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RESEARCH ARTICLE

CLINICAL PROFILE OF PYOGENIC MENINGITIS AND ITS OUTCOME IN PEDIATRIC AGE GROUP.

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Key words:-

Abstract

Objectives:- To analyse demographic factors & clinical, biochemical, bacteriological profile, to study complications, outcome & antibiotic sensitivity pattern among different isolates identified in pyogenic meningitis in paediatric age group.

Design:- Prospective observational study

Methods:- Study subjects between ages of 1 month to 12 years with acute bacterial meningitis were enrolled. Clinical details were recorded. CSF was analysed by routine biochemical method and microbiological studies on special media. Management was as per standard protocols.

Results:- In study period of 18 months 84 children satisfied the criteria of acute bacterial meningitis in childhood. 46.43% ≤1 years, chief presentation was fever, convulsion, vomiting, irritability, headache, refusal to feed/ poor feeding. Meningeal signs present in 40.47%, CSF gram stain positive in 8.33%, blood culture positive in 15.47%, CSF culture positive in 5.95%. The final etiological diagnosis as per CSF culture/ blood culture/ gram stain were streptococcus pneumonie (10.71%), staphylococcus auereus (2.38%), haemophilusinfluenzae type b (1.19%) & pseudomonas aeuriginosa(1.19%). 33.33% cases develop complications during hospital course. Mortality seen in 15.47% patients.

Conclusions:- Acute bacterial meningitis has considerable mortality & morbidity in childhood. Neurodevelopmental follow up and therapy should begiven early. High mortality associated with duration of illness > 7 days, CSF sugar was < 20mg/dl, malnutrition and in cases where organisms identified. Good sensitivity observed among 3rd generation cephalosporin.

Introduction:-

Acute bacterial meningitis is an important disease of early childhood with high mortality and risk of neurological handicaps.[1]The community incidence of acute bacterial meningitis in India is not known. The exact etiological diagnosis is often not possible because of poor culture facilities.[2,3] The three organism commonly associated with

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acute bacterial meningitis in early childhood in western countries are Haemophilusinfluenzae type b, Streptococcus pneumoniae, Neisseria meningitidis. However etiology may vary in different part of world.[1] Many of these infection are likely to be preventable in near future.[4,5]

We have prospectively examined the hospital based frequency of acute bacterial meningitis in childhood especially in relation to its etiology. The clinical diagnostic features, mortality, complications & short term follow up were analysed.

Subjects & methods:-
The study was conducted in paediatric department, Government Medical College & Hospital, Aurangabad which include 3 bedded PICU & 80 bedded general Paediatric Ward. All patient admitted with clinical diagnosis of acute bacterial meningitis during May 2014 to October 2015 were included with satisfying the following criteria.

According to WHO[6] criteria all probable cases of pyogenic meningitis were included. They were the cases presenting with clinical symptoms of meningitis [i.e. fever, headache, stiff neck, bulging fontanels or altered mental status] and CSF with elevated protein [>100mg/dl], decreased glucose [<40mg/dl] or leucocytosis [>100WBC/mm3] with at least 80% neutrophils and lacking an identifiable bacterial pathogen. 2. Any CSF culture positive cases. 3. Age group from 1 month to 12 year.

Other investigations include CBC, CXR, Renal function test, Liver function test, Serum electrolyte, Blood culture, Gram staining, USG, NCCT, BERA, Audiometry & EEG were carried out whenever required. Chi square test is used to determine statistical significance amongst various variable.

Management:-
Following diagnosis the patients were treated with antibiotics as per unit's protocol. We used injectable Ampicillin, Cefotaxime, Ceftriaxone, Vancomycine, Meropenem, piperacillin. Intravenous Dexamethasone was given in a dose of 0.15 mg/kg/dose every 6 hourly for 3 to 4 days (the first dose given with or prior to the first dose of antibiotics). Antibiotics were changed (if required) as per the sensitivity result and clinical response. Appropriate supportive care including attention to fluids, electrolytes, ventilation, parenteral nutrition and neurosurgical interventions were provided. Children who recovered were followed up after 1 month of discharge in outpatient clinic. Evaluation on follow up included detailed neurological examination, Audiometry, BERA, EEG, NCCT/MRI whenever required.

The study was approved by the Institutional Ethics Committee of the hospital & informed consent of the parents was obtained.

Results:-
Of 13500 admissions, 84 children (0.62%) of age 1 month to 12 years had acute bacterial meningitis. 42(50%) were male& 42(50%) were female. 39 patients up to the age of 1 years. Nobody has immunised with pneumococcal, meningococcal &Hemophilusinfluenzae vaccine.

The presenting features include fever (97.61%), convulsions (75%), altered sensorium (59.52%), vomiting (52.35%), irritability (28.57%), headache (27.35%), poor feeding (26.19%) & photophobia (8.33%) cases.

The clinical signs noted were impaired consciousness (59.52%), positive signs of meningeal irritation (40.47%), bulging anterior fontanel (22.61%), cranial nerve palsy (5.95%), papilledema (5.95%) and rash (3.51%).

We were excluded the patients received antibiotics outside the institution before admission which known to cross blood brain barrier. CSF proteins ranges from 45 to 760 mg/dl, CSF sugar ranges from 10 to 120 mg/dl, and leucocytes count ranges from 0 to 1100 cells/ cu^{mm} with neutrophilic count > 80% of total leucocytes. Gram stain was positive in 7 cases (8.33%), CSF culture was positive in 5 cases (5.95%) and blood culture positive in 13 cases (15.47%). All gram stain and CSF culture positive organism were also isolated in blood culture.

Table 1:- Table showing signs and symptoms observed in acute bacterial meningitis.

SYMPTOMS AND SIGNS	NUMBER	PERCENTAGE
FEVER	82	97.61%
CONVULSION	63	75%
ALTERED SENSORIUM	50	59.52%
VOMITING	44	52.38%
IRRITABILITY	24	28.57%
HEADACHE	23	27.38%
POOR FEEDING/ EATING	22	26.19%
PHOTOPHOBIA	7	8.33%
IMPAIRED CONSCIOUSNESS	50	59.52%
POSITIVE MENINGEAL SIGNS	34	40.47%
BULGING AF	19	22.61%
CRANIAL NERVE PALSY	5	5.95%
PAPILLEDEMA	5	5.95%
RASH	3	3.57%

Table 2:- Table showing complications seen during hospital stay in pyogenic meningitis

COMPLICATIONS	NUMBER	PERCENTAGE
NEUROLOGICAL		
PERSISTENT SEIZURES	8	9.52%
HEMIPARESIS	3	3.57%
CRANIAL NERVE PALSY	7	8.33%
SUBDURAL EFFUSION	3	3.57%
CEREBRAL INFARCT	5	5.95%
INTRACRANIAL HAEMORRHAGE	1	1.19%
HYDROCEPHALOUS	6	7.14%
NON NEUROLOGICAL		
DISSEMINATED INTRAVASCULAR COAGULATION	6	7.14%
SHOCK	6	7.14%
ELECTROLYTE IMBALANCE	2	2.38%

Table 3:- Table showing organism identified by gram staining / CSF culture / blood culture.

CAUSATIVE ORGANISM	NUMBER	PERCENTAGE
STREPTOCOCCUS PNEUMONIAE	9	10.71%
STAPHYLOCOCCUS AUREUS	2	2.38%
H. INFLUENZAE	1	1.19%
PSEUDOMONAS	1	1.19%
ISOLATES NOT SEEN	71	84.53%
TOTAL	84	100%

Table 4:- Table showing in vitro antibiotic sensitivity of bacterial isolates in pyogenic meningitis.

Antibiotics	Streptococcus pneumoniae		Staphylococcus Aureus		H. influenzae		Pseudomonas	
	No.	sensitivity	No.	sensitivity	No.	sensitivity	No.	Sensitivity
Piperacillin	9	88.88%	2	100%	1	100%	1	100%
Ampicillin	9	77.77%	2	50%	1	100%		0%
Cefotaxime	9	100%	2	100%	1	100%	1	100%
Ceftriaxone	9	100%	2	100%	1	100%	1	100%
Meropenem	9	100%	2	100%	1	100%	1	100%
Clindamycin	9	77.77%	2	50%	--	--	--	--
Ciprofloxacin	9	100%	2	100%	1	100%	1	100%
Amikacin	9	77.77%	2	50%	1	100%	1	0%
Chloramphenicol	9	77.77%	2	50%	1	100%	1	0%

Most cultures of streptococcus pneumoniae, staphylococcus aureus, H. influenzae were sensitive to standard medication. 2 cases of streptococcus pneumonia & 1 case of staphylococcus aureus were resistant to Ampicillin, Clindamycine, Amikacin, Chloramphenicol. All cases of streptococcus pneumonia & staphylococcus aureus were sensitive to Cefotaxime, Ceftriaxone, Meropenem& Ciprofloxacin. In vitro sensitivity of bacterial isolates in pyogenic meningitis were given in table 4.

Neurological complications seen during hospitalization were persistent seizures (9.52%), cranial nerve palsy (8.33%), hydrocephalous (7.14%), cerebral infarct (5.95%), hemiparesis &subdural effusion each (3.57%) & intracranial haemorrhage (1.19%) cases. 3 cases develop hemiparesis among which 2 died and 1 had persistence of hemiparesis during follow up after 1 month. 1 case develop cerebral infarct with hemiparesis during 1 month follow up. Subdural effusion develop in 3 cases which resolved spontaneously during follow up & 1 new case seen during follow up.

Non neurological complications seen during hospitalization were disseminated intravascular coagulation (7.14%), Shock (7.14%) & Electrolyte imbalance (2.38%) cases. 3 cases died having DIC and shock. 2 cases had electrolyte imbalance among which 1 died and 1 survived. Haemodynamic instability indicate either disseminated infection or raised intracranial pressure.[7]

Prevention of acute complications can be done by early diagnosis & identifying the organism causing it & starting appropriate treatment immediately.

Those patients who survived were followed up after 1 month of discharge to record any new complications arose at home. Total 13 patients died due to pyogenic meningitis after hospitalization. Mortality was 15.47%. Persistent seizures (12.67%), hydrocephalous (9.85%), cerebral infarct (4.22%), cranial nerve palsy (2.81%), hemiparesis (2.81%), hearing loss (2.81%) & subdural effusion (1.4%) were noted during follow up at 1 month of discharge.

Discussion;-

Acute bacterial meningitis accounted for 0.62% of all our paediatric admission during its 18 month of study. We restricted our study age group from 1 month to 12 years to focus on distinct clinical group excluding neonatal meningitis. Kabra et al reviewing a survey of pyogenic meningitis in major centre in India reported frequency of 0.5% to 2.6% of a hospital admission.[2] The community prevalence in international studies have been quoted between 3/100000 in USA[8], 16/100000 in UK[9] to 45.8/100000 in Brazil[8]. Though all these number are relatively small, the importance of acute bacterial meningitis is chiefly because of the associated high mortality and serious morbidity.

In our study of total 84 cases, 13 (15.47%) cases died in hospital. The case fatality rate in India and other developing countries has been quoted as 16 to 30%.[1,3,10,11,12] Approximately 1/3rd of all deaths in our study occurred in the first 48 hours of hospitalization, reflecting the critical condition of the patient at the time of admission. Even in developed countries, in spite of availability of all facilities the case fatality rates of bacterial meningitis in early childhood approaches 10%.[8] The complications rate in acute bacterial meningitis is high in spite of aggressive management.[3,8,13] 33.33% of our patient had acute complications, including subdural effusion, cerebral infarct, hydrocephalous, cranial nerve palsies, persistent seizures, hemiparesis. Even more disturbing than mortality were sequelae& disabling handicaps in survivors. 12.87% with persistent seizures, 9.85% with hydrocephalous, 4.22% with cerebral infarct, 2.81% with cranial nerve palsy, hemiparesis, hearing loss each & 1.4% with subdural effusion during follow up, causing considerable financial and emotional burden to family. Early and careful follow with neurodevelopmental and auditory testing is important because more than half of these disabled children appeared normal at hospital discharge. Overall complications in age group $\leq$ 5 years were 30.94% which is statistically significant than > 5 years (p value 0.034). Complications seen with duration of illness > 7 days were 11.91% which is statistically significant than the illness $\leq$ 7 days (p value 0.0039).

Early diagnosis, prompt initiation of therapy and supportive care are important for improving the long term outcome.[2,8,10] Unfortunately as seen in present study, signs of meningitis can not be used for making early diagnosis as it is seen in 40.47% patients only. Altered sensorium and convulsion are late features. Hence high index of suspicion is necessary to suspect meningitis and perform lumbar puncture. A presumptive diagnosis of acute bacterial meningitis is possible on biochemical analysis of CSF. Difficulties arises when patient are already treated with antibiotics as CSF may show normal sugar content & cells may be predominantly lymphocytes. In such a cases

one has to rely on other CSF parameters and clinical clues. Unfortunately what seems to be difficult especially in our country is accurate diagnosis of acute bacterial meningitis.[2,3,14] Gram staining though chief and easy technique, can identify organism best in 60% of cases[3,10,15], whereas CSF culture results are positive in not more than 15 – 35% patients.[2,3,14] Condition become again worst when patient previously treated with antibiotics. The culture results are perhaps be improved with the use of special media and technique especially for Hemophilusinfluenzae. However most western series quote a culture positivity up to 90%.[8] The reason for low yield in our country are not clear but may include poor quality of culture media and use of antibiotics prior to hospitalization.[3,16] Other quick and sensitive techniques of diagnosis of acute bacterial meningitis need to be urgently explored of great promise is the CSF Latex agglutination test which various authors have confirmed as simple with superior sensitivity and specificity and unaffected by previous antibiotics therapy.[10,16,17] In the present study we have not included this test due to unavailability of kits. These kits are very expensive and available only for common organism and hence not suitable as the lone diagnostic technique in acute bacterial meningitis. Besides kits can not provide information about antibiotic sensitivity and hence both technique (LAT & culture sensitivity) should be used together. In our study among 84 patients 71 patients were negative on culture but the final diagnosis was made on CSF biochemistry and clinical features. In such a cases it is difficult to rule out tuberculous and viral meningitis in initial stages.

The commonest organism associated with acute bacterial meningitis in early childhood was Hemophilus influenzae.[8] However most Indian studies have quoted low isolates of organism.[2,3,14] Whether this is because organism is difficult to grow or the incidence is genuinely low is not clear. In the present study, the contribution by various organism was streptococcus pneumoniae (10.71%), Staphylococcus aureus (2.38%), Hemophilusinfluenzae (1.19%) & pseudomonas (1.19%). The low incidence of infections with N. meningitidis and relatively high incidence pneumococcal infections has been noted by other Indian workers.[3,18]

13 patients died after hospitalization i.e. 15.47% mortality. High mortality is seen which is statistically significant in 1) Malnutrition (p value 0.036) 2) Duration of illness before diagnosis > 7 days (0.034) 3) With different organisms identified by blood culture / CSF culture/ gram staining. 4) CSF sugar < 20mg% at the time of diagnosis (p value 0.011).

There is no statistical difference observed with mortality in patients having predisposing illness before diagnosis than patient having no predisposing illness.

The management of acute bacterial meningitis include suitable combination of antibiotics, dexamethasone for first few days, and importantly intensive care therapy especially for shock and raises intracranial pressure.[2,5,8] Treatment of complications include antiepileptic drugs and neurosurgical procedures. All these adds tremendous financial and emotional burden to family. Measures to prevent acute bacterial meningitis are thus extremely important.

The vaccine against H. influenzae has reduced infections with one of the most important cause of acute bacterial meningitis in advanced countries. This now introduced as optimal vaccine in India. However to be effective it is to be given as early period of infancy as majority of infections occurs during first six months of life. Pneumococcal meningitis is too vaccine preventable disease as both conjugate and polysaccharide vaccine available in India.[5,8] Universal use of meningococcal vaccine is unattractive as the disease is sporadic and is of limited immunogenicity.[8] However if pneumococcal and H. influenzae vaccine become reality in national immunization schedule, the incidence of acute bacterial meningitis in early childhood can reduce by more than 60% with considerable reduction in financial and emotional burden of the disease.

Summary &Conclusion:-

- Higher incidence of acute bacterial meningitis seen in infantile period.
- Streptococcus pneumoniae is the commonest organism causing pyogenic meningitis.
- High mortality is associated with 1) Duration of illness > 7 days. 2) CSF sugar < 20mg/dl. 3) Different organism identified by CSF culture/ blood culture/ Gram staining. 4) Malnutrition
- Streptococcus pneumoniae, Staphylococcus aureus, Hemophilusinfluenzae& pseudomonas aeruginosa identified in pyogenic meningitis were 100% sensitive to Cefotaxime, Ceftriaxone, Piperacillin, Meropenem& Ciprofloxacin & having good sensitivity against Ampicillin, Amikacin& Chloramphenicol.

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