Chapter IV

Results

1. Optimum serum sampling time of once-daily gentamicin dosage regimen and its relatively reference concentration for monitoring nephrotoxicity

1.1 Characteristics of all patients

Fifty admitted patients who met the criteria in this study were monitored. Table 4.1 showed the characteristics of patients. Eighteen and Thirty-two of the patients were hospitalized for the general medical service and the general surgical service in Rajavithi Hospital , respectively. The patients were 25 men and 25 women, their mean age was 49.8 ± 17.9 years (range, 18 - 87 years). The mean dosing weight of the patients was 53.3 ± 7.6 kilograms (range, 40 - 73 kilograms). The mean initial serum creatinine was 0.9 ± 0.2 mg/dl (range, 0.5 - 1.4 mg/dl) and the mean initial estimated creatinine clearance was 72.4 ± 25.9 ml/min (range, 27.4 -128.8 ml/min).

The prescribed doses of once-daily gentamicin by physicians ranged from 120 to 240 mg/day (2.5 - 5.6 mg/kg/day) with the mean value of 210.8 ± 39.8 mg/day (3.97 ± 0.68 mg/kg/day). The doses of twenty-four (48%) patients were prescribed according to the nomogram. Fifteen (30%) and eleven (22%) patients were prescribed with the doses which were higher and lower than 10% of the recommended doses according to the nomogram , respectively.

The median duration of gentamicin therapy was 6 days (range, 4 - 15 days). The percentages of patients as classified by the duration of gentamicin therapy were as follows: 4 to 5 days, 34% ; 6 to 7 days, 26% ; 8 to 10 days, 24% ; 11 to 14 days,

12%; > 14 days, 4%. Fourty percent of the patients received 8 or more days of therapy.

Table 4.2 displayed some clinical status of the patients which may affect the clinical responses of gentamicin therapy.Twelve patients had initial serum potassium levels below 3.5 mEq/L and nine patients had initial serum magnesium levels below 1.7 mg/dl. Six patients had diabetes mellitus , eight patients met the criteria of liver dysfunction , and four patients met the criteria of volume depletion.None of the patients got shock , or concurrent used other nephrotoxic agents ie. amphotericin B , cisplatin , cyclosporin, furosemide more than 160 mg/day , radiocontrast, vancomycin.

Table 4.3 displayed the indication of treatment and clinical responses of the patients. Thirty-eight patients met the criteria for favourable clinical efficacy and twenty-seven patients met the criteria for favourable bacteriological efficacy. The bacteriological efficacy could not evaluated in 13 patients since they had no positive culture at the start of therapy.

The criteria indicated the development of nephrotoxicity was serum creatinine increased for more than or equal to 0.5 mg/dl. from the initial value. In this study , Four patients (8%) showed nephrotoxicity. The changes in serum creatinine levels , serum potassium levels and serum magnesium level from the initial values of the patients in the nephrotoxic group and non-nephrotoxic group are shown in table 4.4A , 4.4B and 4.4C . The four nephrotoxic patients had serum creatinine levels increased according to the criteria after the last day of treatment,i.e., at the tenth day, the fourteenth day , the seventeenth day, and the twentieth day after the starting of gentamicin treatment. All nephrotoxic patients were hypokalemia during the treatment. Three of them had serum potassium levels decreased equal to 3.5 mEq/L since the seventh day of the treatment , one of them had initial serum potassium level lower than the normal range. All nephrotoxic patients were also hypomagnesemia , the

serum magnesium levels of three patients in nephrotoxic group decreased lower than 1.7 mg/dl since the tenth day of the treatment , one of them had initial serum magnesium level less than the normal range.

Comparison of nephrotoxicity and clinical efficacy between patients not using doses according to the nomogram with patients using doses according to nomogram found no significant differences ($P > 0.05$), as shown in Table 4.5 and 4.6.

Table 4.1 Characteristic of all patients

NO.	Ward	SEX	AGE (year)	Dosing Weight (Kg)	SCr (mg/dl)	ClCr (ml./min)	Dose (mg/day)	Dose (mg/kg/day)	Duration (day)
1*	med.	m	20	60.0	1.0	100.0	240	4.0	9
2*	med.	m	43	50.0	0.6	112.3	240	4.8	9
3*	surg.	m	53	60.0	1.3	55.7	240	4.0	6
4*	med.	f	70	47.0	0.9	43.2	120	2.6	5
5	surg.	m	72	41.0	1.3	29.8	120	2.9	6
6*	surg.	m	51	52.0	1.0	64.3	200	3.8	7
7*	med.	f	41	55.0	0.5	128.5	240	4.4	9
8	surg.	f	48	40.0	0.8	54.3	180	4.6	8
9*	med.	f	28	44.0	0.7	83.1	200	4.5	6
10*	med.	f	29	57.5	0.7	107.6	240	4.2	10
11*	med.	f	37	58.0	0.9	88.2	180	3.1	5
12*	surg.	f	28	49.0	0.9	80.9	240	4.9	7
13*	med.	f	32	51.0	1.0	65.0	240	4.7	7
14*	surg.	f	47	63.4	0.8	87.0	240	3.8	6
15*	surg.	f	44	55.0	0.8	77.9	240	4.4	7
16*	surg.	m	45	73.0	0.8	120.4	240	3.3	6
17	med.	m	62	67.0	1.1	65.9	200	3.0	5
18*	med.	f	35	51.0	1.1	70.2	200	3.9	8
19	surg.	f	56	54.0	0.8	66.9	240	4.4	4
20*	surg.	f	82	40.0	1.0	27.4	120	3.0	12
21*	med.	f	34	48.0	0.8	75.1	240	5.0	5
22*	med.	m	69	54.0	0.7	76.1	240	4.4	10
23*	med.	f	35	47.0	0.5	116.5	240	5.1	4
24*	med.	f	52	47.0	0.8	69.8	200	4.3	5
25	surg.	m	21	53.0	1.0	87.6	240	4.5	11
26*	surg.	m	48	59.0	1.1	68.5	240	4.1	6
27	surg.	m	59	57.0	1.1	58.3	240	4.2	12
28*	surg.	f	19	43.0	0.7	87.7	240	5.6	9

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NO.	Ward	SEX	AGE (year)	Dosing Weight (Kg)	SCr (mg/dl)	ClCr (ml./min)	Dose (mg/day)	Dose (mg/kg/day)	Duration (day)
29	surg.	m	40	52.0	0.9	80.2	240	4.6	5
30*	surg.	m	55	62.0	1.1	66.5	240	3.9	8
31*	surg.	m	71	45.0	0.9	47.9	180	4.0	5
32*	surg.	f	18	56.0	1.1	73.3	240	4.3	8
33*	med.	f	36	49.0	0.7	85.9	180	3.7	14
34*	surg.	f	65	58.8	0.8	65.1	240	4.1	15
35	surg.	m	66	56.0	1.4	41.1	180	3.2	5
36	surg.	m	46	58.0	1.0	75.7	240	4.1	5
37*	surg.	m	44	60.0	1.2	66.7	240	4.0	11
38*	surg.	m	76	55.0	1.2	40.7	180	3.3	15
39*	surg.	m	70	48.0	1.1	42.4	180	3.8	12
40	surg.	f	87	61.0	1.0	38.2	160	2.9	5
41*	surg.	f	42	48.0	0.9	69.4	200	4.2	6
42*	med.	f	70	40.0	0.9	41.3	160	4	5
43*	med.	f	77	43.0	0.7	45.7	120	2.8	4
44	surg.	m	39	64.3	0.7	128.8	240	3.7	4
45	surg.	f	34	62.0	1.1	70.5	240	3.9	10
46	surg.	m	58	49.0	0.9	62.0	240	4.9	9
47*	surg.	m	69	51.0	1.0	50.3	180	3.5	6
48*	surg.	m	46	65.0	0.9	94.3	240	3.7	6
49*	surg.	m	44	57.0	0.6	126.6	240	4.2	5
50*	med.	m	81	49.0	1.0	40.2	120	2.5	4
Mean	med=18	f=25	49.88	53.3	0.9	72.42	210.8	3.97	7.42
SD	surg.=32	m=25	17.98	7.58	0.20	25.88	39.84	0.68	2.96
(Range)			(18-87)	(40-73)	(0.5-1.4)	(27.4-128.8)	(120-240)	(2.5-5.6)	(4-15)
Mean	med=17	f=21	52.8	52.8	0.9	68.5	210	4.0	7.7
SD*	surg.=20	m=16	18.7	6.7	0.2	24.1	39.1	0.7	3.4
(Range)*			(18-82)	(40-73)	(0.5-1.3)	(27.4-128.5)	(120-240)	(2.5-5.6)	(4-15)

* : Data of patient with documented infection

Table 4.2 Clinical status of patients

NO.	Nephro-toxicity	Hypokalemia before Tx.	Hypomagnesemia before Tx.	DM.	Liver dysfunction	Shock	Volume Depletion
1	NO	NO	NO	NO	NO	NO	NO
2	NO	YES	NO	NO	NO	NO	NO
3	NO	NO	YES	YES	NO	NO	NO
4	NO	NO	NO	NO	NO	NO	NO
5	NO	NO	YES	NO	NO	NO	NO
6	NO	NO	NO	YES	NO	NO	NO
7	NO	YES	YES	NO	NO	NO	NO
8	YES	YES	NO	NO	YES	NO	NO
9	NO	YES	NO	NO	YES	NO	YES
10	NO	NO	NO	NO	YES	NO	NO
11	NO	YES	NO	NO	NO	NO	NO
12	NO	NO	NO	NO	NO	NO	NO
13	NO	YES	NO	NO	NO	NO	NO
14	NO	YES	NO	NO	NO	NO	NO
15	NO	NO	NO	NO	NO	NO	NO
16	NO	NO	NO	NO	NO	NO	NO
17	NO	NO	NO	NO	NO	NO	NO
18	NO	NO	NO	NO	NO	NO	NO
19	NO	NO	NE	NO	NO	NO	NO
20	NO	YES	YES	NO	NO	NO	NO
21	NO	NO	YES	NO	YES	NO	YES
22	NO	YES	NO	NO	NO	NO	NO
23	NO	NO	NO	NO	NO	NO	NO
24	NO	NO	NO	NO	YES	NO	NO
25	NO	NO	NO	NO	NO	NO	NO

continued.....

NO.	Nephro-toxicity	Hypokalemia before Tx.	Hypomagnesemia before Tx.	DM.	Liver dysfunction	Shock	Volume Depletion
26	NO	NO	NO	NO	YES	NO	NO
27	NO	NO	YES	NO	NO	NO	NO
28	NO	NO	NO	NO	NO	NO	NO
29	NO	NO	NO	NO	NO	NO	NO
30	NO	NO	NO	YES	NO	NO	NO
31	NO	NO	YES	NO	YES	NO	NO
32	NO	NO	NO	NO	NO	NO	NO
33	NO	NO	NO	NO	NO	NO	NO
34	YES	NO	YES	YES	NO	NO	NO
35	NO	NO	NO	NO	NO	NO	NO
36	NO	NO	NO	NO	NO	NO	NO
37	YES	NO	NO	NO	NO	NO	NO
38	YES	NO	NO	NO	NO	NO	YES
39	NO	NO	NO	NO	NO	NO	NO
40	NO	YES	NO	NO	NO	NO	NO
41	NO	NO	NO	NO	NO	NO	NO
42	NO	YES	NO	NO	NO	NO	NO
43	NO	YES	NO	YES	NO	NO	NO
44	NO	NO	NO	NO	NO	NO	NO
45	NO	NO	NO	NO	NO	NO	NO
46	NO	NO	NO	NO	NO	NO	NO
47	NO	NO	YES	NO	YES	NO	NO
48	NO	NO	NO	YES	NO	NO	NO
49	NO	NO	NO	NO	NO	NO	YES
50	NO	NO	NO	NO	NO	NO	NO
Total	4	12	9	6	8	0	4

NE : Not Evaluate

Table 4.3 Indication and clinical responses of patients

NO.	Indication	Favourable clinical efficacy	Favourable bacteriological efficacy	Nephrotoxicity
1*	Pneumonia + Bacteremia	No	No	No
2*	Empyema lung	No	No	No
3*	Abscess at right foot	Yes	Yes	No
4*	UTI	Yes	Yes	No
5	Duodenal obstruction	Yes	NE	No
6*	Wound	Yes	Yes	No
7*	UTI	Yes	Yes	No
8	Obstructive jaundice	No	NE	Yes
9*	UTI	Yes	Yes	No
10*	UTI	Yes	Yes	No
11*	UTI	No	No	No
12*	Acute Cholecystitis	Yes	Yes	No
13*	UTI + Bacteremia	Yes	Yes	No
14*	Acute Cholecystitis	Yes	Yes	No
15*	Empyema Gall bladder	Yes	Yes	No
16*	Abscess	Yes	Yes	No
17	Febrile Neutropenia	Yes	NE	No
18*	UTI	Yes	Yes	No
19	Appendiceal Abscess	Yes	NE	No
20*	Bacteremia	Yes	Yes	No
21*	UTI	Yes	Yes	No
22*	Pneumonia	No	No	No
23*	UTI	No	No	No
24*	UTI	Yes	Yes	No
25	Burn	Yes	NE	No
26*	Perianal abscess	Yes	Yes	No
27	Esophageal obstruction	Yes	NE	No
28*	Acute pancreatitis	No	No	No

continued.....

NO.	Indication	Favourable clinical efficacy	Favourable bacteriological efficacy	Nephrotoxicity
29	DU. perforate	Yes	NE	No
30*	Cellulitis	Yes	Yes	No
31*	Empyema Gall bladder	Yes	Yes	No
32*	Intraabdominal abscess	Yes	Yes	No
33*	Empyema lung	Yes	Yes	No
34*	Cellulitis	Yes	Yes	Yes
35	Cholecystitis	Yes	NE	No
36	Cholangitis	Yes	NE	No
37*	Cellulitis	No	No	Yes
38*	Wound + Bacteremia	Yes	Yes	Yes
39*	Cholangitis e CBD stone	Yes	Yes	No
40	Cholangitis	Yes	NE	No
41*	Empyema Gall bladder	Yes	Yes	No
42*	UTI	Yes	Yes	No
43*	UTI	No	No	No
44	PU. perforate	No	NE	No
45	Cholangitis	Yes	NE	No
46	CBD stone	Yes	NE	No
47*	Empyema Gall bladder	Yes	Yes	No
48*	Cellulitis	Yes	Yes	No
49*	PU. perforate	No	No	No
50*	Pneumonia	No	No	No
Total		38	27	4
Total*		27	27	3

* : Documented infection

NE : Not Evaluate

Table 4.4A Serum creatinine level of the patients at different days

NO.	Serum Creatinine Level (mg/dl)							Nephrotoxicity
	Day0	Day3	Day7	Day10	Day14	Day17	Day20	
1	1.0	1.0	1.0	0.9	1.0	0.9	-	No
2	0.6	0.6	0.7	0.7	-	-	-	No
3	1.3	1.3	1.4	1.4	-	-	-	No
4	0.9	0.9	1.0	-	-	-	-	No
5	1.3	1.4	1.4	1.4	-	-	-	No
6	1.0	1.1	1.0	-	-	-	-	No
7	0.5	0.6	0.7	0.6	0.7	-	-	No
8	0.8	0.8	0.8	1.3	1.5	-	-	Yes
9	0.7	1.1	1.0	-	-	-	-	No
10	0.7	0.7	0.8	0.7	-	-	-	No
11	0.9	0.8	0.7	-	-	-	-	No
12	0.9	1.1	0.9	-	-	-	-	No
13	1.0	0.9	0.8	-	-	-	-	No
14	0.8	0.7	0.9	1.0	-	-	-	No
15	0.8	0.7	0.7	-	-	-	-	No
16	0.8	0.8	0.8	0.8	-	-	-	No
17	1.1	1.1	1.0	-	-	-	-	No
18	1.1	1.0	1.0	0.9	-	-	-	No
19	0.8	0.8	-	-	-	-	-	No
20	1.0	0.9	0.9	0.9	0.9	-	-	No
21	0.8	0.8	0.8	-	-	-	-	No
22	0.7	0.8	0.8	0.8	-	-	-	No
23	0.5	0.5	0.6	-	-	-	-	No
24	0.8	0.9	0.8	-	-	-	-	No
25	1.0	1.0	1.0	0.7	0.6	-	-	No

continued.....

NO.	Serum Creatinine Level (mg/dl)							Nephrotoxicity
	Day0	Day3	Day7	Day10	Day14	Day17	Day20	
26	1.1	1.0	0.8	0.9	-	-	-	No
27	1.1	1.1	1.1	1.1	1.0	-	-	No
28	0.7	0.9	0.6	0.6	0.6	-	-	No
29	0.9	0.9	0.8	-	-	-	-	No
30	1.1	1.0	1.0	0.9	-	-	-	No
31	0.9	1.0	0.9	1.0	-	-	-	No
32	1.1	0.7	0.5	0.5	-	-	-	No
33	0.7	0.7	0.6	0.7	0.6	-	-	No
34	0.8	0.8	0.8	0.7	1.0	1.8	2.3	Yes
35	1.4	1.4	1.4	-	-	-	-	No
36	1.0	1.1	-	-	-	-	-	No
37	1.2	1.2	1.1	1.1	1.8	2.1	-	Yes
38	1.2	1.2	1.5	1.2	1.2	1.3	1.7	Yes
39	1.1	1.1	0.8	1.0	1.1	-	-	No
40	1.0	1.0	1.0	1.1	-	-	-	No
41	0.9	1.0	0.9	-	-	-	-	No
42	0.8	1.0	-	-	-	-	-	No
43	0.7	0.8	0.9	1.1	-	-	-	No
44	0.7	0.7	-	-	-	-	-	No
45	1.1	0.8	0.8	1.1	1.1	1.1	-	No
46	0.9	1.0	1.0	1.0	-	-	-	No
47	1.0	1.1	0.9	-	-	-	-	No
48	0.9	0.9	0.9	0.9	0.8	-	-	No
49	0.6	0.6	0.6	-	-	-	-	No
50	1.0	1.0	-	-	-	-	-	No

Table 4.4B Serum potassium levels of the patients at different days

NO.	Serum Potassium levels (mEq/L)					Nephrotoxicity
	Day0	Day3	Day7	Day10	Day14	
1	3.5	2.6	3.7	3.7	3.5	No
2	3.1	5.1	3.5	3.7	-	No
3	3.9	4.2	4.9	-	-	No
4	4.4	5.7	5.2	-	-	No
5	4.3	4.0	4.1	-	-	No
6	3.8	3.7	3.6	-	-	No
7	3.3	3.3	4.3	4.4	-	No
8	3.4	3.1	3.3	3.1	-	Yes
9	3.3	3.7	-	-	-	No
10	4.6	3.5	4.5	3.8	-	No
11	3.4	4.2	4.2	-	-	No
12	4.3	3.8	3.7	-	-	No
13	3.3	3.4	4.1	-	-	No
14	3.1	5.2	4.3	5.2	-	No
15	4.7	3.3	5.1	-	-	No
16	5.3	4.3	4.8	-	-	No
17	3.7	4.3	4.0	-	3.6	No
18	4.4	3.9	3.8	4.2	-	No
19	4.0	4.1	-	-	-	No
20	2.9	3.5	3.7	3.8	-	No
21	3.7	3.4	3.2	-	-	No
22	3.4	3.8	3.9	3.8	-	No
23	4.1	4.7	3.7	99	-	No
24	3.7	3.8	3.5	99	-	No
25	3.6	4.0	4.4	4.1	-	No

continued.....

NO.	Serum Potassium levels (mEq/L)					Nephrotoxicity
	Day0	Day3	Day7	Day10	Day14	
26	3.8	3.2	3.0	-	-	No
27	4.2	3.5	4.7	5.3	-	No
28	3.8	3.5	3.5	3.5	-	No
29	4.0	3.9	4.2	-	-	No
30	4.0	3.7	3.6	-	-	No
31	4.0	3.2	3.6	-	-	No
32	4.3	3.8	3.7	-	-	No
33	4.4	3.9	3.8	4.2	3.6	No
34	4.5	3.7	3.5	2.9	2.6	Yes
35	4.1	3.7	4.4	-	-	No
36	3.9	4.2	4.5	-	-	No
37	4.6	3.7	3.5	3.1	2.7	Yes
38	4.1	3.3	3.5	2.7	3.1	Yes
39	4.8	3.7	3.7	4.4	4.6	No
40.	2.6	4.2	3.8	4.1	-	No
41	4.7	3.5	5.0	-	-	No
42	3.2	3.4	3.5	-	-	No
43	3.0	4.1	-	4.9	-	No
44	3.8	3.6	-	-	-	No
45	4.2	3.5	4.3	4.2	-	No
46	5.2	99	4.1	4.1	-	No
47	4.0	3.2	3.6	-	-	No
48	4.0	3.6	4.0	-	-	No
49	4.3	3.2	3.5	-	-	No
50	3.9	3.7	-	-	-	No

Table 4.4C Serum magnesium levels of the patients at different days

NO.	Serum Magnesium levels (mg/dl)					Nephrotoxicity
	Day0	Day3	Day7	Day10	Day14	
1	1.8	1.8	1.7	1.7	1.7	No
2	1.8	1.8	1.8	1.7	-	No
3	1.6	1.5	1.6	-	-	No
4	1.9	2.0	2.0	-	-	No
5	1.3	1.3	1.5	-	-	No
6	1.8	1.8	1.8	-	-	No
7	1.5	1.5	1.8	2.1	-	No
8	1.7	1.7	1.7	1.5	-	Yes
9	2.5	2.7	-	-	-	No
10	2.0	2.1	2.2	2.3	-	No
11	1.7	1.7	1.7	-	-	No
12	1.9	1.9	1.8	-	-	No
13	1.8	1.7	1.8	-	-	No
14	1.8	1.8	1.7	1.8	-	No
15	2.3	2.3	2.4	-	-	No
16	2.0	2.0	1.9	-	-	No
17	1.8	1.8	1.7	-	-	No
18	1.9	1.9	1.8	2.1	1.9	No
19	-	-	-	-	-	No
20	1.5	1.4	1.6	1.6	-	No
21	1.4	1.4	1.4	-	-	No
22	1.9	2.2	2.2	2.2	-	No
23	1.9	1.9	1.8	-	-	No
24	1.8	1.8	1.8	-	-	No
25	1.7	2.2	2.2	2.0	-	No

continued.....

NO.	Serum Magnesium levels (mg/dl)					Nephrotoxicity
	Day0	Day3	Day7	Day10	Day14	
26	1.8	1.8	1.8	-	-	No
27	1.1	1.8	2.6	3.4	-	No
28	2.0	2.0	1.8	2.1	-	No
29	1.8	1.8	1.9	-	-	No
30	1.7	1.8	1.8	-	-	No
31	1.6	1.6	1.5	-	-	No
32	1.9	1.9	1.8	-	-	No
33	1.9	1.9	1.8	2.1	1.9	No
34	1.6	1.6	1.6	1.3	1.5	Yes
35	1.8	1.8	1.8	-	-	No
36	1.8	1.7	1.8	-	-	No
37	1.7	1.7	1.7	1.6	1.4	Yes
38	1.9	1.9	1.8	1.5	1.5	Yes
39	1.9	1.9	2.2	2.2	2.2	No
40	1.9	1.9	1.9	2.1	-	No
41	2.2	2.2	2.2	-	-	No
42	1.7	1.7	1.8	-	-	No
43	2.2	1.7	-	1.8	-	No
44	1.8	1.9	-	-	-	No
45	2.2	2.4	2.4	2.4	-	No
46	2.0	-	1.9	-	-	No
47	1.6	1.5	1.5	-	-	No
48	1.9	1.8	1.9	-	-	No
49	1.7	1.8	2.0	-	-	No
50	1.9	1.9	-	-	-	No

Table 4.5 Comparison of the nephrotoxicity between patients not using doses according to the nomogram and patients using doses according to nomogram

Dose of gentamicin	Nephrotoxic Total n = 4	Non-nephrotoxic Total n = 46	P*
Higher than the nomogram	2	13	0.574
According to the nomogram	2	22	1.000
Lower than the nomogram	0	11	0.563

* By Fisher's exact test

Table 4.6 Comparison of the clinical efficacy between patients not using doses according to the nomogram and patients using doses according to nomogram

Dose of gentamicin	Favourable clinical efficacy	Unfavourable clinical efficacy	P*
	Total n = 38	Total n = 12	
Higher than the nomogram	14	1	0.079
According to the nomogram	17	7	0.624
Lower than the nomogram	7	4	0.424

* By Fisher's exact test

1.2 Optimum serum sampling time and its relatively reference concentration for monitoring nephrotoxicity

After starting once-daily gentamicin treatment for 3 days , 3 ml. of blood samples for determination of serum gentamicin concentration were obtained sequentially from all patients at 1 hr. , 2 hr. , 6 hr. , 8 hr. and 24 hr. after beginning of gentamicin IV.infusion.

Table 4.7A and 4.7B showed the serum gentamicin levels at different time points of nephrotoxic patients and non-nephrotoxic patients , respectively. The serum gentamicin levels at 24-hr after starting infusion of 41 (82%) patients were less than 0.3 mg/L which too low to be detected by the TDx assay. The highest concentration found at 24-hr was 1.6 mg/L.

Figure 4.1 and table 4.8 showed comparison of the mean concentrations at different time point between nephrotoxic and non-nephrotoxic groups. The 2-hr, 6-hr and 8-hr serum gentamicin levels in the nephrotoxic group were all significantly higher than the non-nephrotoxic group. The 24-hr serum gentamicin level could not be compared since only 9 out of the 50 patients included in this study had their serum levels which were still detectable at 24 hours. Among these 9 patients , 3 of them showed nephrotoxicity.

Figure 4.2 - 4.6 displayed the percentage of nephrotoxicity in different patient groups classified by serum gentamicin levels at each time points. The percentage of nephrotoxicity was higher in patients with higher serum gentamicin level at 2-hr , 6-hr , 8-hr and 24-hr.

Table 4.9 - 4.12 showed percentages of patients showing nephrotoxicity and not showing nephrotoxicity with different 2-hr , 6-hr , 8-hr , 24-hr serum gentamicin levels, respectively. The serum gentamicin levels were examined to determine for the minimum concentration that would cause a patient to develope nephrotoxicity.

The 6-hr serum gentamicin levels of less than 5.0 mg/L and less than 3.0 mg/L provided the percentages of patients showing nephrotoxicity significantly different from the higher serum drug levels at P= 0.005 and P= 0.021, respectively. Two (4%) of the patients with a 6-hr serum gentamicin level of less than 5.0 mg/L showed nephrotoxicity while none of the patients with 6-hr serum gentamicin level of less than 3.0 mg/L showed nephrotoxicity.

The 8-hr serum gentamicin levels of less than 2.5 mg/L and less than 2 mg/L provided the percentages of patients showing nephrotoxicity significantly different from the higher serum drug levels at P= 0.049 and P=0.01, respectively . And none of the patients with a 8-hr serum gentamicin level of less than 2.0 mg/L showed nephrotoxicity .

The 24-hr serum gentamicin levels of less than 0.3 mg/L provided the percentage of patients showing nephrotoxicity significantly different from the higher serum drug levels , one (2%) of the patients showed nephrotoxicity.

The influence of other clinical factors on nephrotoxicity was also examined as shown in table 4.13. The mean age , baseline serum creatinine level , baseline creatinine clearance and daily dosage of the patients in the nephrotoxic group were not significantly different from the patients in the non-nephrotoxic group. Using a univariate analysis , the only other significantly clinical factor besides serum gentamicin levels that showed statistically significantly different between the patients in the nephrotoxic and non-nephrotoxic groups was the duration of treatment. The longer duration of treatment showed a higher risk of developing nephrotoxicity.

Table 4.7A The serum gentamicin levels at different sampling times of nephrotoxic patients

NO.	Cp1	Cp2	Cp6	Cp8	Cp24
	(mg/L)	(mg/L)	(mg/L)	(mg/L)	(mg/L)
8	11.4	7.4	3.3	2.3	<0.3
34	12.0	8.7	3.8	2.7	0.4
37	11.3	9.0	5.1	3.8	0.6
38	14.0	12.6	6.5	5.1	1.4
mean	12.2	9.4	4.7	3.5	
SD	1.3	2.2	1.4	1.3	
(range)	(11.3-14.0)	(7.4 - 12.6)	(3.3 - 6.5)	(2.3 - 5.1)	(<0.3 - 1.4)

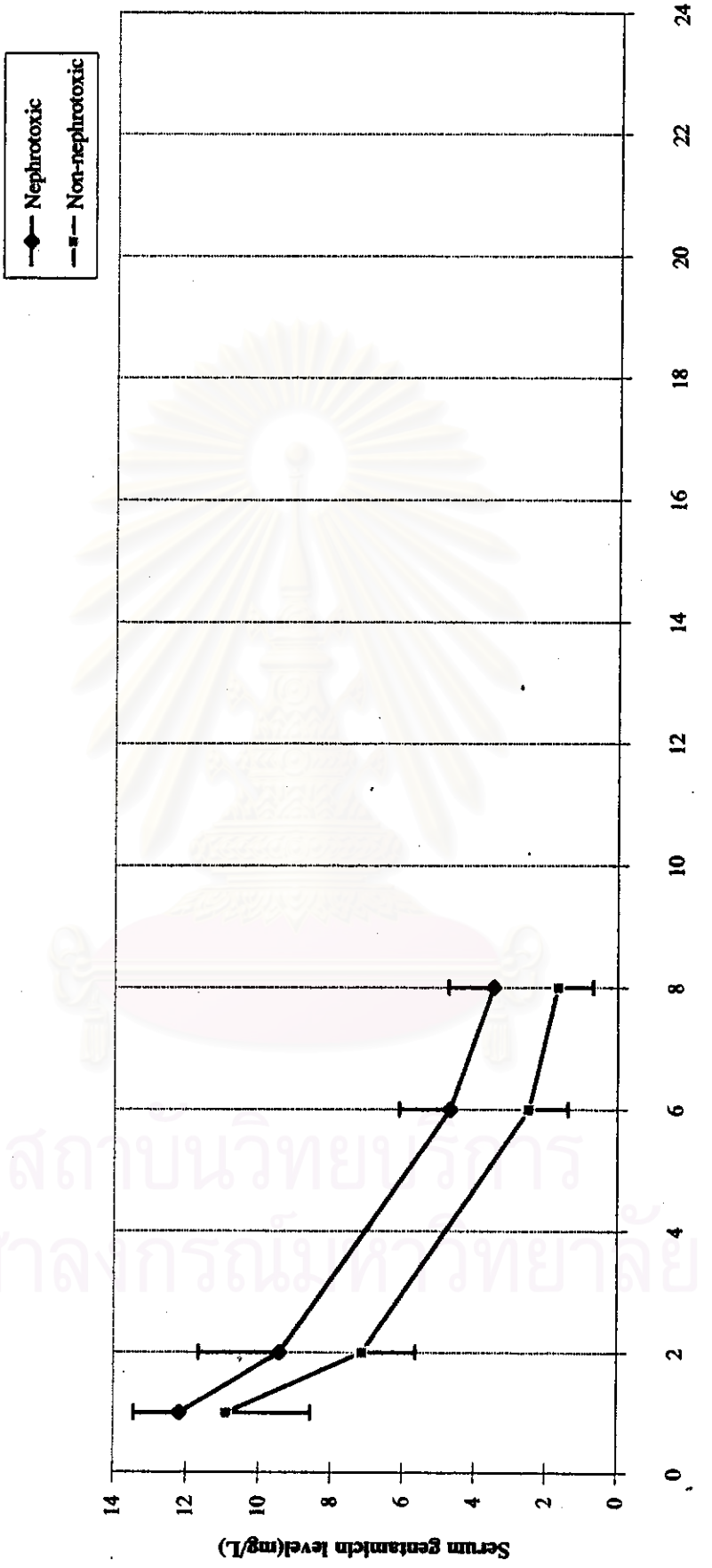
Table 4.7B The serum gentamicin levels at different sampling times of non-nephrotoxic patients

NO.	Cp1	Cp2	Cp6	Cp8	Cp24
	(mg/L)	(mg/L)	(mg/L)	(mg/L)	(mg/L)
1	8.7	5.9	1.6	0.9	<0.3
2	8.9	6.0	2.2	1.1	<0.3
3	13.1	9.9	4.5	3.4	<0.3
4	8.6	7.9	4.7	3.6	0.7
5	10.2	8.1	4.6	3.5	0.5
6	10.3	6.1	1.8	1.1	<0.3
7	10.3	8.4	4.1	3.5	0.4
9	12.9	7.9	2.5	1.7	<0.3
10	13.6	7.6	1.6	0.7	<0.3
11	10.5	5.3	1.6	1	<0.3
12	13.6	7.3	1.6	0.9	<0.3
13	12.8	6.2	2.3	1.3	<0.3
14	11.3	7.2	1.7	0.9	<0.3
15	8.1	4.6	1.0	0.6	<0.3
16	7.7	4.4	1.2	0.6	<0.3
17	11.8	9.4	3.0	2.3	<0.3
18	12.2	6.5	1.5	0.9	<0.3
19	16.4	10	3.1	1.9	<0.3
20	8.6	6.5	2.9	1.9	<0.3
21	13.1	9.5	3.1	1.7	<0.3
22	10.8	6.8	2.1	1.4	<0.3
23	9.2	5.5	1.5	0.9	<0.3
24	14.2	10.1	3.7	2.4	<0.3
25	11.1	7.3	1.3	0.6	<0.3

continued.....

NO.	Cp1	Cp2	Cp6	Cp8	Cp24
	(mg/L)	(mg/L)	(mg/L)	(mg/L)	(mg/L)
26	9.1	5.9	1.8	1.2	<0.3
27	11.4	7.1	3.8	2.5	<0.3
28	12.3	7.5	1.7	1.6	<0.3
29	13.6	7.9	1.2	0.5	<0.3
30	11.5	8.5	3.9	2.9	<0.3
31	9.1	6.6	2.3	1.8	<0.3
32	12.3	6.5	1.4	0.7	<0.3
33	12.0	6.3	1.4	0.8	<0.3
35	10.1	7.8	4.2	3.2	0.5
36	11.8	6.8	1.3	0.6	<0.3
39	13.4	8.4	3.3	2.1	<0.3
40	14.8	9.7	4.1	3.2	0.5
41	12.5	7.4	1.8	1.1	<0.3
42	11.5	9.1	4	3.3	<0.3
43	6.5	6	4.1	3.7	1.6
44	7.5	5	1.1	0.5	<0.3
45	12.8	8.4	3	1.8	<0.3
46	8.8	6	2.1	1	<0.3
47	9.6	7.1	2.5	1.9	<0.3
48	6.5	5	1.9	1.1	<0.3
49	10.4	6.4	2.2	1.2	<0.3
50	6.1	4.7	2	1.4	<0.3
mean	10.9	7.1	2.5	1.7	
SD	2.3	1.5	1.1	1.0	
(range)	(6.1-16.4)	(4.4-10.1)	(1.0-4.7)	(0.5-3.7)	(<0.3 - 1.6)

Fig. 4.1 Comparison of the mean concentrations at different time point between nephrotoxic and non-nephrotoxic groups



Points are means. Bars are SD (Standard deviation)

Table 4.8 Comparison of the mean concentrations at different time point between nephrotoxic and non-nephrotoxic groups.

Concentration factor	Nephrotoxic (n = 4)	Non-nephrotoxic (n = 46)	P*
1-hr serum gentamicin level	12.2 ± 1.3	10.9 ± 2.3	0.292
2-hr serum gentamicin level	9.4 ± 2.2	7.1 ± 1.5	0.007
6-hr serum gentamicin level	4.7 ± 1.4	2.5 ± 1.1	0.001
8-hr serum gentamicin level	3.5 ± 1.3	1.7 ± 1.0	0.001

* By t-test

Figure 4.2 Percentage of nephrotoxicity in patients with different 1-hr serum gentamicin levels

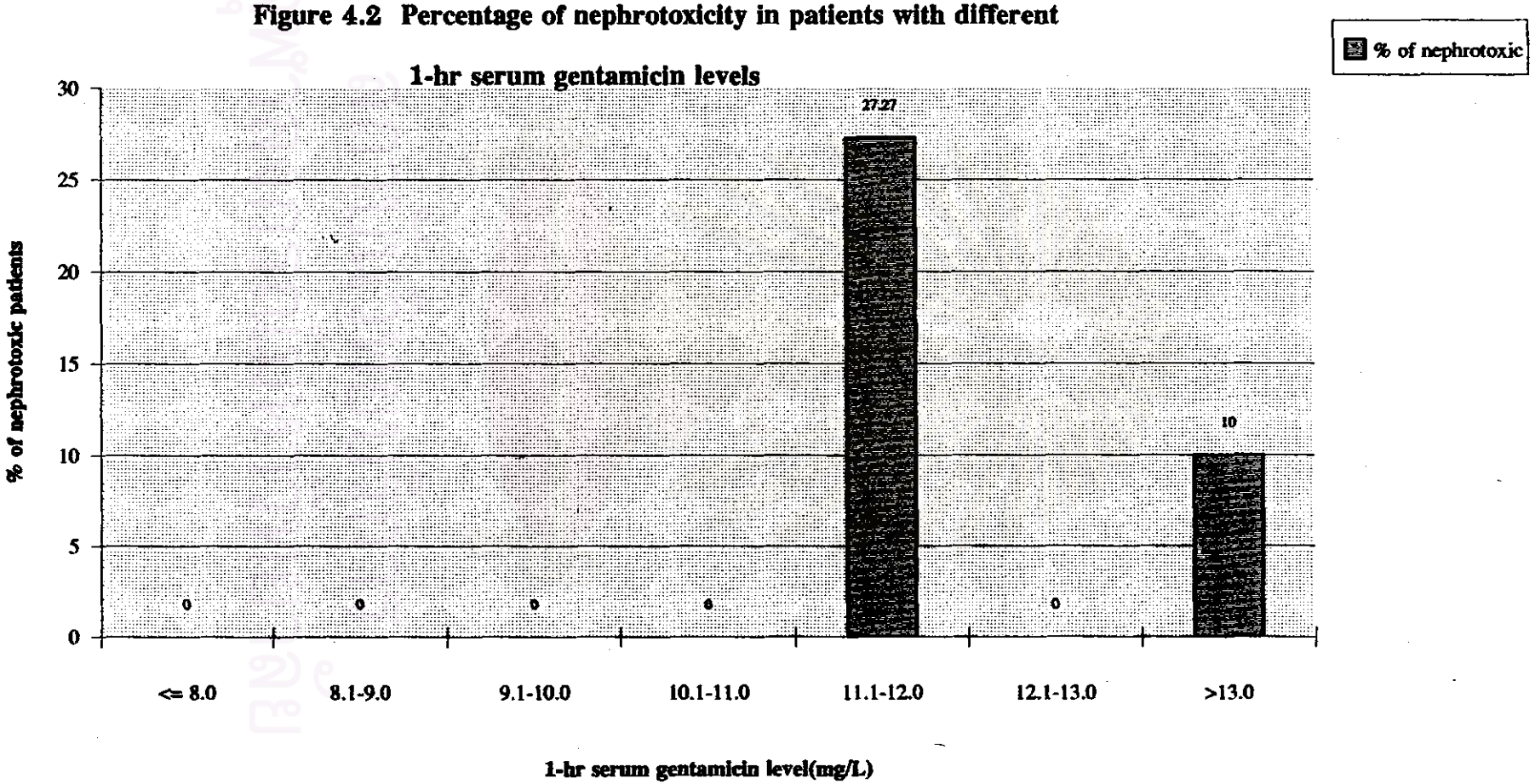


Figure 4.3 Percentage of nephrotoxicity in patients with different 2-hr serum gentamicin levels

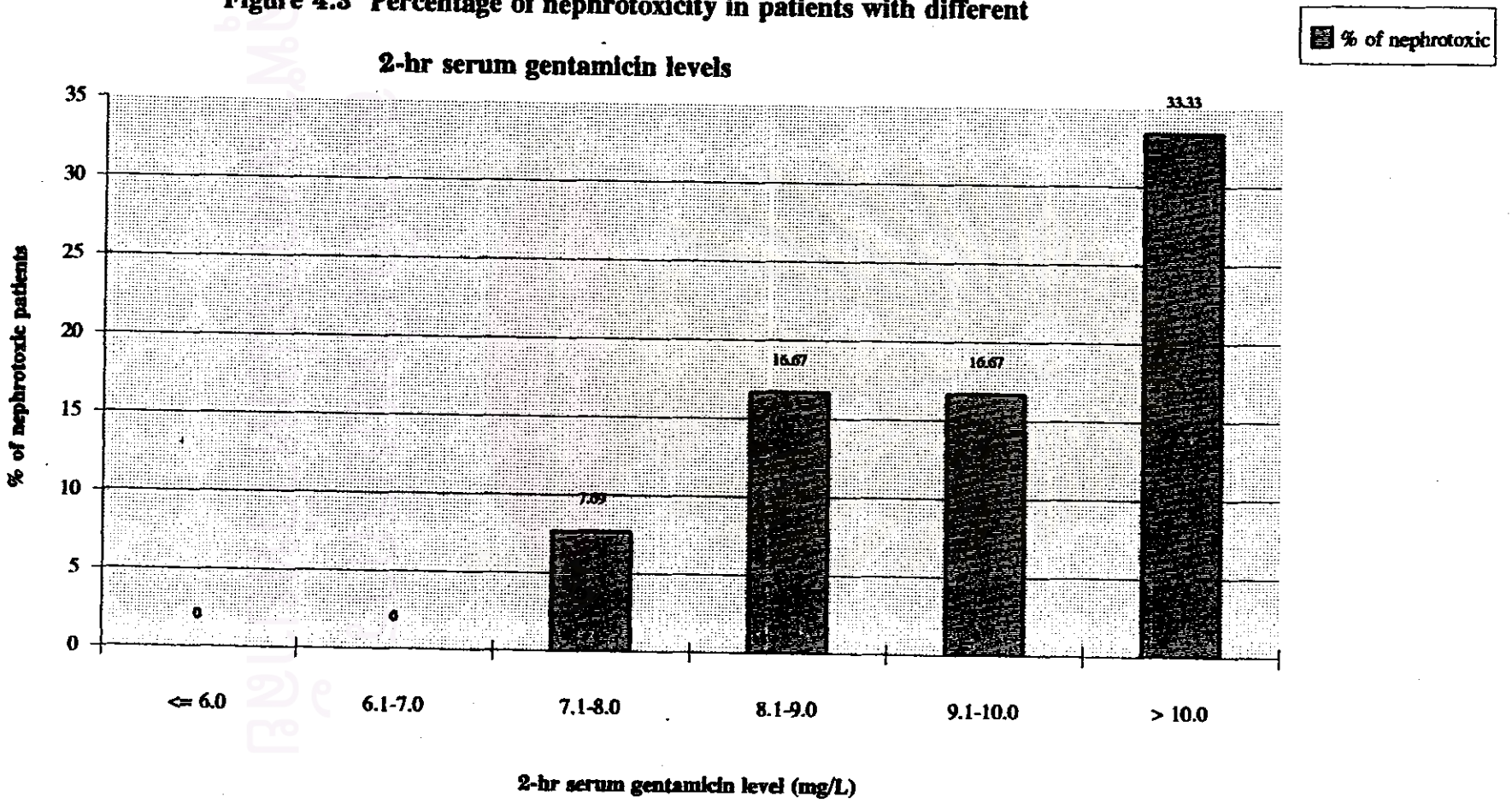


Fig. 4.4 Percentage of nephrotoxicity in patients with different 6-hr serum gentamicin levels

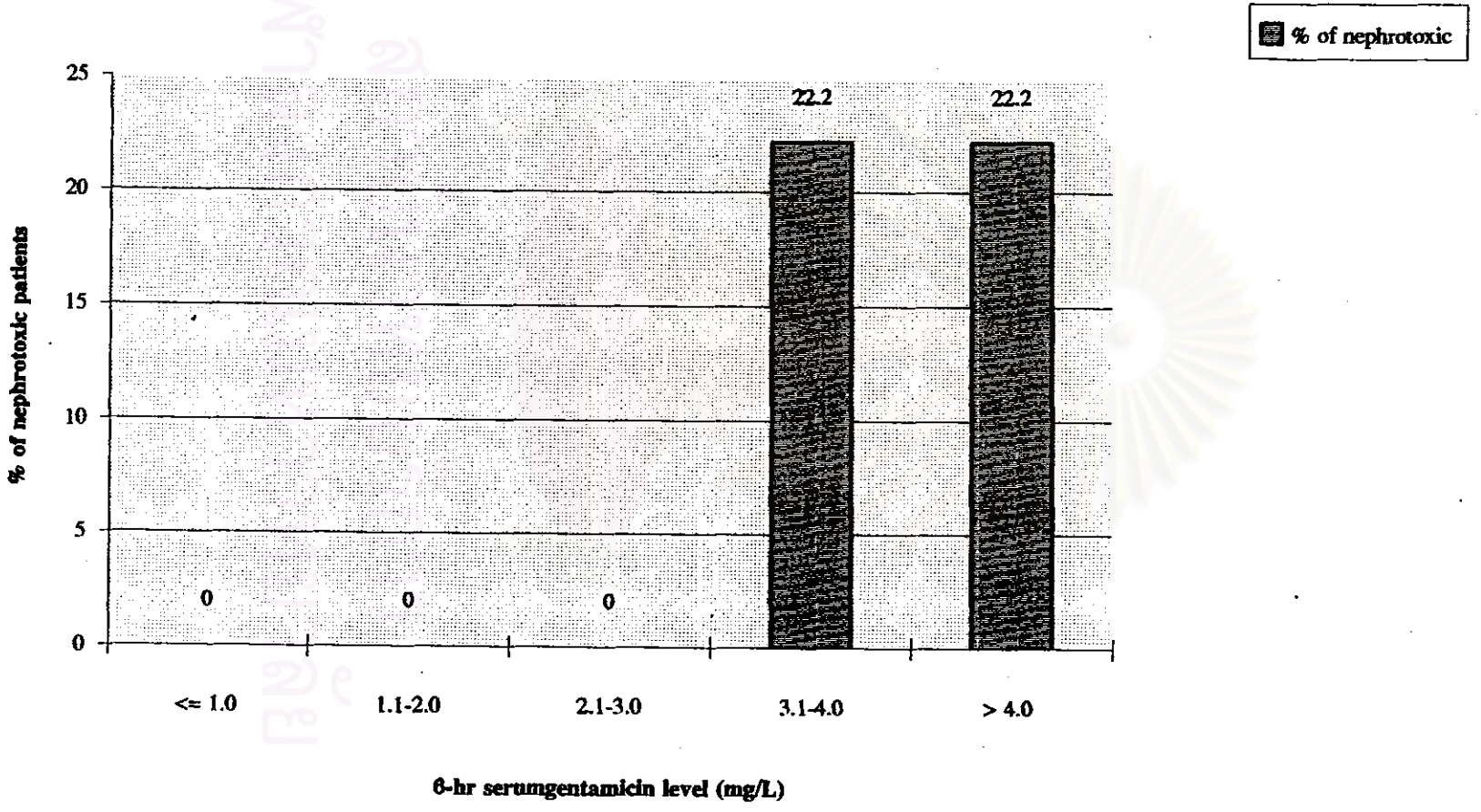


Fig. 4.5 Percentage of nephrotoxicity in patients with different 8-hr serum gentamicin levels

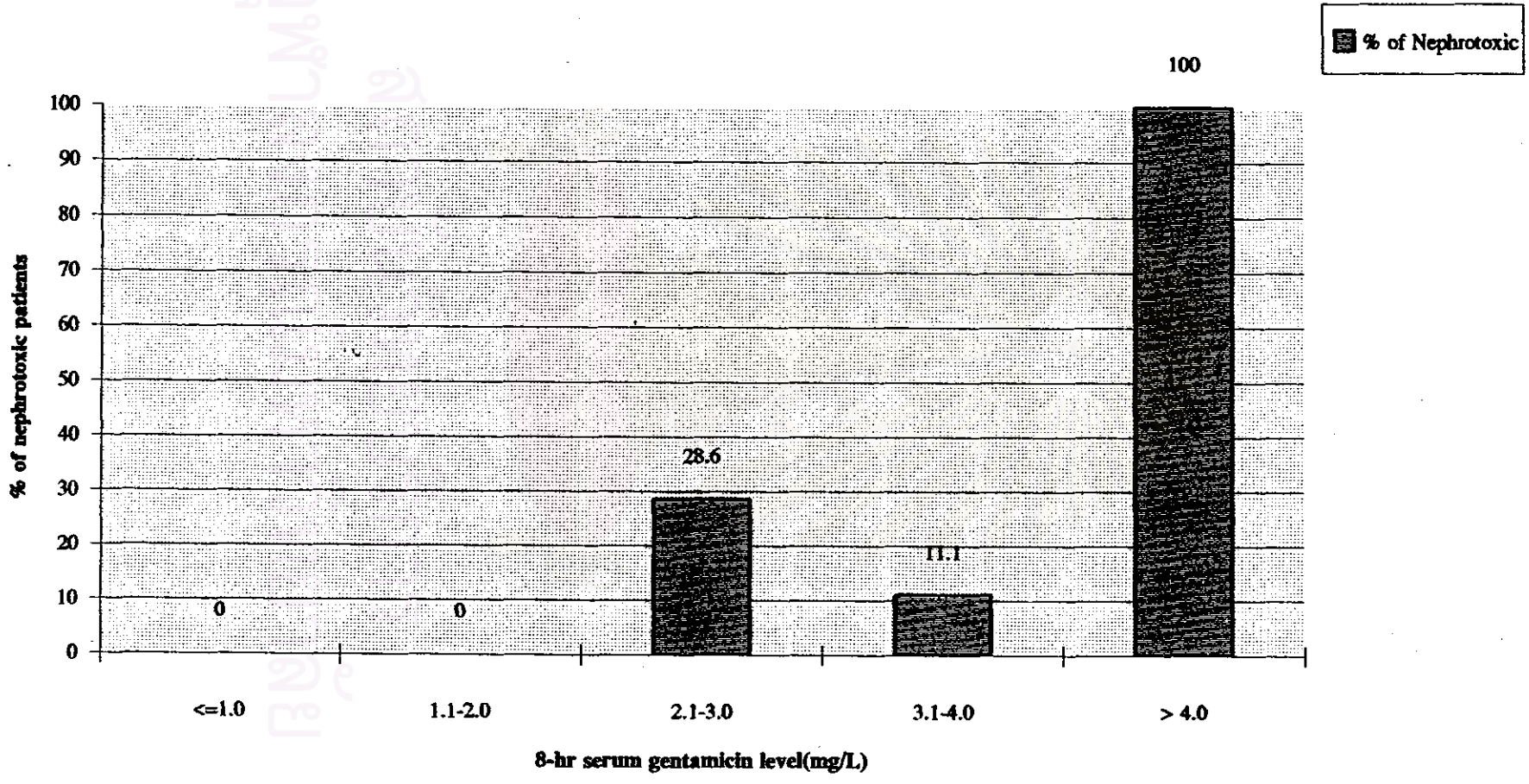


Fig. 4.6 Percentage of nephrotoxicity in patients with different 24-hr serum gentamicin levels

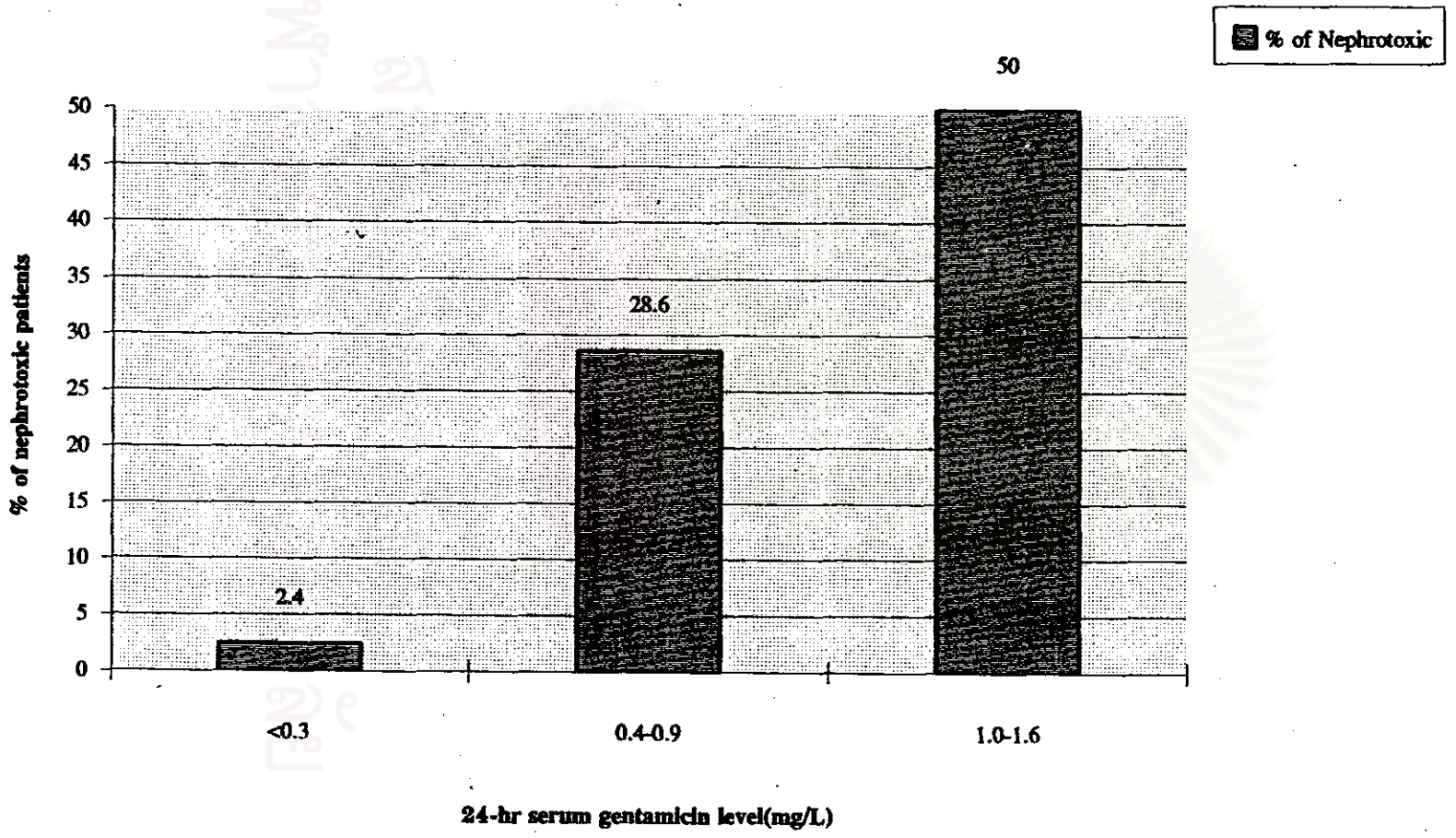


Table 4.9 Percentage of patients showing nephrotoxicity and not showing nephrotoxicity with different 2-hr serum gentamicin levels

2- hr serum gentamicin levels	Nephrotoxic Total n = 4	Non-nephrotoxic Total n = 46	P*
< 11.0 mg/L (n= 49)	3 (6%)	46 (94%)	0.08
< 10.0 mg/L (n= 47)	3 (6%)	44 (94%)	0.225
< 9.0 mg/L (n= 41)	2 (5%)	39 (95%)	0.144
< 8.0 mg/L (n= 35)	1 (3%)	34 (97%)	0.075
< 7.0 mg/L (n= 22)	0	22 (100%)	0.121

* By Fisher's exact test

Table 4.10 Percentage of patients showing nephrotoxicity and not showing nephrotoxicity with different 6-hr serum gentamicin levels

6- hr serum gentamicin levels	Nephrotoxic Total n = 4	Non-nephrotoxic Total n = 46	P*
< 6.0 mg/L (n= 49)	3 (6%)	46 (94%)	0.08
< 5.0 mg/L (n= 48)	2 (4%)	46 (96%)	0.005
< 4.0 mg/L (n= 40)	2 (5%)	38 (95%)	0.174
< 3.0 mg/L (n= 30)	0	30 (100%)	0.021

* By Fisher's exact test

Table 4.11 Percentage of patients showing nephrotoxicity and not showing nephrotoxicity with different 8-hr serum gentamicin levels

8- hr serum gentamicin levels	Nephrotoxic Total n = 4	Non-nephrotoxic Total n = 46	P*
< 4.0 mg/L (n= 49)	3 (6%)	46 (94%)	0.08
< 3.5 mg/L (n= 44)	2 (5%)	42 (95%)	0.06
< 3.0 mg/L (n= 40)	2 (5%)	38 (95%)	0.174
< 2.5 mg/L (n= 37)	1 (3%)	36 (97%)	0.049
< 2.0 mg/L (n= 33)	0	33 (100%)	0.010

* By Fisher's exact test

Table 4.12 Percentage of patients showing nephrotoxicity and not showing nephrotoxicity with different 24-hr serum gentamicin levels

24- hr serum gentamicin levels	Nephrotoxic Total n = 4	Non-nephrotoxic Total n = 46	P*
< 1.5 mg/L (n= 49)	4 (8%)	45 (92%)	0.92
< 1.0 mg/L (n= 48)	3 (6%)	45 (94%)	0.155
< 0.5 mg/L (n= 43)	2 (5%)	41 (95%)	0.089
< 0.3 mg/L (n= 41)	1 (2%)	40 (98%)	0.016

* By Fisher's exact test

Table 4.13 Influence of various clinical factors [a] on nephrotoxicity

Parameter	All Patients (n = 50)	Nephrotoxic (n = 4)	Non-nephrotoxic (n = 46)	*P*
Age (yr.)	49.9 ± 17.9	58.25 ± 14.93	49.15 ± 18.17	0.337 [b]
Baseline serum creatinine (mg/dl)	0.9 ± 0.20	1.0 ± 0.23	0.91 ± 0.20	0.383 [b]
Baseline creatinine clearance (ml/min)	72.4 ± 25.9	56.7 ± 12.0	73.78 ± 26.4	0.209 [b]
Daily Dosage (mg/kg/day)	3.97 ± 0.7	3.97 ± 0.5	3.97 ± 0.7	0.998 [b]
Duration of treatment (days)	7.4 ± 3	12.3 ± 3.4	7 ± 2.5	0.000 [b]
Female gender	25	2	23	1.00 [c]
Hypokalemia before treatment	12	1	11	1.00 [c]
Hypomagnesemia before treatment	9	1	8	0.57 [c]
DM	6	1	5	0.41 [c]
Liver Dysfunction	8	1	7	0.51 [c]
Volume depletion	4	1	3	0.29 [c]

[a] For continuous variables,the mean ± SD is given ;for dichotomous variables,the absolute number of patients is given.

[b] t-test.

[c] Fisher's exact test

2. Optimum serum sampling time of once-daily gentamicin dosage regimen and its relatively reference concentration for monitoring efficacy

2.1 Characteristics of documented infected patients

Of the 50 patients who receieved gentamicin included in this study , a total of 37 patients had been proven of getting bacterial infection. From table 4.1 , the documented infected patients were 16 men and 21 women , their mean age was 52.8 ± 18.7 years (range, 18 - 82 years). The mean duration of gentamicin therapy was 7.7 ± 3.4 days (range, 4 - 15 days).

Sites of infection and causative microorganisms were listed in table 4.14 and 4.15. Urinary tract infection was the most common infectious disease found in the patients , followed by intraabdominal infection and skin or soft tissue infection. The primary site of infection could not be identified for one patient. Most of the cultured microorganisms were aerobic Gram-negative rods. Some patients showed more than one site of infection and several causative microorganisms.

Table 4.16 showed the concurrent antimicrobial agents used. Most patients also received concurrent antimicrobial agents such as metronidazole , penicillin , ampicillin , clindamycin , cloxacillin. Only eight patients (21.6%) received gentamicin as the single antimicrobial agent. Seven patients (18.9%) used 2 concurrent antimicrobial agents, one was metronidazole while the other was Gram-positive sensitive antimicrobial agent.

Table 4.3 displayed the indication of treatment and clinical responses of the patients.The clinical efficacy was defined as favourable if there was clinical improvement with resolution of symptoms of infection , a normal body temparature (37.5^{o}C) for at least 48 hours , and a normal leucocyte count or a 15% or more

decreased in leucocyte count. The bacteriologic efficacy was determined by follow up cultures after discontinuation of the antibiotic therapy. If the post-therapy culture was negative , or no specimens for follow-up culture were available (ie. no sputum in case of respiratory tract infection ,or no pus in patients with the skin or soft tissue infection) , the patients would be determined as having a favourable bacteriologic efficacy. Twenty - seven (73%) of the infected patients fulfilled the criteria for both favourable clinical efficacy and favourable bacteriologic efficacy. Among these 37 patients, three of them developed nephrotoxicity.

Table 4.14 Site of infection

Site of infection	No. of patients (%)
Lower respiratory tract infection	5 (13.5%)
Abdominal infection	10 (27.0%)
Urinary tract infection	12 (32.4%)
Skin/soft tissue infection	9 (24.3%)
Bacteremia	4 (10.8%)

Table 4.15 Causative microorganisms isolated from site of infection

Microorganisms	No. of patients (%)
Gram-negative Organisms	
Enterobacter species	4 (10.8%)
Escherichia coli	17 (45.9%)
Klebsiella species	6 (16.2%)
Proteus species	1 (2.7%)
Pseudomonas species	3 (8.1%)
Other	3 (8.1%)
Gram-positive Organisms	
Enterococcus species	3 (8.1%)
Staphylococcus aureus	3 (8.1%)
Staphylococcus epidermidis	4 (10.8%)
Streptococci	1 (2.7%)
Polymicrobial infection	6 (16.2%)

Table 4.16 Concurrent antimicrobial agents

Concurrent antimicrobial agents	No. of patients (%)
Penicillin G sodium	6 (16.2%)
Ampicillin	6 (16.2%)
Ampicillin + Salbactam	2 (5.4%)
Amoxycillin + Clavulanic	1 (2.7%)
Cloxacillin	3 (8.1%)
Clindamycin	4 (10.8%)
Cefazolin	1 (2.7%)
Cefuroxime	1 (2.7%)
Ceftazidime	1 (2.7%)
Metronidazole	11 (29.7%)

2.2 Optimum serum sampling time and its relatively reference concentration for monitoring efficacy

Table 4.17A and 4.17B showed the serum gentamicin levels at different time points of the patients in favourable efficacy group and unfavourable efficacy group , respectively.

In favourable efficacy group , the means of serum gentamicin levels at 1-hr , 2-hr , 6-hr and 8-hr after starting infusion were 11.3 ± 2.2 mg/L (range, 6.5 - 14.2 mg/L) , 7.5 ± 1.8 mg/L (range, 4.4 - 12.6 mg/L) , 2.7 ± 1.3 mg/L (range, 1.0 - 6.5 mg/L) , 1.8 ± 1.2 mg/L (range, 0.6 - 5.1 mg/L), respectively.

Figure 4.7 and table 4.18 showed comparison of the mean concentration at different time points between favourable efficacy and unfavourable efficacy groups. The 1-hr serum gentamicin level was associated significantly with efficacy at $P < 0.05$ while the 2-hr serum gentamicin level at $P < 0.1$.

Figure 4.8 - 4.12 displayed the percentage of favourable efficacy in different patient groups classified by serum gentamicin levels at each time point. The percentage of favourable efficacy was higher in patients with higher serum gentamicin level at 1-hr and 2-hr.

Table 4.19 and 4.20 showed the percentage of patient showing favourable efficacy and showing unfavourable efficacy with different 1-hr and 2-hr serum gentamicin levels , respectively . The 1-hr serum gentamicin level of more than or equal to 11.0 mg/L and more than or equal to 11.5 mg/L provided the percentage of patients showing favourable efficacy significantly different from the lower drug levels (89% and 94%, respectively) while the 2-hr serum gentamicin level of more than or equal to 6.5 mg/L and more than or equal to 7.0 mg/L did (87% and 89%, respectively).

The influence of the other clinical factors on response was also examined in table 4.21. Univariate analysis showed that the patients who responded with favourable efficacy were more likely to have a lower mean initial temparature , and lower mean initial leukocyte count compared with the patients who did not respond favourably. A lower respiratory tract infection and infection with *Pseudomonas* species were also associated with unfavourable efficacy.

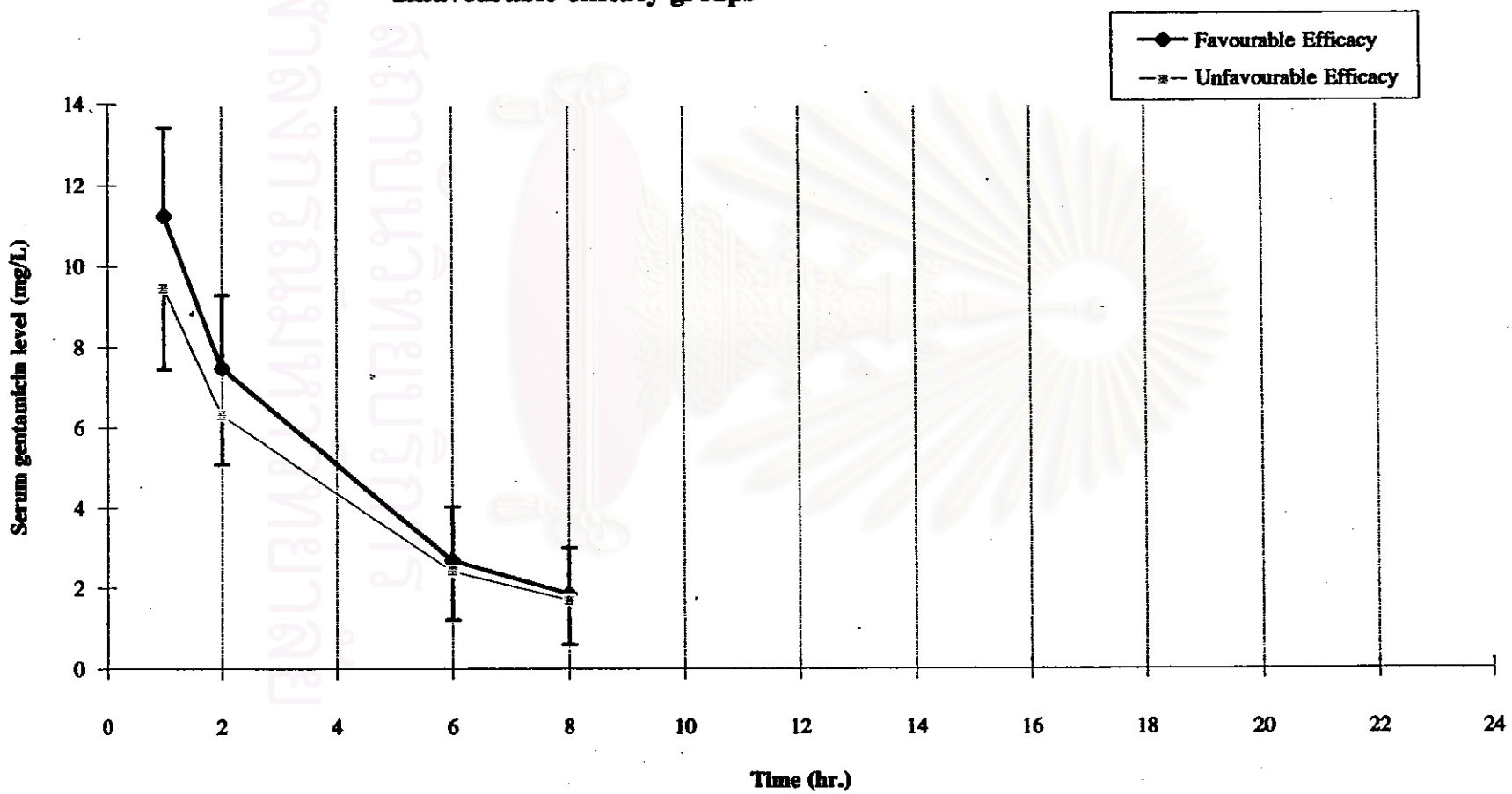
Table 4.17A The serum gentamicin levels at different sampling times of patients showing favourable efficacy .

NO.	Cp1	Cp2	Cp6	Cp8	Cp24
	(mg/L)	(mg/L)	(mg/L)	(mg/L)	(mg/L)
3	13.1	9.9	4.5	3.4	<0.3
4	8.6	7.9	4.7	3.6	0.7
6	10.3	6.1	1.8	1.1	<0.3
7	10.3	8.4	4.1	3.5	0.4
9	12.9	7.9	2.5	1.7	<0.3
10	13.6	7.6	1.6	0.7	<0.3
12	13.6	7.3	1.6	0.9	<0.3
13	12.8	6.2	2.3	1.3	<0.3
14	11.3	7.2	1.7	0.9	<0.3
15	8.1	4.6	1.0	0.6	<0.3
16	7.7	4.4	1.2	0.6	<0.3
18	12.2	6.5	1.5	0.9	<0.3
20	8.6	6.5	2.9	1.9	<0.3
21	13.1	9.5	3.1	1.7	<0.3
24	14.2	10.1	3.7	2.4	<0.3
26	9.1	5.9	1.8	1.2	<0.3
30	11.5	8.5	3.9	2.9	<0.3
31	9.1	6.6	2.3	1.8	<0.3
32	12.3	6.5	1.4	0.7	<0.3
33	12.0	6.3	1.4	0.8	<0.3
34	12.0	8.7	3.8	2.7	0.4
38	14.0	12.6	6.5	5.1	1.4
39	13.4	8.4	3.3	2.1	<0.3
41	12.5	7.4	1.8	1.1	<0.3
42	11.5	9.1	4.0	3.3	<0.3
47	9.6	7.1	2.5	1.9	<0.3
48	6.5	5.0	1.9	1.1	<0.3
mean	11.3	7.5	2.7	1.8	
SD	2.2	1.8	1.3	1.2	
(range)	(6.5-14.2)	(4.4-12.6)	(1.0-6.5)	(0.6-5.1)	(<0.3-1.4)

Table 4.17B The serum gentamicin levels at different sampling times of patients showing unfavourable efficacy .

NO.	Cp1	Cp2	Cp6	Cp8	Cp24
	(mg/L)	(mg/L)	(mg/L)	(mg/L)	(mg/L)
1	8.7	5.9	1.6	0.9	<0.3
2	8.9	6.0	2.2	1.1	<0.3
11	10.5	5.3	1.6	1.0	<0.3
22	10.8	6.8	2.1	1.4	<0.3
23	9.2	5.5	1.5	0.9	<0.3
28	12.3	7.5	1.7	1.6	<0.3
37	11.3	9.0	5.1	3.8	0.6
43	6.5	6.0	4.1	3.7	1.6
49	10.4	6.4	2.2	1.2	<0.3
50	6.1	4.7	2.0	1.4	<0.3
mean	9.5	6.3	2.4	1.7	
SD	2.0	1.2	1.2	1.1	
(range)	(6.1-12.3)	(4.7-9.0)	(1.5-5.1)	(0.9-3.8)	(<0.3-1.6)

Fig. 4.7 Comparison of the mean concentrations at different time point between favourable and unfavourable efficacy groups



Points are means. Bars are SD (Standard Deviation)

Table 4.18 Comparison of the mean concentrations at different time point between favourable and unfavourable efficacy groups.

Concentration factor	Favourable Efficacy (n = 27)	Unfavourable Efficacy (n = 10)	P*
1-hr serum gentamicin level	11.3 ± 2.2	9.5 ± 2.0	0.029
2-hr serum gentamicin level	7.5 ± 1.8	6.3 ± 1.2	0.067
6-hr serum gentamicin level	2.7 ± 1.3	2.4 ± 1.2	0.557
8-hr serum gentamicin level	1.8 ± 1.2	1.7 ± 1.1	0.729

* By t-test

Fig. 4.8 Percentage of favourable efficacy in patients with different 1-hr serum gentamicin levels

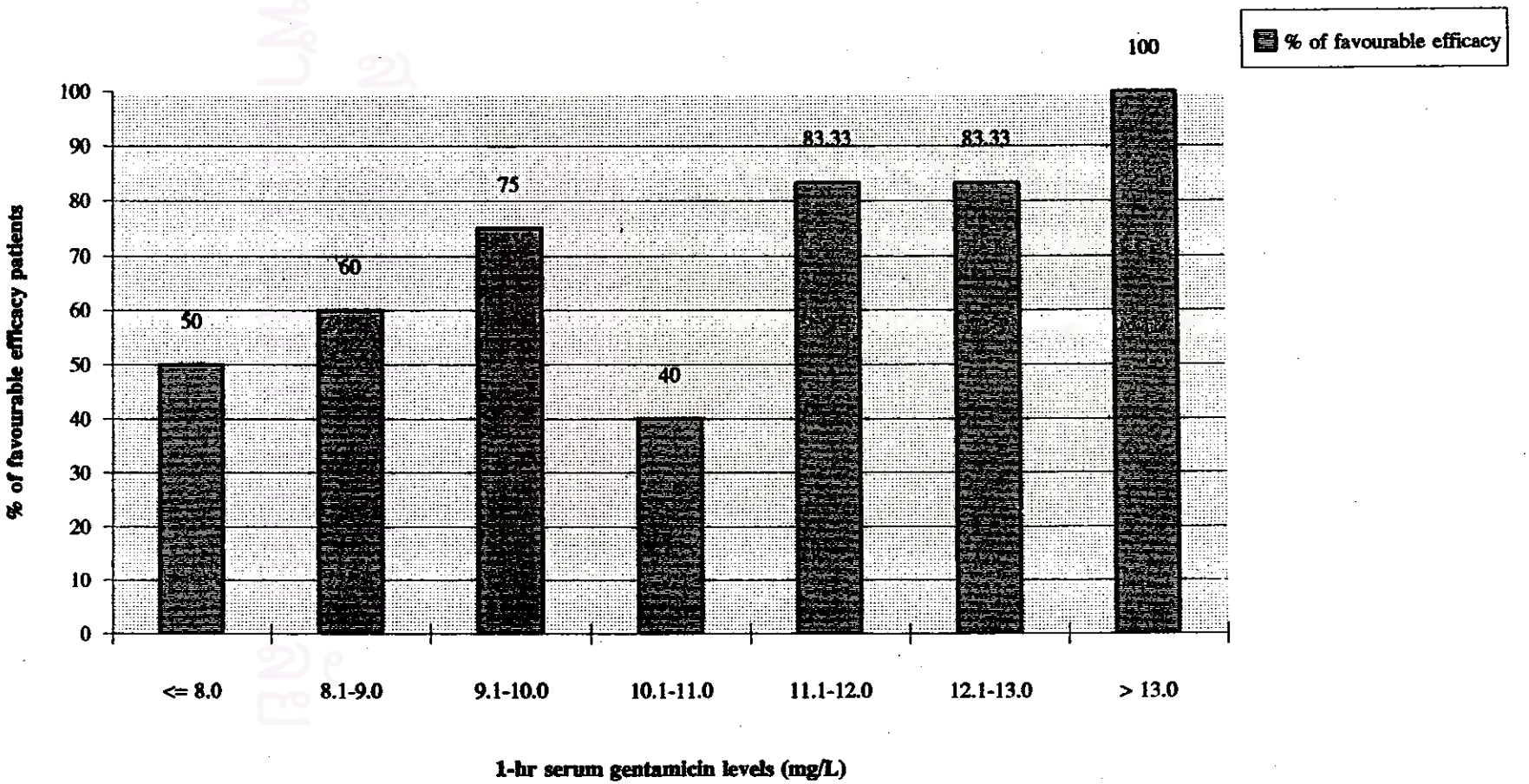


Fig.4.9 **percentage of favourable efficacy in patients with different 2-hr serum gentamicin levels**

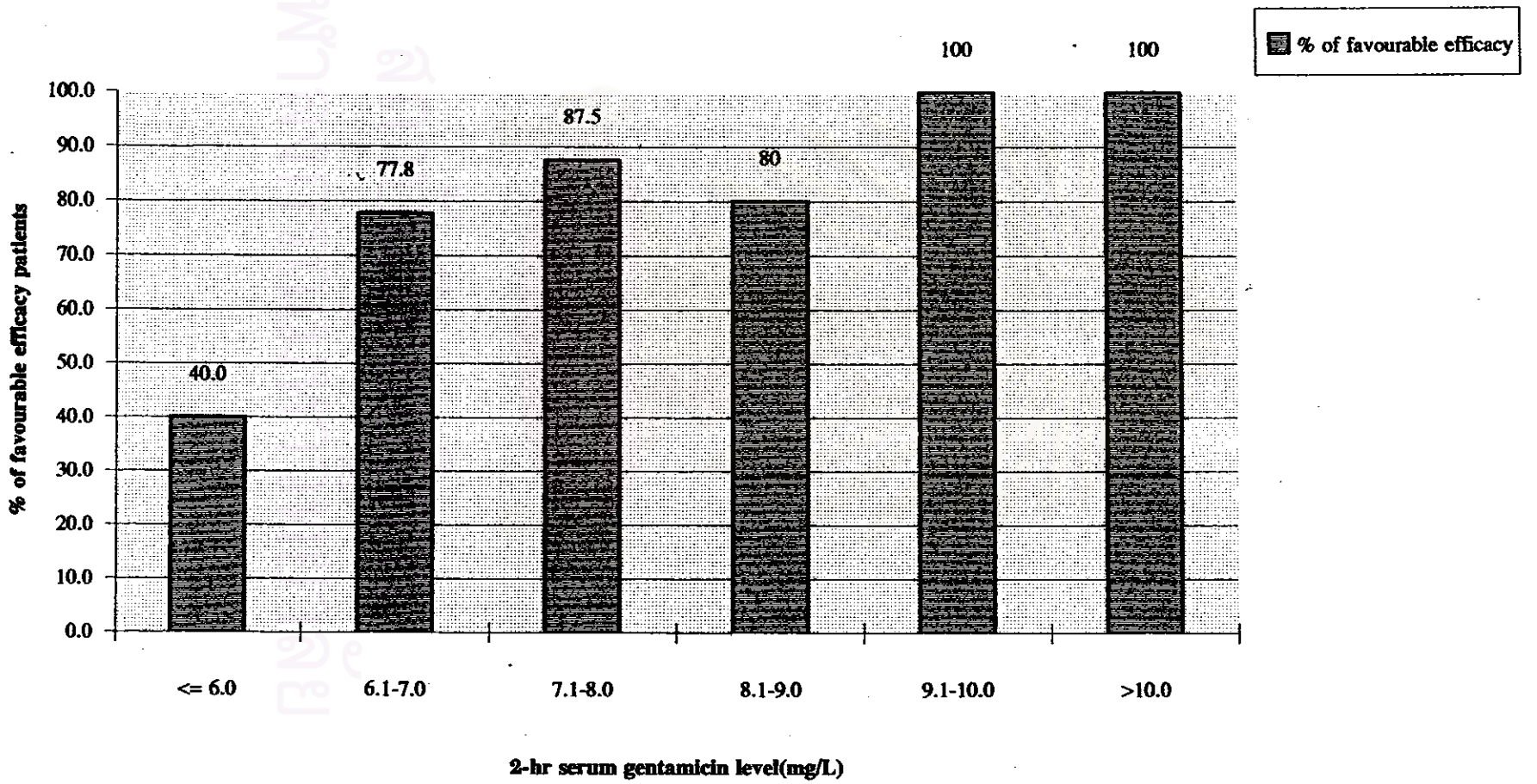


Fig. 4.10 Percentage of favourable efficacy in patients with different 6-hr serum gentamicin levels

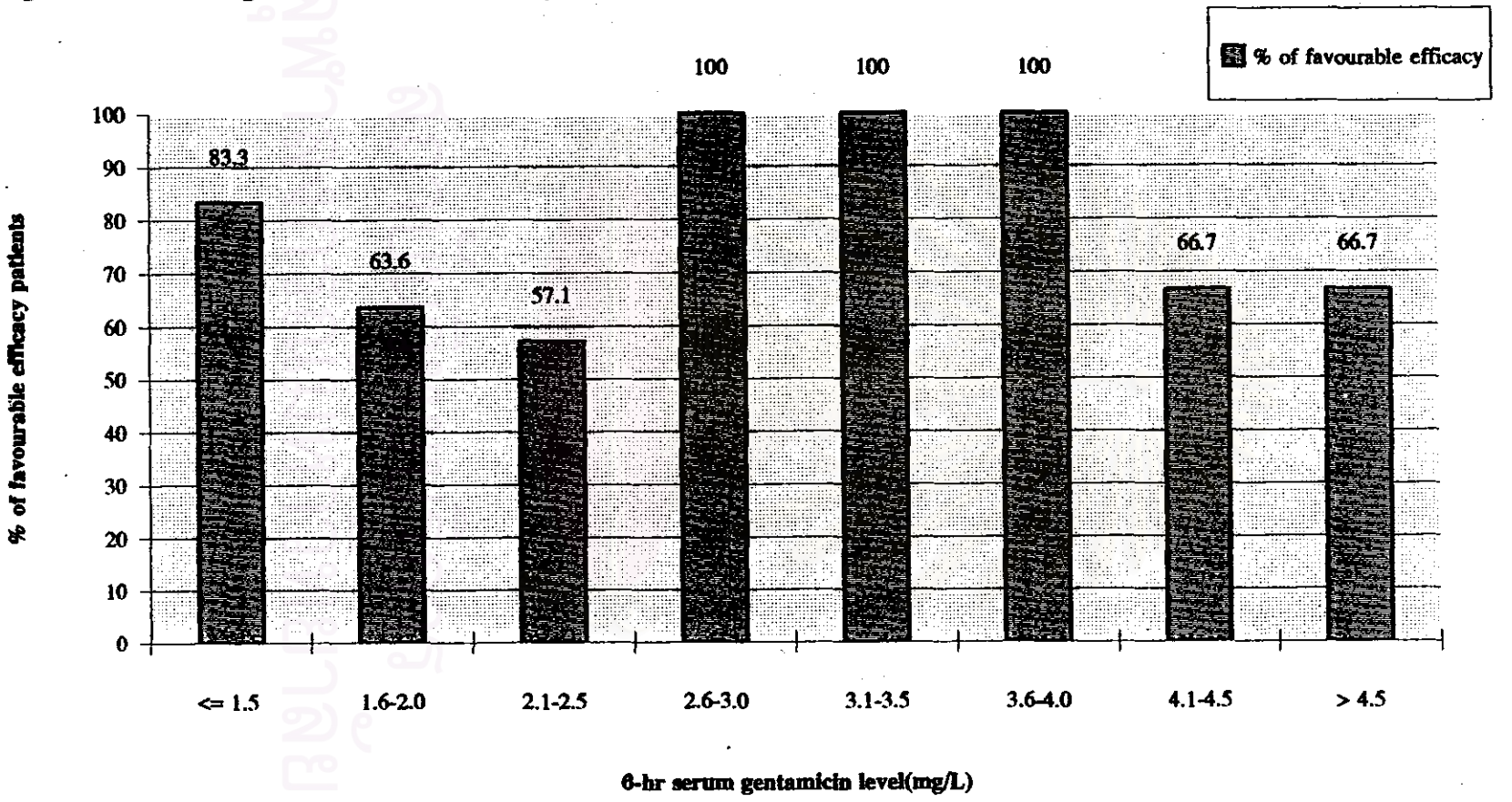


Fig. 4.11 Percentage of favourable efficacy in patients with different 8-hr serum gentamicin levels

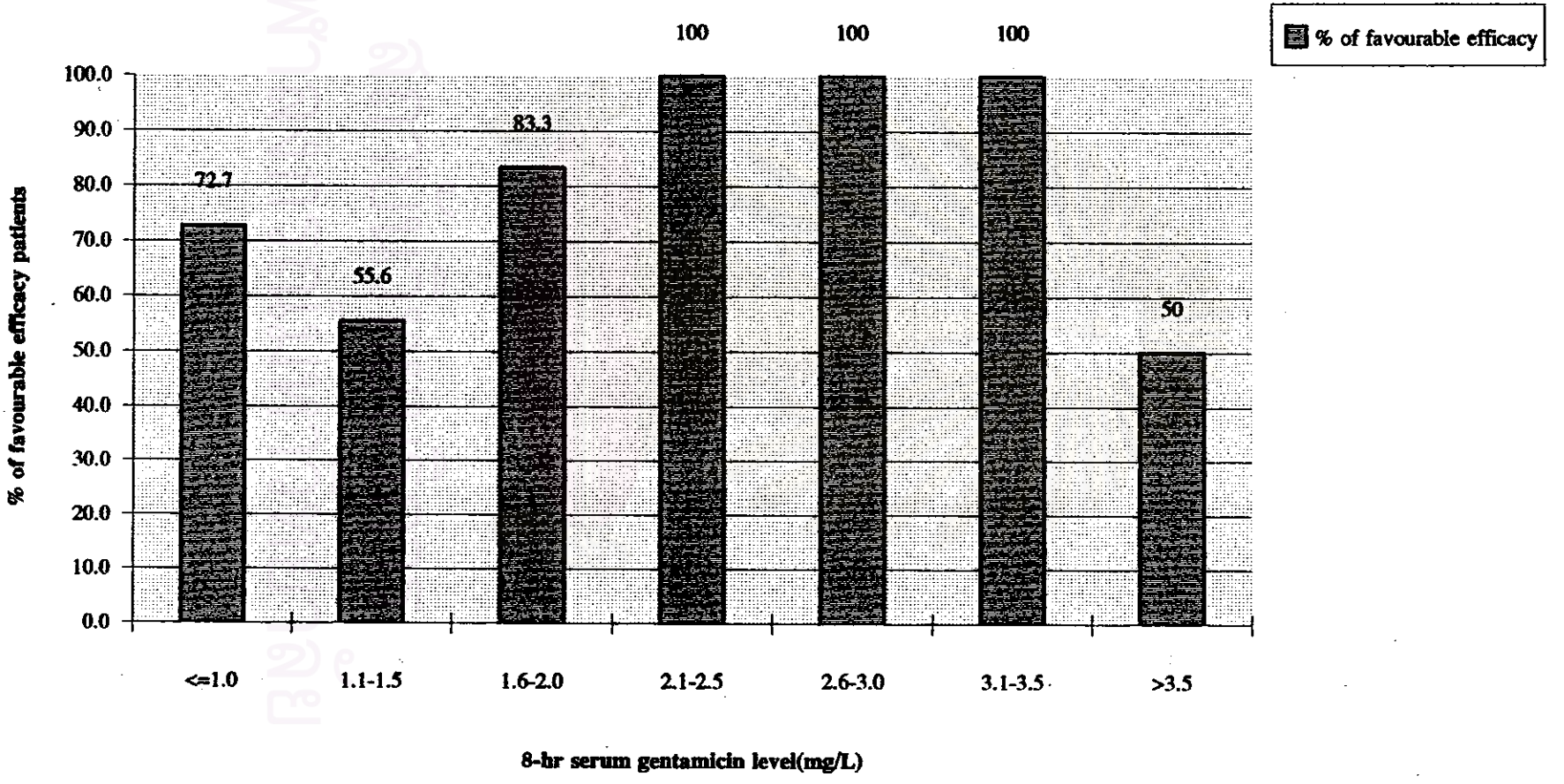


Fig.4.12 Percentage of favourable efficacy in patients with different 24-hr serum gentamicin levels

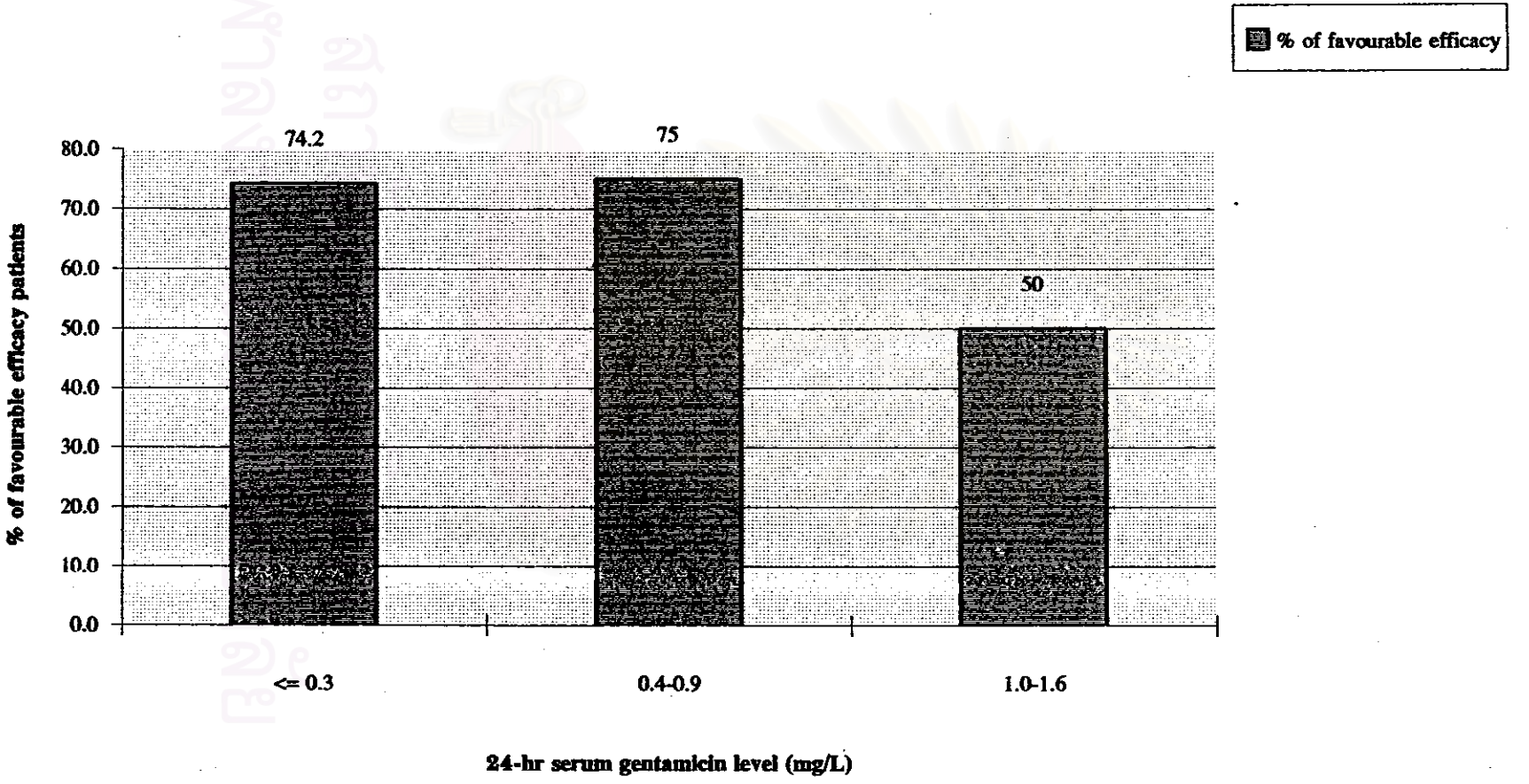


Table 4.19 Percentage of patients showing favourable efficacy and showing unfavourable efficacy with different 1-hr serum gentamicin levels

1- hr serum gentamicin levels	Favourable efficacy Total n = 27	Unfavourable efficacy Total n = 10	P*
>= 10.0 mg/L (n= 24)	19 (79%)	5 (21%)	0.22
>= 10.5 mg/L (n= 21)	17 (81%)	4 (19%)	0.19
>= 11.0 mg/L (n= 19)	17 (89%)	2 (11%)	0.024
>= 11.5 mg/L (n= 17)	16 (94%)	1 (6%)	0.008

* By Fisher's exact test

Table 4.20 Percentage of patients showing favourable efficacy and showing unfavourable efficacy with different 2-hr serum gentamicin levels

2- hr serum gentamicin levels	Favourable efficacy Total n = 27	Unfavourable efficacy Total n = 10	P*
>= 6.0 mg/L (n= 29)	23 (79%)	6 (21%)	0.117
>= 6.5 mg/L (n= 23)	20 (87%)	3 (13%)	0.02
>= 7.0 mg/L (n= 18)	16 (89%)	2 (11%)	0.038
>= 7.5 mg/L (n= 14)	12 (86%)	2 (14%)	0.164
>= 8.0 mg/L (n= 10)	9 (90%)	1 (10%)	0.220

* By Fisher's exact test

Table 4.21 Univariate associations between efficacy in documented infection patients and host factors , infection site ,organism and concurrently administered antibiotic[a]

Factor	Favourable efficacy (n = 27)	Unfavourable efficacy (n = 10)	P
Host factor			
Age	49.52 ± 17.13	46.9 ± 21.94	0.704[b]
Male Sex	10 (37%)	6 (60%)	0.274[c]
Diabetes	4 (14.8%)	1 (10%)	1.000[c]
Initial temperature(^{o}C)	38.7 ± 0.5	39.1 ± 0.5	0.045[b]
Initial leukocyte count (x 1,000 /mm3)	15.65 ± 4.7	20.25 ± 8.9	0.049[b]
Infection site			
Urinary tract	9 (33.3%)	3 (30%)	1.000[c]
Intraabdominal	8 (29.6%)	2 (20%)	0.694[c]
Skin/soft tissue	8 (29.6%)	1 (10%)	0.393[c]
Lower respiratory tract	1 (3.7%)	4 (40%)	0.014[c]
Organism			
E. coli	12 (44.4%)	5 (50%)	1.000[c]
Staphylococcus sp.	5 (18.5%)	2 (20%)	1.000[c]
Klebsiella sp.	6 (22.2%)	0	0.162[c]
Enterobacter sp.	4 (14.8%)	0	0.557[c]
Pseudomonas sp.	0	3 (30%)	0.015[c]
Enterococcus sp.	3 (11.1%)	0	0.548[c]
Streptococcus sp.	0	1 (10%)	0.270[c]
Proteus sp.	1 (3.7%)	0	1.000[c]
Acinetobacter sp.	0	1 (10%)	0.270[c]
Neisseria sp.	0	1 (10%)	0.270[c]
Aeromonas sp.	1 (10%)	0	1.000[c]
Polymicrobial	4 (14.8%)	2 (20%)	0.653[c]
Concurrent antibiotic			
Metronidazole	9 (33.3%)	2 (20%)	0.688[c]
Penicillin G Sodium	4 (14.8%)	2 (20%)	0.653[c]
Ampicillin	6 (22.2%)	0	0.162[c]
Clindamycin	2 (7.4%)	2 (20%)	0.291[c]
Cloxacilin	2 (7.4%)	1 (10%)	1.000[c]
Ampicillin + sulbactam	2 (7.4%)	0	1.000[c]
Amoxycillin + clavulanate	1 (3.7%)	0	1.000[c]
Cefazolin	0	1 (10%)	0.270[c]
Cefuroxime	1 (3.7%)	0	1.000[c]
Ceftazidime	0	1(10%)	0.270[c]

[a] For continuous variables,the mean ± SD is given ; for dichotomous variables , the absolute number of patients (percentage of patients) is given.

[b] By t-test

[c] By Fisher's exact test

3. Pharmacokinetic data of the patients

Table 4.22 illustrated the pharmacokinetic data derived when only two serum drug concentrations at different time points were used and fitted to a one-compartment intermittent infusion model (see Appendix). This is commonly used in clinical settings. In this study, the two points were obtained at 2 hours and 8 hours after the beginning of 30-min intravenous infusion which were expected to be long enough for distribution equilibrium to occur.

Table4.22 Pharmacokinetic data of the patients

NO.	DW (Kg)	Dose (mg/day)	Cp2 (mg/L)	Cp8 (mg/L)	Kd (per hr.)	T1/2 (hr)	Vd (L/kg)	Cl (ml/min)
1	60.0	240	5.9	0.9	0.313	2.21	0.34	105.09
2	50.0	240	6.0	1.1	0.283	2.45	0.42	100.00
3	60.0	240	9.9	3.4	0.178	3.89	0.29	51.09
4	47.0	120	7.9	3.6	0.131	5.29	0.26	26.67
5	41.0	120	8.1	3.5	0.139	4.99	0.28	26.95
6	52.0	200	6.1	1.1	0.285	2.43	0.33	82.17
7	55.0	240	8.4	3.5	0.146	4.75	0.40	53.53
8	40.0	180	7.4	2.3	0.195	3.55	0.42	54.03
9	44.0	200	7.9	1.7	0.256	2.71	0.32	60.89
10	57.5	240	7.6	0.7	0.397	1.75	0.23	85.67
11	58.0	180	5.3	1	0.278	2.49	0.31	84.36
12	49.0	240	7.3	0.9	0.349	1.99	0.31	87.33
13	51.0	240	6.2	1.3	0.26	2.67	0.42	93.70
14	63.4	240	7.2	0.9	0.347	2.00	0.24	88.44
15	55.0	240	4.6	0.6	0.339	2.04	0.44	137.69
16	73.0	240	4.4	0.6	0.332	2.09	0.35	143.21
17	67.0	200	9.4	2.3	0.235	2.95	0.19	49.32
18	51.0	200	6.5	0.9	0.329	2.11	0.29	80.60
19	54.0	240	10	1.9	0.277	2.50	0.24	59.54
20	40.0	120	6.5	1.9	0.205	3.38	0.31	42.17
21	48.0	240	9.5	1.7	0.287	2.41	0.28	63.47
22	54.0	240	6.8	1.4	0.263	2.63	0.36	85.83
23	47.0	240	5.5	0.9	0.302	2.29	0.47	111.51
24	47.0	200	10.1	2.4	0.239	2.90	0.25	46.25
25	53.0	240	7.3	0.6	0.416	1.67	0.24	89.56
26	59.0	240	5.9	1.2	0.265	2.62	0.38	99.21

continued.....

NO.	DW (Kg)	Dose (mg/day)	Cp2 (mg/L)	Cp8 (mg/L)	Kd (per hr.)	T1/2 (hr)	Vd (L/kg)	Cl (ml/min)
27	57.0	240	7.1	2.5	0.174	3.98	0.43	70.30
28	43.0	240	7.5	1.6	0.257	1.51	0.25	82.92
29	52.0	240	7.9	0.5	0.46	3.87	0.38	59.70
30	62.0	240	8.5	2.9	0.179	3.19	0.29	64.26
31	45.0	180	6.6	1.8	0.217	1.87	0.36	99.24
32	56.0	240	6.5	0.7	0.371	2.01	0.24	75.66
33	49.0	180	6.3	0.8	0.344	3.55	0.38	61.27
34	58.8	240	8.7	2.7	0.195	4.68	0.30	43.59
35	56.0	180	7.8	3.2	0.148	1.71	0.25	95.95
36	58.0	240	6.8	0.6	0.405	4.81	0.36	49.55
37	60.0	240	9.0	3.8	0.144	4.59	0.18	27.31
38	55.0	180	12.6	5.1	0.151	3.00	0.25	52.18
39	48.0	180	8.4	2.1	0.231	3.75	0.27	39.99
40	61.0	180	9.7	3.2	0.185	2.18	0.22	70.15
41	48.0	200	7.4	1.1	0.318	4.10	0.27	35.94
42	40.0	160	9.1	3.3	0.169	8.56	0.50	26.80
43	43.0	120	6	3.7	0.081	1.80	0.47	129.69
44	64.3	240	5	0.5	0.384	2.70	0.25	68.83
45	62.0	240	8.4	1.8	0.257	2.32	0.33	101.89
46	49.0	240	6	1	0.299	3.16	0.34	60.03
47	51.0	180	7.1	1.9	0.219	2.75	0.54	114.70
48	65.0	240	5	1.1	0.252	2.48	0.31	93.27
49	57.0	240	6.4	1.2	0.279	3.43	0.30	57.84
50	49.0	120	4.7	1.4	0.202	3.04	0.35	73.25
Mean	53.3	211	7.3	1.8	0.259	3.04	0.32	73.25
SD	7.6	40	1.7	1.1	0.085	1.25	0.08	28.50
Min	40.0	120	4.4	0.5	0.081	1.51	0.18	26.67
Max	73.0	240	12.6	5.1	0.460	8.56	0.54	143.21