



The Role of CSF LDH Estimation to Differentiate Different Types of Meningitis

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Abstract

Introduction: Meningitis is a clinical syndrome characterized by inflammation of the meninges. Meningitis is a medical, neurological and sometimes neurosurgical emergency that requires a multidisciplinary approach. Anatomically meningitis can be divided into the inflammation of the dura (pachymeningitis), which is less common and leptomeningitis, which is more common and is defined as the inflammation of the arachnoid and the subarchanoid space. Examination of the cerebrospinal fluid is the cornerstone of diagnosis. Cerebrospinal fluid analysis includes the total count, differential count, protein, sugar, gram staining culture and sensitivity, AFB staining, in special cases CSF ADA and Tuberculous RNA PCR. Other laboratory tests, which may include CSF lactate, C- Reactive Protein, SGOT, glutamate level and Lactate Dehydrogenase. (LDH). Though CSF abnormalities in meningitis is well documented, only few studies have been conducted in our part of the world. This study is conducted to know the role of CSF LDH to differentiate different types of meningitis.

Materials and Methods: This was a hospital based cross sectional study. All patients with recorded clinical and biochemical evidence of meningitis (viral, bacterial, or tuberculous) admitted in a tertiary care centre in South Kerala during the period of April 2012- 2013 were included. After getting informed consent from Patients after applying inclusion and exclusion criteria, those fulfilling all the inclusion criteria were subjected to detailed evaluation, Lumbar puncture (for CSF collection and analysis of CSF) was done. According to the criteria patients were divided into four groups- Viral, bacterial, tuberculous and partially treated meningitis. CSF LDH was measured and looked for any correlation with the diagnosis. Unpaired T test was used to compare mean LDH level in various types of meningitis. Association was checked with Chi square test.

Observations: 180 patients were included in this study, 111 were males and 69 females. Most of the patients were younger & belonged to the age group of 31-40 years in bacterial and viral meningitis group, whereas in tuberculous meningitis maximum number of patients were elderly, in the age group 61-70years. Among the total 180 patients, 33% were categorized as bacterial, 33% as viral, 4.44% as tuberculous and 28.88% as partially treated meningitis according to the study definitions. The average white blood cell count of the CSF among patients with bacterial meningitis was 613, tuberculous meningitis was 656, and in viral meningitis was 101 cells/mm³. On analysis the differential count was predominantly polymorphs in bacterial whereas it was lymphocytic predominant in other groups. The average CSF protein in bacterial meningitis group was 102.4mg/dl, in viral meningitis group 33.6, tuberculous meningitis group 89.4 and in the partially treated group was 75.47mg/dl. The average CSF sugar value in bacterial meningitis was 29.5mg/dl, in viral 68.4mg/dl, in Tuberculous meningitis 23.3 and in partially treated group

was 43.03mg/dl. The average ADA value in bacterial meningitis group was 6.4, viral meningitis group was 4.8 whereas in tuberculous meningitis group it was 20. We noted that the average ADA value was maximally elevated in the tuberculous group. Among the 18 tuberculous patients, 17 had an ADA of more than 15. The average CSF LDH value was 94.1 IU/L in bacterial meningitis group, 30.2 IU/L in viral meningitis group & 119.9 IU/L in tuberculous meningitis group. Out of the 72 patients who had viral meningitis in our study, 18 (25%) had JE/WEST NILE virus positivity. This high frequency of encephalitis was not observed in other studies, which indicates a high frequency of JE in our part of the world. In those tested positive for JE, the CSF LDH was significantly high. We had 52 (28.88%) patients in the partially treated meningitis group. Among this 34 had features of bacterial & 6 had features of tuberculous meningitis. The CSF LDH value was significantly elevated in these two categories. Rest of the 12 patients with features suggestive of viral meningitis only had a mild elevation of LDH. The mean CSF LDH in viral meningitis & tuberculous meningitis group were 77.2 & 22.5 % respectively.

Conclusion: CSF LDH was significantly elevated in Tuberculous meningitis and bacterial meningitis. In viral meningitis, CSF LDH showed only a mild elevation. Viral meningitis with increased CSF LDH were positive for JE. Hence in Viral meningitis with high LDH should raise suspicion of encephalitis.

Introduction

Meningitis refers to an inflammatory process of the leptomeninges and CSF within the subarachnoid space. Infectious meningitis is broadly classified into acute pyogenic meningitis (usually bacterial), aseptic (usually acute viral meningitis) and chronic (usually tuberculous meningitis or cryptococcal meningitis)^[1]. Antibiotics have reduced the mortality from almost 100% to 8-30%. Early and reliable diagnosis is the key to successful outcome. The information yielded by examination of the Cerebrospinal fluid is often of crucial importance in the diagnosis of neurological disease. Various biochemical markers including Lactate dehydrogenase (LDH) have been studied in diverse neurological conditions like leptomeningeal carcinomatosis, stroke and different types of meningitis^[2-4].

The CSF LDH is around 1/10th of the serum LDH level. Usual source is from the pia and arachnoid cells. Lactate dehydrogenase is an enzyme present in a wide variety of organisms including plants and animals.

High levels of lactate dehydrogenase in the cerebrospinal fluid are associated with bacterial meningitis. High levels are also associated with viral meningitis too, but if so, it indicates encephalitis and a poor prognosis^[5].

The CSF LDH activity was measured using NADH consumption. This was based on the property of pyruvate to reduce lactate at pH 7.4 and temperature 37 °C. the progress of the accompanying oxidation of NADH to NAD is

monitored continuously by measuring the rate of absorbance decreased at 339 nm in a spectrophotometer^[6]. the values of both glutamine and LDH are increased significantly (p <0.001) in patients with meningitis^[6].

CSF level of LDH was found to be elevated in patients with meningitis in some studies^[7]. Nand n, et al has found significantly elevated levels of CSF LDH in all cases of meningitis (p <0.001). they also reported higher LDH activity in patients who die^[7]. LDH and glutamine in CSF may not be useful in differentiating viral from other meningitis but it may act as a corroborative evidence of meningitis.

Levels of lactic acid in the CSF (determined by either gas chromatography or enzymatic analysis) are also elevated in both bacterial and fungal meningitis (above 35mg/dL) and may be helpful in distinguishing these disorders from viral meningitides, in which lactic acid levels remain normal^[8]. CSF LDH value will not be altered with a short period of antibiotic therapy. it needs complete eradication of microorganisms. This is prognostically very significant. Enzymatic study (CSF LDH) is a better sensitive parameter in diagnosis of various types of meningitis when all the above rapid methods fail^[9].

Materials and Methods

The main aims of the study were

- 1) Role of CSF Lactate dehydrogenase (LDH) to differentiate between viral and purulent meningitis.

- 2) Role of CSF LDH in partially treated meningitis.
- 3) Role of CSF LDH in tuberculous meningitis.
- 4) Early rise in CSF LDH in viral meningitis, is it a predictor of meningoencephalitis

It was a hospital based cross sectional study. All patients with recorded clinical and biochemical evidence of meningitis(viral, bacterial, or tuberculous), getting admitted in the Department of Medicine in a tertiary care centre in South Kerala during the period of April 2012 -2013 were included in the study.

Inclusion Criteria

1. All patients admitted with the clinical triad of fever, headache and neck rigidity with other clinical and biochemical evidence of meningitis (tuberculous, bacterial, viral).

Exclusion Criteria

1. Patients with evidence of acute inflammatory demyelinating polyneuropathy, acute disseminated encephalitis or other conditions causing meningeal inflammation like chemical or carcinomatous or chronic meningitis which produce a false elevation in CSF LDH.

2. Hemorrhagic lumbar puncture-causes elevated CSF LDH due to haemolysis.
3. Other organ dysfunction that will alter the serum LDH assay like severe hepatitis, haemolysis, or acute renal failure.
4. Patients with diabetes to avoid variation in sugar value.

After getting informed consent from Patients after applying inclusion and exclusion criteria, those fulfilling all the inclusion criteria were subjected to detailed evaluation. Lumbar puncture (for CSF collection and analysis of CSF) will be done.

According to the criteria patients were divided into four groups.

1. Viral Meningitis
2. Bacterial Meningitis
3. Tuberculous Meningitis
4. Partially Treated Meningitis

CSF LDH was measured and looked for any correlation with the diagnosis.

Observations

Total of 180 patients were enrolled based on the inclusion criteria.

Out of these 180, 111 were males and 69 were females.

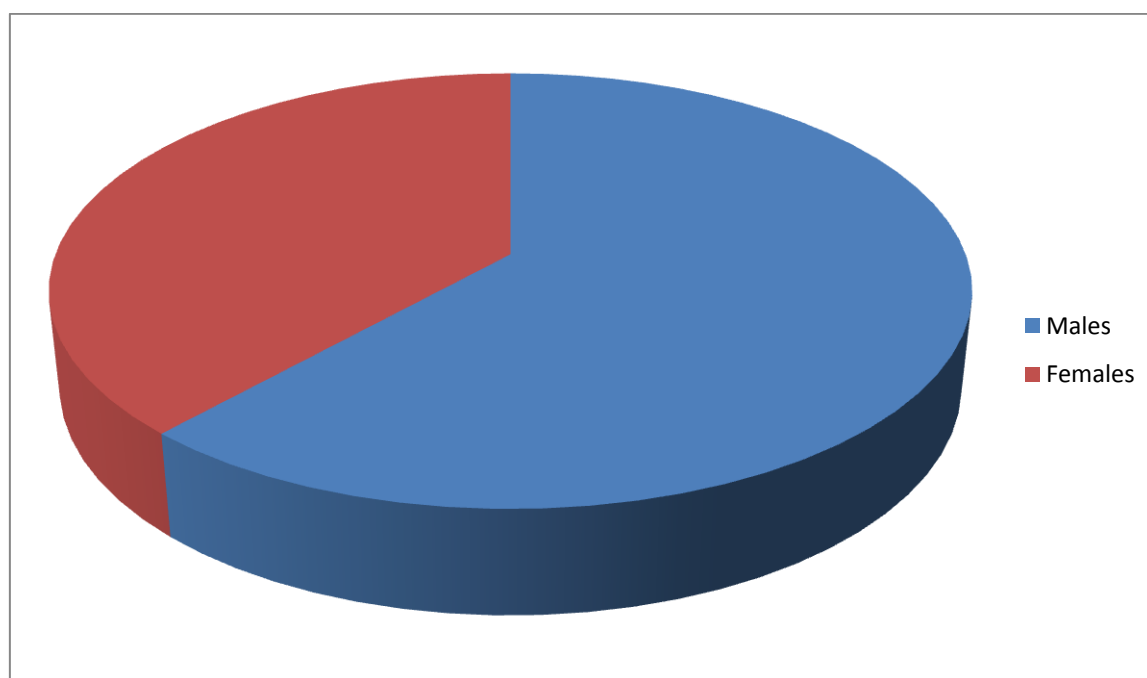


Figure 1: Sex distribution of the subjects.

Most of the patients belonged to the age group of 31- 40 years.

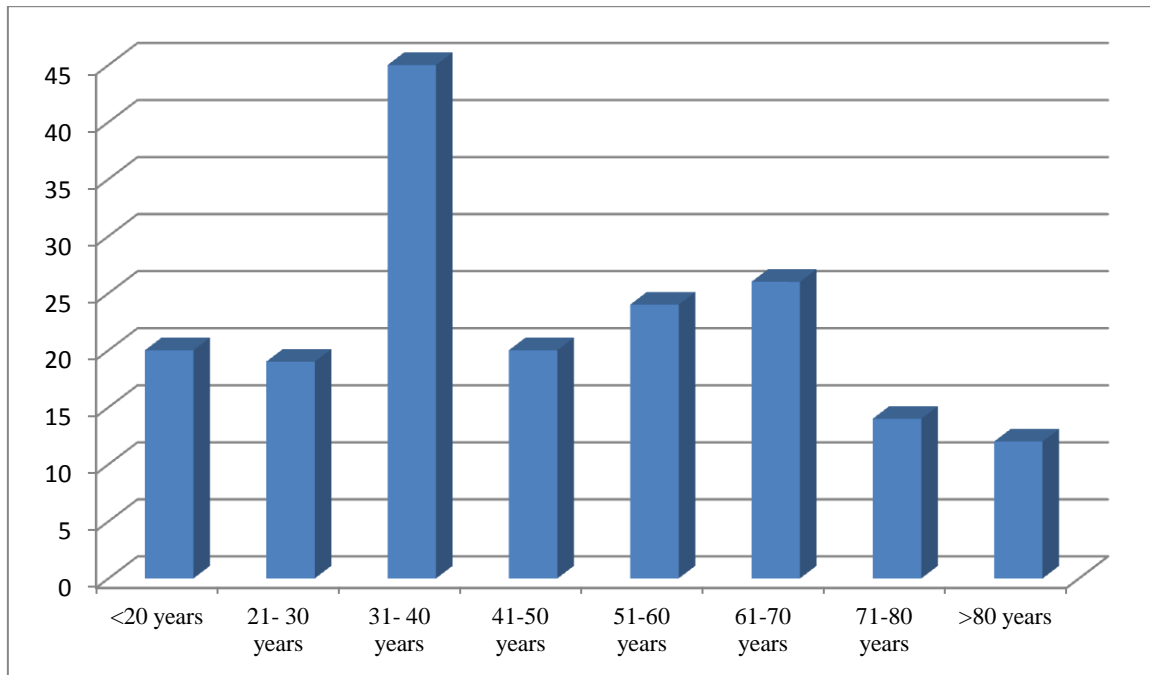


Figure 2: Age distribution of the subjects.

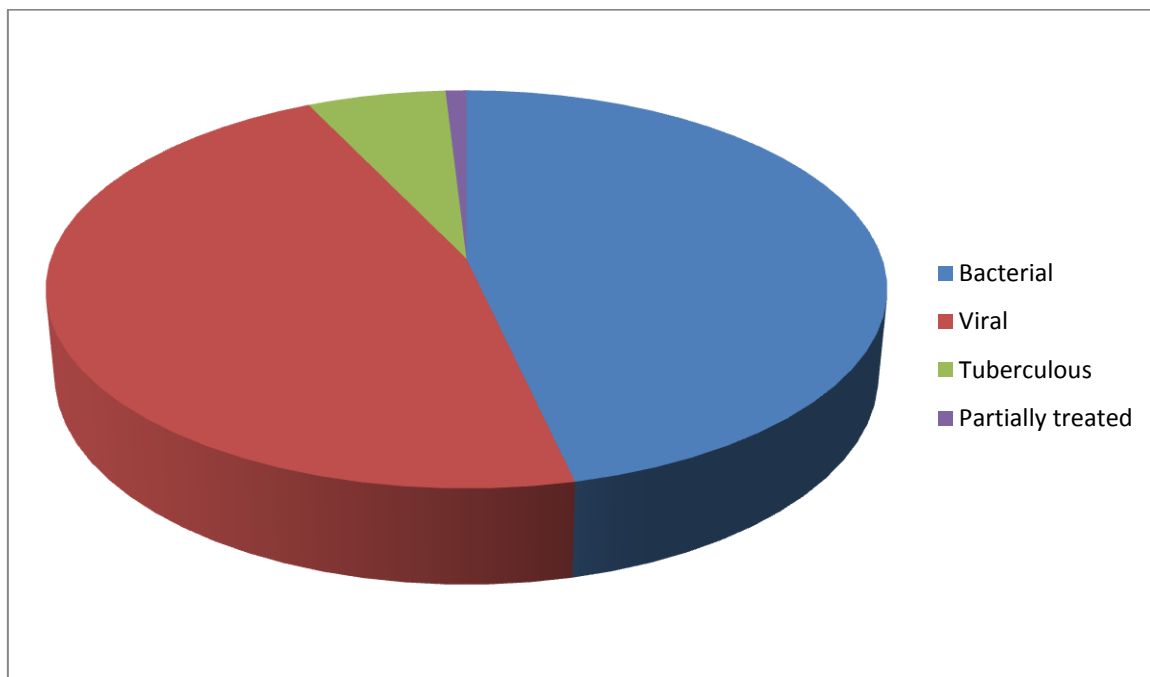


Figure 3: Types of meningitis among the study subjects.

CSF profile of Bacterial Meningitis:

CSF Cell count:

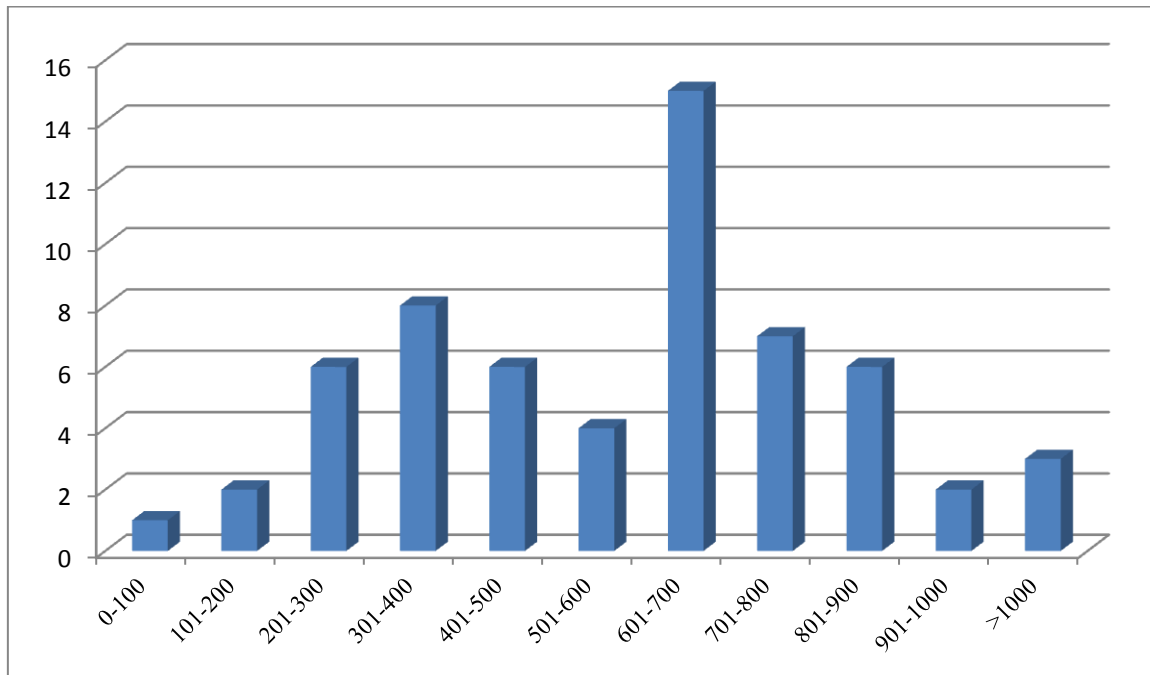


Figure 4: CSF total count in cases of Bacterial meningitis

Mean CSF cell count was 613 cells/mm³.

CSF sugar:

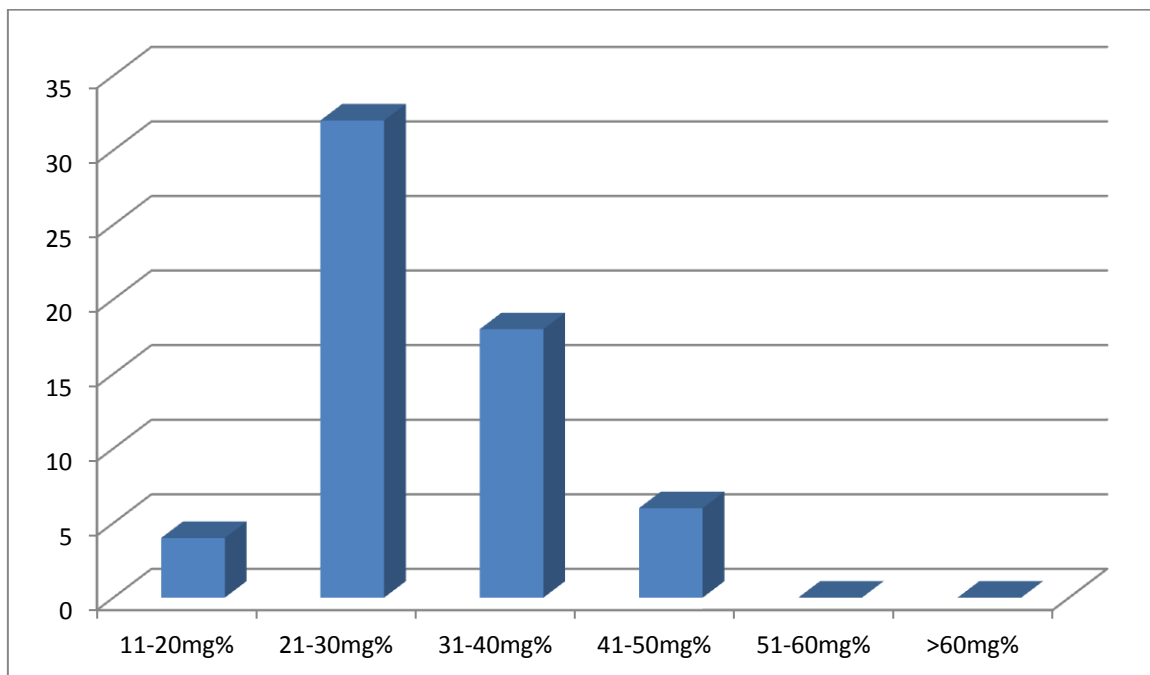


Figure 5: CSF sugar in bacterial meningitis

CSF RBS was very low in bacterial meningitis.

CSF protein

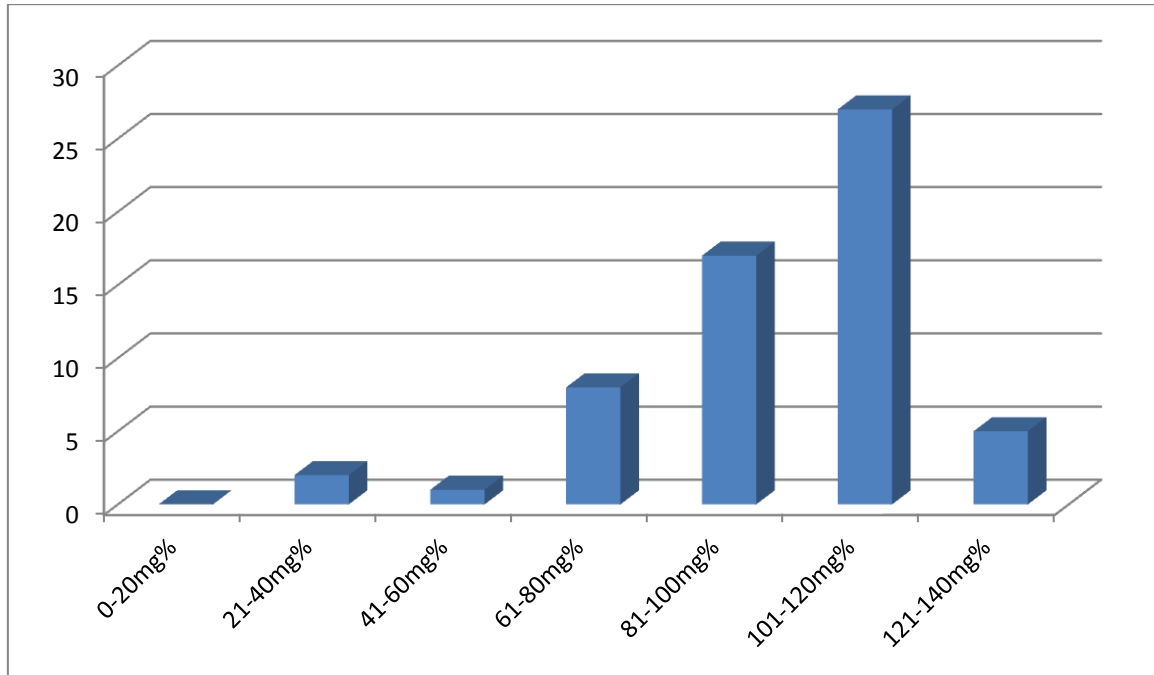


Figure 6: CSF Protein in Bacterial meningitis.

CSF protein was elevated in bacterial meningitis, mean value 102mg/dL

CSF ADA

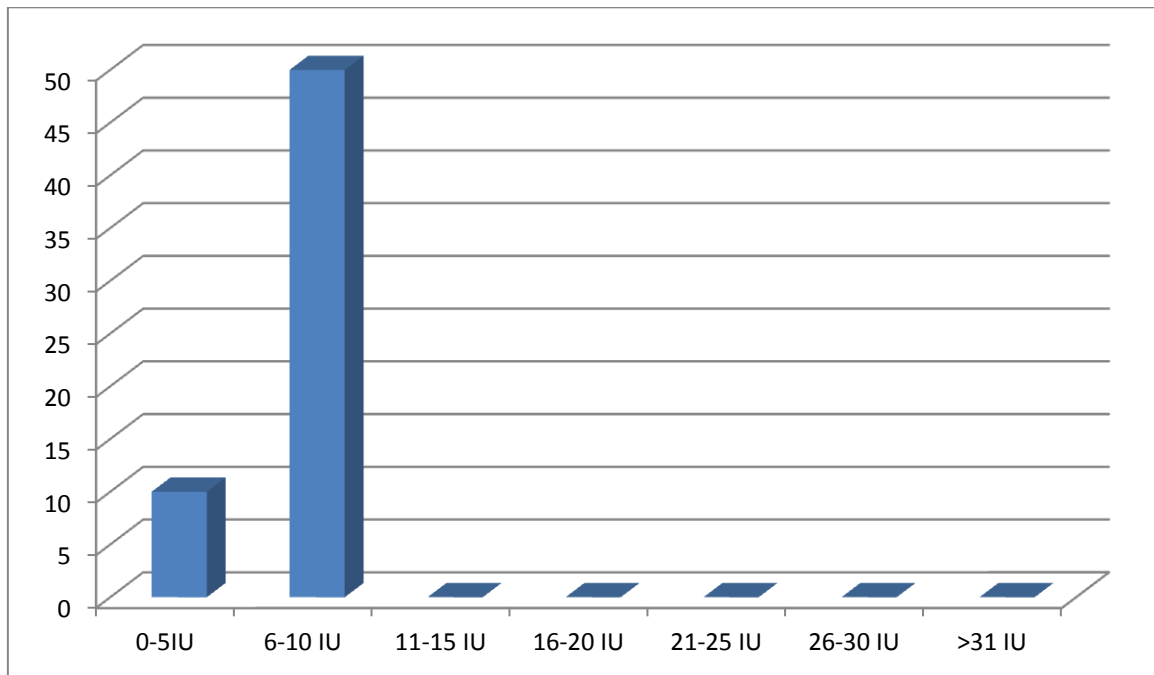


Figure 7: CSF ADA in Bacterial meningitis.

Mean ADA in bacterial meningitis was 6.4 u/l. In all these patients the value was <10u/L

CSF LDH

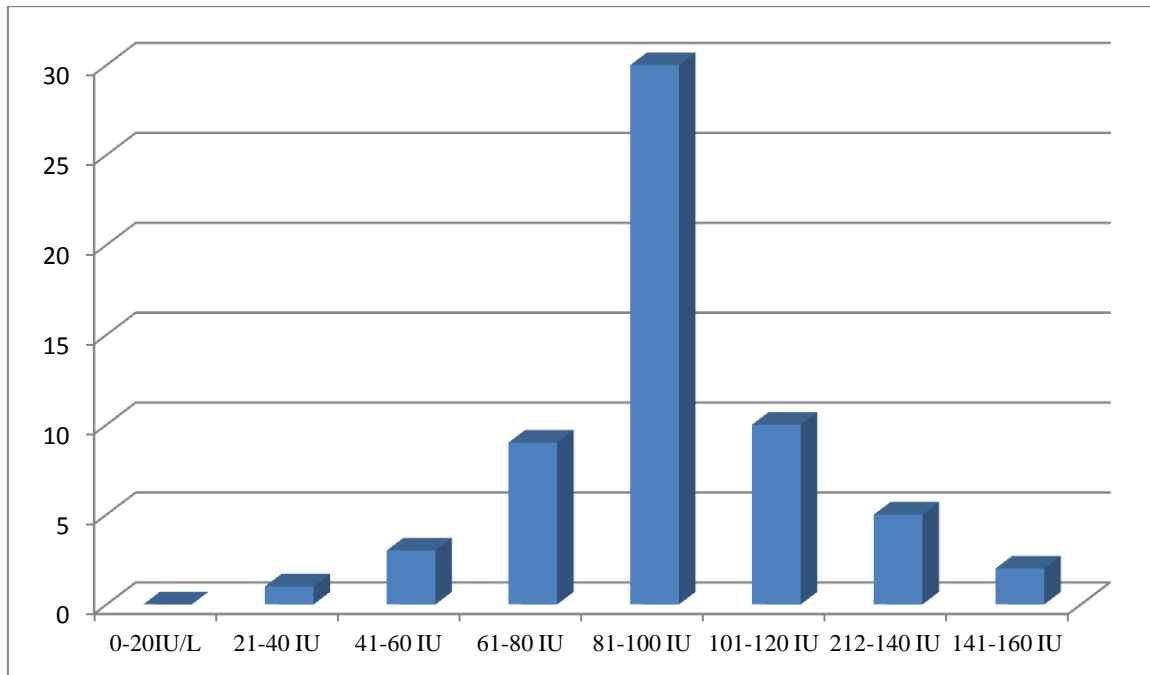


Figure 8: CSF LDH in bacterial meningitis

CSF LDH was normal in half of the patients with bacterial meningitis. Mean value is 94.1IU/L.

CSF profile of Viral Meningitis:

CSF Total Count

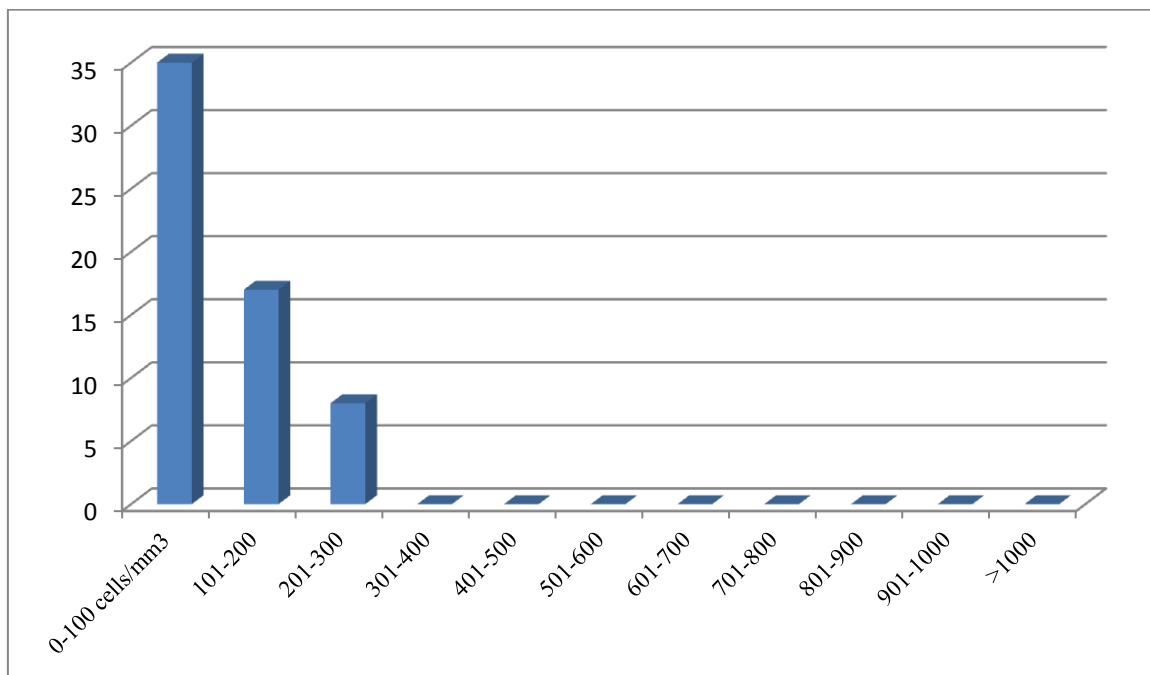


Figure 9: CSF cell count in viral meningitis.

CSF differential count was lymphocyte predominant. Mean lymphocyte is 95.5%. Mean CSF count is 101 cells/mm³

CSF Sugar

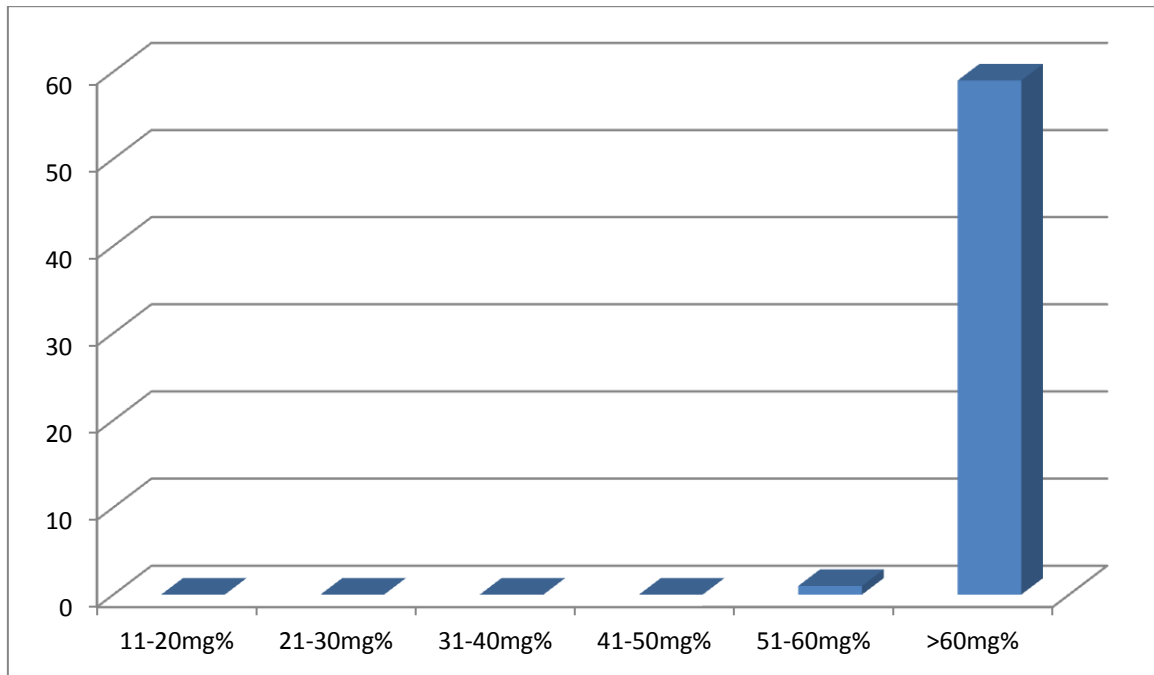


Figure 10: CSF sugar in viral meningitis.

Mean CSF RBS in viral meningitis was 68.6%.

CSF Protein:

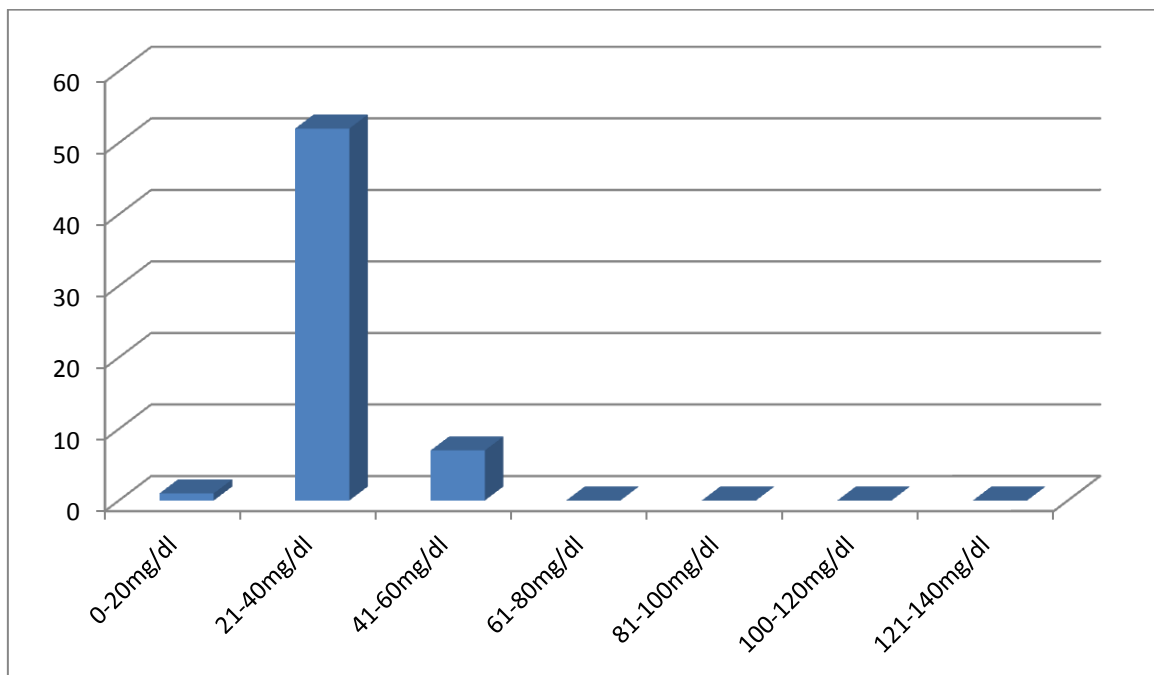


Figure 11: CSF protein in viral meningitis.

CSF protein in viral meningitis was normal. Mean CSF protein was 33.6%

CSF ADA

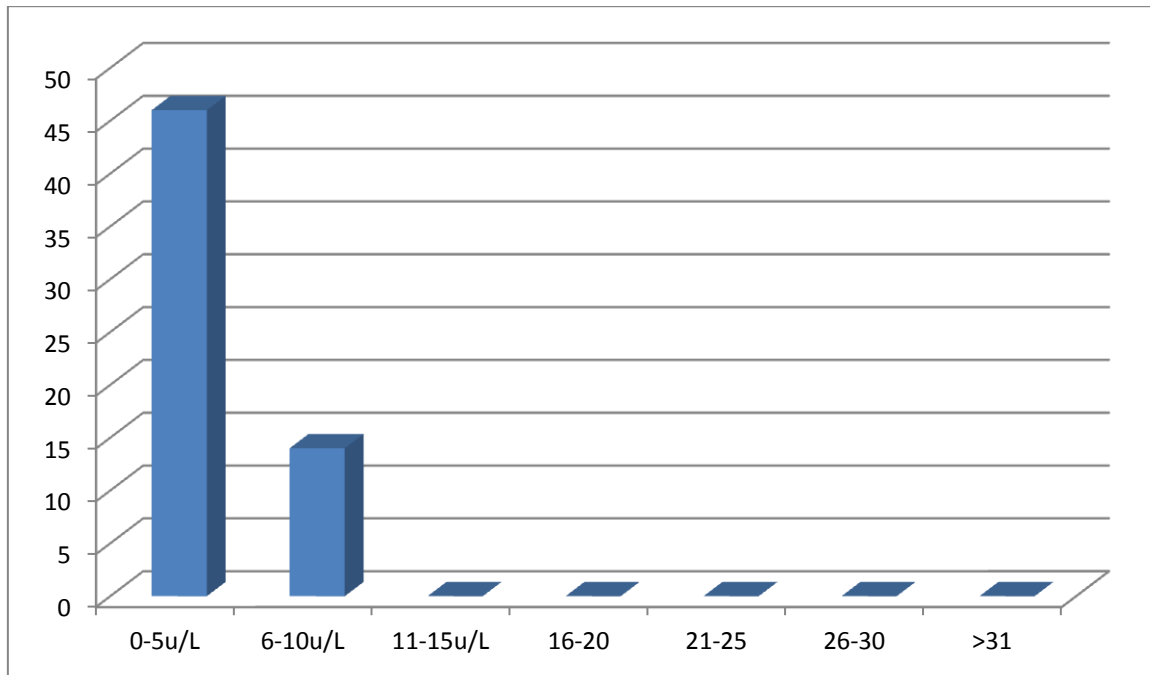


Figure 12: CSF ADA in viral meningitis.

Mean ADA was 4.8U/l

CSF LDH

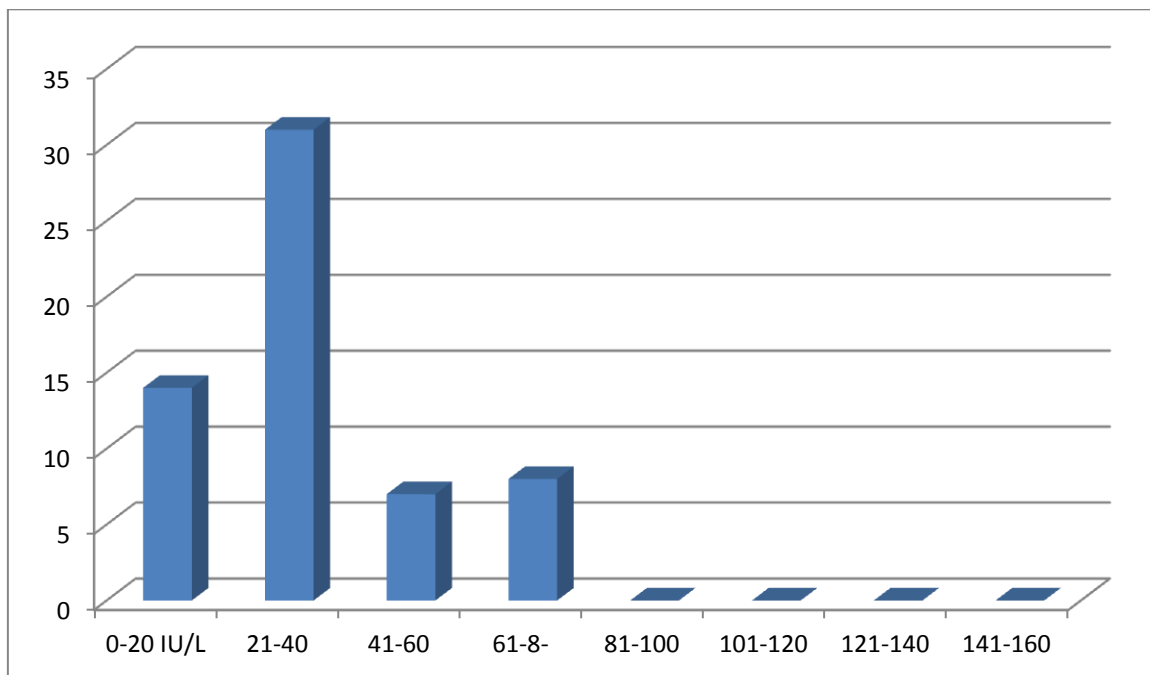


Figure 13: CSF LDH in Viral meningitis.

Mean LDH was 30.2 IU/L. LDH was in the high normal range.

CSF profile of Tuberculous Meningitis:

CSF Total count:

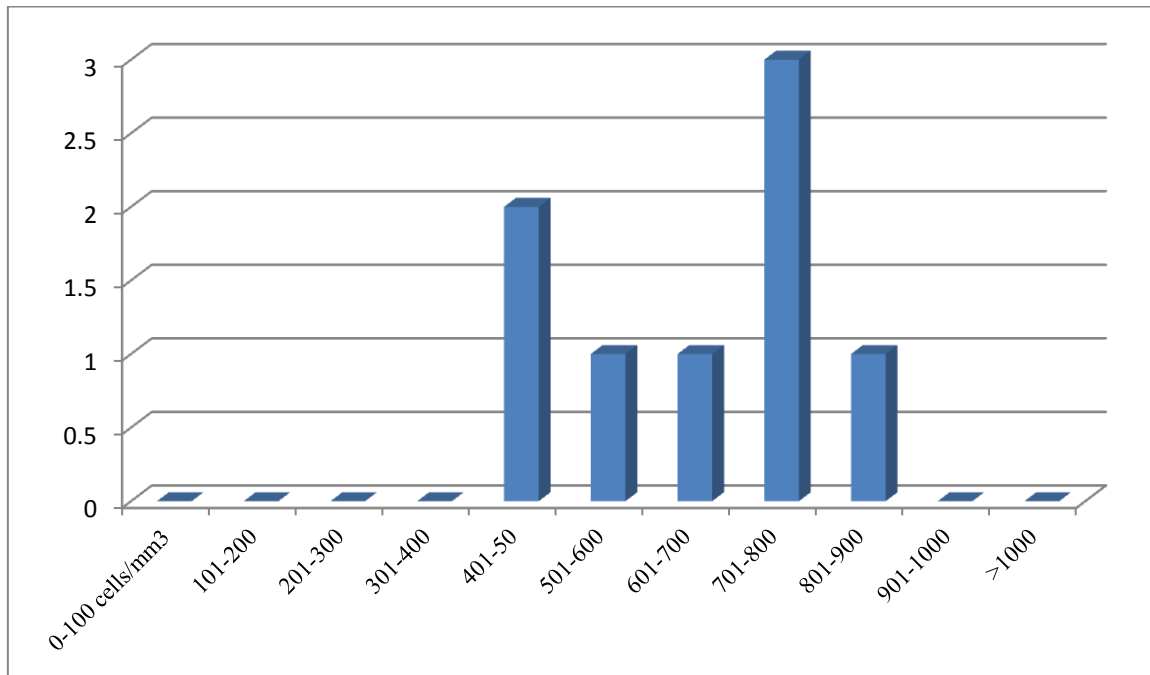


Figure 14: CSF Total Count in tuberculous meningitis.

All patients had lymphocyte predominance. The mean cell count was 656.8.

CSF sugar:

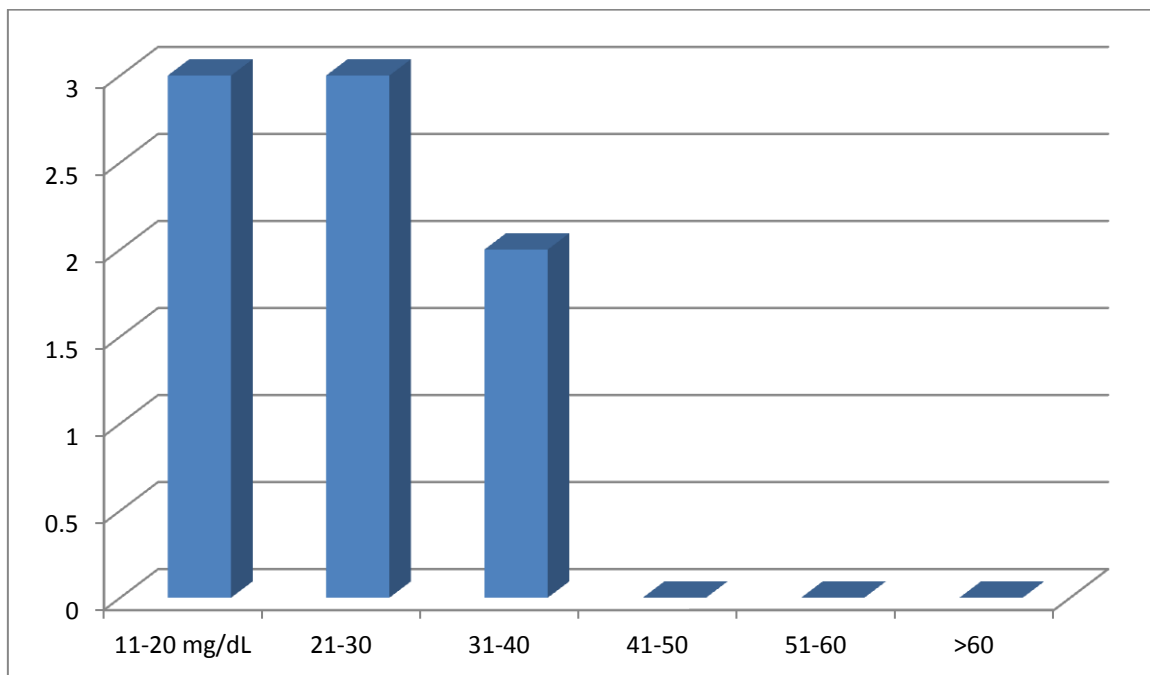


Figure 15 : CSF RBS in Tuberculous Meningitis.

Mean CSF RBS was 23.5mg/dL.

CSF protein

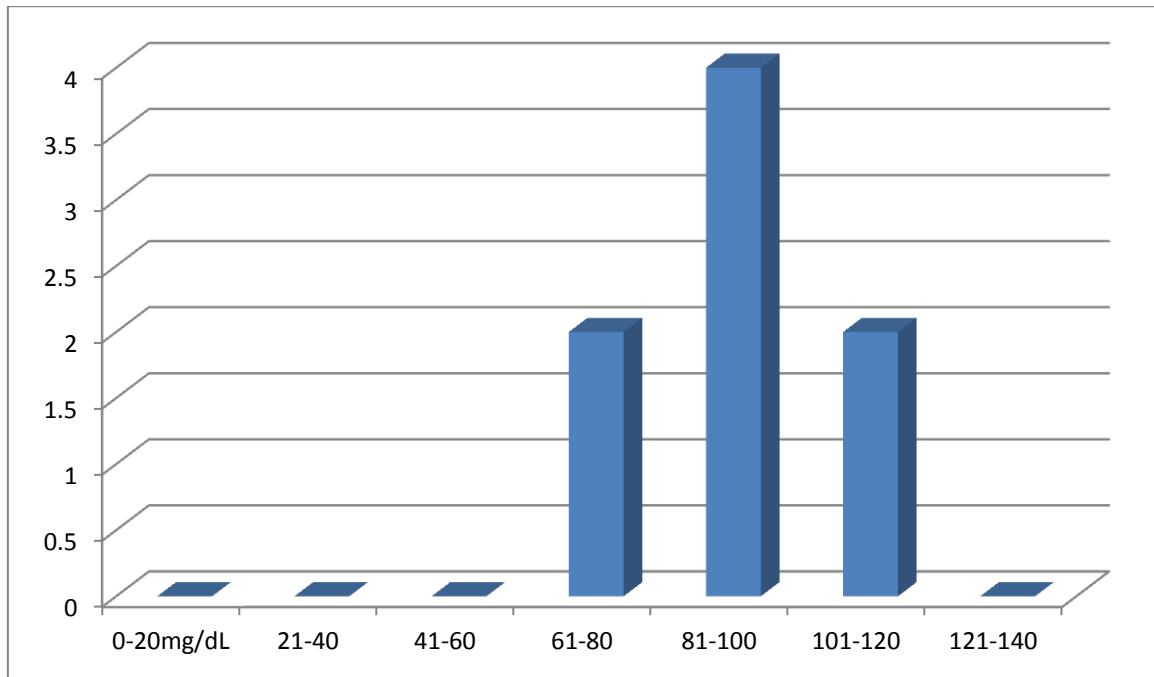


Figure 16: CSF protein in Tuberculous meningitis.

Mean value was 89.4 mg/dL

CSF ADA

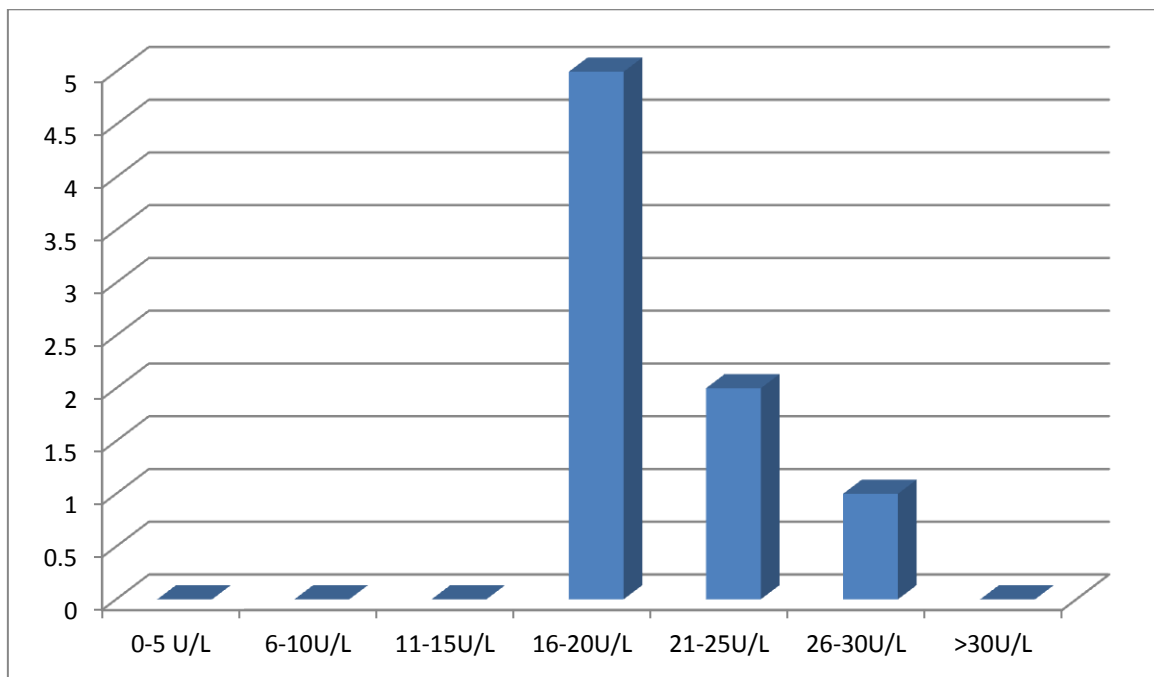


Figure 17: CSF ADA in Tuberculous Meningitis.

Mean ADA value was 20 U/L

CSF LDH

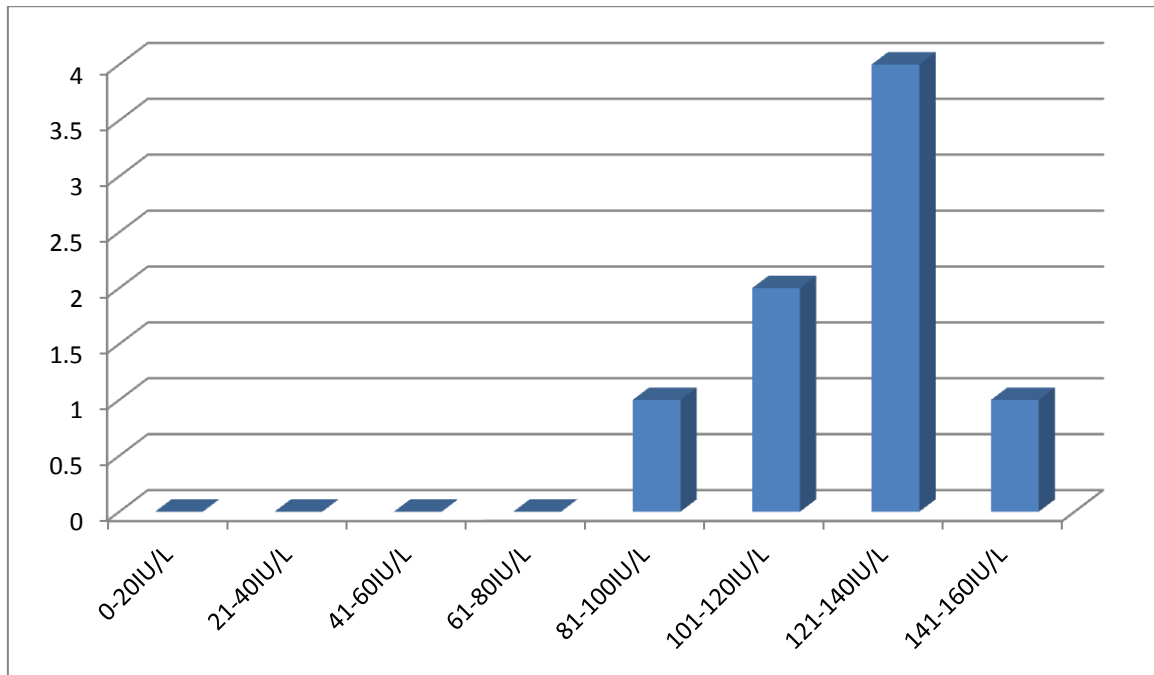


Figure 18: CSF LDH in Tuberculous meningitis.

CSF profile of partially treated meningitis:

CSF Sugar

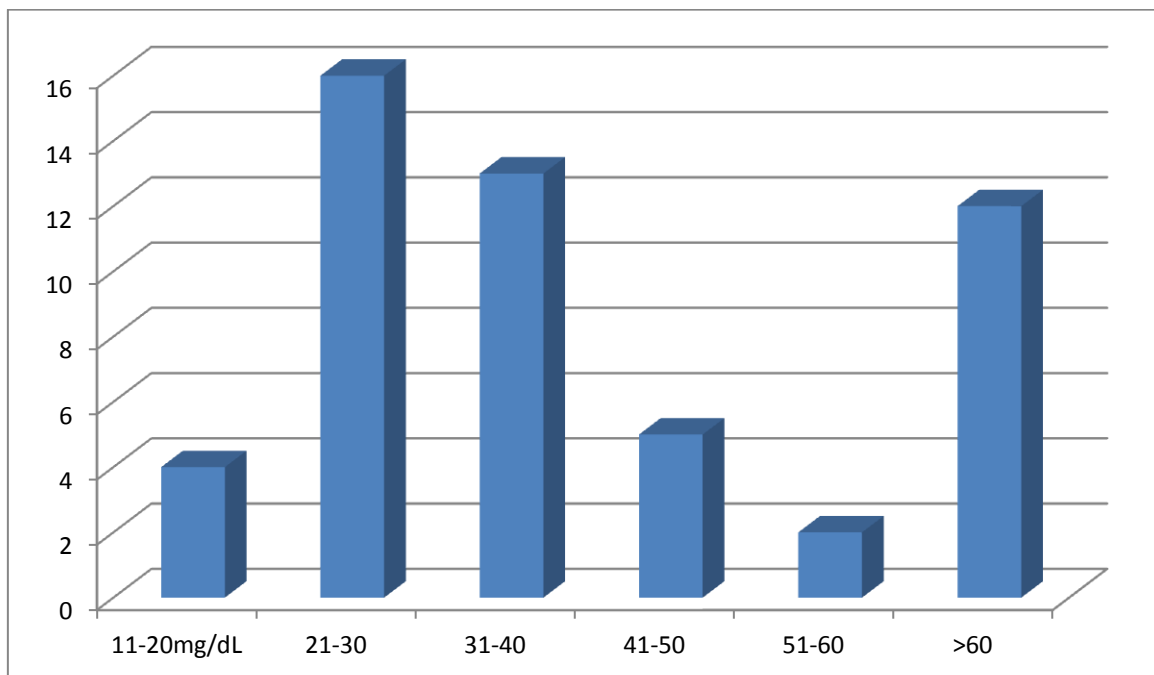


Figure 19: CSF sugar in Partially treated meningitis

CSF Protein:

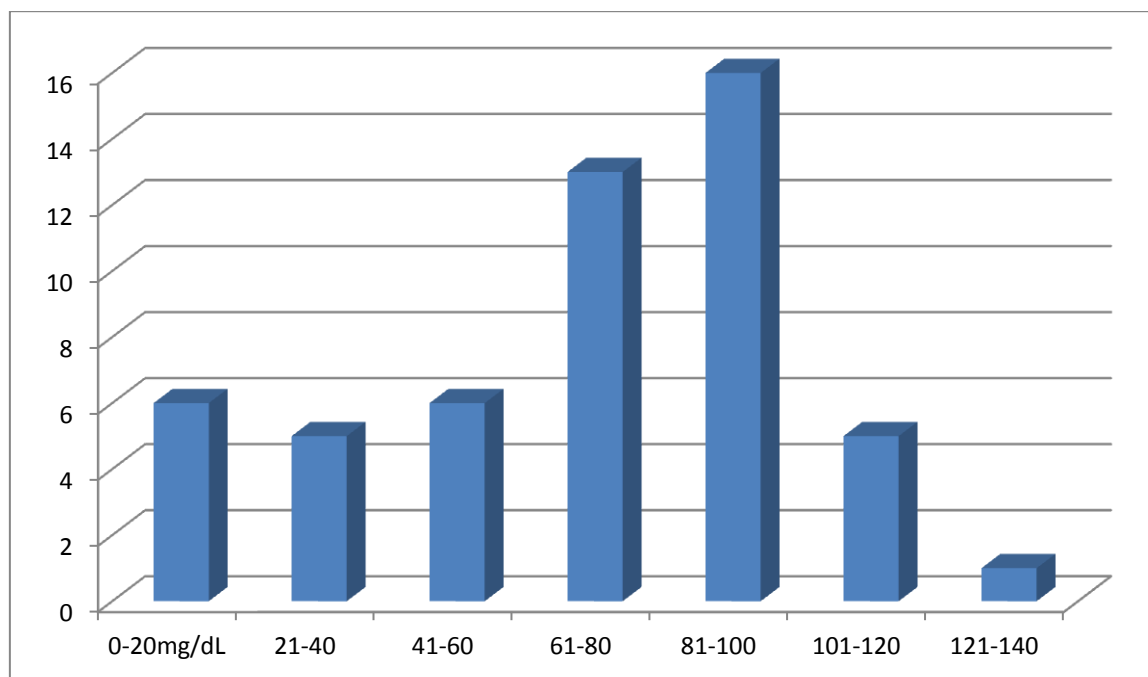


Figure 20: CSF protein in Partially treated meningitis.

CSF ADA:

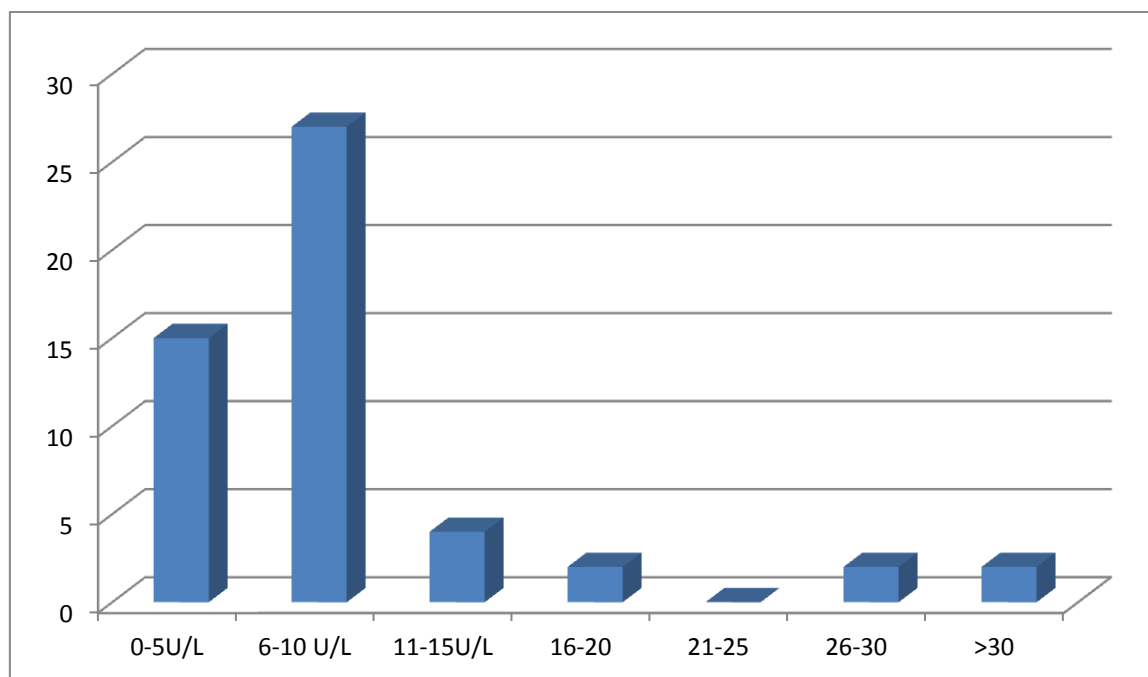


Figure 21: CSF ADA in partially treated meningitis.

CSF LDH

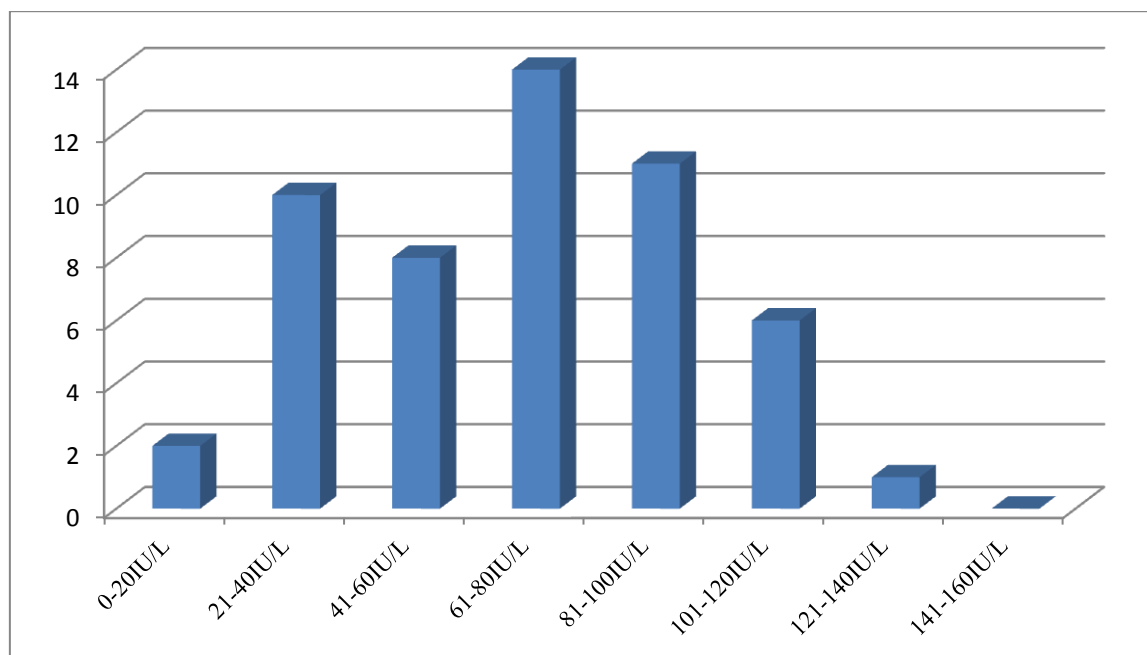


Figure 22: CSF LDH in Partially treated meningitis.

Among the viral meningitis group 25% were Japanese Encephalitis.

CSF LDH in JE positive viral meningitis was significantly high when compared to JE negative meningitis. (p value <0.001).

Discussion

180 patients were included in this study, 111 Male and 69 female. Most of the patients were younger & belonged to the age group of 31-40 years in bacterial and viral meningitis group, whereas in tuberculous meningitis maximum number of patients were elderly, in the age group 61-70 years. Among the total 180 patients, 33% were categorized as bacterial, 33% as viral, 4.44% as tuberculous and 28.88% as partially treated meningitis according to the study definitions.

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The average CSF LDH value was 94.1 IU/L in bacterial meningitis group, 30.2 IU/L in viral meningitis group & 119.9 IU/L in tuberculous meningitis group. Schuchat A et al mentioned that high CSF LDH is associated with bacterial meningitis, whereas high LDH value in viral meningitis indicates an encephalitis. In contrast we observed that LDH is significantly elevated in bacterial and tuberculous meningitis and only mildly elevated in viral meningitis & hence CSF LDH can be used to differentiate bacterial from viral meningitis.

Out of the 72 patients who had viral meningitis in our study, 18 (25%) had JE/WEST NILE virus positivity. This high frequency of encephalitis is not observed in other studies, which indicates a high frequency of JE in our part of the world. In

those tested positive for JE, the CSF LDH was significantly high.

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Conclusions

- 1) CSF LDH was significantly elevated in Tuberculous meningitis and bacterial meningitis.
- 2) In viral meningitis, CSF LDH showed only a mild elevation.
- 3) Viral meningitis with increased CSF LDH were positive for JE. Hence in Viral meningitis with high LDH should raise suspicion of encephalitis.

Limitations

- 1) In partially treated group, prior treatment documents were not available.
- 2) CSF LDH isoenzyme was not done.

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