Predictors of Fertility Quality of Life in infertile patients visiting infertility center in Kathmandu, Nepal: A cross-sectional study.



A Thesis Submitted in Partial Fulfillment of the Requirements for the Degree of Master of Public Health in Public Health COLLEGE OF PUBLIC HEALTH SCIENCES
Chulalongkorn University
Academic Year 2022
Copyright of Chulalongkorn University

ปัจจัยทำนายคุณภาพชีวิตการเจริญพันธุ์ของผู้ป่วยที่มีบุตรยากที่เข้ารับการรักษาในศูนย์รักษาผู้มี
บุตรยาก เมืองกาฐมาณฑุ ประเทศเนปาล: การศึกษาภาคตัดขวาง



วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาสาธารณสุขศาสตรมหาบัณฑิต
สาขาวิชาสาธารณสุขศาสตร์ ไม่สังกัดภาควิชา/เทียบเท่า
วิทยาลัยวิทยาศาสตร์สาธารณสุข จุฬาลงกรณ์มหาวิทยาลัย
ปีการศึกษา 2565
ลิขสิทธิ์ของจุฬาลงกรณ์มหาวิทยาลัย

Thesis Title	Predictors of Fertility Quality of Life in infertile patients visiting infertility center in Kathmandu, Nepal: A cross-sectional study.	
Ву	Miss Shital Shakya	
Field of Study	Public Health	
Thesis Advisor	ALESSIO PANZA, M.D.	
1 2	OLLEGE OF PUBLIC HEALTH SCIENCES, n Partial Fulfillment of the Requirement for the Master of	

Dean of the COLLEGE OF

PUBLIC HEALTH SCIENCES

THESIS COMMITTEE

Chairman

(Assistant Professor MONTAKARN CHUEMCHIT,
Ph.D.)
Thesis Advisor

(ALESSIO PANZA, M.D.)
External Examiner

(Professor RATANA SOMRONGTHONG, Ph.D.)

(Professor CHITLADA AREESANTICHAI, Ph.D.)



ชิทาล ศากยา: ปัจจัยทำนายคุณภาพชีวิตการเจริญพันธุ์ของผู้ป่วยที่มีบุตรยากที่เข้ารับการรักษาในศูนย์รักษาผู้มีบุตรยาก เมืองกาฐมาณฑุ ประเทศแนปาล: การศึกษาภาคตัดขวาง. ( Predictors of Fertility Quality of Life in infertile patients visiting infertility center in Kathmandu, Nepal: A cross-sectional study.) อ.ที่ปรึกษาหลัก: อเรสสิ โอ พันช่า

ในประเทศเนปาล เกิดภาวะมีบุตรยากเพิ่มขึ้น ซึ่งก่อให้เกิดปัญหาด้านการเจริญพันธุ์ โดยมีอัตราความชุกประมาณ 15 % ซึ่งได้มี การศึกษาเกี่ยวกับคุณภาพชีวิตของผ้หญิงที่มีบุตรยากในอัตราที่น้อยมาก ถึงแม้ว่าภาวะมีบุตรยากจะส่งผลกระทบต่อค่สมรส แต่ก็ไม่มีการศึกษาเกี่ยวกับ คุณภาพชีวิตของผู้ชายและผู้หญิงที่มีบุตรยาก วัตถุประสงค์ของการศึกษา เพื่ออธิบายลักษณะต่างๆของผู้ป่วยที่มีภาวะมีบุตรยาก และค้นหาความสัมพันธ์ ระหว่างตัวทำนายเหล่านี้กับคุณภาพชีวิต การศึกษาวิจัยแบบตัดขวาง (cross - sectional study) โดยใช้แบบสอบถาม FertiQoL โดยสำรวจ ชายและหญิงที่มีบุตรยากจำนวน 409 คน ที่ต้องการการรักษาภาวะมีบุตรยากใบศูนย์ดูแลผู้มีบุตรยากในเขต Kathmandu โดยใช้เทคนิคการสุ่ม ตัวอย่างแบบหลายขั้นตอน เจาะจง และสะควก ความถี่และร้อยละ(%) ถูกนำมาใช้เพื่ออธิบายตัวแปรการทำนายทางสังคมและประชากร เศรษฐกิจสังคม ความสัมพันธ์คู่ ลักษณะที่เกี่ยวข้องกับการเจริญพันธุ์ และประวัติทางการแพทย์ ผู้ตอบแบบสอบถามเกือบทั้งหมครู้สึกว่าการมีถูกเป็นสิ่งสำคัญมากสำหรับ ตนเอง และก่สมรสนับสนนตลอดการรักษาภาวะมีบตรยาก 60% ของผู้ตอบแบบสอบถามประสบภาวะมีบตรยากเบื้องต้น และ 53% มีประวัติ ความล้มเหลวของเทคโนโลยีที่ช่วยเรื่องการเจริญพันธุ์ (ART) ผู้ตอบแบบสอบถามร้อยละ 47 และร้อยละ 19 ใค้รับการรักษาด้วยยาต้านไวรัสโดยใช้ เซลล์สืบพันธ์ในตัวเองและคับริจาคตามลำดับ ผัตอบแบบสอบถามร้อยละ 80 ต้องการความช่วยเหลือด้านจิตใจจากผู้เชี่ยวชาญเฉพาะทาง หลังได้รับการ รักษาด้วน(ART) 48% ของผู้ตอบแบบสอบถามมีคุณภาพชีวิตที่ไม่ดี ความสัมพันธ์ของปัจจัยทำนาย กับคุณภาพชีวิต ได้มีการทคสอบเพื่อหา นัยสำคัญโดยการวิเคราะห์แบบสองตัวแปรและหลายตัวแปร วิเคราะห์ความสัมพันธ์ระหว่างตัวแปรทำนายและตัวแปรผลลัพธ์โดยใช้การทดสอบใคส แลวร์ ผลแสดงความสัมพันธ์ทางสถิติที่ p-value 0.001 ได้แก่ การเดินทางไกลเพื่อรับบริการ ความต้องการความช่วยเหลือด้านจิตใจจากผู้เชี่ยวชาญ ระยะเวลาของการมีบุตรยาก ประวัติการรักษาด้วย $\mathbf{ART}$  และการรักษาภาวะมีบุตรยากในปัจจุบัน ในทำนองเดียวกัน พบความสัมพันธ์ที่มีนัยสำคัญทาง สถิติที่ค่า p-value 0.05 สำหรับตัวแปรต่อไปนี้: เพศ ชั่วโมงทำงาน มีวันหยุดจากการทำงาน การรับรู้ถึงความต้องการมีบุตร ระยะเวลาของการมี บุตรยาก และประวัติการผ่าตัดระบบสืบพันธุ์ ตัวแปรอื่นทั้งหมดไม่มีนัยสำคัญ แบบจำลองการถดถอยโลจิสติกหลายตัวแปรป้อนตัวแปรค่อไปนี้ทั้งหมด จากการวิเคราะห์สองตัวแปร ทั้งหมดที่ระบุข้างต้นที่มีค่า p-value 0.05 ที่มีค่า p-value 0.2; อายุ, เชื้อชาติ, ประเภทครอบครัว, ระดับรายได้, การสนับสนุนของคู่สมรส, การเข้าใกล้สุนฮ์มีบุตร, สาเหตุของกาวะมีบุตรยาก, การเจ็บป่วยเรื้อรัง, การรับประทานยา และสุดท้าย ตัวแปรการศึกษาและ ประเภทของภาวะมีบุตรยากซึ่งมีนัยสำคัญในเอกสาร ผลการวิเคราะห์หลายตัวแปรโดยการถดถอยโลจิสติกส์พหคุณใต้แสดงความสัมพันธ์ที่มีนัยสำคัญ ทางสถิติสำหรับตัวแปรต่อไปนี้ เพศหญิง (AOR=1.81, 95% CI=0.32-0.80, p-value 0.004), เข้าถึงเวลาเลิกงานได้ยาก (AOR=1.96, 95% CI=1.24-3.09, p-value 0.004), เดินทางไกล ระยะห่างในการรักษาภาวะมีบุตรยาก (AOR=0.50, 95% CI=1.15-2.86, p-value 0.011), ระชะเวลาสมรสมากกว่า 10 ปี (AOR= 1.68, 95% CI = 1.04-2.71, p-value 0.032) อยู่ระหว่าง ART โดยใช้ self-gametes (AOR=1.71, 95% CI=1.05-2.8, p-value 0.030), อยู่ระหว่างบริจาก ART cycles (AOR=1.99, 95% CI=1.07-3.71, p-value 0.030) และความปรารถนาที่จะ การสนับสนุนทางจิตวิทยาจากผู้เชี่ยวชาญ (AOR=2.21, 95% CI=1.26-3.89, p-value 0.006) เพื่อเป็นการยกระดับคุณภาพชีวิตของผู้ป่วยที่มีบุตรยาก ขอเสนอแนะได้แก่การ ให้การสนับสนุนด้านจิตใจและอารมณ์แก้ผู้ป่วยที่เข้ารับการรักษาภาวะมีบุตรยาก ควรมีการศึกษาเชิงคุณภาพเพื่อทำความเข้าใจว่าคุณภาพชีวิตได้รับ อิทธิพลจากความสามารถในการรับมือและพฤติกรรมของคู่สมรสอย่างไร

##6574009053: MAJOR PUBLIC HEALTH

KEYWORD: Infertility Quality of Life FertiQoL Infertile patients

Shital Shakya: Predictors of Fertility Quality of Life in infertile patients visiting infertility center in Kathmandu, Nepal: A cross-sectional study.. Advisor: ALESSIO PANZA, M.D.

In Nepal, infertility is a rising reproductive health issue with an estimated prevalence of 15%. There are few studies on quality of life in infertile women, but none on quality of life in infertile men and women although infertility is a shared condition and has effects on couples. The study objective is to describe the various predictors of infertile patients seeking infertility treatment and find association between these predictors and the quality of life. A cross-sectional study using a self-administered disease specific FertiQoL questionnaire was conducted among 409 infertile men and women seeking infertility treatment in an infertility center in Kathmandu district. Multistage, purposive, convenience sampling technique was used. Frequency and percentages were used to describe the predictor variables socio-demographic, socio-economic, couple-related, fertility related characteristics and medical history. Almost all the respondents felt that having a child was very important to them and their partners were supportive throughout the infertility treatment. Almost 60% of respondents were experiencing primary infertility and 53% had a history of assisted reproductive technologies (ART) failure. Forty seven percent and 19% respondents were undergoing ART using self-gametes and donor respectively. Eighty percent of respondents desired professional psychological support following ART treatment. Forty eight percent of respondents had poor QoL. Their associations with the outcome variable poor Fertility Quality of Life were tested for significance by bivariate and multivariate analysis. The bivariate association between the predictor and outcome variables were analyzed by using a chi-square test. The results show highly significant statistical association at p-value 0.001 for independent variables; travel long distance for service, desire for professional psychological support, duration of infertility, history of ART treatment and current infertility treatment. Similarly, a statistically significant association at p-value 0.05 was found for the following variables: sex, work hours, access to day-off from work, cognition for need of children, duration of infertility and history of reproductive tract surgery. All other variables were not significant. The multivariate logistic regression model entered all the following variables from bivariate analysis; all those given above with significance p-value 0.05, those with p-value 0.2; age, ethnicity, family type, income level, partner's supportiveness, approach to fertility center, cause of infertility, presence for chronic illness, intake of medications and finally the variables education and type of infertility which were significant in the literature. The multivariate analysis results by multiple logistic regression have shown statistically significant association for the following variables; female gender (AOR=1.81, 95% CI=0.32-0.80, p-value 0.004), difficult access to get time off from work (AOR=1.96, 95% CI=1.24-3.09, p-value 0.004), long travel distance for fertility treatment (AOR=0.50, 95% CI=1.15-2.86, p-value 0.004). value 0.011), more than 10 years of marital duration (AOR= 1.68, 95% CI = 1.04-2.71, p-value 0.032), undergoing ART using self-gametes (AOR=1.71, 95% CI=1.05-2.8, p-value 0.030), undergoing donor ART cycles (AOR=1.99, 95% CI=1.07-3.71, p-value 0.030), and desire for professional psychological support (AOR=2.21, 95% CI=1.26-3.89, p-value 0.006). To further enhance the quality of life among infertile patients, it is recommended to provide psychological and emotional support to the patients undergoing infertility treatment. Qualitative studies are also recommended to understand how the quality of life is influenced by the coping capability and behavior of the partner.



Field of Study:	Public Health	Student's Signature
Academic Year:	2022	Advisor's Signature

### **ACKNOWLEDGEMENTS**

Foremost, I would like to express my sincere gratitude to my advisor Dr. Alessio Panza for guiding me throughout my Master's in Public Health journey. More than that, I am humbly grateful for his invaluable advice and precise guidance which not only helped me accomplish my thesis, but also enhanced my present and future career growth. The completion of this journey wouldn't have been possible without his continuous support and kindness.

I would like to express my greatest thanks to my examination committee, Prof. Ratana Somrongthong and Deputy Dean Asst. Prof. Dr. Montakarn Chuemchit for their wise and diverse opinions and worthy advice on my study. I feel thankful to have both Ajarns and I would like to to express my deepest gratitude to them for their utmost kindness.

Moreover, I would like to extend my gratefulness to Dr. Sanu Maiya Shrestha Pradhan (M.D., Senior Consultant Obstetrician/ Gynecologist, and IVF Specialist), Mr. Dijan Vaidya (Clinical Embryologist, Master's in clinical Embryology) and Mrs. Subhadra Pradhan (Senior Nurse & Lecturer, Nepalese Army Institute of Health Sciences) for their unconditional support in the development and validation of my questionnaire and special thanks to Mr. Prashant Subedi (managing director of Vatsalya Natural IVF) and Dr. Akriti Bharati (senior consultant Gynecologist, Vatsalya Natural IVF) for giving permission and supporting to conduct my research in their infertility center. I am extremely grateful to my aunt Mrs. Durga Rauniyar who is a researcher and statistician based in New Zealand for her immense guidance in statistical analysis. I would like to express my gratitude to Ms. Praju Sharma and Mr. Sulav Bajracharya for helping in data entry and making the raw data presentable.

In addition, I am greatly indebted to all the respondents for their time and kindness and the nursing team of Vatsalya Natural IVF for their help in data collection.

Last but not the least, I express my profound gratitude to my family for always supporting, guiding, and always believing in their daughter. I am thankful to the universe for conspiring this journey for me.

## LIST OF ABBREVIATIONS

AE = An ejaculation

AMH = Anti-Mullerian Hormone

AOF = Acute Ovarian Failure

ART = Assisted Reproduction Technology

DE = Delayed Ejaculation

EDC = Endocrine Disrupting Chemicals

FertiQoL = Fertility Quality of Life

FSH = follicle stimulating hormone (FSH) and

HH = Hypogonadotropic Hypogonadism

HRT = Hormone Replacement Therapy

ICSI = Intra-Cytoplasmic Sperm Injection

IOC = Item-Object Congruence

IUI = Intra-Uterine Insemination

IVF = In-Vitro Fertilization

KS = Klinefilter's Syndrome

LH = Lutenizing Hormone (LH)

LMIC = Low Middle-Income Countries

PE = Premature Ejaculation

PID = Pelvic Inflammatory Disease

QoL = Quality of Life

RE = Retrograde ejaculation

ROS = Reactive Oxidative Species

TESA = Testicular Sperm Extraction

จุฬาลงกรณ์มหาวิทยาลัย Chill Al ONGKORN UNIVERSITY

# TABLE OF CONTENTS

	Page
	iii
ABSTRACT (THAI)	iii
	iv
ABSTRACT (ENGLISH)	iv
ACKNOWLEDGEMENTS	v
LIST OF ABBREVIATIONS	vi
TABLE OF CONTENTS	
LIST OF TABLES	xiii
LIST OF FIGURES	xv
CHAPTER I	16
INTRODUCTION	16
1.1 Problem Statement	16
1.2 Research Gap	
1.3 Research Hypothesis	22
1.3.1 Null Hypothesis	22
1.3.2 Alternative Hypothesis	22
1.4 Research Questions	22
1.5 Research Objectives	22
General Objective	22
Specific Objectives	22
1.6 Conceptual Framework	23
1.7 Operational Definitions	24
1.7.1 Sociodemographic Variables	24
1.7.2 Socioeconomic variables	24
1.7.2 Couple-related variables	25

1.7.3 Fertility-related variables	25
Dependent Variable	27
Quality of life	27
CHAPTER II	28
LITERATURE REVIEW	28
2.1 Problem Statement	28
2.2 Male Infertility	29
2.2.1 Causes of Male Infertility	29
1. Medical Factors	29
1.1 Sperm disorders	29
1.2 Testicular Dysfunction	
1.3 Ejaculatory dysfunction	32
1.4 Hypogonadism	32
1.5 Cancer and Drugs	33
1.6 Unexplained Infertility	34
1.7 Sterilization	34
2. Environmental Causes	34
2.2.2 Risk factors for Male Infertility	34
2.3 Female Infertility	35
2.3.1 Causes for Female Infertility	35
1. Medical Causes	35
1.1 Ovulatory Disorders	35
1.2 Tubal Infertility	36
1.3 Endometriosis	36
1.4 Medicines and Drugs	37
1.5 Unexplained Infertility	37
1.6 Sterilization	37
2. Environmental Causes	38
2.3.2 Risk Factors for Female Infertility	38

2.4 Effects of Infertility	39
A. Psychological effect of couples	39
B. Marital relationship of couples	40
C. Sexual Relationship of couples	40
D. Social stigma among couples	40
E. Quality of Life	41
F. Psychological effects on QoL	43
2.5 Solutions	44
2.5.1 Solutions for Male Infertility	
2.5.2 Solutions for female Infertility	
2.6 Barriers	
Nepal Health System and Infertility	
CHAPTER III	
RESEARCH METHODOLOGY	
3.1 Study Design	49
3.2 Study Area and Population	49
3.3 Data Collection Period	50
3.4 Sample Size	50
3.5 Sampling Method	50
3.6 Inclusion and Exclusion Criteria	53
3.6.1 Inclusion Criteria for Participants	53
3.6.2 Exclusion Criteria for Participants	53
3.7 Measurement tools	54
A. Questionnaire developed by researcher	54
B. FertiQoL Questionnaire	58
C. Back-translation	61
3.8 Validity and Reliability	62
3.8.1 Construct validity	62
A. Questionnaire developed by researcher	62

В	. I	FertiQoL questionnaire6	3
3.	.8.2 0	Content validity6	3
3.	.8.3 I	Face validity6	5
3.	.8.4 I	Pilot Testing6	5
3.	.8.5 I	Reliability6	6
3.9 D	ata C	Collection6	6
3.	.9.1 7	Training the Research Assistant6	6
3.10 1	Data	Entry and Analysis6	8
<u>D</u>	escri	iptive Statistics6	8
<u>Ir</u>	ıferei	iptive Statistics	0
3.11 1	Ethic	al Approval from Chulalongkorn University ERB7	1
		V7	
4.1 B	ackg	round information7	2
4.2 D	escri	ptive analysis7	2
4.	.2.1	General Characteristics of Infertile Patients	3
	1	Socio-demographic factors7	3
	1	II. Socio-economic factors7	4
	1	III. Couple-characteristics7	5
	I	IV. Fertility-related characteristics7	5
	Ţ	V. Medical History7	6
4.	.2.2 (	Quality of Life in Infertile Patients7	7
	1	I. Emotional Domain7	8
	1	II. Mind/ Body Domain7	9
	I	III. Relational Domain8	0
	I	IV. Social Domain8	1
	1	V. Treatment Environment8	2
	1	VI. Treatment Tolerability Domain8	3
4.	.2.3	Categorization of Total FertiQoL scores8	4

4.3 Inferential Statistics	84
4.3.1 Bivariate Analysis	84
A. Sociodemographic variables with FertiQoL	84
B. Socioeconomic variables with FertiQoL	85
C. Couple characteristics with FertiQoL	86
D. Fertility-related characteristics with FertiQoL	88
E. Medical history with FertiQoL	89
4.3.2 Multivariate Analysis	90
CHAPTER V	97
DISCUSSION	97
A. General Characteristics of Infertile patients	97
B. Socio-economic characteristics among infertile patients	98
C. Couple characteristics among infertile patients	100
D. Fertility-related characteristics among infertile patients	100
E. Medical History among infertile patients	101
F. FertiQoL Domains in infertile patients	102
STRENGHTS	105
RECOMMENDATIONS FOR FUTURE RESEARCH	105
RECOMMENDATIONS FOR POLICIES 1778 1781	106
CONCLUSIONS	107
REFERENCES	108
APPENDICES	127
Annex 1: Consent form and Respondent Information Sheet	127
Annex 2: Self-reported questionnaire by the respondent	130
Patient Code:	130
Annex 3: Questionnaire reported by the investigator	132
Annex 4: FertiQoL Questionnaire	133
Annex 5 : Eligiblity Checklist	138
Annex 6 : Questionnaire Translated in Nepali	139

ANNEX 7: Descriptive of FertiQol Domain Classified by Gender sh	own in figures.
	145
Annex 8: Letter of permission from Director of Clinics	153
Annex 9: Gantt chart	154
Annex 10: Budget	154
Annex 11: Researcher Information	155
/ΙΤΔ	156



## LIST OF TABLES

	Page
Table 1 WHO reference range of semen analysis and related abnormalities	29
Table 2 Subscales of FertiQoL	44
Table 3 Summary of evaluation variables	55
Table 4 Subscales of FertiQoL	59
Table 5 Response Category of FertiQoL	59
Table 6 Subscale and total scales of FertiQoL	60
Table 7 Descriptive Statistics	69
Table 8 Socio-demographic characteristics of infertile patients (n=409)	73
Table 9 Socio-economic characteristics of infertile patients (n=409)	74
Table 10 Couple-related characteristics of infertile patients (n= 409)	75
Table 11 Fertility-related characteristics of infertile patients (n=409)	76
Table 12 Medical History related variables in infertile patients (n = 409)	76
Table 13 Descriptive of FertiQoL domains and Total FertiQoL scores	77
Table 14 Descriptive of Emotional Domain based on Gender (n=409)	79
Table 15 Descriptive of Mind/Body Domain based on Gender (n=409)	80
Table 16 Descriptive of Relational Domain based on Gender (n = 409)	81
Table 17 Descriptive of Social Domain based on Gender (n=409)	82
Table 18 Descriptive of Treatment Environment based on Gender (n=409)	83
Table 19 Descriptive of Treatment Tolerability based on Gender (n=409)	83
Table 20 Socio-demographic characteristics and its association with poor Fert (n=409)	-
Table 21 Socio-economic characteristics and its association with FertiQoL (n=	=409)85
Table 22 Couple characteristics and its association with FertiQoL (n=409)	87
Table 23 Fertility-related characteristics and its association with FertiQoL (n=	409) 88
Table 24 Medical History and its association with FertiQoL (n=409)	89
Table 25 List of independent variables which entered the binary logistic mode	190

Table	26 Binary logistic regression for poor FertiQoL (n=409)	.92
Table	27 Multiple logistic regression for poor Fertility Quality of Life (n=409)	.93
Table	28 Comparative table of association between independent and two levels of	
depend	dent variables in bivariate and multivariate analysis (n=409)	.95



# LIST OF FIGURES

		Page
Figure	1 Conceptual Framework	23
Figure	2 Map Indicating different districts and locations in Kathmandu Valley	48
Figure	3 Map showing wards in Kathmandu Metropolitan	49
Figure	4 Sampling Flowchart	52



# CHAPTER I INTRODUCTION

#### 1.1 Problem Statement

Infertility is the disease of the male or female reproductive system defined by the failure to achieve a pregnancy after a year or more of having regular unprotected sexual intercourse. (Organization, 2021) It is categorized as primary and secondary infertility. Globally 15% of couples of reproductive ages are affected by infertility. Estimates show that one in every seven couples are infertile in developed countries whereas one in every four couples experience infertility in developing countries. (Boivin et al., 2007) Globally, 10-15% of couples experience primary infertility while 3-6% couples are affected with secondary infertility. (Inhorn & Patrizio, 2015).

About 14.4 million infertile couples are living in South Asia, thus contributing to the highest incidence of infertility in the world. (Mascarenhas et al., 2012) About 10-15% of reproductive age couples are affected by infertility in Indonesia. (Harzif et al., 2019) A study concluded 12% prevalence of infertility in Vietnam. (N. I. Kim et al., 2022) Similarly, Malaysia has an estimated infertility rate of 15-20%. (*Malaysia Fertility Rate 1950-2023*, n.d., pp. 1950–2023) In Nepal, the prevalence of infertility is estimated to be around 12% (Neupane et al., 2019) and an estimated 7.4% of women face infertility problem. (Khanal & Journals, 2020). A study conducted in Eastern Nepal found a 5.45% prevalence of infertility predominated by secondary infertility. (Subedi et al., 2016)

Infertility can be a caused by male factor, female factor or both factors. Male factors constitute to 30-50% of the cases while female factor contribute to 30% of the infertility cases. About 20-30% of cases result as a combination of both male and female factors. (Agarwal et al., 2015) The prevalence of unexplained infertility or infertility due to unknown causes ranges from 8% to 37%. (Kamath & Deepti, 2016)

Semen disorder accounts to 50% of male infertility cases. (Jungwirth et al., 2012) Low sperm concentrations are major factor causing infertility among 8-18% of men. (Kamath & Deepti, 2016) Similarly, abnormal sperm morphology and low sperm motility accounts to 20-30% of male infertility cases. Testicular defects due to medical conditions like varicocele and acquired genital tract infections contribute to 15-20% (Baazeem et al., 2011) and 10-20% (Henkel et al., 2007) of the cases respectively. Similarly, testicular failure (Jarow et al., 1989), congenital defects in the testicles (Esteves et al., 2011), testicular cancer (Shefi & Turek, 2006) and genetic conditions like Klinefelter syndrome (KS) (Bojesen et al., 2003) affects sperm production leading to testicular failure, thus contributing to further cases of male infertility. About 40% of cases of testicular failure are classified as idiopathic. (A. Sharma et al., 2020)

Similarly, ejaculatory dysfunction is one of the causes for male factor infertility. About 1.2% of infertile men are affected by ejaculatory dysfunction (Esteves et al., 2011) which results in low

volume of semen ejaculation. Furthermore, it can also result in hypogonadism which is a condition characterized by impairment of testicular function. It leads to low testosterone levels thus affecting production of sperm. (Yialamas & Hayes, 2003) Over 10% cases of male-factor infertility are due to hypogonadism. (Soran et al., 2022) Hypogonadism can either result from primary testicular disorder (hypergonadotropic) or secondary to hypothalamic pituitary function (hypogonadotropic). (Fraietta et al., 2013)

Certain medications like chemotherapeutic agents, calcium channel blockers, colchicine, sulphasalazine are associated with testicular failure. (Hendry, 1998) Antidepressant drugs are found to be associated with male factor infertility. (Brezina et al., 2012) Men can pregnant less than 1 out of 1000 woman following male sterilization. (Trussell, 2011) Around 12% of infertility cases remain idiopathic. (Esteves et al., 2011) Male reproductive function is vulnerable to various environmental exposure. (López-Botella et al., 2021) Lacking clinical evidences show that endocrine disrupting chemicals (EDC) like bisphenol A, phthalates, pesticides and other environmental chemicals affect fertility by disrupting development of gonads during fetal life. (Skakkebaek et al., 2016) Exposure to heavy metals like Zn, Cr, Cu, Fe, Pb and As negatively affect male fertility by lowering seminal quality. (Balabanič et al., 2011) Radioiodine therapy for thyroid disease can lead to testicular damage and abnormal spermatogenesis. (Sawka et al., 2008) Radiation from X-rays have harmful effects on sperm parameters and induce oxidative stress. (Kesari et al., 2018) Prolonged exposure to heat and high temperatures induce spermatic damage and reduction in sperm count and concentration. (Hamilton et al., 2016)

Health behaviors like excessive alcohol intake, smoking and use of recreational drugs pose as a risk for reduced fertility in men. (Li et al., 2011) Use of recreational drugs like cannabis, androgens and opioids is associated with reduction in sperm parameters. (Bracken et al., 1990) Men who are inactive and lead a sedentary lifestyle were found to have reduced sperm quality, especially in the presence of concomitant comorbidities like diabetes and obesity. (Vaamonde et al., 2012) Men with high or low BMI (less than 19 kg/m2 or more than 30 kg/m2) are associated with decreased testicular volume and reduced sperm quality due to impairment in spermatogenesis. (Jensen et al., 2004) Exposure of pollutants, sauna, clothing, sleeping position, use of laptop, prolonged driving, welding are associated with scrotal hyperthermia and decreased sperm concentration and motility. (Krzastek et al., 2020) (Jurewicz et al., 2018).

Male infertility can have a significant impact on couple's ability to conceive. Infertile men are found to experience higher levels of psychological distress compared to fertile men. (Dyer et al., 2009) Infertile men are likely to experience anxiety, depression and stress in their life which has negative impact on fertility. Additionally, the psychological effects also impact on infertility treatment and overall Quality of Life (QoL). (Maroufizadeh et al., 2018) Men may experience the feelings of anger, guilt, sadness, and disappointment. They may also struggle with feeling of failure. The diagnosis of male infertility can be difficult for men because the society has more expectations from men to fulfill the desire of a child. (Nieuwenhuis et al., 2009) Ejaculation difficulties may result due to emotional stress and physical demands following fertility treatment which can lead to distress and frustration in men. (Kondoh, 2011) It can contribute to decreased coital frequency resulting in lower sexual satisfaction and thus affecting sexual relationship of the couples which eventually affects the QoL. (Tao et al., 2012)

Medical treatment can help men experiencing infertility. Medications to increase sperm count and surgeries to correct varicocele and other physical abnormalities can aid to mitigate the fertility problems in men. (Dabaja & Schlegel, 2014) Assisted reproductive technologies such as In-vitro fertilization (IVF) and Intracytoplasmic Sperm Injection (ICSI) have helped many infertile men with low sperm count and other fertility issues to father a child. (Merchant et al., 2011) Lifestyle changes such as avoid smoking, decreased alcohol consumption and maintaining body weight can improve sperm parameters in men and hence increase the chances of conception. (Durairajanayagam, 2018) Stress can have a negative impact on the quality of sperm, hence practicing yoga, exercise and meditation is an important aspect to ensure stress management. (Sengupta et al., 2013) Men can seek emotional support from therapist or counselor or support groups to help them cope up with emotional and psychological effects of infertility. Couples should openly communicate and share their feelings throughout the process to conceive. (Fisher & Hammarberg, 2012) Adoption can be another option for couples who are not able to conceive a child.

WHO estimates that female factor is the main cause of infertility among 37% of infertile couples. (Duffy & Allen, 2009) Several causes of female infertility include anatomical abnormalities, ovulatory and menstrual disorders, endometriosis, certain drugs and medications and unexplained infertility. Ovulatory disorders accounts to a major cause of infertility. About 25% cases of female infertility is caused by ovulatory disorders. (Walker & Tobler, 2022) Polycystic Ovarian Syndrome (PCOS) is predominant cause of anovulatory infertility (a condition in which ovulation doesn't occur) thus affecting 7 to 15% of reproductive age women. (Collée et al., 2021) Other causes include premature ovarian failure, autoimmune diseases and thyroid dysfunction. (Szeliga et al., 2021) Premature ovarian failure accounts to 1.1% of global prevalence in female infertility. (Fauser & Van Heusden, 1997) Infertility prevalence of 2-4% was found among women with thyroid disorders. (Krassas, 2000)

Tubal factor infertility accounts to 25-30% of female infertility cases. (Ambildhuke et al., 2022) Tubal factor infertility may occur because of pelvic inflammatory disease (PID), sexually transmitted infection (STI), history of ectopic pregnancy and prior tubal surgery. (Kavanagh et al., 2013) Furthermore, endometriosis may lead to endocrine and ovulatory disorders thus affecting female fertility. (Ozkan et al., 2008) About 30 to 50% of women wfith endometriosis experience infertility. (Counseller, 1938) Prevalence of uterine fibroids is high at 2-3% among infertile women. (Freytag et al., 2021) Endometrial polyps are the commonly reported uterine abnormalities with incidence of 16.7% in patients with recurrent implantation failure after IVF. (Fatemi et al., 2010) Congenital abnormalities like uterine septum accounts to 8% of female infertility cases. (Chan et al., 2011) Problems in cervical mucus can prevent sperm from entering the uterus, thus affecting reproduction. However, this is a rare cause of infertility. (*Infertility Problems With Cervical Mucus - Women's Health Issues*, n.d.)

Use of recreational drugs like marijuana, cocaine, LSD creates slightly elevated risk of ovulatory abnormality. (Mueller et al., 1990) Cytotoxic drugs like cyclophosphamide, methotrexate and 5-fluorouracil used in the treatment of cancer are great stimulators for infertility. Studies show that the treatment resulted in loss of ovarian function among 30% of the patients. (Sonmezer & Oktay, 2006) Anticancer treatments like radiation, chemotherapy and surgery can severely damage ovarian function and lead to premature ovarian failure, thus affecting fertility. (Spears et al., 2019) About 10-17% of infertile women experience

unexplained or idiopathic infertility. (Ehsani et al., 2019) Women who undergo sterilization are more than 99% infertile. (Female Sterilisation, 2017)

Age is one of the major risk factors for female infertility. Increase in age results in decline in the number of oocytes. Quality of existing oocytes and intercourse frequency is also decreased with age. (ESHRE Capri Workshop Group, 2005) Certain lifestyle factors like smoking, alcohol intake and obesity can decrease egg quality and ovulation rate, which can increase the risk of infertility in women. (R. Sharma et al., 2013) Increase in BMI impose an increased risk of ovulatory disorder in women. (Rich-Edwards et al., 2002) Excessive caffeine intake is found to be associated with increased risk of spontaneous abortion (Chen et al., 2014), reduced fecundity, and delayed conception. (Hassan & Killick, 2004) Substance abuse and use of recreational drugs (Monica Bari, 2011) Increased use of pesticides and insecticides, prolonged exposure to endocrine disrupting chemicals (EDCs) (Ding et al., 2016) and use of certain solvents used in paints, pharmaceuticals may negatively affect fertility. (Lipscomb et al., 1991) Certain medications like opioids, antidepressants and chemotherapy can reduce the egg quality and ovulation rate, hence increasing the risk of infertility. (Duffy & Allen, 2009) Exposure to environmental toxins like BPA, lead, cadmium, pesticides also pose a risk for decreased reproductive function in females. (Piazza & Urbanetz, 2019) Noise pollution can have impact on behavioral and physical well-being of individual. (Stansfeld & Matheson, 2003) Exposure to radiation like X-rays can prove to be detrimental to female reproductive function. (De Santis et al., 2007) Overnutrition and undernutrition can negatively affect fertility. (Pasquali et al., 2003) Having a history of medical conditions like diabetes and PCOS can be a risk factor for infertility. (Dennett & Simon, 2015)

Women who experience infertility can have significant effects on emotional and psychological well-being. (Hasanpoor-Azghdy et al., 2014) Infertile women are at high risk of developing depression, anxiety, stress, and relational difficulties. Comparatively, higher levels of anxiety and depression were found among infertile women. (Drosdzol & Skrzypulec, 2009) Infertile women were found to be more distressed than infertile men. (T. Y. Lee & Sun, 2000) The emotional effect can lead to decreased quality of life (QoL). (Rooney & Domar, 2018) Infertility has negative effect on sexual function, body image and self-esteem of women. Consequences of infertility can be seen as relationship difficulties such as decreased sexual and emotional intimacy and increased conflict. The effect of infertility is significantly higher in women compared to men due to physical hardships undergoing treatment and increased pressure of the society on the women for childbearing. It has negative impact on overall QoL in women. (J.-Y. Wang et al., 2022)

Intake of nutrient rich diet is associated with lower risk of ovulatory infertility in women. (Chavarro et al., 2007) Antioxidants can reduce the damage of reactive oxidative species from factors like smoking and drinking thus preventing damage to oocytes, which ultimately reduce its impact on fertility. (Showell et al., 2011) Fertility drugs like clomiphene citrate and gonadotropins are useful to stimulate ovulation in women. (M. Sharma & Balasundaram, 2022) Intrauterine insemination (IUI), In-Vitro Fertilization (IVF), Intracytoplasmic sperm injection (ICSI) are the advancements in assisted reproduction technologies (ART) which can assist the couples experiencing infertility.(Kol, 2014) Exercise can help to reduce stress related to infertility. (Goldman & Hatch, 1999) A reduced risk of ovulatory dysfunction was associated with 30 minutes of exercise per day. (Chavarro et al., 2007) Psychological counselling and support to the couples through the emotional journey of infertility can help them to cope up with the emotional and psychological challenges associated with infertility.(Rooney & Domar,

2018) Adoption is the final option for couples who couldn't conceive a child naturally or through infertility treatments.

Cost is a huge barrier for infertility treatment. (Mosalanejad et al., 2014) Insurance plans usually do not cover the cost of infertility treatments and since the treatment costs are very high, many infertile couple do not seek medical assistance. (Berger et al., 2013) Limited access to infertility care is another barrier for infertility treatment. Couples may need to travel long distances frequently once they enroll in the treatment, thus imposing a financial and logistic burden among the couples. (Blakemore et al., 2020) Alternatively, treatment options including ART may not be available in all areas. Lack of awareness about the available treatment options can also be a barrier among the couples seeking for infertility treatment. (Domar et al., 2021) Increasing age is another barrier for seeking medical treatment. As the age increases among the couples, it becomes more difficult to conceive and treatments may also have lower success rates. (Mosalanejad et al., 2014)

The multiple embryos transferred in the uterus during the IVF cycle increases the chances of multiple pregnancy. ('In Vitro Fertilization and Multiple Pregnancies', 2006) About 30% of pregnancies from IVF treatments result in multiple gestations. Similarly, the incidence of ectopic pregnancy is about 1-2% among women who undergo IVF treatments which is comparatively higher than the risk in fertile population. (Patil, 2012) These complications can be a barrier as they increase the risk associated with pregnancy and childbirth. Apart from that, it can lead to emotional and financial burden among the couples. (Hasanpoor-Azghdy et al., 2014) Many couples hesitate to seek infertility treatment because of the emotional barriers. They may feel ashamed or embarrassed to talk about the infertility issue and hence may be reluctant to access the treatment option. (Domar et al., 2012) Couples may be reluctant to seek for help because of the religious and cultural beliefs present in the society regarding infertility. These beliefs and values may discourage or prohibit the use of certain treatments. (van Balen & Bos, 2009)

Hence, infertility is one of the greatest stressors leading to diminished quality of life. Infertility and its treatment negatively impact on couple's marital relationship, sexual life, psychological state and interpersonal relationships. (Shi et al., 2022) A poor psychological state can have adverse effects on pregnancy rate of ART treatment as well as on pregnancy outcome. (Cooper et al., 2007) Identified factors influencing quality of life include young age, female gender, lower educational level, primary infertility, longer duration of infertility, higher will to have a child, diminished psychological status, altered marital relationship and previous history of assisted pregnancy. (Ni et al., 2021)

#### 1.2 Research Gap

Using the keywords "Infertility" or "infertile" or "childless" AND "Quality of Life", a search was conducted on online databases Medline Ovid and Google Scholar. The search was restricted between 2000-2023. The language used for the search was English. A total of 268 studies were obtained: 164 from Medline Ovid and 57 from Google Scholar. On reviewing the titles of the studies, 133 studies from Medline Ovid were found to be relevant to our study. However, some discrepancies were observed during the search in Google Scholar, hence it was discarded. Only one study out of 133 was conducted in Nepal. However, the study assessed the quality of life among infertile women attending an infertility center using a SF-36

#### [Type here]

questionnaire. (Pradhan Shrestha et al., 2020) Since the study was conducted only in infertile women and used a different measurement tool, it was discarded. Out of remaining 132 relevant studies, 20 were discarded because they didn't use FertiQoL as the measurement tool. Hence, we were left with 103 studies which were conducted using FertiQoL questionnaire. Among them, 86 studies were discarded because the papers studied QoL among either male or female only. Hence, we retrieved only 17 studies related to assessment of QoL among couples. On reading the abstract of the 17 studies, 15 studies were discarded because the studies were not relevant to Low Middle-Income Country (LMIC). Hence, only two relevant studies conducted in LMIC and among infertile couples were obtained.

Additionally, a search was done on Nepal Journals Online (NepJoL) using the keywords "Infertility" or "Infertile" or "Childless" and "Quality of Life" in English and Nepali language which resulted in one study and was a duplication of study retrieved from Medline Ovid. This study was discarded due to assessment only in infertile women and use of a different measurement tool.

However, on accessing the available grey literature in libraries and universities, a thesis abstract was retrieved from the Faculty of Graduate studies, Mahidol University, Thailand. The study was conducted in an infertility center in Kathmandu, Nepal which identified factors associated with QoL among infertile women using FertiQoL as a measurement tool. However, the study doesn't analyze poor QoL and its association with predictor variables. Additionally, the study is conducted only among infertile women. (Pradhan et al., 2013)

The first research gap identified is that only two studies were identified from the search on QoL among infertile patients in LMICs. The second research gap is that based on the search, the principal researcher couldn't find studies on QoL conducted among infertile patients with special attention to infertile couples in Nepal. Third research gap is that only one study has been identified from the search which was conducted in Nepal using disease specific "FertiQoL" questionnaire. Furthermore, no studies were identified from the search which assessed association between patients' characteristics and QoL among patients who individually or as couples seek infertility treatment in Kathmandu, Nepal.

The research aims to study QoL among infertile patients individually or in couples as patients often approach individually to the infertility centers. Additionally, the study will assess association between characteristics of infertile patients and QoL using the standard and valid FertiQoL questionnaire as a measurement tool.

Hence, if the study achieves its objectives, the findings will provide information needed to develop appropriate supportive interventions to serve the needs of infertile patients in Nepal. Additionally, the study will pave a path for future research in Nepal that can easily adopt a validated tool which specifically focuses on accessing the impact of infertility on QoL of infertile patients.

## 1.3 Research Hypothesis

#### 1.3.1 Null Hypothesis

There is no significant association between quality of life and characteristics of infertile men and women visiting infertility center in Kathmandu, Nepal.

## 1.3.2 Alternative Hypothesis

There is significant association between quality of life and characteristics of infertile men and women visiting infertility center in Kathmandu, Nepal.

## 1.4 Research Questions

- 1. Is there any association on quality of life due to sociodemographic characteristics on infertile men and women visiting infertility center?
- 2. Are there any association on quality of life of infertile men and women visiting infertility center based on their socioeconomic status?
- 3. Is there any association of couple-related characteristics on quality of life of infertile men and women visiting infertility center?
- 4. Is there any association of fertility-related characteristics on quality of life of infertile men and women visiting infertility center?
- 5. Are there any association of quality of life based on their medical history of infertile men and women visiting infertility center?

## 1.5 Research Objectives

#### **General Objective**

To describe the characteristics of infertile men and women and to evaluate association between these characteristics and quality of life among men and women visiting infertility center in Kathmandu, Nepal.

## **Specific Objectives**

- 1. To describe socio-demographic, socio-economic, couple-related, fertility related characteristics and medical history of infertile men and women visiting infertility center in Kathmandu, Nepal.
- 2. To determine association of socio-demographic factors on QoL of infertile men and women visiting infertility center in Kathmandu, Nepal.
- 3. To assess the association between socio-economic status and QoL of infertile men and women visiting infertility center in Kathmandu, Nepal.
- 4. To evaluate association between couple-related characteristics and QoL of infertile patients visiting infertility center in Kathmandu, Nepal.
- 5. To assess the association between fertility-related characteristics and QoL of infertile patients visiting infertility center in Kathmandu, Nepal.
- 6. To find association between medical history and QoL of infertile patients visiting infertility center tin Kathmandu, Nepal.

## 1.6 Conceptual Framework

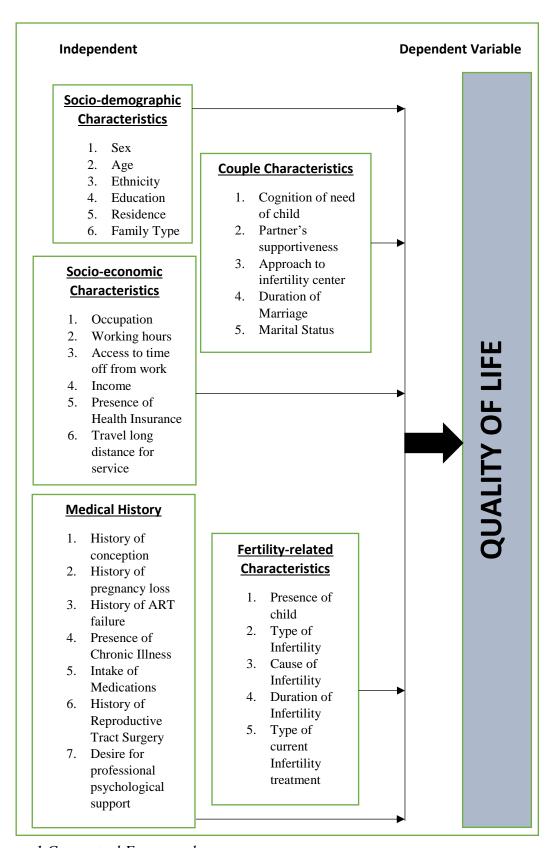


Figure 1 Conceptual Framework

#### 1.7 Operational Definitions

**Independent Variables** 

## 1.7.1 Sociodemographic Variables

- **1.1 Age (in years)**: refers to the self-reported completed age at the last birthday of the participant at the time of the interview.
- **1.2 Sex**: refers to the self-reported biological sex of the respondent.
- **1.3 Ethnicity**: refers to the self-reported ethnicity of the respondent. It was classified according to Nepal DHS survey as Brahmin, Chhetri, Newar, Janajati and Others.
- **1.4 Education level**: refers to the self-reported highest level of education that the participant had attained at the time of the interview. It was classified according to sociodemographic studies as not literate (never went to school but can read and write in Nepali), primary education (grade 1-8), secondary education (grade 9-12), Bachelors, and Masters and above.
- 1.5 Residential area: refers to the self-reported area of current and permanent residence. It was classified as urban and rural. According to Nepal DHS survey, urban area and rural area is represented by the presence of urban municipality (Nagarpalika) and rural municipality/ Village Development Committee (Gaupalika) respectively in the area of residence.

Metropolitan, Sub-Metropolitan and Urban Municipality (Nagarpalika) are considered as urban area.

Rural Municipality and Village Development Committee (Gaupalika) are considered as rural area.

**1.6 Family type**: refers to the self-reported type of family the participants are living in. It was classified according to Nepal DHS survey as nuclear and extended family.

Nuclear family = consists of husband, wife, and children without any other relative living in the same house.

Extended family = consists of husband, wife, and children with other relative living in the same house.

#### 1.7.2 Socioeconomic variables

**1.7 Occupation**: refers to the self-reported type of work in which the respondents were involved in at the time of interview. It was classified as Laborer, Service-oriented, Self-employed, and Unemployed.

Laborer represents manual laborer who work on the basis of daily wages.

Service-oriented represents private and/or public service-oriented work.

Self-employed represents freelance, business or entrepreneur.

- **1.8 Access to time off from work**: refers to the self-reported access granted by the workplace to take time-off for frequent visit to the infertility center for treatment. It was classified as: Very Easy, Easy, Neither Easy nor Hard, Hard, Very Hard. It was later categorized as Easy, Neutral and Hard.
- **1.9 Working hours**: refers to the self-reported daily hours of work related to the respondent's occupation. Those who responded as unemployed mentioned zero

- working hours. It was open-ended which was classified as zero hours, 1-8 hours and >9hours.
- **1.10 Income level:** refers to the self-reported monthly individual income of the couple in Nepali Rupees. The categorization of income level was done as such; less than NRs. 20,000, between NRs. 20,000-50,000, between NRs. 50,000-100,000 and above NRs. 100,000.
- **1.11 Travel long distance for service**: refers to self-reported answer to whether the respondents had travelled to Kathmandu valley specifically for fertility treatment. It was classified as yes and no.
- **1.12 Presence of health insurance:** Refers to the self-reported presence or absence of any health insurance which covers the infertility treatment cost. It was classified as yes and no.

## 1.7.2 Couple-related variables

- **1.13 Marital status**: Refers to the self-reported number of marital partners that the respondent had by the time of interview. It was classified into first marriage and second marriage.
- **1.14 Duration of marriage**: Refers to the self-reported duration (in years) of marriage with the current partner.
- **1.15 Presence of biological child:** Refers to the self-reported number of living biological child/children the respondent has at the time of interview. It was dichotomized as no children and one or more children.
- **1.16** Cognition for need of children: Refers to the self-reported perception on the cognition for need of a child for the respondent at the time of interview. It was classified as very important and not very important.
- **1.17Supportiveness of partner:** Refers to the self-reported support of partner throughout the fertility treatment. It was classified under Likert Scale as not supportive at all, not so supportive, neither supportive nor non supportive, supportive, and very supportive.
- **1.18 Approaching infertility center:** Refers to whether the respondent visited the clinic for treatment alone or with the partner at the time of interview. It was reported by the investigator. It was classified as Individually and With Partner.

## 1.7.3 Fertility-related variables

- 1.19 Type of Infertility: Refers to the type of infertility the patients are experiencing. It was assessed through medical records and reported by the investigator. It was classified as Primary Infertility and Secondary Infertility.
- 1.20 Cause of Infertility: Refers to the factor associated for infertility as diagnosed by the obstetrician/ gynecologist. It was reported by the investigator by referring to the medical record of the patient. It was classified as male factor, female factor, combined factor and unexplained (unknown).
- **1.21 Duration of infertility:** Refers to the duration (in years) which the patients have spent trying to conceive which includes with and without medical help. It was reported by the researcher by reviewing the medical history.
- **1.22 Type of current infertility treatment:** Refers to the type of infertility treatment the patients are undergoing at the time of survey. It was reported by the investigator by

referring to the medical record of the patient. It was classified as timed intercourse (TI), Intrauterine insemination (IUI) with husband sperm, IUI with donor sperm, IVF/ ICSI using self gametes (sperm and egg), IVF/ICSI with donor sperm, egg donation and embryo donation. It was later categorized as TI, ART (self) which included IUI(H) and IVF/ICSI (H), and ART(donor) which included IUI(D) IVF/ICSI(D), egg donation and embryo donation.

**Timed Intercourse** = "A simple treatment option for infertility which involves monitoring of ovarian cycle via ultrasound and hormone testing and then having sexual intercourse around the time of ovulation."

**Ovarian stimulation** = "Pharmacological treatment in which ovaries are stimulated with gonadotropins and/or other pharmacological compound with the intention of inducing the development of ovarian follicles."

**Intrauterine Insemination (IUI)** = "A procedure in which laboratory processed sperm are placed in the uterus to attempt a pregnancy." It can be done using the sperm from a husband or a donor which is called IUI(H) or IUI(D) respectively.

**In-vitro fertilization (IVF)** = "A sequence of procedures that involves extracorporeal fertilization of gametes. It includes conventional invitro insemination and ICSI."

**Intracytoplasmic Sperm Injection (ICSI)** = "A procedure in which a single spermatozoon is injected into the oocyte cytoplasm."

**Testicular Sperm Aspiration (TESA)** = "A surgical procedure involving one or more testicular biopsies or needle aspirations to obtain sperm for use in IVF and/or ICSI"

The definitions are obtained from "The International Glossary on Infertility and Fertility Care 2017".

### 1.7.5 Medical History

- **1.23 Presence of chronic illness:** Refers to the presence of any comorbid conditions at the time of data collection. It was reported by the investigator by referring to the medical record of the patient. It was categorized as yes and no. In case of presence of chronic illness, it was specified by the investigator.
- **1.24 Intake of medicines**: refers to the medications except fertility drugs which the respondents were taking at the time of interview. It was reported by the investigator by referring to the medical record of the patient. It was dichotomized as yes and no. In case of taking any medications, it was specified by the investigator.
- **1.25 History of pregnancy loss**: Refers to the history of pregnancy loss by the time of survey. It was reported by the investigator by referring to the medical record of the patient. It was classified as no history of pregnancy loss, missed abortion, spontaneous abortion, and induced abortion.

**Spontaneous abortion**= Spontaneous demise of a pregnancy, which has been confirmed by at least two positive b-hCGs in the serum or urine. (ESHRE)

**Induced abortion**= Termination of pregnancy using drugs or surgical intervention after implantation and before the embryo or fetus has become independently viable.

- **1.26History of ART failure:** Refers to the history of failing ART treatment in the past. It included history of IUI failure and history of IVF/ICSI failure. It was reported by the investigator by referring to the medical record of the patient. It was classified as yes and no. If presence of history of ART failure, the number of failures was specified by the investigator.
- **1.27History of reproductive tract surgery**: Refers to the history of surgeries related to the reproductive tract including tubal ligation, vasectomy, etc. It was reported by the investigator by referring to the medical record of the patient. It was classified as yes and no. In case of any history of reproductive tract surgery, it was specified by the investigator.
- **1.28Professional psychological support**: Refers to the self-reported desire for psychological support from the provider following infertility and infertility treatment. It was dichotomized as yes and no.

## **Dependent Variable**

## Quality of life

Quality of Life (QoL) refers to infertile patient's or couple's perception of their life in relation to their physical/mental state, relational state, emotional state, social relationships, treatment environment and treatment tolerability. The FertiQoL questionnaire was used to assess the quality of life in infertile patients. The mean total scores obtained from the self-reported FertiQoL questionnaire was used as cut-off point to categorize FertiQoL as good and poor which was used to measure the quality of life.

The values lower than the mean total score indicated poor Quality of Life.

จุฬาลงกรณ์มหาวิทยาลัย Chulalongkorn University

# CHAPTER II LITERATURE REVIEW

#### 2.1 Problem Statement

WHO defines infertility as a disability, "an impairment which is a problem in body function or structure". According to WHO, "Infertility is a disease of the male or female reproductive system defined by the failure to achieve a pregnancy after 12 months or more of regular unprotected sexual intercourse." (Organization, 2021) It is classified as primary infertility and secondary infertility. Primary infertility is the condition when a woman has never conceived after regular unprotected sexual intercourse for 12months or more. Secondary infertility is the condition with at least one successful conception in the past but the incapability to conceive at present despite unprotected sexual intercourse for 12 months or more.

Globally, infertility affects 8-12% of couples of reproductive age. (Ombelet et al., 2008) Prevalence of infertility ranges between 3% and 25% (Dohle et al., 2005). The prevalence of infertility ranges from 6.9% to 9.3% in developing countries. (Boivin et al., 2007) A study concluded that 56% of couples in developed countries and 51% of couples in developing countries were seeking for medical assistance. (Ledger, 2009)

Low middle income countries of South Asia and sub-Saharan regions have higher infertility prevalence rates from 22% to 29% which accounts to about 14.4 million and 10 million couples respectively. (Mascarenhas et al., 2012) A systematic review of national health surveys reported that out of 186 million infertile couples, around 18 million experienced primary infertility and 168 million suffer from secondary infertility which accounts to 2.5% and 25% of the couples respectively. (Sun et al., 2019) By 2010, Sub-Saharan Africa and South Asia had the fourth and second highest prevalence of primary infertility respectively. (Mascarenhas et al., 2012) A prevalence of 25% cases of infertility was reported in China. (Zhou et al., 2018)

Nepal has observed a steady decline in total fertility rate (TFR) from 4.8 births per women in 1996 to 2.1 births per woman in 2022. National Demographic and Health Survey conducted in 2022 estimates that 13-15% of couples are living with infertility in Nepal based on the TFR. (Nepal Demographic and Health Survey 2022 - Key Indicators (English), n.d.) A survey conducted in eight districts of Nepal concluded that 7.4% of reproductive aged woman had infertility problem. (*Adhikari et al. - Infertility, Childlessness, and Healthcare Seeking.Pdf*, n.d.) A study conducted by Pradhan Shrestha et al. in an infertility center of Kathmandu found higher prevalence of primary infertility at 63.38% compared to 24.93% prevalence of secondary infertility. (Pradhan Shrestha et al., 2020) A hospital based study in Nepal found that 65.8% and 34.2% infertile women had primary and secondary infertility respectively. (Subedi et al., 2016) A retrospective study conducted in a hospital from 2008-2018 found that 74.7% of the cases were primary and the remaining 26.5% were secondary infertility. (Tamrakar & Bastakoti, 2019)

Both men and female contribute more or less equally to the infertility problem. Incidence for male infertility is between 30-50% and female infertility accounts to 50% of the cases. Similarly, 20-30% of cases are due to the combination of both male and female factors. (Agarwal et al., 2015) One in eight women and one in ten men aged 15-49 years have experienced infertility. (Datta et al., 2016)

## 2.2 Male Infertility

Around 40-50% of infertility cases are caused by male-factor infertility. (Speroff & Fritz, 2005) The prevalence of infertility in age-standardized to 15-49 years among men increased by around 8% in 2017. (Sun et al., 2019) Approximately 7% men faced fertility problems during their reproductive life. (Nieschlag & Behre, 2001) A study done by Liang et. al found that male infertility contributed to 13.91% of the cases and prevalence of unexplained factor infertility was 23.48%. (Liang et al., 2021) Male infertility is caused by various medical and environmental factors.

### 2.2.1 Causes of Male Infertility

#### 1. Medical Factors

#### 1.1 Sperm disorders

Sperm Disorders refer to problems in the sperm resulting in low sperm count, abnormal sperm morphology or low motility. Semen disorder contribute to 50% of male infertility cases. (Jungwirth et al., 2012) Globally, it is predicted that low sperm concentrations are the major factor causing infertility among 8-18% of men. (WHO Laboratory Manual for the Examination and Processing of Human Semen, n.d.) Similarly, abnormal sperm morphology and low sperm motility accounts to 20-30% of male infertility cases.

Men having sperm parameters below WHO normal range (refer to Table 2) are termed as infertile. (Plachot, Belaisch-Allart et al. 2002) Low sperm count is defined by the count less than 15 million sperm per milliliter per ejaculate. (Low Sperm Count, 2017) Abnormal sperm morphology refers to the abnormality in the shape and size of the sperm. Low sperm motility is the condition where only 40% or fewer sperm can efficiently move through the reproductive tract to reach an egg. About 90% of male infertility problems arise due to abnormality in sperm count and significant association have been studied between abnormal semen parameters and sperm count. (Sabra and Al-Harbi 2014)

Table 1 WHO reference range of semen analysis and related abnormalities

Semen	Reference	Abnormality	Description
Parameter	Range		
Semen	≥1.5ml		
volume			
, , , , , , , , , , , , , , , , , , , ,			

Sperm concentration	≥15 million	Azoospermia	Absence of sperm in the ejaculate.
		Aspermia	Absence of seminal fluid on ejaculation.
		Oligospermia	<15million spermatozoa/ml
Total sperm count	≥39 million sperm/ ejaculate		
Total sperm motility	≥40% motile sperm	Asthenozoospermia	<40% total motile spermatozoa or <32% progressive motile spermatozoa
Sperm Morphology	≥4% morphologically normal sperm	Teratozoospermia	<4% normal form/ morphology

์ วุฬาสงกรณมหาวทยาสย

Studies showed significant decline in semen quality, sperm count, motility, and morphology in relation to age. (Molina, Martini et al. 2010)(Mukhopadhyay et al., 2010) A study concludes that there has been a steady decline of sperm count among

healthy men by 1% per year and sperm density has decreased by 50% for over past 50-60 years. (Carlsen et al., 1992) A 10-year comparison study conducted in India on sperm quality and quantity showed that ejaculate volume decreased from 15% to 3% and sperm morphology was reduced by 7%. (Sengupta 2012) The decline in sperm quality has increased due to increasing incidence of male genital tract abnormalities like testicular cancer and cryptorchidism. (Bussen et al., 2004)(Giwercman & Skakkebaek, 1992)

## 1.2 Testicular Dysfunction

Defects in testicles is characterized by any structural or functional abnormality in one or both testicles thus affecting men's ability to produce or release healthy sperm. A study found 12% prevalence of testicular defects in infertile men seeking treatment. Testicular dysfunction may be due to acquired causes like infections, varicoceles, testicular trauma or torsion or

malignancy; congenital causes like Klinefelter's syndrome (KS) or due to idiopathic causes. (A. Sharma et al., 2020)

Varicocele is a common condition leading to male infertility due to the poor development of testicles. The condition is characterized by enlargement of veins within the skin that holds the testicles (scrotum). (Varicocele - Symptoms and Causes, n.d.) It is one of the major causes for testicular dysfunction leading to semen disorders with a prevalence of around 15-20%. (Baazeem et al., 2011) Some studies has also found an incidence between 35% to 40%. (Rotker & Sigman, 2016) WHO conducted a multicenter study among infertile couples of different geographical regions and found that the prevalence of varicocele ranged from 6% to 47%. (World Health Organization, 1992) A study conducted among infertile males in Pakistan concluded that 22.8% of the cases accounted to varicocele. Additionally, varicocele prevalence was 26% among Chinese male and 42.7% among Indian men. (Karimpour Malekshah et al., 2011) (Zhang et al., 2017)

Infertility due to acquired genital tract infection varies between 10-20%. (Henkel et al., 2007) Infections in male infertility present as urethritis, prostatitis, orchitis or epididymitis and are curable causes of male infertility. The infection prevalence is more common in developing countries. (A. Sharma et al., 2020) Infection leads to inflammation of epididymis which can affect fertility through sperm tract obstruction. (Stojanov et al., 2018) Increased risk and incidence of infertility has been studies among men with Hepatitis B and Hepatitis C infections. (A. Sharma et al., 2020) Some of the viral infections like HSV or HIV-1 are found to be associated with poor semen and sperm quality. (Kapranos et al., 2003)(Umapathy et al., 2001) Viruses like Human Papilloma virus (HPV) has been found in the semen of men experiencing male infertility. (Lyu et al., 2017)

Testicular trauma is an acquired cause of male infertility. It can lead to testicular torsion, displacement of testes and epididymitis. Studies on testicular trauma leading to infertility is rare. (Kukadia et al., 1996) With a prevalence of 19% cases of azoospermia, it is one of the leading causes of male factor infertility. (Öztekin et al., 2019) About 50% of men with testicular cancer experience infertility (Shefi & Turek, 2006) and 22% of men with history of testicular cancer require assisted reproductive technology to fulfill the desire of having a child. (Brydøy et al., 2005) Approximately 1% of men with testicular failure are affected by azoospermia which is its severe manifestation. (Jarow et al., 1989)

Congenital conditions like KS, can affect the production of sperm. KS is a common genetic defect leading to testicular failure which affects 1/1000 to 1/500 males. (Bojesen et al., 2003) Around 95-99% people with KS are infertile. Congenital defect in one or both testicles can result in oligozoospermia or azoospermia. (Esteves et al., 2011) Congenital bilateral absence of vas deferens is a rare obstructive testicular defect which contributes to male infertility. The prevalence is approximately 1 in 1000. (Lin & Huang, 2020) Undescended testis (UDT) or cryptorchidism is the developmental defect in testicles leading to impaired spermatogenesis and testicular germ cell tumors, thus affecting male fertility. (Niedzielski et al., 2016) Men with cryptorchidism have poor sperm quality in terms of motility and morphology and lower sperm counts. The increased duration for testicles remaining undescended pose a greater risk for future fertility. (Leslie et al., 2022)

Underlying genetic conditions, exposure to certain environmental factors and adverse lifestyle behaviors contribute to testicular dysfunction. However, 40% of cases of testicular defects are classified as idiopathic. (A. Sharma et al., 2020)

## 1.3 Ejaculatory dysfunction

Infertility due to ejaculatory dysfunction is a serious problem among young men. Ejaculatory dysfunction is the complete absence of ejaculation and is one of the most prevalent male sexual disorders. Retrograde Ejaculation (RE) and Anejaculation (AE) are the most common causes of ejaculatory dysfunction. About 1.2% of infertile men are affected by ejaculatory dysfunction. (Esteves et al., 2011) An desired ejaculate volume is required to transport male gametes into female reproductive tract, hence ejaculate volume is essential component to achieve fertility. (Roberts & Jarvi, 2009) It includes premature ejaculation, inhibited ejaculation, anejaculation, retrograde ejaculation, and anorgasmia.

Premature Ejaculation (PE) is "ejaculation that nearly or always occurs prior to or within about 1 min of vaginal penetration, an inability to delay ejaculation on all or nearly all vaginal penetrations." Various epidemiological studies have concluded that 20-30% of men experience premature ejaculation. (Rowland et al., 2010). The onset of ejaculation might be sudden or gradual. Conditions like thyroid dysfunction, urological disorders, psychological factors or combination factors can lead to PE. (Kondoh, 2011) PE can lead to reduced semen quality. Retrograde ejaculation (RE) is the disorder in which seminal fluid propels from posterior urethra into the bladder instead of emerging through penis during orgasm. RE accounts to 0.3-2% of male infertility cases. (Yayetz et al., 1994) A study concluded the prevalence of retrograde ejaculation to be 3.2% among infertile men. (Juárez-Bengoa et al., 2011) RE can result due to structural or functional abnormalities. Peripheral neuropathy due to diabetes mellitus, surgery, trauma and unknown causes can be contributing factors for RE. (Kamischke & Nieschlag, 1999) Delayed Ejaculation (DE) or inhibited ejaculation is defined as "persistent or recurrent difficulty, delay in, or absence of attaining orgasm after sufficient sexual stimulation, which causes personal distress." (McMahon et al., 2008) It is one of the least studied ejaculatory dysfunctions in men which results in reduced volume of semen and decreased sensation of ejaculation. Anorgasmia or perceived absence of orgasm experience is related to DE. (Kondoh, 2011) Anejaculation (AE) is the condition with complete absence of ejaculation. AE is rare cause of sexual dysfunction leading to infertility problems. (Stewart & Ohl, 1990) Sexual intercourse in the absence of ejaculate leads to complications for conception. Men with these conditions in their reproductive phase suffer from infertility. (Kondoh, 2011)

#### 1.4 Hypogonadism

Male hypogonadism is a common endocrine disorder in which testicular function is impaired which ultimately affects spermatogenesis and testosterone synthesis. Primary hypogonadism also known as hypergonadotropic hypogonadism is a common form of hypogonadism seen in men. The exact prevalence of the disease is not known. (Fraietta et al., 2013) A study reported an incidence of 12.3 cases per 1000 individuals per year. (Araujo et al., 2004) It is characterized by decreased production of testosterone and increased levels of follicle stimulating hormone (FSH) and Luteinizing hormone (LH). (Darby & Anawalt, 2005) Congenital conditions like KS results in primary hypogonadism among approximately one in 500 men. Acquired causes may be due to medicines, infections or use of abusive drugs or excessive alcohol. The prevalence is approximately 4.1% in men between age of 40-49 years. (Zitzmann & Nieschlag, 2000) Secondary hypogonadism is characterized by normal testicles but altered function due to

problems with pituitary or hypothalamus. It may be caused due to pituitary disorders, inflammatory disease, medications, obesity and aging. (*Male Hypogonadism - Symptoms and Causes*, n.d.) The prevalence of secondary hypogonadism is not well-known. Approximately 2/3 and 1/3 cases of hypogonadotropic hypogonadism are caused by KS and idiopathic causes respectively. (Fraietta et al., 2013)

#### 1.5 Cancer and Drugs

Infertility risk subsequently rises with patients and treatment factors. An increased risk of infertility and impairment in sperm production was evident among male cancer survivors who received alkylating chemotherapy to treat Hodgkin Lymphoma and other malignancies. (Green, Nolan, et al., 2014) About 25% patients developed azoospermia and 28% were oligospermic following treatment with alkylating chemotherapy. (Green, Liu, et al., 2014) Additionally, cisplatin, a DNA crosslinking agent, was found to be associated with reduction in male fertility. (Chow et al., 2016) Radiation exposure on testes have effect on spermatogenesis depending on the exposed dose and radiation. (Wallace et al., 2005) Treatment of bilateral testicular cancer leads to sterility in men. (M. Che et al., 2002)Retrograde ejaculation was observed among 10% of men with testicular cancer. (Brydøy et al., 2010)

Use of antidepressant medications are found to alter testosterone levels thus leading to male factor infertility. (Hendrick et al., 2000) DNA fragmentation was significantly higher in men using antidepressants compared to control. (Brezina et al., 2012) Decreased sperm motility and invitro spermicidal effect were observed with patients on antidepressants. (Relwani et al., 2011)(Kumar et al., 2006) Calcium channel blockers have dose-dependent effect on reduction of sperm motility. (Aaberg et al., 1989) Exposure to calcium channel blockers were also linked with disrupted sperm morphology and inhibition of sperm ability to bind to an egg. (Kanwar et al., 1993)(Benoff et al., 1994) Pregnancy rate per embryo transfer derived from men taking calcium channel blockers was found to be only 17.4%. (Katsoff & Check, 1997) Alpha-adrenergic blockers were found to be associated with ejaculatory disorders. About 30% of men taking these drugs experienced anejaculation. (Hellstrom & Sikka, 2006)Also, sperm concentration and motility were negatively affected with the intake of anti-adrenergic blocker medications. (Hellstrom & Sikka, 2009)

Effects of anti-epileptic drugs on male factor infertility are not well studied. A study found that men on highly active antiretroviral therapy demonstrated 60% reduction in sperm motility. (van Leeuwen et al., 2008) Similarly, decrease in ejaculate volume, disrupted sperm morphology and reduced sperm motility were observed following antiretroviral therapy. (Kehl et al., 2011) However, despite the abnormalities, men undergoing the therapy could highly achieve pregnancy. (Nicopoullos et al., 2010) Patients treated with antibiotics like tetracyclines for testicular infection were found to have deleterious effect on semen quality. (Farombi et al., 2008) Anabolic steroids have been found to be associated with oligo or azoospermia. (Tan & Scally, 2009)

#### 1.6 Unexplained Infertility

Unexplained infertility is the infertility among men with normal semen values and absence of physical as well as endocrinal abnormalities. Approximately 15% of average incidence of unexplained male infertility has been assumed. Erectile problems, coital factors, certain immunological causes, and sperm dysfunction may contribute to unexplained infertility. Sperm DNA damage, high levels of seminal ROS and sperm dysfunction might be possible factors leading to unexplained infertility. (Hamada et al., 2012)

#### 1.7 Sterilization

Male sterilization is done by cutting and sealing the tubes that carry sperm. (Vasectomy - Mayo Clinic, n.d.) Hence, it is irreversible. Less than 1 out of 1000 woman becomes pregnant after the male partner is sterilized. (Trussell, 2011)

#### 2. Environmental Causes

Male reproductive function is vulnerable to various environmental exposures, however only few have been studied. Endocrine disrupting chemicals (EDC) may induce hormonal changes or directly induce testicular toxicity, increase oxidative stress or sperm DNA damage. (Sidorkiewicz et al., 2017) Studies suggest that EDC like bisphenol A, phthalates, pesticides, and other environmental chemicals affect fertility by disrupting development of gonads during fetal life and lead to cryptorchidism, poor sperm quality and predisposition to testicular germ-cell cancers. (Skakkebaek et al., 2016) However, we lack clinical evidence. In-utero exposure to exogenous estrogenic compounds can alter neonatal development of testicles and reduce sperm production in adult men. (Sharpe, 1993)(Andolz et al., 1999) Exposure to heavy metals negatively affect male fertility by lowering seminal quality, thus leading to infertility. (Balabanič et al., 2011) A study showed that men residing in contaminated areas had higher concentrations of heavy metals like Zn, Cr and Cu and lower Fe concentrations in semen, decreased sperm motility and DNA damage was higher. (Bergamo et al., 2016) Similarly, heavy metals like Pb or As present in tobacco smoke adversely affect reproductive outcomes in male. (Hruska et al., 2000)

Male infertility can be caused due to the extreme exposure to heat and radiation and other hazardous substances. Radiation from X-rays have harmful effects on sperm parameters and induce oxidative stress. (Kesari et al., 2018) Prolonged exposure to heat causes testicular damage due to oxidative stress. High temperatures increase testicular metabolism and result in spermatic damage. (Hamilton et al., 2016) Also, prolonged cycling may increase the scrotal temperature which leads to sperm damage, reduced sperm count and concentration and elevation in sperm DNA fragmentation. (Jung et al., 2008)

#### 2.2.2 Risk factors for Male Infertility

Age is an important risk factor for decline in semen quality in men. The presence of spermatids in the seminiferous tubules declined to 50% among men aged 40-50 years. (Sasano & Ichijo, 1969) A decline of 3-12% in sperm motility(Harris et al., 2011) and 4-18% in sperm morphology has been observed in relation to age. (Andolz et al., 1999)(Auger et al., 1995) Health behaviors like excessive alcohol intake, smoking and use of recreational drugs pose as

a risk for reduced fertility in men. (Li et al., 2011) A study showed negative association between smoking and semen parameters. (R. Sharma et al., 2016) Smoking is associated with low sperm motility and concentration. (Mitra et al., 2012) Clinically, it leads to poorer outcomes of assisted reproduction technologies ART. (Waylen et al., 2009) Alcohol exposure in high levels is negatively associated with sperm quality and fertilization ability. (Anderson et al., 1983) Heavy alcohol intake leads to decrease in semen volume and affect sperm morphology. (Ricci, Al Beitawi, et al., 2017) Men with high or low BMI (less than 19 kg/m2 or more than 30 kg/m2) are associated with decreased testicular volume and reduction in sperm quality due to impairment in spermatogenesis. (Jensen et al., 2004) Men who are inactive and lead a sedentary lifestyle were found to have reduced sperm quality, especially in the presence of concomitant comorbidities like diabetes and obesity. (Vaamonde et al., 2012) Men with type 2 diabetes are found to have low testosterone level (Dandona & Dhindsa, 2011) and sleep apnea is also associated with decreased testosterone level and erectile function (Luboshitzky et al., 2005) which impose a risk factor to male infertility.

Use of recreational drugs like cannabis, androgens and opioids is associated with reduction in sperm parameters. (Bracken et al., 1990) Opioids may have direct effect on testicles due to the presence of endogenous opioid receptors. (Subirán et al., 2011) Long term use of opioids lead to decrease in sperm motility, hypogonadism and increase in prolactin levels. (Farag et al., 2018) Use of certain medications like anti-depressants, alpha blockers and antiretrovirals (Brezina et al., 2012) are found to affect testicular tissue, impair ejaculation and affect fertility in men. (Drobnis et al., 2017) Exposure of pollutants is associated with increased sperm DNA fragmentation and decreased sperm motility. (Jurewicz et al., 2018) Sauna, clothing, sleeping position, use of laptop, prolonged driving, welding are associated with scrotal hyperthermia. (Krzastek et al., 2020) Hyperthermia leads to impaired testicular function and decreased sperm concentration and motility. (Mieusset & Bujan, 1995)(Rao et al., 2015) Caffeine consumption has been found to be associated with increased sperm aneuploidy and DNA breaks. (Ricci, Viganò, et al., 2017) Certain history of past infection, presence of chronic medical condition, trauma in testicles, surgery, vasectomy, undescended testicles, further impose a risk to male fertility. (Male Infertility - Symptoms and Causes, n.d.)

# จุฬาลงกรณ์มหาวิทยาลัย

## 2.3 Female Infertility WALDWGKORN WERSITY

WHO estimates that female factor is the main cause among 37% of infertile couples. (Duffy & Allen, 2009) One third of infertility cases is due to female factor (Female Infertility - an Overview | ScienceDirect Topics, n.d.) which accounts to about 9% of women worldwide experiencing infertility. (Boivin et al., 2007) Several causes of female infertility include anatomical abnormalities, ovulatory and menstrual disorders, endometriosis, certain drugs and medications and unexplained infertility.

## 2.3.1 Causes for Female Infertility

#### 1. Medical Causes

### 1.1 Ovulatory Disorders

Ovulatory disorders accounts to a major cause of infertility. About 25% cases of female infertility is caused by ovulatory disorders. (Walker & Tobler, 2022) Polycystic Ovarian Syndrome (PCOS) is predominant cause of anovulatory infertility which affects 7 to 15% of

reproductive age women. (Collée et al., 2021) PCOS is associated with dysfunction in developing a mature follicle hence leading to anovulation and infertility. (Fauser & Van Heusden, 1997)

Premature ovarian failure is the loss of ovarian activity under the age of 40 years which severely affects female fertility. It has a global prevalence of approximately 1.1%. (Fauser & Van Heusden, 1997) A study in 2004 showed that 2.8% of Chinese women are affected by premature ovarian failure. (Wu et al., 2014) About 20% of premature ovarian cases result due to autoimmune diseases. (Szeliga et al., 2021) Gene mutation in women can result in elevated depletion of ovarian reserve leading to early menopause, hence affecting fertility. (Finch et al., 2013) Thyroid dysfunction is a common cause of infertility. Hypothyroidism in reproductive age women has been the cause of infertility with a prevalence of 2-4%. (Lincoln et al., 1999)(Krassas, 2000) It can lead to anovulatory cycles, defects in luteal phase, hyperprolactinemia and sex hormone imbalance leading to infertility. Hypothyroid infertile women are also associated with hyperprolactinemia or high prolactin. A prevalence of 18.3% cases of hyperprolactinemia was found among infertile women. (Verma et al., 2012) It affects by impairing release of GnRH and thereby affecting ovarian function.(Poppe & Velkeniers, 2003)

# 1.2 Tubal Infertility

Tubal factor infertility is a common cause of infertility. The incidence of tubal factor infertility ranges between 25-30%. (Ambildhuke et al., 2022) Factors that contribute to development of tubal factor infertility include pelvic inflammatory disease, previous history of ectopic pregnancy and prior tubal surgery. Sexually Transmitted Infection (STI) is associated with tubal factor infertility. (Kavanagh et al., 2013) The risk of tubal infertility is between 0.1-6% after chlamydial infection. (Land et al., 2010) Pelvic Inflammatory Disease (PID) is the most common cause of acquired infertility among women resulting from infection. One in 10 women with pelvic inflammatory disease becomes infertile. (Pelvic Inflammatory Disease (PID), n.d.) A study found that tubal occlusion due to PID led to infertility among 10.8% women. (Westrom, 1995) History of pelvic surgery pose a significantly higher risk for tubal infertility. (Ramos et al., 2008) Past history with pelvic operations increase the risk for ectopic pregnancy by 9-folds. (Michalas et al., 1992) Incidence of ectopic pregnancy is increasing with increased incidence of PIDs. (Weström et al., 1981) A pregnancy is considered ectopic when embryo implants in the fallopian tube or outside the uterine cavity. (Xue et al., 2022) Ectopic pregnancy can result in infertility and about 35% women with this condition have difficulty getting pregnant. (Ectopic Pregnancy, n.d.)

#### 1.3 Endometriosis

Endometriosis is the condition characterized by presence of tissue like lining of the womb outside the uterus that distort the anatomy of pelvis in women. (Kennedy et al., 2005) The prevalence of endometriosis is estimated to be approximately 6-8%. (Hummelshoj et al., 2006) About 25%-50% of infertile women have endometriosis and 30 to 50% of women with endometriosis experience infertility. (Counseller, 1938) Infertile women are 6 to 8 times more likely to develop endometriosis. (Verkauf, 1987) Endometriosis may lead to endocrine and ovulatory disorders. (Ozkan et al., 2008) Uterine fibroids are common tumor occurring in women. The prevalence of uterine fibroids is high at 2-3% among women experiencing

infertility. Fibroids can cause recurrent pregnancy loss and infertility depending on its location on the uterus. (Freytag et al., 2021) Endometrial polyps are the commonly reported uterine abnormalities with incidence of 16.7% in patients with recurrent implantation failure

after IVF. (Fatemi et al., 2010) A study identified polyps among 32% of patients undergoing IVF. (Hinckley & Milki, 2004) Polyps are characterized by focal growths of uterine mucosa and considered to be a factor to contribute to infertility and recurrent pregnancy loss.(Al Chami & Saridogan, 2017) They are usually diagnosed by hysteroscopy during infertility treatment.

Commonly found congenital uterine abnormalities are uterine septum which is associated with infertility and recurrent pregnancy loss.(Walker & Tobler, 2022) Roughly 8% of female infertility causes are due to congenital abnormalities in the uterus. (Chan et al., 2011) A study reported that congenital uterine anomality like septate uterus have higher incidence of infertility but it was not significant. (Shuiqing et al., 2002) Problems in cervical mucus can prevent sperm from entering the uterus, thus affecting reproduction. However, this is a rare cause of infertility. (Infertility Problems With Cervical Mucus - Women's Health Issues, n.d.)

# 1.4 Medicines and Drugs

Use of recreational drugs like marijuana, cocaine, LSD creates slightly elevated risk of ovulatory abnormality. (Mueller et al., 1990) Anticancer treatments like radiation, chemotherapy and surgery can severely damage ovarian function and lead to premature ovarian failure, thus affecting fertility. (Spears et al., 2019) Cytotoxic drugs like cyclophosphamide, methotrexate and 5-fluorouracil used in the treatment of cancer are great stimulators for infertility. Studies show that the treatment resulted in loss of ovarian function among 30% of the patients. (Sonmezer & Oktay, 2006) Exposure to higher levels of alkylating chemotherapy during cancer treatment using drugs like doxorubicin, bleomycin, vinblastine are associated with lower Anti-Mullerian Hormone (AMH) in women which impacts infertility in women (Decanter et al., 2010) including acute ovarian failure (AOF) and premature menopause. (Thomas-Teinturier et al., 2015) Cell transplantation during the treatment of leukemia pose a greater risk for ovarian failure and infertility in women. (Watson et al., 1999) Radiation can affect fertility when targeted to reproductive organs or structures producing hormones required for reproduction. (Wallace et al., 2003) The risk of infertility following hysterectomy is 100%. However, pregnancies can be achieved by oocyte retrieval and surrogacy. (Giacalone et al., 2001)

# 1.5 Unexplained Infertility

Unexplained infertility is the condition in which there is no definite medical cause for infertility. About 10-17% of infertile women experience unexplained or idiopathic infertility. (Ehsani et al., 2019)

# 1.6 Sterilization

Female sterilization involves surgical procedure to block the fallopian tubes, thus preventing sperm to reach and fertilize the ovum. (Female Sterilization - an Overview | ScienceDirect Topics, n.d.) Women who undergo sterilization are more than 99% infertile. (Female Sterilisation, 2017)

#### 2. Environmental Causes

Studies suggest that physical and psychological stress faced by women reduce the chances of conception. Almost 30% of women seeking infertility treatment are affected by it. (Barzilai-Pesach et al., 2006) Consumption of alcohol beyond the threshold increases the risk of infertility in women.(Jensen et al., 1998) Similarly, excessive smoking increases the risk for ovulatory disorders and hence affect fertility. (Stene-Larsen et al., 2009) Excessive caffeine intake is found to be associated with increased risk of spontaneous abortion, (Chen et al., 2014) reduced fecundity, and delayed conception. (Hassan & Killick, 2004) Substance abuse and use of recreational drugs like cannabis, heroin, cocaine disturbs the reproductive process affecting implantation failure, embryo development and spontaneous abortion hence leading to infertility. (Monica Bari, 2011)

Increased use of pesticides and insecticides is found to correlate with decreased fertility rates, spontaneous abortion, and multiple ovarian disorders. (Record Details, n.d.) Prolonged exposure to endocrine disrupting chemicals (EDCs) present in pesticides, fertilizers, plasticizers is found to reduce fertility by causing hormonal imbalance. (Ding et al., 2016) Exposure to heavy metals like lead, cadmium and arsenic can affect reproductive function and increase the risk for spontaneous abortion, preterm birth, and menstrual irregularities. (H. Wang et al., 2017)(Sabra et al., 2017) Air pollutants like heavy metals or hydrocarbons generate reactive oxygen species and produce oxidative stress which affect female reproduction system in regulating follicular growth and ovulation. (Hernández-Ochoa et al., 2009) Noise pollution can have impact on behavioral and physical well-being of individual. It can cause anger, stress, anxiety, agitation, sleep disturbances, sexual impotence, and emotional instability. (Stansfeld & Matheson, 2003) Solvents used in pharmaceuticals, paints, electronics, etc. may negatively affect fertility (Lipscomb et al., 1991). Indoor pollution due to use of wood and coal for cooking can increase the risk for defects in pregnancy. (Lacasaña et al., 2006) Gonads are highly sensitive to radiation exposure. Hence, exposure to radiation like X-ray, ultrasound can have detrimental effect on pregnancy, increase the risk of implantation failure and cause mental retardation. (De Santis et al., 2007) Studies have shown that exposure to gamma-radiation during cancer treatment results in depletion of ovarian follicles and premature ovarian failure. (C. J. Lee & Yoon, 2005)

# CHULALONGKORN UNIVERSITY

## 2.3.2 Risk Factors for Female Infertility

Age is one of the risk factors for infertility. Fertility declines with age in women (May-Panloup et al., 2016) which is as early as the mid-thirties.(Leridon, 2004) Increase in age results in decline in the number of oocytes and quality of existing oocytes and intercourse frequency is also decreased with age. (ESHRE Capri Workshop Group, 2005) Studies suggest that fertility significantly fell with age above 30 years. (Fédération et al., 1982) Increased aneuploidy in embryos among older women contributes to inability to bear a child as risk for implantation loss and pregnancy failure is increased. (Munné et al., 1995) With increase in age, women respond poorly to ovarian stimulation during IVF treatment. This is a strong predictor of declining ovarian reserve, resulting in reduced fertility and early menopause. (de Boer et al., 2002)(Lawson et al., 2003) Age at marriage also plays a vital role. People tend to delay marriages and get married at an older age resulting in females being older when attempting for first pregnancy. (Leke et al., 1993)

Studies show that intake of nutrient rich diet is associated with lower risk of ovulatory infertility in women. (Chavarro et al., 2007) Certain lifestyle factors like smoking, alcohol intake and

obesity can decrease egg quality and ovulation rate, which can increase the risk of infertility in women. (R. Sharma et al., 2013) Smokers are more likely to experience infertility compared to non-smokers. (Augood et al., 1998) Also, a significant delay in conception was observed among female smokers. (Hull et al., 2000) Exposure to toxic components from smoking may induce intrafollicular stress (Paszkowski et al., 2002) and DNA damage. (Sinkó et al., 2005) Overnutrition and undernutrition can negatively affect fertility. (Pasquali et al., 2003) Increase in BMI impose an increased risk of ovulatory disorder in women. (Rich-Edwards et al., 2002) The risk of infertility is three times higher in those obese than nonobese. (Rich-Edwards et al., 1994)

Certain medications like opioids, antidepressants and chemotherapy can reduce the egg quality and ovulation rate, hence increasing the risk of infertility. (Duffy & Allen, 2009) Exposure to environmental toxins like BPA, lead, cadmium, pesticides also pose a risk for decreased reproductive function in females. (Piazza & Urbanetz, 2019) Having a history of medical conditions like diabetes and PCOS can be a risk factor for infertility. (Dennett & Simon, 2015)

# 2.4 Effects of Infertility

Childbearing is considered a crucial part of married life, hence couples who fail to conceive face pressure from family and the society. Infertility has negative effect on infertile couples, affecting various aspects of their life like marital relationship, sexual satisfaction, psychosocial well-being and overall Quality of life (QoL). (Luk & Loke, 2015)

# A. Psychological effect of couples

Infertile couples are twice more likely to experience anxiety, depression and stress in their life which negatively impact fertility, infertility treatment and overall QoL. (Holter et al., 2006)(Maroufizadeh et al., 2018) Psychological factors may also contribute to negative effects on sexual performance and increased marital conflicts. (Gourounti et al., 2012) In addition, it also play a major role in increased rates of treatment dropout. (Ragni et al., 2005) (Dube et al., 2023)

#### a. Psychological effect on infertile women

Studies show that infertile women experience more stress than infertile men. (T. Y. Lee & Sun, 2000) This is because, in many cultures (including in Nepal), infertility is considered as a failure to fulfill her role as a woman. (Onat & Kizilkaya Beji, 2012) Thereby, women feel incomplete if they are unable to bear children.(Loke et al., 2012) A study conducted in Japan found a significant association between anxiety and depression among infertile women. Also, lack of support from their spouse and feelings of stress was found significant. (Matsubayashi et al., 2004) Studies by Albayrak et al and Noorbala et al found that infertile women experienced higher levels of distress, depressive disorders, anxiety and psychiatric disorders compared to fertile women. (Albayrak & Günay, 2007)(Noorbala et al., 2009) This might be due to the complex process of infertility treatment and stronger desire for a child among women. (Greil et al., 2010)

## b. Psychological effect on infertile men

Infertile men were found to experience higher levels of psychological distress compared to fertile men. (Dyer et al., 2009) A study conducted in Iranian men found that the depression rate

was higher among infertile men than those in western countries.(Ahmadi et al., 2011) Thus, these studies highlight the importance of addressing the psychological needs of male partners in the management of infertility.

#### B. Marital relationship of couples

Infertile couples are two times more likely to divorce than the fertile couples. (Y. Che & Cleland, 2002) A study done in Taiwan found that infertile women were less satisfied with their marriage than their spouse. Wives worried about being accepted by in-laws and family members from husband's side showed aggressive behavior towards them to end a childless marriage. To the contrary, wives' family gave less trouble to the couple even when male factor was the cause for infertility. (T. Y. Lee & Sun, 2000) The situation of Nigeria is such that the husbands take another wife in response to infertility. (Nieuwenhuis et al., 2009) These cases are very much relevant with rural areas of Nepal.

However, some studies have also found that infertile couples have significantly better relationship than fertile couples. They indicated that infertility was not associated with negative effect on marital relationship and additionally, quality of their marital relationship was even higher among infertile couples than that of fertile couples. (Drosdzol & Skrzypulec, 2009) A study in which more than two-thirds of infertile couples were married for more than five years found that QoL was higher among them. However, this can be due to the shared crisis of infertility for a longer duration. (Onat & Kizilkaya Beji, 2012) Better marital functioning can be explained by the ability of the couples to talk about their fertility problems and discuss about future. Greater emotional intimacy between partners and feelings of commitment and loyalty might have strengthened the marital relationships in infertile couples.(Drosdzol & Skrzypulec, 2009)

## C. Sexual Relationship of couples

Difficulties with ejaculation can result in negative personal consequences in men like distress and frustration. Chronic cases of male factor infertility can also lead to decreased coital frequency. (Kondoh, 2011) A study conducted in China found higher incidences of premature ejaculation and higher degree of erectile dysfunction among infertile men. (Gao et al., 2013) Similarly, infertile women were found to have higher sexual dysfunction compared to fertile women. (Oskay et al., 2010) Additionally, infertile wives showed higher levels of sexual dissatisfaction compared to their husbands. (Oskay et al., 2010)(T. Y. Lee & Sun, 2000) The inability to delay ejaculation can further affect sexual intimacy among the couples. (Kondoh, 2011)

#### D. Social stigma among couples

Infertile couples experienced feelings of incompleteness, shame, guilt, and isolation.(Loke et al., 2012) A study conducted in Nigeria show that psychological disturbances faced by infertile men and women were mainly due to the social effect. Infertile women were more worried about their situation, felt depressed and often had suicidal thoughts. (Nieuwenhuis et al., 2009) A study by Loke et. al also support that psychological effect was more prevalent among infertile women. (Loke et al., 2012)

# E. Quality of Life

Infertility has negative impact in marital relationship, sexual satisfaction, psychological well-being, and societal relationships, which ultimately affects the Quality of Life (QoL). (J. Chachamovich et al., 2009)

QoL is defined as "an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, values and concerns". ('The World Health Organization Quality of Life Assessment (WHOQOL)', 1995) Assessment of QoL allows better understanding of the impact of fertility conditions on patients in a broader perspective including emotional symptoms like emotional behavior, self-esteem and mental health. (Aarts et al., 2011) (J. R. Chachamovich et al., 2010) Furthermore, QoL addresses physical, cognitive, relationship, psychological and social domains of the individuals. Hence, determining the factors affecting QoL can help improve patient care and compliance in the treatment domain. (Karabulut et al., 2013)

# a. QoL in infertile female

Infertile women were found to have lower quality of life. A study by Ragni et al. demonstrated that women measured significantly lower on QoL scores in terms of social functioning, emotional and mental health. (Ragni et al., 2005) Another study showed that women scored significantly lower in overall scores while higher in psychological and social relationship domain in comparison to men. (J. Chachamovich et al., 2009)

Similarly, impaired scores were observed in emotional, social, and mental domains among young women. (Souter et al., 2002)(J. R. Chachamovich et al., 2007) In a study conducted by Fekkes et al., social domain was highly affected among young women compared to old (Fekkes et al., 2003) which is assumed to be due to lesser life experience and lack of developmental strategies to cope up with stress. However, the study by Karabulut et al. found no difference in emotional, mind/body and social scores among younger age group. This difference in results is thought to be due to the supportive family behaviors in the culture of study population. (Karabulut et al., 2013)

Lower scores in QoL were observed in women experiencing primary infertility. Having at least one child decreased the distress while having no children resulted in social isolation and reduced tolerability to treatment. (Karabulut et al., 2013) This was supported by studies which compared couples with and without children and concluded that QoL was significantly impaired due to the absence of children. (Monga et al., 2004)(Johansson et al., 2009) Social isolation and decreased treatment tolerability might be the impact of conservative communities surrounding parenthood.

Lower educational status was related to poorer scores in social and mental health domains which assumes the association of higher educational status with higher income and better mental health. (J. R. Chachamovich et al., 2007) In a study conducted by Karabulut et al., high education status was associated with higher scores in the QoL domains. However, their total scores were lower among highly educated primary infertile women which indicates the intense effect of primary infertility on QoL domains. (Karabulut et al., 2013) Hence, specific study needs to be conducted to find the association of higher educational status with high income, housing, and better mental health.

The QoL among those residing in rural areas was lower as compared to the urban residents. (Namdar et al., 2017) It was supported by the findings from study by Dong et. al which

concluded lower QoL scores among rural residents. (Dong & Zhou, 2016)Emotional domain was found to be lower among those living in extended families compared to nuclear families. This can suggest that women are pressurized by the elders in the extended family to achieve a pregnancy. (Karabulut et al., 2013)

History of ART failure was associated with low mental health scores and psychological health. (J. R. Chachamovich et al., 2007) (Ragni et al., 2005) Studies found that social, psychological and mind/body domains of QoL were affected by the number of ART failures, with women presenting lower scores than men in each domain. (Agostini et al., 2017)(Moura-Ramos et al., 2012) Similarly, lower scores in mind/body, social and tolerability subscales of QoL were associated with increased duration of infertility. (Ragni et al., 2005)

Furthermore, the stigma associated with infertility led patients to not talk about infertility issue which resulted in lack of social support. (Malik & Coulson, 2008) Fatigue was found to be an influential factor of QoL in infertile women. (Nho & Kim, 2022) Women with recurrent miscarriage were found to have negative effects on their functional ability and scored lower in well-being. (Tavoli et al., 2018) The women who had desire for psychological support demonstrated lower scores in QoL domains. Women with health insurance were found to have a better relationship with their partners and hence scored higher in relation domain. (Karabulut et al., 2013) It can be hypothesized that since infertility treatments are not supported by public health system, emotions evoked by financial impact is partially mitigated by being insured.

#### b. QoL in infertile men

Most of the findings in QoL among men is obtained from couple study. Men scored higher in terms of QoL scores as compared to women. However, on comparing with the normal population, the infertile men had similar QoL scores, thus suggesting that the scores were independent of infertility problems. (Ragni et al., 2005) The sensitivity of QoL measurement instrument used in the study can explain the discrepancy of the results. To the contrary, comparing against normative data, men scored lower in emotional and social functioning domains (Fekkes et al., 2003) and in mental health domains. (Shindel et al., 2008) Also, men scored lower in self-esteem and social functioning domains. (El-Messidi et al., 2004)

A group of studies have investigated the predictors of low QoL in infertile men. The findings concluded that strong will to have children, lower education level, poor marital relationship, history of ART failure and prolonged duration of infertility were associated with lower scores in mental health domains. (Lau et al., 2008)(Ragni et al., 2005) Planning for ART was also associated with impaired emotional behavior. (Fekkes et al., 2003)

# c. QoL in couples

It has been assumed that individual QoL is influenced by partner's QoL. (Andrews et al., 1991) (Greil, 1997) Hence study regarding QoL should focus on men and women as a dyad rather than individual. Family system theory also suggests that studying individuals in integration with their relationship with family members is a better approach. (Peterson et al., 2003) Studies found that infertility stress has negative effect on individual's QoL but also has significant effect on QoL of his/her spouse. (J. H. Kim et al., 2018) (J. H. Kim & Shin, 2013) Individual and partner perception on infertility may also result in distress. (Benyamini et al., 2009) Lower congruence levels among couples were associated with marital satisfaction and lower levels of adaptation. (Peterson et al., 2006) Infertility related distress, marital relationship and

depression were found to be the main factors influencing QoL. (J. H. Kim & Shin, 2013) QoL scores were found to be intrinsically linked to the presence of the clinical conditions like endometriosis, PCOS and cancer which result in infertility. (J. R. Chachamovich et al., 2010) A study conducted in rural China found 80% of infertile couples were desperate for a child and they felt that they could not live well without a child. This indicates that desire for a child was a major concern for them. (Lau et al., 2008)

Couples undergoing infertility treatment often struggle to balance job responsibilities with their treatments. The treatment process may include frequent and unpredictable visits in coordination with menstrual cycle. A study conducted in Japan found significant association between reduced access to time off at work and increased job demand and lower scores in QoL. (Maeda et al., 2022)

# F. Psychological effects on QoL

Psychosocial studies illustrate a highly negative impact of infertility and its treatment on QoL and well-being. (Greil, 1997) (Verhaak et al., 2007) Psychological difficulties among couples relates to the cognition and personal beliefs regarding parenthood and childlessness. (Verhaak et al., 2007) A longitudinal study on psychosocial predictors of QoL among infertile couples found that parenthood was associated with increased QoL scores in infertile women and diminished marital life scores in the couples. (ABBEY et al., 1994) Some studies have found association between impact of partner's coping mechanism and couple's experience with infertility. (Peterson et al., 2006)(Berghuis & Stanton, 2002) Also, a partner's coping pattern influences women's ability to cope with infertility and vice versa. (Jordan & Revenson, 1999)(Peterson et al., 2006) Studies show strong association between depression and psychological domain of QoL.(J. R. Chachamovich et al., 2010)(Berlim et al., 2008)(J. Chachamovich et al., 2009) Hence, minimizing emotional distress may positively influence QoL and treatment compliance.

# Measurements of QoL

Some of the generic instruments used for the assessment of QoL are Short Form 36 (SF-36), World Health Organization Quality of Life Brief Version (WHOQoL-BREF), Core Quality of Life Questionnaire (QLQ-C30), SF-12, General Health Questionnaire- 28 (GHQ-28), Enrich Inventory and Quality of Well-being scale. Similarly, specific instruments include Fertility Problem Inventory (FPI), Fertility Quality of Life (FertiQoL), Fertility Problem Stress (FPS), Infertility Questionnaire (IFQ) and Illness Cognitions Questionnaire adopted for Infertility (ICQ-I).

However, SF-36 and WHOQoL-BREF are the most widely used generic measures (Mousavi et al., 2013) and FertiQoL is the mostly used specific measure for assessing QoL in infertile patients. (Kitchen et al., 2017)

Disease-specific measure like FertiQoL is preferred due to its focus on specific aspects of the condition. FertiQoL is an internationally developed instrument used to measure QoL in male and female experiencing infertility problems. The questionnaire also includes an additional module for the assessment of treatment satisfaction. FertiQoL provides an adequate face and content validity in terms of number of items included (n=36), respondent's burden, clarity of instructions and balance in response options. It has strong evidence for internal consistency reliability measured by Cronbach's alpha values which range between 0.72 to 0.92 and

construct validity to support the structure of conceptual framework of FertiQoL. (Boivin et al., 2011) Hence, FertiQoL is a reliable and valid measure to assess changes in QoL or treatment satisfaction in clinical studies with patients following treatment.

Table 2 Subscales of FertiQoL

S.No.	Subscale	Description		
1.	Emotional	"Impact of Negative emotions like sadness, depression,		
		jealousy, and resentment on QoL"		
2.	Mind/ Body	"Impact on physical health (eg. Fatigue, pain), Cognition (eg.		
		Concentration), Behavior (eg. Disrupted daily activities,		
		delayed life plans)"		
3.	Relational	"Impact on marriage or partnership (eg. Sexuality, communication, commitment)"		
4.	Social	"Impact on social interactions (eg. Social inclusion, expectations, stigma, support)"		
5.	Treatment Environment	"Impact of accessibility and quality of treatment on QoL."		
6.	Treatment Tolerability	"Extent to which fertility medical services impact on daily life"		

#### 2.5 Solutions

## 2.5.1 Solutions for Male Infertility

Acquired infections in male infertility can be treated with antibiotics which can help improve sperm quality and prevent further testicular damage and complications. (A. Sharma et al., 2020) Antioxidants can help reduce the damage of reactive oxidative species from factors like smoking and drinking and thus prevent damage to sperm and sperm DNA, thus reducing its impact on fertility. (Showell et al., 2011) Oral pharmacotherapy is an effective, noninvasive treatment option for cases of ejaculatory dysfunction. The condition can be treated effectively by Alpha-adrenergic agonists or anticholinergic and antihistaminic drugs. (Roberts & Jarvi, 2009)(Kamischke & Niesha, 2002, p. 1) Intrauterine Insemination (IUI) is less expensive and non-invasive which makes it more convenient treatment option. (Fraietta et al., 2013) IUI is a procedure in which laboratory processed sperm are placed in the uterus to attempt a pregnancy. It is a preferred treatment option for men who have sperm concentration higher than  $5 \times 106/\text{mL}$  but fail for conception.

Hormone replacement therapy (HRT) with urinary or recombinant gonadotropins is widely accepted treatment option for hypogonadism cases. Men with hypogonadotropic hypogonadism were found to achieve 67% fertilization and 30% pregnancy rate per cycle on HRT following ICSI cycle.(Zorn et al., 2005) Progression in the field of ART (IVF, ICSI, sperm cryopreservation) has increased the treatment and management options among infertile men and women. Using these technologies, sperm can be retrieved from target sites like vas deferens, epididymis and testis (Kondoh, 2011) which is referred as Testicular sperm extraction

(TESA) or testicular microdissection. TESA is a surgical procedure involving one or more testicular biopsies or needle aspirations to obtain sperm for use in IVF and/or ICSI. Intracytoplasmic Sperm Injection (ICSI)- a procedure in which a single spermatozoon is injected into the oocyte cytoplasm, can be opted for individuals with sperm concentrations >5×106/mL but fail for conception. (Bakircioglu et al., 2007) These are possible treatment options for male infertility. (Fraietta et al., 2013) Additionally, reproductive potential of female partner should also be evaluated. Male patients can seek ART services for sperm banking or cryopreservation of sperm before undergoing cancer treatment or exposure to chemotherapy.

# 2.5.2 Solutions for female Infertility

Exercise can help to reduce stress related to infertility. (Goldman & Hatch, 1999) A reduced risk of ovulatory dysfunction was associated with 30 minutes of exercise per day. (Chavarro et al., 2007) Mutual support and consideration of partners are helpful ways to cope up with infertility for marital adjustment. (Peterson et al., 2006) It was reported that lack of support from husband increased distress and decreased marriage satisfaction among infertile women. (T. Y. Lee & Sun, 2000) Hence, support from husband can help protect women against negative thoughts and ultimately save marriage. (Albayrak & Günay, 2007) If couples can support each other, the infertility experience can bring them closer and strengthen their marital relationship. Couple's ability to talk about their fertility problem and plans further strengthens the feelings of commitment and loyalty among them and creates a stronger emotional intimacy. (Drosdzol & Skrzypulec, 2009) Providing psychological counselling and support to the couples through the emotional journey of infertility can help them to cope up with the emotional and psychological challenges associated with infertility. (Rooney & Domar, 2018) Patients who received psychological treatment during infertility treatment were 25% more likely to achieve a pregnancy. (Dube et al., 2023) Fertility drugs like clomiphene citrate and gonadotropins are useful to stimulate ovulation in women. (M. Sharma & Balasundaram, 2022) The first baby conceived by invitro fertilization, ART services brings hope to many infertile couples. (Ni et al., 2021) Advances in medical technology introduced IVF, ICSI and cryopreservation, which provides an opportunity for couples to become parents.

# CHULALONGKORN UNIVERSITY

#### 2.6 Barriers

Increasing age is a barrier for seeking medical treatment. As the age increases among the couples, it becomes more difficult to conceive and treatments may also have lower success rates. (Mosalanejad et al., 2014) In many cultures, infertility still remains a taboo and childlessness is stigmatized which makes it difficult for couples to talk about the issue and seek for help. (Onat & Kizilkaya Beji, 2012) Infertile couples become more vulnerable to suffering from depression and feeling of shame. They often exhibit dysfunctional coping strategies and score lower in psychological functioning which can lead to emotional burden among the couples. (Hasanpoor-Azghdy et al., 2014) They may feel ashamed or embarrassed to talk about the infertility issue and hence may be reluctant to access the treatment option. (Domar et al., 2012) Lack of awareness about the available treatment options can also be a barrier among the couples to seek for infertility treatment. (Domar et al., 2021)

Despite the vast worldwide diffusion of IVF, political and social reactions about these treatments are heterogeneous. Criticisms towards these technologies have been raised that might result in patients being ashamed of their condition. Moreover, performing IVF may be

considered a highly stressful event per se since patients generally feel it is the last chance to conceive. (Ragni et al., 2005) Repeated treatment failures with ART can lead to low compliance in treatment among the individuals and cause further anxiety and discomfort. It also pose an increased burden on the finance. (Akarsu et al., 2009) Multiple pregnancies and ectopic pregnancies are possible complications of infertility treatments like IVF. About 30% of pregnancies from IVF treatments result in multiple gestations. The multiple embryos transferred in the uterus during the IVF cycle increases the chances of multiple pregnancy. ('In Vitro Fertilization and Multiple Pregnancies', 2006) Similarly, the incidence of ectopic pregnancy is about 1-2% among women who undergo IVF treatments which is comparatively higher than the risk in fertile population. (Patil, 2012) These complications can be a barrier as they increase the risk associated with pregnancy and childbirth. Increased treatment duration is also a barrier for seeking fertility care. Couples may need to travel long distances frequently once they enroll in the treatment, thus imposing a financial and logistic burden among the couples. (Blakemore et al., 2020) Alternatively, treatment options including ART may not be available in all areas.

Infertility is a major reproductive health issue which is stigmatized and still remains a taboo in developing countries like Nepal. Infertility can cause mental problems and hence, this issue can be a stressful experience for infertile patients. Many couples face difficult challenges in physical, mental, social, emotional and relationship domains. Neglecting the emotional needs and other adverse effects of infertility in infertile patients can have a negative impact in the treatment of the couples. Hence, quality of life assessment should be conducted among patients experiencing infertility. Only two quality of life studies have been conducted in Nepal while only one study has used FertiQoL as a measurement tool. A study was identified on quality of life among infertile women in Nepal through gray literature in the library of Mahidol University which was conducted in an infertility center in Kathmandu. The study identified that 48.9% respondents had good level of Core QoL with mean score of 61.58 and 53.7% respondents had good level of Treatment QoL with mean score of 68.45. The study found significant association between Core QoL and education level of the respondent and her husband, duration of treatment, income of her husband, social support level, social pressure from female relatives and treatment service affordability. Also, it concluded significant association between Treatment QoL and husband's education, social support level and treatment service affordability.

# Nepal Health System and Infertility

Nepal Demographic and Health Survey (DHS) has not yet considered the prevalence of infertility in Nepal. Additionally, there is no national registry for activities involving IVF. IVF/ICSI, sperm donation and gamete donation are permitted Assisted Reproduction Technology (ART) practices in Nepal. A maximum of three embryos per transfer are allowed.

Nepal Law Commission under "The Right to Safe Motherhood and Reproductive Health Act, 2018" Act No. 9 states infertility under the definition of "Morbidity" as the state that affects reproductive system. In Chapter 5 - "Right to Morbidity Care", it states that "Every woman shall have the right to get her examined, obtain counseling and receive treatment relating to morbidity by or in the health system." However, with high out-of-pocket expenditure for health at 51%, low public health expenditure at 1.5% of gross domestic product (GDP) and only 0.4% of total federal government health budget allocated for sexual and reproductive health as in fiscal year 2019/2020, the right for fertility care has not been met. (United Nations Population Fund 2022, n.d.)

With the introduction of IVF technology in 2004, ART has existed for nearly two decades in Nepal. Given the minimal allocation of budget to sexual and reproductive health, ART remains either unavailable or inaccessible to most people. On conducting an online search, the principal researcher couldn't gather any information on infertility and infertility services from the website of Ministry of Health and Population (MoHP) in Nepal, hence it was not possible to find any information on publicly funded infertility treatments in Nepal. On asking key informants, the researcher found that infertility care is not included in the health insurance packages.

The infertility services are available only in privately owned institutions. Since the data on the number of available service providers for infertility care was not available in the MoHP or other authorized source, the principal researcher conducted an intensive online search on Google and Facebook using the keyword "Nepal infertility center" followed by a search using "IVF Nepal" which ended up with 53 results. However, the search didn't include some of the infertility centers known to the researcher. Hence, the principal researcher added three more names to the results thus, the search resulted in 56 infertility centers in Nepal. However, the names of three infertility centers in Nepal were mentioned in "OVU Fertility" website but were not identified, the name of one infertility center was repeated, three infertility centers were based in Delhi, India and three other infertility centers were not identified by location, hence ten infertility centers were discarded. A total of 46 functional infertility centers were identified in Nepal. 27 out of 46 service providers are located inside the Kathmandu Valley.

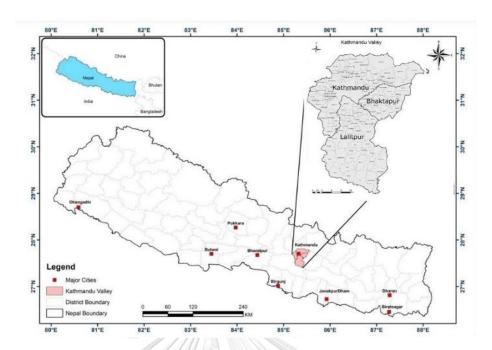


Figure 2 Map Indicating different districts and locations in Kathmandu Valley

The services offered by the providers are infertility diagnosis, infertility treatment, fertility preservation and donor treatment. Infertility treatment varies from pharmacotherapy with ovarian stimulation using oral medications or combined with intravenous gonadotropins, to expensive ART options. The diagnostic tests start from NRs. 10,000, infertility treatment ranges from NRs. 30,000 – 4,00,000, fertility preservation costs NRs. 25000 – 50000 and donor treatment cost ranges from NRs. 10,000 – 2,00,000 depending on the diagnosis. Hence, the overall cost for infertility treatment ranges between NRs. 75,000-700,000 which is approximately 570 – 5300 USD. With a Gross National Income (GNI) per capita of 1170 USD as per World Bank's data 2021, the infertility treatment cost is not affordable to the Nepali infertile patients seeking fertility treatment. Hence, financial burden is most important barrier for patients seeking infertility treatment. The author after five years of working experience in infertility center in Nepal has found that the couples consented for first IVF cycles despite financial constraints but had to stop treatment when they failed the cycle and had to repeat the treatment. Patients often turn to seek alternative measures for treatment which includes faith healing and ayurvedic medicine in hope for quick and successful outcome.

# CHAPTER III RESEARCH METHODOLOGY

# 3.1 Study Design

The study design was a cross-sectional study.

# 3.2 Study Area and Population

The study area was Kathmandu district, which is located in Kathmandu valley, situated in Bagmati Province of Nepal.

There are seven provinces in Nepal formed by the grouping of the existing districts. Every district has local government authorities which are classified under metropolitan, submetropolitan, urban municipality, and rural municipality or Village Development Committee (VDC). Each district is a composite of any or all the four authorities. Each local government authorities have its smallest unit for the management of public administrative functions which are known as "Wards".

Kathmandu valley comprises of three districts – Kathmandu, Bhaktapur and Lalitpur. Kathmandu district is the capital of Nepal. It covers an area of 49.45 sq.km and consists of 2,017,532 population as per census 2021. It has 11 local government authorities: one metropolitan and ten urban municipalities. Kathmandu Metropolitan is the main local government authority of the district and constitutes of 32 wards. The study area was situated in Ward No.1, Naxal, Kathmandu.

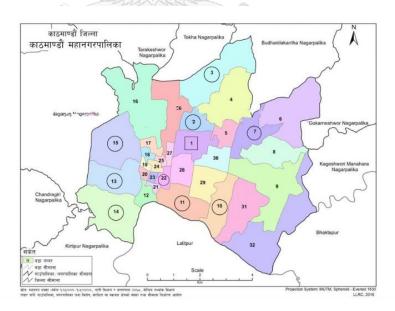


Figure 3 Map showing wards in Kathmandu Metropolitan

Note: Circles indicate the wards with infertility centers, Square indicate the ward with study site.

As Kathmandu is the capital and most developed urban center in Nepal, it attracts huge population for better facilities including healthcare. A total of 46 service providers for infertility care has been identified in Nepal out of which 27 are located inside Kathmandu valley. There are 22 infertility centers in Kathmandu district alone. The National Demographic Health Survey data of Nepal doesn't cover the infertile population; hence no data could be retrieved on the number of infertile couples in Nepal.

#### 3.3 Data Collection Period

The study period was 7<sup>th</sup> June to 15<sup>th</sup> June 2023.

#### 3.4 Sample Size

The sample size was calculated by using the Cochran's formula. As no previous studies on quality of life among infertile men and women using disease specific FertiQoL in Nepal was found, the proportion of infertile patients with poor quality of life was set as 50% in the equation.

$$n_0 = \frac{(za/2)^2 \times p \times (1-p)}{d^2}$$

$$n_0 = \frac{(1.96)^2 \times 0.5 \times (1-0.5)}{(0.05)^2}$$

$$n_0 = 384$$

A refusal of 25 patients was expected and hence, added to the calculated sample which resulted in 409 patients. Hence, the data was collected from 409 eligible atients. The patients were either individuals or couples.

#### 3.5 Sampling Method

The sampling technique was multistage convenience sampling. All the patients presenting at the clinic every day, therefore, were recruited till the required sample size necessary for inferential statistical testing was reached.

The data on infertile population and list of infertility centers was not available on the website of Ministry of Health and Population (MoHP) of Nepal or any other authentic sources. Hence, the principal researcher conducted an intensive online search on Google and Facebook using the keyword "Nepal infertility center" followed by a search using "IVF Nepal" which ended up with 53 results. However, the search didn't include some of the service providers but was known to the researcher. Hence, the principal researcher added three more names, thus identifying 56 infertility centers in Nepal. Among the 56 infertility centers, the names of three infertility centers in Nepal were mentioned in "OVU Fertility" website but were not identified, the name of one infertility center was repeated, three infertility centers were based in Delhi,

India and three other infertility centers were not identified by location, hence ten infertility centers were discarded. A total of 46 functional infertility centers were identified in Nepal. 27 out of 46 service providers are located inside the Kathmandu Valley. Multistage sampling technique was applied to obtain the representative sample of infertile couples in Kathmandu valley.

**First Stage** – Among the three districts inside Kathmandu valley- Kathmandu, Lalitpur and Bhaktapur, there are 22, five and null infertility centers respectively. Since Bhaktapur doesn't have any infertility centers, it was excluded from the study. Therefore, Kathmandu and Lalitpur district were selected by purposive sampling.

**Second Stage** – In Kathmandu district, there are 11 local government authorities – one metropolitan and ten urban municipalities. Kathmandu Metropolitan is the major local government authority of Kathmandu district. Additionally, 16 out of 22 infertility clinics are located inside Kathmandu Metropolitan. Hence, Kathmandu Metropolitan was selected purposively.

In Lalitpur district, there are six local government authorities- one metropolitan, two urban municipalities and three rural municipalities. Lalitpur Metropolitan is the major local government authority of Lalitpur district. Also, all the five identified infertility centers are located within Lalitpur Metropolitan; hence it was selected purposively.

**Third Stage** – A search was conducted on the website of "Nepal Society of Obstetrician and Gynecologists" to obtain the list of senior gynecologists involved in infertility care. Most of them were providing their services in private clinics rather than hospitals. So, infertility clinics were chosen over hospitals in Kathmandu and Lalitpur Metropolitan. Some infertility clinics were inside hospital premises but functioned as a separate unit from the hospital authority. Hence, choosing clinics would indicate better services and increased number of respondents.

In Kathmandu Metropolitan, two infertility hospitals, and 14 infertility clinics were identified. The six infertility hospitals were discarded and thus, the 14 infertility clinics were selected purposively. Among the five identified infertility centers in Lalitpur Metropolitan, three of them were private clinics and two of them were run by hospital. The hospitals were discarded and thus the three clinics were selected purposively.

**Fourth Stage** – The researcher searched whether more than one service providers (gynecologist) were available in one clinic, so that maximum number of respondents can be collected.

In Kathmandu district, one infertility center was identified where four gynecologists are providing IVF services in a single clinic. The name of the clinic is Vatsalya Natural IVF located in Ward No. 1, Naxal, Kathmandu. Additionally, the clinical records showed a huge number of patients visiting the clinic for infertility treatment. Hence, the clinic was selected purposively for the study.

However, there were only three infertility centers in Lalitpur and none of them had more than one gynecologist providing their service in one center. Since this would lead to insufficient respondents for our data collection, the clinics in Lalitpur district were discarded.

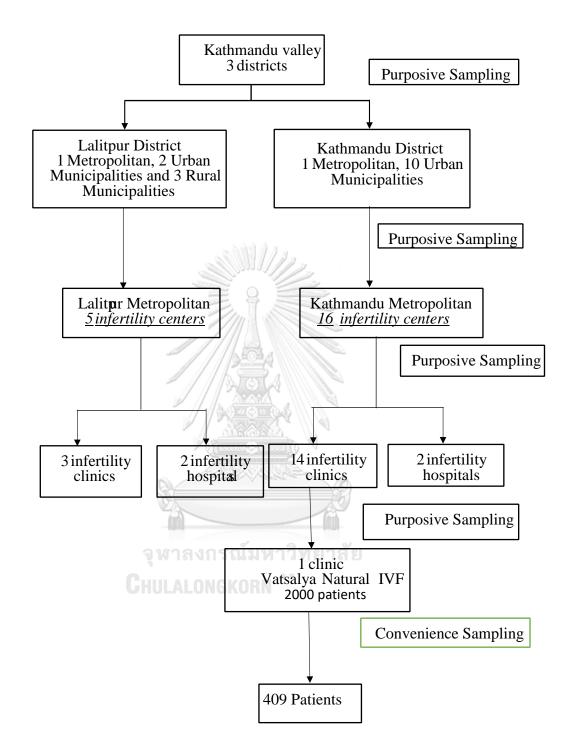


Figure 4 Sampling Flowchart

**Fifth Stage** – After interviewing the clinical director of the clinic, the principal researcher was informed that, at present, there were 2000 patients visiting the selected infertility center located in Kathmandu district. To meet the sample size of our study, 409 patients were selected conveniently from the selected clinic.

Having the full list of patients available, the principal researcher could have selected the patients by random sampling, and it would also have been beneficial in generalizing the outcome. However, due to the time constraint for the data collection, the researcher chose not to use random sampling and instead go for convenience sampling.

#### 3.6 Inclusion and Exclusion Criteria

- 3.6.1 Inclusion Criteria for Participants
- 1. Patients who were willing to participate in the study and gave written consent to participate.
- 2. Patients who were unable to conceive after at least a year of timed unprotected sexual intercourse. (Karabulut et al., 2013)
- 3. Patients who had been diagnosed for infertility.
- 4. Patients who could read/ write the questionnaire.

# 3.6.2 Exclusion Criteria for Participants

- 1. Patients who had a history of cancer treatment. (Karabulut et al., 2013)
- 2. Patients who were taking psychiatric medications/therapy or medications that may interfere with sex life. (J.-Y. Wang et al., 2022)
- 3. Patients who had experienced major life events like death of close relatives or a biological child during past twelve months prior to the interview. (Mao et al., 2022)
- 4. Patients with any form of disability. (Mao et al., 2022)

The patients with the above mentioned exclusion criteria were exluded from the study because from the literature review, we found that these conditions have effect on the quality of life. (Karabulut et al., 2013) (Mao et al., 2022) (J.-Y. Wang et al., 2022)

The participants were screened for inclusion and exclusion criteria by one nurse, trained as a research assistant, who was experienced in data collection and was working in the same clinic. She screened the respondents for duration of infertility, diagnosed cause of infertility and history of cancer treatment and intake of psychiatric medications through the medical records.

Additionally, the nurse orally screened the participants for assessing whether they had experienced major life events like death of close relatives or a biological child during the past twelve months prior to the interview. The nurse also screened for the presence of any form of disability and the ability to read/ write the questionnaire.

If the participants didn't meet the eligibility criteria from medical records and oral screening, the nurse expressed gratitude to the participant for their time and excluded them from the study.

#### 3.7 Measurement tools

The data was collected by using two questionnaires; one of them is developed by the researcher and remaining one is FertiQoL questionnaire developed by experts. The questionnaire developed by the researcher consisted of two sets; one set of questionnaires was reported by the principal investigator and the other set of questionnaires were self-reported by the respondent. The FertiQoL questionnaire was given to the respondents for self-report.

# A. Questionnaire developed by researcher

The questionnaire developed by the researcher is divided into two parts; "Self-reported questionnaire by the respondent" (Annex 2) and "Questionnaire filled by the investigator". (Annex 3) There are 16 questions in the self-reported questionnaire (Part 1) and 16 questions in the questionnaire filled by investigator (Part 2). A total of 32 structured questions on sociodemographic, socioeconomic, couple related, fertility related, and medical characteristics of the respondent were used in the study. The adaptation of questionnaire on the characteristics were done by considering the results of former studies which used quantitative methods to assess QoL among infertile patients. (Karabulut et al., 2013) (Dong & Zhou, 2016) Item-objective congruence (IOC) index was also considered. The questionnaires are given as in Annex 2 and Annex 3. The questionnaires in Nepali which were given out to the respondents does not contain any complex questions to ensure readability. The questionnaires were translated in Nepali and back translated in English by reproductive health experts. Details can be found below under the sub-heading "Back-translation".

The questionnaires consist of five main parts which consisted of 32 questions.

```
Part 1: Sociodemographic factors (6 questions) – See Q. No. 1.1-1.6
```

Part 2 : Socioeconomic factors (6 questions) – See Q. No. 1.7 – 1.11, 1.14

Part 3: Couple-related factors (5 questions) – See Q. No. 1.13, 1.15, 2.1, 2.7, 2.15

Part 4: Fertility-related factors (7 questions) – See Q. No. 1.12, 2.2, 2.3, 2.5, 2.8, 2.11, 2.16

Part 5 : Medical History (8 Questions) – See Q. No. 1.16, 2.4, 2.6, 2.9, 2.10, 2.12, 2.13, 2.14

Question No. 1.1-1.16 as in Annex 2 were self-reported by the respondent and Question No. 2.1-2.16 as in Annex 3 were reported by the investigator.

Table 3 Summary of evaluation variables

	3 Summary of evaluation variables				
S.No.	Variables	Description	Variable Coding		
Part 1	[•				
Socio	demographic				
1	Sex (Q1.1)	The information was	0 = Female		
		collected under two groups.	1 = Male		
2	Age	The information was	1 =≤30		
	(Q1.2)	first collected with	2 = 31-35		
		open ended question	$3 = \ge 36$		
		and later grouped into three categories.			
3	Ethnicity (Q1.3)	The ethnicity of the	0 = Others		
	Lumienty (Q1.3)	respondent was	1 = Janajati/		
		collected under seven	Newar		
		groups and later	2 = Bahun/ Chhetri		
		categorized into three			
4	Education	groups. This information was	0 = Below High		
'	Education	collected under 6	School		
	(Q1.4)	groups and later	1 = Above High School		
		grouped as above			
		high school education			
		and below high school education.			
5	Residence	The information was	0 = Rural		
-	(0)	collected under two	1 = Urban		
	(Q1.5) awas	groups. หาวิทยาลั	E		
	CHULALO	ngkorn Univers	ITY		
6	Family type	The information was	0 = Nuclear		
	(Q 1.6)	collected under two	1 = Joint		
Dont 1	l Sagio agamemia	groups			
factor	2: Socio-economic s				
7	Occupation	The information was	0=Unemployed		
	(Q1.7)	collected under four	1= Laborer		
		groups and was later grouped later into	2=Service/Self-		
		three.	employed		
8	Working hours	The information was	$0 = \le 0 \text{ hours}$		
	(Q1.8)	collected with open-	1 = 1-8  hours		
	,	ended question and	$2 = \ge 9$ hours		

		was later grouped into three categories.	
9	Access to take day off from work (Q1.9)	The information was collected under 5-point Likert scale. It was categorized under three groups.	0 = Easy 1 = Neutral 2 = Hard
10	Income level (Q1.10)	The information was collected under four groups	0 = Less than 20,000 NRs 1 = 20,000 - 50,000 NRs 2 = 50,000 - 1,00,000 NRs. 3 = Above 1,00,000 NRs.
11	Presence of Health Insurance (Q1.11)	The information was collected under two groups.	0 = No 1 = Yes
12 Part 3 factor	Travel long distance for service (Q1.14)  3: Couple-related	The information was collected under two groups.	0 = No 1 = Yes
13	Cognition of need of children (Q1.13)	The information was collected under two groups.	0 = Not so Important IT 1 = Very Important
14	Partner's supportiveness during treatment (Q1.15)	The information was collected under 5-point Likert scale. It was categorized under three groups.	0 = Not Supportive 1 = Neither Supportive nor Non-Supportive 2 = Supportive
15	Approaching infertility center (Q2.1)*	The information was collected under two groups.	0 = Individually 1 = With Partner
16	Duration of partnership (Q2.7)*	The information was collected with open ended question and	$0 = \le 5 \text{ years}$ $1 = 6-9 \text{ years}$ $2 = \ge 10 \text{ years}$

		later grouped as such.	
17	Marital Status (Q2.15)*	The information was collected under two groups.	0 = First Marriage 1 = Second Marriage
Part facto	4: Fertility-related		
18	Presence of biological child (Q1.12) (Q2.5, Q2.16) *	The information was collected under two groups.	0 = No children 1 = One or more children
19	Type of Infertility (Q2.2) *	The information was collected under two groups.	1 = Primary Infertility 2 = Secondary Infertility
20	Cause of infertility (Q2.3) *	The information was collected under four groups and later categorized into three.	0 = Female 1 = Male 2 = Both and Unexplained
21	Duration of infertility (Q2.8) *	The information was collected with openended question and was later grouped	$0 = \le 3$ years 1 = 4-5 years $2 = \ge 6$ years
22	Type of current Infertility treatment (Q2.11) *	The information was collected under seven groups and then categorized under three groups.	0= Timed Intercourse 1= Assisted Reproduction (self) 2= Assisted Reproduction (donor)
	Part 5: Medical History		
23	Professional psychological support (Q1.16)	The information was collected under two groups.	0 = No 1 = Yes
24	History of conception (Q2.4)	The information was collected under two groups.	0 = No 1 = Yes
25	History of pregnancy loss (Q2.6) *	The information was collected under two groups.	0 = No 1 = Yes

26	History of ART treatment (Q2.9, Q2.10) *	The information was collected under two groups.	
27	Presence of	The information was	0 = No
	chronic	collected under two	1 = Yes
	illness	groups.	
	(Q2.12) *		
28	Intake of	The information was	$0 \qquad 0 = No$
	Medications	collected under two	1 = Yes
	(Q2.13) *	groups.	
29	History of	The information was	0 = No
	reproductive tract	collected under two	1 = Yes
	surgery (Q2.14) *	groups.	

<sup>\*</sup> Reported by the investigator

# B. FertiQoL Questionnaire

FertiQoL is a gold standard for assessing QoL among infertile patients which is developed by a team of experts from European Society of Human Reproduction and Embryology (ESHRE) and the American Society for Reproductive Mediscine in 2011. Fertility Quality of life (FertiQoL) is one of the sensitive, reliable, and valid measure of QoL among infertile patients which assesses the mind/body, relational, social, and emotional domains. (Boivin et al., 2011) Additionally, it measures the treatment tolerability and treatment environment as well. The questionnaire is in Annex 4. IOC index was considered. The questionnaire in Nepali which will be given out to the respondents does not contain any complex words to ensure readability. The questionnaire was translated in Nepali and back translated in English by reproductive health experts. Further details can be found below under the title "Back-translation".

FertiQoL yielded six subscale and three total scores with a range of 0 to 100. Two additional items (marked A and B on the FertiQoL questionnaire given in Annex 3) captured an overall evaluation of physical health and satisfaction with quality of life and are not used in FertiQoL scoring. The questionnaire consisted of 36 items.

It yielded six subscales which are as such:

- 1. Emotional Subscale 6 questions
- 2. Mind/ Body Subscale 6 questions
- 3. Relational Subscale 6 questions
- 4. Social Subscale 6 questions
- 5. Treatment Environment Subscale 6 questions
- 6. Treatment Tolerability Subscale 4 questions

The Core FertiQoL represented the average fertility quality of life across all domains. There are four subscales for Core FertiQoL – Emotional, Mind-Body, Relational and Social subscales.

The Treatment FertiQoL represents the average quality of life across treatment domains. There are two treatment subscales – Treatment Environment and Treatment Tolerability.

Table 4 Subscales of FertiQoL

S.No.	Subscale	Description	Question No.
			(refer to Annex 3)
1.	Emotional	"Impact of Negative emotions like	Q4, Q7, Q8, Q9,
		sadness, depression, jealousy, and	Q16, Q23
		resentment on QoL"	
1.	Mind/ Body	"Impact on physical health (eg.	Q1, Q2, Q3, Q12,
		Fatigue, pain), Cognition (eg.	Q18, Q24
		Concentration), Behavior (eg.	
		Disrupted daily activities, delayed life	
		plans)"	
3.	Relational	"Impact on marriage or partnership	Q6, Q11, Q15,
		(eg. Sexuality, communication,	Q19, Q20, Q21
		commitment)"	
4.	Social	"Impact on social interactions (eg.	Q5, Q10, Q13,
		Social inclusion, expectations, stigma,	Q14, Q17, Q22
	j.	support)"	
5.	Treatment	"Impact of accessibility and quality of	T2, T5, T7, T8, T9,
	Environment	treatment on QoL."	T10
6.	Treatment	"Extent to which fertility medical	T1, T3, T4, T6
	Tolerability	services impact on daily life"	
	8	<b>18</b>	

FertiQoL questionnaire consisted of 36 items which were scored according to five response categories. The response scale ranged from 0 to 4. Respondents were asked to rate the statements which reflected their current feelings and thoughts. Scores lower than mean value indicated poor quality of life. The categories and subscales are as such:

Table 5 Response Category of FertiQoL

Response	Scale	Scale		
Category				
Evaluation	0	-	Very Poor	
	1	-	Poor	
	2	-	Neither Poor nor Good	
	3	-	Good	
	4	-	Very Good	
Satisfaction	0		- Very Dissatisfied	
	1		- Dissatisfied	
	2		- Neither Dissatisfied nor Satisfied	
	3		- Satisfied	

	4	-	Very Satisfied	
-				
Frequency	0	-	Always	
	1	-	Very often	
	2	-	Quite Often	
	3	-	Seldom	
	4	-	Never	
Intensity	0	-	An extreme amount	
	1	-	very much	
	2	shirit da	moderate amount	
	3		a little	
	4		not at all	
	- inning			
Capacity	_0	////-	Completely	
	1//		a great deal	
	2		moderately	
	3///	A O A	not much	
	Ø4 // //	AIAIA	not at all	

Table 6 Subscale and total scales of FertiQoL

	Core FertiQ	oL	Treatment FertiQoL			
	Emotional Mind/Body		Relational	Social	Environment	Tolerabilit
		0.000.00	7010100000			у
Item	Q4R	Q1	Q6	Q5	T2R	T1
	Q7	Q2LALONG	Q11R	Q10 S T	T5R	T3
	Q8	Q3	Q15R	Q13	T7	T4
	Q9 Q16	Q12	Q19	Q14R	Т8	T6
	Q10 Q23	Q18	Q20	Q17	Т9	
	\\\ \( \) \(	Q24	Q21R	Q22	T10	

<sup>&</sup>quot;The item numbers are the questions in the FertiQoL questionnaire. The items marked as "Q" and "T" represent "Core" and "Treatment" FertiQoL. Items with R require reverse marking before summing."

The scoring was done in three steps.

- 1.The items marked with "R" required reverse marking before summing. The items were reversed first.
- 2. The raw scores were calculated by summing all the items which belonged to the subscale or total subscale. For the Total FertiQoL, core (24 items) and treatment (10 items) were added.

3. The scaled scores for the subscale and total scores were computed by multiplying the relevant raw score by 25/k. Here, k is the number of items in the subscale. The scales scores range is 0 to 100.

#### C. Back-translation

All the above-described questionnaires were translated in Nepali language and didn't contain complex questions to ensure readability among the respondents. The principal researcher proficient in reproductive health and English and Nepali language translated the English version of all the above-described sections of questionnaires in Nepali. The Nepali translation was back translated by another key person who is an undergraduate in Social Sciences and have three years of experience in conducting Reproductive Health programs. The back translator did not have access to any of the above-described parts of the original questionnaires in English.

The translator read all the back-translated sections of the questionnaires. However, the translator didn't correspond to translation of the word "fertility problem". The literal translation of fertility problem in Nepali language would indicate overall reproductive problem. Since there is no specific word for fertility problem and the questionnaire will be specifically distributed to infertile patients, both the translator and the back-translator agreed to use the term "infertility problem" instead of "fertility problem" wherever the terms were mentioned in the researcher developed questionnaire and FertiQoL questionnaire. Apart from that, there were minor words and phrases which the translator didn't correspond to the back translator. However, the translator and back-translator discussed on the translated questionnaires and concluded with necessary modifications.

The questionnaires thus translated were verified with another reproductive health expert, working as an embryologist in an infertility center for the past seven years. He was proficient in both Nepali and English language. The translator and the expert both had access to both the original English and back-translated Nepali questionnaires i.e. Questionnaire developed by researcher and FertiQoL questionnaire. No modifications were required for the questionnaire developed by researcher. However, for the FertiQoL questionnaire, both the English and backtranslated Nepali questionnaire were placed together and subjected for necessary corrections. The Core and Treatment Domains of FertiQoL questionnaire were intensely discussed with the expert. Both the translator and expert having access to the original FertiQoL searched for synonyms of specific words like "impaired" (Q1), "cope" (Q4), "support" (Q5), "resentment" (Q7), "grief" (Q8), isolated (Q10), affectionate (Q11), obligations (Q12) and "bothered" (Q18). Thus, the back-translated Nepali words were made simpler, and the sentences were refined to make it convenient and understandable for the patient. In the treatment domain, the words "Surgery and medical treatments" as used in "T8" and "T9" were translated as "medical services and treatment" because the use of word "surgery" translated in Nepali language sounded more intense and complicated. Thus, the final questionnaires were prepared.

In this way, the questionnaires developed by the researcher and the FertiQoL questionnaire were translated in Nepali language.

# 3.8 Validity and Reliability

#### 3.8.1 Construct validity

## A. Questionnaire developed by researcher

The important characteristics were drafted from relevant studies in literature review. (J. R. Chachamovich et al., 2010) (Karabulut et al., 2013) (Dong & Zhou, 2016)

The construct validity for the characteristics presented in conceptual framework (Figure 1) are explained as below:

# 1. Sociodemographic Characteristics

It included age, sex, ethnicity, education level, residence, and family type. The sociodemographic characteristics had construct validity because they are confounders in any kind of research, and they should be included in any kind of conceptual framework to control for the confounding.

#### 2. Socioeconomic Characteristics

It included occupation, income level, working conditions (work hours, access to time off from work), travel long distance for service and presence of Health Insurance. The first two characteristics occupation and income level had construct validity because they are confounders in any kind of research and should be included in conceptual framework to control for confounding. Similarly, working conditions and presence of health insurance had construct validity because the characteristics were derived from a literature review. (Maeda et al., 2022) (Karabulut et al., 2013) Hence, these variables were valid for measuring an association with quality of life (QoL).

# 3. Couple Characteristics

It included marital status, duration of marrigae, cognition of need of children, partner supportiveness in the treatment and approaching infertility center as couple. These variables were derived from systematic review paper and published articles. (J. R. Chachamovich et al., 2010; Fekkes et al., 2003) Hence, they were valid for measuring an association with QoL.

# 4. Fertility-related Characteristics

It included presence of biological children, type of infertility, cause of infertility, duration of infertility, duration of treatment, and type of current treatment. These variables were derived from published study. (Karabulut et al., 2013) Hence, they had construct validity to measure association with QoL.

## 5. Medical History

It included the following variables: desire for professional psychological suppor, history of conception, history of pregnancy loss, history of ART failure, presence of chronic illness, intake of medications, and history of reproductive tract. The variables were derived from

literature review which had found association between medical history and QoL. (J. R. Chachamovich et al., 2010; Karabulut et al., 2013)

Since we had the construct validity for all the variables inside conceptual framework, we automatically had the construct validity of the questionnaires because each section of the questionnaires in Annex 2 and Annex 3 corresponded to the sections of the conceptual framework.

- 1. Sociodemographic factors (8 questions) See Q. No. 1.1-1.6
- 2. Socioeconomic factors (6 questions) See Q. No. 1.7 1.11, 1.14
- 3. Couple-related factors (6 questions) See Q. No. 1.13, 1.15, 2.1, 2.7, 2.15
- 4. Fertility-related factors (8 question) See Q. No. 1.12, 1.15, 2.3, 2.4, 2.5, 2.6, 2.7, 2.9, 2.12, 2.17
- 5. Medical History (6 Questions) See Q. No. 1.16, 2.4, 2.6, 2.9, 2.10, 2.12, 2.13, 2.14

The questionnaires corresponded with the conceptual framework and operational definitions which were based on the literature review indicating association with QoL. Hence, the questionnaires had construct validity.

## B. FertiQoL questionnaire

The FertiQoL questionnaire is derived from an initiative of two largest reproductive medical societies namely European Society of Human Reproduction and Embryology (ESHRE) and the American Society of Reproductive Medicine (ASRM). Hence, FertiQoL is the first and internationally validated instrument to measure QoL among individuals experiencing infertility issues. It provides an integral means for QoL issues in clinical care and research endeavors. FertiQoL provides an adequate face and content validity in terms of number of items included (n=36), acceptable respondent's burden, clarity of instructions and balance in response options. (Boivin et al., 2011)

# CHULALONGKORN UNIVERSITY

#### 3.8.2 Content validity

Two questionnaires were used in the study. The questionnaires developed by the researcher was derived mainly from literature review. (J. R. Chachamovich et al., 2010) (Karabulut et al., 2013) (Dong & Zhou, 2016) The FertiQoL questionnaire is developed by a team of experts. (Boivin et al., 2011)

The content validity for the translated questionnaires were done by consultation with experts. The questionnaires were validated by three experts for content and construct validity to confirm whether the questionnaire measures what it has claimed in the conceptual framework and operational definitions. The individuals involved in the validation of the questionnaire were two experts with more than five years of experience in providing infertility services - Dr. Sanu Maiya Shrestha Pradhan (M.D., Senior Consultant Obstetrician/ Gynecologist, and IVF Specialist) and Mr. Dijan Vaidya (Clinical Embryologist, Master's in clinical Embryology) and one expert who is a researcher and lecturer with more than seven years of experience in teaching

- Mrs. Subhadra Pradhan (Senior Nurse & Lecturer, Nepalese Army Institute of Health Sciences). Index of item-objective congruence (IOC) was used by summing up the scores from the experts. In each item, the experts were asked to determine the content validity score:

Score = 1 (for clear measuring),

Score = -1 (for not measuring clearly) or

Score = 0 (degree to which it measures the content area is unclear)

IOC index less than 0.66 was received from experts with comments for the following questions; Q 2.10"Has the patient been under ART treatment before?", Q1.6 "How many members are there in your family?", "Does the patient have any history of pregnancy loss?" Q2.11 "What type of infertility treatment is the patient going through in this cycle?" Hence, they were subjected for revision.

The experts suggested that the term ART used in Q2.10 was vague and hence Q2.10 was divided into two questions; "Has the patient been under IUI treatment before?" and "Has the patient been under IVF treatment before?" Similarly, the experts commented that Q1.7 doesn't measure the parameter for family size. Hence, the question was changed to "What type of family are you living in?" And the choices were a. Nuclear family (with husband and children) b. Joint family (with husband and his family). The category for Q2.8 "Does the patient have any history of pregnancy loss?" was changed to a. No history b. Spontaneous Abortion and c. Induced Abortion. The experts suggested that spontaneous and missed abortion can be classified under the same category to avoid confusions during data collection. Similarly, the categorization of options for Q2.11 was also changed to avoid confusion and easy analysis of the data. The categorization was modified as a. Timed Intercourse (TI) b. IUI with Husband Sperm (IUI-H) c. IUI with donor sperm (IUI-D) d. IVF with husband sperm e. IVF with donor sperm f. ICSI with husband sperm g. ICSI with donor sperm h. Egg donation i. Embryo donation.

Following questions from received IOC index 0.66 and hence it was revised; Q1.12 "Monthly income of the couples", Q3 "Do you feel drained or worn out because of fertility problems?" and Q18 "Are you bothered by fatigue because of fertility problems?".

One of the experts advised to review the monthly income of the couples through guidelines in Central bureau of statistics Nepal. But the researcher found out that there is no standardized scale to assess the socioeconomic status of the Nepalese population. However, Kuppuswamy's scale was identified to be the commonly used tool to classify socioeconomic status in the Nepalese context. (Joshi & Acharya, 2019) Thus, taking reference from a recent study on socioeconomic determinants in Nepal which used the Kuppuswamy's scale (Sherchand et al., 2022), the income category was reclassified.

For Q3 and Q18 from FertiQoL questionnaire, since the questions seemed to be a repetition on "fatigue", two experts marked them as unclear. However, on discussion with the study advisor who is also an Editor-in-Chief for Journal of Health Research and an experienced freelance consultant, we concluded that the repetition of the questions may have been a strategy to psychologically test whether the respondents are attentively and correctly answering all the

questions in the questionnaire. Hence, we keep both the questions in our study questionnaire. Thus, IOC was carried out to ensure content validity.

Apart from the above-mentioned questions, all the other questions received an IOC index of 1 and hence, they didn't require any modifications.

# 3.8.3 Face validity

The face validity was checked as one of the objectives of the pilot testing. The details of pilot study are as follows.

# 3.8.4 Pilot Testing

The pilot testing was conducted by the principal researcher. The pilot study was done among 15 infertile patients visiting an infertility center in "Kathmandu Fertility Center", which is an infertility clinic located in Ward no. 3, Kathmandu Metropolitan. The selected pilot study site is similar in characteristics to the real study site. The patients in the pilot study represents the infertile patients from the clinical setting and infertility service in the center is provided by senior gynecologist.

The infertility center lies 4.5 km northwards to the selected clinic in Kathmandu. Thus, the site for pilot study is far from the selected study site which ensures avoidance of contamination with infertile patients participating in the real study.

The pilot testing was done among respondents who were present in the clinic for fertility treatment at the time of study and those who met the eligibility criteria for the study. The respondents were screened for eligibility with the help of nurse by checking their medical records. The medical records of the eligible participants were masked to ensure that the principal researcher doesn't know the name of the participant. The pilot testing was done among the eligible patients who gave consent to participate in the study. They were asked to participate in the survey while waiting for the ultrasound. Those who agreed to participate were included in the pilot testing and the purpose of study, process of face validation and researcher's inclusion criteria were explained to them. The questionnaires in Annex 2 and Annex 4 were given to the respondents for self-report. The respondents were requested to fill in all the answers so that there are no missing data. Meanwhile, the questionnaires in Annex 3 were reported by the investigator by assessing the medical records of the patient.

The details of administered questionnaires are same as in measurement tools described above.

The pilot testing of the questionnaires was conducted to make sure that the respondents understand the questionnaires well, to avoid misinterpretation of the questions and offensive, demotivation and ambiguous words. Through pilot testing, the questionnaires were pre-tested for usability and were ensured that its burden is least to the respondent. Moreover, the time to answer the questionnaires, and the clear flow of the questions were also checked with the respondents. Then, Cronbach's alpha was calculated for reliability.

# 3.8.5 Reliability

The researcher used two questionnaires - one is developed by the researcher and the other is FertiQoL. There were 32 questions in the questionnaire developed by researcher as in Annex 2 and Annex 3. None of the questions in the questionnaires required internal validity because one question represented one variable measuring one fact. The only questionnaire that required internal validity is FertiQoL. However, the FertiQoL questionnaire has already been subjected to reliability testing. A study has found that Cronbach reliability for the Core and Treatment FertiQoL (and subscales) were satisfactory and in the range of 0.72 and 0.92 respectively. (Boivin et al., 2011) On conducting the pilot study, the Cronbach's alpha calculated for reliability was 0.835. Hence, the questionnaire is a reliable tool for measurement of fertility quality of life.

## 3.9 Data Collection

The principal researcher submitted a formal letter in the selected study clinic asking for permission from the clinical administration to conduct the research. On receiving the consent from the selected clinic, the principal researcher went to the clinic for data collection.

The researcher recruited the nurses from the selected clinic as the research assistants. The nurses who had been working for more than a year in the clinic, had completed a Diploma course in Nursing and had experience in data collection and conducting research were recruited as the research assistants.

The researcher collected data from four individuals at a time. It required 15-20 minutes for everyone to fill the questionnaire, hence, the researcher got about 50 responses in a day. With six working days per week, the researcher completed the data collection within two weeks. The principal researcher was assisted by the nurse duly trained as research assistant.

# 3.9.1 Training the Research Assistant

The nurses who were already working in the infertility center were recruited as the research assistants. The qualifications and experience in data collection were checked before recruiting them for data collection. A training of three hours was enough to recruit the nurse as research assistants.

- 1. **Place of training**: Interview room of the infertility center.
- 2. **Duration of training**: 3 hours
- 3. Objective of the training

The training objective were as such:

3.1 Explain to the nurse regarding the process and objective of the study.

- 3.2 Training the nurse to screen the participants according to their eligibility criteria
- 3.3 Train to mask the medical records of the eligible participants.
- 3.4 Train regarding the consent form and the questionnaire.
- 3.5 Train the nurse on answering likely questions from participants in a standard way.
- 3.6 Train to receive written consent form from the participants.
- 3.7 Train to hand out the questionnaires to the consenting participants.
- 3.8 Train the nurse to check for any missing answers in the questionnaire once the respondent completes it.
- 3.9 Train the nurse to collect the questionnaire by expressing gratitude once the respondent completes the questionnaire.

# 4. Method of training

- 4.1 The training started with an oral presentation explaining the process and objective of the study.
- 4.2 Question and answer session was conducted with the research assistant.
- 4.3 A role play from two nurses was introduced: one as a research assistant and one as a participant.
- 4.4 The researcher observed the role play. After the role play, the principle researcher gave feedback with recommendations of improvement if necessary.

A list of patient's names was retrieved from the clinical database of both the clinics with the help of nurses in the respective clinics. The name list remained with the nurses, and they coded the names with specific numbers to ensure the process of masking of data from the principal researcher. An eligibility checklist as in Annex 5 was handed to the trained nurse.

The study was conducted while the patients waited for their consultation with the doctor. The nurse duly trained as research assistant screened for eligibility of the participants by orally asking and accessing the medical records. If the patients met all eligibility criteria, the nurse approached the participant and explained the process and purpose of the study. If the participant was willing to participate in the study, the nurse covered the name of the patient in the medical record file and wrote the number code from the name list to ensure the masking of data from the principal researcher. If the patients were not willing to participate, the nurse expressed gratitude to the patients for their time and excluded them from the study. Eligible patients (in a group of four) were requested to follow the nurse in a separate room where the patients would informed regarding the objectives of the study and confidentiality of the data. She explained to the patients regarding consent, freedom to participate, right to withdraw, confidentiality, access to the final report and no use of the data for other purposes. She requested the participant to sign on a written consent to participate in the study. If the participants didn't give written

consent to participate, the nurse expressed her gratitude towards the patient for their time and exclude them from the study. The participants who were willing to sign the consent form were provided with a coded questionnaire to fill up.

The consenting participants were explained that the informed consent form which included the participant's name, and the signature will be kept separately from the questionnaire and that their answers could not be traced back to them. Once the researcher received the written consent from the participants, the consent form was kept separately. Then the researcher coded the questionnaires based on the code number mentioned on the medical record file of the participant. Thus, the self-reported questionnaires were coded before handing them to the respondents.

The translated Nepali questionnaire which consisted of self-reported sections and investigator reported sections of the questionnaire were used for data collection. The self-reported questionnaire was provided directly to the respondents. While the patients filled the self-reported questionnaires, the investigator assessed the medical file and filled out clinical characteristics of the respondent. The questionnaire items were explained to the participants when necessary. In case of any doubts or comprehension difficulties about the questions or the responses, the investigator personally cleared all the confusions. It required 15-20 minutes to complete the questionnaires. After the respondents completed the questionnaire, the researcher asked the respondents to recheck the involuntarily missed answers. Finally, the completed questionnaires received from the patients were kept in a sealed envelope.

During treatment, while female patients require frequent visits to the clinic for oocyte monitoring throughout the menstrual cycle, male patients are obliged to visit only for diagnostics and sperm collection. Hence, if the female patient approached the fertility clinic with their partner and both consented to participate in the study, data was collected from both the patients individually and independently. Finally, the completed questionnaires from the dyad couple were kept in one sealed envelope.

The answers from the participants were kept confidential and coded to identify the data collection form. The data of the respondents were coded to ensure anonymity and concealment of allocation. At the end of the research, the encoded name list of patients was destroyed.

#### 3.10 Data Entry and Analysis

The data was entered in Epidata V3.1 and then transferred to Microsoft Excel. The data was cleaned and was transferred for analysis to Statistical Package of Social Sciences (SPSS software version 26.0) subjected to College of Public Health Sciences, Chulalongkorn University, Thailand. The answers were scored and grouped as mentioned in the description in measurement tool.

# **Descriptive Statistics**

Participants' characteristics (independent variables) were summarized using frequencies and percentages.

The descriptive statistics were conducted which are as summarized in the following table.

Table 7 Descriptive Statistics

Variables	Types of variables	Descriptive statistics
Sex of the respondent	Categorical (nominal)	Frequency, percentage
Age of the respondent	Categorical (discrete) <sup>1</sup>	Frequency, percentage
Ethnicity of the respondent	Categorical (nominal)	Frequency, percentage
Education level of the respondent	Categorical (ordinal)	Frequency, percentage
Residence of the respondent	Categorical (nominal)	Frequency, percentage
Family type of the respondent	Categorical (nominal)	Frequency, percentage
Occupation of the respondent	Categorical (nominal)	Frequency, percentage
Working hours of the respondent	Categorical (discrete) <sup>2</sup>	Frequency, percentage
Access to time off from work of the respondent	Categorical (nominal)	Frequency, percentage
Income level of the respondent	Categorical (ordinal)	Frequency, percentage
Presence of health insurance	Categorical (ordinal)	Frequency, percentage
Travel long distance for treatment	Categorical (ordinal)	Frequency, percentage
Cognition for need of children	Categorical (ordinal)	Frequency, percentage
Supportiveness of partner	Categorical (ordinal)	Frequency, percentage
Approach to infertility center	Categorical (ordinal)	Frequency, percentage
Duration of marriage	Categorical (ordinal) <sup>3</sup>	Frequency, percentage
Marital Status of the respondent	Categorical (ordinal)	Frequency, percentage
Presence of biological child	Categorical (ordinal)	Frequency, percentage
Type of infertility	Categorical (ordinal)	Frequency, percentage

Cause of Infertility	Categorical (ordinal)	Frequency, percentage
Duration of Infertility	Categorical (ordinal) <sup>4</sup>	Frequency, percentage
Type of Current infertility treatment	Categorical (ordinal)	Frequency, percentage
Desire for psychological support	Categorical (ordinal)	Frequency, percentage
History of conception	Categorical (ordinal)	Frequency, percentage
History of pregnancy loss	Categorical (ordinal)	Frequency, percentage
History of ART failure	Categorical (ordinal)	Frequency, percentage
Presence of Chronic Illness	Categorical (ordinal)	Frequency, percentage
Intake of Medications	Categorical (ordinal)	Frequency, percentage
History of Reproductive Tract Surgery	Categorical (ordinal)	Frequency, percentage

#### Note:

- 1 ≤31 years, 32-35 yrs, ≤36 years
- 2 ≤0 hours, 1-8hours, ≥9hours
- 3 ≤ 5 years, 6-9 years, ≥ 10 years
- 4 ≤3 years, 4-5 years, ≥6 years GHULALONGKORN UNIVERSITY

# **Inferential Statistics**

Based on the literature review, the researcher focused on the outcome in QoL score as a categorical variable and used multiple logistic regression.

In bivariate analysis, the association between independent variable and the dependent variable- quality of life were assessed using Chi-square test.

Independent variables with P<0.2 in bivariate analysis were included in a multivariate logistic regression model to determine which ones are associated with QoL. The multivariate model was fitted in hierarchical manner using the stepwise method. Variance inflation factors was used to assess multicollinearity and variables of VIF of >2.5 were excluded from the final model. Associations were expressed as beta-

coefficients (mean differences) with 95% confidence intervals. All the analysis was done by using SPSS V.28.

# 3.11 Ethical Approval from Chulalongkorn University ERB

The ethical approval to conduct this study was obtained from Chulalongkorn University Ethical Review Board, Bangkok, Thailand. Permission was received from the Administrative Committee of Vatsalya Natural IVF to conduct the research in the clinical setting. Furthermore, written consent was taken from the participants before enrolling them for the study. Those who didn't consent for the study were not included in the study. The data received from the participants were kept confidential.



# CHAPTER IV RESULTS

#### 4.1 Background information

The study aimed to describe the socio-demographic factors, socio-economic factors, couple-related factors, fertility-related factors, and medical history which may have association with quality of life of infertile patients visiting fertility clinic in Kathmandu, Nepal. The study was conducted in the selected infertility clinic situated at Naxal, Kathmandu. The sample size requested for statistical testing of the study hypothesis was 384. Following 25 refusals to participate, the researcher continued to recruit consenting eligible patients till the number of 385 was reached. To this number, 25 consenting patients were further recruited to make up for those who did not consent to participate. The total participants' data presented in the results is therefore 409. All patients who consented to participate, completed the questionnaire. The required sample size was achieved within nine days in June 2023. The data was entered daily in EpiData version 3.1, exported to Microsoft Excel, cleaned, and then analyzed using Statistical Package of Social Sciences (SPSS software version 26.0) subjected to College of Public Health Sciences, Chulalongkorn University, Thailand.

The patients were provided with a self-reported questionnaire whose item-objective congruence (IOC) score was greater than and equal to 0.66. The pilot testing was done among 15 infertile patients from an infertility center located at 4km distance from our original study site. The self-reported questionnaire and the data from medical records didn't require reliability test. Hence, after pilot study, the Cronbach's alpha coefficient was calculated for FertiQoL questionnaire which was 0.835. After the data collection, the mean scores were 67.8±16.1(22.9-98.9) for core FertiQoL, 67.7±13.2(27.5-97.5) for treatment FertiQoL and 67.7±13.2 (35.3-96.3) for total FertiQoL. The results are presented in two parts; descriptive statistics and inferential statistics.

# 4.2 Descriptive analysis

In descriptive analysis, the socio-demographic factor, age variable was described using mean, standard deviation, maximum and minimum values, frequency, percentage, and cumulative percentage. Similarly, socio-economic variables – working hours, couple related variables-duration of marriage and medical history variable - duration of infertility were also described using mean, standard deviation, maximum and minimum values, frequency, percentage, and cumulative percentage. Using the percentile value, these variables were then categorized into three groups and described using frequency, percentage, and cumulative percentage.

For categorical socio-demographic variables (sex, ethnicity, education, residence and family type), socioeconomic variables (employment status, ease of access from work, income level, travel long distance for service and presence of health insurance), couple-related variables (marital status, cognition of need of child, partner's supportiveness in treatment, approach to fertility center), fertility-related variables (presence of biological child, type of infertility, cause

of infertility, duration of infertility and type of current treatment) and medical variables (desire for psychological support, presence of chronic illness, history of medication intake, history of ART failure, history of conception, history of pregnancy loss and history of reproductive tract surgery) only frequency, percentage and cumulative percentage were used for descriptive data. Following the resulting descriptive data, the variables (except with dichotomous attributes) were categorized into three attributes except for monthly income.

For Quality-of-life assessment, the scores were first described in mean, standard deviation, maximum and minimum values. Then, using the mean value, the variables were categorized into two levels – good and poor FertiQoL, and described using frequency, percentage, and cumulative percentage.

#### 4.2.1 General Characteristics of Infertile Patients

# I. Socio-demographic factors

Table 8 shows all the socio-demographic factors.

The mean age of the respondents was  $33.1 \pm 5.0$  (21-47) years. Most of the respondents were females (68.9%) with a mean age of  $32.4 \pm 4.9$  (21-45) years while 31.1% were male with a mean age of  $34.8 \pm 4.9$  (24-47) years. The percentile range was used to group the age of the respondents into three groups. 53.5% respondents had education above high school. 47.7% respondents belonged to a higher ethnicity i.e. Brahmin and Chhetri while 44% belonged to the indigenous ethnic groups. 76.3% respondents belonged to urban area and 70.2% of the respondents lived in a joint family.

Table 8 Socio-demographic characteristics of infertile patients (n=409)

S.No.	Variables	Frequency	Percentage
		(n)	(%)
1.	Gender		
	Male	127	31.1%
	Female	282	68.9%
2.	Age		
	≤31 years	145	35.5
	32-35 years	141	34.5
	≥36 years	123	30.1
3.	Ethnicity		
	Brahmin/Chhetri	195	47.7%
	Janajati (Indigenous)	180	44%
	Others	34	8.3%
4.	Education		
	Above High School	219	53.5%
	Below High School	190	46.5%

5.	Residence		
	Rural	97	23.7%
	Urban	312	76.3%
6.	Type of family		
	Nuclear	122	29.8%
	Joint	287	70.2%

# II. Socio-economic factors

Table 9 presents the socio-economic factors. Majority of the respondents (55%) were service/self-employed while 36.9% were unemployed. Majority (43.8%) had an income between NRs. 20,000-50,000. The mean duration of daily work hours was  $5.4\pm4.3$  (0-12) hours. All the respondents were paying out-of-pocket for infertility treatment as only 25.7% had health insurance but didn't cover any fertility expenses. 58.7% respondents had travelled to Kathmandu only to receive fertility services. However, 32.3% respondents found it difficult to get access to day-off from work for coming to receive fertility treatment.

Table 9 Socio-economic characteristics of infertile patients (n=409)

S. No.	Variables	Frequency	Percentage
		(n)	(%)
1.	<b>Occupation</b>		
	Unemployed	151	36.9%
	Service/ Self-Oriented	225	55%
	Laborer	33	8.1%
2.	Monthly income		
	Less than NRS. 20,000	129	31.5%
	Between NRs. 20,000 –	179	43.8%
	50,0000 3 175011117711		
	Between NRs. 50,000 –	60	14.7%
	1,00,000	/ERSITY	
	Above NRs. 1,00,000	41	10%
3.	Work hours		
	≤0 hours	150	36.7%
	1-8 hours	166	40.6%
	≥9 hours	93	22.7%
4.	Access to day-off		
	Easy	103	25.2%
	Neither Easy nor Difficult	174	42.5%
	Difficult	132	32.3%
5.	Presence of Health Insurance		
	No	304	74.3%
	Yes	105	25.7%
6.	Travel for service		
	No	169	41.3%
	Yes	240	58.7%

# III. Couple-characteristics

Table 10 shows couple-related characteristics. Majority 92.2% respondents didn't have any children, 98.5% responded that the cognition of children was very important to them and 98.3% responded that they have supportive partners. The mean duration of marriage was  $7.8 \pm 4.1$  (1-20) years. Almost all the participants 57.9% of the patients approached to the fertility center as couples while the remaining came for service as individuals.

*Table 10 Couple-related characteristics of infertile patients* (n=409)

S.No.	Variables	Frequency	Percentage
		(n)	(%)
1.	Marital Status		
	First Marriage	403	98.5%
	Second Marriage	6	1.5%
2.	Duration of marriage		
	≤5 years	142	34.7%
	6-9 years	132	32.3%
	≥10 years	135	33%
3.	Children Present		
	No	377	92.2%
	Yes	32	7.8%
4.	Perception of need of		
	children		
	Very Important	404	98.78%
	Not so Important	5	1.22%
5.	Partner's		
	Supportiveness		
	Not Supportive	NIVE 4SITY	0.97%
	Neither Supportive nor	3	0.73%
	non-supportive		
	Supportive	402	98.3%
6.	Approach to fertility		
	center		
	Couple	237	57.9%
	Individual	172	42.1%

# IV. Fertility-related characteristics

Table 11 shows fertility related characteristics. 58.9% of the patients were experiencing primary infertility and the female cause of infertility was prevalent at 48.7%. The mean duration of infertility was  $4.5 \pm 3.1(1-15)$  years. Majority of the respondents 46.9% were undergoing ART cycles using self-gametes (sperm and egg) while 19.1% were undergoing donor ART cycles (donor sperm, egg, or embryo).

*Table 11 Fertility-related characteristics of infertile patients* (n=409)

S.No	Variables	Frequency	Percentage (%)
1.	Type of Infertility		
	Primary	241	58.9%
	Secondary	168	41.1%
2.	Cause of Infertility		
	Female	199	48.7%
	Male	71	17.4%
	Both + unexplained	139	34.0%
3.	<b>Duration of infertility*</b>		
	≤3 years	205	50.1%
	4-5 years	94	23%
	≥6 years	110	26.9%
4.	Type of Infertility	>	
	treatment		
	Timed Intercourse	139	34%
	Assisted Reproduction (self)	192	46.9%
	Assisted Reproduction (donor)	78	19.1%

# V. Medical History

Table 12 shows the medical history variables. About a quarter of respondents (25.4%) had chronic conditions and 23% of them were taking medications. 64.5% respondents had a history of pregnancy loss while 52.8% had a history of ART failure. Only 11.5% respondents had a history of reproductive tract surgery. Majority of the respondents (80.7%) desired professional psychological support.

Table 12 Medical History related variables in infertile patients (n = 409)

S.No.	Variables	Frequency	Percentage (%)
1.	Presence of Chronic		
	Illness		
	No	305	74.6%
	Yes	104	25.4%
2.	<b>Intake of Medications</b>		
	No	315	77%
	Yes	94	23%
3.	History of conception		
	No	248	60.6%
	Yes	161	39.4%

4.	History of Pregnancy		
	Loss	145	35.5%
	Yes	264	64.5%
	No		
5.	History of Childbirth		
	No	367	89.7%
	Yes	42	10.3%
6.	History of ART		
	failure		
	No	216	52.8%
	Yes	193	47.2%
7.	History of		
	Reproductive Tract		
	Surgery		
	No .	362	88.5%
	Yes	47	11.5%
8.	Desire for		
	professional		
	psychological support		
	Yes	330	80.7%
	No	79	19.3%

# 4.2.2 Quality of Life in Infertile Patients

Table 13 shows the descriptive of FertiQoL domains and total FertiQoL scores. The mind/body domain had a mean score of  $60.5 \pm 23.3$  (0 – 100) which was the lowest score observed among all other domains. Similarly, the emotional domain had a mean score of  $62.4 \pm 20.5$  (8.3 - 100) which was the second lowest score observed. However, the relational domain had a mean score of  $82.7 \pm 12.7$  (50-100) which was the highest score among all other domains. The mean scores for total core FertiQoL and total treatment FertiQoL were  $67.8 \pm 16.1$  (22.9-98.9) and  $67.75 \pm 14.1$  (27.5-97.5) respectively. The sum of the means of six domains of FertiQoL (mind/body, emotional, relational, social, environment and tolerability) is 406.5 divided by 6 categories gives a total FertiQoL mean of  $67.7 \pm 13.2$  (35.2-96.3).

Table 13 Descriptive of FertiQoL domains and Total FertiQoL scores

S.No.	Domain	Mean	SD	Minimum	Maximum
1.	Emotional	62.4	20.5	8.3	100
2.	Mind/Body	60.5	23.3	0	100
3.	Relational	82.7	12.7	50	100
4.	Social	65.1	20.4	0	100
5.	Environment	69.4	15.0	29.1	100

6. Tolerability	65.1	21.4	6.2	100
7. Total Core	67.8	16.1	22.9	98.9
8. Total Treatment	67.7	14.1	27.5	97.5
<ol><li>Total FertiQoL</li></ol>	67.7	13.2	35.2	96.3

#### I. Emotional Domain

Table 14 shows the descriptive of Emotional Domain based on gender of the respondents. While 37.6% male and 31% female respondents felt that they can cope with fertility problems to a great extent, about 16% of both respondents felt that they are not able to cope up with the fertility problems. About 46% of both respondents seldom had the feeling of jealousy and resentment. While 43% females seldom had feelings of grief and loss, 37.8% of men never had feelings of grief and loss. About 40.1% females often had had the feelings of fluctuation between hope and despair while these feelings were comparatively lower at 34.4% among men. 47.9% females seldom fluctuated between hope and despair.

Majority 32.7% females felt sad and depressed at an extreme amount while only 16% men felt extremely sad and depressed. 30.3% females had very much to moderate levels of sadness and depression. About 36% men responded to being sad and depressed to very much and moderate levels. 19% females felt very much anger because of their fertility problems compared to 8.8% men. A total of 33.1% females felt anger in extreme and moderate levels while 66.4% men felt little to no anger at all.

จุฬาลงกรณ์มหาวิทยาลัย Chulalongkorn University

*Table 14 Descriptive of Emotional Domain based on Gender (n=409)* 

S.NO.	Core	Frequenc	y (Percenta	σe)				,			
0.110.	FertiQoL Statements	Completely					ely	Not Much		Not at All	
Emotio	onal Domain	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	
Q4R	Cope with	34	75	47	88	24	76	10 (8%)	28	10 (8%)	17 (6%)
	fertility	(27.2%)	(26.4%)	(37.6%)	(31%)	(19.2%)	(26.8%)		(9.9%)		
	problem										
		Always		Very Oft	en	Quite Of	ten	Seldom		Never	
Q7	Feeling of	5 (4%)	10	14	24	9	39	58	133	39	78
	jealousy and		(3.5%)	(11.2%)	(8.5%)	(7.2%)	(13.7%)	(46.4%)	(46.8%)	(31.2%)	(27.5%)
	resentment										
Q8	Feelings of	6	16	15	26	11	37	47	122	46	83
	grief and loss	(4.8%)	(5.6%)	(12%)	(9.2%)	(8.8%)	(13%)	(37.6%)	(43%)	(36.8%)	(29.2%)
Q9	Fluctuate	9	30	16	41	18	43	51	136	31	34
	between hope	(7.2%)	(10.6%)	(12.8%)	(14.4%)	(14.4%)	(15.1%)	(40.8%)	(47.9%)	(24.8%)	(12%)
	and despair										
		An Extre	eme	Very Mu	ch	A Moder	ate	A Little		Not At A	11
		Amount				Amount					
		Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Q16	Feelings of	20	93	26	56	19	30	40	87	20	18
-	being sad and	(16%)	(32.7%)	(20.8%)	(19.7%)	(15.2%)	(10.6%)	(32%)	(30.6%)	(16%)	(6.3%)
	depressed			·	, , , , , , , , , , , , , , , , , , ,				ĺ .		<u> </u>
Q23	Feeling of	9	40	11	54	22	34	42	102	41	54
-	Anger	(7.2%)	(14.1%)	(8.8%)	(19%)	(17.6%)	(12%)	(33.6%)	(35.9%)	(32.8%)	(19%)

#### II. Mind/ Body Domain

Table 15 shows the descriptive of Mind/ Body Domain based on gender in infertile patients. 42.9% of female respondents and 35.2% of male respondents had impaired attention due to infertility. Likewise, 54.4% male respondents and 48.2% female respondents didn't have any thoughts about not being able to move ahead to other life goals due to infertility problems. While 40.8% of females felt drained to a complete and greater extent, 47.2% male participants were not drained because of fertility issues. However, about 30% of both respondents felt drained and worn out moderately.

32.7% females and 36.8% males seldom felt that the infertility problems interfered with their day-to-day work. Conversely, about 43% of both respondents felt that the infertility problems didn't interfere with their day-to-day work at all. Fatigue was prevalent among 37.3% females while only 24% men felt extreme to moderate fatigue. 40.8% men didn't feel any fatigue at all due to infertility problems. Majority (75.2%) men didn't have any pain and discomfort following infertility treatment while 35.3% females experienced the feeling of pain and discomfort.

*Table 15 Descriptive of Mind/Body Domain based on Gender (n=409)* 

Mind	/ Body Domain	An Extres Amount	ne	Very Mu	ch	A Moderate A Little Amount		Not at Al	Not at All		
		Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Q1	Impaired attention and concentration	19 (15.2%)	39 (13.7%)	25 (20.0%)	83 (29.2%)	45 (36%)	102 (35.9%)	23 (18.4%)	43 (15.1%)	13 (10.4%)	17 (6%)
Q2	Not able to move ahead with life goals	8 (6.4%)	21 (7.4%)	23 (18.4%)	57 (20.1%)	26 (20.8%)	69 (24.3%)	26 (20.8%)	58 (20.4%)	42 (33.6%)	79 (27.8%)
Q3	Feeling drained and worn out	8 (6.4%)	29 (10.2%)	23 (18.4%)	87 (30.6%)	35 (28%)	83 (29.2%)	18 (14.4%)	35 (12.3%)	41 (32.8%)	50 (17.6%)
		Always		Very Often		Quite Often		Seldom		Never	
		Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Q12	Interferance with day-to-day work	5 (4%)	10 (3.5%)	8 (6.4%)	28 (9.9%)	12 (9.6%)	31 (10.9%)	46 (36.8%)	93 (32.7%)	54 (43.2%)	122 (43%)
		An Extres Amount	ne	Very Much		A Moder Amount	ate	A Little		Not At A	11
		Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Q18	Bothered by fatigue	14 (11.2%)	56 (19.7%)	16 (12.8%)	50 (17.6%)	20 (16%)	30 (10.6%)	24 (19.2%)	80 (28.2%)	51 (40.8%)	68 (23.9%)
Q24	Feelings of pain and physical discomfort	(8.8%)	30 (10.6%)	7 (5.6%)	38 (13.4%)	13 (10.4%)	32 (11.3%)	32 (25.6%)	90 (31.7%)	62 (49.6%)	94 (33.1%)

#### III. Relational Domain

Table 16 represents the descriptive of Relational Domain categorized under gender among infertile patients. Over 70% respondents were sexually satisfied with their partners even though they had fertility problems. However, 16.2% females and 14.4% men expressed dissatisfaction with sexual relationship with their partner. More than 85% respondents were always affectionate with their partner while less than 4% respondents were not affectionate with their partners. 78.4% males and 71.1% females had strengthened commitment with their partner following fertility problems. In 19.7% females and 15.2% males, infertility had moderately strengthened the commitment between the partners. Likewise, 72.8% males and 67.3% females felt that infertility didn't have any negative impact in their relationship. However, 23.9% females and 13.6% males responded that infertility had had a little negative impact in their relationships.

*Table 16 Descriptive of Relational Domain based on Gender* (n = 409)

Relati	Relational Domain		Very Dissatisfied Dissatisfied		issatisfied Neither Satisfied nor Dissatisfied		Satisfied		Very Satisfied		
		Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Q6	Satisfaction with	7	23	11	23	15	39	52	140	40	59
	sexual relationship	(5.6%)	(8.1%)	(8.8%)	(8.1%)	(12%)	(13.7%)	(41.6%)	(49.3%)	(32%)	(20.8%)
		Always		Very Oft	en	Quite Oft	en	Seldom		Never	
		Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Q11R	Affectionate	110	242	8	23	3 (2.4%)	11	0	2	4	6
	with partner	(88%)	(85.2%)	(6.4%)	(8.1%)		(3.9%)		(0.7%)	(3.2%)	(2.1%)
		An Extreme Very		Very Mu	Very Much A Moderate			A Little		Not at All	
		Amount		Amoi		Amount	unt				
		Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Q15R	Strengthening of	57	116	41	86	19	56	4	17 (6%)	4	9
	commitment to partner	(45.6%)	(40.8%)	(32.8%)	(30.3%)	(15.2%)	(19.7%)	(3.2%)		(3.2%)	(3.2%)
Q19	Negative impact	2	3	6	9	9 (7.2%)	13	17	68	91	191
	on relationship with partner	(1.6%)	(1.1%)	(4.8%)	(3.2%)		(4.6%)	(13.6%)	(23.9%)	(72.8%)	(67.3%)
Q20	Difficulty in	4	10	1	4	9 (7.2%)	15	12	36	99	219
	talking to partner	(3.2%)	(3.5%)	(0.8%)	(1.4%)		(5.3%)	(9.6%)	(12.7%)	(79.2%)	(77.1%)
Q21R	Contentment	71	156	33	65	10 (8%)	39	5 (4%)	12	6	12
	with relationship	(56.8%)	(54.9%)	(26.4%)	(22.9%)		(13.7%)		(4.2%)	(4.8%)	(4.2%)

#### IV. Social Domain

Table 17 represents the descriptive of social domain among infertile men and women. About 45% respondents were satisfied with the support they receive from their friends regarding their fertility problems. Nearly 70% of both respondents never felt socially isolated due to infertility issues. However, 20.8% males and 18% females seldom felt isolated. 45.6% males never felt uncomfortable attending any social events while 65.1% females felt uncomfortable to attend social events in extreme to moderation.

Majority 72.8% males and 64.1% females felt that their family could understand what they are going through while 23.9% females felt that the family seldom understands them, and less than 15% respondents felt that their families don't understand what they are going through. While 65.6% females felt inferior to people with children in extreme to moderate levels, 59.2% men felt inferior in extreme to moderate while 40.8% didn't felt inferior at all.

Among females, 46.2% felt extreme to moderate, 28.5% felt a little and 25.4% didn't feel any social pressure on them due to infertility issues. Likewise, 39.2% men felt extreme to moderate pressure, 29.6% felt little pressure and 31.2% felt no social pressure at all.

*Table 17 Descriptive of Social Domain based on Gender* (n=409)

Social Domain		Very Dissatisfied		Dissati	sfied	Neither nor Diss	Satisfied atisfied	Satisfic	ed	Very Sa	Very Satisfied	
		Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	
<b>Q</b> 5	Support from	8	20	18	31	42	115	43	95	14	23	
	friends	6.4%	7%	14.4%	10.9%	33.6%	40.5%	34.4%	33.5%	11.2%	8.1%	
	'	Always		Very O	ften	Quite O	ften	Seldon	1	Never		
		Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	
Q10	Social isolation	2.	14	5	12.	9	16	2.6	51	83	191	
		1.6%	4.9%	4%	4.2%	7.2%	5.6%	20.8%	18%	66.4%	67.3%	
Q13	Uncomfortable	3	22	11	29	11	30	43	104	57	99	
	attending social events	2.4%	7.7%	8.8%	10.2%	8.8%	10.6%	34.4%	36.6%	45.6%	34.9%	
Q14R	Understanding	36	71	28	58	27	53	17	68	17	34	
	by family	28.8%	25%	22.4%	20.4%	21.6%	18.7%	13.6%	23.9%	13.6%	12%	
		An Extr	eme	Very N	Iuch	A Mode	rate	A Littl	e	Not at A	.11	
		Amount	:			Amount						
		Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	
Q17	Feelings of	17	57	16	32	9	23	32	74	51	98	
	inferiority	13.6%	20.1%	12.8%	11.3%	7.2%	8.1%	25.6%	26.1%	40.8%	34.5%	
Q22	Social Pressure	17	46	15	55	17	30	37	81	39	72	
		13.6%	16.2%	12%	19.4%	13.6%	10.6%	29.6%	28.5%	31.2%	25.4%	

#### V. Treatment Environment

Table 18 shows the descriptive of Treatment Environment domain in infertile men and women. 93.3% women and 88.8% men responded that the fertility medical services that they want are available to them. Majority of respondents 89.6% men and 88% women found that the fertility staffs understood what they are going through. However, the incidence decreased to about 65% of both the respondents regarding satisfaction of quality of services available to them to address their emotional needs. 67% respondents were satisfied with the services that they were receiving. More than 70% respondents were satisfied with the quality of information they received. Nearly 80% respondents were satisfied with the interaction they had with the fertility staff regarding their fertility issues.

*Table 18 Descriptive of Treatment Environment based on Gender (n=409)* 

	Treatment Environment	Always	,	Very Of	en	Quite Of	ten	Seldom	,	Never	
		Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
T2	Availability of	33	64	40	102	38	99	11	16	3	3
	medical services	(26.4%)	(22.5%)	(32%)	(35.9%)	(30.4%)	(34.9%)	(8.8%)	(5.6%)	(2.4%)	(1.1%)
		An Extre	me	Very Mu	ich	A Moder	ate	A Little		Not At A	Ш
		Amount				Amount					
T5	Understanding by	33	68	36	104	43	78	9	25	4	9
	fertility staff	(26.4%)	(23.9%)	(28.8%)	(36.6%)	(34.4%)	(27.5%)	(7.2%)	(8.8%)	(3.2%)	(3.2%)
		Very Dis	,		Neither Satisfied nor Dissatisfied		Satisfied		Very Satisfied		
T7	Quality of	4	8	5	12	34	77	60	148	22	39
	treatment fulfill emotional need	(3.2%)	(2.8%)	(4%)	(4.2%)	(27.2%)	(27.1%)	(18%)	(52.1%)	(17.6%)	(13.7%)
T8	Rate the received	3	3	4	10	34	79	57	157	27	35
	treatment	(1.1%)	(1.1%)	(3.2%)	(3.5%)	(27.2%)	(27.8%)	(45.6%)	(55.3%)	(21.6%)	(12.3%)
T9	Received quality	2	4	4	11	30	62	61	166	28	41
	of information	(1.6%)	(1.4%)	(3.2%)	(3.9%)	(24%)	(21.8%)	(48.8%)	(58.5%)	(22.4%)	(14.4%)
T10	Interaction with	6	7	2	16	16	38	55	151	46	72
	medical staff	(4.8%)	(2.5%)	(1.6%)	(5.6%)	(12.8%)	(13.4%)	(44%)	(53.2%)	(36.8%)	(25.4%)

# VI. Treatment Tolerability Domain

Table 19 shows the descriptive of Treatment Tolerability Domain among infertile men and women. 40.1% females seldom had negative effect on their mood due to infertility treatment while 49.6% men never had any negative effect. 40.8% and 29.3% females thought that dealing with the procedures and administration of drugs during the treatment process was moderately and extremely complicated respectively. 45.6% men thought the same with the treatment in a moderate level. 57.4% females and 60% males were not bothered by the effect of treatment in their daily or work-related activities. While 48.6% female respondents were moderately bothered by physical side effects of fertility medications and treatments, 48% men were not bothered by physical side effects at all.

*Table 19 Descriptive of Treatment Tolerability based on Gender (n=409)* 

	Treatment Tolerability	Always		Very O	ften	Quite Of	sen Seldom			Never
		Male	Female	Male	Female	Male	Female	Male	Female	Male
T1	Negative effect on	2	14	1	28	6	29	54	114	62
	mood	(1.6%)	(4.9%)	(0.8%)	(9.9%)	(4.8%)	(10.2%)	(43.2%)	(40.1%)	(49.6%
		An Extreme		Very M	ery Much A Moder		rate A Little			Not A
		Amount				Amount		1		
T3	Complications with	13	26	12	57	57	116	10 (8%)	43	33
	treatment	(10.4%)	(9.2%)	(9.6%)	(20.1%)	(45.5%)	(40.8%)		(15.1%)	(26.4%
T4	Effect of treatment	13	23	15	47	22	51	39	85	36
	in daily life	(10.4%)	(8.1%)	(12%)	(16.5%)	(17.6%)	(18%)	(31.2%)	(29.9%)	(28.8%
T6	Bothered by	5 (4%)	28	9	34	27	60	24	78	60
	physical side effects	, ,	(9.9%)	(7.2%)	(12%)	(21.6%)	(21.1%)	(19.2%)	(27.5%)	(48%)
	of treatment									

# 4.2.3 Categorization of Total FertiQoL scores

The quality-of-life scores were categorized by taking the mean of the score as the cutoff point. The scores equal to and greater than the mean value was considered as good QoL, and the scores less than the mean value was taken as the poor QoL. 52.3% respondents had good QoL while 47.7% had poor QoL.

#### 4.3 Inferential Statistics

#### 4.3.1 Bivariate Analysis

Bivariate analysis was done using the Pearson's Chi-square between each independent categorical variable and the dependent variable.

# A. Sociodemographic variables with FertiQoL

Table 20 shows the socio-demographic characteristics and its association with FertiQoL among infertile patients. Females (52.1%) were found to have poor quality of life compared to males (37.8%) and the difference was significant at p-value 0.007.

Table 20 Socio-demographic characteristics and its association with poor FertiQoL (n=409)

S.	Variables	Poor	Good	Chi-	P-value
No.	-(0))			square	
1.	Gender				
	Male	48	79	7.210	0.007
		(37.8%)	(62.2%)		
	Female	147	135		
		(52.1%)	(47.9%)		
2.	Age				
	≤31 years	62	83	4.350	0.114
		(42.8%)	(57.2%)		
	32-35 years	77	64		
		(54.6%)	(45.4%)		
	≥36 years	56	67		
		(45.5%)	(54.5%)		
3.	Ethnicity				
	Others	21	13	4.771	0.092
		(61.8%)	(38.2%)		
	Janajati	77	103		
	-	(42.8%)	(57.2%)		
	Bahun/ Chhetri	97	98		
		(49.7%)	(50.3%)		

4.	Education					
	Below High	97	93	1.621	0.203	
	School	(51.1%)	(48.9%)			
	Above High	98	121			
	School	(44.7%)	(55.3%)			
5.	Residence	,	,			
	Urban	149	163	0.003	0.954	
		(47.8%)	(52.2%)			
	Rural	46	51			
		(47.4%)	(52.6%)			
6.	Family type	, ,	,			
	Nuclear	67	55	3.654	0.056	
		(54.9%)	(45.1%)			
	Joint	128	159			
		(44.6%)	(55.4%)			

#### B. Socioeconomic variables with FertiQoL

Table 21 describes the relationship between socio-economic characteristics and FertiQoL. There was significant association between working hours and FertiQoL at a significance of 0.008. Similarly, FertiQoL was found to be significantly associated with access to time off from work (p-value 0.011). 56.7% respondents who had to travel long distance for fertility treatment had poor quality of life compared to 39.4% who didn't have to travel more, and the difference was highly significant at a p-value <0.001.

#### **จหาลงกรณ์มหาวิทยาลัย**

Table 21 Socio-economic characteristics and its association with FertiQoL (n=409)

S.	Variables	Poor	Good	Chi-	P-value
No.				Square	
1.	Employment				
	Unemployed	79	72	2.255	0.324
		(52.3%)	(47.7%)		
	Laborer	16	17		
		(48.5%)	(51.5%)		
	Service/ Self-	100	125		
	employed	(44.4%)	(55.6%)		
2.	Income level				
	Below 20,000	70	59		
		(54.3%)	(45.7%)	5.693	0.128
	Between 20,000-	86	93		
	50,000	(48%)	(52%)		

-	Between 50,000	24	36		
	- 1,00,000	(40%)	(60%)		
	Above 1,00,000	15	26		
	A00ve 1,00,000	(36.6%)	(63.4%)		
		(30.070)	(03.470)		
3.	Work Hours				
	≤0 hours	79	71	9.565	0.008
		(52.7%)	(47.3%)		
	1-8 hours	64	102		
		(38.6%)	(61.4%)		
	≥9 hours	52	41		
		(55.9%)	(44.1%)		
4.	Access to day off				
	Easy	42	61	9.090	0.011
		(40.8%)	(59.2%)		
	Neutral	76	98		
	-	(43.7%)	(56.3%)		
	Hard	77	55		
		(58.3%)	(41.7%)		
5.	Presence of				
	Health Insurance				
	No	145	159	0.000	0.989
	V //	(47.7%)	(52.3%)		
	Yes	50	55		
		(47.6%)	(52.4%)		
_			6		
6.	Travel for		- 35		
	service				
	No	59	110	18.815	< 0.001
	<u>-</u> จุฬาลงก	(34.9%)	(65.1%)		
	Yes	136	104		
	<u>GHULALON</u>	(56.7%)	(43.3%)		

# C. Couple characteristics with FertiQoL

Table 22 describes the relationship between couple characteristics and FertiQoL. FertiQoL was found to be highly significant with duration of marriage (p-value <0.001). 48.3% respondents who thought that having a child is very important had a poor quality of life and the difference was significant at p-value 0.032.

Table 22 Couple characteristics and its association with FertiQoL (n=409)

	le characteristics and				
S. No.	Variables	Poor	Good	Chi-	P-
				square	value
1.	Marital Status				
	Second Marriage	2	4	0.502	0.479
		(33.3%)	(66.7%)		
	First Marriage	193	210		
		(47.9%)	(52.1%)		
2.	Duration of	400			
	marriage	11/12.			
	≤5 years	52	90	15.204	< 0.001
		(36.6%)	(63.4%)		
	6-9 years	62 (47%)	70 (53%)		
	≥10 years	81 (60%)	54 (40%)		
3.	Presence of				
	Biological Child				
	No //	180	197	0.009	0.925
	W // // // // // // // // // // // // //	(47.7%)	(52.3%)		
	Yes	15	17		
	571	(46.9%)	(53.1%)		
4.	Cognition of	HIGH TO HE TO THE			
	children				
	Very Important	195	209	4.612	0.032
		(48.3%)	(51.7%)		
	Not so important	0 (0%)	5 (100%)		
5.	Supportiveness of				
	partner				
	Not Supportive	4 (100%)	0 (0%)	4.894	0.087
	Neutral	2	1		
		(66.7%)	(33.3%)		
	Supportive	189	213		
		(47%)	(53%)		
6.	Approach to the				
	clinic				
	With partner	104	133	3.254	0.071
	-	(43.9%)	(56.1%)		
	Individually	91	81		
	-	(52.9%)	(47.1%)		

# D. Fertility-related characteristics with FertiQoL

Table 23 describes the fertility-related characteristics and its association with FertiQoL.

FertiQoL was highly significant with type of current treatment (p-value <0.001). Similarly, FertiQoL was significant with duration of infertility (p-value 0.010).

Table 23 Fertility-related characteristics and its association with FertiQoL (n=409)

S. No.	Variables	Poor	Good	Chi- square	P-value
1	. Type of		Ž.	•	
	infertility				
	Primary	120	121	1.052	0.305
	-//	(49.8%)	(50.2%)		
	Secondary	75	93		
		(44.6%)	(55.4%)		
2	. Cause of				
	infertility				
	Male	40	31	3.741	0.176
	58	(56.3%)	(43.7%)		
	Female	87	112		
		(43.7%)	(56.3%)		
	Both +	68	71		
	unexplained	(48.9%)	(51.1%)		
3	. Duration of	,			
	infertility				
	≤3 years	90	115	9.310	0.010
	GHULALON	(43.9%)	(56.1%)		
	4-5 years	39	55		
	, , , , , , , , , , , , , , , , , , ,	(41.5%)	(58.5%)		
	≥6 years	66(60%)	44 (40%)		
4	. Type of current		( )		
	treatment				
	Timed	48	91	14.754	< 0.001
	Intercourse	(34.5%)	(65.5%)		
	ART (self)	103	89		
	<b>,</b>	(53.6%)	(46.4%)		
	ART (donor)	44	34		
	( )	(56.4%)	(43.6%)		

# E. Medical history with FertiQoL

Table 24 describes the relationship between FertiQoL and medical history among infertile patients. 56.5% respondents who had a history of ART failure had poor FertiQoL compared to 39.8% patients who didn't have failure history and the difference was highly significant at <0.001. 63.8% patients with a history of reproductive tract surgery had a poor quality of life. The difference was statistically significant at p-value 0.018. Patients who desired for professional psychological support (51.8%) had highly significant poor quality of life at p-value <0.001.

Table 24 Medical History and its association with FertiQoL (n=409)

S.	Variables	Poor	Good	Correlation	P-value
No.	Monte			Coefficient	
1.	Presence of				
	chronic illness				
	No	152	153	2.241	0.134
	-////	(49.8%)	(50.2%)		
	Yes	43	61		
		(41.3%)	(58.7%)		
2.	Intake of				
	medications				
	No	157	158	2.573	0.109
		(49.8%)	(50.2%)		
	Yes	38	56		
	TT: 0	(40.4%)	(59.6%)		
3.	History of	<b>ณ์มหาวิ</b> า			
	pregnancy loss	121	122	1 120	0.200
	No CHULALONG	(40, 60())	(50.40())	1.128	0.288
	Vaa	(49.6%) 64	(50.4%) 81		
	Yes	0 <del>4</del> (44.1%)	-		
4.	History of	(44.170)	(55.9%)		
4.	conception				
	No	122	126	0.581	0.446
	INO	(49.2%)	(50.8%)	0.361	0.440
	Yes	73	88		
	103	(45.3%)	(54.7%)		
5.	History of	(43.370)	(34.770)		
٥.	Childbirth				
	No	175	192	0.000	0.994
	1.0	(47.7%)	(52.3%)	3.300	0.771
	Yes	20	22		
	_				
	108	(47.6%)	(52.4%)		

6.	History of ART				
	failure	86	130		
	No	(39.8%)	(60.2%)	11.343	< 0.001
		109	84		
	Yes	(56.5%)	(43.5%)		
7.	History of				
	Reproductive				
	Tract Surgery				
	No	165	197	5.554	0.018
		(45.6%)	(54.4%)		
	Yes	30	17		
		(63.8%)	(36.2%)		
8.	Desire for				
	psychological	11/13			
	support	100000			
	No	24	55	11.744	< 0.001
	-	(30.4%)	(69.6%)		
	Yes	171	159		
		(51.8%)	(48.2%)		

# 4.3.2 Multivariate Analysis

The multivariate analysis was undertaken to analyze the relationship between the independent variables and the dependent variable. As the dependent variable was total FertiQoL scores which was categorized into two levels; good and poor FertiQoL, binary logistic regression was used.

The independent variables which entered the binary logistic regression were those whose p-values were less than 0.2 in bivariate analysis and those whose p-values were greater than 0.2 in current study but significant in other studies.

The independent variables entered in the binary logistic model were as follows:

Table 25 List of independent variables which entered the binary logistic model

S.No.	Variables	p-value	p-value <0.2	Significant in
		< 0.05	but greater	other studies
			than 0.05	
A.	Socio-demographic			
1.	Sex	<b>~</b>		
2.	Age		<b>~</b>	
3.	Ethnicity		<b>✓</b>	

4.	Education		<b>✓</b>
5.	Family Type	<b>✓</b>	
	Socio-economic	•	
1.	Income Level		
2.	Occupation		<b>✓</b>
3.	Work hours	<b>✓</b>	
4.	Access to day-off	<b>✓</b>	
_	from work		
5.	Travel for service	<b>✓</b>	
<b>C</b> . (	Couple-related	10 11	
1.	Partner's	11/122	
	Supportiveness		
2.	Approach to fertility		
2	clinic		
3.	Duration of marriage	<b>Y</b>	
<b>D.</b> 1	Fertility-related		
1.	Cause of Infertility		
2.	Duration of Infertility		
3.	Type of Infertility		<b>~</b>
4.	Type of current		·
	treatment	33	
<b>1</b> 5.			
	Medical History		
1.	Presence of Chronic Illness	เหมามยาล	
2.	Intake of Medications	n University	
3.	History of ART failure	<b>✓</b>	
4.	History of	·	
	Reproductive Tract	▼	
	Surgery		
5.	Desire for	<b>✓</b>	
	psychological support		

i. For p-value<0.05 – sex, work hours, access to time off, migration for service, cognition of child, desire for psychological support, duration of marriage, duration of infertility, history of ART failure, history of reproductive tract surgery, type of current treatment.

- ii. For p-value <0.2, but greater than 0.05 age, ethnicity, family type, income, supportiveness of partner, approach for service, cause of infertility, presence of chronic illness, intake of medications.
- iii. Independent variables that were significant in other studies –Education, Occupation, Type of Infertility.

Table 26 shows the results of binary logistic regression of fertility quality of life at 95% confidence interval. In the table, only the results of variables of column 1 (p<0.05) in Table 25 are shown because all the variables of column 2 (p<0.2) and column 3 (from literature) were not significant. Among all the independent variables, sex, working hours, access to time off, duration of infertility and history of reproductive tract surgery were found to have significant association with poor QoL. And, travel long distance for service, desire for professional psychological support, duration of marriage, history of ART treatment and type of current infertility treatment were found to have highly significant association with poor QOL.

*Table 26 Binary logistic regression for poor FertiQoL* (n=409)

S.	Variables	<b>B</b> ///	Sig.	Adjust.	95% Co	ıfidence
No.				OR	Interval	
		110	EMODERAL A		Lower	Upper
1.	Sex	0.583	0.008	1.792	1.168	2.750
2.	Working hours					
	0 hours <sup>(R)</sup>	3	0.009			
	1-8 hours	0.573	0.012	1.773	1.133	2.775
	≥9 hours	-0.131	0.622	0.877	0.522	1.476
3.			น์มหาวิท			
	off Easy (R)		0.011			
	Neutral	-0.119	0.637	0.888	0.542	1.455
	Hard	-0.710	0.008	0.492	0.291	0.830
4.	Travel long	0.710	0.000	0.152	0.271	0.050
	distance <sup>(R)</sup>	-0.891	< 0.001	0.410	0.273	0.616
5.	Desire for	0.001	0.001	0.110	0.275	0.010
	psychological	-0.902	< 0.001	0.406	0.240	0.686
	support <sup>(R)</sup>	0.502	0.001	01100	0.2.0	0.000
6.	Duration of					
0.	marriage					
	≤5 years <sup>(R)</sup>		< 0.001			
	6-9 years	-0.427	0.083	0.652	0.402	1.057
	≥10 years	-0.954	< 0.001	0.385	0.237	0.626
7.	Duration of	0.50	0.001	0.202	3.23 /	0.020
, •	infertility					
	≤3 years <sup>(R)</sup>		0.010			

0.099	0.696	1.104	0.673	1.809	
-0.651	0.007	0.522	0.326	0.835	
of ART					
$t^{(R)}$ -0.674	< 0.001	0.510	0.344	0.756	
of					
ctive -0.745	0.020	0.475	0.253	0.891	
V					
t					
:se <sup>(R)</sup>	< 0.001				
lf) -0.786	< 0.001	0.456	0.291	0.715	
onor) -0.897	< 0.002	0.408	0.231	0.719	
	-0.651 of ART t <sup>(R)</sup> of of ctive rgery <sup>(R)</sup> y t t rse <sup>(R)</sup> lf) -0.786	-0.651 0.007 of ART t <sup>(R)</sup> -0.674 <0.001 of of of ctive rgery <sup>(R)</sup> y t  rse <sup>(R)</sup> <0.001 -0.786 <0.001	-0.651 0.007 0.522  of ART  t <sup>(R)</sup> -0.674 <0.001 0.510  of  ctive rgery <sup>(R)</sup> y  t  rse <sup>(R)</sup> <0.001  -0.786 <0.001 0.456	-0.651 0.007 0.522 0.326  of ART  t <sup>(R)</sup> -0.674 <0.001 0.510 0.344  of  ctive rgery <sup>(R)</sup> -0.745 0.020 0.475 0.253  y  t  rse <sup>(R)</sup> <0.001  lf) -0.786 <0.001 0.456 0.291	-0.651 0.007 0.522 0.326 0.835  of ART  t <sup>(R)</sup> -0.674 <0.001 0.510 0.344 0.756  of  ective -0.745 0.020 0.475 0.253 0.891  rgery <sup>(R)</sup> y  t  -0.786 <0.001 0.456 0.291 0.715

Note: Good FertiQoL is the reference. (R) = Reference group

As shown in table 27, the variables that maintained their significance for its association with poor FertiQoL are 1) gender of the patient, 2) access to time off from work 3) migration for service 4) duration of marriage, 5) type of current treatment, 6) Desire for professional psychological support, while the variables; working hours, duration of infertility, history of ART failure and history of Reproductive Tract Surgery lost their significance. There is no variable which is not significant in bivariate analysis and becomes significant in multivariate analysis. There is no variable which is not significant in bivariate analysis and from literature review (see table 25) that becomes significant in multivariate analysis.

*Table 27 Multiple logistic regression for poor Fertility Quality of Life (n=409)* 

S.	Variables	В	Sig.	Adjust.	95% Con	fidence
No.				OR	Interval	
					Lower	Upper
1.	Sex	-0.680	0.004	0.507	0.319	0.805
2.	Access to time off					
	Hard	0.674	0.004	1.962	1.244	3.093
3.	Travel for service	0.595	0.011	1.812	1.149	2.858
4.	Desire for psychological support <sup>(R)</sup>	0.794	0.006	2.213	1.259	3.889
5.	Current Infertility treatment					
	ART (Self)	0.540	0.030	1.716	1.055	2.791
	ART (Donor)	0.689	0.030	1.991	1.068	3.712

6.	Duration of marriage					
	≥10 years	0.521	0.032	1.684	1.046	2.713

Note: Good FertiQoL is the reference. (R) = Reference group

In detail, table 27 showed the results of multivariate logistic regression of fertility quality of life at 95% confidence interval. The significant observations were as such:

- 1. Females were 50% more likely to have poor quality of life compared to males. (AOR=0.50, 95% CI = 0.319-0.805, p-value 0.004)
- 2. Infertile patients who had hard access to time off from work were 1.9 times more likely to have poor quality of life compared to those who had easy access to time off from work. (AOR= 1.96, 95% CI = 1.24-3.09, p-value 0.004)
- 3. Infertile patients who had to travel long distance for service were 1.8 times more likely to have poor quality of life compared to those who didn't have to travel long distance. (AOR= 1.81, 95% CI = 1.15-2.86, p-value 0.011)
- 4. Infertile patients who desired professional psychological support were 2.2 times more likely to have poor quality of life compared to those who didn't desire for professional psychological support. (AOR= 2.21, 95% CI = 1.26-3.89, p-value 0.006)
- 5. Infertile patients who were undergoing ART using self-gametes (sperm, egg) were 1.7 times more likely to have poor quality of life compared to those who were undergoing Timed Intercourse. (AOR= 1.71, 95% CI = 1.05-2.8, p-value 0.030)
- 6. Infertile patients who were undergoing ART using donor gametes (sperm, egg, embryo) were 1.99 times more likely to have poor quality of life compared to those who were undergoing timed intercourse. (AOR= 1.99, 95% CI = 1.07-3.71, p-value 0.030)
- 7. Infertile patients who were married for more than 10 years were 1.6 times more likely to have poor quality of life. (AOR= 1.68, 95% CI = 1.04-2.71, p-value 0.032)

Table 28 Comparative table of association between independent and two levels of dependent variables in bivariate and multivariate analysis (n=409)

dependent variables in bivariate and Independent variables	Analytical results of two levels of dependent variable			
	Bivariate analysis	Multivariate analysis		
Age	Statistical association	-		
Sex	Statistical association	Statistical association		
Ethnicity	Statistical association	-		
Education	-	-		
Residence	11/1/11	-		
Family type	2000 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	-		
Migration for service	Statistical association	Statistical association		
Employment Status	7-3	-		
Working hours	Statistical association	-		
Access to take day off	Statistical association	Statistical association		
Income Level		-		
Presence of Health Insurance	14 (2) 24 (2) (3) (4) (4) (4) (4) (4) (4) (4) (4) (4) (4	-		
Marital History		-		
Duration of marriage	Statistical association	Statistical association		
Presence of Biological Child		-		
Perception of need of child	ณ์มหาวิทยาลัย	-		
Partner's supportiveness in treatment	KORN UNIVERSITY	-		
Approach to fertility center	-	-		
Type of Infertility	-	-		
Cause of Infertility	-	-		
Duration of infertility	-	-		
Type of current treatment	Statistical association	Statistical association		
Presence of Chronic Illness	-	-		
Intake of Medications	-	-		
History of ART failure	Statistical association	-		
History of pregnancy loss	-	-		

History of reproductive tract	Statistical association	-
surgery		
Desire for professional	Statistical association	Statistical association
psychological support		



# CHAPTER V DISCUSSION

The study was a cross-sectional descriptive study carried out among 409 infertile patients attending an infertility center in Kathmandu, Nepal. It aimed at describing the characteristics and fertility quality of life among infertile patients and to evaluate any association between these characteristics and fertility QoL among the infertile patients.

Twenty-five eligible participants refused to participate in the study. So, 25 consenting eligible patients were recruited to make up for those who did not consent to participate. Thus, data was collected from 409 consenting participants. Unlike in many studies, most of the eligible participants consented to participate in the study. This might be because the researcher approached the eligible respondents as the medical staff of the clinic to participate in the study. The researcher received a verbal consent and then requested for a written consent. The researcher requested the respondents to utilize their time by filling up the questionnaire while they wait to meet the doctor.

# A. General Characteristics of Infertile patients

The respondents were 68% females, and more than half of the respondents approached to the infertility center as couples while remaining 41.4% approached as individuals. Females had to visit the clinic frequently for monitoring the development of egg, hence most of the respondents who approached as individuals were females. Thus, the higher percentage of female respondents is justified. Also, majority of the male participants were reluctant to participate in the study and hence, they were excluded from the study as they didn't give their consent. In our study, females were more likely to have poor quality of life compared to men. (AOR=0.50, 95% CI = 0.319-0.805, p-value 0.004) The findings are relevant with the systematic study conducted by J. Chachamovich in 2009 which showed that women scored significantly lower in overall FertiQoL scores compared to men. (J. Chachamovich et al., 2009) Another study by Ragni et al. conducted among infertile couples in Italy in 2005 also supports our findings as it has demonstrated that women measured significantly lower in QoL scores. (Ragni et al., 2005) This can be explained as women experience major physical and emotional consequences of infertility as well as infertility treatment. Also, the stronger desire to have children among women further aids in diminishing the quality of life compared to men.

The mean age of respondents was  $33.1\pm5.0$  (21-47) years. The mean age for male was  $34.8\pm4.9$  (24-47) years and the mean age for female was  $32.4\pm4.9$  (21-45) years. The result from our study is comparable to a cross-sectional study conducted on infertile

patients in Nepal by Pradhan et al in 2013 which showed the mean age of the females to be 30 years. (Pradhan et al, 2013) A case control study with 180 infertile women in Iran had a mean age  $33.19 \pm 5.9$  among infertile women. (Bakhtiyar et al., 2019) Similarly, the result is also comparable to a case-controlled study by Valsangkar et al conducted with 106 infertile women in India in 2011 which resulted in mean age of 35 years. (Valsangkar et al., 2011) In Nepali society, the age of marriage is usually between 25-30 years. Many couples plan for a child few years after marriage and seek for fertility treatment, thus a mean age of 33 years is an ideal age for seeking fertility treatment among Nepali respondents. However, our study didn't find any significant difference between age and poor FertiQoL. The results contrast with a study conducted by Fekkes et al. in Netherlands among infertile men and women which found that QoL of young women were more affected compared to old. (Fekkes et al., 2003) Alternatively, a study by Karabulut among infertile women in Turkey found no difference in QoL scores among young and old age groups. (Karabulut et al., 2013) Another study conducted among 135 infertile women in Iran didn't find any significant association between age and FertiQoL.(Maroufizadeh et al., 2017) These findings suggest that although age is a major risk factor for infertility and has a declining effect on fertility, other factors might be more significant as a predictor for low QoL.

Three quarter of respondents in our study belonged to urban area. This might be because the study was conducted in urban area. In our study, the place was residence was not found to be significantly associated with fertility quality of life (FertiQoL). However, findings from a study conducted by Dong et. al in China among infertile couples in 2016 found that couples residing in rural areas had considerably lower FertiQoL scores than those from urban residents. (Dong & Zhou, 2016) However, he also mentions the difference of coping style, cognition of children, family monthly net income, employment status, educational level, and social support in the rural counterparts as the risk factors for predicting FertiQoL in rural infertile patients. This contrasting result in our study could be explained by the fact that the respondent's permanent area of residence was taken as the basis for categorizing the place of residence. Since some respondents belonged to rural area but had been staying in Kathmandu (urban area) since a long time for employment and education, the risk factors associated with the difference in FertiQoL in rural and urban counterparts might have been affected. To address this discrepancy, the researcher added one more variable to the study i.e., travel long distance for service.

#### B. Socio-economic characteristics among infertile patients

In our study, we found that around 37% of the respondents were unemployed yet were seeking expensive fertility treatment. This shows that in the cultural setting of Nepal, having children and giving continuity to one's generation is considered a social norm with very high positive value. Despite being unemployed, couples may feel immense pressure from family and society to have children. Additionally, individuals may feel a strong personal desire to become parents regardless of their employment status. This

cultural emphasis on procreation might have driven the respondents to seek for fertility treatments even while facing financial constraints. Also, individuals might have been willing to invest financially in the fertility treatment as these treatments offer higher chances of success, potentially overlooking their employment status as they prioritize starting a family. Additionally, the infertile patients might have received financial support from their family, relatives or by selling assets such as land and livestock (goats, cows, cattle, etc.) which might have enabled them to afford fertility treatments despite not having an income of their own. Only additional qualitative research could provide clearer, evidence-based understanding of the previously suggested explanations.

About 1/3<sup>rd</sup> of the respondents had a monthly income of less than NRs. 20,000. An increase in job demand and decrease in market might be the major reason for high unemployment. While 1/4<sup>th</sup> of the respondents in our study had health insurance, all the respondents were paying out-of-pocket for the fertility treatment. This is because the Nepal Health System doesn't cover the cost of fertility treatment. However, despite high unemployment and low income, people are seeking expensive treatment like Assisted Reproduction Technologies (ART) to fulfill the desire to have a child.

Our study found that those who had difficulty in accessing time off from work for fertility treatment had significantly poor QoL. (AOR= 1.96, 95% CI = 1.244-3.093, p-value 0.004) While there is limited research on predicting QoL based on access from work, our findings are comparable to a study conducted in 2022 among infertile patients in Japan which found that work related stress had an impact on FertiQoL. (Maeda et al., 2022) Fertility treatment requires frequent visits to service provider and often requires time off from work. While providing flexibility among patients with infertility issues could help improve job retention, such flexibility is not included in workplace policies in the context of Nepal. Hence, work related factors like reduced access to time off can have significant effect on QoL among infertile patients.

A predictor variable "travel long distance for service" was later addition after conducting the pilot study which was responded by the participant through self-report. Our study found that more than half of the respondents had travelled to Kathmandu to specifically receive fertility services. Since Kathmandu is the capital of the country and vast range of facilities and services including infertility treatment are available here, the patients might have travelled to Kathmandu in the hope to conceive a child. In our study, a significant association was found between travel long distance for service and FertiQoL. (AOR= 1.81, 95% CI = 1.149-2.858, p-value 0.011) A study conducted among 137 Chinese infertile women with recurrent implantation failure in 2019 showed that patients who had to travel long distances for fertility treatment exhibit poor fertility QoL compared to those who belonged to urban areas and didn't have to travel much. (Ni et al., 2021) Another study which was conducted among North American men in 2022 found that men who travelled long distances for fertility treatment have a lower QoL. (Chen et al., 2022) Hence, these studies support our findings on the effect of travel distance on FertiQoL. The need to travel far from home for frequent examinations and prolonged duration of treatment causes hardships among infertile patients specifically

with transportation and accommodation costs. The emotional and financial burden to travel for fertility treatment further leads to poor QoL.

# C. Couple characteristics among infertile patients

Almost all the respondents felt that having a child is very important for them. This is specifically due to the cultural norms in the Nepali society where a couple is expected to provide a child to the family within few years of marriage. Since almost all the respondents had the same answer to this predictor, the association of cognition of need of child couldn't be determined with FertiQoL in our study.

Our study showed that patients who were married for more than 10 years significantly had poor quality of life. (AOR= 1.68, 95% CI = 1.046-2.713, p-value 0.032) A study by above mentioned Karabulut found that prolonged duration of infertility had negative impact on total QoL scores. (Karabulut et al., 2013) Also, study by above mentioned Ragni et al. found that increased duration of infertility was associated with lower QoL scores. (Ragni et al., 2005) To the contrary, a case-control study conducted among 58 Turkish women found that QoL was higher among infertile couples who were married for more than five years. (Onat & Kizilkaya Beji, 2012) Our findings could be explained by the inability to jointly cope up with the crisis of infertility. With increase in duration of marriage and the inability to have a child, the couples may be reluctant to talk about their fertility problems and discuss about their future together which negatively impacts the QoL. Additionally, in the context of Nepal, increased duration of marriage without a child is considered as a failed marriage which further builds stress among the infertile couples, thus leading to poor QoL.

# D. Fertility-related characteristics among infertile patients

Additionally, our study didn't observe any significant associations between poor FertiQoL and duration of infertility. The result contrasts with the study by above mentioned Ragni et al. who found that duration of infertility affected QoL. (Ragni et al., 2005) However, a study conducted by Lau et al. among infertile couples in China found no significant difference between FertiQoL and duration of infertility. (Lau et al., 2008) This might be because the patients experiencing infertility might have adapted and developed coping mechanisms over time to deal with the challenges associated to infertility. The adaptation and coping process among the patients might have attenuated the impact of duration of infertility on FertiQoL. It is also possible that majority of the respondents in our study didn't have a longer duration of infertility to have a significant association with QoL.

However, our study found that infertile patients undergoing ART using self-gametes had significantly poor quality of life. (AOR= 1.71, 95% CI = 1.055-2.791, p-value 0.030) Also, significantly poor QoL was observed among patients undergoing ART using donor gametes. (AOR= 1.99, 95% CI = 1.068-3.712, p-value 0.030) A study

conducted among 1062 infertile Chinese women in 2019 found that women undergoing ART treatment had poor quality of life. (Song et al., 2021) Another study conducted among 432 infertile women in China concluded that IVF treatment cycles had negative impact on FertiQoL and the risk of anxiety and depression gradually increased. (Ni et al., 2023) A study by Imrie et al. among couples who underwent ART cycles with donor egg in UK fertility clinic found significantly poorer psychological health compared to those who underwent ART cycles using self-gametes. (Imrie et al., 2019) ART treatments can be emotional burden with additional physical and logistic demands including frequent visits to the clinic, multiple doses of hormonal injections and medical procedures which impacts on patients' well-being and overall QoL. Additionally, the financial burden and uncertainty of success associated with ART cycles further impacts FertiQoL negatively. Furthermore, patients undergoing donor ART cycles can be accompanied by social stigma and judgement which can contribute to feelings of shame and reduced QoL. Additionally, patients undergoing donor cycles need to face complex decisions regarding donor selection and the fear of disclosure. Such challenges further adds up emotional burden and impacts FertiQoL.

# E. Medical History among infertile patients

Our study couldn't find significant association between having a history of ART failure and poor QoL. However, a study by above mentioned J.R. Chachamovich et al. found lower scores in mental and psychological health among patients with a history of ART failure. (J. R. Chachamovich et al., 2007) Similarly, a longitudinal study by Agostini et al. in 2017 among 85 sub-fertile men and women in Italy found that QoL domains were affected by the number of ART failures and women presented with lower scores compared to men. (Agostini et al., 2017) To the contrary, the study by El-Messidi et al. conducted among infertile women in Spain didn't find any significant association between history of ART failure and QoL. (Heredia et al., 2013) The results might have varied between the studies due to the influence of other factors beyond the history of ART failure in determining the QoL among infertile patients. It is possible that other variables might have had a stronger impact on FertiQoL in our study population. Also, we included failure of both IUI (intrauterine insemination) and IVF/ICSI cycles under ART failure which might have resulted in its inability to find significant association with QoL. Although having a history of ART failure includes physical, emotional and financial burden, probably other predictors of fertility have major effect on QoL among infertile patients.

Our study demonstrated that those who desired for professional psychological support had poor quality of life. (AOR= 1.68, 95% CI = 1.046-2.713, p-value 0.032) The findings can be compared to a study conducted by above mentioned Karabulut which found that women desiring psychological support demonstrated lower QoL in all core domains. (Karabulut et al., 2013) Another study conducted among 536 infertile German men and women concluded that psychosocial counselling was an integral part in fertility treatment and it could help improve FertiQoL. (R. E. Sexty et al., 2018) It is justifiable that those who are facing major challenges with infertility have poor QoL

and desire for psychological support to cope up with the stress. Hence, psychological support is a crucial aspect in improving FertiQoL among infertile patients. Additionally, psychological support can minimize the treatment drop-out rates and minimize the stress related to infertility and its treatment.

#### F. FertiQoL Domains in infertile patients

The mean Core FertiQoL score was found to be  $66.9\pm17.3$  which is comparative to the study conducted in Nepal by Pradhan et al. among infertile women in 2013. (Pradhan et al., 2013) This might be explained probably due to similar methodology and similar setting. Also, the scores are comparative to a cross-cultural comparative study among infertile couples of Germany, Hungary and Jordan which found the mean QoL scores to be  $64.1\pm12.3$ . (R. Sexty et al., 2016) The study revealed only a few culturally based differences in FertiQoL between couples of the three countries. Another study by above mentioned Valsangkar et. al found a mean score of  $65.97\pm2.8$  which is comparable to our study. (Valsangkar et al., 2011) This might be due to the shared cultural similarities among Nepali and Indian individuals.

The mean score for mind/body domain in our study was  $60.5 \pm 23.3$  which is the lowest score obtained compared to other domains. Indeed, a study conducted among German infertile women found a mean score of  $75\pm17$  which is higher compared to our study. (Neumann et al., 2018) The difference can be explained as the study took place in a high-income country and thus, the socioeconomic conditions of the study population might have contrasted the results in our study. The study by above mentioned Valasangkar et al. found a relatively low mean score of  $42.1\pm4.3$ . (Valsangkar et al., 2011) The study involved participation of young females so they might have found it difficult to cope up with the physical and mental effects of fertility on QoL compared to older women. Thus, they might have experienced impaired attention and inability to move forward with other life goals. Also, our study included the participation of both men and women. A study by Hsu et al. by Taiwanese couples showed that men were more likely to cope up with fertility stress and had minimum physical effects in terms of infertility and infertility treatment, thus scored higher in terms of mind/body domain of FertiQoL compared to women. (Hsu, Lin et al. 2013)

The mean score for emotional domain was found to be  $62.4 \pm 20.5$  in our study which is comparatively higher than the results from above mentioned Pradhan et al. (Pradhan et al., 2013) with mean score of  $48.0 \pm 21.2$ . This can be explained by the participation of both male and female participants in our study while the study conducted by Pradhan et al was carried out only among infertile female patients. Since females experience more emotional challenges related to infertility and the concerns about self-identity, femininity and desire for biological motherhood, these factors can contribute to heightened emotional experiences in FertiQoL domain for females. This is supported by a study conducted in Iran by Keramat et al. which found that emotional domain was

significantly better in men compared to women as the respondents. (Keramat et al., 2014)

The mean score in relational domain was highest compared to the other domains at  $82.7\pm12.7$  which is comparable to the study by above mentioned Pradhan et al. at  $79.7\pm12.4$ . (Pradhan et al., 2013) It is possible that despite infertility issues, couples are happy and satisfied with their relationship. Conversely, it might also be possible that in a patriarchal setting of Nepali society, patients are not willing to share negative aspects about their relationship even though they might be facing hardships in their relationship due to fertility problems.



## **LIMITATIONS**

- 1. Due to the time constraints, a random selection of the respondents could not be carried out. Since a convenience sampling is conducted in the study, the outcomes couldn't be generalized to a larger population.
- 2. The data was collected from individuals as well as couples. However, the couple data are treated as individual data to meet the required sample size. The effect of responses couldn't be measured among the couples.
- 3. Due to the limitation in setting of the clinic, the couples couldn't be kept in separate spaces to complete the responses. Hence, there might be some influence of each other in the responses received in the final data.
- 4. The questionnaire consisted of 68 questions which is quite long. Thus, it might have exhausted the respondents and made them answer it without reading carefully.
- 5. The multiple choices and yes/no questions in the questionnaire might not have possibly determined the actual responses from the respondents.
- 6. Due to the sensitive nature of the questionnaire, despite measures to ensure privacy and comfort through utilization of female interviewers, some questions regarding marital life and sexual life may not have obtained accurate responses.

CHILLALONGKORN UNIVERSITY

#### **STRENGHTS**

- 1. The study includes both the infertile men and women. While majority of the studies only consider females in infertility studies, male responses are equally important while assessing quality of life in infertile patients as both the partners are equally involved throughout the infertility journey.
- 2. This is the first study on Fertility Quality of Life using a standard back translated FertiQoL questionnaire which finds significant association between characteristics of infertile patients and their QoL. It is a significant contribution to the knowledge on fertility quality of life among Nepali infertile patients.
- 3. As it is the first study, it provides a baseline data of infertile patients' quality of life in Nepal as well as provides points to consider in future research.
- 4. The study provides suggestions for specific needs for assessing quality of life among infertile patients including focus on psychological needs of infertile patients.

# RECOMMENDATIONS FOR FUTURE RESEARCH

- 1. Dyad studies on couples should be conducted to observe the proper findings on fertility quality of life and its effect.
- 2. Qualitative research should be conducted on infertile patients to explore further regarding the effect of infertility in their quality of life.
- 3. Qualitative research to understand the unexpected finding of relatively high number of unemployed respondents and the ability to pay for expensive fertility treatment service.
- 4. Further research on fertility quality of life in other districts and regions of Nepal are recommended.
- 5. A longer duration available for research can use a random sampling and hence, the results can be generalized to a population.

#### RECOMMENDATIONS FOR POLICIES

- 1. Patients undergoing infertility treatments might require additional emotional support and counseling to navigate the challenges they face. Proper counselling and emotional support services should be made available throughout the fertility treatment process to address the emotional impact of infertility.
- 2. Patient-centered care should be given emphasis as the foundation of fertility services. Patients should be involved in decision-making, and they should be provided comprehensive information.
- 3. Fertility services should be made accessible and affordable. Policies should be implemented to address financial barriers like insurance coverage for those who cannot afford fertility treatment but are desperately seeking for one.
- 4. Considerations should be made in drafting workplace policies with regard to people experiencing infertility and seeking treatment.
- 5. Quality assurance measures should be developed and enforced to maintain the standard of care. Assessment and monitoring for effectiveness, safety and outcomes of fertility services should be involved.
- 6. Fertility services should be decentralized and made available in other districts and regions of the country with ample manpower and resources.



# **CONCLUSIONS**

This is the very first study on the Fertility Quality of Life among infertile patients including male and females using a specific tool FertiQoL questionnaire in Nepal. This is an important study as it provides the baseline information on predictors of fertility quality of life in infertile patients including both men and women. This study highlighted a need of similar research on psychological support among the infertile patients to cope with the stress related to infertility and to minimize the increased treatment drop-out rates due to stress. It further focused on the development of standard policies to assess and monitor the patients for effectiveness, safety, and outcomes of fertility services. The findings of this study can summarize below.

- 1. Majority of female infertile patients had poor QoL.
- 2. Difficult access to time off from work lead to poor QoL among infertile patients.
- 3. The patients who have travelled long distance only to receive fertility services had a poor QoL.
- 4. Increased marital duration result in poor QoL.
- 5. Patients undergoing ART using self-gametes and donor gametes had poor QoL compared to those undergoing natural cycles.
- 6. Patients who desire for psychological support have poor QoL.



# **REFERENCES**



- Aaberg, R. A., Sauer, M. V., Sikka, S., & Rajfer, J. (1989). Effects of Extracellular Ionized Calcium, Diltiazem and Camp on Motility of Human Spermatozoa. *The Journal of Urology*, *141*(5), 1221–1224. https://doi.org/10.1016/S0022-5347(17)41225-0
- Aarts, J. W. M., van Empel, I. W. H., Boivin, J., Nelen, W. L., Kremer, J. A. M., & Verhaak, C. M. (2011). Relationship between quality of life and distress in infertility: A validation study of the Dutch FertiQoL. *Human Reproduction*, 26(5), 1112–1118. https://doi.org/10.1093/humrep/der051
- ABBEY, A., ANDREWS, F. M., & HALMAN, L. J. (1994). Psychosocial Predictors of Life Quality: How Are They Affected by Infertility, Gender, and Parenthood? *Journal of Family Issues*, 15(2), 253–271. https://doi.org/10.1177/0192513X94015002006
- Adhikari et al. Infertility, childlessness, and healthcare seeking.pdf. (n.d.). Retrieved 2 January 2023, from https://snis.ch/wp-content/uploads/2020/01/Working-paper\_WOREC.pdf
- Agarwal, A., Mulgund, A., Hamada, A., & Chyatte, M. R. (2015). A unique view on male infertility around the globe. *Reproductive Biology and Endocrinology*, 13(1), 1–9.
- Agostini, F., Monti, F., Andrei, F., Paterlini, M., Palomba, S., & La Sala, G. B. (2017). Assisted reproductive technology treatments and quality of life: A longitudinal study among subfertile women and men. *Journal of Assisted Reproduction and Genetics*, 34(10), 1307–1315. https://doi.org/10.1007/s10815-017-1000-9
- Ahmadi, H., Montaser-Kouhsari, L., Nowroozi, M. R., & Bazargan-Hejazi, S. (2011). Male Infertility and Depression: A Neglected Problem in the Middle East. *The Journal of Sexual Medicine*, 8(3), 824–830. https://doi.org/10.1111/j.1743-6109.2010.02155.x
- Akarsu, C., Caglar, G., Vicdan, K., Isik, A., & Tuncay, G. (2009). Pregnancies achieved by testicular sperm recovery in male hypogonadotrophic hypogonadism with persistent azoospermia.

  \*Reproductive BioMedicine Online, 18(4), 455–459. https://doi.org/10.1016/S1472-6483(10)60119-8
- Al Chami, A., & Saridogan, E. (2017). Endometrial Polyps and Subfertility. *Journal of Obstetrics and Gynaecology of India*, 67(1), 9–14. https://doi.org/10.1007/s13224-016-0929-4
- Albayrak, E., & Günay, O. (2007). State and trait anxiety levels of childless women in Kayseri, Turkey. The European Journal of Contraception & Reproductive Health Care: The Official Journal of the European Society of Contraception, 12(4), 385–390. https://doi.org/10.1080/13625180701475665
- Ambildhuke, K., Pajai, S., Chimegave, A., Mundhada, R., & Kabra, P. (2022). A Review of Tubal Factors Affecting Fertility and its Management. *Cureus*, *14*(11), e30990. https://doi.org/10.7759/cureus.30990
- Anderson, R., Willis, B., Oswald, C., & Zaneveld, L. (1983). Ethanol-induced male infertility: Impairment of spermatozoa. *Journal of Pharmacology and Experimental Therapeutics*, 225(2), 479–486.
- Andolz, P., Bielsa, M., & Vila, J. (1999). Evolution of semen quality in North-eastern Spain: A study in 22 759 infertile men over a 36 year period. *Human Reproduction*, 14(3), 731–735.
- Andrews, F. M., Abbey, A., & Halman, L. J. (1991). Stress from infertility, marriage factors, and subjective well-being of wives and husbands. *Journal of Health and Social Behavior*, 238–253.
- Araujo, A. B., O'Donnell, A. B., Brambilla, D. J., Simpson, W. B., Longcope, C., Matsumoto, A. M., & McKinlay, J. B. (2004). Prevalence and incidence of androgen deficiency in middleaged and older men: Estimates from the Massachusetts Male Aging Study. *The Journal of Clinical Endocrinology & Metabolism*, 89(12), 5920–5926.
- Auger, J., Kunstmann, J. M., Czyglik, F., & Jouannet, P. (1995). Decline in semen quality among fertile men in Paris during the past 20 years. *New England Journal of Medicine*, 332(5), 281–285.
- Augood, C., Duckitt, K., & Templeton, A. A. (1998). Smoking and female infertility: A systematic review and meta-analysis. *Human Reproduction (Oxford, England)*, *13*(6), 1532–1539.
- Baazeem, A., Belzile, E., Ciampi, A., Dohle, G., Jarvi, K., Salonia, A., Weidner, W., & Zini, A.
- (2011). Varicocele and Male Factor Infertility Treatment: A New Meta-analysis and Review of the Role of Varicocele Repair. *European Urology*, *60*(4), 796–808. https://doi.org/10.1016/j.eururo.2011.06.018

- Bakircioglu, M. E., Erden, H. F., Çiray, H. N., Bayazit, N., & Bahçeci, M. (2007). Gonadotrophin therapy in combination with ICSI in men with hypogonadotrophic hypogonadism. *Reproductive BioMedicine Online*, 15(2), 156–160. https://doi.org/10.1016/S1472-6483(10)60703-1
- Balabanič, D., Rupnik, M., & Klemenčič, A. K. (2011). Negative impact of endocrine-disrupting compounds on human reproductive health. *Reproduction, Fertility and Development*, 23(3), 403–416.
- Barzilai-Pesach, V., Sheiner, E. K., Sheiner, E., Potashnik, G., & Shoham-Vardi, I. (2006). The Effect of Women's Occupational Psychologic Stress on Outcome of Fertility Treatments. *Journal of Occupational and Environmental Medicine*, 48(1), 56–62.
- Bakhtiyar, K., Beiranvand, R., Ardalan, A., Changaee, F., Almasian, M., Badrizadeh, A., Bastami, F., & Ebrahimzadeh, F. (2019). An investigation of the effects of infertility on Women's quality of life: A case-control study. *BMC Women's Health*, *19*(1), 114. https://doi.org/10.1186/s12905-019-0805-3
- Benoff, S., Cooper, G. W., Hurley, I., Mandel, F. S., Rosenfeld, D. L., Scholl, G. M., Gilbert, B. R., & Hershlag, A. (1994). The effect of calcium ion channel blockers on sperm fertilization potential\*†\*Supported in part by an office based research grant from the American Foundation for Urologic Disease with funds contributed by Searle.†The Society for Assisted Reproductive Technology Prize Paper presented at the 49th Annual Meeting of The American Fertility Society, Montreal, Quebec, Canada, October 11 to 14, 1993. Fertility and Sterility, 62(3), 606–617. https://doi.org/10.1016/S0015-0282(16)56953-2
- Benyamini, Y., Gozlan, M., & Kokia, E. (2009). Women's and men's perceptions of infertility and their associations with psychological adjustment: A dyadic approach. *British Journal of Health Psychology*, 14(1), 1–16.
- Bergamo, P., Volpe, M. G., Lorenzetti, S., Mantovani, A., Notari, T., Cocca, E., Cerullo, S., Di Stasio, M., Cerino, P., & Montano, L. (2016). Human semen as an early, sensitive biomarker of highly polluted living environment in healthy men: A pilot biomonitoring study on trace elements in blood and semen and their relationship with sperm quality and RedOx status. *Reproductive Toxicology*, 66, 1–9. https://doi.org/10.1016/j.reprotox.2016.07.018
- Berger, R., Paul, M., & Henshaw, L. (2013). Women's Experience of Infertility: A Multi-systemic Perspective. *Journal of International Women's Studies*, *14*(1), 54–68.
- Berghuis, J. P., & Stanton, A. L. (2002). Adjustment to a dyadic stressor: A longitudinal study of coping and depressive symptoms in infertile couples over an insemination attempt. *Journal of Consulting and Clinical Psychology*, 70(2), 433.
- Berlim, M. T., McGirr, A., & Fleck, M. P. (2008). Can sociodemographic and clinical variables predict the quality of life of outpatients with major depression? *Psychiatry Research*, 160(3), 364–371.
- Blakemore, J. K., Maxwell, S. M., Hodes-Wertz, B., & Goldman, K. N. (2020). Access to infertility care in a low-resource setting: Bridging the gap through resident and fellow education in a New York City public hospital. *Journal of Assisted Reproduction and Genetics*, *37*(7), 1545–1552. https://doi.org/10.1007/s10815-020-01781-y
- Boivin, J., Bunting, L., Collins, J. A., & Nygren, K. G. (2007). International estimates of infertility prevalence and treatment-seeking: Potential need and demand for infertility medical care. *Human Reproduction*, 22(6), 1506–1512.
- Boivin, J., Takefman, J., & Braverman, A. (2011). The fertility quality of life (FertiQoL) tool: Development and general psychometric properties†. *Human Reproduction*, *26*(8), 2084–2091. https://doi.org/10.1093/humrep/der171
- Bojesen, A., Juul, S., & Gravholt, C. H. (2003). Prenatal and postnatal prevalence of Klinefelter syndrome: A national registry study. *The Journal of Clinical Endocrinology & Metabolism*, 88(2), 622–626.
- Bracken, M. B., Eskenazi, B., Sachse, K., McSharry, J.-E., Hellenbrand, K., & Leo-Summers, L. (1990). Association of cocaine use with sperm concentration, motility, and morphology. *Fertility and Sterility*, *53*(2), 315–322.

- Brezina, P. R., Yunus, F. N., & Zhao, Y. (2012). Effects of pharmaceutical medications on male fertility. *Journal of Reproduction & Infertility*, *13*(1), 3.
- Brydøy, M., Fosså, S. D., Klepp, O., Bremnes, R. M., Wist, E. A., Wentzel-Larsen, T., & Dahl, O. (2005). Paternity following treatment for testicular cancer. *Journal of the National Cancer Institute*, 97(21), 1580–1588.
- Brydøy, M., Fosså, S. D., Klepp, O., Bremnes, R. M., Wist, E. A., Wentzel-Larsen, T., & Dahl, O. (2010). Paternity and Testicular Function Among Testicular Cancer Survivors Treated With Two to Four Cycles of Cisplatin-Based Chemotherapy. *European Urology*, *58*(1), 134–141. https://doi.org/10.1016/j.eururo.2010.03.041
- Bussen, S., Sütterlin, M., Steck, T., & Dietl, J. (2004). Semen parameters in patients with unilateral testicular cancer compared to patients with other malignancies. *Archives of Gynecology and Obstetrics*, *269*, 196–198.
- Carlsen, E., Giwercman, A., Keiding, N., & Skakkebæk, N. E. (1992). Evidence for decreasing quality of semen during past 50 years. *British Medical Journal*, *305*(6854), 609–613.
- Chachamovich, J., Chachamovich, E., Fleck, M. P., Cordova, F. P., Knauth, D., & Passos, E. (2009). Congruence of quality of life among infertile men and women: Findings from a couple-based study. *Human Reproduction (Oxford, England)*, 24(9), 2151–2157. https://doi.org/10.1093/humrep/dep177
- Chachamovich, J. R., Chachamovich, E., Ezer, H., Fleck, M. P., Knauth, D., & Passos, E. P. (2010). Investigating quality of life and health-related quality of life in infertility: A systematic review. *Journal of Psychosomatic Obstetrics & Gynecology*, *31*(2), 101–110. https://doi.org/10.3109/0167482X.2010.481337
- Chachamovich, J. R., Chachamovich, E., Zachia, S., Knauth, D., & Passos, E. P. (2007). What variables predict generic and health-related quality of life in a sample of Brazilian women experiencing infertility? *Human Reproduction (Oxford, England)*, 22(7), 1946–1952. https://doi.org/10.1093/humrep/dem080
- Chan, Y. Y., Jayaprakasan, K., Zamora, J., Thornton, J. G., Raine-Fenning, N., & Coomarasamy, A. (2011). The prevalence of congenital uterine anomalies in unselected and high-risk populations: A systematic review. *Human Reproduction Update*, 17(6), 761–771. https://doi.org/10.1093/humupd/dmr028
- Chavarro, J. E., Rich-Edwards, J. W., Rosner, B. A., & Willett, W. C. (2007). Diet and lifestyle in the prevention of ovulatory disorder infertility. *Obstetrics & Gynecology*, *110*(5), 1050–1058.
- Che, M., Tamboli, P., Ro, J. Y., Park, D. S., Ro, J. S., Amato, R. J., & Ayala, A. G. (2002). Bilateral testicular germ cell tumors. *Cancer*, *95*(6), 1228–1233. https://doi.org/10.1002/cncr.10804
- Che, Y., & Cleland, J. (2002). Infertility in Shanghai: Prevalence, treatment seeking and impact. Journal of Obstetrics and Gynaecology: The Journal of the Institute of Obstetrics and Gynaecology, 22(6), 643–648. https://doi.org/10.1080/0144361021000020457
- Chen, L.-W., Wu, Y., Neelakantan, N., Chong, M. F.-F., Pan, A., & van Dam, R. M. (2014). Maternal caffeine intake during pregnancy is associated with risk of low birth weight: A systematic review and dose-response meta-analysis. *BMC Medicine*, *12*, 174. https://doi.org/10.1186/s12916-014-0174-6
- Chen, J., Jarvi, K., Lajkosz, K., Smith, J., Lau, S., Lo, K., Grober, E., & Samplaski, M. K. (2022). How far will they go? Distance and driving times that north American men travel to see a reproductive urologist. *Andrologia*, *54*(10), e14551. https://doi.org/10.1111/and.14551
- Chow, E. J., Stratton, K. L., Leisenring, W. M., Oeffinger, K. C., Sklar, C. A., Donaldson, S. S., Ginsberg, J. P., Kenney, L. B., Levine, J. M., Robison, L. L., Shnorhavorian, M., Stovall, M., Armstrong, G. T., & Green, D. M. (2016). Pregnancy after chemotherapy in male and female survivors of childhood cancer treated between 1970 and 1999: A report from the Childhood Cancer Survivor Study cohort. *The Lancet Oncology*, *17*(5), 567–576. https://doi.org/10.1016/S1470-2045(16)00086-3
- Collée, J., Mawet, M., Tebache, L., Nisolle, M., & Brichant, G. (2021). Polycystic ovarian syndrome and infertility: Overview and insights of the putative treatments. *Gynecological Endocrinology: The Official Journal of the International Society of*

- *Gynecological Endocrinology*, *37*(10), 869–874. https://doi.org/10.1080/09513590.2021.1958310
- Cooper, B. C., Gerber, J. R., McGettrick, A. L., & Johnson, J. V. (2007). Perceived infertilityrelated stress correlates with in vitro fertilization outcome. *Fertility and Sterility*, 88(3), 714–717.
- Counseller, V. S. (1938). Endometriosis: A clinical and surgical review. *American Journal of Obstetrics and Gynecology*, *36*(5), 877–888.
- Dabaja, A. A., & Schlegel, P. N. (2014). Medical treatment of male infertility. *Translational Andrology and Urology*, *3*(1), 9–16. https://doi.org/10.3978/j.issn.2223-4683.2014.01.06
- Dandona, P., & Dhindsa, S. (2011). Update: Hypogonadotropic hypogonadism in type 2 diabetes and obesity. *The Journal of Clinical Endocrinology & Metabolism*, 96(9), 2643–2651.
- Darby, E., & Anawalt, B. D. (2005). Male hypogonadism: An update on diagnosis and treatment. *Treatments in Endocrinology*, *4*, 293–309.
- Datta, J., Palmer, M., Tanton, C., Gibson, L., Jones, K., Macdowall, W., Glasier, A., Sonnenberg, P., Field, N., & Mercer, C. (2016). Prevalence of infertility and help seeking among 15 000 women and men. *Human Reproduction*, *31*(9), 2108–2118.
- de Boer, E. J., den Tonkelaar, I., te Velde, E. R., Burger, C. W., Klip, H., & van Leeuwen, F. E. (2002). A low number of retrieved oocytes at in vitro fertilization treatment is predictive of early menopause. *Fertility and Sterility*, 77(5), 978–985. https://doi.org/10.1016/S0015-0282(02)02972-2
- De Santis, M., Cesari, E., Nobili, E., Straface, G., Cavaliere, A. F., & Caruso, A. (2007). Radiation effects on development. *Birth Defects Research Part C: Embryo Today: Reviews*, *81*(3), 177–182. https://doi.org/10.1002/bdrc.20099
- Decanter, C., Morschhauser, F., Pigny, P., Lefebvre, C., Gallo, C., & Dewailly, D. (2010). Anti-Müllerian hormone follow-up in young women treated by chemotherapy for lymphoma: Preliminary results. *Reproductive BioMedicine Online*, *20*(2), 280–285. https://doi.org/10.1016/j.rbmo.2009.11.010
- Dennett, C. C., & Simon, J. (2015). The Role of Polycystic Ovary Syndrome in Reproductive and Metabolic Health: Overview and Approaches for Treatment. *Diabetes Spectrum : A Publication of the American Diabetes Association*, *28*(2), 116–120. https://doi.org/10.2337/diaspect.28.2.116
- Ding, R., Jin, Y., Liu, X., Zhu, Z., Zhang, Y., Wang, T., & Xu, Y. (2016). Characteristics of DNA methylation changes induced by traffic-related air pollution. *Mutation Research/Genetic Toxicology and Environmental Mutagenesis*, 796, 46–53. https://doi.org/10.1016/j.mrgentox.2015.12.002
- Dohle, G. R., Colpi, G. M., Hargreave, T. B., Papp, G. K., Jungwirth, A., Weidner, W., & EAU Working Group on Male Infertility. (2005). EAU guidelines on male infertility. *European Urology*, 48(5), 703–711. https://doi.org/10.1016/j.eururo.2005.06.002
- Domar, A., Gordon, K., Garcia-Velasco, J., La Marca, A., Barriere, P., & Beligotti, F. (2012). Understanding the perceptions of and emotional barriers to infertility treatment: A survey in four European countries. *Human Reproduction (Oxford, England)*, 27(4), 1073–1079. https://doi.org/10.1093/humrep/des016
- Domar, A., Vassena, R., Dixon, M., Costa, M., Vegni, E., Collura, B., Markert, M., Samuelsen, C., Guiglotto, J., Roitmann, E., & Boivin, J. (2021). Barriers and factors associated with significant delays to initial consultation and treatment for infertile patients and partners of infertile patients. *Reproductive BioMedicine Online*, *43*(6), 1126–1136. https://doi.org/10.1016/j.rbmo.2021.09.002
- Dong, Y., & Zhou, F. (2016). Comparison of fertility quality of life between urban and rural infertile couples. *Fertility and Sterility*, *106*(3), e118. https://doi.org/10.1016/j.fertnstert.2016.07.354
- Drobnis, E. Z., Nangia, A. K., Drobnis, E. Z., & Nangia, A. K. (2017). Male reproductive functions disrupted by pharmacological agents. *Impacts of Medications on Male Fertility*, 13–24.
- Drosdzol, A., & Skrzypulec, V. (2009). Evaluation of marital and sexual interactions of Polish infertile couples. *The Journal of Sexual Medicine*, 6(12), 3335–3346. https://doi.org/10.1111/j.1743-6109.2009.01355.x

- Dube, L., Bright, K., Hayden, K. A., & Gordon, J. L. (2023). Efficacy of psychological interventions for mental health and pregnancy rates among individuals with infertility: A systematic review and meta-analysis. *Human Reproduction Update*, *29*(1), 71–94. https://doi.org/10.1093/humupd/dmac034
- Duffy, C., & Allen, S. (2009). Medical and Psychosocial Aspects of Fertility After Cancer. *Cancer Journal (Sudbury, Mass.)*, 15(1), 27–33. https://doi.org/10.1097/PP0.0b013e3181976602
- Durairajanayagam, D. (2018). Lifestyle causes of male infertility. *Arab Journal of Urology*, *16*(1), 10–20. https://doi.org/10.1016/j.aju.2017.12.004
- Dyer, S., Lombard, C., & Van der Spuy, Z. (2009). Psychological distress among men suffering from couple infertility in South Africa: A quantitative assessment. *Human Reproduction* (Oxford, England), 24(11), 2821–2826. https://doi.org/10.1093/humrep/dep278
- Ectopic Pregnancy. (n.d.). Reproductive Science Center of New Jersey. Retrieved 24 January 2023, from https://fertilitynj.com/infertility/female-infertility/ectopic-pregnancy/
- Ehsani, M., Mohammadnia-Afrouzi, M., Mirzakhani, M., Esmaeilzadeh, S., & Shahbazi, M. (2019). Female Unexplained Infertility: A Disease with Imbalanced Adaptive Immunity. *Journal of Human Reproductive Sciences*, 12(4), 274–282. https://doi.org/10.4103/jhrs.JHRS\_30\_19
- El-Messidi, A., Al-Fozan, H., Lin Tan, S., Farag, R., & Tulandi, T. (2004). Effects of repeated treatment failure on the quality of life of couples with infertility. *Journal of Obstetrics and Gynaecology Canada: JOGC = Journal d'obstetrique et Gynecologie Du Canada: JOGC*, 26(4), 333–336. https://doi.org/10.1016/s1701-2163(16)30361-9
- ESHRE Capri Workshop Group. (2005). Fertility and ageing. *Human Reproduction Update*, *11*(3), 261–276. https://doi.org/10.1093/humupd/dmi006
- Esteves, S. C., Miyaoka, R., & Agarwal, A. (2011). An update on the clinical assessment of the infertile male. *Clinics*, 66(4), 691–700. https://doi.org/10.1590/S1807-59322011000400026
- Farag, A. G. A., Basha, M. A., Amin, S. A., Elnaidany, N. F., Elhelbawy, N. G., Mostafa, M. M. T., Khodier, S. A., Ibrahem, R. A., & Mahfouz, R. Z. (2018). Tramadol (opioid) abuse is associated with a dose- and time-dependent poor sperm quality and hyperprolactinaemia in young men. *Andrologia*, *50*(6), e13026. https://doi.org/10.1111/and.13026
- Farombi, E. O., Ugwuezunmba, M. C., Ezenwadu, T. T., Oyeyemi, M. O., & Ekor, M. (2008). Tetracycline-induced reproductive toxicity in male rats: Effects of vitamin C and Nacetylcysteine. *Experimental and Toxicologic Pathology*, 60(1), 77–85. https://doi.org/10.1016/j.etp.2008.02.002
- Fatemi, H., Kasius, J., Timmermans, A., Van Disseldorp, J., Fauser, B., Devroey, P., & Broekmans, F. (2010). Prevalence of unsuspected uterine cavity abnormalities diagnosed by office hysteroscopy prior to in vitro fertilization. *Human Reproduction*, *25*(8), 1959–1965.
- Fauser, B. C., & Van Heusden, A. M. (1997). Manipulation of human ovarian function: Physiological concepts and clinical consequences. *Endocrine Reviews*, *18*(1), 71–106. https://doi.org/10.1210/edrv.18.1.0290
- Fédération, C., Schwartz, D., & Mayaux, M. J. (1982). Female fecundity as a function of age: Results of artificial insemination in 2193 nulliparous women with azoospermic husbands. *New England Journal of Medicine*, 306(7), 404–406.
- Fekkes, M., Buitendijk, S. E., Verrips, G. H. W., Braat, D. D. M., Brewaeys, A. M. A., Dolfing, J. G., Kortman, M., Leerentveld, R. A., & Macklon, N. S. (2003). Health-related quality of life in relation to gender and age in couples planning IVF treatment. *Human Reproduction*, 18(7), 1536–1543. https://doi.org/10.1093/humrep/deg276
- Female Infertility—An overview | ScienceDirect Topics. (n.d.). Retrieved 24 January 2023, from https://www.sciencedirect.com/topics/medicine-and-dentistry/female-infertility
- Female sterilisation. (2017, December 21). Nhs.Uk.
  - https://www.nhs.uk/conditions/contraception/female-sterilisation/
- Female Sterilization—An overview | ScienceDirect Topics. (n.d.). Retrieved 24 January 2023, from https://www.sciencedirect.com/topics/nursing-and-health-professions/female-sterilization

- Finch, A., Valentini, A., Greenblatt, E., Lynch, H. T., Ghadirian, P., Armel, S., Neuhausen, S. L., Kim-Sing, C., Tung, N., Karlan, B., Foulkes, W. D., Sun, P., & Narod, S. (2013). Frequency of premature menopause in women who carry a BRCA1 or BRCA2 mutation. *Fertility and Sterility*, 99(6), 1724–1728. https://doi.org/10.1016/j.fertnstert.2013.01.109
- Fisher, J. R., & Hammarberg, K. (2012). Psychological and social aspects of infertility in men: An overview of the evidence and implications for psychologically informed clinical care and future research. *Asian Journal of Andrology*, *14*(1), 121–129. https://doi.org/10.1038/aja.2011.72
- Fraietta, R., Zylberstejn, D. S., & Esteves, S. C. (2013). Hypogonadotropic Hypogonadism Revisited. *Clinics*, *68*(Suppl 1), 81–88. https://doi.org/10.6061/clinics/2013(Sup01)09
- Freytag, D., Günther, V., Maass, N., & Alkatout, I. (2021). Uterine Fibroids and Infertility. *Diagnostics*, 11(8), 1455. https://doi.org/10.3390/diagnostics11081455
- Gao, J., Zhang, X., Su, P., Liu, J., Shi, K., Hao, Z., Zhou, J., & Liang, C. (2013). Relationship between sexual dysfunction and psychological burden in men with infertility: A large observational study in China. *The Journal of Sexual Medicine*, *10*(8), 1935–1942. https://doi.org/10.1111/jsm.12207
- Giacalone, P.-L., Laffargue, F., Bénos, P., Dechaud, H., & Hédon, B. (2001). Successful in vitro fertilization–surrogate pregnancy in a patient with ovarian transposition who had undergone chemotherapy and pelvic irradiation. *Fertility and Sterility*, *76*(2), 388–389. https://doi.org/10.1016/S0015-0282(01)01895-7
- Giwercman, A., & Skakkebaek, N. E. (1992). The human testis—An organ at risk? In *International Journal of Andrology* (Vol. 15, Issue 5, pp. 373–375). Wiley Online Library.
- Goldman, M. B., & Hatch, M. C. (1999). Women and health. Elsevier.
- Gourounti, K., Anagnostopoulos, F., Potamianos, G., Lykeridou, K., Schmidt, L., & Vaslamatzis, G. (2012). Perception of control, coping and psychological stress of infertile women undergoing IVF. *Reproductive Biomedicine Online*, 24(6), 670–679.
- Green, D. M., Liu, W., Kutteh, W. H., Ke, R. W., Shelton, K. C., Sklar, C. A., Chemaitilly, W., Pui, C.-H., Klosky, J. L., Spunt, S. L., Metzger, M. L., Srivastava, D., Ness, K. K., Robison, L. L., & Hudson, M. M. (2014). Cumulative alkylating agent exposure and semen parameters in adult survivors of childhood cancer: A report from the St Jude Lifetime Cohort Study. *The Lancet Oncology*, *15*(11), 1215–1223. https://doi.org/10.1016/S1470-2045(14)70408-5
- Green, D. M., Nolan, V. G., Goodman, P. J., Whitton, J. A., Srivastava, D., Leisenring, W. M., Neglia, J. P., Sklar, C. A., Kaste, S. C., Hudson, M. M., Diller, L. R., Stovall, M., Donaldson, S. S., & Robison, L. L. (2014). The cyclophosphamide equivalent dose as an approach for quantifying alkylating agent exposure: A report from the childhood cancer survivor study. *Pediatric Blood & Cancer*, 61(1), 53–67. https://doi.org/10.1002/pbc.24679
- Greil, A. L. (1997). Infertility and psychological distress: A critical review of the literature. *Social Science & Medicine*, *45*(11), 1679–1704.
- Greil, A. L., Slauson-Blevins, K., & McQuillan, J. (2010). The experience of infertility: A review of recent literature. *Sociology of Health & Illness*, *32*(1), 140–162.
- Hamada, A., Esteves, S. C., Nizza, M., & Agarwal, A. (2012). Unexplained male infertility:

  Diagnosis and management. *International Braz J Urol: Official Journal of the Brazilian Society of Urology*, *38*(5), 576–594. https://doi.org/10.1590/s1677-55382012000500002 Hamilton, T. R. dos S., Mendes, C. M., de Castro, L. S., de Assis, P. M., Siqueira, A. F. P., Delgado,
  J. de C., Goissis, M. D., Muiño-Blanco, T., Cebrián-Pérez, J. Á., Nichi, M., Visintin, J. A., & Assumpção, M. E. O. D. (2016). Evaluation of Lasting Effects of Heat Stress on Sperm Profile and Oxidative Status of Ram Semen and Epididymal Sperm. *Oxidative Medicine and Cellular Longevity*, *2016*, 1687657. https://doi.org/10.1155/2016/1687657
- Harris, I. D., Fronczak, C., Roth, L., & Meacham, R. B. (2011). Fertility and the aging male. *Reviews in Urology*, 13(4), e184.
- Harzif, A. K., Santawi, V. P. A., & Wijaya, S. (2019). Discrepancy in perception of infertility and attitude towards treatment options: Indonesian urban and rural area. *Reproductive Health*, 16, 126. https://doi.org/10.1186/s12978-019-0792-8

- Hasanpoor-Azghdy, S. B., Simbar, M., & Vedadhir, A. (2014). The emotional-psychological consequences of infertility among infertile women seeking treatment: Results of a qualitative study. *Iranian Journal of Reproductive Medicine*, 12(2), 131–138.
- Hassan, M. A., & Killick, S. R. (2004). Negative lifestyle is associated with a significant reduction in fecundity. *Fertility and Sterility*, *81*(2), 384–392.
- Hellstrom, W. J. G., & Sikka, S. C. (2006). Effects of Acute Treatment With Tamsulosin Versus Alfuzosin on Ejaculatory Function in Normal Volunteers. *The Journal of Urology*, 176(4), 1529–1533. https://doi.org/10.1016/j.juro.2006.06.004
- Hellstrom, W. J. G., & Sikka, S. C. (2009). Effects of Alfuzosin and Tamsulosin on Sperm Parameters in Healthy Men: Results of a Short-Term, Randomized, Double-Blind, Placebo-Controlled, Crossover Study. *Journal of Andrology*, 30(4), 469–474. https://doi.org/10.2164/jandrol.108.006874
- Hendrick, V., Gitlin, M., Altshuler, L., & Korenman, S. (2000). Antidepressant medications, mood and male fertility. *Psychoneuroendocrinology*, *25*(1), 37–51. https://doi.org/10.1016/S0306-4530(99)00038-4
- Hendry, W. (1998). Disorders of ejaculation: Congenital, acquired and functional. *British Journal of Urology (Print)*, 82(3), 331–341.
- Henkel, R., Maaß, G., Jung, A., Haidl, G., Schill, W., & Schuppe, H. (2007). Age-related changes in seminal polymorphonuclear elastase in men with asymptomatic inflammation of the genital tract. *Asian Journal of Andrology*, *9*(3), 299–304.
- Heredia, M., Tenías, J. M., Rocio, R., Amparo, F., Calleja, M. A., & Valenzuela, J. C. (2013). Quality of life and predictive factors in patients undergoing assisted reproduction techniques. *European Journal of Obstetrics* & *Gynecology and Reproductive Biology*, *167*(2), 176–180. https://doi.org/10.1016/j.ejogrb.2012.12.011
- Hernández-Ochoa, I., Karman, B. N., & Flaws, J. A. (2009). The role of the aryl hydrocarbon receptor in the female reproductive system. *Biochemical Pharmacology*, 77(4), 547–559. https://doi.org/10.1016/j.bcp.2008.09.037
- Hinckley, M. D., & Milki, A. A. (2004). 1000 office-based hysteroscopies prior to in vitro fertilization: Feasibility and findings. *JSLS: Journal of the Society of Laparoendoscopic Surgeons*, 8(2), 103–107.
- Holter, H., Anderheim, L., Bergh, C., & Möller, A. (2006). First IVF treatment—Short-term impact on psychological well-being and the marital relationship. *Human Reproduction*, *21*(12), 3295–3302.
- Hruska, K. S., Furth, P. A., Seifer, D. B., Sharara, F. I., & Flaws, J. A. (2000). Environmental factors in infertility. *Clinical Obstetrics and Gynecology*, *43*(4), 821–829.
- Hsu, P.-Y., et al. (2013). "The fertility quality of life (FertiQoL) questionnaire in Taiwanese infertile couples." <u>Taiwanese Journal of Obstetrics and Gynecology</u> **52**(2): 204-209.
- Hull, M. G., North, K., Taylor, H., Farrow, A., & Ford, W. C. L. (2000). Delayed conception and active and passive smoking. *Fertility and Sterility*, 74(4), 725–733.
- Hummelshoj, L., Prentice, A., & Groothuis, P. (2006). *Update on Endometriosis: 9th World Congress on Endometriosis, 14–17 September 2005, Maastricht, the Netherlands.*
- Imrie, S., Jadva, V., & Golombok, S. (2019). Psychological well-being of identity-release egg donation parents with infants. Human Reproduction (Oxford, England), 34(11), 2219–2227. https://doi.org/10.1093/humrep/dez201
- In Vitro Fertilization and Multiple Pregnancies. (2006). *Ontario Health Technology Assessment Series*, 6(18), 1–63.
- Infertility Problems With Cervical Mucus—Women's Health Issues. (n.d.). MSD Manual Consumer Version. Retrieved 24 January 2023, from https://www.msdmanuals.com/home/women-s-health-issues/infertility/infertilityproblems-with-cervical-mucus
- Inhorn, M. C., & Patrizio, P. (2015). Infertility around the globe: New thinking on gender, reproductive technologies and global movements in the 21st century. *Human Reproduction Update*, *21*(4), 411–426. https://doi.org/10.1093/humupd/dmv016

- Jarow, J. P., Espeland, M. A., & Lipshultz, L. I. (1989). Evaluation of the azoospermic patient. *The Journal of Urology*, 142(1), 62–65.
- Jensen, T. K., Andersson, A.-M., Jørgensen, N., Andersen, A.-G., Carlsen, E., & Skakkebæk, N. E. (2004). Body mass index in relation to semen quality and reproductive hormonesamong 1,558 Danish men. *Fertility and Sterility*, 82(4), 863–870.
- Jensen, T. K., Hjollund, N. H. I., Henriksen, T. B., Scheike, T., Kolstad, H., Giwercman, A., Ernst, E., Bonde, J. P., Skakkebæk, N. E., & Olsen, J. (1998). Does moderate alcohol consumption affect fertility? Follow up study among couples planning first pregnancy. *BMJ*, 317(7157), 505–510. https://doi.org/10.1136/bmj.317.7157.505
- Johansson, M., Adolfsson, A., Berg, M., Francis, J., Hogström, L., Janson, P. O., Sogn, J., & Hellström, A.-L. (2009). Quality of life for couples 4-5.5 years after unsuccessful IVF treatment. Acta Obstetricia Et Gynecologica Scandinavica, 88(3), 291–300. https://doi.org/10.1080/00016340802705956
- Jordan, C., & Revenson, T. A. (1999). Gender differences in coping with infertility: A metaanalysis. *Journal of Behavioral Medicine*, *22*, 341–358.
- Joshi, S. K., & Acharya, K. (2019). Modification of Kuppuswamy's Socioeconomic Status Scale in the Context of Nepal, 2019. *Kathmandu University Medical Journal (KUMJ)*, 17(65), 1–2.
- Juárez-Bengoa, A., Bagnarello-González, F., Rodríguez-Perdomo, D. F., & Rodríguez-Yee, E. (2011). [Prevalence of retrograde ejaculation in infertility associated to hypospermia]. Ginecologia Y Obstetricia De Mexico, 79(2), 61–66.
- Jung, A., Strauss, P., Lindner, H., & Schuppe, H. (2008). Influence of moderate cycling on scrotal temperature. *International Journal of Andrology*, *31*(4), 403–407.
- Jungwirth, A., Giwercman, A., Tournaye, H., Diemer, T., Kopa, Z., Dohle, G., Krausz, C., & European Association of Urology Working Group on Male Infertility. (2012). European Association of Urology guidelines on Male Infertility: The 2012 update. *European Urology*, 62(2), 324–332. https://doi.org/10.1016/j.eururo.2012.04.048
- Jurewicz, J., Dziewirska, E., Radwan, M., & Hanke, W. (2018). Air pollution from natural and anthropic sources and male fertility. *Reproductive Biology and Endocrinology*, 16(1), 1–18.
- Kamath, M., & Deepti, M. (2016). Unexplained infertility: An approach to diagnosis and management. In *Current Medical Issues* (Vol. 14, Issue 4, pp. 94–100). Wolters Kluwer Medknow Publications.
- Kamischke, A., & Nieschlag, E. (1999). Mini symposium: Non-surgical sperm recovery: Part II. Treatment of retrograde ejaculation and anejaculation. *Human Reproduction Update*, 5(5), 448–474.
- Kamischke, A., & Nieschlag, E. (2002). Update on medical treatment of ejaculatory disorders 1. *International Journal of Andrology*, *25*(6), 333–344.
- Kanwar, U., Anand, R. J. K., & Sanyal, S. N. (1993). The effect of nifedipine, a calcium channel blocker, on human spermatozoal functions. *Contraception*, *48*(5), 453–470. https://doi.org/10.1016/0010-7824(93)90135-T
- Kapranos, N., Petrakou, E., Anastasiadou, C., & Kotronias, D. (2003). Detection of herpes simplex virus, cytomegalovirus, and Epstein-Barr virus in the semen of men attending an infertility clinic. *Fertility and Sterility*, 79, 1566–1570.
- Karabulut, A., Özkan, S., & Oğuz, N. (2013). Predictors of fertility quality of life (FertiQoL) in infertile women: Analysis of confounding factors. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, 170(1), 193–197. https://doi.org/10.1016/j.ejogrb.2013.06.029
- Karimpour Malekshah, A., Esmailnejad Moghaddam, A., Moslemizadeh, N., Peivandi, S., Barzegarnejad, A., Musanejad, N., & Jursarayee, G. (2011). Infertility in Mazandaran province north of Iran: An etiological study. *Iranian Journal of Reproductive Medicine*, 9(1), 21–24.
- Katsoff, D., & Check, J. H. (1997). A challenge to the concept that the use of calcium channel blockers causes reversible male infertility. *Human Reproduction*, *12*(7), 1480–1482. https://doi.org/10.1093/humrep/12.7.1480

- Kavanagh, K., Wallace, L. A., Robertson, C., Wilson, P., & Scoular, A. (2013). Estimation of the risk of tubal factor infertility associated with genital chlamydial infection in women: A statistical modelling study. *International Journal of Epidemiology*, 42(2), 493–503. https://doi.org/10.1093/ije/dyt011
- Kehl, S., Weigel, M., Müller, D., Gentili, M., Hornemann, A., & Sütterlin, M. (2011). HIV-infection and modern antiretroviral therapy impair sperm quality. *Archives of Gynecology and Obstetrics*, 284(1), 229–233. https://doi.org/10.1007/s00404-011-1898-6
- Kennedy, S., Bergqvist, A., Chapron, C., D'Hooghe, T., Dunselman, G., Greb, R., Hummelshoj, L., Prentice, A., & Saridogan, E. (2005). ESHRE guideline for the diagnosis and treatment of endometriosis. *Human Reproduction*, *20*(10), 2698–2704.
- Kesari, K. K., Agarwal, A., & Henkel, R. (2018). Radiations and male fertility. *Reproductive Biology and Endocrinology*, 16(1), 1–16.
- Khanal, P., & Journals, E. (2020). Infertility: An Emerging Issue in Nepal.
- Kim, J. H., & Shin, H. S. (2013). A structural model for quality of life of infertile women. *Journal of Korean Academy of Nursing*, 43(3), 312–320.
- Kim, J. H., Shin, H. S., & Yun, E. K. (2018). A Dyadic Approach to Infertility Stress, Marital Adjustment, and Depression on Quality of Life in Infertile Couples. *Journal of Holistic Nursing*, *36*(1), 6–14. https://doi.org/10.1177/0898010116675987
- Kim, N. I., Chamchan, C., & Tangchonlatip, K. (2022). Prevalence and Social Risk Factors of Infertility in Vietnam. *Illness, Crisis & Loss, 30*(4), 756–769. https://doi.org/10.1177/10541373211022103
- Kitchen, H., Aldhouse, N., Trigg, A., Palencia, R., & Mitchell, S. (2017). A review of patientreported outcome measures to assess female infertility-related quality of life. *Health and Quality of Life Outcomes*, *15*(1), Article 1. https://doi.org/10.1186/s12955-017-0666-0
- Kol, S. (2014). Assisted Reproductive Technology (ART). In *Reference Module in Biomedical Sciences*. Elsevier. https://doi.org/10.1016/B978-0-12-801238-3.03880-0
- Kondoh, N. (2011). Ejaculatory dysfunction as a cause of infertility. *Reproductive Medicine and Biology*, *11*(1), 59–64. https://doi.org/10.1007/s12522-011-0108-3
- Krassas, G. E. (2000). Thyroid disease and female reproduction. *Fertility and Sterility*, 74(6), 1063–1070.
- Krzastek, S. C., Farhi, J., Gray, M., & Smith, R. P. (2020). Impact of environmental toxin exposure on male fertility potential. *Translational Andrology and Urology*, 9(6), 2797–2813. https://doi.org/10.21037/tau-20-685
- Kukadia, A. N., Ercole, C. J., Gleich, P., Hensleigh, H., & Pryor, J. L. (1996). Testicular trauma: Potential impact on reproductive function. *The Journal of Urology*, 156(5), 1643–1646. https://doi.org/10.1016/s0022-5347(01)65472-7
- Kumar, V. S. K., Sharma, V. L., Tiwari, P., Singh, D., Maikhuri, J. P., Gupta, G., & Singh, M. M. (2006). The spermicidal and antitrichomonas activities of SSRI antidepressants. *Bioorganic & Medicinal Chemistry Letters*, 16(9), 2509–2512. https://doi.org/10.1016/j.bmcl.2006.01.078
- Lacasaña, M., Vázquez-Grameix, H., Borja-Aburto, V. H., Blanco-Muñoz, J., Romieu, I., Aguilar-Garduño, C., & García, A. M. (2006). Maternal and paternal occupational exposure to agricultural work and the risk of anencephaly. *Occupational and Environmental Medicine*, 63(10), 649–656. https://doi.org/10.1136/oem.2005.023333
- Land, J. A., Van Bergen, J. E. A. M., Morré, S. A., & Postma, M. J. (2010). Epidemiology of Chlamydia trachomatis infection in women and the cost-effectiveness of screening.

  \*Human Reproduction Update, 16(2), 189–204. https://doi.org/10.1093/humupd/dmp035
- Lau, J. T. F., Wang, Q., Cheng, Y., Kim, J. H., Yang, X., & Yi Tsui, H. (2008). Infertility-Related Perceptions and Responses and Their Associations With Quality of Life Among Rural Chinese Infertile Couples. *Journal of Sex & Marital Therapy*, 34(3), 248–267. https://doi.org/10.1080/00926230701866117
- Lawson, R., El-Toukhy, T., Kassab, A., Taylor, A., Braude, P., Parsons, J., & Seed, P. (2003). Poor response to ovulation induction is a stronger predictor of early menopause than elevated basal FSH: A life table analysis. *Human Reproduction (Oxford, England)*, 18(3),

- 527-533. https://doi.org/10.1093/humrep/deg101
- Ledger, W. L. (2009). Demographics of infertility. Reproductive Biomedicine Online, 18, S11-S14.
- Lee, C. J., & Yoon, Y.-D. (2005). γ-Radiation-induced follicular degeneration in the prepubertal mouse ovary. *Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis*, *578*(1), 247–255. https://doi.org/10.1016/j.mrfmmm.2005.05.019
- Lee, T. Y., & Sun, G. H. (2000). Psychosocial response of Chinese infertile husbands and wives. *Archives of Andrology*, 45(3), 143–148. https://doi.org/10.1080/01485010050193913
- Leke, R. J., Oduma, J. A., Bassol-Mayagoitia, S., Bacha, A. M., & Grigor, K. M. (1993). Regional and geographical variations in infertility: Effects of environmental, cultural, and socioeconomic factors. *Environmental Health Perspectives*, 101(suppl 2), 73–80.
- Leridon, H. (2004). Can assisted reproduction technology compensate for the natural decline in fertility with age? A model assessment. *Human Reproduction*, 19(7), 1548–1553. https://doi.org/10.1093/humrep/deh304
- Leslie, S. W., Soon-Sutton, T. L., & Khan, M. A. (2022). Male Infertility. In *StatPearls*. StatPearls Publishing. http://www.ncbi.nlm.nih.gov/books/NBK562258/
- Li, Y., Lin, H., Li, Y., & Cao, J. (2011). Association between socio-psycho-behavioral factors and male semen quality: Systematic review and meta-analyses. *Fertility and Sterility*, 95(1), 116–123.
- Liang, S., Chen, Y., Wang, Q., Chen, H., Cui, C., Xu, X., Zhang, Q., & Zhang, C. (2021). Prevalence and associated factors of infertility among 20–49 year old women in Henan Province, China. *Reproductive Health*, *18*(1), 254. https://doi.org/10.1186/s12978-021-01298-2
- Lin, C.-H., & Huang, T.-Y. (2020). Congenital bilateral absence of the vas deferens (CBAVD) with bilaterally present seminal vesicles. *Urology Case Reports*, *31*, 101131. https://doi.org/10.1016/j.eucr.2020.101131
- Lincoln, S. R., Ke, R. W., & Kutteh, W. H. (1999). Screening for hypothyroidism in infertile women. *The Journal of Reproductive Medicine*, *44*(5), 455–457.
- Lipscomb, J. A., Fenster, L., Wrensch, M., Shusterman, D., & Swan, S. (1991). Pregnancy Outcomes in Women Potentially Exposed to Occupational Solvents and Women Working in the Electronics Industry. *Journal of Occupational Medicine*, *33*(5), 597–604.
- Loke, A. Y., Yu, P.-L., & Hayter, M. (2012). Experiences of sub-fertility among Chinese couples in Hong Kong: A qualitative study. *Journal of Clinical Nursing*, 21(3–4), 504–512. https://doi.org/10.1111/j.1365-2702.2010.03632.x
- López-Botella, A., Velasco, I., Acién, M., Sáez-Espinosa, P., Todolí-Torró, J.-L., Sánchez-Romero, R., & Gómez-Torres, M. J. (2021). Impact of Heavy Metals on Human Male Fertility—An Overview. *Antioxidants*, *10*(9), 1473. https://doi.org/10.3390/antiox10091473
- Low sperm count. (2017, October 19). Nhs.Uk. https://www.nhs.uk/conditions/low-spermcount/
- Luboshitzky, R., Lavie, L., Shen-Orr, Z., & Herer, P. (2005). Altered luteinizing hormone and testosterone secretion in middle-aged obese men with obstructive sleep apnea. *Obesity Research*, *13*(4), 780–786.
- Luk, B. H.-K., & Loke, A. Y. (2015). The Impact of Infertility on the Psychological Well-Being, Marital Relationships, Sexual Relationships, and Quality of Life of Couples: A Systematic Review. *Journal of Sex & Marital Therapy*, 41(6), 610–625. https://doi.org/10.1080/0092623X.2014.958789
- Lyu, Z., Feng, X., Li, N., Zhao, W., Wei, L., Chen, Y., Yang, W., Ma, H., Yao, B., & Zhang, K. (2017). Human papillomavirus in semen and the risk for male infertility: A systematic review and meta-analysis. *BMC Infectious Diseases*, 17, 1–9.
- Maeda, E., Hiraike, O., Sugimori, H., Kinoshita, A., Hirao, M., Nomura, K., & Osuga, Y. (2022). Working conditions contribute to fertility-related quality of life: A cross-sectional study in Japan. *Reproductive Biomedicine Online*, 45(6), 1285–1295. https://doi.org/10.1016/j.rbmo.2022.07.006
- Malaysia Fertility Rate 1950-2023. (n.d.). Retrieved 18 January 2023, from https://www.macrotrends.net/countries/MYS/malaysia/fertility-rate
- Male hypogonadism—Symptoms and causes. (n.d.). Mayo Clinic. Retrieved 23 January 2023, from https://www.mayoclinic.org/diseases-conditions/male-hypogonadism/symptomscauses/syc-20354881

- Male infertility—Symptoms and causes. (n.d.). Mayo Clinic. Retrieved 25 January 2023, from https://www.mayoclinic.org/diseases-conditions/male-infertility/symptoms-causes/syc-20374773
- Malik, S. H., & Coulson, N. (2008). The male experience of infertility: A thematic analysis of an online infertility support group bulletin board. *Journal of Reproductive and Infant Psychology*, *26*(1), 18–30. https://doi.org/10.1080/02646830701759777
- Mao, J., Guo, H., Wang, J., Li, Y., & Xu, M. (2022). Analysis of Related Factors of Coping Styles in Infertile Patients in Central China. *Patient Preference and Adherence*, *16*, 1605. https://doi.org/10.2147/PPA.S364345
- Maroufizadeh, S., Ghaheri, A., Almasi-Hashiani, A., Mohammadi, M., Navid, B., Ezabadi, Z., & Omani Samani, R. (2018). The prevalence of anxiety and depression among people with infertility referring to Royan Institute in Tehran, Iran: A cross-sectional questionnaire study. *Middle East Fertility Society Journal*, 23(2), 103–106. https://doi.org/10.1016/j.mefs.2017.09.003
- Mascarenhas, M. N., Flaxman, S. R., Boerma, T., Vanderpoel, S., & Stevens, G. A. (2012).

  National, Regional, and Global Trends in Infertility Prevalence Since 1990: A Systematic Analysis of 277 Health Surveys. *PLoS Medicine*, *9*(12), e1001356.

  https://doi.org/10.1371/journal.pmed.1001356
- Matsubayashi, H., Hosaka, T., Izumi, S., Suzuki, T., Kondo, A., & Makino, T. (2004). Increased depression and anxiety in infertile Japanese women resulting from lack of husband's support and feelings of stress. *General Hospital Psychiatry*, *26*(5), 398–404. https://doi.org/10.1016/j.genhosppsych.2004.05.002
- May-Panloup, P., Boucret, L., Chao de la Barca, J.-M., Desquiret-Dumas, V., Ferre-L'Hotellier, V., Moriniere, C., Descamps, P., Procaccio, V., & Reynier, P. (2016). Ovarian ageing: The role of mitochondria in oocytes and follicles. *Human Reproduction Update*, *22*(6), 725–743. McMahon, C. G., Althof, S. E., Waldinger, M. D., Porst, H., Dean, J., Sharlip, I. D., Adaikan, P., Becher, E., Broderick, G. A., & Buvat, J. (2008). An evidence-based definition of lifelong premature ejaculation: Report of the International Society for Sexual Medicine (ISSM) ad hoc committee for the definition of premature ejaculation. *The Journal of Sexual Medicine*, *5*(7), 1590–1606.
- Merchant, R., Gandhi, G., & Allahbadia, G. N. (2011). In vitro fertilization/intracytoplasmic sperm injection for male infertility. *Indian Journal of Urology : IJU : Journal of the Urological Society of India*, 27(1), 121–132. https://doi.org/10.4103/0970-1591.78430
- Michalas, S., Minaretzis, D., Tsionou, C., Maos, G., Kioses, E., & Aravantinos, D. (1992). Pelvic surgery, reproductive factors and risk of ectopic pregnancy: A case controlled study. *International Journal of Gynaecology and Obstetrics: The Official Organ of the International Federation of Gynaecology and Obstetrics*, 38(2), 101–105. https://doi.org/10.1016/0020-7292(92)90044-j
- Mieusset, R., & Bujan, L. (1995). Testicular heating and its possible contributions to male infertility: A review. *International Journal of Andrology*, *18*(4), 169–184.
- Mitra, A., Chakraborty, B., Mukhopadhay, D., Pal, M., Mukherjee, S., Banerjee, S., & Chaudhuri, K. (2012). Effect of smoking on semen quality, FSH, testosterone level, and CAG repeat length in androgen receptor gene of infertile men in an Indian city. *Systems Biology in Reproductive Medicine*, 58(5), 255–262.
- Monga, M., Alexandrescu, B., Katz, S. E., Stein, M., & Ganiats, T. (2004). Impact of infertility on quality of life, marital adjustment, and sexual function. *Urology*, 63(1), 126–130. https://doi.org/10.1016/j.urology.2003.09.015
- Monica Bari, M. M., Natalia Battista, Valentina Pirazzi. (2011). The manifold actions of endocannabinoids on female and male reproductive events. *FBL*, *16*(2), 498–516. https://doi.org/10.2741/3701
- Mosalanejad, L., Parandavar, N., & Abdollahifard, S. (2014). Barriers to Infertility Treatment: An Integrated Study. *Global Journal of Health Science*, 6(1), 181–191. https://doi.org/10.5539/gjhs.v6n1p181
- Moura-Ramos, M., Gameiro, S., Canavarro, M. C., & Soares, I. (2012). Assessing infertility stress: Reexamining the factor structure of the Fertility Problem Inventory. *Human Reproduction*, *27*(2), 496–505.

- Mousavi, S. A., Masoumi, S. Z., Keramat, A., Pooralajal, J., & Shobeiri, F. (2013). Assessment of Questionnaires Measuring Quality of Life in Infertile Couples: A Systematic Review. *Journal of Reproduction & Infertility*, 14(3), 110–119.
- Mueller, B. A., Daling, J. R., Weiss, N. S., & Moore, D. E. (1990). Recreational drug use and the risk of primary infertility. *Epidemiology (Cambridge, Mass.)*, 1(3), 195–200. https://doi.org/10.1097/00001648-199005000-00003
- Mukhopadhyay, D., Varghese, A. C., Pal, M., Banerjee, S. K., Bhattacharyya, A. K., Sharma, R. K., & Agarwal, A. (2010). Semen quality and age-specific changes: A study between two decades on 3,729 male partners of couples with normal sperm count and attending an andrology laboratory for infertility-related problems in an Indian city. *Fertility and Sterility*, 93(7), 2247–2254. https://doi.org/10.1016/j.fertnstert.2009.01.135
- Munné, S., Alikani, M., Tomkin, G., Grifo, J., & Cohen, J. (1995). Embryo morphology, developmental rates, and maternal age are correlated with chromosome abnormalities\*\*Presented at the 50th Annual Meeting of The American Fertility Society, San Antonio, Texas, November 4 to 9, 1994, where it was awarded the prize paper of the Society for Assisted Reproductive Technology. Fertility and Sterility, 64(2), 382–391. https://doi.org/10.1016/S0015-0282(16)57739-5
- Namdar, A., Naghizadeh, M. M., Zamani, M., Yaghmaei, F., & Sameni, M. H. (2017). Quality of life and general health of infertile women. *Health and Quality of Life Outcomes*, *15*(1), 139. https://doi.org/10.1186/s12955-017-0712-y
- Nepal Demographic and Health Survey 2022—Key Indicators (English). (n.d.). Retrieved 5 January 2023, from https://dhsprogram.com/publications/publication-PR142-Preliminary-Reports-Key-Indicators-Reports.cfm
- Neumann, K., Kayser, J., Depenbusch, M., Schultze-Mosgau, A., & Griesinger, G. (2018). Can a quality-of-life assessment assist in identifying women at risk of prematurely discontinuing IVF treatment? A prospective cohort study utilizing the FertiQoL questionnaire. *Archives of Gynecology and Obstetrics*, 298. https://doi.org/10.1007/s00404-018-4797-2
- Neupane, P., Sharma, D., Panta, P. P., Aryal, B., Poudel, T., & Amgain, K. (2019). Causes of Infertility amongst Couples Visited at Infertility Centre Kathmandu, Nepal. *Journal of Karnali Academy of Health Sciences*, 2(2), Article 2. https://doi.org/10.3126/jkahs.v2i2.25180
- Nho, J.-H., & Kim, E. J. (2022). Relationships among Type-D Personality, Fatigue, and Quality of Life in Infertile Women. *Asian Nursing Research*, *16*(4), 208–214. https://doi.org/10.1016/j.anr.2022.08.001
- Ni, Y., Shen, H., Yao, H., Zhang, E., Tong, C., Qian, W., Huang, L., Wu, X., & Feng, Q. (2023). Differences in Fertility-Related Quality of Life and Emotional Status Among Women Undergoing Different IVF Treatment Cycles. *Psychology Research and Behavior Management*, *16*, 1873–1882. https://doi.org/10.2147/PRBM.S411740
- Ni, Y., Tong, C., Huang, L., Zhou, W., & Zhang, A. (2021). The analysis of fertility quality of life and the influencing factors of patients with repeated implantation failure. *Health and Quality of Life Outcomes*, 19(1), 32. https://doi.org/10.1186/s12955-021-01666-3
- Nicopoullos, J. D. M., Almeida, P., Vourliotis, M., Goulding, R., & Gilling-Smith, C. (2010). A decade of sperm washing: Clinical correlates of successful insemination outcome. *Human Reproduction*, 25(8), 1869–1876. https://doi.org/10.1093/humrep/deq134
- Niedzielski, J. K., Oszukowska, E., & Słowikowska-Hilczer, J. (2016). Undescended testis–current trends and guidelines: A review of the literature. *Archives of Medical Science*, *12*(3), 667–677.
- Nieschlag, E., & Behre, H. M. (2001). *Andrology: Male reproductive health and dysfunction*. Springer Science & Business Media.
- Nieuwenhuis, S. L., Odukogbe, A.-T. A., Theobald, S., & Liu, X. (2009). The impact of infertility on infertile men and women in Ibadan, Oyo State, Nigeria: A qualitative study. *African Journal of Reproductive Health*, 13(3), 85–98.

- Noorbala, A. A., Ramezanzadeh, F., Abedinia, N., & Naghizadeh, M. M. (2009). Psychiatric disorders among infertile and fertile women. *Social Psychiatry and Psychiatric Epidemiology*, 44(7), 587–591. https://doi.org/10.1007/s00127-008-0467-1
- Ombelet, W., Cooke, I., Dyer, S., Serour, G., & Devroey, P. (2008). Infertility and the provision of infertility medical services in developing countries. *Human Reproduction Update*, 14(6), Article 6
- Onat, G., & Kizilkaya Beji, N. (2012). Effects of infertility on gender differences in marital relationship and quality of life: A case-control study of Turkish couples. *European Journal of Obstetrics, Gynecology, and Reproductive Biology, 165*(2), 243–248. https://doi.org/10.1016/j.ejogrb.2012.07.033
- Organization, W. H. (2021). WHO fact sheet on infertility. *Global Reproductive Health*, 6(1), e52. https://doi.org/10.1097/GRH.000000000000052
- Oskay, Ü., Beji, N., & Serdaroglu, H. (2010). The Issue of Infertility and Sexual Function in Turkish Women. *SEXUALITY AND DISABILITY*, 28(2). https://doi.org/10.1007/s11195-010-9158-4
- Ozkan, S., Murk, W., & Arici, A. (2008). Endometriosis and infertility: Epidemiology and evidence-based treatments. *Annals of the New York Academy of Sciences*, 1127(1), 92–100.
- Öztekin, Ü., Caniklioğlu, M., Sarı, S., Selmi, V., Gürel, A., & Işıkay, L. (2019). Evaluation of Male Infertility Prevalence with Clinical Outcomes in Middle Anatolian Region. *Cureus*. https://doi.org/10.7759/cureus.5122
- Pasquali, R., Pelusi, C., Genghini, S., Cacciari, M., & Gambineri, A. (2003). Obesity and reproductive disorders in women. *Human Reproduction Update*, *9*(4), 359–372.
- Paszkowski, T., Clarke, R. N., & Hornstein, M. D. (2002). Smoking induces oxidative stress inside the Graafian follicle. *Human Reproduction*, *17*(4), 921–925.
- Patil, M. (2012). Ectopic pregnancy after infertility treatment. *Journal of Human Reproductive Sciences*, 5(2), 154. https://doi.org/10.4103/0974-1208.101011
- Pelvic Inflammatory Disease (PID). (n.d.). Retrieved 24 January 2023, from https://www.acog.org/en/womens-health/faqs/pelvic-inflammatory-disease
- Peterson, B. D., Newton, C. R., & Rosen, K. H. (2003). Examining congruence between partners' perceived infertility-related stress and its relationship to marital adjustment and depression in infertile couples. *Family Process*, 42(1), 59–70.
- Peterson, B. D., Newton, C. R., Rosen, K. H., & Skaggs, G. E. (2006). Gender differences in how men and women who are referred for IVF cope with infertility stress. *Human Reproduction*, *21*(9), 2443–2449.
- Piazza, M. J., & Urbanetz, A. A. (2019). Environmental toxins and the impact of other endocrine disrupting chemicals in women's reproductive health. *JBRA Assisted Reproduction*, 23(2), 154–164. https://doi.org/10.5935/1518-0557.20190016
- Poppe, K., & Velkeniers, B. (2003). Thyroid disorders in infertile women. 64(1), 45–50.
- Pradhan, P. (2013). Factors associated with Quality of Life among Infertile Women Receiving Treatment at an Infertility Center in Kathmandu, Nepal. Graduate Studies Mahidol University. https://graduate.mahidol.ac.th/engine/current-
- students/detail/abstract\_view.php?id=5536823&fac=23&prg=2327M&gp=3
- Pradhan Shrestha, S., Bhandari, S. D., & Pradhan, S. (2020). Quality of Life among Infertile Women Attending an Infertility Treatment Center, Kathmandu. *Journal of Nepal Health Research Council*, 18(3), 394–400. https://doi.org/10.33314/jnhrc.v18i3.2639
- Psychological and social aspects of infertility in men: An overview of the evidence and implications for psychologically informed clinical care and future research—PMC. (n.d.). Retrieved 25 January 2023, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3735147/
- Ragni, G., Mosconi, P., Baldini, M. P., Somigliana, E., Vegetti, W., Caliari, I., & Nicolosi, A. E. (2005). Health-related quality of life and need for IVF in 1000 Italian infertile couples. *Human Reproduction (Oxford, England)*, 20(5), 1286–1291. https://doi.org/10.1093/humrep/deh788
- Ramos, R. R., Gutiérrez, G. R., Monroy, I. A., & Sánchez, H. G. M. (2008). Risk factors associated to female infertility. *Ginecologia y Obstetricia de Mexico*, 76(12), 717–721.

- Rao, M., Zhao, X.-L., Yang, J., Hu, S.-F., Lei, H., Xia, W., & Zhu, C.-H. (2015). Effect of transient scrotal hyperthermia on sperm parameters, seminal plasma biochemical markers, and oxidative stress in men. *Asian Journal of Andrology*, *17*(4), 668.
- Recent advances in medically assisted conception. Report of a WHO Scientific Group. (1992). World Health Organization Technical Report Series, 820, 1–111.
- Record Details. (n.d.). Retrieved 24 January 2023, from https://krishi.icar.gov.in/ohs-2.3.1/index.php/record/view/229831
- Relwani, R., Berger, D., Santoro, N., Hickmon, C., Nihsen, M., Zapantis, A., Werner, M., Polotsky, A. J., & Jindal, S. (2011). Semen Parameters are Unrelated to BMI But Vary With SSRI Use and Prior Urological Surgery. *Reproductive Sciences*, *18*(4), 391–397. https://doi.org/10.1177/1933719110385708
- Ricci, E., Al Beitawi, S., Cipriani, S., Candiani, M., Chiaffarino, F., Viganò, P., Noli, S., & Parazzini, F. (2017). Semen quality and alcohol intake: A systematic review and meta-analysis. *Reproductive Biomedicine Online*, *34*(1), 38–47.
- Ricci, E., Viganò, P., Cipriani, S., Somigliana, E., Chiaffarino, F., Bulfoni, A., & Parazzini, F. (2017). Coffee and caffeine intake and male infertility: A systematic review. *Nutrition Journal*, *16*(1), 1–14.
- Rich-Edwards, J. W., Goldman, M. B., Willett, W. C., Hunter, D. J., Stampfer, M. J., Colditz, G. A., & Manson, J. E. (1994). Adolescent body mass index and infertility caused by ovulatory disorder. *American Journal of Obstetrics & Gynecology*, 171(1), 171–177. https://doi.org/10.1016/0002-9378(94)90465-0
- Rich-Edwards, J. W., Spiegelman, D., Garland, M., Hertzmark, E., Hunter, D. J., Colditz, G. A., Willett, W. C., Wand, H., & Manson, J. E. (2002). Physical activity, body mass index, and ovulatory disorder infertility. *Epidemiology*, 13(2), 184–190.
- Roberts, M., & Jarvi, K. (2009). Steps in the investigation and management of low semen volume in the infertile man. *Canadian Urological Association Journal*, *3*(6), 479.
- Rooney, K. L., & Domar, A. D. (2018). The relationship between stress and infertility. *Dialogues in Clinical Neuroscience*, 20(1), 41–47.
- Rotker, K., & Sigman, M. (2016). Recurrent varicocele. Asian Journal of Andrology, 18(2), 229.
- Rowland, D., McMahon, C. G., Abdo, C., Chen, J., Jannini, E., Waldinger, M. D., & Ahn, T. Y.
- (2010). Disorders of Orgasm and Ejaculation in Men. *The Journal of Sexual Medicine*, 7(4, Part 2), 1668–1686. https://doi.org/10.1111/j.1743-6109.2010.01782.x
- Sabra, S., Malmqvist, E., Saborit, A., Gratacós, E., & Gomez Roig, M. D. (2017). Heavy metals exposure levels and their correlation with different clinical forms of fetal growth restriction. *PloS One*, *12*(10), e0185645. https://doi.org/10.1371/journal.pone.0185645 Sasano, N., & Ichijo, S. (1969). Vascular patterns of the human testis with special reference to its senile changes. *The Tohoku Journal of Experimental Medicine*, *99*(3), 269–280.
- Sawka, A. M., Lea, J., Alshehri, B., Straus, S., Tsang, R. W., Brierley, J. D., Thabane, L., Rotstein, L., Gafni, A., & Ezzat, S. (2008). A systematic review of the gonadal effects of therapeutic radioactive iodine in male thyroid cancer survivors. *Clinical Endocrinology*, 68(4), 610–617.
- Sengupta, P., Chaudhuri, P., & Bhattacharya, K. (2013). Male reproductive health and yoga. *International Journal of Yoga*, 6(2), 87–95. https://doi.org/10.4103/0973-6131.113391 Sexty, R. E., Griesinger, G., Kayser, J., Lallinger, M., Rösner, S., Strowitzki, T., Toth, B., & Wischmann, T. (2018). Psychometric characteristics of the FertiQoL questionnaire in a German sample of infertile individuals and couples. *Health and Quality*
- Sexty, R., Hamadneh, J., Rösner, S., Strowitzki, T., Ditzen, B., Toth, B., & Wischmann, T. (2016). Crosscultural comparison of fertility specific quality of life in German, Hungarian and Jordanian couples attending a fertility center. *Health and Quality of Life Outcomes*, *14*, 27. https://doi.org/10.1186/s12955-016-0429-3
- Sharma, A., Minhas, S., Dhillo, W. S., & Jayasena, C. N. (2020). Male infertility due to testicular disorders. *The Journal of Clinical Endocrinology and Metabolism*, 106(2), e442–e459. https://doi.org/10.1210/clinem/dgaa781
- Sharma, M., & Balasundaram, P. (2022). Ovulation Induction Techniques. In *StatPearls*. StatPearls Publishing. http://www.ncbi.nlm.nih.gov/books/NBK574564/

- Sharma, R., Biedenharn, K. R., Fedor, J. M., & Agarwal, A. (2013). Lifestyle factors and reproductive health: Taking control of your fertility. *Reproductive Biology and Endocrinology:* RB&E, 11, 66. https://doi.org/10.1186/1477-7827-11-66
- Sharma, R., Harlev, A., Agarwal, A., & Esteves, S. C. (2016). Cigarette smoking and semen quality: A new meta-analysis examining the effect of the 2010 World Health Organization laboratory methods for the examination of human semen. *European Urology*, 70(4), 635–645.
- Sharpe, R. (1993). Declining sperm counts in men-is there an endocrine cause? *Journal of Endocrinology*, 136(3), 357–360.
- Shefi, S., & Turek, P. J. (2006). Definition and current evaluation of subfertile men. *International Braz j Urol*, *32*, 385–397.
- Sherchand, O., Baranwal, J. K., & Gelal, B. (2022). Socioeconomic Determinants of Vitamin D Status in Women. *Jundishapur Journal of Health Sciences*, 14(3), Article 3. https://doi.org/10.5812/jjhs-129396
- Shi, Z., Mao, Z., Nie, H., Geng, L., Chen, G., & Li, S. (2022). Development and validation of the health-related quality of life instrument for Chinese infertile couples: A mixed-methods study protocol. *Health and Quality of Life Outcomes*, *20*(1), 54. https://doi.org/10.1186/s12955-022-01957-3
- Shindel, A. W., Nelson, C. J., Naughton, C. K., Ohebshalom, M., & Mulhall, J. P. (2008). Sexual function and quality of life in the male partner of infertile couples: Prevalence and correlates of dysfunction. *The Journal of Urology*, *179*(3), 1056–1059. https://doi.org/10.1016/j.juro.2007.10.069
- Showell, M. G., Brown, J., Yazdani, A., Stankiewicz, M. T., & Hart, R. J. (2011). Antioxidants for male subfertility. *The Cochrane Database of Systematic Reviews*, 1, CD007411. https://doi.org/10.1002/14651858.CD007411.pub2
- Shuiqing, M., Xuming, B., & Jinghe, L. (2002). Pregnancy and its outcome in women with malformed uterus. *Chinese Medical Sciences Journal= Chung-Kuo i Hsueh k'o Hsueh Tsa Chih*, 17(4), 242–245.
- Sidorkiewicz, I., Zaręba, K., Wołczyński, S., & Czerniecki, J. (2017). Endocrine-disrupting chemicals—Mechanisms of action on male reproductive system. *Toxicology and Industrial Health*, *33*(7), 601–609.
- Sinkó, I., Mórocz, M., Zádori, J., Kokavszky, K., & Raskó, I. (2005). Effect of cigarette smoking on DNA damage of human cumulus cells analyzed by comet assay. *Reproductive Toxicology*, 20(1), 65–71.
- Skakkebaek, N. E., Rajpert-De Meyts, E., Buck Louis, G. M., Toppari, J., Andersson, A.-M., Eisenberg, M. L., Jensen, T. K., Jørgensen, N., Swan, S. H., & Sapra, K. J. (2016). Male reproductive disorders and fertility trends: Influences of environment and genetic susceptibility. *Physiological Reviews*, *96*(1), 55–97.
- Song, D., Li, X., Yang, M., Wang, N., Zhao, Y., Diao, S., Zhang, X., Gou, X., & Zhu, X. (2021). Fertility quality of life (FertiQoL) among Chinese women undergoing frozen embryo transfer. *BMC Women's Health*, 21(1), 177. https://doi.org/10.1186/s12905-021-01325-1
- Sonmezer, M., & Oktay, K. (2006). Fertility preservation in young women undergoing breast cancer therapy. *The Oncologist*, *11*(5), 422–434.
- Soran, V., Knell, A., Tharakan, T., Cayetano-Alcaraz, A., Jayasena, C., & Minhas, S. (2022). Investigating the prevalence of hypogonadism and associated cardiovascular risk of males presenting with infertility: Results from a diverse and multi-ethnic UK patient cohort. *Endocrine Abstracts*, 81. https://doi.org/10.1530/endoabs.81.EP852
- Souter, V. L., Hopton, J. L., Penney, G. C., & Templeton, A. A. (2002). Survey of psychological health in women with infertility. *Journal of Psychosomatic Obstetrics and Gynaecology*, 23(1), 41–49. https://doi.org/10.3109/01674820209093414
- Spears, N., Lopes, F., Stefansdottir, A., Rossi, V., De Felici, M., Anderson, R. A., & Klinger, F. G. (2019). Ovarian damage from chemotherapy and current approaches to its protection. *Human Reproduction Update*, *25*(6), 673–693.
- Speroff, L., & Fritz, M. A. (2005). *Clinical gynecologic endocrinology and infertility*. lippincott Williams & wilkins.

- Stansfeld, S. A., & Matheson, M. P. (2003). Noise pollution: Non-auditory effects on health. *British Medical Bulletin, 68,* 243–257. https://doi.org/10.1093/bmb/ldg033
- Stene-Larsen, K., Borge, A. I. H., & Vollrath, M. E. (2009). Maternal Smoking in Pregnancy and Externalizing Behavior in 18-Month-Old Children: Results From a Population-Based Prospective Study. *Journal of the American Academy of Child & Adolescent Psychiatry*, 48(3), 283–289. https://doi.org/10.1097/CHI.0b013e318195bcfb
- Stewart, D. E., & Ohl, D. A. (1990). Idiopathic anejaculation treated by electroejaculation. *The International Journal of Psychiatry in Medicine*, 19(3), 263–268.
- Stojanov, M., Baud, D., Greub, G., & Vulliemoz, N. (2018). Male infertility: The intracellular bacterial hypothesis. *New Microbes and New Infections*, *26*, 37–41.
- Subedi, S., Lamichhane, S., & Chhetry, M. (2016). Study of Infertile Couples Attending a Teaching Hospital in Eastern Nepal. *Jnma, Journal of the Nepal Medical Association*, 55(203), 22–25
- Subirán, N., Casis, L., & Irazusta, J. (2011). Regulation of male fertility by the opioid system. *Molecular Medicine*, 17(7), 846–853.
- Sun, H., Gong, T.-T., Jiang, Y.-T., Zhang, S., Zhao, Y.-H., & Wu, Q.-J. (2019). Global, regional, and national prevalence and disability-adjusted life-years for infertility in 195 countries and territories, 1990–2017: Results from a global burden of disease study, 2017. *Aging (Albany NY)*, 11(23), 10952–10991. https://doi.org/10.18632/aging.102497
- Szeliga, A., Calik-Ksepka, A., Maciejewska-Jeske, M., Grymowicz, M., Smolarczyk, K., Kostrzak, A., Smolarczyk, R., Rudnicka, E., & Meczekalski, B. (2021). Autoimmune Diseases in Patients with Premature Ovarian Insufficiency—Our Current State of Knowledge. *International Journal of Molecular Sciences*, 22(5), 2594.
- Tamrakar, S. R., & Bastakoti, R. (2019). Determinants of Infertility in Couples. *Journal of Nepal Health Research Council*, *17*(1), 85–89. https://doi.org/10.33314/jnhrc.1827
- Tan, R. S., & Scally, M. C. (2009). Anabolic steroid-induced hypogonadism Towards a unified hypothesis of anabolic steroid action. *Medical Hypotheses*, 72(6), 723–728. https://doi.org/10.1016/j.mehy.2008.12.042
- Tao, P., Coates, R., & Maycock, B. (2012). Investigating marital relationship in infertility: A systematic review of quantitative studies. *Journal of Reproduction & Infertility*, 13(2), 71.
- Tavoli, Z., Mohammadi, M., Tavoli, A., Moini, A., Effatpanah, M., Khedmat, L., & Montazeri, A. (2018). Quality of life and psychological distress in women with recurrent miscarriage: A comparative study. *Health and Quality of Life Outcomes*, *16*, 150. https://doi.org/10.1186/s12955-018-0982-z
- The World Health Organization Quality of Life assessment (WHOQOL): Position paper from the World Health Organization. (1995). *Social Science & Medicine (1982)*, 41(10), 1403–1409. https://doi.org/10.1016/0277-9536(95)00112-k
- Thomas-Teinturier, C., Allodji, R. S., Svetlova, E., Frey, M.-A., Oberlin, O., Millischer, A.-E., Epelboin, S., Decanter, C., Pacquement, H., Tabone, M.-D., Sudour-Bonnange, H., Baruchel, A., Lahlou, N., & De Vathaire, F. (2015). Ovarian reserve after treatment with alkylating agents during childhood. *Human Reproduction*, *30*(6), 1437–1446. https://doi.org/10.1093/humrep/dev060
- Trussell, J. (2011). Contraceptive failure in the United States. *Contraception*, 83(5), 397–404. https://doi.org/10.1016/j.contraception.2011.01.021
- Umapathy, E., Simbini, T., Chipata, T., & Mbizvo, M. (2001). Sperm characteristics and accessory sex gland functions in HIV-infected men. *Archives of Andrology*, *46*(2), 153–158.
- United Nations Population Fund 2022. (n.d.). Executive Board of the United Nations

  Development Programme, the United Nations Population Fund and the United Nations Office
  for Project Services.
- Vaamonde, D., Da Silva-Grigoletto, M. E., García-Manso, J. M., Barrera, N., & Vaamonde-Lemos, R. (2012). Physically active men show better semen parameters and hormone values than sedentary men. *European Journal of Applied Physiology*, 112, 3267–3273.
- Valsangkar, S., Bodhare, T., Bele, S., & Sai, S. (2011). An evaluation of the effect of infertility on marital, sexual satisfaction indices and health-related quality of life in women. *Journal of Human Reproductive Sciences*, 4(2), 80–85. https://doi.org/10.4103/0974-1208.86088

- van Balen, F., & Bos, H. M. W. (2009). The social and cultural consequences of being childless in poor-resource areas. *Facts, Views & Vision in ObGyn*, 1(2), 106–121.
- van Leeuwen, E., Wit, F. W., Repping, S., Eeftinck Schattenkerk, J. K. M., Reiss, P., van der Veen, F., & Prins, J. M. (2008). Effects of antiretroviral therapy on semen quality. *AIDS*, 22(5), 637. https://doi.org/10.1097/QAD.0b013e3282f4de10
- Varicocele—Symptoms and causes. (n.d.). Mayo Clinic. Retrieved 23 January 2023, from https://www.mayoclinic.org/diseases-conditions/varicocele/symptoms-causes/syc-20378771
- Vasectomy—Mayo Clinic. (n.d.). Retrieved 24 January 2023, from https://www.mayoclinic.org/tests-procedures/vasectomy/about/pac-20384580 Verhaak, C. M., Smeenk, J. M. J., Evers, Awm. al, Kremer, J. A., Kraaimaat, F. W., & Braat, D. D. M. (2007). Women's emotional adjustment to IVF: a systematic review of 25 years of research. Human Reproduction Update, 13(1), 27–36.
- Verkauf, B. (1987). Incidence, symptoms, and signs of endometriosis in fertile and infertile women. *The Journal of the Florida Medical Association*, 74(9), 671–675.
- Verma, I., Sood, R., Juneja, S., & Kaur, S. (2012). Prevalence of hypothyroidism in infertile women and evaluation of response of treatment for hypothyroidism on infertility. *International Journal of Applied and Basic Medical Research*, 2(1), 17–19. https://doi.org/10.4103/2229-516X.96795
- Walker, M. H., & Tobler, K. J. (2022). Female Infertility. In *StatPearls*. StatPearls Publishing. http://www.ncbi.nlm.nih.gov/books/NBK556033/
- Wallace, W. H. B., Thomson, A. B., & Kelsey, T. W. (2003). The radiosensitivity of the human oocyte. *Human Reproduction*, *18*(1), 117–121. https://doi.org/10.1093/humrep/deg016
- Wallace, W. H. B., Thomson, A. B., Saran, F., & Kelsey, T. W. (2005). Predicting age of ovarian failure after radiation to a field that includes the ovaries. *International Journal of Radiation Oncology\*Biology\*Physics*, *62*(3), 738–744. https://doi.org/10.1016/j.ijrobp.2004.11.038
- Wang, H., Li, J., Hao, J.-H., Chen, Y.-H., Liu, L., Yu, Z., Fu, L., Tao, F.-B., & Xu, D.-X. (2017). High serum lead concentration in the first trimester is associated with an elevated risk of small-forgestational-age infants. *Toxicology and Applied Pharmacology*, 332, 75–80. https://doi.org/10.1016/j.taap.2017.07.020
- Wang, J.-Y., Lv, X.-Q., Wu, J.-M., Tang, W.-Q., Luo, G.-Y., Liang, C.-M., Wang, D.-N., Hong, J.-F., & Cao, Y.-X. (2022). Sexual Function, Self-Esteem, and Quality of Life in Infertile Couples Undergoing in vitro Fertilization: A Dyadic Approach. *Psychology Research and Behavior Management, Volume 15*, 2449–2459. https://doi.org/10.2147/PRBM.S378496
- Watson, M., Wheatley, K., Harrison, G. A., Zittoun, R., Gray, R. G., Goldstone, A. H., & Burnett, A. K. (1999). Severe adverse impact on sexual functioning and fertility of bone marrow transplantation, either allogeneic or autologous, compared with consolidation chemotherapy alone. *Cancer*, 86(7), 1231–1239. https://doi.org/10.1002/(SICI)1097-0142(19991001)86:7<1231::AID-CNCR18>3.0.CO;2-Y
- Waylen, A. L., Metwally, M., Jones, G. L., Wilkinson, A. J., & Ledger, W. L. (2009). Effects of cigarette smoking upon clinical outcomes of assisted reproduction: A meta-analysis. *Human Reproduction Update*, 15(1), 31–44.
- Westrom, L. (1995). Effect of pelvic inflammatory disease on fertility. *Venereology: Official Publication of the National Venereology Council of Australia*, 8(4), 219–222.
- Weström, L., Bengtsson, L. P., & Mårdh, P. A. (1981). Incidence, trends, and risks of ectopic pregnancy in a population of women. *British Medical Journal (Clinical Research Ed.)*, 282(6257), 15–18. https://doi.org/10.1136/bmj.282.6257.15
- WHO laboratory manual for the examination and processing of human semen. (n.d.). Retrieved 19 January 2023, from https://www.who.int/publications-detailredirect/9789240030787
- World Health Organization. (1992). The influence of varicocele on parameters of fertility in a large group of men presenting to infertility clinics. *Fertility and Sterility*, *57*(6), 1289–1293.

- Wu, X., Cai, H., Kallianpur, A., Li, H., Yang, G., Gao, J., Xiang, Y.-B., Ji, B.-T., Zheng, W., & Shu, X.O. (2014). Impact of premature ovarian failure on mortality and morbidity among Chinese women. *PloS One*, *9*(3), e89597.
- Xue, Y., Zhang, F., Zhang, H., & Zhang, S. (2022). Time to pregnancy in women with previous ectopic pregnancy undergoing in vitro fertilization treatment: A retrospective cohort study. *Scientific Reports*, 12(1), Article 1. https://doi.org/10.1038/s41598-022-13027-1
- Yavetz, H., Yogev, L., Hauser, R., Lessing, J. B., Paz, G., & Homonnai, Z. T. (1994). Retrograde ejaculation. *Human Reproduction (Oxford, England)*, 9(3), 381–386. https://doi.org/10.1093/oxfordjournals.humrep.a138513
- Yialamas, M. A., & Hayes, F. J. (2003). Androgens and the ageing male and female. *Best Practice & Research Clinical Endocrinology & Metabolism*, 17(2), 223–236.
- Zegers-Hochschild, F., Adamson, G. D., Dyer, S., Racowsky, C., De Mouzon, J., Sokol, R., Rienzi, L., Sunde, A., Schmidt, L., & Cooke, I. D. (2017). The international glossary on infertility and fertility care, 2017. *Human Reproduction*, 32(9), 1786–1801.
- Zhang, Y., Ma, T., Su, Z., Ye, M., Tian, H., Li, J., & Liu, J. (2017). Varicoceles affect semen quality of infertile men in Southern China: A cross-sectional study of 5447 cases. *Medicine*, 96(31), e7707. https://doi.org/10.1097/MD.000000000007707
- Zhou, Z., Zheng, D., Wu, H., Li, R., Xu, S., Kang, Y., Cao, Y., Chen, X., Zhu, Y., & Xu, S. (2018). Epidemiology of infertility in China: A population-based study. *BJOG: An International Journal of Obstetrics & Gynaecology*, 125(4), 432–441.
- Zitzmann, M., & Nieschlag, E. (2000). Hormone substitution in male hypogonadism. *Molecular and Cellular Endocrinology*, 161(1–2), 73–88.
- Zorn, B., Pfeifer, M., Virant-Klun, I., & Meden-Vrtovec, H. (2005). Intracytoplasmic sperm injection as a complement to gonadotrophin treatment in infertile men with hypogonadotrophic hypogonadism. *International Journal of Andrology*, *28*(4), 202–207. https://doi.org/10.1111/j.1365-2605.2004.00519.x



#### **APPENDICES**

#### **Annex 1: Consent form and Respondent Information Sheet**

**Research Title:** Predictors of Fertility Quality of Life among infertile patients visiting two infertility centers in Kathmandu, Nepal: A cross-sectional study.

You are invited to take part in a research project. Before you decide to participate it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and do not hesitate to ask if anything is unclear or if you would like more information.

The research aims to study the quality of life among patients facing infertility issues through a self-reported questionnaire. The questionnaire includes questions on general sociodemographic factors like age, ethnicity, and education, socioeconomic factors like income, presence of health insurance, and couple characteristics related to fertility. Additionally, the questionnaire includes various questions on your physical, mental, social, relationship, and treatment-related effects of fertility issues. Furthermore, the researcher will access your medical records for medical data on the cause of infertility, treatment history, and type of undergoing treatment. The researcher has already received permission from the fertility center to access your medical records.

The study will include 456 eligible patients facing fertility problems. However, you should meet the following criteria to be eligible to participate in the study.

- 1. You are facing fertility problems and are unable to conceive after at least a year or more of regular unprotected sexual intercourse.
- 2. You are able to read and write in Nepali.
- 3. You consent to participate in the study by providing a signature on the written consent form provided by the researcher.
- 4. You have been diagnosed with infertility at the time of the study.

You are not eligible to participate in the study if you meet one or more of the following conditions.

- 1. You or your partner have or have had a history of cancer treatment.
- 2. You are taking psychiatric medications or therapy at the time of the study.
- 3. You have experienced major life events like the death of close relatives or a biological child during the past twelve months prior to the interview.
- 4. You or your partner have any form of disability.

You will be requested to fill up the questionnaire completely and reach out to the researcher in case of any inconvenience. If you (and your partner) consent, you will be given the questionnaire to fill out anonymously which you will hand over to the researcher after

completion. The researcher will check the completeness of the responses and then keep the completed responses in an envelope to be sealed in front of you.

The researcher will access your medical records to screen your eligibility for the study. You will be approached and invited to a separate room while you wait for your consultation with the doctor in the infertility center. You will be orally screened for accessing certain eligibility criteria which are not available in your medical records. You will be explained about the purpose of the study, its objective, the anonymity of responses, and the confidentiality of the final data. If you meet all the eligibility criteria, you will be requested to provide your signature on a written consent form. In case the husband is interviewed, he must also sign his name on the consent form. However, the consent form will be kept separate from the questionnaire and hence, the signature on the consent form cannot be tracked back to the questionnaires. Additionally, the questionnaire will not include your names or any other details which can identify the individual filling the questionnaire. All the information received from the questionnaire will be anonymous, kept confidential, and will not be shared with anybody. All the consent forms and questionnaires will be stored confidentially.

It would require 15-20 minutes for you to complete the questionnaire. The researcher will be available all the time in case of any queries or confusion while filling up the questionnaire. If you require any further information regarding the study, it will be provided by the principal researcher. Moreover, any advice related to the study from your side is welcome and you can contact the researcher freely at any time.

There are a few negligible risks related to the research. The study includes some questionnaires which require information regarding your sexual life. You may feel uncomfortable or inconvenient to answer the questions. However, the information is required to assess all the aspects which affect your quality of life due to fertility problems. Also, since the questionnaire doesn't consist your name, the information provided is strongly anonymous. Thus, you are requested to answer the questions without the fear of being judged or misinterpreted. In case you feel uncomfortable, or are not willing to answer the questions, you can freely reach out to the researcher and drop out of the study. Choosing not to participate in the study will not have any negative consequences on you. Your support to answer all questions in the questionnaire precisely would be greatly appreciated. In case of any concerns or questions before, during, or after filling out the questionnaires, you can speak to the researcher without any hesitation.

There will be no compensation for participation in the study. As the research study doesn't have any budget, the researcher would not be able to give you any physical presents. However, the researcher expresses gratitude for your time and effort in participation in the study. There might not be an immediate benefit to participating in the study. But the information that you provide will be very helpful for assessing the effects of infertility on Quality of life which will eventually benefit in terms of developing appropriate supportive interventions to serve the needs of infertile patients in Nepal. The information from this study will pave a path for future

studies in Nepal which can benefit other patients suffering from infertility problems.

In case of any questions or any complaints about the study or the researcher, please contact Ms. Shital Shakya, +977-9860013043 <a href="mailto:shakya.shital1996@gmail.com">shakya.shital1996@gmail.com</a> or report any misbehavior or misconduct during the study to the Research Ethics Review Committee for Research Involving Human Research Participants, Health Sciences Group, Chulalongkorn University (RECCU), Chamchuri 1 Building, 2<sup>rd</sup> Floor, 254, Phayathai Road, Pathumwan District, Bangkok 10330, Thailand, Tel./Fax. 0-2218-3202

Email: eccu@chula.ac.th

I have been explained by researcher and i	understand all the details
provided. And I voluntarily signed my name to enroll	l in this project and receive
a copy of this document.	
SignSig	n
(	()
Principal investigator	Research participant
SA AV	

จุฬาลงกรณ์มหาวิทยาลัย Chulalongkorn University

## Annex 2: Self-reported questionnaire by the respondent

#### **Patient Code:**

Q.N	Questions	Response
1.1	Sex	☐ Male ☐ Female
1.2	Age at last birthday	Answer:
1.3	Ethnicity	Answer:  Brahmin Chhetri Dalit Newar Janjati Madhesi Others
1.4	Highest level of education	Answer:  Literate (never been to school but can read and write simple Nepali language)  Basic education level (1-8)  Secondary Education level (9-12)  University Degree (Bachelors)  Post graduate degree (Masters or Higher)
1.5	What kind of family are you living in?	Metropolitan/Municipality/ VDC  Answer:  Nuclear family (with husband and children)  Joint family (with husband and his family)
1.7	What type of occupation are you involved in?	Answer:  Worker/ Laborer/ Daily wages Government/ private service oriented Self-employed (Business/Freelance/ Entrepreneur) Unemployed

1.8	How many hours do you have to	hours
1.0	work per week?	A
1.9	How easy is it for you to get time off from work to visit the	Answer:
	clinic for treatment?	<ul><li></li></ul>
	chine for treatment:	☐ Neither Easy nor difficult
		Difficult
		Very difficult
1.10	What is the total monthly	Answer:
	income of the couples?	Less than NRs. 20,000
		☐ Between NRs. 20,000 – 50,000
	China a	
		☐ More than 1,00,000
1.11	Do you have a health insurance	Answer:
	that covers the cost of infertility	No
	treatment? If yes, then what type	Community-based Health Insurance
	of health insurance are you	Health Insurance through employer
	covered by?	Social Security
		Other Privately Purchased Health
		Insurance
	If you have health insurance,	<u> </u>
	does it cover all treatment cost?	2
		No Insurance
	8	Doesn't cover the cost of fertility treatment
		Partially covered
	1011	Fully covered
1.12	Do you have any child/children?	lo No ยาลัย
	CHILLAL ONGKORI	Yes
	If yes, mention number and	MI/ E I
	gender of child/children.	Male/Female
1.13	How important it is for you to	☐ Very Important
	have a child?	☐ Not so important
1.14	Did you travel to Kathmandu	Yes
	only for fertility treatment?	□No
1.15	How supportive is your partner	Answer:
	during the infertility treatment	
	process?	☐ Not supportive at all
		☐ Not so supportive
		☐ Neither supportive nor non-supportive
	·	

		Supportive
		☐ Very supportive
1.16	Would you want to receive any	Yes
	psychological support from the	□No
	healthcare provider to facilitate	
	your infertility treatment?	

## Annex 3: Questionnaire reported by the investigator

## **Patient Code:**

2.1	Visiting the clinic for treatment	Individually
	-////	With Partner
2.2	Type of infertility	Primary
	1/2003	Secondary
2.3	Diagnosed cause of infertility	Unexplained
		Female factor
		☐ Male factor
	ZACHOROWOW.	☐ Both male and female factor
2.4	Has the patient conceived before?	Yes No
2.5	Has the patient ever given birth?	Yes
	in	□ No
2.6	Does the patient have any history of	Answer:
	pregnancy loss?	☐No History
	CHILALONGKORN UNIV	Spontaneous abortion
	OHOLALONGKOM OM	Induced abortion
	If was mantion how many times?	
2.7	If yes, mention how many times?	
2.7	For how long has the patient been	years
2.8	married to current partner?	
2.8	Since how long has the patient been	years
2.9	trying to conceive? Has the patient been under IUI	No
2.9	treatment before?	Yes
	treatment before:	Lites
	If yes, how many times.	times
2.10	Has the patient been under IVF	□No
	treatment before?	Yes
	If yes, how many times?	times

2.11	What type of infertility treatment is the patient going through in this cycle?	☐ TI ☐ IUI (H) ☐ IUI (D) ☐ IVF/ ICSI (Husband sperm) ☐ IVF/ ICSI (Donor sperm) ☐ Egg donation ☐ Embryo donation
2.12	Does the patient have any chronic	No
	disease conditions?	Yes
	If yes, mention it.	
2.13	Is the patient currently taking any	No
	medications?	Yes
	If yes, mention it.	> ::::::::::::::::::::::::::::::::::::
2.14	Does the patient have any history of	No
	reproductive tract surgery?	Yes
2.15	Is this first marriage of patient?	Yes No
2.16	Does the patient have any children	Yes No
	from previous partner?	

# Annex 4: FertiQoL Questionnaire

	For each question, check the response that is closest to your current thoughts and feelings.	Very Poor	Poor ERSITY	Neither Good nor Poor	Good	Very Goo d
A.	How would you rate your health?					
	For each question, check the response that is closest to your current thoughts and feelings.	Very Dissati sfied	Dissatisfi ed	Neither Satisfie d nor Dissatisf ied	Satisf ied	Very Satis fied
В.	Are you satisfied with your quality of life?					

	For each question, check the response that is closest to your	Compl etely	A Great Deal	Modera tely	Not Much	Not at
Q1	Are your attention and concentration impaired by the thoughts of infertility?					All
Q2	Do you think you cannot move ahead with other life goals and plans because of fertility problems?					
Q3	Do you feel drained or worn out because of fertility problems?		n h			
Q4	Do you feel able to cope with your fertility problems?					
	For each question, check the response that is closest to your current thoughts and feelings.	Very Dissati sfied	Dissatisfi ed	Neither Satisfie d Nor Dissatisf ied	Satisf ied	Very Satis fied
Q5	Are you satisfied with the support you receive from friends with regard to your fertility problems?					
Q6	Are you satisfied with your sexual relationship even though you have fertility problems?	Magae Minn N	ERSITY			
	For each question, check the response that is closest to your current thoughts and feelings.	Alway s	Very Often	Quite Often	Seldo m	Neve r
Q7	Do your fertility problem cause feelings of jealousy and resentment?					
Q8	Do you experience grief and/or feelings of loss about not being able to have a child (or more children)?					

Q9	Do you fluctuate between hope and despair because of fertility problems?					
Q10	Are you socially isolated because of fertility problems?					
Q11	Are you and your partner affectionate with each other even though you have fertility problems?					
Q12	Do your fertility problems interfere with your day-to-day work or obligations?					
Q13	Do you feel uncomfortable attending social situations like holidays and celebrations because of your fertility problems?					
Q14	Do you feel your family can					
	understand what you are going through?					
	through?  For each question, check the	An	Very	A	A	Not
	For each question, check the response that is closest to your	Extre	Very Much	Modera	A little	at
	For each question, check the response that is closest to your current thoughts and feelings.	Extre me	A V/			
	For each question, check the response that is closest to your	Extre	A V/	Modera te		at
Q15	For each question, check the response that is closest to your current thoughts and feelings.	Extre me Amou	A V/	Modera te		at
Q15	For each question, check the response that is closest to your current thoughts and feelings.  Have fertility problems strengthened your commitment to your partner?  Do you feel sad and depressed about your fertility problems?	Extre me Amou	A V/	Modera te		at
	For each question, check the response that is closest to your current thoughts and feelings.  Have fertility problems strengthened your commitment to your partner?  Do you feel sad and depressed	Extre me Amou	A V/	Modera te		at

Q19	Have fertility problems had a negative impact on your relationship with your partner?					
Q20	Do you find it difficult to talk to your partner about your feelings related to infertility?					
Q21	Are you content with your relationship even though you have fertility problems?					
Q22	Do you feel social pressure on you to have (or have more) children?					
Q23	Do your fertility problems make you angry?					
Q24	Do you feel pain and physical discomfort because of your fertility problems?					
	For each question, check the	Alway	Very	Quite	Seldo	Neve
	response that is closest to your	S	Often	Often	m	r
	current thoughts and feelings.					
T1	Does fertility treatment negatively affect your mood?		าลีย ERSITY			
T2	Are the fertility medical services you would like available to you?					
	For each question, check the response that is closest to your current thoughts and feelings.	An Extre me Amou nt	Very Much	A Modera te Amount	A little	Not at All
T3	How complicated is dealing with the procedure and/or administration of medication for your infertility treatment (s)?					

T4	Are you bothered by the effect of treatment on your daily or work-related activities?					
T5	Do you feel the fertility staff understand what you are going through?					
T6	Are you bothered by the physical side effects of fertility medications and treatment?					
	For each question, check the response that is closest to your	Very Dissati	Dissatisfi ed	Neither Satisfie	Satisf ied	Very Satis
	current thoughts and feelings.	sfied	eu	d Nor	ieu	fied
			a di M	Dissatisf ied		
T7	Are you satisfied with the quality of services available to you to address your emotional needs?					
Т8	How would you rate the surgery and/or medical treatment(s) you have received?					
T9	How would you rate the quality of information you received about medication, surgery and/or medical treatment?	มาวิทย				
T10	Are you satisfied with your interactions with fertility medical	N UNIV	ERSITY			

## **Annex 5 : Eligiblity Checklist**

S.No.	Criteria	Eligible	Non-	Comments
			Eligible	
1.	The patient consents to participate in			
	the study.			
2.	The patient can read and write in			
	Nepali.			
3.	The patient and their partner doesn't			
	have any form of physical disability.	7		
4	The patient has been unable to			
4.	conceive after at least a year of time			
	unprotected sexual intercourse.			
5.	The patient has been diagnosed for			
	infertility.			
6.	The patient or their partner doesn't			
	have a history of cancer treatment.			
	The patient or their partner doesn't			
	have a history of taking psychiatric			
	medications or psychiatric therapy.			
	จุฬาสงกรณมหาวา	ายาลย		
7.	The patient and their partner have not	IVERSITY	<b>/</b>	
	experienced any major life events like			
	death of close relatives or biological child during the past twelve months.			
	china during the past twelve months.			

#### **Annex 6 : Questionnaire Translated in Nepali**

#### भाग १

## सहभागीले भर्ने प्रश्नावली

सहभागीको परिचय नं. :	मिति:
दिइएको हरेक प्रश्नमा आफ्नो सोचाइ र भावना	लाई सबैभन्दा नजिकबाट चिनाउने प्रतिक्रियामा (ठिक) चिन
लगाउनुहोस्। तपाईँको प्रतिक्रियालाई हालको सो	चाइ र भावनाहरूसँग जोडेर उत्तर दिनुहोस्। कुनै कुनै प्रश्नहरू

एकदम तपाईंको निजी जीवनसँग गाँसिएका हुनसक्छन् तर यी प्रश्नहरू तपाईंको जीवनको सबै पक्षहरूको पूर्णरूपले मापन गर्नका लागि महत्वपूर्ण छन्।

प्र नं	प्रश्नहरू	प्रतिक्रिया
१.१	लैंगिक पहिचान	🗌 पुरूष 🔲 महिला
१.२	गएको जन्मदिनमा तपाईँ कति वर्ष हुनुभयो?	वर्ष
१.३	तपाईँ कुन समुदायबाट हुनुहुन्छ?	🔲 बाहुन 🔲 क्षेत्री
		🔲 दलित 🔲 नेवार
		🔲 जनजाति. 🔲 मधेसी
		□ अन्य
१.४	तपाईँले हालसम्ममा हासिल गर्नुभएको सबैभन्दा उच्च	🔲 उच्च अध्ययन (मास्टर वा सोभन्दा
	शैक्षिक योग्यतामा चिन्ह लगाउनुहोस्।	माथि)
		🔲 विश्वविद्यालय (ब्याचलर)
		🔲 माध्यमिक तह ( कक्षा ९ – कक्षा १२)
	<u> </u>	🔲 प्रारम्भिक तह (कक्षा १ – कक्षा ८)
	(1) (1) (1) (1) (1) (1) (1) (1) (1) (1)	🔲 साक्षर (कहिल्यै विद्यालय नगएको
		तर नेपाली भाषामा सामान्य लेखपढ
		गर्न सक्ने)
१.५	स्थायी ठेगाना लेख्नुहोस्।	जिल्ला/
	(पालिका सहित लेख्नुहोस्)	महा/उप –
	21700 1070111100111100	नगरपालिका/ गाउँपालिका
१.६	दिइएको मध्ये तपाईँ कस्तो कसिमको परिवारमा बस्नुहुन्छ?	🔲 एकल परिवार (श्रीमान्, श्रीमती)
	CHULALONGKORN UNIVERS	TV
	Oliotheolidical Olivein	🔲 संयुक्त परिवार (श्रीमान्, श्रीमती र
	* 00 ) ;	श्रीमानको परिवार)
१.७	तपाईँ कुन किसिमको पेशामा संलग्न हुनुहुन्छ?	🔲 कामदार ज्यालाम्जदुरी
		🔲 सरकारी वा प्राइभेट सेवा क्षेत्र
		स्वरोजगार
		🔲 बेरोजगार
१.८	तपाईँ दिनको कति घण्टा काम गर्नुहुन्छ?	
,,,,		घण्टा
१.९	उपचारको निम्ति क्लिनिकमा आउनको लागि कामबाट	🔲 एकदम सजिलो छ 🗌 गाऱ्हो छ
	समय निकाल्न वा छुट्टी लिन कत्तिको सजिलो छ?	🔲 सजिलो नै छ 🔲 एकदम गाऱ्हो
		<u> </u>
		🔲 सजिलो पनि होइन गाऱ्हो पनि होइन
१.१०	तपाईँ र तपाईँको जीवनसाथीको कुल मासिक आम्दानी कति	🗌 २०,००० भन्दा कम
	ন্ত?	🔲 २०,००० देखि ५०,०००
		🔲 ५०,००० देखि १,००,०००
		🗌 १.००.००० भन्दा माथि

8.88	के तपाँईले आफ्नो नाममा कुनै किसिमको स्वास्थ्य बीमा गर्नुभएको छ? यदि गर्नुभएको छ भने कुन किसिमको स्वास्थ्य बीमा गर्नुभएको छ?	□ छैन □ सामुदायिक स्तरको स्वास्थ्य बीमा □ कर्मचारी स्वास्थ्य बीमा □ सामाजिक सुरक्षा □ अन्य संस्थामार्फत किनेको बिमा				
	यदि स्वास्थ्य बीमा गर्नुभएको छ भने के त्यस बीमाले यस क्लिनिकमा उपचार गरेको खर्चको भुक्तानी गर्छ?	बीमा गरेको छैन     बीमा छ तर खर्च भुक्तानी गर्दैन     जांशिक रूपमा गर्छ     पूर्णरूपमा गर्छ				
१.१२	के तपाँईको सन्तान छ?	□				
	छ भने कति जना छोरा/छोरी उल्लेख गर्नुहोस्।	छोरा / छोरी				
१.१३	हालको अवस्थामा तपाईँको निम्ति आफ्नै सन्तान हुनु कत्तिको महत्वपूर्ण लाग्छ?	☐ एकदम महत्वपूर्ण छ ☐ त्यति धेरै महत्वपूर्ण छैन				
१.१४	के तपाईँ निसन्तान स्वास्थ्य सेवा लिनको लागि मात्रै काठमाडौँ आउनुभएको हो?	्रा हो 				
१.१५	निसन्तान उपचारको क्रममा तपाईँको जिवनसाथीले तपाईँलाई कत्तिको साथ दिनुहुन्छ?	<ul><li>□ पटक्कै साथ दिँदैन</li><li>□ खासै साथ दिँदैन</li><li>□ साथ दिने पिन होइन निदने पिन होइन</li><li>□ साथ दिन्छ</li></ul>				
	3	□ एकदम साथ दिन्छ				
१.१६	निसन्तान उपचारको क्रममा के तपाईँले स्वास्थ्यकर्मी मार्फत कुनै किसिमको मनोवैज्ञानिक परामर्श पाउने ईच्छा राख्नुभएको छ?	ੁ छ □ छैन ਭ				
	UNULALUNURURU URITERS	71 1 1				
भाग २						
गगाउन <u>ु</u> ह	हरेक प्रश्नमा आफ्नो सोचाइ र भावनालाई सबैभन्दा नजिक ोस्। तपाँईको प्रतिक्रियालाई हालको सोचहरू र भावनाहरूसँग	ा जोडेर उत्तर दिनुहोस्। कुनै कुनै प्रश्नहरू				
أحتجي	ी नागर्रेको निजी जीवनगँग गाँगियका स्नागरूका का भी ए०	टिस्ट नागर्टेको जीवनको गर्ने गथरस्क				

वि एकदम<sup>ँ</sup> नै तपाँईको निजी जीवनसँग गाँसिएका हुनसक्छन् तर यी प्रश्नहरू तपाँईको जीवनको सबै पक्षहरूको पूर्णरूपले मापन गर्नका लागि महत्वपूर्ण छन्।

दिइएको	हरेक प्रश्नमा, तपाईँको हालको सोचाइ र	एकद	कम	राम्रो पनि	रा	एकदम
भावनाहर	रूसँग नजिक रहेको प्रतिक्रियामा चिन्ह	म	जोर	होइन	म्रो	राम्रो
लगाउनुह	<u>शेस्</u> ।	कम		कमजोर		
		जोर		पनि होइन		
क)	तपाँईले आफ्नो स्वास्थ्यलाई कसरी					
	मूल्याङ्कन गर्नुहुन्छ?					
		एकद	असन्तु	सन्तुष्ट पनि	सन्तुष्ट	एकदम
		म	ष्ट	होइन		सन्तुष्ट

दिइएको	हरेक प्रश्नमा, तपाईँको हालको सोचाइ र	असन्तु		असन्तुष्ट		
	रूसँग नजिक रहेको प्रतिक्रियामा चिन्ह	ष्ट		पनि होइन		
लगाउनुह	होस्।					
ख)	के तपाईँ आफ्नो जीवनस्तरबाट सन्तुष्ट					
	हुनुहुन्छ?					
दिइएको	हरेक प्रश्नमा, तपाईँको हालको सोचाइ र	पूर्णरू	एकद	ठिकठिकै	धेरै	कदापि
	रूसँग नजिक रहेको प्रतिक्रियामा चिन्ह	पले	·म		छैन	छैन
लगाउनुह	होस्।					
प्र.१.	निसन्तानपनले तपाईँको कुनै कुरामा ध्यान					
	दिने वा केन्द्रित रहने क्षमतालाई प्रभाव					
	पारेको छ?					
प्र.२.	निसन्तान समस्याहरूको कारण के तपाईँ					
·	आफ्नो जीवनको अन्य लक्ष्यहरूमा अघि					
	बढ्न सक्दिनँ भन्ने सोच्नुहुन्छ?	7				
Я.३.	निसन्तान समस्याहरूका कारण के तपाई	1	× 🔲			
	गलेको अथवा थिकत भएको महसूस					
	गर्नुहन्छ?					
प्र.४.	के तपाईँलाई आफ्नो निसन्तान		0.			
	समस्याहरूको सामना गर्न सक्छु भन्ने					
	महसुस हुन्छ?					
दिइएको	हरेक प्रश्नमा, तपाईँको हालको सोचाइ र	एकद	असन्तु	सन्तुष्ट पनि	सन्तुष्ट	एकदम
	रूसँग नजिक रहेको प्रतिक्रियामा चिन्ह	·н	ष्ट	होइन	0-	सन्तुष्ट
लगाउनुह		असन्तु	0	असन्तुष्ट		30
3		رو		पनि होइन		
प्र.५.	के तपाईँ आफ्नो निसन्तान समस्याहरूको					
	विषयमा आफ्ना साथीहरूबाट प्राप्त					
	सहयोगसँग सन्तुष्ट हुनुहुन्छ?	and I	(A)			
प्र.६.	आफ्नो निसन्तान समस्याहरू भए पनि के					
	तपाईँ आफ्नो यौन सम्बन्धबाट सन्तुष्ट					
	हुनुहुन्छ?					
दिइएको	हरेक प्रश्नमा, तपाईँको हालको सोचाइ र	सधैँ	धेरैज	प्राय:	कहिले	कहिल्यै
भावनाह	रूसँग नजिक रहेको प्रतिक्रियामा चिन्ह		सो		काहीँ	पनि छैन
लगाउनुह	होस्। GHULALONGKORN ।	JNIVE	RSITY			
प्र.७.	के तपाईको निसन्तान समस्याले ईर्ष्या र					
	आक्रोशको भावना पैदा गर्छ?					
Я.८.	के तपाईंले सन्तान (वा धेरै सन्तानहरू)					
	जन्माउन नसकेकोमा शोक अथवा केही					
	गुमाउनु परेको भावना अनुभव गर्नुहुन्छ?					
प्र.९.	निसन्तान समस्याहरूका कारण के तपाईंमा					
	आशा र निराशा बीच उतारचढाव आएको					
	छ?					
प्र.१०.	निसन्तान समस्याका कारण के तपाईँ					
	सामाजिक रूपमा अलग्गिनु भएको छ?					
प्र.११.	के तपाई र तपाईको जीवनसाथी निसन्तान					
	समस्याका बावजुद एकअर्कालाई स्नेह र					
	माया गर्नुहुन्छ?					

प्र.१२.	के तपाईंको निसन्तान समस्याहरूले तपाईंको दैनिक कार्य वा दायित्वहरूमा					
प्र.१३.	हस्तक्षेप गरेको छ? के तपाईँ आफ्नो निसन्तान समस्याका कारण सामाजिक भेटघाट र उत्सवहरूमा सहभागी					
	हुन असहज महसुस गर्नुहुन्छ?					
प्र.१४.	के तपाँईले अनुभव गरिरहनु भएको अवस्थालाई तपाँईको परिवारले बुझ्न सक्छन् भन्ने महसुस गर्नुहुन्छ?					
दिइएको	हरेक प्रश्नमा, तपाईँको हालको सोचाइ र	एकद	धेरै	ठिक्क मात्र	अलि	पटक्कै
	रूसँग नजिक रहेको प्रतिक्रियामा चिन्ह	म नै			कति	छैन
लगाउनुह	होस।	धेरै				
प्र.१५.	के निसन्तान समस्याहरूले तपाईंको जीवनसाथीप्रतिको तपाईंको प्रतिबद्धतालाई बलियो बनाएको छ?					
प्र.१६.	के तपाँईलाई आफ्नो निसन्तान					
	समस्याहरूको बारेमा सोच्दा दु:ख तथा		>			
	निराशा महसुस हुन्छ?					
प्र.१७.	के निसन्तान समस्याहरूका कारण					
	तपाँईलाई सन्तान भएका अन्य		97			
	व्यक्तिहरूको अगाडि सानो महसुस हुन्छ?					
प्र.१८.	निसन्तान समस्याहरूका कारण के तपाई					
·	थकान भएको महसुस गर्नुहुन्छ?	8				
	3	एकद	धेरै	ठिक्क मात्र	अलि	पटक्कै
	F	म नै			कति	छैन
	ZIOONONON	धेरै				
प्र.१९.	के निसन्तान समस्याहरूले तपाईंको		B			
	जीवनसाथीसँगको सम्बन्धमा नकारात्मक		95/			
	असर पारेको छ?					
प्र.२०.	के तपाईलाई निसन्तानपनसँग सम्बन्धित					
, <u>,</u>	आफ्नो भावनाको बारेमा आफ्नो	วิทยา	าลัย			
	जीवनसाथीसँग कुरा गर्न गाह्रो लाग्छ?					
प्र.२१.	निसन्तान समस्याहरू भए पनि के तपाई	JMVE	RSHTY			
ZI. ( ).	आफ्नो वैवाहिक सम्बन्धमा सन्तुष्ट हुनुहुन्छ?					
प्र.२२.	के तपाईँलाई सन्तान (वा थप सन्तान) पाउन					
<b>Л.</b> ( \.	सामाजिक दबाव परेको महसुस हुन्छ?					]
प्र.२३.	के आफ्नो निसन्तान अवस्थाले गर्दा					
A. ( <del>Q</del> .	तपाईँलाई रिस उठ्छ?					
प्र.२४.	के निसन्तानपनका कारणले तपाईँलाई					
71. ( • .	दुखाइ तथा शारीरिक असहजता महसुस					
	हुन्छ?					_
दिदाग्को	हरेक प्रश्नमा, तपाईँको हालको सोचाइ र	सधैँ	धेरैज	प्राय:	कहिले	कहिल्यै
1467-11	CAT MATH, CHIEFT CICIFFI CHIEF C	(1-1		ZII 1.		
भावनाहर			स्रो		काहीँ	पनि नादँ
•	रूसँग नजिक रहेको प्रतिक्रियामा चिन्ह		सो		काहीँ	पनि नाइँ
लगाउनुह	रूसँग नजिक रहेको प्रतिक्रियामा चिन्ह होस्।		सो		काहीँ	पनि नाइँ
•	रूसँग नजिक रहेको प्रतिक्रियामा चिन्ह होस्। के निसन्तानपनको उपचारले तपाईँको		सो		काहीँ	पनि नाइँ
लगाउनुह	रूसँग नजिक रहेको प्रतिक्रियामा चिन्ह होस्।		सो □ □		काहीँ	पनि नाइँ

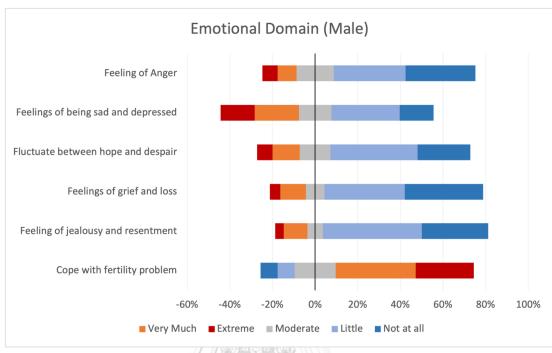
	को हरेक प्रश्नमा, तपाईँको हालको सोचाइ र ।हरूसँग नजिक रहेको प्रतिक्रियामा चिन्ह	एकद म नै	धेरै	ठिकठिकै	अलि कति	छैन
	नुहोस्।	धेरै				
Т3	तपाईँले लिइरहनुभएको निसन्तान उपचारको प्रक्रिया (औषधी सेवन, सुइ लिने) कत्तिको जटिल छ?					
T4	के निसन्तान उपचारको असरले तपाईँको दैनिक जीवन वा पेशागत गतिविधिहरूमा कुनै प्रभाव परेको छ?					
T5	के निसन्तान उपचार सेवामा संलग्न स्वास्थ्यकर्मीहरूले तपाईँको अवस्था बुझ्नुभएको महसुस गर्नुहुन्छ?					
Т6	निसन्तान उपचार र त्यस क्रममा प्रयोग हुने औषधीबाट सिर्जना हुने शारीरिक असरले तपाँईलाई दिक्क पारेको छ?					
	दिइएको हरेक प्रश्नमा, तपाईँको हालको सोचाइ र भावनाहरूसँग नजिक रहेको प्रतिक्रियामा चिन्ह लगाउनुहोस्।	एकद म असन्तु ष्ट	असन्तु ष्ट	सन्तुष्ट पनि होइन असन्तुष्ट पनि होइन	सन्तुष्ट	एकदम सन्तुष्ट
Т7	के तपाईं आफ्नो भावनात्मक आवश्यकताहरू सम्बोधन गर्न उपलब्ध सेवाहरूको गुणस्तरसँग सन्तुष्ट हुनुहुन्छ?					
Т8	आफूलाई प्राप्त निसन्तान सम्बन्धी स्वास्थ्य उपचार र सेवालाई तपाँई कसरी मूल्याङ्कन गर्नुहुन्छ?					
Т9	स्वास्थ्य तथा औषधी उपचारको क्रममा तपाँईलाई उपलब्ध गराइएको जानकारीको गुणस्तरलाई तपाँई कसरी मूल्याङ्कन गर्नुहुन्छ?		3			
T10	आफ्नो उपचारको क्रममा स्वास्थ्यकर्मीहरूसँग भएको अन्तरक्रियाबाट के तपाईँ सन्तुष्ट हुनुहुन्छ?	วิทย	าลัย าลัย			
	भाग	1 <b>5</b>	:NƏIII			
सहभागी		मेति:				
प्र.नं.	प्रश्नहरू	Τ,	प्रतिक्रिया			
7.8	निसन्तान सेवा लिन एक्लै आएको वा जीवनसाथ		ा एक्ल <u>ै</u>	जीवन	ा साथीसँग	
7.7	कुन प्रकारको निसन्तान समस्या देखिएको छ?		<u></u>		न्डेरी	
7.3	निसन्तान हुनुको कारण के हो?				नलागेको	
٧.٧	पहिले बच्चा बसेको छ कि छैन?		🗌 छ	□ छैन		
ર.પ	सन्तानलाई जन्म दिएको छ कि छैन?		🗌 छ	🗌 छैन		_
ર.६	विगतमा बच्चा खेर गएको छ कि छैन?			ntaneous abor		
	यदि छ भने कतिपटक खेर गएको छ?			cu Abortion		

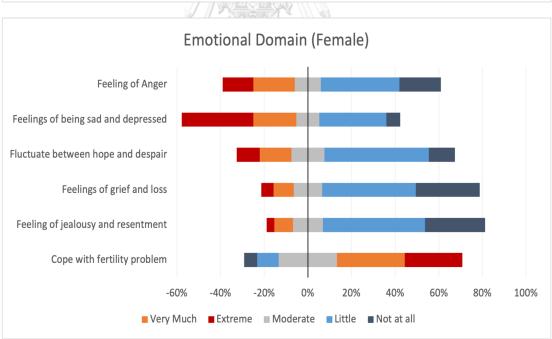
		पटक
9.6	वैवाहिक सम्बन्ध कति वर्षको भयो?	वर्ष
7.6	बच्चा पाउने प्रयास गरेको कति वर्ष भयो?	वर्ष
7.9	विगतमा IUI विधिबाट उपचार गरेको छ कि छैन? छ	□ छ 🔲 छैन
	भने कति पटक?	पटक
२.१०	विगतमा IVF विधिबाट उपचार गरेको छ कि छैन? छ	🗌 छ 🔲 छैन
	भने कति पटक?	पटक
२.११	यस महिनावारी चक्रमा कुन उपचार प्रक्रियामा	TI IUI (H)
	लागिरहनु भएको छ?	☐ IUI (D) ☐ IVF (Husband
		sperm)
		IVF (Donor sperm)
		Egg donation Embryo donation
२.१२	कुनै किसिमको दीर्घ रोग छ कि छैन?	ाछ □ छैन
(,,,		
	छ भने कुन?	
२.१३	कुनै किसिमको औषधी सेवन गरिरहेको छ कि छैन?	🗌 छ 🔲 छैन
	ਲ भने कुन?	<u> </u>
२.१४	विगतमा कुनै किसिमको प्रजनन प्रणालीसँग सम्बन्धित	🔲 छ 🔲 छैन
	शल्यक्रिया गरेको छ कि छैन?	
	<b>छ भने कुन</b> ?	
२.१५	के यो पहिलो विवाह हो?	🔲 हो 🔲 होइन
૨.શદ	के पहिलेको जीवनसाथीबाट सन्तान भएको छ?	ा छ           । छैन



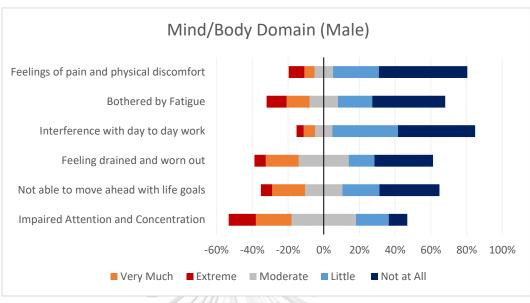
# ANNEX 7: Descriptive of FertiQol Domain Classified by Gender shown in figures.

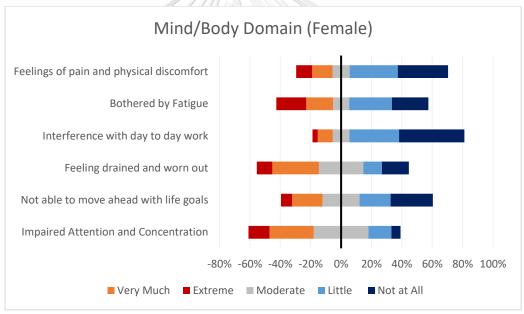
#### A. Emotional Domain



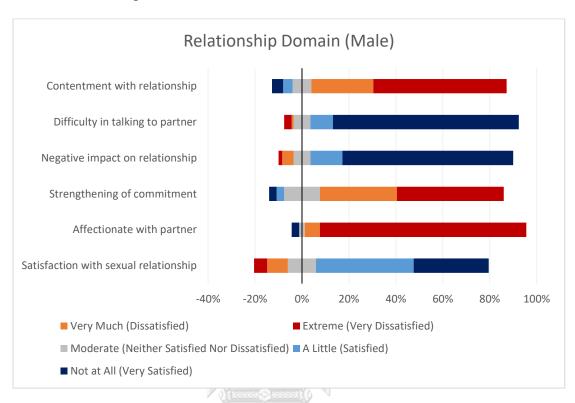


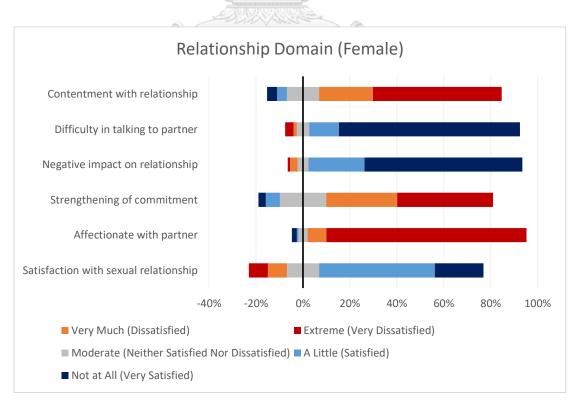
# B. Mind/Body Domain



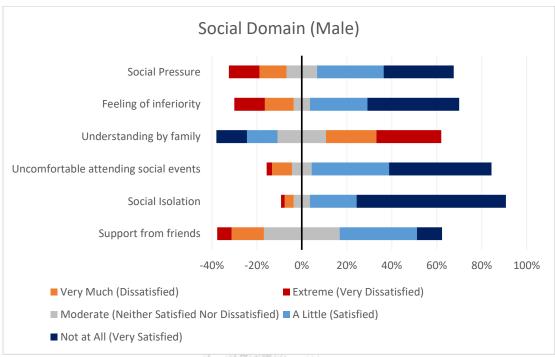


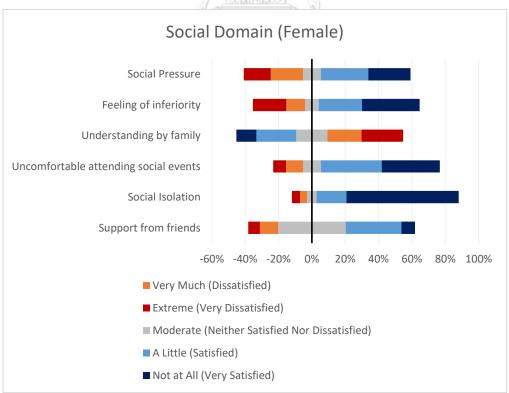
# C. Relationship Domain



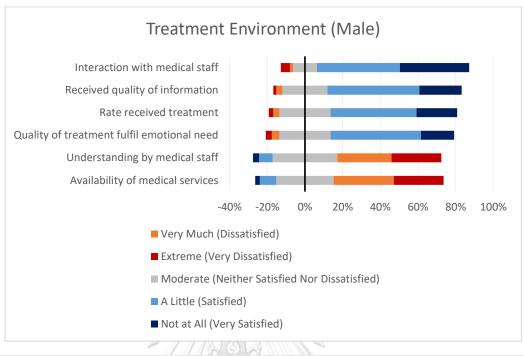


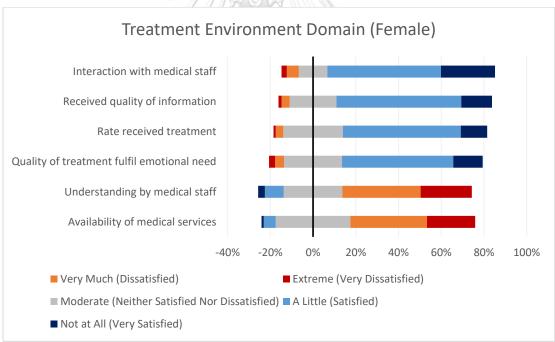
#### D. Social Domain



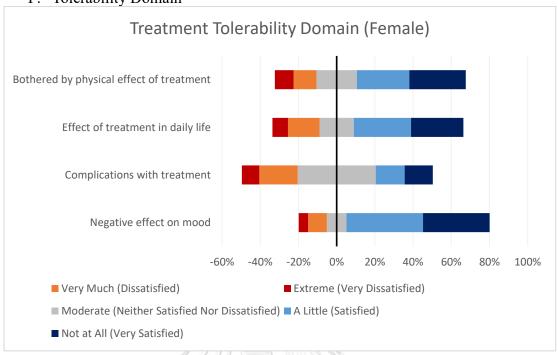


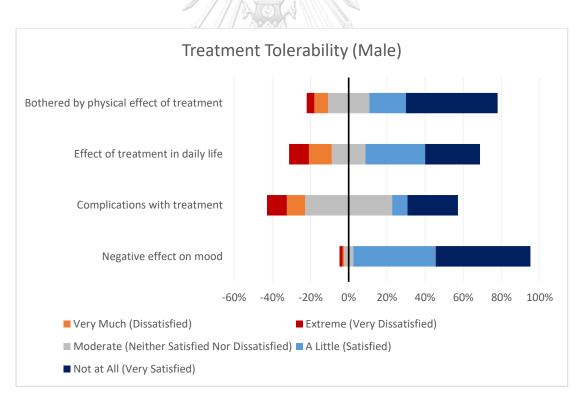
#### E. Environment Domain





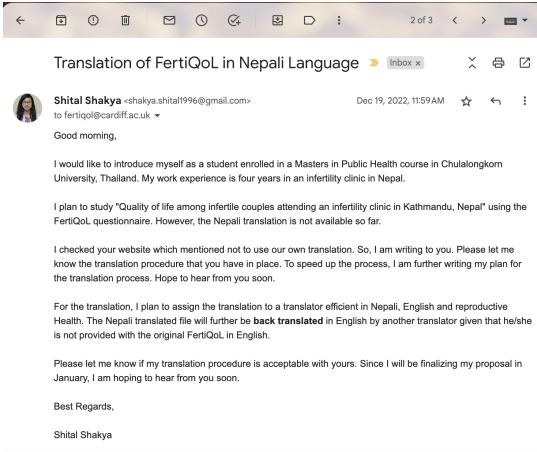
# F. Tolerability Domain





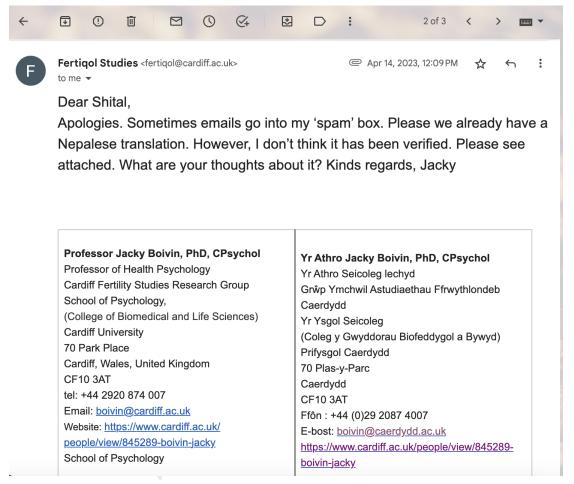
## Annex 7: Letter of permission to use FertiQoL questionnaire

#### Mail sent by the researcher



CHULALONGKORN UNIVERSITY

#### Mail received from FertiQoL studies



CHULALONGKORN UNIVERSITY

### **Annex 8: Letter of permission from Director of Clinics**



<u>Letter of permission to access medical records from Vatsalya Healthcare, Kathmandu, Nepal.</u>

**Annex 9: Gantt chart** 

	Dec	Jan	Feb	Mar	April	May	June	July
Proposal								
preparation								
Proposal								
submission								
Proposal								
Examination			Ni Ba					
Pilot test		(17						
Ethical consideration								
Data collection,								
entry, analysis,								
and defense					11 4			
writing		V	() Leccor	() ()				

# Annex 10: Budget

No	Item จุฬาลงกรณง	Cost	าลย	Unit	Total	
	CHILL AL ONCKOL	a Harre		cost		
	GHULALUNGKUI	Nepali	Thai baht		Nepali	Thai
		Rupees			Rupees	Baht
1.	Photocopies (questionnaire,	40	~ 10	500	20,000	5,200
	consent, and information sheet)					
2.	Stationary	50	~ 15	500	25,000	6,500
5.	Transportation Cost	200	~ 50	60	12,000	3,000
6.	Translation of the English	1000	~250	6	6,000	1,500
	documents to Nepali language					
7.	Book binding and preparation of	24000	~6000	1	24,000	6,000
	thesis paper					ŕ
	Total		1		87000	22,200
					Nepali	Thai
					Rupees	Baht

### **Annex 11: Researcher Information**

Principal Researcher's Name – Ms. Shital Shakya

Position – Master student of Public Health

Date of Birth – 26th Jan 1996

Home Address – Natole-20, Lalitpur, Nepal

Phone No. +977-9860013043

Email: shakya.shital1996@gmail.com



## **VITA**

**NAME** Shital Shakya

**DATE OF BIRTH** 26 January 1996

PLACE OF BIRTH Lalitpur, Nepal

INSTITUTIONS Kathmandu University

**ATTENDED** 

**HOME ADDRESS** Natole-20, Lalitpur, Nepal.

**PUBLICATION** Swastika Hada, Rojeena Koju Shrestha, Pushpa Parajuli,

Jenisha Timalsina, Supriya Dhungel, Shital Shakya, Manika Humagain (2018) "Prevalence of Cardiovascular Disease and Prescribing Pattern of Drugs in Patients admitted in Cardiovascular Unit in Dhulikhel Hospital", International Journal of Advances in Science, Engineering and Technology (IJASEAT), pp. 23-26, Volume-6, Issue-

4, Spl. Iss-2

AWARD RECEIVED None

จุฬาลงกรณ์มหาวิทยาลัย

CHULALONGKORN UNIVERSITY