

Study of Pyogenic Meningitis in Under 5 Children with Special Reference to Antigen Detection in CSF in a Tertiary Care Hospital

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Abstract

Original Research Article

During the last two decades, significant changes have taken place in the epidemiology of meningitis, especially due to the global availability and expanding use of Hib vaccines. We conducted an observational study with the aim of our study was to isolate and identify the pathogen causing pyogenic meningitis in children under 5 years during December 2012 to May 2013 in Paediatrics department of Dhaka Shishu (Children) Hospital Dhaka. Our study participants are clinically suspected cases of pyogenic meningitis in children below 5 years of age admitted in the selected hospital. All the data were collected and recorded systematically in a questionnaire and entered into computer software SPSS (Statistical package for social sciences) version 20.0 edited and analyzed with plotted in graphs and tables. Sensitivity and specificity of Gram stain, CSF latex were calculated. Main outcome measure (s): Results of CSF cell count, Gram stain, Culture, LAT and Blood culture are the main outcome variables. A total of 100 cases of suspected meningitis in the age group below 5 years comprised the study population. Majority of the patients belonged to ≤ 12 months. Male to female ratio was 1.6:1. The most common clinical presentation was fever (100.0%) with median duration of 2 days. Ninety six patients had convulsion and the median duration of continuation of convulsion was 1 day. Thirty eight patients had vomiting and median duration of continuation of vomiting was 1 day. A total of 100 clinically suspected cases of acute bacterial meningitis, laboratory confirmed cases were 36(36.0%), out of which 14(38.9%) cases were CSF culture positive, 10(27.8%) were Gram stain positive and 36(36.0%) were Latex agglutination test positive. Most frequently isolated organism were *Streptococcus pneumoniae* 34(94.4%). *Haemophilus influenzae* was isolated in 2 cases. The validity of test of serology (LAT) sensitivity was 100.0% and specificity was 74.4%, Gram stain sensitivity was 71.4% and specificity 100.0% to detect capsular polysaccharide antigen in CSF. In the conclusion, we can say Pyogenic meningitis is more common during infancy and is more common in males. Fever, convulsion, vomiting and lethargy were the commonest symptoms. CSF culture is the 'Gold standard' and positive in 38.9% cases, but Latex agglutination test was 100.0% sensitive for detection of Antigen in CSF.

Keywords: Pyogenic Meningitis, Antigen detection, CSF.**Copyright © 2019:** This is an open-access article distributed under the terms of the Creative Commons Attribution license which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use (NonCommercial, or CC-BY-NC) provided the original author and source are credited.

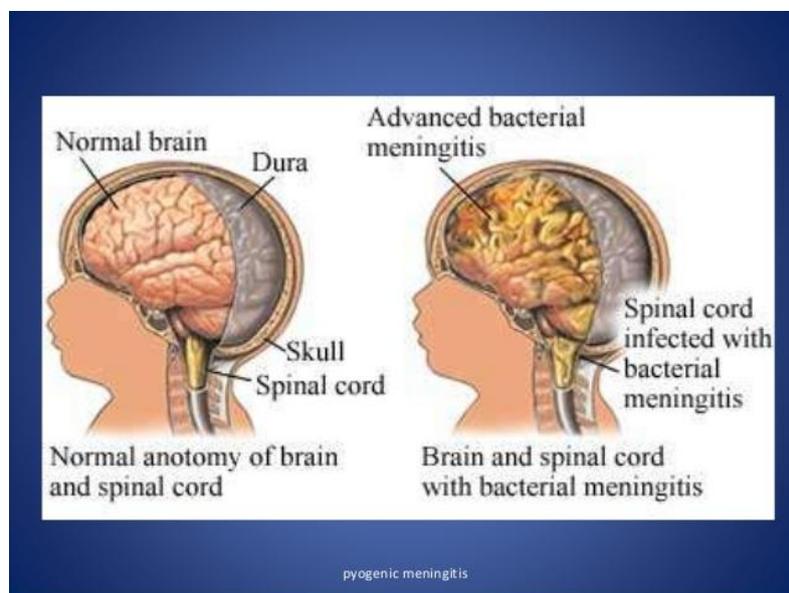
INTRODUCTION

Pyogenic meningitis is one of the most potentially serious infections in infants and children. It is associated with acute complications and risk of chronic morbidity [1]. Acute bacterial meningitis is seen more in children than in adults and it is caused by a variety of micro organisms; the most important among them are *Haemophilus influenzae*, *Neisseria meningitidis* and *Streptococcus pneumoniae* [2]. They are most commonly associated with bacterial meningitis globally accounting for almost 90% of reported cases between 2 months to 5 years of age [3]. CNS is normally sterile unless the barrier between brain and blood are broken or infection enters from outside. Meningitis is the inflammation of the pia and arachnoid

matter surrounding the brain and spinal cord [4]. Bacterial meningitis most commonly results from haematogenous dissemination of micro organism from a different site of infection. Bacterial colonization in the nasopharynx with a potentially pathogenic micro organism is the usual source of the bacteremia [1]. The clinical symptoms and signs of bacterial meningitis in children vary depending on the age of the child and duration of disease. Non specific signs include abnormal vital signs such as tachycardia and fever, poor feeding, irritability, lethargy and vomiting. Signs of fulminant sepsis such as shock disseminated intravascular coagulation (DIC), purpuric rash and coma may be present and are more common in meningococcal meningitis. Classical signs of meningitis

such as nuchal rigidity, bulged fontanelle, photophobia and positive Kernig's and Brudzinski's sign may also be present. Seizure may be present in 20-30% of children with bacterial meningitis more commonly with *S. pneumoniae* and *H. influenzae* infection than *N. meningitidis* [5]. However, in early stage of the disease

and in young children, the symptoms and signs are often non-specific. Fever may be absent up to 30% of individuals and 20-30% does not have signs of meningism at presentation. Previous antibiotic therapy may also mask the significance of the presenting illness [6].



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No pathognomonic signs or symptoms will accurately diagnose the cause of meningitis. The etiological diagnosis mainly depends on CSF analysis and culture. Alternative methods of CSF study has been developed which may be useful in patients commenced with antibiotic therapy before lumbar puncture. Where culture is negative, detection of soluble bacterial antigen can help to reach a diagnosis. Latex agglutination test has been introduced for this purpose because it can detect comparatively very small quantity of antigen present in CSF. The antigen is common meningeal pathogen eg. *H. influenzae* type b, *S. pneumoniae*, *E. coli*, Group B. Strep. and *N. meningitidis* are detected by LAT. The LAT can diagnose these specific bacterial pathogens and specific antibiotic therapy can be given to reduce the emergence of bacterial resistance [7]. Particularly when antibiotic treatment is already started and it has been suggested that such diagnostic techniques may be more sensitive than Gram staining or standard bacterial culture [8]. Latex agglutination test is very useful in the diagnosis of bacterial meningitis with sensitivity and specificity ranging from 95-100% [7]. Seizures occur more commonly with *S. pneumoniae* and *H. influenzae* infection. Signs of fulminant sepsis such as shock, DIC, purpuric rash and coma may present and are more common in meningococcal meningitis [5]. Incidence rates of *N. meningitidis* meningitis are generally highest in children <5 years of age and adolescents. *N. meningitidis* can also cause a severe bacteremia called meningococcaemia [9] in young children; the case-fatality rate for meningitis due to *H. influenzae* is

generally higher than that for meningitis due to *N. meningitidis*. The case fatality rate for meningitis due to *S. pneumoniae* in children less than five years of age exceeds 73% in some parts of the world [10]. The mortality of untreated bacterial meningitis approaches 100% and even with optimum treatment mortality and morbidity might happen. Neurological sequelae are relatively common in survivors of meningitis [11]. Sensorineural hearing loss, seizures, motor problems, hydrocephalus and mental retardation, as well as more subtle problems are observed in post meningitis children [12]. Early clinical suspicion supplemented with CSF study to confirm meningeal inflammation and identification of organism helps in timely intervention and optimum outcome. Meningitis in children constitutes a formidable illness worldwide due to its high morbidity and mortality [13]. One hundred and fifty patients with a clinical diagnosis of pyogenic meningitis were studied by Awari and Nighute [14]. Incidence of the disease was more common in low socioeconomic group. Awari and Nighute [14] determined the prevalence of pyogenic meningitis in their hospital and to find out the sensitivity of Gram stain, CRP and latex agglutination tests for diagnosis of pyogenic meningitis from CSF sample. Out of 150 samples studied 50 were diagnosed as pyogenic meningitis. *Haemophilus influenzae* was the commonest organism 12 (24%) followed by the *Staphylococcus aureus* 8 (16%), *Streptococcus pneumoniae* 6 (12%), *Acinetobacter* species 5 (10%), coagulase negative *Staphylococcus* 2 (4%), *E. coli* 3 (6%), *Klebsiella* species 3 (6%), *Pseudomonas* species 2 (4%), Group-B

Streptococci 1(2%), Enterococci 1(2%). The sensitivity of Gram stain and latex agglutination test was 98% and 92% respectively. Sensitivity of CRP was 70%. Hence Gram stain and latex agglutination test were found to be most reliable tests for diagnosis of pyogenic meningitis. Examined the distribution of acute meningoenephalitis and its etiological agents in admitted children of a tertiary hospital of Southern Bangladesh. Their study was carried out in Khulna Medical College Hospital from 2007-2009. All the admitted children between one month to 12 years of age were inducted during two years on the inclusion criteria: acute onset of fever (≤ 14 days) followed by any one of the three signs-neck stiffness, convulsion or altered mental status. Cerebrospinal fluid (CSF) was collected within hours and sent to laboratory for cytology and biochemistry. CSF was examined by Gram stain and latex agglutination test to detect the common bacteria. Serum and CSF were also tested for Japanese encephalitis virus antibody. A total of 140 children were included in the study, which was 2.5% of total admission between 2009 and 2010. Acute meningoenephalitis cases were relatively higher (37.9%) during monsoon. CSF report was pyogenic in 24 (18.5%) and viral in 13 (10%) cases. Altered mental status was significantly lower in pyogenic (62.5%) meningoenephalitis compared to non-pyogenic (93.4%) variety ($p < 0.001$). Bacterial cause was determined in 11 (8.5%) children- *S pneumoniae* (n = 8). *N meningitidis* (n = 2) and *H.influenzae* (n = 1). Three (2.3%) patients were positive for Japanese encephalitis virus. *S pneumoniae* is found as the most common bacteria for acute meningoenephalitis and Japanese encephalitis virus is present in small number.

This study is undertaken to aid in rapid diagnosis of acute bacterial meningitis cases by Gram stain and LAT and to carry out the comparative evaluation with culture which is the 'Gold standard' with Gram stain and antigen detection in CSF in cases of acute bacterial meningitis and to study antibiotic susceptibility pattern of isolates. Bacterial meningitis is an important serious illness worldwide. CSF study is important in diagnosis and management of a case of meningitis. Identifying the specific agent with their sensitivity helps in management. Although CSF culture

is the 'Gold standard' for the diagnosis of meningitis but if antibiotic is given prior any investigation then diagnosis become difficult. For such instances and also for rapid diagnosis, detection of antigen by LAT should be employed. LAT identifies bacterial antigen and this can be identified earliest. Gram stain also identifies organism earliest but in a non specific manner. This present study is placed to identify the organisms causing meningitis in a tertiary care Hospital and their sensitivity. Study also compares the usefulness of LAT and Gram stain in identifying organisms.

OBJECTIVE

General Objectives

- To isolate and identify the pathogen causing pyogenic meningitis in children under 5 years.

Specific Objectives

- To detect capsular polysaccharide antigen in CSF by latex agglutination test.
- To do comparative evaluation of Gram stain, culture and Antigen detection in CSF.

METHODS AND MATERIALS

We conducted an observational study with the aim of our study was to isolate and identify the pathogen causing pyogenic meningitis in children under 5 years during December 2012 to May 2013 in Paediatrics department of Dhaka Shishu (Children) Hospital Dhaka, Our study participants are clinically suspected cases of pyogenic meningitis in children below 5 years of age admitted in the selected hospital. All the data were collected and recorded systematically in a questionnaire and entered into computer software SPSS (Statistical package for social sciences) version 20.0 edited and analyzed with plotted in graphs and tables. Sensitivity and specificity of Gram stain, CSF latex were calculated. Main outcome measure (s): Results of CSF cell count, Gram stain, Culture, LAT and Blood culture are the main outcome variables. A total of 100 cases of suspected meningitis in the age group below 5 years comprised the study population.

RESULTS

Table-1: Presenting symptoms with duration of the study patients (n=100)

symptoms	Number	Duration of symptoms (days)	
		Median	Range(Min/max)
Fever	100	2	1.5
Convulsion	96	1	1.3
Vomiting	38	1	1.2
Lethargy	35	1	1.2
Excessive Crying	11	1	1.2
Unconsciousness	7	1	1.1

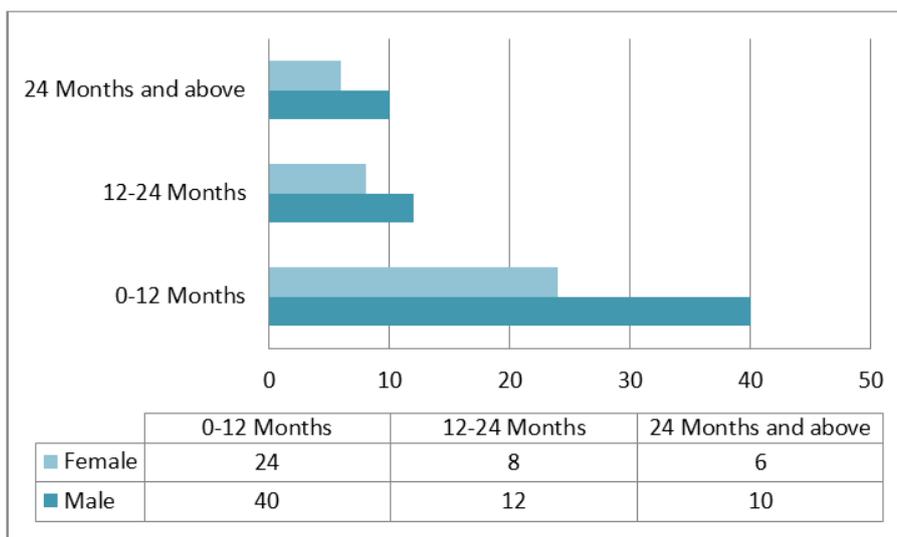


Fig-1: Distribution of the study patients by age & Sex (n=100)

Table-2: CSF findings of the study patients (n=100)

Investigation	Median	(Min/Max)
Total Cell Count/cu mm	700	45,12000
Neutrophil (%)	83	10,95
Lymphocyte (%)	16	5,90
Sugar(mg/dl)	45	6,58
Protin(mg/dl)	220	80,1000

Table-3: laboratory confirmed cases of acute bacterial meningitis by different lab methods (n=36)

Tests	Number of Patients
Gram stain+LAT+ Culture	10
Culture+LAT	14
LAT	12
Culture alone	0
Total	36

Table-4: Comparison of CSF Gram stain and LAT with Culture (n=100)

Test	Culture		Total
	Positive	Negative	
Gram stain			
Positive	10	0	10
Negative	4	22	26
Total	14	22	36
LAT			
Positive	14	22	36
Negative	0	0	0
Total	14	22	36

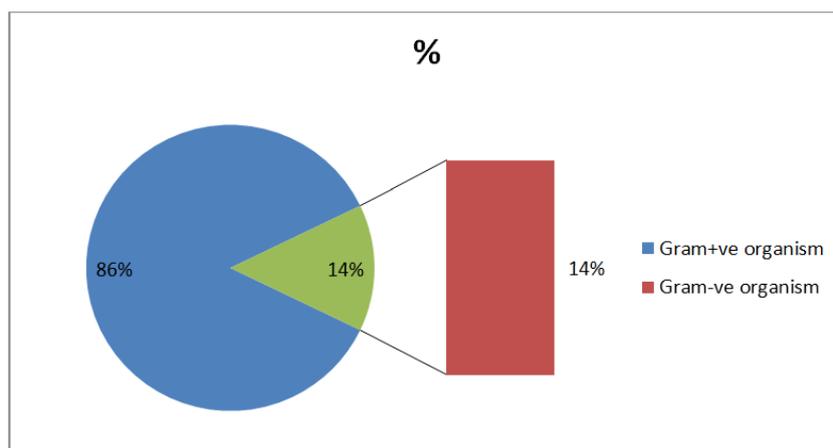


Fig-2: CSF Gram positive and Gram negative culture isolation in the study (n=14)
Among 14 CSF culture positive cases, Gram positive 12(85.7%) and 2(14.3%) Gram negative.

CSF Gram Stain

Table-5: Organisms detected by Gram stain (n=10)

Organism seen in Gram Stain	Total cases	(%)
Gram positive cocci	8	80.0%
Gram positive bacilli	2	20.0%
	10	100%

CSF Latex Agglutination test (LAT)

Table-6: Organisms detected by LAT in the study (n=36)

Organism Detected by LAT	Total cases +ve for LAT	(%)
S.pneumoniae	34	94.4%
H.influenzae type b	2	5.6%
	36	100%

Table-7: percentage of sensitivity of the organisms (n=34)

Organism	No. Tested	P (%)	A (%)	G (%)	Co (%)	Ch (%)	E (%)	Chef (%)	CF (%)
S.pneumoniae	34	34 (100%)	34 (100%)	6 (16.7%)	20 (58.3%)	34 (100%)	25 (75.0%)	34 (100%)	34 (100%)
H.influenzae type b	2	2 (100%)	2 (100%)	NT	0(0.0)	1 (50.0%)	NT	2 (100%)	NT

Table-7: Sensitivity, Specificity, accuracy, positive and negative predictive values of the serology (LAT) and Gram stain

Test of Validity	Serology(LAT)	Gram Stain
Sensitivity	100.0	71.4
Specificity	74.4	100.0
Accuracy	78.0	96.0
Positive predictive Value	38.9	100.0
Negative predictive Value	100.0	95.6

The validity of serology (LAT) and Gram Stain Correlated by calculating were sensitivity, specificity, Accuracy, Positive Negative predictive Values.

DISCUSSION

This observational study was carried out with an aim to detect capsular polysaccharide antigen in CSF by latex agglutination test and to do comparative

evaluation of Gram stain, culture and Antigen detection in CSF. A total of 100 patients, clinically suspected cases of pyogenic meningitis in children below 5 years of age admitted in Paediatrics department of Dhaka Shishu (Children) Hospital Dhaka, from December, 2012 to May, 2013, were included in this study. Children with history of fever, bulged fontanelle, convulsion, neck stiffness, altered sensorium and meningeal signs were enrolled in this study. Any

contraindication to do lumbar puncture, eg. Papilloedema, bleeding disorder, previously treated and referred from other hospitals were excluded from the study. The present study findings were discussed and compared with previously published relevant studies. Pyogenic meningitis occurs in all ages but it is commonest infancy. In this study it was observed that majority (70.0%) patients belong to ≤ 12 months, in this study all patients had fever their median duration was 2 days. Ninety six patients had convulsion with median duration 1 day. Thirty eight patients had vomiting and median duration 1 day. In present study CSF culture, Gram stain and Latex agglutination test was done. CSF culture is the "Gold standard" and these positive cases could be identified by other tests too, as being found here.

Although specificity of LAT is good, Sensitivity is not better than Gram stain. Therefore, negative result for specific bacterial antigen do not rule out bacterial meningitis⁷ In this study it was observed that in the test of validity of serology (LAT) sensitivity 100.0% , specificity 47% , accuracy 78.0% , positive predictive Values 38.9% and negative predictive values 100% to deduct capsular polysaccharide antigen in CSF. The Study Showed that a high sensitivity (100%) and specificity (98-100%) of LAT compared to culture (40%) isolation and gram stain 25-30% positivity. Maxson *et al.*, [15]. Study showed sensitivity and specificity of bacterial antigen test for *S. pneumoniae*, Hib and *N. meningitis* as 66% and 100%, 89% and 99% and 83% and 100% respectively and Group B *Streptococcus* was both 100%.

CONCLUSION

This study was undertaken to isolate identify the pathogen causing pyogenic meningitis in children less than 5 years. Pyogenic meningitis is more common during infancy and in males. Fever, Convulsion, Vomiting, and Lethargy were the commonest symptoms. Only culture could identify the agent in 38.9% cases. Latex could identify 36.0% cases. *S. Pneumoniae* was the most common identified organism in this study. A collaboration of methods may help to diagnose bacterial meningitis. However, Majority of the cases are diagnosed on clinical ground.

Limitations of the study

The study population was selected from one selected hospital in Dhaka city; So that the results of the study may not reflect the exact picture of the country. The present study was conducted at a very short period of time. Small sample size was also a limitation of the study as it was conducted at a very short period of time. Although culture is the "Gold Standard" for diagnosis but it has limited value in case of low bacterial load in CSF.

Recommendation

Further studies can be undertaken by including large number of patients.

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