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Epidemiology of Invasive Pneumococcal Disease in Pediatric Age Group in a Tertiary Care Hospital

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ABSTRACT
The diagnosis of pneumococcal infection is established by the recovery of S. pneumoniae from the site of infection or the blood/sterile body fluid. Blood cultures/relevant body fluid culture should be obtained in children with pneumonia, meningitis, arthritis, osteomyelitis, peritonitis, pericarditis, or gangrenous skin lesions. All the prospective data were collected from patients using structured proforma along with their culture reports with the help of the microbiology labs. The data for the present study was collected from microbiology unit and was recorded in pre designed study proforma. The data edited for completeness and consistency before transferring into MS Excel for further analysis. Since the present study was descriptive, MS excel was used for the analysis purposes. The continuous variables were expressed as mean and as frequency distribution for categorical variables. The organism separation, susceptible and resistant were analyzed using formal method of MS-excel. In this study over period of one year 41 children were diagnosed with IPDs. Age group under study was 0-18 years, with <1 month being 1, 1-12 months being 12, 1-5 years are 18 cases and >5 yrs being 10 cases with mean age of 39.6 months and median of 36 months among total 41 children, 27 males (65.9%) and 14 were females (34.1%). 4 children had CNS infections (9.8%), 5 children had LRTI (12.2%), 1 child had combined LRTI and CNS infection (2.4% and 31 children had pneumococcal sepsis (75.6%).

INTRODUCTION

Invasive pneumococcal disease (IPD) refers to a disease in which the bacterium enters a sterile site such as blood, cerebrospinal fluid (CSF), pleural fluid, joint fluid, or pericardial fluid. Bloodstream infection (sepsis) is common in cases of IPD, either alone or in combination with focal disease. Pneumococcal meningitis usually develops after pneumococcal bacteremia, present at a sustained high level for 12-24 h before bacteria cross the blood-brain barrier. S. pneumoniae remains the most frequently identified pathogen of bacterial meningitis The risk of pneumococcal meningitis is increased in children with congenital or acquired CSF leak across a mucocutaneous barrier, such as a lumbar Dural sinus, cranial or midline facial defects (cribriform plate), fistulas of the middle ear (stapedial footplate) or inner ear (oval window, internal auditory canal, cochlear aqueduct), or CSF leakage as a result of basilar or other skull fracture. Mortality is higher in pneumococcal meningitis than in meningococcal or Haemophiles influenzas meningitis, at approximately 8% for children in developed countries[1,2]. Pneumococcal pneumonia most often occurs when the trachea is colonized, which may also result from direct seeding of lung tissue after bacteremia. It is the most common cause of community-acquired bacterial pneumonia in children under 2 years. Only 10-15% of children have positive blood cultures if hospitalized for pneumonia. Pneumococcal pneumonia is often uncomplicated, with complete recovery. A significant and common complication of pneumococcal pneumonia is pleural effusion and empyema which continue to be seen despite vaccination[3]. Before the routine use of PCVs, pneumococci caused >80% of bacteremia episodes in infants 3-36 months old with fever without an identifiable source (i.e., occult bacteremia). Bacteraemia may be followed by meningitis, osteomyelitis, suppurative (septic) arthritis, endocarditis and rarely, brain abscess. Primary peritonitis may occur in children with peritoneal effusions caused by nephrotic syndrome and other ascites-producing conditions[4]. Local complications of infection may occur, causing empyema, pericarditis, mastoiditis, epidural abscess, periorbital cellulitis, or meningitis. Abdominal infections such as peritonitis, ileitis and appendicitis have been reported, as have abscesses in solid organs. HUS and disseminated intra vascular coagulation (DIC) can also occur as a rare complication[5]. The diagnosis of pneumococcal infection is established by the recovery of S. pneumoniae from the site of infection or the blood/ sterile body fluid. Blood cultures/relevant body fluid culture should be obtained in children with pneumonia, meningitis, arthritis, osteomyelitis, peritonitis, pericarditis, or gangrenous skin lesions[6]. While significant protection from pneumococcal disease has been achieved by the use of polysaccharide and polysaccharide-protein conjugate vaccines, capsule-independent protection has been limited by serotype replacement along with disease caused by non-encapsulated Streptococcus pneumoniae (NESp). NESp strains compose approximately 3-19% of asymptomatic carriage isolates and harbor multiple antibiotic resistance genes. Surface proteins unique to NESp enhance colonization and virulence despite the lack of a capsule even though the capsule has been thought to be required for pneumococcal pathogenesis[7]. Genes for pneumococcal surface proteins replace the capsular polysaccharide (cps) locus in some NESp isolates and these proteins aid in pneumococcal colonization and otitis media (OM). NESp strains have been isolated from patients with invasive and noninvasive pneumococcal disease, but noninvasive diseases, specifically, conjunctivitis (85%) and OM (8%), are of higher prevalence. Conjunctival strains are common of the so-called classical NESp lineages defined by multi locus sequence types (STs) ST344 and ST448, while sporadic NESp lineages such as ST1106 are more commonly isolated from patients with other diseases. Higher rates of recombination can lead to increased acquisition of antibiotic resistance and virulence factors, increasing the risk of disease and hindering treatment. NESp strains are a significant proportion of the pneumococcal population, can cause disease and maybe increasing in prevalence in the population due to effects on the pneumococcal niche caused by pneumococcal vaccines. Current vaccines are ineffective against NESp and further research is necessary to develop vaccines effective against both encapsulated and non-encapsulated pneumococci[8].

MATERIALS AND METHODS

Study Area/Study Site: In-patient department of pediatrics and neonatology of Rainbow Children's Hospital and perinatal center.

Study Population: Pediatric age group 0-18 yrs of age.

Inclusion Criteria:

- All children who were admitted and diagnosed with IPD and had laboratory-confirmed pneumococcal positive culture.

Exclusion Criteria:

- Children with noninvasive pneumococcal infections (sinusitis, pharyngitis, conjunctivitis, otitis media).

Sample Size:

- The sample size was not estimated based on power calculation. The sampling procedure adopted is purposive. The samples that were analyzed during the study period were considered for analysis. As this is a descriptive study having no intervention and no control group, the sampling is purposive in nature. All the patients who are positive to culture during the study period were

included. The expected total number of cases was 41 during the study period who had IPDs.

Study Design: Prospective Observational Study.

Methods:

- All the prospective data were collected from patients using structured proforma along with their culture reports with the help of the microbiology labs.

Patient Enrolment:

- Patients meeting the following criteria were included in the study: Children of age 0-18 yrs admitted with Positive pneumococcal Cultures.

Statistical Analysis: The data for the present study was collected from microbiology unit and was recorded in pre-designed study proforma. The data edited for completeness and consistency before transferring into MS Excel for further analysis. Since the present study was descriptive, MS excel was used for the analysis purposes. The continuous variables were expressed as mean and as frequency distribution for categorical variables. The organism separation, susceptible and resistant were analyzed using formal method of MS-excel.

RESULTS AND DISCUSSIONS

Age under study is 0-18 years, with <1 month being 1, 1-12 months being 12, 1-5 years are 18 cases and >5 yrs being 10 cases with mean age of 39.6 months and median of 36 months.

Table 1: Age Group

	Frequency	Percent
<1M	1	2.4
1M-1Y	12	29.3
1-5YRS	18	43.9
>5YRS	10	24.4
Total	41	100.0

Table 2: Mean Age Distribution

Age		
Mean		39.561
Median		36.000
Std. Deviation		33.8423
Minimum		1.0
Maximum		126.0
Percentiles	25	7.500
	50	36.000
	75	59.500

Among total 41 children, 27 males (65.9%) and 14 were females (34.1%).

Table 3: Sex Distribution

	Frequency	Percent
Female	14	34.1
Male	27	65.9
Total	41	100.0

Mean hospital stay was 5.98 days. minimum being zero days i.e. treated on OPD basis and maximum being 19 days.

Table 4: Hospital Stay

	Frequency	Percent
0-5 Days	26	63.4
6-10 Days	8	19.5
11-15 Days	4	9.8
>15 Days	3	7.3
Total	41	100.0

Table 5: Mean Hospital Stay

Duration of Hospital Stay	
Mean	5.98
Median	4.00
STD. Deviation	4.698
Minimum	0
Maximum	19

25 children were completely immunized (61%), 6 were partially immunized (14.6%) and 10 were un immunized (24.4%).

Table 6: Immunization Status

	Frequency	Percent
Immunized	25	61.0
Partial	6	14.6
Un immunized	10	24.4
Total	41	100.0

28 children were immuno competent without any underlying risk factors (68.3%), while 13 children had underlying immuno deficiency (31.7%).

Table 7: Immunity Status

	Frequency	Percent
Immuno competent	28	68.3
Immuno compromised	13	31.7
Total	41	100.0

Risk Factors: Out of 41 children, 13 children had underlying risk factors 4 children had cns infections (9.8%), 5 children had LRTI (12.2%), 1 child had combined LRTI and CNS infection (2.4%) and 31 children had pneumococcal sepsis (75.6%).

Table 8: Diagnosis

Diagnosis	Frequency	Percent
CNS infections	4	9.8
LRTI	5	12.2
LRTI with CNS infection	1	2.4
Sepsis	31	75.6
Total	41	100.0

Among total 13 immuno compromised children 1 had LRTI and 12 had sepsis.

Table 9: Comparing Diagnosis with Immunity Status

	Frequency	immuno competent	immuno compromised
CNS infections	4	4	0
LRTI	5	4	1
LRTI with CNS infection	1	1	0
Sepsis	31	19	12
Total	41	28	13

Table 10: Risk Factors Associated with IPDs

Disease	Number(n)
H1N1	1
Nephrotic Syndrome	2
Chronic Liver Failure	5
Downs Syndrome	1
Dengue Fever	1
ALL	2
HLH	1

Streptococcus pneumoniae is a main pathogen high associated morbidity and mortality worldwide. It causes otitis media, sinusitis, pneumonia and invasive pneumococcal diseases (IPD). Diagnosis of IPD requires pneumococcus isolation from a normally sterile site, such as blood, cerebrospinal fluid (CSF) and pleural or ascitic fluid. Despite the availability of vaccines and antibiotics, a 2008 report from the World Health Organization (WHO) indicated that S. Pneumoniae is responsible for approximately 1.6 million deaths annually, particularly among young children and the elderly[9]. During the last decade, the clinical management of respiratory infections has become increasingly complicated by the emergence and spread of resistance in S. Pneumoniae to commonly used antibacterial drugs, particularly ß-lactams and macrolides, both in India and worldwide. Due to disproportionate Exposure to Antibiotics in Children they are at Risk for Invasive Pneumococcal Disease and the Potential for Emerging drug Resistance. Certain group of children are vulnerable for IPDs like neonates and infants below the age group of vaccination, children with asplenia, preceding a viral infection, any immuno compromised situations like leukemia, nephrotic syndrome, chronic liver and renal disease and in children with CSF leak syndromes. Even after PCV vaccination era we are still seeing increase in IPDs among children with Non vaccine serotypes and non-capsular pneumococcal strains, which are potentially dangerous, causing mortality and morbidity, prolonged hospital and multi drug resistence, despite vaccine coverage[10]. In this study over period of one year 41 children were diagnosed with IPDs. Age group under study was 0-18 years, with <1 month being 1, 1-12 months being 12, 1-5 years are 18 cases and >5 yrs being 10 cases with mean age of 39.6 months and median of 36 months. Among total 41 children, 27 males (65.9%) and 14 were females (34.1%). In study conducted by Godwin Oligbu *et al.* only 72 children (64%) had been appropriately immunized according to their age. In our study 25 children were completely immunized (61%), 6 were partially immunized (14.6%), and 10 were un immunized (24.4%) with PCV[11]. In this study 28 children were immunocompetent without any underlying risk factors (68.3%), while 13 children had underlying immuno deficiency (31.7%). 31.7% (n=13) of the patients had risk factors like H1N1 (n=1), nephritic syndrome (n=2), chronic liver disease (n=5), downs syndrome (n=1), dengue fever (n=1), ALL (n=2) and HLH (n=1). In study conducted by Viktor molander *et al.* between age group of 0-84 years 62% (n=151) of patients had risk factors like chronic kidney disease (n=37), cardiovascular disease (n=31), malignant disease (n=31), diabetes (n=27) and chronic liver disease (n=20). l skull fracture (n=18) immuno suppressive treatment (n=32)[12]. Godwin oligbu *et al.* studied about risk factors associated with IPDs. there were patients with comorbidities like prematurity (12%), immuno suppression (3.3%), asclepia (3.3%), chronic liver disease (0.6%), chronic respiratory disease (2%), Chromosomal disorders (2.6%) were present. In our study 75.6% children had pneumococcal sepsis (n=31), 9.8% children had cns infections (n=4), 12.2% children had LRTI (n=5), 2.4% had combined LRTI and CNS infection (n=1).

CONCLUSION

- IPDs were more common in children between 1-5 years of age.
- Males were affected >females.
- Mean hospital stay was 5.98 days.
- 25 children were completely immunized (61%), 6 were partially immunized (14.6%) and 10 were un immunized (24.4%).
- 28 children were immunocompetent without any underlying risk factors (68.3%), while 13 children had underlying immuno deficiency (31.7%).
- Pneumococcal sepsis (75.6%) was the most common presentation (n=31), LRTI (12.2%) (n=5), CNS infection (9.8%) (n=4), LRTI with CNS infection (2.4%) (n=1).

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