Significance of CSF-LDH in various types of meningitis

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Abstract
The cerebrospinal fluid concentration of Lactate dehydrogenase (LDH) was studied in patients with pyogenic and tubercular meningitis. Significant increase in LDH level (P<0.001) were observed in the test group when compared to the control group. LDH may useful in differentiating viral from other meningitis. It may act as corroborative evidence of meningitis.

Keywords: meningitis, cerebrospinal fluid, lactate,

1. Introduction
Meningitis refers to an inflammatory process of the leptomeninges and CSF within the subarachnoid space. Infectious meningitis is broadly classified into acute pyogenic (usually bacterial meningitis) aseptic (usually acute viral meningitis) and chronic usually (tuberculous, spirochetal or cryptococcal)[1].

Pyogenic meningitis is a major pediatric problem all over the world, especially in developing countries like India[2]. Antibiotics have reduced the mortality from almost 100% to 8-30%. Early and reliable diagnosis is the key to successful outcome[2].

As presenting signs and symptoms may be inconclusive laboratory tests are essential in establishing a definite diagnosis. So, the rapid diagnosis of bacterial meningitis is an important function of most laboratories and usually based on CSF examination[3].

Many test for rapid diagnoses of bacterial meningitis have been introduced including the nitroblue tetrazolium test, litmus test, counter immunoelctrophoresis and gram stain. Even though the above tests, favors rapid diagnosis, they have their own drawbacks. Counter immunoelctrophoresis is utilized in the diagnosis of meningitis due to haemophilus, pneumococi and meningococci but the method requires specific high tittered antisera and overall false negative rate is about 10%.

The litmus lysate test for endotoxin is rapid and accurate in diagnosing gram negative meningitis but is of no value in cases of gram positive etiology further more if the gram negative bacterial count in the CSF is below 3000 to 400 microorganisms per cubic centimeter, a false negative litmus lysate test may result[4].

The information yielded by examination of Cerebrospinal fluid (CSF) is often of crucial importance in the diagnosis of neurological disease[5]. Various biochemical markers in CSF including lactate dehydrogenase (LDH) have been studied in diverse neurological conditions like leptomeningeal carcinomatosis, stroke and different types of meningitis[6]-[8].

The gram stain may be negative in as many as 30% of cultured proved bacterial meningitis prior antibiotic treatment may also alter bacteria, so as to
obscure their morphological and staining characteristic[4].

Enzymatic study (CSF-LDH) is a better sensitive parameter in diagnosis of various types of meningitis when all the above rapid diagnostic method fail[4].

1.1 Aims and Objectives
- The purpose of this study was to establish early diagnosis and therapeutic value of CSF-LDH in bacterial and non bacterial meningitis.
- To evaluate the importance of CSF-LDH estimation as compared to other investigation in diagnosis of bacterial meningitis in adults as well as in children.
- To find out whether it is specific, superior and faster as in children.
- To evaluate the importance of CSF LDH estimation as compared to other investigation in differential diagnosis of bacterial and non bacterial meningitis.
- To find out its usefulness in differential diagnosis of meningitis.

2. Material and Methods
The present study consisted of 100 cases of suspected meningitis to differentiate them in to pyogenic of non pyogenic including tuberculous and viral meningitis. Where as in females frequency of pyogenic meningitis (24%) was more as compared to tuberculous (18%) and viral meningitis. In case of tuberculous meningitis, majority of cases below 5 year of age (72.5%) with the maximum incidence being in the age group of 1-2 years (25%) fallowed by 0-12 month (20%) and 3-5 years (25%).

In all cases, detailed history including age, sex, duration of symptoms, presenting symptoms, history of treatment prior to hospitalization.

Routine hematological investigation, X-ray, USG and CT scan finding were noted. CSF was obtained by lumbar puncture and examined in detail including physical appearance, turbidity, presence of xanthochromia, cobweb, clot etc.

CSF microscopic examination including total cell count and differential count were done. Biochemistry analysis like (Sugar, Protein, Chloride, ADA and LDH) was also done.

3. Result
The present study consisted of 100 cases of suspected meningitis to differentiate them in to pyogenic of non pyogenic including tuberculous and viral meningitis. The present study was carried out at Department of Pathology, Shree M.P. Shah Medical College and Guru Govind Singh Hospital, Jamnagar during the period from July 2004 to July 2006.

Total 140 CSF samples were examined. Out of them 100 patients of all age groups and either sex of clinically suspected cases of meningitis were taken as test group. The physical, Biochemical and microscopic examination of CSF were done in all cases of pyogenic, tuberculous and viral meningitis. 40 control subjects of all age and either sex were taken as control group.

Table No: 01 Age distribution in various disease and control group.

| age        | Pyogenic meningitis | Tuberculous meningitis | Viral meningitis | Total |
|------------|---------------------|------------------------|-----------------|-------|
|            | No. of cases | %               | No. of cases | %               | No. of cases | %               | No. of cases | %               |
| 0-12 Month | 24              | 60                | 8              | 20               | 3              | 15               | 35              | 17.5            |
| 12-24 Month| 03              | 7.5               | 10             | 25               | 2              | 10               | 15              | 6               |
| 25-36 Month| 02              | 5                 | 3              | 7.5              | 2              | 10               | 7               | 12.5            |
| 3-5 year   | 01              | 2.5               | 8              | 20               | 4              | 20               | 13              | 6               |
| 6-7 years  | 01              | 2.5               | 4              | 10               | 2              | 10               | 7               | 12.5            |
| 8-12 Year  | 02              | 5                 | 2              | 5                | 4              | 20               | 8               | 3               |
| 13-20 year | 03              | 7.5               | 2              | 5                | 1              | 5                | 6               | 10              |
| 21-40 year | 02              | 5                 | 2              | 5                | 2              | 10               | 6               | 2               |
| >40 year   | 02              | 5                 | 1              | 2.5              | 0              | 0                | 3               | 2               |
| Total      | 40              | 100               | 40             | 100              | 20             | 100              | 40              | 100             |

Table no.01 shows that majority of cases (72.5%) occurred below 3 year of age in cases of pyogenic meningitis. The vast majority of cases (60%) were below one year. The cause of increase incidence during the first 3 year of life is possibly due to increase meningeal permeability.

Table 02: Sex distribution of disease cases

| Type of meningitis | Male | Female |
|-------------------|------|--------|
| No. of cases      | No. of cases | percentage | No. of cases | percentage |
| Pyogenic          | 40   | 24     | 16            | 16        |
| Tuberculosis      | 40   | 22     | 18            | 18        |
| Viral             | 20   | 12     | 8             | 8         |
| Total             | 100  | 58     | 42            | 42        |

Table no. 2 is showing male predominance as compared to frequency of meningitis is female. In males pregnancy of pyogenic meningitis (24%) was more as compared to tuberculous (18%) and viral (12%) meningitis. Where as in females frequency of tuberculous meningitis was 22%, 16% for pyogenic meningitis and 8% for viral meningitis.
Table 03: CSF-LDH (Level) in various disease and control group

| Type of meningitis     | No. of cases | CSF-LDH Range     | Mean       |
|------------------------|--------------|-------------------|------------|
| Pyogenic meningitis    | 40           | 35.5-750 U/L      | 171.25 U/L |
| Tuberculous meningitis| 40           | 20.4-315 U/L      | 105.65 U/L |
| Viral meningitis       | 20           | 17-75 U/L         | 35.6 U/L   |
| Control group          | 40           | 05-53 U/L         | 21.30 U/L  |

The table no.03 shows that CSF-LDH level increases maximally in pyogenic meningitis with range of 35.5-750 U/L and mean 171.25 U/L. There was mild increase of CSF-LDH in aseptic meningitis (17-75 U/L range and mean 35.6 U/L) and moderate increase in tuberculous meningitis (range 20.4-315 U/L and mean 105.65 U/L). CSF-LDH activity in the control group ranges from 05-53 U/L with the mean of 21.30 U/L and it is taken as a normal mean value in the present study.

Table 04: CSF –LDH Positivity & Negativity in various disease and control groups

| Type of meningitis     | CSF-LDH Positive | CSF-LDH Negative | Total No. |
|------------------------|-------------------|-------------------|-----------|
|                        | No. of cases      | Percentage        | No. of cases | Percentage |          |
| Pyogenic meningitis    | 35                | 87.5              | 5          | 12.50      | 40        |
| Tuberculous meningitis| 31                | 77.5              | 9          | 22.50      | 40        |
| Viral meningitis       | 11                | 55                | 9          | 45         | 20        |
| Control group          | 00                | 00                | 40         | 100        | 40        |

Table no 04 shows that LDH activity is increased in 87.5% of pyogenic meningitis, 77.5% of tuberculous meningitis cases and 22.5% of viral meningitis.

Table No. 05: Sensitivity, specificity and predictive value in pyogenic meningitis

|                   | Disease present | Disease absent |
|-------------------|-----------------|---------------|
| Test positive     | 33              | 05            |
| Test negative     | 07              | 35            |

Sensitivity = 33/40 = 82.5%
Specificity = 35/40 = 87.5%
Predictive value of positive test = 33/38 = 86.8%
Predictive value of Negative test = 35/42 = 83.3%

Table no.05 shows that in case of pyogenic meningitis sensitivity was 82.5 % and specificity was 87.5%. The Predictive value of positive test was 86.3% and the Predictive value of Negative test was 83.3 % in present study.

In cases of pyogenic meningitis detection of ‘p’ value is <0.001 is highly significant.

So, this shows that test is highly significant for diagnosis of bacterial meningitis to other meningitis group.

4. Discussion

Meningitis is a significant cause of morbidity and mortality in children worldwide. Neurological outcome and survival depend largely on damage to central nervous system prior to effective treatment. Quick diagnosis in acute bacterial meningitis is due to large spectrum of signs and symptoms. However, it is usual practice to start antibiotics before the complete laboratory results are available. Such blind prescriptions are usually in non meningitis doses. Majority of children who reported to hospital, therefore, have already been treated with inadequate dose of antibiotics and present atypical features in CSF.

The activity of LDH varies from person to person and also from laboratory due to variation in the standardization of apparatus and reagents used.

Table no 06: Comparative analysis of age distribution in pyogenic meningitis.

| Authors               | Year | 0-1 year | 1-3 year | >3 year |
|-----------------------|------|----------|----------|---------|
| Achar and Thambiah[9] | 1954 | 82.60    | 5.80     | 11.60   |
| Paul[10]              | 1960 | 71.00    | 13.00    | 16.00   |
| Vashi and Joshi[11]   | 1968 | 58.00    | 18.00    | 24.00   |
| Gandhi[12]            | 1969 | 25.00    | 31.70    | 43.30   |
| Kumar et al[13]       | 1980 | 54.50    | 19.70    | 25.80   |
| Merchant and Patil[14] | 1984 | 85.00    | 0.00     | 0.00    |
| Present study         | 2007 | 60.00    | 12.50    | 27.50   |

Table no.06 shows that comparative analysis of only pediatric patient done as pediatric age group constituted about 82.5 % of total cases in the present study. Children up to 12 years of age were taken and calculations were done accordingly in present study.
Table no 07: Comparative analysis of age distribution in tuberculous meningitis.

| Authors                  | Year | Age          |
|--------------------------|------|--------------|
| Udani et al [15]         | 1970 | 0-1 year     |
|                          |      | 15.60        |
|                          |      | 1-2 year     |
|                          |      | 20.80        |
|                          |      | 3-5 year     |
|                          |      | 39.20        |
|                          |      | 6-7 year     |
|                          |      | 11.80        |
|                          |      | >7 year      |
|                          |      | 12.60        |
| Benakappa et al [16]     | 1975 | 26.00        |
| Present study            | 2000 | 20.00        |
|                          |      | 25.00        |
|                          |      | 20.00        |
|                          |      | 10.00        |
|                          |      | 5.00         |

As mention in table No.07 the age distribution in the present study correlated with that reported by Udani et al and Benakappa et al [16]. In the present study the highest incidence of disease i.e. 65% occurred in children under 5 years of age.

Table No. 08: Comparative analysis of CSF-LDH value in Bacterial meningitis and control group.

| Authors        | Year | CSF-LDH Bacterial meningitis | CSF-LDH Control group |
|----------------|------|-----------------------------|------------------------|
| P.V. Nelson    | 1975 | 31-1498 U/L                 | 3.17 U/L               |
| Knight[4]      | 1981 | 88-2451 U/L                 | 0.23-5 U/L (10.5 U/L)  |
| Present study  | 2006 | 35.5-750 U/L                | 5-53 U/L (21.3 U/L)    |

In the present study the mean value was 21.3 U/L in the control group which is more or less equated the past study group.

CSF-LDH activity is markedly increased in pyogenic meningitis group in the present study and it is correlated well with study of P.V. Nelson and study of Knight.

5. Conclusion

Bacterial meningitis is more common than non-bacterial meningitis. Pyogenic meningitis is more prevalent under 1 year of age group while tuberculous meningitis is seen most frequently between 3 to 5 year of age. Estimation of CSF-LDH activity shows more sensitive (82.5%) and specificity (87.5%) to differentiate pyogenic meningitis from non bacterial meningitis. CSF-LDH level has inverse relationship with meningitis and direct relationship with leucocytosis.

So, overall conclusion of study is that estimation of CSF-LDH activity is not only supplementary aid but diagnostic and differentiating aid for meningitis.

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