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Evaluation of latex agglutination test (LAT) and efficacy in diagnosis of pyogenic meningitis in children

Dr. Kisoar Farhana Keya[1*], ASM Nawshad Uddin Ahmed[2], Dr. Amal Kanti banik[3]
[1] Registrar, Adolescent Unit (Female), Department of Paediatrics, Dhaka Shishu (Children) Hospital, Dhaka, Bangladesh
[2] Professor, Department of Paediatrics, Bangladesh Institute of Child Health & Dhaka Shishu Hospital, Dhaka, Bangladesh
[3] Registrar, Department of Paediatrics, Dhaka Shishu (Children) Hospital, Dhaka, Bangladesh

Abstract
Pyogenic meningitis is one of the most common and devastating disease of Central Nervous System, especially in children. We carried out an observational study with the aim was Evaluation of Latex Agglutination Test Efficacy in Diagnosis of Pyogenic Meningitis in children under 5 years during December 2012 to May 2013 in Paediatrics department of Dhaka Shishu (Children) Hospital, Dhaka, Bangladesh. We took our participants who were clinically suspected cases of pyogenic meningitis in children below 5 years of age admitted in our 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. Sensitivity and specificity of Gram stain, CSF latex were calculated. CSF cell count, Gram stain, Culture, LAT and Blood culture were the main outcome variables. A total of 100 cases of suspected meningitis in the age group below 5 years selected the study population. Majority of the patients belonged to ≤12 months. The most common clinical presentation was fever (100.0%) with median duration of 2 days. Ninety six (96) 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%). 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%. 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. In the conclusion, we can say. LAT can be a valuable tool in early diagnosis of acute pyogenic meningitis cases even after administration of antibiotics.

Keywords: evaluation, latex agglutination test, pyogenic meningitis, efficacy

1. Introduction
Pyogenic meningitis is one of the most common and devastating disease of Central Nervous System, especially in children. Acute bacterial meningitis is seen more in children than in adults and it is caused by a variety of microorganisms; the most important among them are Haemophilus influenzae, Neisseria meningitides 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. meningitides [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].

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 lumber 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 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. pneumonae and H. influenzae infection. The case fatality rate for meningitis due to S. pneumonae 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 sequel 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 [11]. 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 as its high morbidity and mortality [11] One hundred and fifty patients with a clinical diagnosis of pyogenic meningitis were studied by Awari and Nighute [12]. 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.

2. Objectives

General Objective

- To Evaluate Latex Agglutination Test (LAT) Efficacy in Diagnosis of Pyogenic Meningitis in children

Specific Objectives

- To detect capsular polysaccharide antigen in CSF by latex agglutination test.
- To make a comparison among Gram stain, culture and Antigen detection in CSF.

3. Method and Materials

We carried out an observational study with the aim was to Evaluation of Latex Agglutination Test Efficacy in Diagnosis of Pyogenic Meningitis in children under 5 years during December 2012 to May 2013 in Paediatrics department of Dhaka Shishu (Children) Hospital, Dhaka, Bangladesh., 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. Sensitivity and specificity of Gram stain and CSF latex were calculated. Main outcome measures were Results of CSF cell count, Gram stain, Culture, LAT and Blood culture.A total of 100 cases of suspected meningitis in the age group below 5 years were enrolled in our study. Before going to conduct study, we had taken approval from the authority. As well as we taken informed written consent from the guardians of the study children.

4. Results

A total of 100 cases of suspected meningitis in the age group below 5 years selected the study population. Majority of the patients belonged to ≤12 months. The most common clinical presentation was fever (100.0%) with median duration of 2 days. Ninety six (96) 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 was Streptococcus pneumonae 34(94.4%). 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%. 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

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

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
Protein(mg/dl)	220	80,1000

CSF Latex Agglutination test (LAT)

Table 3: Organisms detected by LAT in the study (n=36)

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

Table 4: Percentage of sensitivity of the organisms of positive cases (n=36)

Organism	N	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 5: 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.

5. Discussion

We carried out an observational study with the aim was Evaluation of Latex Agglutination Test Efficacy in Diagnosis of Pyogenic Meningitis in children under 5 years during December 2012 to May 2013 in Paediatrics department of Dhaka Shishu (Children) Hospital, Dhaka, Bangladesh. We took our participants who were clinically suspected cases of pyogenic meningitis in children below 5 years of age admitted in our 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. Sensitivity and specificity of Gram stain, CSF latex were calculated. CSF cell count, Gram stain, Culture, LAT and Blood culture were the main outcome variables. A total of 100 cases of suspected meningitis in the age group below 5 years selected the study population. Majority of the patients belonged to ≤12 months. The most common clinical presentation was fever (100.0%) with median duration of 2 days. Ninety six (96) 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 was Streptococcus pneumonae 34(94.4%). 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%. 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. Children with history of fever, bulged fontanelle, convulsion, neck stiffness, altered sensorium and meningeal sings were enrolled in this study. Any unexpected conditions like lumber 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 2days. Ninety six patients had convulsion with median duration 1day. Thirty eight patients had vomiting and median duration 1day. 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.

Latex Agglutination Test (LAT) is good for Sensitivity but not for specificity than Gram stain. In this study it was observed that in the test of validity of serology (LAT) sensitivity 100.0%, specificity 74.4%, 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.

6. Limitations of the study

This study was conducted in one centre with small sample size, which can't reflect the scenarios of the whole country. Although culture is the 'Gold Standard" for diagnosis but it has limited value in case of low bacterial load in CSF.

7. Conclusion and recommendation

This study was undertaken to see evaluation of Latex Agglutination Test Efficacy in Diagnosis of Pyogenic Meningitis in children under 5 years. 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. Further studies can be undertaken by including large number of patients.

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