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Haemophilus influenzae infection among children with acute bacterial meningitis.

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ABSTRACT… Objective: To determine the frequency of haemophilus influenzae infection in children less than 5 years with acute bacterial meningitis (ABM). **Study Design:** Descriptive Cross Sectional study. **Setting:** Department of Pediatric Medicine, The Children's Hospital and Institute of Child Health, Multan. **Period:** October 2019 to March 2020. **Material & Methods:** A total of 165 children aged 5 – 60 months of either gender having acute bacterial meningitis with duration of < 2 weeks were enrolled. Cerebrospinal fluid (CSF) of each child was sent for microbiological analysis. **Results:** There were 106 (64.2 %) boys and 59 (35.8 %) girls. Mean age was 2.72 ± 1.07 years. Most cases, 112 (67.9 %) belonged to urban areas. Maternal literacy was positive in 65 (39.4%) cases while 59 (35.8%) were fully vaccinated. Mean disease duration was 56.25 ± 15.36 hours and 112 (67.9%) had duration of illness more than 36 hours. Frequency of Haemophilus Influenzae was noted in 35 (21.2%) cases. **Conclusion:** Frequency of Haemophilus Influenzae was high among children with acute bacterial meningitis. Early diagnosis and appropriate management might help reducing prolonged hospitalization and disease morbidity related to Haemophilus Influenza.

Key words: Acute Bacterial Meningitis, Grequency, Haemophilus Influenzae.

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INTRODUCTION

Haemophilus influenza is known to be a gram-negative human bacteria found residing in the upper respiratory tract.[1] In terms of serotypes, encapsulated H. influenzae type b (Hib) and type f (Hif) are noted to be the commonest and linked to invasive disease. H. influenzae has been observed to harm the host innate immunity response and includes bactericidal effects of the complement system.[2,3]

Variability exists regarding incidence of bacterial meningitis (BM) around the world but most of the data represents a cumulative incidence of 3/100000 population.[4] Race, gender and age seem to affect the incidence of BM. Incidence of BM is noted to be 77/110,000 infants under the age of 1 year. Overall, its incidence is 3.3 cases vs. 2.6 cases among male and female children respectively.[5] H. Influenzae, Neisseria meningitidis and Streptococcus pneumoniae are found to be the commonest pathogens involved and account for over 80% of the BM cases. Before H. Influenzae serotype b (Hib) conjugate vaccine period, Hib was responsible for more than 95% of the invasive H. influenza infections among younger pediatric age groups. Among those young children having invasive Hib disease, meningitis was noted in about 2/3rd of the cases while about 15 to 30% of the survivors were found to have major neurological sequelae like hearing impairments, mental retardation or seizure disorders.[6] Nhantumbo AA et al from Mozambique noted 12.2% children with acute BM (ABM) to have presence of H. influenzae.[7] "Center for Disease Control and Prevention Emerging Infection Program's Active Bacterial Core Surveillance (ABCs)" estimated Hib to account for 0.20/100000 cases among children aged less than 5 years.[8]

This study was aimed to determine the frequency of H. influenza in ABM among children aged < 5 years. Limited local data exists about current scale of the problem. In the past 5 years, no research has been seen in Southern Punjab, so

we planned this study. The results will be helpful to diagnose and manage these patients early, and thought to help decreasing morbidity and mortality affected by H. influenzae.

MATERIAL & METHODS

This descriptive cross-sectional study was conducted at "The Department of Pediatric Medicine, The Children's Hospital and Institute of Child Health, Multan", from October 2019 to March 2020. Sample size of 165 children estimated using formula; $n = z^2pq/d^2$, where $z = 1.96$, $p = 12.2\%$[7] (frequency of H. Influenza in meningitis), $q = 100\text{-}p$, $d = 5$ %. Approval from Institutional Ethical Committee was obtained.

We included a total of 165 children aged 5 – 60 months of either gender having ABM with duration < 2 weeks. As per WHO, ABM was labeled as a child having age less than 5 years along with sudden onset of fever (>38.5°C rectal or 38.0°C axillary) and CSF examination showing any two of these: i) Turbid appearance ii) Leukocytosis (> 100 cells/mm^3), iii) Leukocytosis (10 – 100 cells/mm^3) and either raised protein (100 mg/dl) or declined glucose (<40 mg/dl) levels. Children with perforations, shock or seizures (on history and clinical records), or with congenital anomalies or with acquired immunodeficiency, and those with malignancies or viral meningitis, were excluded.

All the study data was collected on a specialized proforma. Informed consent was sought from parents/guardians. CSF sample adopting aseptic measures was obtained from each child employing lumber puncture (LP). One ml of CSF was obtained into 3.0 ml sterile tubes and immediately dispatched to "Central Institutional Laboratory" aiming microbiological analysis including cytochemical study. CSF was considered purulent in case of at least one of the following: i) leukocyte count of more than or equal to 100 mm^3 ii) leukocyte count between 10 to 100 mm^3 and either a glucose level of less than 40 mg/dL or presence of protein using a semi-quantitative method (Pandy). Growth of H. Influenzae was reported as small non-motile, gram-negative cocco-bacillus under light microscope on CSF culture (on blood agar containing haemin and NAD under anaerobic conditions) as reported by Microbiology laboratory. Fully vaccinated was those who have completed full course of vaccination as recommended by EPI and not missed any dose of vaccination, partially vaccinated children will include those who have missed at least one dose of vaccination and unvaccinated are those who have not received any dose of vaccination as recommended by EPI (as reported by the parents).

For data analysis, SPSS-20 was employed. Mean and standard deviation calculated for Age. Frequencies and percentage were used to represent gender, monthly family income, vaccination status, age groups, residential area, frequency of H. Influenzae, and mother's education. Effect modifiers like age, gender, residential area, monthly family income, vaccination status and mother's education were controlled by making stratified tables. Applying chi-square test, P value < 0.05 was taken as significant.

RESULTS

There were 106 (64.2 %) male and 59 (35.8 %) were female cases. Overall, mean age was 2.72 ± 1.07 years (ranging 1 year to 5 years). Most cases i.e. 129 (78.2 %) were aged less than 3 years. No significant difference was found among male and female cases in terms of age (2.73 ± 0.941 years vs. 2.71 ± 1.28 years, p=0.934). Majority, 112 (67.9 %) children belonged to urban areas while monthly family income < 25000 PKR was recorded in 106 (64.2%) cases. Maternal literacy was positive in 65 (39.4%) while 100 (60.4%) mothers were illiterate. Of these 165 study cases, 18 (10.9%) were un-vaccinated, 88 (53.3%) were partially vaccinated and 59 (35.8%) were fully vaccinated. Mean disease duration was 56.25 ± 15.36 hours and 112 (67.9%) had duration of illness more than 36 hours. Table-I is showing characteristics of study participants.

Frequency of H. Influenza was noted in 35 (21.2%) cases. Age less than 3 years (p=0.002), urban residential status (p=0.041), monthly family income < Rs. 25000 (p=0.010) and incomplete

vaccination status (p<0.001) were found to have significant association with frequency of H. Influenza (Table-II).

Characteristics		Number (%)
Gender	Male	106 (64.2)
	Female	59 (35.8)
Age Groups (years)	< 3 Years	129 (78.2)
	> 3 Years	36 (21.8)
Residential Status	Rural	53 (32.1)
	Urban	112 (67.9)
Monthly Family Income (PKR)	< Rs. 25000	106 (64.2)
	> Rs. 25000	59 (35.8)
Maternal Education	Illiterate	100 (60.6)
	Literate	65 (39.4)
Vaccination Status	Un-vaccinated	18 (10.9)
	Partially vaccinated	88 (53.3)
	Vaccinated	59 (35.8)
Duration of Symptoms (hours)	< 36	53 (32.1)
	> 36 hours	112 (67.9)

Table-I. Characteristics of study participants. (n = 165)

DISCUSSION

Infants with ABM are usually presenting with non-specific features.[9] Thorough evaluation involving respiratory and neurological exams to identify any focal neurological indicator, posturing, cranial nerve abnormality and level of consciousness needs to be done.

In this study, 64.2% cases with ABM were boys. Bari et al in a local study[10] found 69.8% of the cases with meningitis to be boys while in another study from Rawalpindi[11], male predominance as 58% was reported which is again close to what we noted in the present study. A study from Yemen also recorded 69% of the study participants to be male which shows that the regional data in terms of gender distribution also favoring our findings.[12]

Mean age among our study cases was noted to be 2.72±1.07 years. It was also observed that most cases, 78.2% were above 3 years of age. Bari et al[10] from Lahore found mean age among children with meningitis to be 11.3±12 months while in another study by Tajdin et al[13] also recorded similar findings. Another study from Karachi[14] noted mean age of study participants with meningitis to be 4.8±4.14 years mean age which is slightly higher to what we found.

Study Variables		Haemophilus Influenza		P-Value
		Yes (n=35)	No (n=130)	
Gender	Male	23 (65.7%)	83 (63.8%)	0.838
	Female	12 (34.3%)	47 (36.2%)	
Age Groups (years)	< 3	34 (97.1%)	95 (73.1%)	0.002
	> 3	1 (2.9%)	35 (26.9%)	
Residential Status	Rural	6 (17.1%)	47 (36.2%)	0.041
	Urban	29 (82.9%)	83 (63.8%)	
Monthly Family Income (PKR)	< Rs. 25000	29 (82.9%)	77 (59.2%)	0.010
	> Rs. 25000	06 (17.1%)	53 (40.8%)	
Maternal Education	Illiterate	23 (65.7%)	77 (59.2%)	0.561
	Literate	12 (34.3%)	53 (40.8%)	
Vaccination Status	Un – vaccinated	12 (34.3%)	6 (4.6%)	<0.001
	Partially vaccinated	23 (65.7%)	65 (50.0%)	
	Fully vaccinated	0 (0%)	59 (45.4%)	
Duration of Symptoms (hours)	< 36	12 (34.3%)	41 (31.5%)	0.839
	> 36	23 (65.7%)	89 (68.5%)	

Table-II. Stratification of Haemophilus Influenza with regards to Study Variables. (n = 165)

Difference among different researchers could be because of difference in inclusion criteria as we enrolled children under 5 years of age. A research from Rawalpindi[11] also elaborates mean age of the study participants with meningitis to be 6 years which is again due to the reason just mentioned above. We noted mean disease duration was 56.25 ± 15.36 hours and 112 (67.9%) had duration of illness more than 36 hours. Fayyaz et al[14] also posted similar results. The present study also found out incomplete vaccination status to be significantly associated with presence of H. Influenza which is again reiterating the importance of Hib conjugate vaccine.[15] As H Influenza is a major cause of morbidity and mortility in this part of the world, compliance to Hib vaccines will benefit children of our region.[16]

Of these 165 study cases, Haemophilus Influenza was noted in 21.2%. Al-Khorasani et al[17] also reported H. influenza to be found in 15% of ABM cases. Nhantombu et al[7] observed 12.2% H. influenzae in children with ABM. Other regional data has also identified as H. Influenza as one of the most common bacterial pathogen involved in ABM among young pediatric age group whereas in Africa N meningitides is found more common.[19,20]

Our study had few limitations as well. In the study protocol, we did not plan to include recording of clinical signs of symptoms which would have enlightened us further about the presentation of study participants. Detailed findings about CSF examination would further add to what is known about the CSF characteristics of children having H. Influenza related ABM. Further studies should be done exploring other commonly involved bacterial pathogens in ABM among children.

CONCLUSION

Frequency of Haemophilus Influenza was high among children with acute bacterial meningitis. Frequency of Haemophilus Influenza was linked with younger age, urban residential status, low socio-economic status and incomplete vaccination status. Early diagnosis followed by appropriate management may help reducing prolonged hospitalization and disease morbidity which will provide psychological and economic relief to the suffering families.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

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2	Safdar Hussain	Methodology, Literature review, Discussion.	
3	Asim Khurshid	Study concept, Supervision, Proof reading.	