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ORIGINAL RESEARCH

Clinical presentation and CSF analysis in childhood meningitis and role of CSF LDH in diagnosis

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ABSTRACT

Introduction: Meningitis is one of the commonest diseases in children. Standard routine analysis of CSF in meningitis does not always provide rapid definitive information as for as causative agent is concerned. **Objective of the study**: To evaluate the clinical presentation and CSF analysis in childhood meningitis with special reference to LDH estimation. **Material & methods:** Study was conducted in the department of Pediatrics Institute of Medical sciences & SUM Hospital. Cases of different types of meningitis between 1 month to 14 yrs were taken and 21 cases of febrile convulsion were taken as controls. Cases below 1 month age and traumatic or dry tap were excluded from the study. Results were analyzed by descriptive statistical analysis, Kruskall Wallis test, chi-square/fisher exact test were used. **Results:** Viral meningitis was the commonest type of meningitis in this study comprising 38.7%. Male cases were more comprising 66.7%. TBM common in >5 yr age group, pyogenic and viral meningitis were common in 1-5yrs age group. Fever, convulsion, vomiting and headache were the commonest symptoms. Neck rigidity, altered sensorium, cranial nerve palsy and motor weakness were the commonest signs. CSF protein was significantly high in TBM, slightly elevated in pyogenic meningitis. LDH was elevated (>60IU/dl) in 100% cases in pyogenic meningitis and 87.5% in TBM, 24% cases of viral meningitis. **Conclusion:** To conclude, even though LDH activity is used as supportive evidence of meningeal inflammation, as this test is cost effective can be used on regular basis along with other routine tests to diagnose meningitis and for differentiation of pyogenic, tubercular and viral meningitis**.**

Key Words: Meningitis, Lactate dehydrogenase, Cerebrospinal fluid.

INTRODUCTION

Many organisms can cause central nervous system infection. Acute infection of Central Nervous System (CNS) is the most common cause of fever associated with signs and symptoms of CNS disease in children. Most common infection of CNS are meningitis and encephalitis. Meningitis implies primary involvement of meninges whereas encephalitis indicates brain parenchymal involvement. Because these anatomic boundaries are often not distinct, many patients have evidence of both meningeal and parenchymal involvement and should be considered to have meningoencephalitis[1].Nonetheless, specific pathogens are identifiable and are influenced by the age and immune status of the host and epidemiology of the pathogen[2].

Various factors that determine the outcome of disease are age, early diagnosis, early treatment, duration of treatment and type of microorganism[3].The information yielded by examination of Cerebrospinal fluid is often of crucial importance in the diagnosis of neurological disease[4].

Prompt and precise etiological diagnosis remains a challenge and often a thorough cerebrospinal fluid examination may not give a precise diagnosis. Many enzymes are known to be present in abundance in the nervous system. Meningitis disturbs the blood brain

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barrier and is expected to cause rise in enzymatic activity.

Therefore, various investigators have used them for the diagnosis as well as for determining the prognosis in cases of meningitis[5-10].

However, the role of various cerebrospinal fluid enzymes needs to be evaluated as not enough work has been carried out and majority of researchers have estimated one of these enzymes either in cerebrospinal fluid or serum[11].

It is in this context that the present study was planned to evaluate the diagnostic significance of Cerebrospinal fluid Lactate Dehydrogenase in cases of tuberculosis and pyogenic meningitis.

The current study was conducted among children with suspected meningitis admitted in the department of Pediatrics, Institute of Medical Sciences & SUM Hospital, Odisha.

MATERIAL & METHODS

The present study was conducted in the Department of Pediatrics, Institute of Medical Sciences& SUM Hospital, Odisha. Patient's attendant were appraised of the purpose of the study and written consent was taken prior to commencement of the study. Ethical clearance was obtained by the ethical clearance committee of the institution. The study included clinical evaluation and CSF analysis of 54 cases of meningitis and 21 cases of febrile convulsion as controls admitted to Pediatrics wards during the period of December 2019 to July 2021.

STUDY GROUP:

Selection of cases:

Those cases admitted with fever, headache, vomiting, altered sensorium, with or without convulsion in the age group of 1 month to 14 years were examined in detail for any clinical evidence of meningitis. Clinically evident cases of meningitis were randomly selected and submitted for detailed history and careful physical examination. In the clinical evaluation special attention was given for detection of any other associated pyogenic infection, h/o ear discharge and h/o contact with tuberculosis.

After detailed clinical and fundus examination, blood was drawn for estimation of blood sugar. In stable cases Lumbar puncture was performed immediately, in sick cases and cases with evidence of raised intracranial tension lumbar puncture was postponed till the patient stabilizes.

During Lumbar puncture pressure was assessed and macroscopic appearance of fluid was noted. Altogether 5-6 ml of CSF was collected in 5 clean sterile bottles. For culture and sensitivity CSF was directly collected into glucose broth and sent to microbiology lab. During lumbar puncture, one drop of CSF was collected directly over three clean glass slides. One slide was used to study pleocytosis and type of cells. The other two slides were used for preparation of smear by heat fixation for Gram's stain and Z-N stain.

Those cases of dry or traumatic tap and age less than 1 month were excluded from the study.

Analysis of CSF:

All the samples were immediately taken for analysis. Biochemical analysis for protein, sugar, chloride was done in the department of biochemistry using standard methods. CSF cytology was studied in the department of cytology after centrifugating the specimen.

The diagnosis of meningitis was made on the basis of clinical evidence of meningeal irritation, CSF protein, glucose and pleocytosis. The diagnosis of pyogenic meningitis was made on the basis of CSF leucocytic pleocytosis with >90% neutrophils and CSF glucose less than 1/3rd of corresponding blood glucose with or without positive CSF culture or Gram stain. The diagnosis of TBM was made on the basis of leucocytic pleocytosis with >80% lymphocytes and increased protein with or without positive PCR and CT scan brain evidence.CSF LDH was estimated in the central lab with the help of Calorimeter.

Statistical analysis:

The Statistical software namely SPSS 15.0, Stata 8.0, MedCalc 9.0.1 and Systat 11.0 were used for the analysis of the data. Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Median± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance.

RESULTS

Table 1: Diagnosis of the Patients

Diagnosis	Number	Percentage
Pyogenic	17	22.7
Tubercular	8	10.7
Viral	29	38.7
Control	21	28.0

Table 1 shows Total 75 cases were studied among which 8(10.7%) were tubercular meningitis, 17cases (22.7%) were pyogenic meningitis, 29(38.7%) cases were viral meningitis and 21 cases(28%) were controls.

Table 2: Age & Sex Distribution of Patients

Age & Sex	Pyogenic No (%)	Tubercular No (%)	Viral No (%)	Control No (%)	Total No (%)
Age in Years					
<1 year	3 (17.6)	0 (0.0)	4 (13.8)	2 (9.5)	9 (12.0)

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1-5 year	10 (58.8)	1(12.5)	15 (51.7)	9(42.9)	35(46.7)
>5 year	4(23.5)	7(87.5)	10(34.5)	10 (47.6)	31(41.3)
Sex					
Male	12(70.6)	7(87.5)	20(69.0)	11(52.4)	50(66.7)
Female	5(29.4)	1(12.5)	9(31.0)	10(47.6)	25(33.3)

Table 2 shows the age distribution in the study and control group the majority of patients were in the age group of 1-5 years. In TBM cases (12.5%)of patient was in the age group of 1-5 years and 7 cases (87.5%) were in >5 years age. In pyogenic meningitis 10 cases (58.8%) were 1-5 years age. In viral meningitis majority of cases were in the 1-5 years age group. Among total 75 cases 66.7% were males and 33.3% were females. Males are predominant in pyogenic & viral meningitis and TBM & control group.

Table 3: Presenting Complaints

Symptoms	Pyogenic (n=17) No (%)	Tubercular (n=8) No (%)	Viral (n=29) No (%)	control (n=21) No (%)	*P value
Fever	15(88.2)	7 (87.5)	29(100.0)	21 (100.0)	0.100
Convulsion	9(52.9)	8(100.0)	18(62.1)	20(95.2)	0.004
Headache	9(52.9)	2 (25.0)	14 (48.3)	7 (33.3)	0.411
Vomiting	10(58.8)	1 (12.5)	20 (69.0)	11 (52.4)	0.040
Cough	0(0.0)	2(6.9)	0(0.0)	4 (19.0)	0.127
Altered sensorium	3 (17.6)	4 (50.0)	12(41.4)	10 (47.6)	0.221
Others	2(11.8)	1(12.5)	11 (37.9)	2 (10.0)	0.057

*Statistically Significant (Chi-Square test)

Table 3 Showed Fever was the most consistent symptom in all type of cases, 87.5% in TBM, 88.2% in pyogenic meningitis, 100% in viral meningitis & control group. The other presenting symptoms in TBM included convulsions in 100%, headache in 25 %, vomiting in 12.5% & altered sensorium in 50% of cases.

The symptoms in pyogenic meningitis included convulsion in 52.9%, headache in 52.9%, vomiting in 58.8%, & altered sensorium in 17.6% of cases. In viral meningitis 62.1% had convulsions, 48.3% had headache, 69% had vomiting & 41.4% had altered sensorium, other evidence of viral fever like skin rash, coryza, pharyngitis, and redness of eyes is seen in 37.9% of cases.

In control group 95.2% had convulsions, 52.4% had vomiting &19% cough, 47% altered sensorium.

Table 4- Clinical Features

Symptoms	Pyogenic (n=17) No (%)	Tubercular (n=8) No (%)	Viral (n=29) No (%)	control (n=21) No (%)	*P value
CN Palsy	2(11.8)	1(12.5)	7(24.1)	0(0.0)	0.282
CN Deficit	2(11.8)	0(0.0)	0(0.0)	0(0.0)	0.108
Neck Rigidity	2(11.8)	1 (12.5)	12(41.4)	0(0.0)	0.103
Kernig's sign	5(29.4)	1(12.5)	13(44.8)	0(0.0)	0.665
Brudzinski sign	5(29.4)	1(12.5)	9(31.0)	0(0.0)	0.486
Papilledema	2 (11.8)	1(12.5)	2(6.9)	0(0.0)	0.935

*Statistically Significant (Chi-Square/Fisher's Exact test)

Table 4 showed the most consistent finding in all groups of meningitis was neck rigidity observed in 68.4% of cases. In TBM group cranial nerve palsy was seen in 1(12.5%) case among which 3rd, 6th& 7thnerve were commonly involved. Kernig's sign was positive in 1 (12.5%) of cases, fundus showed papilledema in 1 case. In pyogenic meningitis group 2 (11.8%) cases showed cranial nerve involvement, 2 (11.8%) cases showed motor weakness, neck rigidity is seen in 2 (11.8%) cases, Kernig's sign positive in 5(29.4%) cases. In viral meningitis group 12(41.4%) cases had neck rigidity, 13(44.8%) had Kernig's sign positive.

In control group No history of CN palsy, Neck rigidity, kernig's sign, papilledema

Table 5- CSF Profile Among Different Type of Cases

CSF Parameter	Diagnosis				
	Pyogenic Median(Q1-Q3)	Tubercular Median(Q1- Q3)	Viral Median(Q1- Q3)	Febrile Median(Q1- Q3)	*P value
Total cell	245.0(142.0-292.5)	105(92.5-135)	21.0(9.3-50.3)	4.00(2.0-4.0)	<0.001
Polymorphs	67.5(36.9-188.8)	19(15.7-32.2)	0.9(0.03-12.6)	0.0(0.0-0.8)	<0.001
Lymphocytes	113.9(81.8-160.5)	82(73.2-111.2)	20.4(8.9-34.0)	3.0(2.0-4.0)	<0.001
Glucose (mg/dl)	50.0(45.0-52.5)	95.0(92.3-95.5)	88.5(78.0-97.3)	98.0(91.0-102.0)	<0.001
Protein (mg/dl)	95.0(66.9-123.5)	155.0(101.3-192.5)	55.0(41.2-66.5)	45.0(36.0-53.0)	<0.001

*Statistically significant (Kruskal wallis test)

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Table 5 shows in TBM group the median cell count was 105(92.5-135) cells/cumm, median polymorphs 19(15.7-32.2), median lymphocytes 82(73.2-111.2), the median protein of 155(107-185mg/dl) and the median sugar 50(45-52.5mg/dl). In pyogenic meningitis group the median cell count was 245(145-290) cells/cumm, the median polymorphs 67.5(40-183) and the median lymphocyte 113.9(89.2-158.6) the median protein of 95(73.9-115) mg/dl and the mean sugar of 96(80-114) mg/dl. In viral meningitis group the median cell count was 21(9.5-48.5) cells/cumm, the median polymorphs of 0.9(0.03-123.1), the mean lymphocytes of 20.4(8.9-33.3), protein mean of 55(42.5-66) mg/dl & mean sugar of 88.5(78-96.5) mg/dl.
Control group showed cell count of 4(2-4) cells/cumm, with lymphocytes of 3(2-4) protein of 45(37-52mg/dl), & mean sugar of 98(92-102) mg/dl. P value is significant (<0.001) for all the parameters in all the groups

Table 6: Elevated LDH Status Among Different Type of Cases

LDH Level	Pyogenic (n=17) No (%)	Tubercular (n=8) No (%)	Viral (n=29) No (%)	control (n=21) No (%)	P value*
Normal (≤60)	0 (0.0)	1 (12.5)	22 (75.9)	20 (95.2)	
Elevated (>60)	17 (100)	7 (87.5)	7 (24.1)	1 (4.8)	<0.001

*Statistically Significant (Chi-Square test)

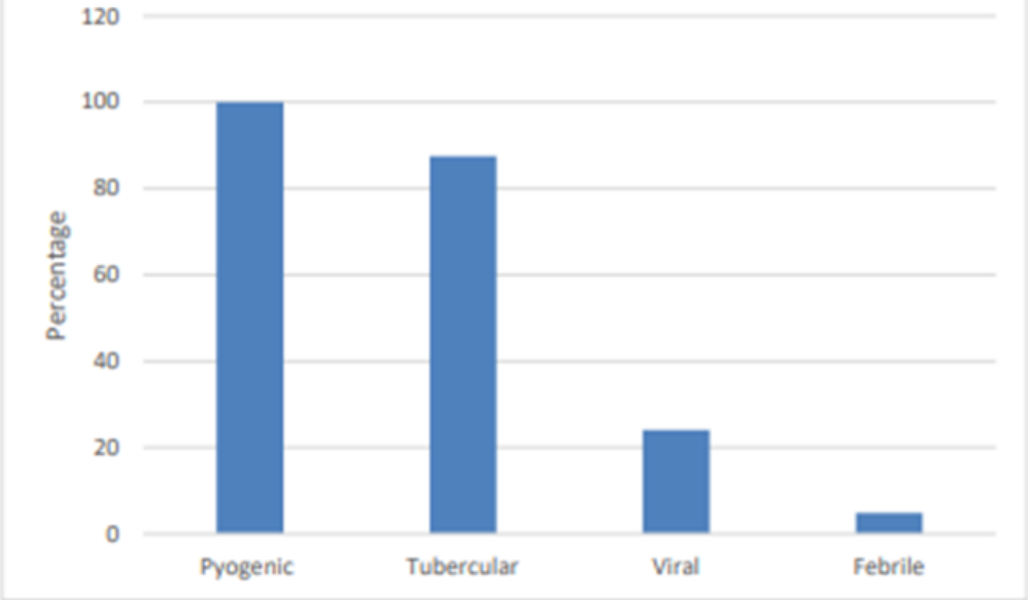

Figure 1: Elevated LDH Status Among Type of Cases

In Table 6 LDH levels are presented & graphically projected in Fig.1. LDH is elevated (LDH>60 IU/dl) in 100% cases in pyogenic meningitis and 87.5% in TBM, 24% cases of viral meningitis. Control group: 1% elevated.

DISCUSSION

In this study of CSF analysis in childhood meningitis with special reference to LDH estimation, 75 cases were studied. Out of 75 cases, 8 children had TBM, 17 children had pyogenic meningitis, and 29 children had viral meningitis and 21 febrile convulsion cases were taken as controls.

Among 17 cases of pyogenic meningitis 70.6% were males and 29.4% were females. Majority of them (58.8%) were between 1-5 years age group, while 23.5% cases were above 5years and 17.6% were below 1 year of age.In other studies, done by Kabra et al[12] 56% of cases were above 5 years, 22% between 1-5 years, Chitale et al[13] found 44% of cases between 1-5 years age group.

Among 8 cases with TBM, 87.5% were males & 12.5% were found to be females. Cases above 5 years were 87.5% and 1-5 years 12.5%, no case was below 1 year.

In a study by Chitale et al[13] maximum cases of TBM were found in above 5 years, in another study by Shah et al14 3/4th cases were below 5 years. Present studies data are consistent with study done by Chitale et al[13].In 29 viral meningitis cases 69% were males and 31% were female with majority of cases were in the age group of 1-5yrs.

In present study fever was present in 88.2% of cases, as compared to other studies done by Gaikwad et al[15] found in 90%, Stair et al[16] in 90% and Laditan et al[17] (64,65,67) in 91.7%. Convulsion in present study was seen in 52.9% of cases, as compared to 9.1% in Laditan et al[17], 40% in Gaikwad et al[15] and 24% in Stair et al16. In present study headache was complained by 52.9% of cases, as compared to 54.5% in Laditan et al[17], 84% in Gaikwad et al[15].

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In present study fever is the most consistent symptom (87.5%) which is consistent with other studies, Thilothammal et al[18] 65 found in 100% of cases and Lincoln et al19 in 97.5% cases. Convulsion in present study was found in 100% of cases as compared to other studies Thilothammal et al[18] 79% and Lincoln et al19 9.5%.In present study headache was present in 25% as compared to study done by Thilothammal et al18where headache was found in 34% and Lincoln et al[19] found in 12.5%. Vomiting in present study was found in 64.7% of patients as compared to other studies Thilothammal et al[18] 76% and Lincoln et al 51%. Altered sensorium in present study was presenting complaint in 50% as compared to study by Thilothammal et al[18] where 80% had altered sensorium.

Altered sensorium was found in 17.6% of cases in present study as compared to 22% in Gaikwad et al[15] and 60% in Minns et al[20]. Cranial nerve palsy was seen in 11.8% in present study as compared to 8% in Gaikwad et al[15] and 31% in Minns et al[20]. Meningeal signs were seen in 70.6% of cases in present study as compared to 88% cases in Gaikwad[15] and 23% cases in Minns et.al[20].

In present study cranial nerve palsy was observed in 12.5% of cases as compared to other studies done by Thilothammal et al[18] observed in 28% and Kennedy et al[21] observed in 17.5%. Motor deficit was present in 12.5% of cases in present study as compared to 47% in study by Thilothammal et al[18]. In present study neck rigidity was observed in 12.5% of cases as compared to 65% cases in a study done by Thilothammal et al[18] and 90% cases in Kennedy et al21. Papilledema in present study was demonstrated in 0% of cases as compared to 12% in Thilothammal et al[18] and 31% in Kennedy et al[21].

In this study the median cell count was found to be 245 (145-290) cells/cumm with predominance of polymorphs 67.5% (40-183.7%). In other studies, like Jain et al[6], Chowdhary et al[22]. Cell count was between 2000-3000 cells/cumm. The median protein value was 105.93(41.54-170.35) mg/dl in present study as compared to 163(28-297.2) mg/dl in Jain et al and 469.6(218.1721.1)mg/dl in study done by Sharma et al[23].

CSF LDH was elevated in all type of meningitis. The highest titre of CSF LDH was observed in pyogenic meningitis. LDH titres were marginally elevated in viral meningitis and intermediate values were observed in TBM. When 60 IU/L was taken as highest normal LDH activity, LDH estimation has showed high sensitivity and specificity to diagnose meningitis. Jain et al and Gupta et al found a linear relationship between rise in LDH activity and cell count that is consistent with our study[6,24].

CONCLUSION

Meningitis is one of the commonest diseases in children. Although majority of cases manifest typically with fever, convulsion, headache, vomiting and altered sensorium, atypical presentations are not uncommon. In majority of the cases, detailed history and clinical examination was helpful in diagnosing meningitis, CSF analysis was helpful in majority of the patients for diagnosis of meningitis. Even though LDH activity is used as supportive evidence of meningitis, as this test is cost effective can be used on regular basis along with other routine tests to support the diagnosis of meningitis and to differentiate between the pyogenic, tubercular and viral meningitis.

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