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**Original research article**

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**A CASE CONTROL STUDY FOR DIAGNOSTIC SIGNIFICANCE OF CEREBROSPINAL FLUID (CSF) & SERUM LACTATE DEHYDROGENASE (LDH) AND TOTAL CREATINE KINASE (CK) LEVEL IN MENINGITIS.**

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**Abstract:**

**Introduction :** Meningitis is the most common sequelae to microbial invasion of the CNS. Neurological sequelae are serious and rather common among survivors. Meningitis disturbs the blood brain barrier (BBB) and is expected to cause rise in enzymatic activity. For that reason some enzymes are used for the diagnosis in cases of meningitis.

Since prompt and precise etiological diagnosis remains a challenge and often a thorough cerebrospinal fluid examination may not give a precise diagnosis, a quick and reliable test is required for rapid bedside diagnosis. This study was planned to find out the role of diagnostic significance of CSF & serum LDH & Total CK levels in meningitis.

**AIM :** Diagnostic significance of CSF & serum LDH & Total CK levels in meningitis.

**Objectives :** To measure and estimate the level of Cerebrospinal fluid (CSF) & Serum LDH & Total CK in pyogenic meningitis and tuberculous meningitis. **Material and methods :** This Case control study was carried out at Clinical Chemistry Laboratory, Medical College Baroda and Sir Sayajirao General (S.S.G.) Hospital, Vadodara. Approval of Institute's Scientific Review Committee and Ethical Clearance were obtained from the Institutional Ethics Committee for Human Research, Medical College Baroda and S.S.G. Hospital, Vadodara. 30 diagnosed patients of Meningitis and 30 patients who were operated under spinal anesthesia (Patient who met with an accident without any major illness) between the age group of 18 to 60 years were enrolled in my study. Detailed history and record findings of examination were done as per proforma and data were recorded in proforma sheet. For laboratory investigation, 5 ml blood sample by venipuncture was taken in plain vacutainer and 1 ml CSF sample by lumbar puncture were collected in plain vacutainer. Blood and CSF samples were processed in clinical chemistry laboratory and tests were performed. **Results:** As defined in materials and methods, the study group consisted of 30 cases in group I (Clinically diagnosed cases of meningitis) and 30 age & sex matched controls in group II (Patients undergoing surgery under spinal anesthesia from Ortho and Surgery i.e patients with accidents were taken as Control). Statistical analyses were done by using unpaired Student's t-test to find out significance of difference between two groups. The Mean  $\pm$  SD of S. LDH, CSF LDH, S. Total CK, CSF Total CK in group I and group II, were  $232.10 \pm 27.79$  (161.0 – 280.1) IU/L,  $248.68 \pm 44.48$  (148.0 – 320.8) IU/L,  $201.34 \pm 19.84$  (167.8 – 236.7) IU/L,  $31.80 \pm 9.44$  (18.2 – 56.0) IU/L,  $140.01 \pm 13.92$  (115.2 – 167.0) IU/L,  $35.73 \pm 10.40$  (18.9 – 66.9) IU/L,  $115.87 \pm 52.52$  (29.0 – 198.0) IU/L,  $7.89 \pm 3.61$  (3.9 -17.0) IU/L, respectively. There was statically significant difference found between these two groups. ( $P < 0.0001$ ). The Mean  $\pm$  SD of S. LDH, CSF LDH, S. Total CK, CSF Total CK in Pyogenic meningitis and Tuberculous meningitis in group I were  $233.45 \pm 30.43$  (161 – 280.1) IU/L,  $251.36 \pm 46.66$  (148.0 – 320.8) IU/L,  $202.93 \pm 19.70$  (167.8 – 230.0) IU/L,  $33.76 \pm 9.80$  (18.2 – 56.0) IU/L,  $227.68 \pm 17.54$  (198.5 – 244.0) IU/L,  $239.88 \pm 38.20$  (180.0 – 286.0) IU/L,  $196.10 \pm 20.93$  (175.9 – 236.7) IU/L,  $25.37 \pm 3.92$  (19.8 – 30.4) IU/L, respectively. There was statistically significant difference was not found in between Pyogenic meningitis and Tuberculous meningitis. ( $P > 0.05$ ). **Conclusion :** This study was carried out to measure the levels of Lactate dehydrogenase (LDH) and Total Creatine Kinase (CK) in serum and Cerebrospinal fluid (CSF) in patients with meningitis. LDH and Total CK in serum and CSF may not be useful in differentiating types of meningitis but it may act as a corroborative evidence of meningitis. So along with routine CSF parameters CSF LDH and Total CK level may add in the diagnosis of meningitis

**Key words: CSF Meningitis , LDH , Total CK,**

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### **Introduction:**

Infectious disease remains a major cause of death and disability for millions of people around the world. Acute Infections of the nervous system are among the most important problems in medicine. Early recognition, efficient decision making and rapid intervention of therapy can be lifesaving.

Meningitis is the most common sequelae to microbial invasion of the CNS. Neurological sequelae are serious and rather common among survivors<sup>1</sup>. Meningitis disturbs the blood brain barrier (BBB) and is expected to cause rise in enzymatic activity. For that reason some enzymes are used for the diagnosis in cases of meningitis<sup>2</sup>. It is one of the dreadful infectious diseases and more common in developing countries than developed countries. So, early diagnosis and treatment remains a challenge to the clinician<sup>1</sup>.

Many enzymes are present in abundance in the nervous system. Besides routine cerebrospinal fluid analysis (protein, sugar, and cell count), other additional tests like latex agglutination, counter-immuno electrophoresis, radio – immunoassay<sup>1</sup> and measurement of CSF lactate have been utilised with varying degrees of success for the diagnosis of bacterial meningitis. The limitation of these options is however considerable as some require specific anti sera and some are too slow and laborious procedures. More over no single test mentioned above could achieve a high degree of sensitivity and specificity required for a definitive diagnosis<sup>1</sup>.

The culture of CSF which gives a definite diagnosis and most importantly the antibiotic sensitivity pattern of the infecting organism, takes longer time. More over CSF culture for pyogenic organisms are positive only in 30%-60%<sup>1</sup>.

Since prompt and precise etiological diagnosis remains a challenge and often a thorough cerebrospinal fluid examination may not give a precise diagnosis, a quick and reliable test is required for rapid bedside diagnosis. Many enzymes are known to be present in abundance in the nervous system. Meningitis disturbs the blood brain barrier (BBB) and is expected to cause rise in enzymatic activity<sup>1</sup>.

This study is planned to find out the role of diagnostic significance of CSF & serum LDH & Total CK levels in meningitis.

### **Aims and Objectives :**

AIM : Diagnostic significance of CSF & serum LDH & Total CK levels in meningitis.

**OBJECTIVES :**

- 1.To measure the level of Cerebrospinal fluid (CSF) LDH & Total CK in pyogenic meningitis and tuberculous meningitis.
2. To estimate serum LDH & Total CK levels in pyogenic meningitis and tuberculous meningitis.
3. To estimate the levels of LDH & Total CK in serum & Cerebrospinal fluid (CSF) in normal subjects.(CSF obtained from surgical and orthopedic OT undergoing operation under spinal anesthesia specially patient who came with accidental injury)
4. To compare LDH & Total CK enzymes levels in serum & CSF of patients of meningitis with age and sex matched controls.

**Materials and Methods:**

This Case control study was carried out at Clinical Chemistry Laboratory, Medical College Baroda and Sir Sayajirao General (S.S.G.) Hospital, Vadodara. Approval of Institute's Scientific Review Committee and Ethical Clearance were obtained from the Institutional Ethics Committee for Human Research, Medical College Baroda and S.S.G. Hospital, Vadodara. 30 diagnosed patients of Meningitis and 30 patients who were operated under spinal anesthesia (Patient who met with an accident without any major illness) between the age group of 18 to 60 years were enrolled in my study.

**Inclusion Criteria:**

**Group 1:** Clinically diagnosed cases of meningitis.(Cases )

**Group 2:** Age & sex matched controls (Patients undergoing surgery under spinal anesthesia from Ortho and Surgery i.e patients with minor accidents were taken as Control)

**Exclusion Criteria:**

- Below the 20 years and above the 60 years.
- Diagnosed cases of liver and kidney disease.
- Refusal of patients to enroll into the study

**METHOD OF DATA COLLECTION :**

Detailed history and record findings of examination were done as per proforma and data were recorded in proforma sheet. For laboratory investigation ,5 ml blood sample by venipuncture was taken in plain vacutainer and 1 ml CSF sample by lumbar puncture were collected in plain vacutainer. Blood and CSF samples were processed in clinical chemistry laboratory and tests were performed .

Methods employed for the investigations were as follow:

1. CSF LDH(U/L) : Kinetic IFCC method

2. CSF Total CK(U/L): Kinetic IFCC method
3. Serum LDH (U/L) : Kinetic IFCC method
4. Serum Total CK(U/L) : Kinetic IFCC method

### Results and Analysis :

As defined in materials and methods, the study group consisted of 30 cases in group I (Clinically diagnosed cases of meningitis) and 30 age & sex matched controls in group II (Patients undergoing surgery under spinal anesthesia from Ortho and Surgery i.e patients with accidents were taken as Control).

Statistical analyses were done by using unpaired Student's t-test to find out significance of difference between two groups.

**Table 1 : Results of S. LDH ,CSF LDH, S. Total CK , CSF Total CK in group I and group II,**

		Group I (Cases)		Group II (Controls)		P value
No. of Patients		30		30		
Sex (M/F)		23(76%)/7(23.33)		22(73%)/8(26.33%)		
Parameter	Reference Range	Mean (range)	SD	Mean (range)	SD	
Serum LDH (IU/L)	114-240	232.1 (161.0-280.1)	27.79	140.01 (115.2-167.0)	13.92	P<0.0001
CSF LDH (IU/L)	<40	248.68 (148.0-320.8)	44.48	35.73 (18.9-66.9)	10.40	P<0.0001
Serum Total CK (IU/L)	M: 25-200 F : 25-170	201.34 (167.8-236.7)	19.84	115.87 (29.0-198.0)	52.52	P<0.0001
CSF Total CK (IU/L)	<18	31.80 (18.2-56.0)	9.44	7.89 (3.9-17.01)	3.61	P<0.0001

Table 1 shows that Mean  $\pm$  SD of S. LDH ,CSF LDH, S. Total CK , CSF Total CK in group I and group II, were  $232.10 \pm 27.79$  (161.0 – 280.1) IU/L,  $248.68 \pm 44.48$  ( 148.0 – 320.8 ) IU/L,  $201.34 \pm 19.84$  (167.8 – 236.7) IU/L,  $31.80 \pm 9.44$  (18.2 – 56.0) IU/L,  $140.01 \pm 13.92$  ( 115.2 – 167.0 ) IU/L,  $35.73 \pm 10.40$  (18.9 – 66.9) IU/L,  $115.87 \pm 52.52$  (29.0 – 198.0) IU/L,  $7.89 \pm 3.61$  (3.9 -17.0) IU/L, respectively. There was statically significant difference found between these two groups. (P < 0.0001)

**TABLE 2 : COMPARISON OF DIFFERENT PARAMETER BETWEEN  
PYOGENIC MENINGITIS AND TUBERCULOUS MENINGITIS IN STUDY GROUPS**

		Pyogenic Meningitis (n=23)		Tuberculous Meningitis (n=7)		P value
Parameter	Reference Range	Mean (range)	SD	Mean (range)	SD	
Serum LDH (IU/L)	114-240	233.45 (161.0-280.1)	30.43	227.68 (198.5-244.0)	17.54	P=0.6390
CSF LDH (IU/L)	<40	251.36 (148.0-320.8)	46.66	239.88 (180.0-286.0)	38.20	P=0.5592
Serum Total CK (IU/L)	M: 25-200 F : 25-170	202.93 (167.8-236.7)	19.70	196.10 (175.9-236.7)	20.93	P0.5371

<b>CSF Total CK (IU/L)</b>	<b>&lt;18</b>	33.76 (18.2-56.0)	9.80	25.37 (19.8-30.4)	3.92	P=0.4343
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Table : 2 shows the Mean  $\pm$  SD of S. LDH , CSF LDH, S. Total CK , CSF Total CK in Pyogenic meningitis and Tuberculous meningitis in group I were  $233.45 \pm 30.43$  (161 – 280.1) IU/L,  $251.36 \pm 46.66$  (148.0 – 320.8 ) IU/L,  $202.93 \pm 19.70$  ( 167.8 – 230.0) IU/L,  $33.76 \pm 9.80$  ( 18.2 – 56.0 ) IU/L,  $227.68 \pm 17.54$  ( 198.5 – 244.0 ) IU/L,  $239.88 \pm 38.20$  (180.0 – 286.0 ) IU/L,  $196.10 \pm 20.93$  (175.9 – 236.7 ) IU/L,  $25.37 \pm 3.92$  (19.8 – 30.4) IU/L, respectively. There was statistically significant difference was not found in between Pyogenic meningitis and Tuberculous meningitis. (P > 0.05)

**FIGURE : 1 – COMPARISION OF SERUM LDH IN GROUP I (CASES) & GROUP II (CONTROL)**

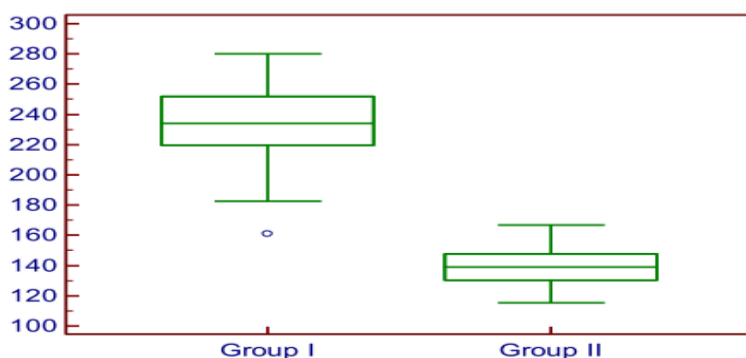


Table 1 and Fig:1 shows that Mean  $\pm$  SD of serum LDH in group I (cases) and group II (control) were  $232.1 \pm 27.79$  IU/L and  $140.01 \pm 13.92$  IU/L, respectively. There was statistically significance difference found in level of serum LDH between two groups. (P < 0.0001).

**FIGURE:2 - COMPARISION OF CSF LDH IN GROUP I (CASES) & GROUP II (CONTROL)**

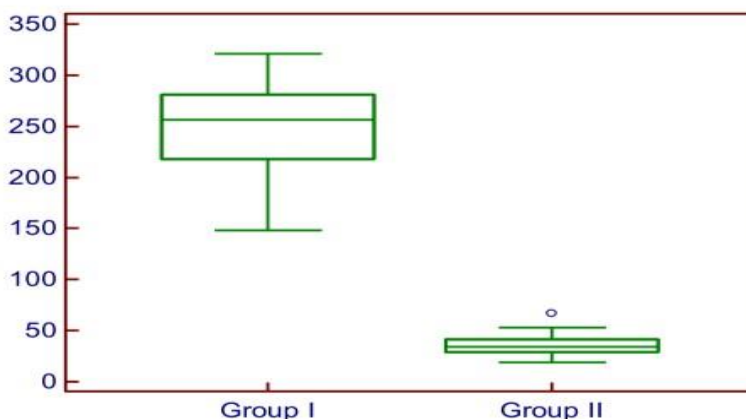


Table 1 and Fig:2 show that Mean  $\pm$  SD of CSF LDH in group I (cases) and group II (control) were  $248.68 \pm 44.48$  IU/L,  $35.73 \pm 10.4$  IU/L, respectively. There was statistically significance difference found in level of CSF LDH between two groups. ( $P < 0.0001$ ).

**FIGURE 3: – COMPARISION OF SERUM TOTAL CK IN GROUP I (CASES) & GROUP II (CONTROL)**

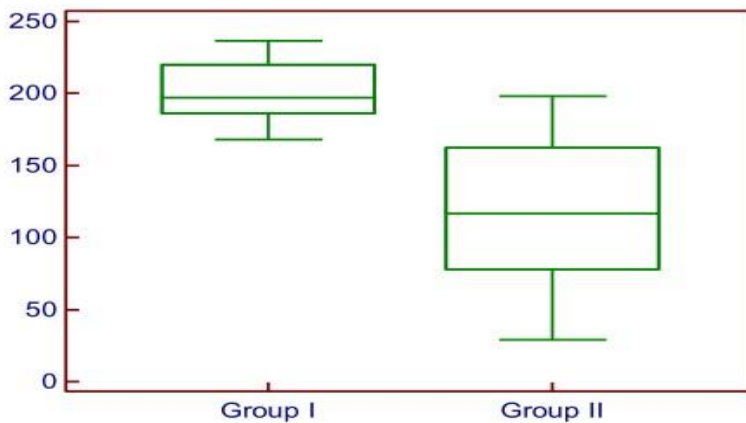


Table 1 and Fig:3 show that Mean  $\pm$  SD of serum total CK in group I (cases) and group II (control) were  $201.34 \pm 19.84$  IU/L,  $115.87 \pm 52.52$  IU/L, respectively. There was statistically significance difference found in level of serum Total CK between two groups. ( $P < 0.0001$ ).

**FIGURE 4: – COMPARISION OF CSF TOTAL CK IN GROUP I (CASES) & GROUP II (CONTROL)**



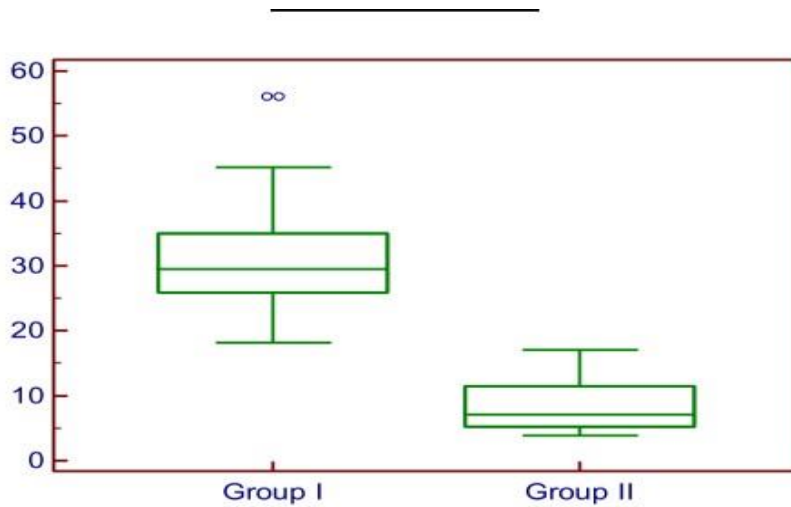


Table 1 and Fig:4 shows that Mean  $\pm$  SD of CSF total CK in group I and group II, were  $31.8 \pm 9.44$  IU/L,  $7.89 \pm 3.61$  IU/L, respectively. There was statistically significance difference found in level of CSF Total CK between two groups. ( $P < 0.0001$ ).

**FIGURE 5: – COMPARISION OF CSF, LDH IN PYOGENIC MENINGITIS & TUBERCULOUS MENINGITIS**

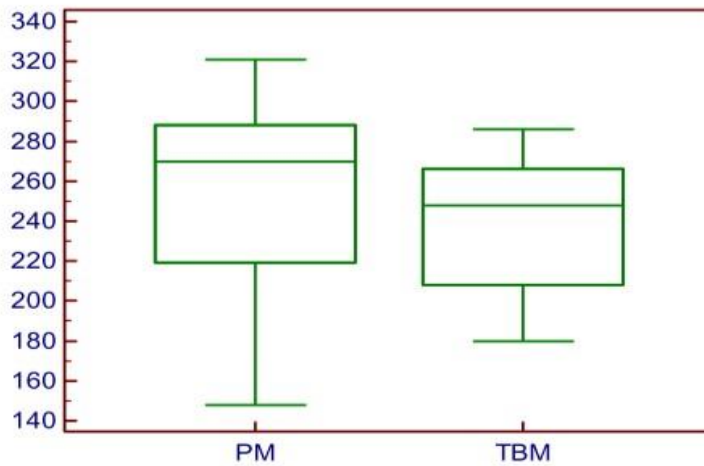


Table 2 and Fig:5 shows that Mean  $\pm$  SD of CSF total CK in Pyogenic meningitis (PM) & Tuberculous meningitis (TBM),were  $251.36 \pm 45.66$  IU/L,  $239.88 \pm 38.2$  IU/L, respectively. There was no statistically significance difference found in level of CSF LDH between Pyogenic meningitis & Tuberculous meningitis. ( $P > 0.05$ )

**FIGURE 6: COMPARISON OF CSF TOTAL CK IN PYOGENIC MENINGITIS & TUBERCULOUS MENINGITIS**

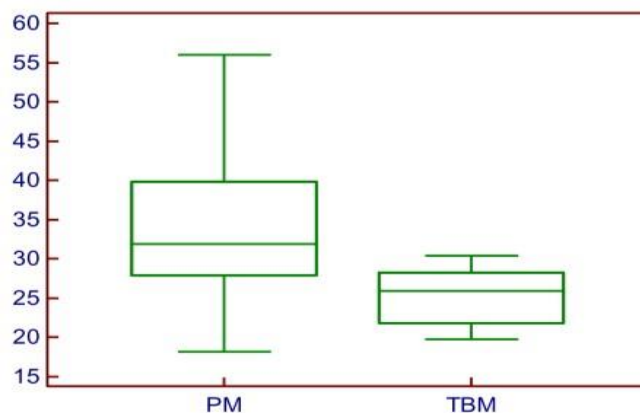


Table 2 and Fig:6 shows that Mean  $\pm$  SD of serum and CSF LDH in group I and group II were  $33.76 \pm 9.8$  IU/L,  $25.37 \pm 3.92$  IU/L, respectively. ( $P > 0.05$ ). There was no statistically significance difference found in level of CSF LDH between Pyogenic meningitis & Tuberculous meningitis. ( $P > 0.05$ ).

### Discussion:

Acute infections of the nervous system are among the most important problems in medicine because early recognition, efficient decision-making, and rapid initiation of therapy can be lifesaving. In this study we observed that enzyme activity was elevated in serum as well as in Cerebrospinal fluid (CSF) in meningitic patients compare to controls. Our observation was matched with other studies Purna Chandra Dash et al<sup>1</sup> and M. Sharma et al<sup>2</sup>.

The serum and CSF LDH and Total CK level was estimated in patients of pyogenic meningitis and tuberculous meningitis. We observed that the mean  $\pm$  SD of CSF LDH and Total CK was more than the mean  $\pm$  SD of serum LDH and Total CK in both pyogenic meningitis and tuberculous meningitis. Our results were same as Purna Chandra Dash et al<sup>1</sup> and M. Sharma et al<sup>2</sup>.

In this study CSF and serum LDH and Total CK levels were higher in Pyogenic meningitis than Tuberculous meningitis. It was same as Purna Chandra Dash et al<sup>1</sup> and M. Sharma et al<sup>2</sup>.

Bacterial meningitis is more common than non bacterial meningitis. Estimation of CSF LDH activity shows more sensitivity to differentiate pyogenic meningitis from non bacterial meningitis. Creatinine phosphokinase (CPK), an enzyme involved in the phosphorylation of the creatinine with ATP from ADP and creatinine phosphate is markedly elevated in meningitis of varied etiology. CPK elevation is found in the CSF than serum. A high level of CSF CPK in cases of meningitis and have both diagnostic and prognostic significance and present study results correlate well with other studies which has done previously.

**LIMITATIONS OF PRESENT STUDY WERE:**

- The sample size was small.
- Only Clinically diagnosed patients were taken.
- The Parameters were analyzed on semi- autoanalyzer.
- The follow- up of patients has not been taken.

**Conclusion**

This study was carried out to measure the levels of Lactate dehydrogenase (LDH) and Total Creatine Kinase (CK) in serum and Cerebrospinal fluid (CSF) in patients with meningitis. LDH and Total CK in serum and CSF may not be useful in differentiating types of meningitis but it may act as a corroborative evidence of meningitis. So along with routine CSF parameters CSF LDH and Total CK level may add in the diagnosis of meningitis. However, study with larger group is required to establish good correlation.

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Conflict of interest Nil

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