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Original Research Article

A Hospital-Based Assessment of the Diagnostic Role of CSF C-Reactive Protein Quantitatively in Acute Meningitis and Differentiating Pyogenic Meningitis from Non-Pyogenic Meningitis

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Abstract

Aim: The present study was undertaken to assess the diagnostic role of CSF C-reactive protein quantitatively in acute meningitis and differentiating pyogenic meningitis from non-pyogenic meningitis.

Methods: The present study was conducted in the Department of Pathology, Anugrah Narayan Magadh Medical College and Hospital (ANMMCH) Gaya, Bihar, India for one year and patients with suspected cases of meningitis with clinical signs and symptoms of acute meningitis, aged 1 month to 18 years were included.

Results: In most of the cases 58 (61.05%) of the study population were in the age group of 1 month to 5 years. The age distribution among Pyogenic meningitis (50) shows the maximum of 17 cases (34%) in the age group 1 month to 1 year followed by 13 (26%) in the age of >1 year to 5 years. Sex distribution of study population where male patients were 55 (57.90%) and female 40 (42.10%). Clinical findings of acute meningitis in the study population where all of the study population (95) were suffering from fever (95%), Headache were present in Pyogenic meningitis 15 (30%) and Non-Pyogenic meningitis 6 (24%) respectively. In 49 cases (98%) of Pyogenic meningitis had elevated CSF-CRP level >1.1µg/ml and 1 case (2%) were in the range of 0.05-0.10 µg/ml. In the case of non-Pyogenic meningitis 24 (96%) were found to have in the range of 0.05-0.10 µg/ml. CSF CRP value of >0.1 µg/ml has a good sensitivity (98.22%), specificity (96.24%), good positive predictive value (98.12%), and good negative predictive value (96.14%) and good Diagnostic Accuracy (97.43%) for Pyogenic meningitis.

Conclusion: In conclusion we found that CSF-CRP level is significantly higher in pyogenic meningitis compared to non-pyogenic meningitis patients. It is a good indicator to diagnose pyogenic meningitis. It can be used to differentiate pyogenic from non-pyogenic meningitis also.

Keywords: Bacterial Meningitis, C-Reactive Protein, Cerebrospinal Fluid.

Introduction

Meningitis is a neurological emergency with high mortality and morbidity in the past few years. Significant advances have been made in the meningitis. Various pathogens are involved in the etiology of meningitis. The most commonly responsible organisms for pyogenic meningitis are s. pnemoniae in 50%, N. meningitides in 25%, Grp B. streptococci in 10%, L. Monocytogenes in 10%. [1] Tubercular meningitis is the most common cause of chronic meningitis and incidence in patients with tuberculosis varies from 7 to 12 %. [2] Enteroviruses (polio, coxsackie, Echo) are most common cause of viral meningitis in more than 75% cases.

Meningitis is one of the dangerous infections associated with significant morbidity and mortality (1-8%) throughout the world. [3,4] The exact incidence of meningitis in children and infants is unknown, however diagnosis of meningitis should be considered as major differential criteria in newborn with high fever and altered level of consciousness. [5] Although viral infection has been reported more than other microbial meningitis [6,7], the infection caused by bacteria is a more significant problem in most of country in the world,

especially in developing countries. [8,9] Most patients without bacterial meningitis have a negative Gram's stain (specificity 99.9%) with a negative predictive value of 99.9%. [10] Detection of nuclear polymorph leukocytes in the CSF is a fairly reliable indicator of pyogenic meningitis. But CSF leukocyte count < 250/mm3 may be present in as many as 20% of patients with bacterial meningitis. Pleocytosis may be absent in patients with severe overwhelming sepsis. Pleocytosis with a lymphocytic predominance may be present during the early stage of acute bacterial meningitis; conversely, neutrophilic pleocytosis may be present in patients during the early stages of acute viral meningitis Use of antibiotics makes the gram's stain and culture-negative and may alter the CSF cytology from neutrophilic to lymphocytic predominance. [11] Because of these limitations, several rapid diagnostic tests have been developed to aid in the diagnosis& to discriminate rapidly between viral meningitis and bacterial meningitis. [12] These techniques include Counter Immuno Electrophoresis of the CSF for the immunoglobulins, lactic acid, creatine phosphokinase and C-reactive protein. [13] As CRP is the fastest reacting and most sensitive indicator of an acute inflammatory reaction, it is a useful aid in preliminary differentiation between acute bacterial and nonbacterial meningitis. Detection of CSF-CRP appears to provide a new dimension to the diagnosis of meningitis. [14]

The present study was undertaken to assess the diagnostic role of CSF C-reactive protein quantitatively in acute meningitis and to evaluate the efficacy of CSF C-reactive protein in differentiating pyogenic meningitis from non-pyogenic meningitis.

Materials and Methods

The present study was conducted in the Department of Pathology Anugrah Narayan Magadh Medical College and Hospital (ANMMCH) Gaya, Bihar, India for one year. and patients with suspected cases of meningitis with clinical signs and symptoms of acute meningitis, aged 1 month to 18 years were included.

Inclusion Criteria

- Age 1 month to18 years
- Clinical features are suggestive of meningitis
- Patients with high body temperature
- Feeding problems. Vomiting.
- Irritability
- Seizures or sluggishness. High pitched crying

Exclusion Criteria

- Patients in whom lumbar puncture was contraindicated
- Sepsis at the local site
- Papilloedema or other signs of raised intracranial pressure
- Marked spinal deformity
- Bleeding diathesis or on anticoagulant therapy Patients on steroid
- Traumatic lumbar puncture Refusal to consent
- Patients having congenital CNS abnormality and who is known case of neurodegenerative disorder of the brain.

Sample Size: 95 patients were included after the protocol was approved by an ethical review committee of ANMMCH, GAYA, Bihar, India. Informed written consent was taken. A detailed history has been taken. A general physical and systemic examination was done. Investigations including Complete Blood Count with CSF analysis (appearance, cell count & differential, sugar, protein, gram's stain, culture), quantitative CSF- CRP, blood sugar, Mantoux Test (MT) in tubercular suspected, cranial CT scan and MRI brain if indicated was done.

Patients investigated as above were divided into three groups as mentioned below:

Group-I: Pyogenic meningitis

Group-II: Non-Pyogenic meningitis (Tubercular meningitis, Aseptic meningitis, etc.)

Group-III: No Meningitis (Normal CSF: cerebral malaria, febrile convulsion, dyselectrolytemia etc.)

We assessed the role of CSF C-reactive protein quantitatively in acute meningitis by using compute-based program statistical package for social science (SPSS) version 20.0 programs. Statistical Method: ANOVA, unpaired t-test.

Results

Table 1: Demographic data

Age groups	Pyogenic meningitis	Non-Pyogenic meningitis	Normal CSF (Controls)	Total
1 month to 1 year	17 (34)	4 (16)	3 (15)	24 (25.26%)
>1year to 5 years	13 (26)	10 (40)	11 (55)	34 (35.78%)
>5 years to 10 year	12 (24)	3 (12)	5 (25)	20 (21.05%)
>10 years to 18 years	8 (16)	8 (32)	1 (5)	17 (17.89%)
Total	50 (100%)	25 (100%)	20 (100%)	95 (100%)
Sex				
Male	30 (60)	14 (55)	11 (55)	55 (57.90)

Female	20 (40)	11 (44)	9 (45)	40 (42.10)
Total	50 (100%)	25 (100%)	20 (100%)	95 (100%)

In most of the cases 58 (61.05%) of the study population were in the age group of 1 month to 5 years. The age distribution among Pyogenic meningitis (50) shows the maximum of 17 cases (34%) in the age group 1 month to 1 year followed by 13 (26%) in the age of >1 year to 5 years. Sex distribution of study population where male patients were 55 (57.90%) and female 40 (42.10%).

Table 2: Clinical presentation and cytological and biochemical examination of CSF of the study population

Clinical findings	**Pyogenic meningitis (Group I)**	**Non-Pyogenic meningitis (Group III)**	**Normal CSF (Controls) (Group III)**	**Total**
Fever	50 (100%)	25 (100%)	20 (100%)	102 (100%)
Headache	15 (30%)	6 (24%)	2 (10%)	23 (24.21)
Nausea/ Vomiting	33 (66%)	16 (64%)	12 (60%)	61 (64.21%)
Altered Sensorium	44 (88%)	22 (88%)	12 (60%)	78 (82.10%)
Convulsion	28 (56%)	12 (48%)	20 (100%)	60 (63.15%)
Neck Rigidity	26 (52%)	15 (60%)	0	41 (43.15%)
Kerning' Sign	20 (40%)	7 (28%)	0	27 (28.42%)
Brudzinski' Sign	16 (32%)	8 (32%)	0	24 (25.26%)
Parameters	**Pyogenic meningitis (Group I)**	**Non-Pyogenic meningitis (Group III)**	**Normal CSF (Controls) (Group III)**	**P value**
Cell Count (cells/cmm)	912.18+ 810.60	156.34+138.12	1.88+1.52	0.0001
Cell_type	73.07+10.40 (Polymorphs)	76.24+9.01 (Lymphocytes)	68.22+48.52 (Lymphocytes)	0.0001
CSF Sugar (mg/dl)	42.58+14.36	64+18.52	64.36+5.45	0.0001
CSF Protein (mg/dl)	142.28+55.35	84.16+62.68	65.75+5.55	0.0001
CSF CRP (µg/ml)	5.52+1.44	0.09+0.040	0.01+0.010	0.0001

Clinical findings of acute meningitis in the study population where all of the study population (95) were suffering from fever (95%), Headache were present in Pyogenic meningitis 15 (30%) and Non-Pyogenic meningitis 6 (24%) respectively. All 50 (100.0%) cases of Pyogenic meningitis had low glucose level <90 mg/dl of CSF which is less than two-third of blood glucose level. The mean value of Glucose level (mg/dl) in CSF, in pyogenic meningitis was 42.58+14.36, in non-Pyogenic meningitis was 64+18.52and in the case of normal CSF was 64.36+5.45. All 50 (100.0%) cases of Pyogenic meningitis had elevated protein levels>45 mg/dl of CSF. The mean value of protein level (mg/dl) in CSF, in Pyogenic meningitis was 142.28+55.35, in non-Pyogenic meningitis was 84.16+62.68 and in the case of normal CSF was 65.75+5.55.

Table 3: CSF-CRP level among the study population

CSF CRP (µg/ml)	**Pyogenic meningitis (n=50)**	**Non-Pyogenic meningitis (n=25)**	**Normal CSF (Controls) (n=20)**	**Total**
more than 0.1ug/ml	49	1	0	50
less than 0.1ug/ml	1	24	20	45
Total	50	25	20	95

In 49 cases (98%) of Pyogenic meningitis had elevated CSF-CRP level >1.1µg/ml and 1 case (2%) were in the range of 0.05-0.10 µg/ml. In the case of non-Pyogenic meningitis 24 (96%) were found to have in the range of 0.05-0.10 µg/ml.

Table 4: CSF-CRP Test Estimation

Parameters	**Estimate**
Sensitivity	98.22%
Specificity	96.24%
Positive Predictive Value	98.12%
Negative Predictive Value	96.14%
Diagnostic Accuracy	97.43%
Positive Likelihood Ratio	26.48
Negative Likelihood Ratio	0.02

CSF CRP value of >0.1 µg/ml has a good sensitivity (98.22%), specificity (96.24%), good positive predictive value (98.12%), and good negative predictive value (96.14%) and good Diagnostic Accuracy (97.43%) for Pyogenic meningitis.

Discussion

Meningitis is defined as an inflammatory condition involving the membranes (meninges) covering the brain and spinal cord. It can have infectious causes, such as bacteria, mycobacteria, viruses, fungi, or parasites, or be associated with autoimmunity, cancer, or reactions to medication. [15] Meningitis continues to be a formidable illness with high morbidity and mortality in India. Gram positive cocci and gram-negative bacilli have been incriminated as bacterial aetiological agents of pyogenic meningitis in various studies. [16,17] Bacterial meningitis is a life-threatening illness. Early recognition and appropriate antibiotic treatment is crucial to reduce morbidity and mortality. Polymorphonuclear leukocytosis, low glucose concentration, and increased protein concentration in CSF are characteristics for bacterial meningitis. [18] Sometimes, bacterial meningitis presents with atypical CSF manifestations [19] and the white blood cell count, total protein and glucose levels were often unreliable markers for differential diagnosis, greatly due to low sensitivity. [20] Glucose concentrations in the CSF of patients with viral meningitis often overlap those characteristic of bacterial meningitis; but, CRP, a non-specific indicator, was very reliable in estimating the type of infection. [21] CSF-CRP is not an alternative of examination of CSF biochemistry, cytology and culture [22] and used to confirm the diagnosis, especially in restrictions on diagnostic tests.

In most of the cases 58 (61.05%) of the study population were in the age group of 1 month to 5 years. The age distribution among Pyogenic meningitis (50) shows the maximum of 17 cases (34%) in the age group 1 month to 1 year followed by 13 (26%) in the age of >1 year to 5 years. Sex distribution of study population where male patients were 55 (57.90%) and female 40 (42.10%). Clinical findings of acute meningitis in the study population where all of the study population (95) were suffering from fever (95%), Headache were present in Pyogenic meningitis 15 (30%) and Non-Pyogenic meningitis 6 (24%) respectively. A similar observation was also recorded by other authors. [23,24]

All 50 (100.0%) cases of Pyogenic meningitis had low glucose level <90 mg/dl of CSF which is less than two-third of blood glucose level. The mean value of Glucose level (mg/dl) in CSF, in pyogenic meningitis was 42.58+14.36, in Non-Pyogenic meningitis was 64+18.52and in the case of normal CSF was 64.36+5.45. All 50 (100.0%) cases of Pyogenic meningitis had elevated protein levels>45 mg/dl of CSF. The mean value of protein level (mg/dl) in CSF, in Pyogenic meningitis was 142.28+55.35, in Non-Pyogenic meningitis was 84.16+62.68 and in the case of normal CSF was 65.75+5.55. In 49 cases (98%) of Pyogenic meningitis had elevated CSF-CRP level >1.1µg/ml and 1 case (2%) were in the range of 0.05-0.10 µg/ml. In the case of Non-Pyogenic meningitis 24 (96%) were found to have in the range of 0.05-0.10 µg/ml. CSF CRP value of >0.1 µg/ml has a good sensitivity (98.22%), specificity (96.24%), good positive predictive value (98.12%), and good negative predictive value (96.14%) and good Diagnostic Accuracy (97.43%) for Pyogenic meningitis. This report demonstrates the usefulness of a latex agglutination test for the detection of CSF-CRP as a rapid and simple, method in diagnosing and differentiating cases of bacterial and non-bacterial meningitis in children. [25] The concentration of CSF CRP is raised in patients with meningitis. CSF-CRP has been reported to be one of the most reliable and early indices to differentiate bacterial from non-bacterial meningitis. [26] CRP estimation can help in diagnosing cases of acute bacterial meningitis more effectively than culture. It is also useful in monitoring the clinical course of meningitis. [27]

Conclusion

In conclusion we found that CSF-CRP level is significantly higher in pyogenic meningitis compared to non-pyogenic meningitis patients. It is a good indicator to diagnose pyogenic meningitis. It can be used to differentiate pyogenic from non-pyogenic meningitis also. It is recommended to detect CSFCRP level as a rapid diagnostic test to start appropriate antibiotic therapy, As Early, accurate and appropriate therapy can ameliorate the mortality and morbidity rates, the overall cost of the treatment and the duration of hospitalization.

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