

# Vaccination Status and Clinical Spectrum of Children with Pyogenic Meningitis in A Tertiary Care Hospital of Hazara Division, Pakistan

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## ABSTRACT

**Background:** Pyogenic meningitis is one of the serious causes of mortality and morbidity in children. It is more prevalent in third world countries with poor vaccination coverage. This study was done to determine the vaccination status and clinical spectrum of pyogenic meningitis in children presenting to a tertiary care hospital.

**Methods:** This cross-sectional study was carried out from August, 2017 till January, 2020 over 2.5 years. Records of children who got admitted in pediatric B ward, of either gender between ages of 1 month to 14 years diagnosed as case of pyogenic meningitis were included. Records of vaccination status along with signs of meningeal irritation, complications and outcome during hospital stay were documented. Data was analyzed by SPSS 20 and chi square test applied. P value < 0.05 was taken as significant.

**Results:** There were 117 patients, 78 males and 39 females. Age ranged from 1 month to 14 years with mean age of  $5.51 \pm 4.19$  years. Patients who were vaccinated up to date were 49.6% and 37.6% were not vaccinated at all. Main presenting feature was fever and seizures especially under one year of age. There was significant association between seizures and age group with p value of 0.001. Signs of meningeal irritation (neck stiffness, brudzinski sign, kerning sign) and paradoxical irritability were present in 85 (72.6%) patients mostly above 1 year of age. There was significant association between signs of meningeal irritation and age group (5 years and above) with p value of <0.001. 110 (94%) got discharged and one (0.9%) patient was referred while 6 (5.1%) patients expired. There was significant association between stay duration and vaccination status. ( $p = 0.018$ )

**Conclusion:** Fever was the most common presentation and vaccinated children with pyogenic meningitis had shorter stay in hospital.

**Keywords:** irritability, meningitis, paradoxical, seizures, vaccination

### Authors' Contribution:

<sup>1-2</sup>Conception; Literature research; manuscript design and drafting; Critical analysis and manuscript review; Data analysis; Manuscript Editing.

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## Introduction

Pyogenic or bacterial meningitis is inflammation of meninges of spinal cord and brain. It is still one of the major causes of mortality and morbidity in children all over the world.<sup>1</sup> Worldwide there are almost 135000 deaths due to bacterial meningitis

every year.<sup>2</sup> Streptococcus pneumonia is one of the leading pathogens in children causing the meningitis along with Neisseria meningitides. Haemophilus influenzae type b is also one of the major pathogens in infants and early childhood.<sup>3</sup> Streptococcus

pneumonia and Haemophilus influenzae type b (Hib) are responsible for the most of the bacterial meningitis sequelae in children.<sup>4,5</sup>

After introduction of pneumococcal conjugate vaccines including PCV-10 and PCV-13, reduction in rates of pneumococcal infections was expected globally.<sup>6</sup> In Pakistan, extended program on immunization (EPI) was started in 1978 and it included vaccination against Haemophilus influenza. In 2012 vaccine against streptococcus pneumonia was also included in EPI schedule.<sup>7,8</sup> Though due to coverage of vaccination, there is decrease in incidence of pyogenic meningitis yet it is prevalent in the country. One of surveillance studies done in southern Pakistan showed that majority of pyogenic meningitis in children is caused by Streptococcus pneumonia and Hib.<sup>9</sup> Another study done in Lahore showed that pneumonia followed by meningitis are the leading infectious diseases especially in rural areas.<sup>10</sup> The frequency of pyogenic meningitis was 7.6% in children presenting with fever with fits in one of the hospitals of Islamabad, Pakistan.<sup>11</sup>

The number of patients presenting and admitting with diagnosis of pyogenic meningitis has increased over the last few years. This study was conducted to determine the vaccination status and clinical spectrum of pyogenic meningitis in our setup that may help the health care professionals and public health administrators in identifying the magnitude of the problem and allocation of resources, giving emphasis on vaccination and educating masses.

## Material and Methods

This cross-sectional study was conducted in paediatric B ward of Ayub Teaching Hospital, Abbottabad. The data was collected retrospectively after taking approval from institutional review board. Sample size was calculated by open epi sample size calculator taking frequency of pyogenic meningitis as 7.6%.<sup>11</sup> The calculated sample size was 108 patients. Data was retrieved from patient files from August, 2017 till January, 2020. Records of

children of either gender between ages of 1 month to 14 years were included who were diagnosed as case of pyogenic meningitis on clinical basis, cerebrospinal fluid (CSF) findings along with CT scan. The CSF finding suggestive of bacterial meningitis was increase in cell count and presence of neutrophils. Records of patients with diagnosis of tuberculous meningitis, meningo-encephalitis/encephalitis, febrile seizures and seizure disorders were excluded. Records of vaccination status were considered as up to date vaccinated, if vaccine schedule was complete according to EPI vaccine card. If any dose was found to be missed, according to age, it was taken as partially vaccinated and if none of vaccine given apart from polio drops then taken as not vaccinated. All patients initially suspected or diagnosed with pyogenic meningitis were started on intravenous antibiotics including ceftriaxone and vancomycin. Due to non-availability of CSF cultures, antibiotics covering gram negative and gram-positive bacteria were given. Dexamethasone was also given as anti-inflammatory for 72 to 96 hours. Retrieved from data, presenting features included, fever, signs of meningeal irritation including neck stiffness, brudzinski sign, kerning sign, paradoxical irritability in children less than 1.5 years of age. Development of complications during hospital stay secondary to meningitis were documented on specific proforma. Data was analyzed using SPSS version 20. Vaccination status, clinical spectrum of the disease, duration of hospital stays and patient's outcome was analyzed and chi square test applied as test of significance. P value < 0.05 was considered as statistically significant.

## Results

In this study total of 117 patients were included. Out of 117 patients, 78 (66.7%) were males and 39 (33.3%) were females. Age of patients ranged from 1 month to 14 years. Their baseline details have been given in (table I). Total 82 (70.1%) patients

stayed in hospital for up to 7 days. Stay of remaining 35 (29.9%) patients was 8 days or more. Majority (58.1%) of patients of pyogenic meningitis were less than five years of age. The main presenting feature of patients was fever present in 86 (73.5%) patients while 31 (26.5%) patients were not having history of fever. Association of fever with gender and age category did not reveal any significant relation (P value 0.8 and 0.1 respectively). Another presenting feature was seizure; which was present in 46 (39.3%) patients. Out of 46 patients, 36 (78.3%) patients were having generalized tonic clonic seizures and 10 (21.7%) patients were having focal seizures. There was significant association between seizures and age group. Majority of patients having seizures were under one year of age. Association of seizures with gender was also significant. Larger number of patients having seizures were males. Association of seizures with fever was also significant. Majority of patients presenting with seizures also had fever (Table II). At time of presentation, signs of meningeal irritation (neck stiffness, brudzinski sign, kerning sign) and paradoxical irritability were present in 85 (72.6%) patients. There was significant association between signs of meningeal irritation and age group. Majority of patients presenting with seizures were above 5 years of age. Association of meningeal irritation with gender was non-significant (Table III).

Out of 117 patients, 58 (49.6%) were vaccinated up to date, 15 (12.8%) were partially vaccinated while 44 (37.6%) were not vaccinated at all apart from taking polio drops. Male children who were not vaccinated were 35.89% while female non-vaccinated children were 41%. Fever, seizures and signs of meningeal irritation were not having significant relationship with vaccination status (p value > 0.5). Association of vaccination status with patients stay in hospital was significant. Children who were vaccinated up to date had stay duration of up to 7 days while unvaccinated children had more duration of stay in hospital (Table IV).

Out of 117 patients, 110 (94%) got discharged and one (0.9%) patient was referred while 6 (5.1%) patients expired. Majority (88.9%) were not having any complication at time of discharge from hospital. The most common complication observed in hospital was hydrocephalus which was present in 7 (6%) patients followed by Hemiplegia in 5 (4.2%) patients. Dural sinus thrombosis was present in one (0.9%) patient.

There was also significant association between seizures as presenting feature and CT scan findings with p value of 0.033. Association of duration of stay in hospital and outcome, complications or age category was non-significant.

**Table I: Baseline data of patients in study (n=117).**

	Minimum	Maximum	Mean	Std. Deviation
Stay duration (days)	1	16	6.75	2.796
Age (years)	0.10	13.00	5.1517	4.19448
CSF cell count (cells/ul)	2	28000	3550.44	4841.232
Polymorphs (percent)	0	95	64.85	30.390
Lymphocytes (percent)	5	100	35.38	30.516
CSF sugar (mg/dl)	1	157	47.11	29.075
CSF protein (mg/dl)	5	649	125.32	106.891

**Table II: Association of seizures with age, gender and fever (n=117)**

Variables	Seizures		Total n (%)	P value
	Yes n (%)	No n (%)		

Age (Years)				
Up to 1	20 (17.09)	12 (10.26)	32 (27.35)	0.001
1-5	16 (13.68)	20(17.09)	36(30.77)	
More than 5	10 (8.55)	39(33.33)	49(41.88)	
Gender				
Male	36 (30.77)	42 (35.90)	78 (66.67)	0.032
Female	10 (8.55)	29 (24.79)	39 (33.33)	
Fever				
Yes	39 (33.33)	47 (40.17)	86 (73.50)	0.026
No	7 (5.98)	24 (20.51)	31 (26.49)	
Total	46 (39.32)	71 (60.69)	117 (100)	

Table III: Association of signs of meningeal irritation with age and gender (n=117)				
Gender	Signs of meningeal irritation		Total n (%)	P value
	Yes n (%)	No n (%)		
Age (Years)				
Up to 1	15 (12.82)	17(14.53)	32 (27.35)	0.001
1-5	27(23.08)	9 (7.69)	36(30.77)	
More than 5	43 (36.75)	6(5.13)	49(41.88)	
Gender				
Male	57 (48.72)	21 (17.95)	78 (66.67)	0.883
Female	28 (23.93)	11 (9.40)	39 (33.33)	
Total	85 (72.65)	32 (27.35)	117 (100)	

Table IV: Association of vaccination status with duration of stay in hospital (n=117)					
Duration of stay (days)	Vaccination status			Total n (%)	P valu e
	Up to date n (%)	Partially vaccinated n (%)	Not vaccinated n (%)		
Up to 7	40 (34.19)	15 (12.82)	27 (23.08)	82 (70.08)	0.018
8 or more	18 (15.38)	0 (0)	17 (14.53)	35 (29.91)	
Total	58 (49.57)	15 (12.82)	44 (37.61)	117 (100)	

## Discussion

Though the incidence of bacterial meningitis has decreased with inclusion of new vaccines and expansion of immunization program especially in third world countries yet the morbidity and mortality associated with it is quite high. Therefore, timely diagnosis of bacterial meningitis is one of the most important aspects in management including status epilepticus and prevention of the sequelae.<sup>8</sup> The presenting features of bacterial meningitis are

fever, neck stiffness, seizures and altered consciousness level. Children appear sicker and in infants, the main presenting features are poor feeding, lethargy, seizures and paradoxical irritability.<sup>12,13</sup> Studies have shown that fluid management may be associated with decrease in neurological sequelae in children.<sup>14</sup> Hadi N et al<sup>15</sup> did one study in Iran and in their study positive CSF cultures were more in children less than five years of age in 57.1% patients while in our

study about 60% of patients were aged less than five years. Sallam AKA<sup>16</sup> study done in Yemen showed that the age group which presented with meningitis was between 4 months and 3 years. Bari A et al<sup>17</sup> studied the clinical spectrum in children 1 month to 5 years of age with bacterial meningitis at Children hospital, Lahore. Their male to female ratio was 1.7:1 in comparison to our study ratio of 2:1. Majority of patients (68.3%) in Bari A et al study was less than one year of age while in our study 27.4% children were less than one year of age. Fayyaz J et al<sup>18</sup> published one study about CT scan in children presenting with acute bacterial meningitis. Their study male to female ratio was 2.3:1 while in our study it was 2:1.

Fayyaz J et al<sup>19</sup> did study in Aga Khan University hospital and studied the presenting features of children with acute bacterial meningitis. Their study included 192 patients. In their study the main presenting feature was fever in 86% of patients while in our study fever as presenting feature was present in 73.5% patients. We included the paradoxical irritability as signs of meningeal irritation, 72.6% patients in our study had signs of meningeal irritation at presentation, while in Fayyaz J et al study, 78.56% patients had signs of meningeal irritation. Their findings also included that the signs of meningeal irritation were more elicitable in children who were more than five years of age like in our study. Complications were noted in 3.12% patients in contrast to our study in which complications were noted in 11.1% patients. Iio K et al<sup>20</sup> in one case report emphasized that absence of neck stiffness cannot rule out meningitis in infants, physical appearance and fever also matters. In our study 27.2% patients had no sign of meningeal irritation at time of presentation. In one of the studies by Amin M et al<sup>21</sup> done in Bhawal Victoria Hospital, 63.2% children presented with history of seizures while in our study 39.3% children had history of seizures at presentation.

In Fayyaz J et al<sup>18</sup> study, CT scan was done in 59.4% of patients and it was reported normal in 78.94%

patients. While in our study CT scan was done in 40.2% of patients.

In Bari A et al<sup>17</sup> study, 45.2% children were vaccinated up to date, as in our study where 49.6% children were vaccinated up to date. Bari A et al study was done in Lahore and patients presenting to children hospital were from rural areas. In our hospital also the majority of children presenting with meningitis are from rural areas that may be the reason for majority of children not being vaccinated. In Amin M et al<sup>17</sup> study, only 50.5% children with meningitis were vaccinated up to date and 22.7% were not vaccinated at all while in our study 45.2% children were vaccinated up to date and 37.6% children were not vaccinated at all. In their study, 63.2% children presented with history of seizures while in our study 39.3% children had history of seizures at presentation. Though they did CSF culture yet in their study 24.1% patients had *Neisseria meningitidis*. In our study 12% with meningococemia were having meningitis. Truong J et al<sup>22</sup> studied the impact of incorrect vaccination in France leading to meningitis in children. They reported 48 cases which were due to vaccine preventable bacteria. On the top of list was *Neisseria meningitidis* which was in 54.2% cases. In our study only 45.2% were vaccinated up to date and 12% cases were with meningococcal meningitis.

Andriatahirintsoa EJPR et al<sup>23</sup> in their study observed for the impact of pneumococcal conjugated vaccine (PCV)10 in children and concluded that incidence of meningitis caused by pneumococcal bacteria was reduced after introduction of vaccine in immunization program. In Pakistan, PCV was introduced in EPI program in October 2012. In our study 37.6% children were not vaccinated at all and 12.8% children were only partially vaccinated. Shrestha RG et al<sup>24</sup> did one study in one of the hospitals of Nepal and the objective was doing CSF culture in children with meningitis. Their study showed that 72.2% meningitis was caused by *Haemophilus influenzae*. In Pakistan, EPI program

includes Haemophilus influenzae vaccine. We did not do any CSF culture due to various reasons.

In Sallam AKA<sup>16</sup> study; mortality was 14.28% in children with pyogenic meningitis. In comparison mortality was 5.13% in our study, which is quite less as compared to Sallam AKA study. In a study done by Fayyaz J et al<sup>18</sup> the mortality was 3.1%.

There are limitations in this study as the data was collected retrospectively. Also, we only documented the outcome in hospital. Patients follow up is required for the possible long term neurological sequelae.

## Conclusion

Fever was most common presentation in patients of pyogenic meningitis. Seizures were common in infants reporting with meningitis, whereas signs of meningeal irritation were mostly absent in them. Male gender was more likely to have seizures. Vaccinated children had shorter stay in hospital.

## Recommendations

Infants less than one year presenting with paradoxical irritability and history of seizures, should be worked up for possible meningitis. Multicenter studies are required to further confirm the findings. Also, there are significant numbers of children who are not vaccinated at all or not up to date. Public awareness on vaccination should be the priority.

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