CHAPTER II

LITERATURE REVIEW

Over the past decade there has been a growing awareness of the problem of ARI among children in the developing world; the high morbidity and mortality among children in both rural and urban areas can be attributed to ARI. The problem was outlined first by Bulla and Hitze (1978).

Data on the incidence of acute lower respiratory tract infection (LRI) in the developing world , on the case-fatality rate, on microbial etiologies and on mortality at various ages were available from various sources , but methodologies were diverse and not always clearly described.

The Board on Science and Technology for International Development (BOSTID) undertook a coordinated research effort between 1983 and 1988 to establish the etiology and epidemiology of ARI in children in the developing world.

The case definition in the BOSTID research was that upper respiratory tract infection (URI) and lower respiratory tract infection (LRI) were grouped together as cases of ARI. Children with URI had at least one of the following signs : purulent runny nose,sore throat,cough,earache or ear discharge without findings for LRI.

Children with LRI had at least one of the following signs : wheezing, stridor,respiratory rate more than 50/minute,cyanosis, chest indrawing, or rales or crepitations.

In October 1988 results from the BOSTID research project were presented at the ARI symposium held at the National Academy of Sciences Beckman Center in Irvine, California, as follows :

1. In population in developing countries, the incidence of LRI varies widely, while ARI incidence is more similar.
2. The incidence of ARI, the incidence of LRI, and the fatality rate are higher among children < 18 months than those > 18 months.
3. Viruses were more frequently responsible than bacteria for episodes of ARI. Respiratory Syncytial Virus (RSV) was the virus most commonly found to cause ARI; parainfluenza 1,2 and 3 viruses, influenza A and B viruses and adenovirus also were responsible, to varying degrees and in different projects.
4. The major bacterial pathogens causing ARI were Streptococcus pneumoniae and Haemophilus influenzae.

   Both S.pneumoniae and H.influenzae were isolated from the throats of healthy children; the percentage of carriers varied widely in different populations.

In all studies, rales occured in a great percentage of patients, approximately 72-94% of cases . Respiratory rates >50/m and chest indrawing appeared in a much lower percentage of outpatients than inpatients (Bale, 1990).

Among children with cough or difficult breathing, those having pneumonia need to be identified to ensure that they receive antibiotics. The traditional method in making a clinical diagnosis of pneumonia was the recognition of auscultatory signs, in particular, crepitations.

However, according to Leventhal (1982) in Philadelphia, auscultatory signs are not very reliable in children, even when they are examined by a paediatrician .

Fast breathing was found to be a better predictor of pneumonia than auscultatory findings.The validity of this approach was confirmed by studies which determined the pathognomonic value of clinical signs for the diagnosis of pneumonia in children in Papua New Guinea,the Gambia and India. The results confirmed that fast breathing is a sensitive and specific indicator of pneumonia and that observation of this sign can help to categorize children with cough into 2 groups with high and low probability of pneumonia (Shann et al.,1984;Campbell et al.,1988;Cherian et al., 1988).

Effects of age on the sensitivity and specificity of the respiratory rate (RR) as a sign of pneumonia

Study	2 - 11 months		1 - 4 years	
	RR >50	RR >40	RR >50	RR >40
SENSITIVITY	%	%	%	%
Gambia	85	100	64	87
India	89	96	57	71
Papua New Guinea	80	89	57	74
SPECIFICITY				
Gambia	98	55	98	82
India	93	62	96	87
Papua New Guinea	81	59	90	72

In all studies,the sensitivity increases if the cut-off point is lowered from 50 to 40.The increases observed were from 80-89% to 89-100% in infants 2-11 months old,and from 57-64% to

71-87% in children 1-4 years old.The same change in the cut-off point produces a decrease in the specificity for both age group. The combined cut-off of 50 in infants 2-11 months old and of 40 in children 1 - 4 years old produces the best compromise in the trade off between sensitivity and specificity.

In the United States , Leventhal (1982) showed that tachypnea was a good clinical predictor of pneumonia that could be confirmed radiologically, but he did not specify respiratory rate used for defining tachypnea.

Lucero et al.(1990) in the Philippines made a prospective study of 2 groups of 199 children less than 5 years old , to test the validity of RR >50/minute and >40/minute as an indication of pneumonia. Chest roentgenograms were used in the diagnosis of pneumonia.There were two groups studied,the first group presented at the Outpatient Clinic of the Research Institute of Tropical Medicine for cough of less than 3 weeks and the prevalence of pneumonia was 69%; the second group presented at the Outpatient Department of the Makati Medical Center for cough of less than 1 week duration and the prevalence of pneumonia was 29%. In both groups,the RR was measured when the child was quiet or asleep. No further explanation about the method of counting (observation, auscultation or monitoring),the time and interval of counting RR. Inclusion of other clinical signs in the second group, such as chest retraction, and/or cyanosis, and/or failure to eat normally increased the sensitivity of tachypnea as indicator of pneumonia.

Validation of RR >50/min and >40/min as indicator of pneumonia in 2 population of children in Manila

Pneumonia prevalence, RR		Pn+/Pn-	Sens. %	Spec. %	Predictive value +	Predictive value -	LR +	95%CI
1.69%								
>50/min	y	74/10	54	84	88	44	5.90	2.77,12.56
	n	64/51						
>40/min	y	101/26	73	57	80	49	3.67	1.95,6.91
	n	37/35						
2.29%								
>50/min	y	11/24	19	83	31	71	1.14	0.52,2.51
	n	47/115						
>40/min	y	26/45	45	68	37	75	1.73	0.92,3.24
	n	32/96						
>50/m+sc	y	19/29	33	79	40	74	1.88	0.95,3.73
	n	39/112						
>40/m+sc	y	28/46	48	68	38	76	1.93	1.03,3.60
	n	30/95						

* y=yes n=no
\+ sc=symptom complex including chest retraction, and/or cyanosis, and/or failure to eat normally

It was concluded,that in population where the prevalence of pneumonia was low,tachypnea was of limited use in the diagnosis of pneumonia. While in the population with a high prevalence,a RR of >50/min had a high specificity (84%) and moderate sensitivity (54%),giving a low false-positive rate. Conversely,a RR of >40/min had a high sensitivity (73%) and 57% specificity.

Harari et al. (1991) studied prospectively clinical and chest radiographic findings in 185 children with cough aged 8 weeks-6 years who attended an Outpatient Clinic in Papua New Guinea. They found that the presence of either a RR of >50/min or chest indrawing ,or both signs, was a good indicator of pneumonia, with a

predictive power of 46% for positive test and 83% for a negative test,and 69% sensitivity and 65% specificity.This study also showed that a more complex definition of tachypnea as a RR >40 /min in children over 12 months old and >50/min in infants had only little additional benefit.

Contrary to Harari , Berman et al. (1990) showed in 90 infants less than 3 months old , a RR >60/min was significantly associated with LRI which was confirmed either radiologically or based on rales, the sensitivity was 62%, specificity 63%, the positive predictive value 79.6%, and negative predictive value 41.5%. If a threshold of 50 is used,the specificity decreases to 56%.

As varying prevalences will give a different results in a diagnostic test,it is important to know what is the prevalence of pneumonia in a target population. But unfortunately there were only a few data on the prevalence of ARI in Indonesia. In 1986,a survey conducted in a rural area in West Java found the point prevalence of ARI was 16.9 in underfives (Rosmayudi et al., 1986). Other reports from Indonesia were between 21-28.9% (Hadiwinoto and Prihatini,1989).

According to several studies, the incidence of ARI in urban areas is greater than that in rural areas. However, it is difficult to compare the prevalence of ARI among the studies because of different study methods and designs, and criteria of diagnosis.

Because ARI consists of URI and LRI,while pneumonia is one of LRI,prevalence of pneumonia may be somewhat lower than 20% in the population.

In 2 hospitals in Manila,the prevalence of pneumonia were 29% and and 69 %, showing a big difference with prevalence of pneumonia in the population.

So, it is justified to estimate that the prevalence of pneumonia in a university teaching hospital is approximately 20%.