

ETIOLOGY OF ACUTE LOWER RESPIRATORY INFECTION IN FILIPINO CHILDREN UNDER FIVE YEARS

Ma Rosario Z Capeding¹, Lydia T Sombrero¹, Fe Julia Paladin¹, Hiroshi Suzuki², Yoshio Numazaki², and Mediadora C Saniel¹

¹Research Institute for Tropical Medicine, Alabang, Muntinlupa Metro Manila, Philippines ²Sendai National Hospital, Virus Research Center, Sendai, Japan

Abstract. This study conducted at the Research Institute for Tropical Medicine from April 1990 to December 1992, identified the etiology of acute lower respiratory tract infection (ALRI) in 119 (36.9%) of 317 hospitalized children < 5 years of age. A higher proportion of respiratory viruses (27.2%) than bacterial agents (10.7%) were identified. Viral agents (adenovirus, RSV, parainfluenza 3, influenza A and influenza B) and bacterial agents (mainly *Haemophilus influenzae* and *Streptococcus pneumoniae*) are the pathogenic agents involved in ALRI among Filipino children less than 5 years old.

INTRODUCTION

Acute lower respiratory infection (ALRI) is a major cause of morbidity and mortality among children worldwide. In most developing countries like the Philippines, data on the etiologic diagnosis is limited, primarily because of difficulties in obtaining adequate samples and the low sensitivity of presently available diagnostic methods, such as blood culture and serological tests. Viral etiology studies likewise are uncommon. Knowledge of the etiologic agents of ALRI would be very useful for proper treatment or prevention of ARI. Here we present the bacterial and viral findings in hospitalized children with pneumonia under five years of age.

MATERIALS AND METHODS

All children less than 5 years old admitted at the Research Institute for Tropical Medicine (RITM) for pneumonia from April 1990 to December 1992, were prospectively enrolled into the study. Informed consent was obtained from each parent. Upon enrollment into the study, a standardized clinical evaluation was done by the pediatrician on duty. Data were recorded into a pre-coded patient entry form.

Blood was obtained by venipuncture. Bacterial cultures which included blood and nasopharyngeal aspirate cultures were performed following the recommended standard techniques (Balows *et al*,

1991). Antimicrobial susceptibility testing was done by the Kirby-Bauer disk diffusion method on Mueller-Hinton agar enriched with 5% sheep blood. Cefinase disk was used for predicting beta-lactamase resistance. Virus isolation was carried out by inoculating an aliquot of NPA suspended in virus transport medium onto confluent monolayers of HEP 2, MA-104, MDCK Hela-Ohio and Human Foreskin Fibroblast cells grown on tissue culture tubes or plates. The cultures were observed for 2-3 weeks for any cytopathic effect or hemadsorption reactions. Isolates were identified by immunofluorescence test using specific monoclonal antibodies and FITC-labeled antimouse IgG. Detection of viral antigens of RSV, Adenovirus, Parainfluenza, Influenza A and B and measles were carried out using the immunofluorescence technique. Briefly, cell smears prepared from nasopharyngeal aspirates were stained with specific monoclonal antibodies and FITC-labeled anti-mouse IgG. The cells were examined under a fluorescence microscope for typical apple-green fluorescence pattern.

RESULTS

A total of 322 patients were enrolled during the study period. There were 184 (57%) boys and 138 (43%) girls. Five patients lacked blood and NPA samples and were excluded from the etiologic part of the analysis.

The median age of patients was 8 months (range, 1 month to 59 months). Table 1 shows the age

Table 1

Age distribution of children with ALRI

Age (months)	No. of cases	(%)
0 - 11	199	(61)
12 - 24	80	(25)
25 - 59	43	(14)

distribution of children. The greatest number of patients were less than 2 years old (85%); of these, 199 (61%) were less than 1 year of age.

The severity of illness of the children studied was classified according to the World Health Organization (WHO) ARI management algorithm (WHO, 1990).

Table 2 shows the severity of illness of patients with and without measles. Pulmonary complications were pleural effusion (2), empyema (2), emphysema (1) and lung abscess (1). Of the 322 patients, 32 died, a mortality rate of 10%. Of those who died, twenty (62%) were less than a year old.

Based on their nutritional status (FNRI-PPS, 1992), 56 (18%) were normal; 109 (33%) were first degree malnourished; 104 (32%) second degree malnourished and 53 (17%) had third degree malnutrition. Of the five patients who were qualified to receive vaccination, 53 had no measles while 32 had no DPT immunization. Forty-two percent or 138 patients had received antibiotics prior to hospitalization. Amoxicillin, trimethoprim/sulfamethoxazole and ampicillin were the most common antibiotics taken.

Thirty-four blood cultures yielded growth of pathogenic bacteria. Among the bacterial agents

Table 2

Admitting diagnoses of children with ALRI.

Classification	With measles		Without measles	
	No.	(%)	No.	(%)
Pneumonia	1	(0.3)	8	(2.0)
Severe	96	(30.0)	181	(56)
Very severe	13	(4.0)	24	(7.0)

Table 3

Bacteriologic results from blood and nasopharynx.

Bacterial agents and source	No. of cases	(%)
A. Blood culture		
<i>H. influenzae</i>	14	(4.4)
<i>S. pneumoniae</i>	12	(3.7)
<i>S. aureus</i>	3	(0.9)
<i>K. pneumoniae</i>	2	(0.6)
<i>S. viridans</i>	1	(0.3)
<i>Salmonella</i> group 0	1	(0.3)
<i>A. anitratum</i>	1	(0.3)
Total	34	(10.7)
B. Nasopharynx		
<i>H. influenzae</i>	84	(26)
<i>S. pneumoniae</i>	40	(13)
<i>S. pneumoniae</i> + <i>H. influenzae</i>	38	(12)
<i>S. aureus</i>	18	(0.6)
<i>K. pneumoniae</i>	10	(0.3)
<i>H. parainfluenzae</i>	8	(0.3)
Others (<i>S. viridans</i>)	68	(21)
Total	266	(83.5)

(Table 3), *H. influenzae* and *S. pneumoniae* were the most common findings. Other microorganism isolated were: *S. aureus*, *K. pneumoniae*, *S. viridans*, *Salmonella* group 0 and *A. anitratum*. Table 3 likewise shows the bacterial agents isolated from the nasopharynx. *H. influenzae* and *S. pneumoniae* comprised 51% of the upper respiratory tract carriage. All invasive strains of *S. pneumoniae* isolated were susceptible to penicillin, as determined by screening with oxacillin disks. None of the invasive strains of *H. influenzae* produced B-lactamase.

A total of 85 respiratory viruses and 125 other viruses (48 entero-like virus, 43 measles virus, 30 rhinovirus and 4 H. simplex virus) were identified by cell culture or by rapid viral diagnosis. RSV accounted for 69% of the respiratory viruses detected (Table 4). The rest of the viral findings were adenovirus, parainfluenza 3, influenza B and influenza A. Only adenovirus was found with a concomitant bacterial agent in 3 patients.

DISCUSSION

This study showed similar findings of previous etiology studies on ALRI that reported *H. influenzae*

Table 4

Respiratory viruses identified in children with ALRI by cell culture and rapid viral diagnosis.

Virus	Cell culture	Rapid viral diagnosis	Total positive	
	No. of cases	No. of cases	No.	(%)
Adenovirus	16	3	19	(6.0)
RSV	6	53	59	(18.9)
Parainfluenza 3	3		3	(0.9)
Influenza A		1	1	(0.3)
Influenza B	1	2	3	(0.9)
Total	26	59	85	(27.2)

and *S. pneumoniae* as the most common bacterial agents (Shann, 1986; Nohynek *et al*, 1991). In the Philippines until recently, there have been few investigations on this subject. From the early 1980s until 1991, the Research Institute for Tropical Medicine which is the research arm of the Department of Health and one of the infectious disease centers of the country has conducted both community and hospital-based etiology studies. In these studies, *H. influenzae* and *S. pneumoniae* were the most frequently isolated pathogens (Tupasi *et al*, 1990 a, b).

The documentation of the etiologic diagnosis of bacterial ALRI is a problem. Blood culture, which is the standard method to diagnose bacterial pneumonia is specific but insensitive in children (Teele *et al*, 1985). Although culture was performed promptly after obtaining the samples, the viability of the bacteria may have been lost during transport of the sample. In addition, antibiotic usage by patients before admission could have diminished the isolation of bacteria. In this study 42% of patients received antibiotic prior to hospitalization. Considering the fastidious nature of *H. influenzae* and *S. pneumoniae*, the low yields are likely underestimate of the true incidence.

The upper respiratory tract carriage of *H. influenzae* and *S. pneumoniae* is very common in children (Converse and Dillon, 1977) especially so in developing countries where the carriage rate is high (Gratten *et al*, 1989). Some investigators were able to relate colonization to the development of respiratory tract infections (Gray *et al*, 1980; Montgomery *et al*, 1990). The process from colonization to

invasion however, is still poorly understood. Upper respiratory tract carriage studies are also important both in monitoring the resistance patterns of antibiotics (Mastro *et al*, 1990) and the efficacy of conjugate vaccines such as *H. influenzae* type b (Hib) conjugate (Takala *et al*, 1991).

A higher proportion of viruses (27.2%) than bacterial agents (10.7%) were identified. This finding was similar to a previous local study done in 1984-1986 which documented more respiratory viral infections than bacterial infection in children with pneumonia less than 5 years old (Tupasi *et al*, 1990 a, b), although the sensitivity issue of bacterial culture should be considered. The high incidence of clinically identified measles in 34% of patients strongly suggest that viral infection facilitates bacterial invasion of the lower respiratory tract.

In the three age group studied, the high incidence rates of ALRI was high in less than 24 months and more in boys than in girls is in agreement with studies of other developing countries (Selweyn, 1990). The high case fatality rate in the infancy group confirms previous observations that infants and young children are clearly at risk for serious respiratory infections and thus emphasizes the need for vaccination against the most common infectious agents. Since majority (61%) of our cases of pneumonia remained without etiologic diagnosis, there is a need for a sensitive, accurate and rapid diagnostic procedures.

In summary, respiratory viruses and bacterial agents, mainly *H. influenzae* and *S. pneumoniae* are

the pathogenic agents involved in ALRI among Filipino children less than 5 years old.

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