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Garcia RDJ. The Etiology of Childhood Inpatient Pneumonias in Two Private, Tertiary, Metro Manila Hospitals from 1993-2021 Seen By One Pediatric Infectious Disease Specialist
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ORIGINAL ARTICLE

THE ETIOLOGY OF CHILDHOOD INPATIENT PNEUMONIAS IN TWO PRIVATE, TERTIARY, METRO MANILA HOSPITALS FROM 1993-2021 SEEN BY ONE PEDIATRIC INFECTIOUS DISEASE SPECIALIST

Robert Dennis J. Garcia, MD, MHSA
Section Head, Pediatric Infectious Diseases, Makati Medical Center
Active Staff, Pediatric Infectious Diseases, Cardinal Santos Medical Center

ABSTRACT

Introduction: The scarce local data on the etiology of childhood pneumonia admitted in a hospital has come from a few urban and rural government hospitals. There is no data from private hospitals. Knowing the most likely etiology of pneumonia is of outmost importance as this has implications on the diagnostic modalities requested and the institution of therapy.

Objectives: The purpose of this study is to identify clinical and microbiologic diagnoses of clinically- and radiographically-confirmed pediatric pneumonia cases admitted in a private hospital. Secondarily, a discussion of specific etiologies is made.

Methodology: Each consecutive, inpatient, pneumonia referral/admission in either one of two private, urban, tertiary hospitals, of a child 18 years and below from 1993 to 2021 was logged into a computer daily by a single pediatric infectious disease specialist. Clinical, epidemiologic, diagnostic and therapeutic data were recorded. All pneumonia cases, except those seen in newborns before their discharge from the nursery, were included.

Results: Of the 496 cases**,** there was a clinical and/or microbiologic etiology in 43% of cases. The bacteremia rate was 6.3%. The most common identifiable etiologies were *Mycoplasma pneumoniae* (11.9%), *Mycobacterium tuberculosis* (5.2%), and *Staphylococcus aureus* (4.2%), while bronchiolitis (5.5%) and measles (4.8%) were the most common clinical diagnoses. There were several cases of ventilator-associated pneumonia and *Pneumocystis jirovecii* pneumonia.

Conclusions: *Mycoplasma pneumoniae*, tuberculosis, *Staphylococcus aureus* and *Pneumocystis jirovecii* are important pneumonia etiologies that have not been widely considered locally. The data presented here mirrors the practice of one pediatric infectious disease doctor in two hospitals where diagnostic and treatment options are readily available and utilized.

KEYWORDS: *Etiology; Pediatric Community Acquired Pneumonia*

Correspondence:
Dr. Robert Dennis J. Garcia
Email: rdgarcia59@yahoo.com

The author declares that the data presented are original material and has not been previously published, accepted or considered for publication elsewhere; that the manuscript has been approved by the author, and that the author has met the requirements for authorship.

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INTRODUCTION

Childhood pneumonia is generally treated empirically, often based on data from the West, or from WHO data that was based on third world reports which were mostly from the 1980s and 1990s.[1] The scarce local data on etiology of pneumonia have been reported from Metro Manila government hospitals (Philippine General Hospital [PGH], Philippine Children's Medical Center [PCMC], Regional Institute for Tropical Medicine [RITM], and Quezon City General Hospital [QCGH]) and rural government hospitals from Bohol and Tacloban.[2-5] There is no data from private hospitals.

The 2021 PAPP-PIDSP Clinical Practice Guidelines in the evaluation and management of Pediatric Community-acquired Pneumonia (PCAP) indicated that there is a lack of local data on PCAP etiology, and do not include viruses other than influenza, bacteria like pertussis and *Mycoplasma pneumoniae*, specifically; and fungi like *Pneumocystis jirovecii*; and only briefly mentions *Staphylococcus aureus* and *Mycobacterium tuberculosis* as possible pneumonia etiologies. The PCAP guidelines are a classification of community-acquired pneumonia in children, based on clinical assessment of disease severity, and its corresponding treatment; etiology is not emphasized as much due to the dearth of published information.[6] In an era where there is a heightened awareness of the need for rational antimicrobial use due to high rates of multi-drug resistant organisms seen in hospitals and the community, an improved knowledge of the likely organism(s) involved in a specific type of pneumonia, will allow the clinician to choose antimicrobials, if necessary, that are more specifically directed to such an organism or organisms.

The primary objective of this study is to provide local data on specific etiologic organisms and clinical diagnoses of all pneumonia cases admitted and seen by a single pediatric infectious disease practitioner over a 29-year period.

Secondarily, a discussion of specific etiologies is made.

MATERIALS AND METHODS

Cases in this paper included all cases of pneumonia compiled from 1993 to 2021. Each consecutive inpatient admission or referral of a patient 18 years or younger was routinely logged into a personal computer daily. Cases in which a discharge diagnosis of pneumonia of any severity together with the eventual identified etiology to explain the pneumonia (if any was arrived at) were included in this study. Clinical, epidemiologic, diagnostic and therapeutic data relevant to the pneumonia diagnosis were routinely recorded in each patient's account. The inclusion criteria for pneumonia were a child with cough, with or without tachypnea, with or without fever, and with a chest radiograph showing evidence of acute lung parenchymal disease. The etiologic diagnosis was made as follows:

- Bacterial organisms (from blood, sputum, pleural fluid, endotracheal aspirate) by standard laboratory methods
- Mycoplasma disease by the Immunocard Mycoplasma IgM^{R} test
- *Pneumocystis jirovecii* by a methenamine silver stain of Gomori, direct fluorescent antigen stain or by PCR testing
- Tuberculous (TB) pneumonia based on clinical findings, a positive 5 TU PPD test or serum TB Quantiferon result, characteristic radiographic findings, epidemiology, and laboratory findings (positive AFB smear, TB GeneXpert^{R}, and/or identification of *Mycobacterium tuberculosis* in culture)
- Leptospirosis by the presence of serum IgM antibody
- COVID-19 infection by a COVID RT-PCR test from a nasopharyngeal and oropharyngeal swab
- Influenza virus by a rapid point-of-care antigen test
- Pertussis, bronchiolitis, measles and varicella were identified clinically

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Although as a general statement, diagnostic tests were largely done as needed, without concern for cost, the diagnostic tests varied according to clinical state and epidemiology. In general, a blood culture was done for all patients referred to the author.

Excluded were newborns born at the study institutions with pneumonia, who had not been discharged from the nursery yet. Cases with a diagnosis of primary TB, without a clinical and progressing pneumonia, were excluded.

This study was approved by each hospital's Institutional Review Board. As all the cases were obtained from the author's personal files in a password-protected personal computer, no medical records were accessed from the hospitals' medical records department.

The author has no conflict of interest in the conduct of this study.

RESULTS

Table 1. Etiology of childhood inpatient pneumonia cases seen by one pediatric infectious disease physician from 1993 to 2021, from two private, urban, tertiary hospitals. *(N=496)*

Etiology (source)	No. (%)
Mycoplasma pneumoniae	59 (11.9%)
Bronchiolitis (clinical)	27 (5.5%)
Mycobacterium tuberculosis	26 (5.2%)
Measles (clinical)	24 (4.8%)
Staphylococcus aureus	21 (4.2%)
Blood culture-positive	14
Pleural fluid culture-positive	7
Bordetella pertussis (clinical)	12 (2.4%)
Influenza AH1N1 antigen positive	8 (1.6%)
Pneumocystis jirovecii	7 (1.4%)
Streptococcus pneumoniae (blood)	6 (1.2%)
Salmonella spp. (blood)	6 (1.2%)
COVID-19 (RT-PCR positive)	6 (1.2%)
Varicella (clinical)	4 (0.8%)
Leptospirosis (serum leptospirosis IgM)	2 (0.4%)
Serratia marcescens (blood)	2 (0.4%)
Mycobacterium abscessus (B.A.L. aspirate and mycobacerial culture)	1 (0.2%)
Pseudomonas spp. (blood)	1 (0.2%)
Stenotrophomonas maltophilia (blood)	1 (0.2%)
Chromobacterium anthropi (blood)	1 (0.2%)
Rhizopus spp. (lung biopsy and fungal culture)	1 (0.2%)
No etiology	281(56.7%)

Table 2. Endotracheal aspirate growths in children with ventilator-associated pneumonia seen by one infectious disease physician from 1993 to 2021, from two private, urban, tertiary hospitals. *(N=26)*

Organism	No. (%)
Pseudomonas aeroginosa	7 (27%)
Klebsiella spp.	3 (12%)
Staphylococcus aureus	3 (12%)
Serratia marcescens	3 (12%)
Stenotrophomonas maltophilia	2 (8%)
Candida spp.	1 (4%)
Acinetobacter spp.	1 (4%)
Enterobacter aerogenes	1 (4%)
No growth	5 (19%)

DISCUSSION

Ninety-eight percent of the cases in this study were referrals to the author from general pediatricians and the rest are the author's own patients. This 29-year retrospective study of childhood inpatient pneumonia in two private, urban, tertiary hospitals found a clinical and/or microbiologic etiology in 43% of the 496 cases. Of those with a known cause, the most common etiologies were *Mycoplasma pneumoniae* (11.9%), bronchiolitis (5.5%), *Mycobacterium tuberculosis* (5.2%), measles (4.9%) and *Staphylococcus aureus* (4.8%). Endotracheal growths for mechanically-ventilated children, tabulated separately, showed mostly gram-negative bacillary growths and *S. aureus*. The bacteremia rate was 6.3%.

I. Viral Pneumonia

Community-acquired pneumonia is defined as an illness with signs and symptoms of an acute infection of the pulmonary parenchyma, while bronchiolitis is broadly defined as a clinical syndrome of respiratory distress that occurs in children <2 years of age and is characterized by upper respiratory symptoms eventually followed by lower respiratory (e.g., small airway/bronchiole) infection with inflammation. Bronchiolitis is generally caused by several viruses, the most common of which is RSV. RSV bronchiolitis is often indistinguishable from RSV pneumonia and, frequently, the two coexist.[7]

With this significant overlap in the clinical manifestations, the author included bronchiolitis under the viral pneumonias in this paper.

Bronchiolitis was the second most frequent diagnosis (5.5%). This is a common viral lower respiratory tract illness usually seen in children less than two years of age, with its highest incidence between 6 weeks to 7 months. The hospitalization rate for healthy infants with RSV bronchiolitis is 0.5-4%.[7] In the present study, although our laboratory can identify RSV by PCR testing at the present time, all the bronchiolitis cases were seen before PCR testing was available, so that none of the cases was documented to be due to RSV. In studies from Tacloban City and Baguio City among children with severe inpatient pneumonia in whom viruses were identified, RSV was the virus present in 24% and 88% of cases, respectively, when a virus was isolated. Disease peaked in October, and 70% of RSV cases were seen in children aged <1 year, while 23% were between 1-2 years.[5,8] In a study in Metro Manila of infants <90 days of age evaluated for sepsis, pneumonia, or meningitis, for whom viruses were identified, RSV-positive cases were seen from July to October, with a peak in October.[4] The illness usually manifests with rhinorrhea, cough and an inconsistent fever, progressing over 2-5 days to tachypnea, wheezing, chest retractions and cyanosis; chest radiograph will usually show hyperinflation, bilateral interstitial infiltrates, and peribronchial cuffing.[7] In Tacloban City, the case-fatality rate for RSV-positive children was 7.5%.[5] Other known causes of bronchiolitis are human metapneumovirus, rhinovirus, parainfluenza, influenza, bocavirus and adenovirus.[7]

Measles-associated pneumonia was the 4th most frequent etiology, seen in 4.8% of cases. Locally, during a measles outbreak, pneumonia cases can rise sharply. It is generally difficult to distinguish a purely measles pneumonia from a measles pneumonia complicated by a secondary bacterial pathogen.

All of the measles pneumonia cases reported in this study were empirically treated with antibacterial due to the recognized significant morbidity and mortality accompanying such cases. In an RITM study of 537 children <5 years of age admitted for pneumonia, 48% had measles; among the measles cases, 14.8% had bacteremia, with *Salmonella spp*. and *Haemophilus influenzae* most commonly identified.[2] In a National Children's Hospital study, among the 425 pediatric inpatients admitted for measles, 77% developed pneumonia. Of these, 15% were 0-6 months of age, 34% were 7-12 months of age, and 28% were 13-23 months of age. Younger age (18 months for measles pneumonia vs. 37 months for measles alone), wasting and stunting were associated with an increased risk for measles pneumonia.[9] In a study from RITM of 71 children under five years of age who died of pneumonia, 35 children (49%) had clinically diagnosed measles. To determine the etiology of death for those with measles, ante-mortem blood culture, lung aspirate culture, post-mortem lung swab culture, and tissue gram stain were done; 25% of the children had measles virus only isolated, 43% had measles virus with bacterial super-infection, and 29% had bacteria only isolated.[10] Of the bacterial infections complicating measles, *S. aureus* was identified in 12 of 35 (34%) and *Pseudomonas aeruginosa* in 8 of 35 (23%); all of the *P. aeruginosa*-measles cases had received antibacterial at home before being admitted.[10]

Influenza with pneumonia was seen in 1.6%; most of the cases were seen during the 2009 influenza AH1N1 pandemic when the cases were documented to have the virus as reported in a previous study from one of the institutions in the present study.[11] In local reports, among severe pneumonia cases in whom viruses were specifically identified, a study in Baguio City of 377 children under six years isolated Influenza B in 6%, Influenza A in 4%, and Influenza AH1N1 in 2%.[8]

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In a study done in Tacloban City of 819 children under 14 years with pneumonia, Influenza A was identified in 2.2%.[5] During the 2009 Influenza AH1N1 pandemic, three local studies showed that 2%, 2.5% and 14% of children documented to have Influenza AH1N1 infection developed clinical and/or radiographic pneumonia.[8,12-13] In Baguio City and Metro Manila studies among children with influenza pneumonia, ages were <5 years old in 9-20%; 6-10 years old in 23-33%; 11-15 years old in 32%;[11-12] this is unlike RSV bronchiolitis, in which children are <2 years of age. Locally, children with documented influenza infection have fever (92-100%), cough (80-85%), colds (47-76%), throat pain (33-42%), vomiting (8-22%), headache (18-19%), diarrhea (4-18%), dyspnea (7%) and respiratory failure (0-1.5%).[11-13]

Pneumonia was due to COVID-19 in 1.2% of children in this study. All had a known adult exposure at home, had minimal radiographic infiltrates, and all recovered from the pneumonia. Four of the six children were between 8-22 months of age. The other two were both 13 years old; one was initially admitted for hemophagocytic lymphohistiocytosis, whose illness was complicated by COVID-19 infection, Multisystem Inflammatory Syndrome in Children (MIS-C), and a mild pneumonia; the second adolescent was undergoing chemotherapy for acute myelogenous leukemia and developed COVID-19 infection and a mild pneumonia. Both recovered from COVID-19. Children are far less infected by COVID-19 infection compared to adults, and when the former are infected, they often have a mild illness which does not require hospitalization; rarely is intensive care treatment necessary.[14-16]

Varicella pneumonia was seen in 0.8%. Varicella is known to be complicated by skin and soft tissue infections, pneumonia and encephalitis. Pneumonia has been reported in 6%, 8% and 17% of children admitted for varicella complications, and one population-based estimate of varicella pneumonia indicated a rate of 4.3 cases per 10,000 varicella infections.[17-19]

Due to the market population of the two hospitals, there is a high likelihood that a big proportion of the children catered to were vaccinated for varicella, to explain the low rate of cases admitted with varicella pneumonia. Like the measles virus, varicella virus causing pneumonia versus a secondary bacterial infection complicating the disease is hard to distinguish. These cases were admitted and given antimicrobials, and treated as varicella with secondary bacterial pneumonia.

II. Community-Acquired Bacterial Pneumonia

Bacteremia and/or a pleural fluid growth occurred in 7.7% of cases, with *S. aureus* (4.2%), *S. pneumoniae* (1.2%) and *Salmonella spp.* (1.2%) being the only blood culture isolates in community-acquired pneumonia in this study. Worldwide, the microbiologic etiology of childhood pneumonia has always been an enigma because the gold standard, obtaining lung samples through an invasive procedure like a percutaneous lung aspirate for specimen collection, is accompanied by significant risks and costs. On the other hand, more readily available tests, sputum culture and blood culture, are often not available or have a low yield: most children under six years cannot be expected to provide a good sputum sample. Blood cultures are known to grow a pathogen only infrequently, with bacteremia only detected in 2.3% to 3.9% in the West.[20-21] At the RITM, among children <5 years of age admitted with pneumonia, 44% had an identified etiology and the bacteremia rate was 13%.[2] In a multi-center study from PGH, QCGH and RITM of infants <3 months old with severe pneumonia, the bacteremia rate was 7%;[4] in a study done in Bohol of infants <2 months of age, the bacteremia rate was 5%;[3] while in a study done in Tacloban City of children <14 years old, it was 2.9%.[5]

Staphylococcus aureus was the 5th most common pneumonia etiology (4.8%) identified and was the top cause of community-acquired bacteremic pneumonia.

Children often had pyoderma as a primary focus (skin abscesses, intravascular catheter-related phlebitis, cellulitis, or fasciitis), while the pleural isolates were from pleural extension of staphylococcal pneumonia, usually with pneumatocoeles on radiography, or through downward extension of complicated neck infections (neck abscess, Ludwig's angina, and subsequent mediastinitis) as was seen in a previous report from one of the institutions in this study.[22] Locally, a rural PCAP study in Tacloban City of children <14 years old, who were admitted, reported a *S. aureus* growth in 0.5% of blood cultures.[5] In a study done at PCMC, among all *S. aureus* isolates from different body fluids, 17% were obtained from pneumonia and empyema cases; 7% were isolated from blood.[23] In a study done at RITM of 71 fatal pneumonias seen in children under 5 years of age, *S. aureus* was the most commonly identified organism, with 13 obtained from ante-mortem blood culture and 7 from tissue; 61% of the staphylococcal pneumonia cases were associated with measles, while the rest were associated with a primary skin lesion.[10] In a World Health Organization (WHO) programme report on ARI, a study of blood isolates from 167 of 8,418 infants with pneumonia from Gambia, Papua New Guinea and Philippines was cited, and the top organisms reported were *S. aureus* (20%), Group A Streptococcus (17%), *E. coli* (11%), *Salmonella spp*. (10%) and *H. influenzae* (4%).[24] Known risk factors for *S. aureus* pneumonia are untreated skin and soft tissue infections, *S. aureus* bacteremia, measles, influenza and pertussis.[25] Radiographically, *S. aureus* pneumonia may distinctively show cavitations, pneumatocoeles and pleural effusion or empyema.

Clinically diagnosed pertussis with pneumonia was seen in 2.4%. These patients were mostly infants under six months of age who had not finished their primary pertussis vaccination series.

In a study done at the PGH, 93% of pertussis admissions were less than four months old, and 36% were not even old enough to have received their first DPT vaccine.[26] Infants <2 months old who get pertussis have the highest hospitalization rates, with 25% developing pneumonia, and mortality is 1%.[27] Other than age, clues for pertussis are the absence of fever despite a radiographic pneumonia, the paroxysmal nature of the attacks of coughing, a peripheral leukocytosis with a lymphocytic predominance, thrombocytosis, a radiograph which may only be mildly abnormal with a perihilar infiltrate and/or atelectasis, and the presence of a recent or ongoing cough among the infant's caretakers. Consolidation in the radiograph of an infant with pertussis suggests a secondary bacterial infection due *S. aureus*, *S. pneumoniae* and/or oropharyngeal flora.[27]

Streptococcus pneumoniae was the 9th most frequent etiology, identified by blood culture in 1.2%. This organism has traditionally been the top cause of bacterial PCAP, although this has not been reflected in local studies. In a study done in Bohol, the bacteremia rate for infants <2 months of age admitted with pneumonia was 5%, with only 1.3% being due to *S. pneumoniae*.[3] In a Metro Manila study of children <5 years of age with suspected invasive bacterial disease, 0.8% grew *S. pneumoniae* in blood culture.[28] In a PGH-RITM-QCGH study of infants <3 months of age admitted for sepsis, pneumonia or meningitis, among 198 who had pneumonia, 7% were bacteremic but only one blood culture grew *S. pneumoniae* (0.5%).[4] In a study done in Tacloban City of children <14 years old with severe pneumonia, only 0.5% had a blood culture growth of *S. pneumoniae*.[5] In a study done in Central Visayas of 956 children <6 years old with pneumonia, sepsis and/or meningitis, 1.3% grew *S. pneumoniae*, with 9 of 12 invasive pneumococcal isolates seen at age 12 months or younger.[29] These numbers are less, but not far from, those reported in the West.

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In Spain, 2.1% of 884 children admitted with community-acquired pneumonia grew *S. pneumoniae* in blood cultures, while in the U.S., the rate was 2.8% among pediatric community-acquired pneumonia cases admitted to four large Children's Hospitals.[20-21] In this study, only 23% of all growths in blood cultures for community-acquired pneumonia was due to *S. pneumoniae*. Among all blood culture growths in other local reports, *S. pneumoniae* was the growth in 14% in Tacloban City and 27% in Bohol.[4-5] Even as this organism is considered to be the most common pathogen for pneumonia at 3 weeks to 4 years of age,[30] much of this data was obtained in the 1980s and 1990s using poorly validated body fluid antigen and antibody tests.[21]

Salmonella spp. bacteremia with pneumonia was seen in 1.2%; all were in infants <12 months of age. Non-typhoidal salmonella is known to be potentially invasive when infection occurs in infancy. Among 198 infants <90 days of age with inpatient pneumonia at PGH, QCGH and RITM, 7% had a positive blood culture growth; of these, *Salmonella spp.* was the top growth (3 of 14; 21%). Half of the infants who had salmonella bacteremic pneumonia were born at home.[4] Among children <14 years old in Tacloban City with severe pneumonia, only 2.3% were bacteremic; of the 17 with bacteremia, one was due to Salmonella spp.[5] In other countries, among 1,032 children <6 years old in Ghana admitted for pneumonia, 9% of 173 children who were bacteremic grew a non-typhoidal salmonella, even more frequent than bacteremic *Streptococcus pneumoniae* (4.6%).[31] Among 152 Thai children <16 years old with inpatient PCAP, only six (3.9%) were bacteremic, with blood culture growths of *S. pneumoniae*, *E. coli* and *Salmonella* group B.[32] As salmonella is not generally a respiratory pathogen, the pneumonia seen in salmonella-bacteremic infants is possibly a complication of the bacteremia.

Leptospirosis with pneumonia was seen in 0.4%; neither of the two cases was suspected to have pulmonary hemorrhage. Leptospirosis can be accompanied by pneumonia in 6-50% of cases, and pulmonary symptoms include cough, shortness of breath, cyanosis and hemoptysis.[33-35] Among the 85 children with leptospirosis in Tondo General Hospital, 14% had cough or dyspnea, but there was no mention of pneumonia.[36] A known complication of leptospirosisis is pulmonary hemorrhage, which may bring about radiographic infiltrates and acute respiratory distress syndrome.[33-35]

Haemophilus influenzae type B (HiB) is a known pneumonia pathogen, but was not identified in this series. The organism is known to cause a low-grade intermittent bacteremia and is rarely cultured from blood. The clientele in the two hospitals are known to be in the middle-class socio-economic bracket, with a high likelihood to have received HiB vaccination, to possibly explain the absence of documented HiB cases. Locally, a rural study among children <6 years of age with pneumonia reported HiB in 1.3% of blood cultures, with 11 of 12 cases seen in children <1 year of age.[29]

Among the above community-acquired bacterial pneumonia etiologies, all can be seen in the first 12 months of age. As children get vaccinated for HiB and pertussis, these two are less likely to be seen after five to six months of age. Salmonella can be seen sporadically and may be influenced by socio-economic factors and young age; pneumonia is likely secondary to bacteremia. *Staphylococcus aureus* pneumonia is associated with untreated pyodermas and *S. aureus* bacteremia. Radiography will not generally distinguish bacterial etiology, but when pneumatocoeles are present, the etiology will likely be *S. aureus*.

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After age 12 months, in DPT-HiB-vaccinated communities, *S. pneumoniae* becomes the predominant community-acquired bacterial pathogen, as current pneumococcal vaccines do not prevent disease due to non-vaccine pneumococcal serotypes and pneumococcal vaccines are not routinely available in most local health centers.

III. Atypical Pneumonia

Mycoplasma pneumoniae was the top pneumonia etiology (11.9%) identified. In four local pneumonia studies on admitted patients, three of which were done in the same two institutions in this study, this organism was detected in 4%, 22%, 26% and 28% of childhood inpatient pneumonias.[37-40] In one published prospective local study of PCAP in children under six years of age, *Mycoplasma pneumoniae* was detected in 26%, indicating that this organism is not only seen in older school-aged children.[38] In the West, *Mycoplasma pneumoniae* has been reported to cause 20% of PCAP among high school students and is considered to be the most commonly identified bacterial pathogen for children 5 years of age and older.[41] The local studies, including the present one, used a serologic IgM test, which is known to show a positive result for up to 6-12 months after the acute infection. Pneumonia due to *Mycoplasma pneumoniae* is generally indistinguishable from other bacterial pneumonia causes, but a clue may be a normal WBC count in the presence of a moderately elevated ESR and/or CRP.[39-41] Chest radiograph often shows an interstitial pneumonia, but it may also appear as bronchopneumonia.[39-41] The organism, in general, does not cause a hypoxemic illness, thereby causing a classical “walking” pneumonia.

Though the study hospitals can now identify chlamydophyla by PCR testing, no cases had been identified at the time of this study, as no other chlamydophyla testing kits were available over the previous 25 years.

IV. Ventilator-Associated Pneumonia

Blood culture grew gram-negative bacillary organisms (*Serratia marcescens*, *Pseudomonas spp.*, *Stenotrophomonas maltophilia* and *Chromobacterium anthropi*) among children with pneumonia in this study (1% of cases); all were treated for healthcare-associated pneumonia. For ETA isolates (see Table 2) from mechanically-ventilated children, *Pseudomonas aeruginosa* was the top isolate with 26%, followed by *Klebsiella spp.*, *S. aureus*, *B. cepacia* and *S. marcescens* at 12%, each. In a study done in Cebu of 343 children <6 years old with severe PCAP who were intubated and mechanically ventilated, in which an ETA culture was obtained within three days of admission (which the authors considered to be community-acquired infections), 19% had a growth, with the organisms being *Klebsiella pneumoniae* (38%), *P. aeruginosa* (26%), *Acinetobacter baumanii* (15%), *Enterobacter cloacae* (12%) and *S. aureus* (6%). Of those with an ETA growth, 92% had been given antibiotics at home.[42] Hospital-acquired gram-negative bacilli are the usual causes of ventilator associated pneumonia. Risk factors are neurologic incompetence, seizure disorder, surgery, inappropriate feeding of children in respiratory distress, prior antibiotic use and contaminated respiratory equipment.[43] The usual clinical manifestations are a new-onset fever in a hospitalized child who has new radiographic infiltrates, an increasing oxygen requirement, and leukocytosis.[43] The patients in this study were mostly neurologically impaired due to infection or seizures, or were post-operative cases which entailed extended mechanical ventilation support. The organisms obtained in ETA culture are similar to other reports in the literature, in which gram negative bacilli, notably *P. aeruginosa* and *Klebsiella spp.,* and *S. aureus* are the predominant isolates.[44-45]

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In a local study done where post-mortem lung aspiration was performed in 50 children who died of very severe pneumonia, the top four isolates were *Pseudomonas spp.* (28%), *Enterobacter spp.* (18%), *S. aureus* (11%), *E. coli* (10%) and *Klebsiella spp*. (8%). However, the authors did not indicate if these were ventilator-associated or community-acquired; 52% of the patients were in the hospital for more than seven days before death and 86% were infants.[46]

V. Tuberculous Pneumonia

Tuberculous pneumonia was the third most common etiology (5.2%) in this study. It is important to be aware that TB can cause pneumonia, especially in the local setting. In this study, cases often manifested as a sub-acutely evolving (2-6 weeks) illness with clinical and radiographic pneumonia, usually with prolonged fever, productive cough, with poor response to different oral and intravenous antimicrobials and, often, with an adult pulmonary TB contact at home, which are findings similar to that reported in the literature.[47] In the present study, continued fever despite one or more courses of oral antibiotics was usually the reason for the hospital admission. Otherwise, a frequent observation among the TB pneumonia cases was that these children were usually not hypoxemic, despite a prolonged illness. The availability of the TB GeneXpert^{R} test has greatly aided in a more prompt diagnosis of TB pneumonia because prior to its availability, it would take 3-5 weeks before a sputum mycobacterial culture yielded the diagnosis if the initial acid-fast bacilli (AFB) smear was negative. Clinically, TB pneumonia may be seen in two situations: progressive primary TB pneumonia occurring in very young infants who have marked weight loss, fever, cough and fatigue; while reactivation TB with pneumonia is usually seen in older children and adolescents who have fever, anorexia, malaise, weight loss, night sweats, productive cough, hemoptysis and chest pain.[48-49]

Radiographically, TB pneumonia is indistinguishable from other causes, unless thick-walled cavities, usually in the upper lobes, are seen, in older children; pleural effusion may be present.[48]

In this study, there was one case of *Mycobacterium abscessus* pneumonia in a diabetic 18-year-old girl with a 12-year history of achalasia and repeated aspiration pneumonia. The organism was obtained through bronchoalveolar lavage. She presented with a 4-month long fever, like what is seen with TB pneumonia, but she did not respond to anti-TB medications nor did she have a documented TB contact at home. When the mycobacterial susceptibility result was obtained, her medications were adjusted and she recovered after the treatment course.

VI. *Pneumocystis jirovecii* and Other Fungal Pneumonia

There were seven cases (1.4%) of *Pneumocystis jirovecii* pneumonia, none of whom had HIV infection. One was a 13-month-old girl with post-measles pneumonia complicated by respiratory failure. A 2nd case was a 4-year-old girl with severe pneumonia and respiratory failure; she was found to have CD4-lymphocytpenia but her HIV test was negative. A 3rd case was a 17-year-old male with fever of unknown origin for four weeks and insidious pneumonia, who was found to have CD4-lymphocytopenia but was HIV-negative. A 4th case was a 6-month-old preterm boy with bronchopulmonary dysplasia, who had three pneumonia episodes after being discharged from the nursery at three months of age; during the 3rd pneumonia episode, he was found to have pneumocystis. A 5th case was a 6-year-old boy with Acute lymphocytic leukemia who developed pneumonia after intensive chemotherapy. A 6th case was a 5-year-old with a sellar tumor who was on radiotherapy and corticosteroid treatment. A 7thcase was a 1-year-old with severe combined immunodeficiency.

All cases had the organism identified from an endotracheal aspirate, except for the 3rd case for whom a sputum sample was the source. Of the seven cases, three died even with the standard care provided. Risk factors for pneumocystis pneumonia are HIV/AIDS and other T-cell immunodeficiencies, immunosuppression, idiopathic CD4 lymphocytopenia, malignancy and organ transplantation. Most patients with pneumocystis pneumonia will have the five findings of fever, cough, tachypnea, hypoxemia, and a high serum LDH. If the diagnosis is suspected, and an HIV test is negative, a CD4 lymphocyte count may be requested to see if this is low. The chest radiograph classically shows bilateral diffuse ground-glass infiltrates, which start at the perihilum, after which, these progress outwards.[50] Early in the AIDS era, the mortality rate for mechanically ventilated adults with pneumocystis pneumonia was 60-100%.[51] In a meta-analysis of risk factors for death for children under 5 years of age with acute lower respiratory infection in low to middle-income countries, a diagnosis of *Pneumocystis jirovecii* pneumonia had an odds ratio of 4.79 for death.[52]

There was one case of fatal *Rhizopus spp.* pneumonia identified through a lung biopsy in a child with acute myelogenous leukemia in relapse. The biopsy was done because of continued fever and a progressively worsening radiograph despite broad-spectrum antibacterial and antifungal treatment, and the patient did not survive. One non-immunocompromised patient had growth of *Candida spp.* from an ETA sample who recovered with anti-fungal treatment.

Determining the definite or likely (in resource-limited settings) etiology of childhood pneumonia is important for the clinician because treatment will vary considerably between organisms, although this paper purposely did not address specific treatments.

For many viral pneumonias, antimicrobials are not necessary, or available; these pneumonias may, however, be secondarily complicated by bacterial infections. For the different bacterial pneumonias, antibacterial choices may and will differ widely. For pneumocystis pneumonia, which is a life-threatening illness, antimicrobial treatment is different from the usual choices for pneumonia. For tuberculous pneumonia, anti-TB drugs are given. For some pneumonias (pneumocystis), corticosteroid treatment may be necessary or supportive oxygen therapy will more likely be required.

CONCLUSION

In this 29-year retrospective study of childhood pneumonias in two private, urban, tertiary hospitals, an etiology was determined in 43%. Of those with a known etiology, *Mycoplasma pneumoniae* (11.9%), bronchiolitis (5.5%), *Mycobacterium tuberculosis* (5.2%), measles (4.8%) and *S. aureus* (4.2%) were the most common. The bacteremia rate was 6.3%. The data presented here mirrors the practice of one pediatric infectious disease doctor in two urban, private, tertiary hospitals where diagnostic and treatment options are readily available and utilized.

LIMITATIONS OF THE STUDY

This study has several limitations. Not all pneumonia cases were referred to the author. There was a selection bias, as the milder pneumonias were generally managed by the general pediatricians while the ones which did not improve after two days or more, upon the discretion of the attending pediatrician, were referred to the infectious disease specialist and/or a pediatric pulmonologist. The author is not the sole pediatric infectious disease specialist in the two private hospitals included in this study.

Furthermore, there are several pediatric pulmonologists who see admitted patients with pneumonia. Lastly, the diagnostic procedures have greatly evolved in the last three decades when data collection was done.

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