CSF C – REACTIVE PROTEIN ESTIMATION FOR THE BED SIDE DIAGNOSIS OF PYOGENIC MENINGITIS

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CERTIFICATE

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INTRODUCTION

Infections of the central nervous system are fairly common in pediatric practice. The clinical profile is protean. A high index of suspicion of the treating physician is essential to make an early diagnosis. The need for early diagnosis is imperative. Potent antibiotics have reduced mortality, but do not prevent sequelae especially if therapy is delayed. The newer rapid diagnostic tests and imaging modalities have improved the holistic management of children with CNS infections. Pretreatment with antibiotics of patients with purulent meningitis can modify the clinical picture and CSF findings. So distinctive etiological diagnosis becomes difficult. Gram' staining of CSF can provide a rapid preliminary identification of infective organism, but is liable to misinterpretation especially in inexperienced hands.

Culture of CSF takes 24 to 48 hours for isolating the causative organism. Further more culture may not always be positive in children who have received antibiotics prior to hospitalization.

Bacterial polysaccharide antigen of microorganisms can be detected by newer immunological tests like Counter immuno electrophoresis, Latex agglutination tests etc. Since antigen may be present in the CSF even after lysis of bacteria, these immunological tests could prove useful even in partially treated patients. The present

study was therefore designed to evaluate the utility of CRP in CSF in diagnosing cases of pyogenic meningitis, to study the spectrum of bacterial pathogens causing acute bacterial meningitis, their sensitivity pattern to antibiotics, and to analyse the clinical profile of bacterial meningitis.

OVERVIEW OF PYOGENIC MENINGITIS IN CHILDREN

Infections of central nervous system can be broadly classified into

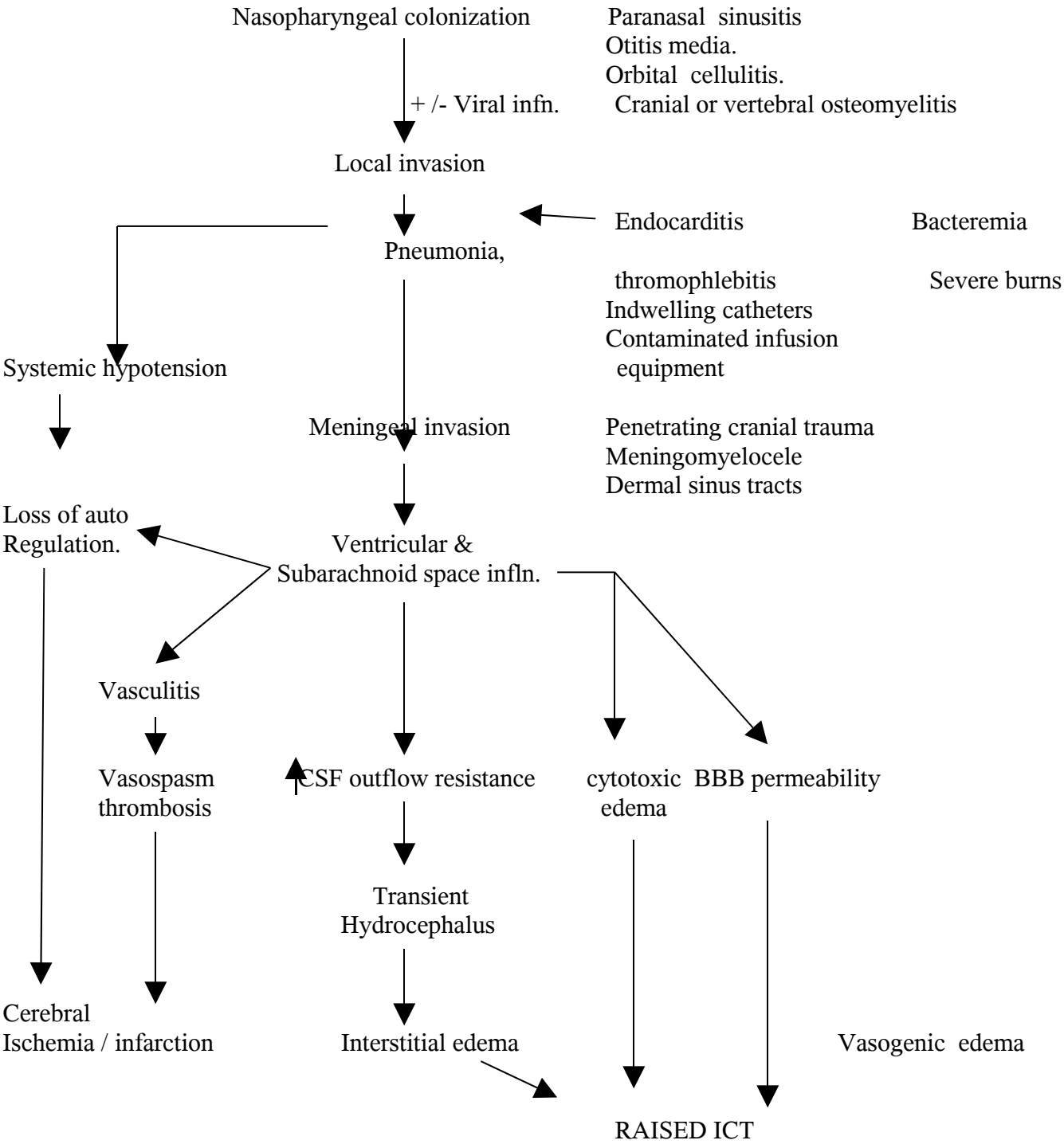
1) Meningitis – acute, subacute, chronic
2) Encephalitis and infective encephalopathy
3) Cerebral abcess, granuloma, parasitic infestations

Meningitis may be

i. Acute- bacterial, viral.
ii. Subacute or chronic- TB, fungal, parasitic, neoplastic or chemical.
iii. Partially treated

Acute bacterial meningitis which is a major cause of mortality and morbidity among children occurs both in epidemic and sporadic pattern. It may follow septicemia, apparently trivial illness like upper respiratory tract infections, otitis media, pyoderma and minor head trauma. Patients with diminished host resistance as in diabetes mellitus, malignancies, and patients on immunosuppresive drugs are more susceptible to develop meningitis.

PATHOPHYSIOLOGY OF BACTERIAL MENINGITIS



Common etiological pathogens:[1]

AGE GROUP	COMMON BACTERIAL PATHOGENS
NEWBORN	Escherichia coli Klebseilla pneumoniae Listeria monocytogenes Enterococcus Sp. Salmonella Sp.
4 WEEKS TO 12 WEEKS	Hemophilus influenza Streptococcus pneumoniae Gp . B streptococcus Listeria monocytogenes
MORE THAN 12 WEEKS	Hemophilus influenza Streptococcus pneumoniae Nisseriea miningitidis

Epidemiology of acute bacterial meningitis is primarily a reflection of epidemics of bacteremia.

Incidence of pyogenic meningitis

In developed countries: 1.5 / 100000

In developing countries: 20 / 100000

The case fatality rate in early childhood is 10 %

Incidence in ICH

YEAR	**2003**	**2004**	**2005**	**2006**
NO. OF CASES	126	120	84	55

PREDISPOSING FACTORS:

Acute otitis media

Chronic sinusitis

Pneumonia

Endocarditis

Head injury

Recent neurosurgery

Neurosurgical devices

Altered immune status

CSF leak

FACTORS CONTRIBUTING TO INFECTION LEADING TO MENINGITIS:

Host factors:

Age

Sex : Male infants have higher incidence of Gram neg organisms

Female infants are more susceptible to L.monocytogenes

Group B streptococcus affects both sexes equally

Race: blacks have a higher incidence rate

Immunity level of host

Genetic predisposition: presence of HLA B12

Presence of HLA BW 40 – H influenza

Presence of HLA B27 - N .meningitidis

Environmental factors: incidence more in

Winter season

Overcrowding

Poor socioeconomic conditions

HOST DEFENSE MECHANISMS IN SUBARACHNOID SPACE

The host response to infection is by way of cerebral edema which causes the multitude of features in meningitis.

i. Complement mediated.

Complement levels are low / absent in normal CSF. Complement levels increases in infection, but is insufficient.

Low CSF complement is due to.

Variable permeability of BBB.

Variable degrees of sub arachnoid space inflammation.

Enhanced clearance from subarachnoid space.

Low production rates in CNS.

Degradation at site of infection.

Leukocyte protease degrades functional complement C3b with formation of non-opsonic break down product C3d. Hence opsonic and bacteriocidal activity is absent.

ii. Humoral:

Normal CSF – IgM absent.

IgG levels low.

Immunoglobulins increase in acute bacterial meningitis, but are insufficient.

iii. Cell Mediated:

Hall mark – Neutrophilic phagocytosis

C5a acts as chemotactic factor for neutrophils

Meningeal & perivascular macrophages also play a role.

SPREAD

Hematogenous – most common

Direct

Contiguous

CLINICAL FEATURES[4]:

Neonate:

Usually nonspecific with few signs referable to the CNS

Bulging fontanelle

Seizures (40%)

Temperature instability

Irritability, high pitched cry

Lethargy, poor feeding, vomiting

Apnea, cyanosis

Infants:

Mild irritability, reluctance to flex the neck

Projectile vomiting, vacant stare, convulsions, high pitched cry

Tense and bulging fontanelle

Temperature instability

Older children:

Headache

Projectile vomiting

Lethargy, mental confusion

90 to 95 % have fever

Anorexia, arthralgia, myalgia

Photophobia

Papilloedema

Untreated illness progresses to convulsions, coma and death

Signs of meningeal irritation[43];

Nuchal rigidity

Kernig' sign

Brudzinski' neck and leg sign

Signs of meningeal irritation may be absent in:

Neonates

Young infants

Comatose

Paralyzed children

Pretreatment with antibiotics

Unduly sedated child

Cutaneous manifestations of bacterial meningitis:

Purpura in meningococcal meningitis

Ecthyma gangrenosum in pseudomonas meningitis

Tache cerebrale due to autonomic disturbances

Petichiae and purpura in DIVC

Others:

Waterhouse Friedrichson syndrome in meningococcal meningitis

Other signs of raised ICP like Charcot's triad

Focal neurological signs

DIAGNOSIS:

Complete blood count

Differential count

Blood culture

Gold standard is CSF culture

CSF analysis:

- Cell count
- CSF protein

- CSF sugar
- Gram’ stain

Chest X ray

Others: blood sugar, blood gases and serum electrolytes must be monitored regularly to rule out hypo or hyperglycemia, acidosis, SIADH.

CSF analysis is corner stone for the diagnosis of meningitis; [5]

CSF	NORMAL	BACTERIAL MENINGITIS	TB MENINGITIS	VIRAL MENINGITIS
PROTEIN(mg/dl)	20 - 45	100- 500	100 – 3000	50 - 200
GLUCOSE(mg/dl)	> 50	< 40	< 50	N
CELLS(/mm^3)	< 5	100-10000 Polymorphs	10-500 lymphocytes	UPTO 1000

CSF glucose is not a reliable indicator and is the least informative measurement to confirm the diagnosis of bacterial meningitis. Bacteria have also been isolated from CSF that did not have abnormal protein or abnormal number of cells.

TREATMENT[6]

Stabilise airway, breathing, and circulation

Maintain fluid and electrolyte balance :

By prescribing the correct type and volume of fluid, the risk of development of brain edema can be minimized. The child should receive fluids sufficient to maintain systolic blood pressure at around 80 mm Hg, urinary output of 500 mL/m^2/d, and adequate tissue perfusion. While care to avoid SIADH is important, underhydrating the patient and risk of decreased cerebral perfusion are equally concerning as well.

Dopamine and other inotropic agents may be necessary to maintain blood pressure and adequate circulation.

Management of ICP elevation

Seizure control

Fever control

Treatment of predisposing factors

Nursing care

Immediate Lumbar puncture if not contraindicated

Dexamethasone administration:

Animal models of bacterial meningitis have shown decreased inflammation, reduction in cerebral edema and intracranial pressure, and lessening brain damage with use of dexamethasone.

Adjunctive dexamethasone is recommended in cases of H influenzae type b meningitis.it has to be initiated 10-20 minutes prior to or at least concomitant with the first antimicrobial dose at 0.15 mg/kg q6h for 2-4 days. It decreases in the incidence of neurologic and audiologic sequelae, with evidence of clinical benefit being greatest for overall hearing impairment

Data from pediatric patients so far does not demonstrate a clear clinical benefit with dexamethasone use in patients with S pneumoniae meningitis. Given the lack of clear benefit favoring dexamethasone use in this setting and the concerns about decreased antibiotic penetration in the CSF with its use, decision to use this agent is considered on a case-by-case basis after weighing the potential risks and benefits

Empirical parenteral antibiotics. Prior to its isolation, a combination of antibiotics covering both Gram negative and Gram positive organism is given

AGE	STANDARD	ALTERNATIVE	DOSE/Kg/ DAY
Birth to 2 months	Cefotaxime + Ampicillin	Ampicillin + Gentamycin	Cefatoxime – 200 mg in 4 divided doses Ceftrioxone 100 mg once Ampicilllin 200 mg in 4 divided doses Gentamycin 5 mg to 7.5mg/Kg in 2 to 3 divided doses
2 months to 12 years	Cefatoxime	Chloramphenicol + Ampicillin	

TREATMENT

The choice of antibiotic depends on the isolation of the organism and its sensitivity pattern.

ORGANISM	ANTIBIOTIC	DOSE
H influenza type B	Cefotaxime or ceftrioxone	200 mg/kg/day in 4 div doses 100mg/ kg/day in 2 div doses
Streptococcus pneumoniae If allergic to beta lactam antibiotics	Vancomycin + cefotaxime or ceftrioxone chloramphenicol	60 mg / kg / day in 4 div doses dose same as for HiB 100 mg / kg /day in 4 div doses
Listeria monocytogenes Alternative is	Ampicillin Cotrimoxozole IV	200mg/ kg / day in 4 div doses
Gram negative enteric bacilli If Pseudomonas	Cefotaxime + aminoglycoside ceftazidime	 150mg/kg/day

Duration of antimicrobial therapy:

- N meningitidis - 7 days
- H influenzae - 7 days
- S pneumoniae - 10-14 days
- S agalactiae - 14-21 days
- Aerobic gram-negative bacilli - 21 days or 2 weeks beyond first sterile culture (whichever is longer)
- L monocytogenes - ≥21 days

Indications for repeat lumbar puncture include lack of clinical improvement or meningitis caused by resistant S pneumoniae strains or by gram-negative enteric bacilli. In neonates with gram-negative bacillary meningitis, examination of CSF during treatment is necessary to verify that cultures are sterile. Reexamination of CSF for chemistries and culture should be performed 48-72 hours after treatment initiation; further specimens are obtained based upon demonstrating lack of sterilization or lack of apparent clinical response

PREVENTION[5]

CHEMOPROPHYLAXIS

Chemoprophylaxis is recommended for household contact, which means one who

lives in the residence of the index case or who has spent a minimum of 4 hours with the index case for at least 5 of 7 days preceding the patients' hospitalization. In case of H.influenzae type b infection, the patient and the household contact should receive Rifampicin 20mg/kg/dose every day for 4 days.

In case of meningococcal infection, the close contacts should receive rifampicin 10 mg/kg/dose every 12 hours for two days. Ceftriaxone is an effective alternative for pregnant women.Ciprofloxacin can also be given in a single dose of 500 mg

PRIMARY PREVENTION

Immunisation with H. influenza type B vaccine – HIB OC (3 doses intramuscularly at 2, 4, 6 months and a booster 15 months) or PRP – OMP (2 doses intramuscularly at 2, 4 months and booster at 12 months) causes an impressive decline in incidence of meningitis due to HIB[57]. Pnuemoccocal 7 valent conjugate vaccine (PCV 7) which contains commonly prevalent serotypes can be used. 3 doses PCV 7 are recommended to be given at 2, 4 and 6 months of age and a 4 th dose is given at 12 to 15 months.

Quadrivalent meningococcal vaccine for meningoccocus A,C, Y or W 135 is given in selected groups .

COMPLICATIONS[7]

During treatment the common complications are seizures, syndrome of inappropriate secretion of antidiuretic hormone (SIADH) and subdural effusion. Symptomatic subdural effusion should be treated by aspiration. Persistent fever may complicate the management and may be due to subdural effusion, drug reaction, nosocomial infection, phlebitis, pneumonia, pericarditis or arthritis. Disseminated intravascular coagulation (DIC) is most often common in patients with shock and purpura.

The neurological sequelae are recurrent seizures, sensorineuronal hearing loss,hydrocephalus, hemiparesis and mental retardation.

Recrudescence is the reappearance of infection during therapy with appropriate antibiotics and is usually due to development of bacterial resistant. Relapse occurs between 3 days and 3 weeks after therapy and indicates persistent bacterial infection in the CNS (subdural empyema, ventriculitis, cerebral abscess or mastoiditis, cranial osteomyelitis, orbital infection).

Recurrence is a new episode of meningitis due to reinfection with the same or another pyogenic pathogen and suggests the presence of an anatomic communication or immunocompromised states.

CRP estimation is a simple and rapid test[8] and does not require expertise. It is less expensive and results will be available within a short time. It is an acute phase reactant

belonging to a group of serum proteins called PENTAXTRINS. It is normally present in trace amounts in blood of healthy individuals. Its level increases within hours of acute injury or onset of inflammation and reaches a peak level within 24 to 48 hours[9]. In serum it is found in association with the very low density lipoprotein fraction. Its activity resembles those of an antibiotic. CRP is elevated in all bacterial infections[10] in acute stage. The exact mechanism by which CRP enters the CSF is not known. Probably it reaches the CSF by passive diffusion through the highly inflamed meninges.

BIOCHEMICAL PROPERTIES[11]

It has a molecular weight of approximately 110,000 daltons . CRP consists of five apparently identical noncovalently bound polypeptide units. Each subunit has a molecular weight of 21,500 daltons and is composed of 189 aminoacids residues with one disulphide bond. In electron microscopy the subunit appears spherical and the entire CRP molecule has the shape of a pentagon. Studies of the binding specificities have indicated that CRP has reactivity with (a)phosphocholine and phosphate esters and hence with lipids widely distributed in mammalian and microbial cells. And (b) with multiple widely distributed polycations, including those derived from leucocyte granules. Interaction with either of these ligands has been shown to alter CRP in such a way that it can bring about activation if the complement system with generation of all known C dependant reactivities including complement consumption, adherence, phagocytosis and cytolysis[12].

Experimentally, CRP synthesis and the production of other acute phase reactants have been shown to be induced by a factor released from macrophages. Since this factor has been independently discovered by many investigators it has many names.

Interleukin I

Lymphocyte activating factor

Lymphocyte endogenous mediator

Endogenous pyrogen

REVIEW OF LITERATURE

The meningitis syndrome has been recognized for many centuries. Meningitis may have been described in the Middle Ages, but it was first accurately identified by a scientific-literary association during an outbreak in Geneva, Switzerland in 1805.Meningoccoci was first isolated by Anton Weichselbaum in Veinna.

Quincke introduced lumbar puncture in 1891.

Ajay Gaur, Seshan, S. V et al [13] had studied one hundred children suffering from meningitis and other neurological disorders admitted over a period of one year in a hospital in India. The patients admitted with suspicion of meningitis that later proved to be either tubercular or pyogenic meningitis were included in the study. The control group consisted of patients with febrile convulsions, acute respiratory tract infection with meningismus and acute flaccid paralysis. The C-reactive protein test was able to detect 80% of cases of pyogenic meningitis and was negative in the control group. The positive predictive value of the test for pyogenic and tubercular meningitis was 100%. Similarly, negative cerebrospinal fluid C-reactive protein test was 100% specific for absence of pyogenic and tubercular meningitis. It indicates that estimates of C-reactive protein in cerebrospinal fluid is a valuable and rapid bedside diagnostic test for pyogenic meningitis with reasonably good sensitivity, 100% specificity and positive predictive value.

Ali W; Ahmad et al [14] in their study, C - reactive protein (CRP) levels were studied. 20 cases served as control, 38 had pyogenic meningitis, 4 had Tubercular meningitis, 3 had Aseptic meningitis and 5 had Encephalitis. Mean value of Serum and CSF CRP level in pyogenic meningitis was 32.5 ml/l and 20.5 mg/l respectively. Mean value of serum CRP in Tubercular meningitis was 9 mg/l while as CSF CRP in tubercular meningitis was normal. Serum and CSF CRP levels in case of Aseptic meningitis and Encephalitis were normal. Serial estimation of Serum and CSF CRP levels revealed that CRP levels rapidly returned to normal with clinical recovery and response to therapy. However these patients who showed no response to therapy and who developed sequelae, continued to have raised Serum and CSF CRP levels. Measurement of CRP is therefore an excellent parameter in diagnosis, differentiation and prognosis of C.N.S infections.

Nandita Chinchankar et al [15] in their study conducted in a hospital in Pune done on patients with a provisional diagnosis of acute bacterial meningitis had concluded that etiological diagnosis can be enhanced by LAT and good culture media. H. influenzae b and S. pneumoniae account for more than 60% of acute bacterial meningitis in early childhood In that study, more than two-third patients were positive for LAT whereas cultures were positive in only one-half. However the LAT kits are expensive and available only for common organisms and hence not suitable as the lone diagnostic technique in ABM. Besides, the kits cannot provide information on antibiotics

sensitivity and hence both techniques (LAT and culture sensitivity) should be used together. In their series, 10 patients were negative on culture and LAT, but the final diagnosis was made on CSF biochemistry and clinical features. In such cases, it is difficult to rule out tuberculous and viral meningitis in the initial stages.

Zvezdana et al [16] compared CRP concentrations in the blood and CSF, along with CSF nitric oxide (NO), protein, glucose, and leukocyte count, in 17 consecutive patients (age range, 2 months to 47years) with suspected bacterial meningitis and in noninfected controls($P < 0.001$). . CRP in CSF was significantly higher in patients with gram negative bacterial meningitis as compared to patients with gram-positive bacterial meningitis.

The usefulness of CSF C-reactive protein in differentiating bacterial and non-bacterial meningitis was studied by Vaidya AK et al [17] who concluded that serum CRP levels can been used to monitor the infections of central nervous system and also to differentiate between bacterial and viral meningitis, since the CRP levels have been found to be significantly lower in cases of viral meningitis.CSF- CRP values appeared to be more sensitive in differentiating bacterial and non-bacterial meningitis than the usual parameters measured in CSF like cell count, protein, sugar and Gram stain. Their study demonstrated that CSF-CRP levels are also useful in diagnosing partially treated cases of meningitis, CRP detected by latex agglutination was a helpful screening test to differentiate bacterial and non-bacterial meningitis at the bedside and CRP detected

patients should be considered to have bacterial meningitis until proved otherwise.

In their study on C-reactive protein in childhood meningitides Pemde et al [18] the utility of C-reactive protein (CRP) latex agglutination test in meningitis was evaluated. Serum CRP test was positive in 100% cases of meningitic groups and 53% cases of "no meningitis (NM)" group. Cerebrospinal fluid (CSF) CRP test was positive in 100% cases of pyogenic meningitis, whereas it was negative in 95% cases of tuberculous meningitis and 100% cases of NM group. CSF CRP test showed 100% sensitivity and negative predictive values, 95-100% specificity and 94-100% positive predictive values for various inter-group differentiations. This study concluded that CSF CRP positive cases should be considered as pyogenic meningitis unless proved otherwise. Routine use of this simple, reliable and inexpensive test was recommended for rapid diagnosis and differential diagnosis of meningitis.

Tankhiwale SS et [19] had taken up a study on seventy five clinically, biochemically and microscopically diagnosed cases of pyogenic meningitis including 28 adults and 47 paediatric patients. Gram positive isolates in adults and gram negative bacilli in paediatric age group were the predominant organisms. Estimation of C-reactive protein in cerebrospinal fluid (CSF) and serum was done in all cases as an early marker for rapid diagnosis of pyogenic meningitis. Simultaneous estimation of CRP levels in serum and CSF was found to have a significant diagnostic utility as compared to culture.

Cerebrospinal fluid C-reactive protein in meningitis: diagnostic value and pathophysiology. E. Ben Gersham et al [20] examined the diagnostic value of C-reactive protein in cerebrospinal fluid on initial lumbar puncture in a prospective study including 126 patients (30 neonates, 96 infants and children) suspected of having meningitis. In infants and children, a retrospectively chosen cut-off CRP titre of 4 (i.e. >0.4 mg/l CRP) had a sensitivity of 100% and a specificity of 94% for differentiating bacterial meningitis from both viral meningitis and normal. It was a more sensitive and selective test for differentiating bacterial from viral meningitis on initial CSF examination than was the CSF leucocyte count, glucose concentration or protein concentration.

Sindic CJ et al [21] in an article published in the J Neurol Sci._1984 have determined the level of C-reactive protein was determined in the cerebrospinal fluid by particle counting immunoassay. In non-neurological patients (N = 24), CRP was detectable only in 10 samples at concentrations ranging from 1.5 to 37 micrograms/l.. The highest CRP levels were found in viral and bacterial, including tuberculous, infections of the nervous system, with overlapping results for the various types of infections. However, in serum, the levels of CRP were much higher in pyogenic than in viral meningitis. They compared the CSF CRP/serum CRP ratio to the same ratio for albumin and found a significant correlation between the two ratios in viral, but not in bacterial, infections. These results suggested a local consumption of CRP during bacterial meningitis.

Rajmani et al [22] who estimated of C - reactive protein in Serum and CSF for diagnosis of various meningitis have said that CSF-CRP sensitivity was found in 83.33% cases of pyogenic and none from TBM or viral meningitis. CSF-CRP levels in pyogenic meningitis were very high (104±90.21mg/dL) but within normal range in TBM,viral meningitis and controls (<6 mg/L).Thus CSF-CRP levels above normal (6 mg/L) indicates diagnosis of pyogenic meningitis. They concluded that latex agglutination for serum and CSF is a probable, rapid, simple, economic test and could be performed at bedside and very much helpful for laboratories of developing countries even in rural areas.

John M, Raj IS et al [23] estimated the utility of cerebrospinal fluid C-reactive protein measurement--a bedside test in the rapid diagnosis of bacterial meningitis C-reactive protein determinations were performed by the Latex agglutination method on the cerebrospinal fluid samples of 212 patients with clinical features suggestive of meningitis. Their conclusion was that C-RP was a better indicator of bacterial meningitis (sensitivity 91 per cent) than the Gram's stain (sensitivity 46 per cent).In their study C-RP determination in CSF proved to be a useful indicator of bacterial meningitis and served to distinguish it from viral encephalitis, tuberculous meningitis,febrile convulsions and other central nervous system disorders.

Shaltout A et al [24] had done a study on the. Evaluation of cerebrospinal fluid C-reactive protein in the diagnosis of suspected meningitis. Cerebrospinal fluid C-reactive

protein was studied in 183 consecutive infants and children with suspected meningitis, using a nephelometric technique. Cerebrospinal fluid C-reactive protein was above an empirically chosen level of 1 mg/L in seven of 19 children with culture-proven bacterial meningitis, in only one of 15 children with viral meningitis, and three of 139 children with no meningitis. All 10 children with partially treated meningitis had CSF-CRP levels below 1 mg/1. There was good correlation between CSF-CRP and total protein levels in children with bacterial meningitis (R value 0.4999 P less than 0.05). The test was not sensitive enough for early differentiation between bacterial and viral meningitis. They concluded that CSF CRP also did not add extra information regarding aetiology in partially treated meningitis.

The value of cerebrospinal fluid C-reactive protein determination as a diagnostic aid in infective meningitis was investigated in four groups of children by Donald PR et al.[25] CSF CRP values in the bacterial meningitis group differed significantly from those of each of the other groups (P less than 0.01), but considerable overlap between the groups detracted from the diagnostic value of the test. In six patients with bacterial meningitis with ambiguous conventional CSF chemistry results, normal CSF CRP values were found. Simultaneous serum CRP was determined in nine patients with tuberculous meningitis and 11 with bacterial meningitis. The CRP response in both the serum and CSF appears subdued in tuberculous meningitis in comparison with bacterial meningitis. A considerable and apparently parallel diurnal variation in both values was

seen. CSF CRP values have limited application in the etiologic diagnosis of meningitis.

But de Beer FC, Kirsten GF et al [26] on their observations on the value of C reactive protein measurement in tuberculous, bacterial, and viral meningitis have said that the concentrations of C reactive protein in patients with tuberculous meningitis lay between those of patients with bacterial and viral meningitis - a finding which detracted from the virtually absolute discrimination C reactive protein measurement allows between bacterial and viral meningitis. In all but two of the patients with tuberculous meningitis, C reactive protein concentrations fell rapidly after treatment began and became normal after 10 days. This fall did not, however, exclude the development of hydrocephalus as a complication. They concluded that measurement of C reactive protein remains a useful additional parameter in the diagnosis and management of the various types of meningitis.

Rizzo F et al [27] did a study on, C-reactive protein in the differential diagnosis of infectious meningitis. The authors have determined quantitatively C reactive protein in the serum of twenty patients suffering from acute bacterial meningitis and ten patients suffering from viral meningitis. The values observed, that are higher significantly in the bacterial meningitis, permitted to affirm ,that reactive C-protein as an useful test in the differential diagnosis between bacterial and viral meningitis.

Astruc J et al [28] had evaluated the value of C-reactive protein monitoring in the

reduction of antibiotic treatment of bacterial meningitis in children..21 of 24 meningococcal meningitis were treated for 4 or 5 days, 16 of 22 Haemophilus influenzae and 4 of 6 pneumococcal meningitis were treated for 7 days without increase in neurologic sequelae. A return of blood CRP levels to normal values was observed in all these patients simultaneously. Thus, CRP was a good biological parameter for assesing treatment discontinuation. Furthermore, in some complications such as subdural effusion, a new increase of CRP levels was observed after the 5th day. A sequential follow-up of CRP levels at days J0, 5, 7, 10, seemed to be a very useful tool for management of bacterial meningitis.

Ramos Lizana J et al [29] had given a score for the differential diagnosis of bacterial and viral meningitis The purpose of the study was to verify the statistical validity of the score proposed by Thomé et al. for the differential diagnosis between bacterial and viral meningitis and to study the utility of two new parameters (CRP and the patient's age). They concluded that the score was a useful instrument in the differential diagnosis between bacterial and viral meningitis. Furthermore, the introduction of CRP and the patient's age improved the diagnostic value of the test.

Another study by Sormunen P et al [30] have endorsed the view that C-reactive protein is useful in distinguishing Gram stain-negative bacterial meningitis from viral meningitis in children.The objective was to clarify to what extent Gram stain-negative bacterial meningitis can be distinguished from viral meningitis by assessment of

cerebrospinal fluid and blood indices and serum C-reactive protein in children over 3 months of age. Three hundred twenty-five consecutive patients with CSF culture-proven bacterial meningitis, for whom Gram stain was negative in 55 cases, and 182 children with proven or presumed viral meningitis were included in the study. Of the tests investigated in this study, only serum CRP was capable of distinguishing Gram stain-negative bacterial meningitis from viral meningitis on admission with high sensitivity (96%), high specificity (93%), and high negative predictive value (99%).

Peltola H, Valmari P [31] have used Serum C-reactive protein as detector of pretreated childhood bacterial meningitis.Serum C-reactive protein (CRP) levels were measured at presentation to the hospital in 15 children with proven bacterial meningitis (BM) pretreated with antibiotics. CRP exceeded the upper normal limit of 19 mg/l in all cases; the mean value was 195 mg/l (range, 55 to 375 mg/l). On the other hand, CRP levels were normal in 12 patients with viral meningitis or meningoencephalitis. Rapid determination of serum CRP should be performed whenever BM is suspected.

Serum C-reactive protein in the differential diagnosis of acute meningitis was used by Hansson LO et al [32].The ability of serum C-reactive protein to differentiate between acute bacterial and viral meningitis was evaluated in 235 patients, both children and adults. In patients with bacterial meningitis, 7/60 (12%) had S-CRP concentrations below 50 mg/l. In patients with viral meningitis, 15/146 (10%) had S-CRP concentrations above 50 mg/l. Only 3 children below 6 years of age with viral

meningitis had S-CRP concentration above 20 mg/l, but none exceeded 50 mg/l. An S-CRP value above 50 mg/l in patients with CSF pleocytosis usually indicates bacterial etiology. However, S-CRP values above 50 mg/l may occasionally be seen in viral meningitis.

Another study by Cuevas LE et al [33] on C-reactive protein and bacterial meningitis concluded that CSF CRP should not be used as a useful discriminatory test in areas where malaria and TB meningitis are common.

STUDY JUSTIFICATION

Various indices have been initiated to screen for bacterial meningitis, majority being neither highly sensitive nor specific[34]. The value of certain rapid and easy screening tests to detect the presence of infection has been studied by various authors with varying conclusions. Though various tests are available to detect bacterial infections they are expensive and they need expertise to be done and to be interpreted.

C-reactive protein , an acute phase reactant, has been used to diagnose and follow the course of infection.

The present study was undertaken to establish the utility of C-RP in CSF in early diagnosis of bacterial meningitis in children. This not only enables us to start antibiotics in meningitic doses in cases of pyogenic meningitis but also avoid unnecessary antibiotics in the rest.

Its advantages include:

Rapid diagnosis, can be done within few minutes

Can be performed at hospitals where full fledged microbiology lab is unavailable

Low cost

OBJECTIVES OF THE STUDY

(a) To analyse the diagnostic utility of C reactive protein as a bedside test to diagnose pyogenic meningitis

(b) To analyse the common organisms being isolated from CSF in cases of pyogenic meningitis in our hospital as well as antibiotic susceptibility patterns

MATERIALS AND METHODS

STUDY DESIGN: case control study

STUDY PLACE: Institute of child health and hospital for children,Egmore Chennai

STUDY DURATION: December 2005 to October 2007

STUDY POPULATION: Children aged 1 month to 12 years admitted in various medical wards at Institute of Child Health and Hospital for Children.

INCLUSION CRITERIA

All children with CSF culture positivity are included as cases and those with culture negative are taken as control group.

SAMPLE SIZE

For an alpha error of 0.05, power of 80 % and with an expected positive value of 90 % sample size was calculated to be 46. A total of 50 cases which were CSF culture positive were included in the study group and compared with an equal number of CSF culture negative cases. The study and control group were comparable in age and sex distribution.

CONTROL GROUP

Included all cases for which CSF analysis was done for reasons other than pyogenic meningitis .They consisted of patients with febrile convulsions, acute respiratory tract infection with meningismus and acute flaccid paralysis.

METHODOLOGY

Children in the age group of 1 month and 12 years admitted in various wards of Institute of Child Health in the period between December 2005 and October 2007 with clinical diagnosis of pyogenic meningitis who satisfied inclusion criteria were included in the study. Detailed CNS examination was done and looked for neurological deficit and screened for extra cranial focus of infection. All the findings were entered in the following data entry form. Control group consisted of patients with febrile convulsions, acute respiratory tract infection with meningismus and acute flaccid paralysis etc. Under aseptic precaution lumbar puncture was done with the patient in the left lateral decubitus position, the styletted needle was passed into the L3 – L4 or L4 – L5 intervertebral space and the CSF fluid was taken for culture and biochemical analysis. CRP estimation in the CSF was done in the bedside itself for both the control and the study groups.

Qualitative assessment of CRP was done by slide latex agglutination method. One drop of test specimen was placed on a slide using a disposable pipette to which was added a drop of CRP reagent. Both the test specimen and the reagent were uniformly mixed over the entire circle using a mixing stick. The slide was rocked gently back and forth observing for agglutination macroscopically at the end of 2 mins .CRP was taken as positive if agglutination occured and negative if no agglutination occured. Positive and negative controls were included for each of the CSF CRP tests.

In the microbiology lab CSF was cultured in enriched media like blood agar and chocolate agar for the organisms like pneumococci, beta hemolytic streptococci and H influenza .It was also inoculated in Mac Conky agar for gram negative lactose fermenting and non lactose fermenting organisms like E coli, klebsiella and salmonella respectively . The plates were incubated in a incubator of 37 ^{0}C overnight. The next day colony morphology was read and with help of biochemical reactions the organisms were differentiated and confirmed with special tests. The antibiotic sensitivity with the drugs were done in Mueller Hunten agar

Culture was taken as gold standard. 50 cases of culture positive CSF was taken as the study group of pyogenic meningitis. 50 cases which were culture negative in CSF study were included in the control group CSF analysis for cells; CSF protein , sugar and CRP were simultaneously estimated in the control group samples also.

RESULTS

A total of 100 children were included in the study. Children in the age group of one month to 12 years with a suspicion of meningitis who were later found to have growth in their CSF were included in the study group (n=50). 50 cases of children who did not have any CSF growth and were subsequently diagnosed as non pyogenic causes of encephalopathy were included in the control group. Data was analyzed using SSPS windows statistical software program in the computer. The results were tabulated and the clinical profile was analysed using simple statistical proportions. Sensitivity, specificity, positive predictive value and negative predictive value of CRP against the gold standard of culture in diagnosing bacterial meningitis was calculated.

TABLE I

AGE DISTRIBUTION OF STUDY POPULATION

AGE	STUDY GROUP (n = 50)		CONTROL GROUP (n = 50)	
	n	%	n	%
1 Month to 1 year	25*	50%	25	50%
1 to 3 years	13	26%	9	18%
3 to 6 years	8	16%	11	22%
6 to 12 years	4	8%	5	10 %

In the pyogenic meningitis group 50% of the children were in the age group of one month to one year but it was not statistically significant ($p < .73$ *)

The mean age in the pyogenic meningitis group was 29 months and in the non pyogenic meningitis group was 33 months.

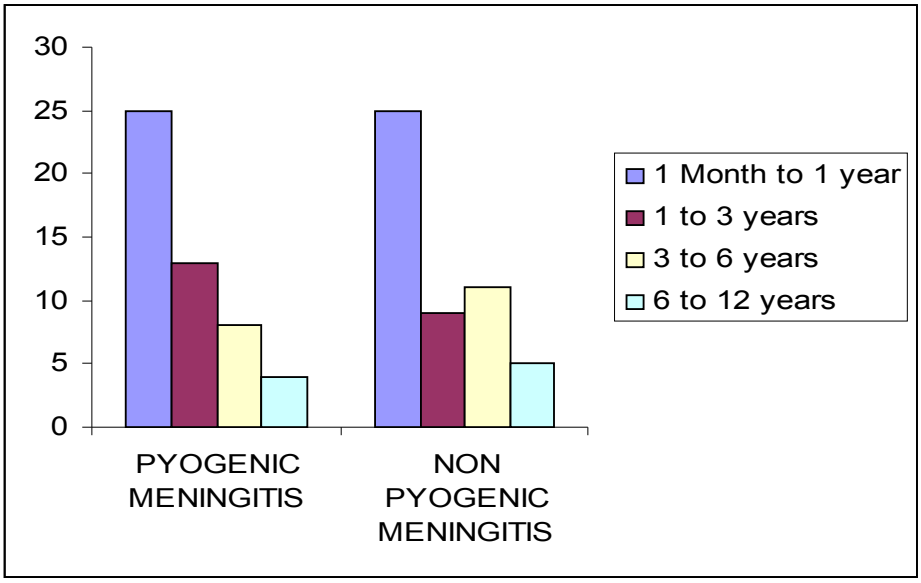


TABLE II

SEX DISTRIBUTION OF THE STUDY POPULATION

SEX	PYOGENIC MENINGITIS (n = 50)	NON PYOGENIC MENINGITIS (n = 50)
MALE	26	27
FEMALE	24	23

There was no difference in sex distribution observed between pyogenic meningitis and non pyogenic meningitis ($p = 0.94$).

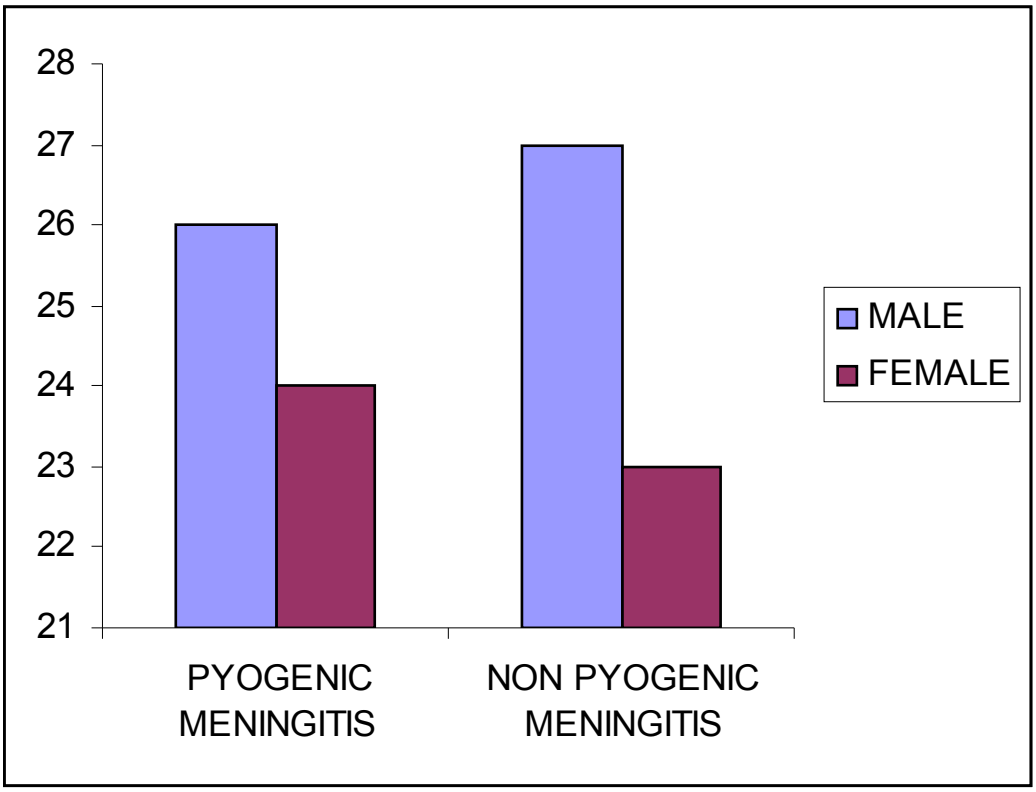


TABLE III

CLINICAL FEATURES OF CHILDREN PRESENTING AS ACUTE CNS INFECTION

CLINCAL FEATURES	PYOGENIC MENINGITIS (n = 50)		NON PYOGENIC MENINGITIS (n = 50)	
SYMPTOMS	n	%	n	%
Fever	44	88	27	54
Headache	9	18	3	6
Vomitting	17	34	5	10

Seizures	45	90	44	88
Alt sensorium	46	92	24	48
SIGNS	n	%	n	%
Neck rigidity	11	22	4	8
Kernig’s	12	24	4	8
Bulg font	5	10	1	2
Shock	23	46	4	8
Aloc	48	96	20	40
FND	19	38	10	28
Papillodema	6	12	1	2

Shock, altered level of consciousness, and a history of fever were most significantly associated with bacterial meningitis (p value < 0.00)

TABLE IV

CSF ANALYSIS – COLOUR

CSF COLOUR	PYOGENIC MEINGITIS (n = 50)		NON PYOGENIC MENINGITIS (n = 50)	
	n	%	n	%
CLEAR	35	70%	50	100 %
TURBID	12	24%	NIL	0%
PURULENT	3	6%	NIL	0%

The CSF color in the pyogenic meningitis group was clear in 35 cases i(70 %) of the cases while in the rest 15 cases (30 %) it was turbid. While in the non pyogenic meningitis group all the CSF specimens were clear (100 %).

TABLE V

CSF ANALYSIS – CELLS

PREDOMINANT CSF CELLS	PYOGENIC MENINGITIS (n = 50)		NON PYOGENIC MENINGITIS (n = 50)	
	n	%	n	%
Polymorphs	25	50%	1	2%
Lymphocytes	3	6%	3	6%
No cells	22	44%	46	92%

In the cases of pyogenic meningitis 25 cases (50%) had predominantly polymorphs in the CSF analysis, 3 (6%) cases had predominantly lymphocytes while about 22 cases (44%) did not show any cells in their CSF.

In the non pyogenic meningitis group, only one case (2%) showed polymorphs, 3 cases (6%) had lymphocytes, while majority of them i.e . 46 cases (92%) did not have any cells in their CSF analysis.

TABLE VI

CSF ANALYSIS – PROTEIN

CSF PROTEIN	PYOGENIC MENINGITIS (n = 50)		NON PYOGENIC MENINGITIS (n = 50)	
	n	%	n	%
< 45 mg%	15	30%	40	80%
45 – 100 mg%	27	54%	7	14%
>100 mg%	8	16%	3	6%

The protein levels in the pyogenic meningitis group was less than 45 mg% in 15 cases (30%) , between 46 to 100 mg% in 27 cases (54%) and in 8 cases (16%) was more than 100 mg%.

The same in the non pyogenic meningitis group: 40 cases (80%) had their CSF protein levels below 45 mg% , 7 cases(14%) had CSF protein levels between 45 to 100 mg % and 3 cases (6%) had protein levels more than 100 mg%.

The mean protein levels in the experimental group was 74.12 mg% and in the control group 53 .52 mg%.

TABLE VII

CSF ANALYSIS - SUGAR

CSF - SUGAR	PYOGENIC MENINGITIS (n = 50)		NONPYOGENIC MENINGITIS (n = 50)	
	n	%	n	%
< 2 / 3 rd OF B.SUGAR	20	40%	10	20%
> 2 / 3 rd OF B.SUGAR	30	60%	40	80%

Only 20 cases (40%) had a CSF sugar less than two thirds of the blood sugar. The rest 30 cases had a CSF sugar more than two thirds of the blood sugar among the cases of pyogenic meningitis.

In the non pyogenic meningitis group 10 cases (20%) had a CSF sugar less than two thirds of the blood sugar and in the rest of the 40 cases (80%) the CSF sugar was more than two thirds of the blood sugar

The mean CSF sugar in the study group was 58.2 mg% and in the control group it was 75.14 mg %.

TABLE VIII

ORGANISMS GROWN IN CSF CULTURE (n = 50)

ORGANISM	n	%
Klebsiella	28	56%
E. coli	9	18%
Pseudomonas	7	14%
H.influenza	1	2%
Pneumococcus	4	8%
Staph.aureus	1	2%
Proteus	1	2%

Among the organisms grown in CSF culture klebsiella was the most commonly isolated one accounting for 28 (56%) of the 50 culture positive cases. The next common organism was E.coli in 9 (18%) cases, followed by pseudomonas in 7 cases (14 %), pneumococcus in 4 cases (8%) and H.infuenza, Staph.aureus, and Proteus in one case (2%) each.

TABLE IX

ANTIBIOTIC SENSITIVITY PATTERN IN CASES OF PYOGENIC MENINGITIS. (n = 50)

ANTIBIOTIC SENSITIVITY	n	%
Amikacin	33	66
Ciprofloxacin	28	56
Cefotaxime	1	2
Erythromycin	1	2
Gentamycin	2	4
Ceftazidime	2	4
Vancomycin	1	2
Mutidrug resistant	1	2
Ampicillin	1	2
Cloxacillin	1	2

The antibiotic sensitivity pattern in the 50 cases of pyogenic meningitis which showed growth in the CSF revealed that amikacin was sensitive in 33 of the cases (66%), ciprofloxacin was sensitive in 28 of them(56%), cefatoxime, erythromycin,

vancomycin, ampicillin and cloxacilin were sensitive in in one cases each (2% each). Gentamycin and

ceftazidime were sensitive in 2 cases each (4% each). One case was multidrug resisistant.

TABLE X

C REACTIVE PROTEIN IN CSF

CSF - CRP	POSITIVE		NEGATIVE		TOTAL
	n	%	n	%	
PYOGENIC MENINGTIS	41	82	9	18	50
NON PYOGENIC MENINGITIS	0	0	50	100	50
TOTAL	41		59		100

CRP in CSF in the pyogenic meningitis group was positive in 41 cases (82%) but was negative in 9 of them (18%). CRP positivity in CSF was statistically significant in the pyogenic meningitis group with a p value < 0.01 according to the Mann – Whitney

test.

In the non pyogenic meningitis group CRP done on CSF was negative in all the cases.

TABLE XI

SENSITIVITY AND SPECIFICITY OF CSF CRP IN CULTURE POSITIVE CASES

CRP	CULTURE		TOTAL
	POSITIVE	NEGATIVE	
POSITIVE	41	0	41
NEGATIVE	9	50	59
TOTAL	50	50	100

Sensitivity was 82%, Specificity 100%, Positive predictive value 100% and Negative predictive value 85 %. Among 50 culture positive cases, 41 children (82%) had CSF CRP positivity (sensitivity 82%), and 50 children who did not show any growth in CSF were negative for CSF CRP also (specificity 100%). Out of the 41 children who show CSF CRP to be positive, all the 41 also had some organism grown in their CSF culture (Positive predictive value 100%) and CSF culture was negative for 50

children among 59 children who tested to be CSF CRP negative (Negative predictive value 85%)

Overall accuracy was 91% (91 / 100)

TABLE XII

SENSITIVITY AND SPECIFICITY OF ABNORMAL BIOCHEMISTRY IN CASES OF BACTERIAL MENINGITIS (ELEVATED PROTEIN OR DECREASED SUGAR)

ABNORMAL BIOCHEMISTRY	CULTURE		TOTAL
	POSITIVE	NEGATIVE	
POSITIVE	37	10	47
NEGATIVE	13	40	53
TOTAL	50	50	100

Abnormal biochemistry of CSF in cases of culture proven pyogenic meningitis had a sensitivity of 74% and specificity of 80%.

TABLE XIII

SENSITIVITY AND SPECIFICITY OF ABNORMAL CSF CELL COUNT IN CASES OF BACTERIAL MENINGITIS

ABNORMAL CSF CELL COUNT	CULTURE		TOTAL
	POSITIVE	NEGATIVE	
POSITIVE	28	4	32
NEGATIVE	22	46	68
TOTAL	50	50	100

The sensitivity of an abnormal cell count in picking up cases of bacterial meningitis was 56% and the specificity was 92%.

TABLE X1V

SENSITIVITY AND SPECIFICITY OF ABNORMAL CSF CELL COUNT AND ABNORMAL CSF BIOCHEMISTRY IN CASES OF BACTERIAL MENINGITIS

ABNORMAL CSF CELL COUNT & ABNORMAL CSF BIOCHEMISTRY	CULTURE		TOTAL
	POSITIVE	NEGATIVE	
POSITIVE	40	11	51
NEGATIVE	10	39	49
TOTAL	50	50	100

The sensitivity when abnormal CSF biochemistry and abnormal CSF cell count were combined in the diagnosis of bacterial meningitis was 80% and the specificity was 78%.

TABLE XVI

SENSITIVITY AND SPECIFICITY OF ABNORMAL CSF CELL COUNT, CSF CRP AND ABNORMAL CSF BIOCHEMISTRY IN CASES OF BACTERIAL MENINGITIS

ABNORMAL CSF CELL COUNT, CSF CRP & ABNORMAL CSF BIOCHEMISTRY	CULTURE		TOTAL
	POSITIVE	NEGATIVE	
POSITIVE	45	12	57
NEGATIVE	5	38	43
TOTAL	50	50	100

The sensitivity when all three parameters i.e CSF CRP, abnormal CSF biochemistry and cell count were combined for the diagnosis of bacterial meningitis was 90% .

DISCUSSION

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. C-reactive protein is the classic acute phase reactant. CRP levels in serum and cerebrospinal fluid have been shown to be increased as a result of invasive central nervous system infection. Isolation of etiological agent by culture is a time consuming process while estimation of CRP is a rapid diagnostic procedure. The diagnostic utility of CSF-CRP is evaluated in the present study.

100 patients in the age group of one month and 12 years who were suspected to have meningitis and other neurological problems were studied. We restricted our study to the age group of 1 month to 12 years to focus on the distinct clinical group excluding neonatal meningitis. 50 cases of them who were admitted with the suspicion of meningitis and later proved to be pyogenic meningitis by culture of the CSF was included in the study group. Control group consisted of 50 patients with neurological illnesses other than pyogenic meningitis and were CSF culture negative. CSF cell count , protein and sugar estimation were done on both the study and control group. Similarly CRP estimation was also done qualitatively in both the study and control groups. The results were then statistically analyzed.

Among the 50 cases of pyogenic meningitis 50 % of the cases were in the age group of 1 month to one year, making it the most vulnerable population to be affected by

bacterial meningitis.

There was no sex predominance noted in our study. Both the males and females were equally affected.

The most common presenting symptom and signs were altered sensorium followed very closely by seizures and the most common signs were altered level of consciousness followed by shock. This observation stresses on the fact that most cases of pyogenic meningitis have to be handled in tertiary level hospitals with dedicated intensive care units capable of managing shock and the resultant morbidity.

The CSF in the pyogenic meningitis group was most commonly clear. It was turbid or frankly purulent in only 15 % of the cases. Although 50 % of the cases had cells in the CSF, mostly polymorphs, the rest of the 25 cases did not show any significant cells. The reason for this observation may be because most of the cases admitted in Institute of Child Health have been treated for variable period of time in other hospitals and so have already received parenteral antibiotics for several days[33].The mean protein level in the study group CSF was 75 mg% and the mean glucose level was 58 mg % .

The most common organism isolated in the case of pyogenic meningitis were klebsiella followed by E.coli and pseudomonas. This observation is in contrast to other studies done elsewhere where the most common isolates were streptococcus pneumoniae and H.influenza [2, 15].

But a similar observation was made by Tankhiwale et al[18] in his study conducted in a tertiary centre in Nagpur which showed that E coli, streptococcus, klebsiella and pseudomonas were the most common isolates.

The antibiotic sensitivity was also likewise altered. Number of studies have shown that gentamycin and third generation cephalosporins covered most of the organisms grown in CSF culture.[41,42,43,44.] But in our study it was observed that amikacin and ciprofloxacin were the most sensitive antibiotics. A combination of amikacin and ciprofloxacin covered almost 96% of the cases. An empirical antibiotic of therapy of cefatoxime that is being followed now does not seem to a benefit, as fewer than 5 patients of pyogenic meningitis were sensitive to it. Given the poor CSF penetration of aminoglycosides, ciprofloxacin can be used in the management of pyogenic meningitis.

CRP in CSF was positive in 41 (82%) of the CSF samples with culture positivity which was statistically significant ($p < .01$) in detecting cases of pyogenic meningitis. The sensitivity was 82% and specificity was 100 %. It had a positive predictive value of 100% and a negative predictive value of 85% .So though CSF CRP is reasonably sensitive in picking up cases of pyogenic meningitis; it can miss upto 18% of the cases. But it is highly specific for bacterial meningitis. So if CSF CRP is positive it virtually makes a diagnosis of bacterial meningitis irrespective of other corraborative evidences whereas a negative test need not necessarily rule out pyogenic meningitis. A similar finding was also reported in various other studies[12, 13].

Our observation was similar to the findings of Ajay Gaur et al who in their study;

CSF C-reactive protein estimation for bedside diagnosis of pyogenic meningitis, concluded that the C-reactive protein test was able to detect 80% of cases of pyogenic meningitis and 15% cases of tubercular meningitis and was negative in the control group. The positive predictive value of the test for pyogenic meningitis was 100%. Similarly, negative cerebrospinal fluid C-reactive protein test was 100% specific for absence of pyogenic meningitis. It is indicated that estimates of C-reactive protein in cerebrospinal fluid is a valuable and rapid bedside diagnostic test for pyogenic meningitis with reasonably good sensitivity, 100% specificity and positive predictive value.[12]

A similar observation was made by Shaltout A et al[23] in his study : Evaluation of cerebrospinal fluid C-reactive protein in the diagnosis of suspected meningitis where he concluded that there was good correlation between CSF-CRP and total protein levels in children with bacterial meningitis (R value 0.4999 P less than 0.05).[20]

But Pemde et al in his study C-reactive protein in childhood meningitides observed that

CSF CRP test showed 100% sensitivity and negative predictive values, 95-100% specificity and 94-100% positive predictive values. This study concluded that CSF CRP positive cases should be considered as pyogenic meningitis unless proved otherwise.[17]

CSF CRP was found to be more sensitive (82%) than abnormal CSF biochemistry (74%) and abnormal CSF cell count (56%) in diagnosing cases of bacterial meningitis

.The sensitivity when both abnormal CSF biochemistry and cell count were combined was 80% but it was observed that when all three parameters were included the sensitivity rose to 90%. So it can be deduced that CSF CRP is a very useful test in diagnosing cases of bacterial meningitis in combination with other factors especially when facilities for culture are not available.

CONCLUSION

1. Altered sensorium, seizures and shock are the most common presenting features of bacterial meningitis in children.

2. Gram negative organisms are most frequently isolated in cases of pyogenic meningitis with sensitivity to ciprofloxacin.

3. CRP estimation can be used as a bedside diagnostic tool in cases of pyogenic meningitis as a supportive evidence of bacterial meningitis with reasonably good sensitivity, and 100% specificity and positive predictive value.

4. Exclusion of bacterial meningitis with only the conventional tests is difficult. Combined with careful physical examination and CSF analyses, CSF CRP measurement affords substantial aid.

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PROFORMA

NAME:

AGE:

SEX:

IP NO.:

WARD:

SYMPTOMS:

FEVER:

HEADACHE:

VOMITING:

SEIZURES:

ALTERED SENSORIUM:

SIGNS:

NECK RIGIDITY:

BULGING FONTANELLE:

SHOCK:

ALOC:

FOCAL NEUROLOGICAL DEFICIT:

PAPILLEDEMA

BLOOD SUGAR:

CSF ANALYSIS:

COLOUR:

CELLS

BIOCHEMICAL ANALYSIS:

PROTEIN:

SUGAR:

CULTURE

SENSITIVITY PATTERN

C REACTIVE PROTEIN

FINAL DIAGNOSIS