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PROGNOSTIC SIGNIFICANCE OF SERUM LDH AND CSF LDH IN CEREBRAL MALARIA AND VIRAL ENCEPHALITIS.

Medicine

Dr. Sarita Behera* Assistant Professor, PG Department of Medicine, SCB Medical College, *Corresponding Author

Dr. Sanjay Kumar Tirkey Post Graduate, Department of Medicine, SCB Medical College,

Dr. Prasanna Kumar Rathor Assistant Professor, PG Department of Medicine, SCB Medical College,

Dr. Sushanta Kumar Bhuyan Post Graduate, Department of Medicine, SCB Medical College,

ABSTRACT

Background: Cerebral malaria and viral encephalitis are two life threatening infections having similar presentation and difficult to diagnose in absence of parasite by slide test or rapid diagnostic test (RDT) and negative serological test in case of viral encephalitis and difficult to predict their prognosis.

Objective: To study the prognostic significance of serum lactate dehydrogenase (LDH) and CSF LDH in patients of cerebral malaria and viral encephalitis.

Method: After fulfilling exclusion criteria, 35 encephalitis patients and 22 cerebral malaria patients are selected clinically and subjected to blood MP, Rapid Diagnostic Test (RDT) and serological tests for Herpes simplex virus (HSV)-1 and HSV-2. Controls are selected from the patients having minor surgical ailment like hernia, hydrocele without neurological, renal, hepatic or cardiac diseases who were to undergo the required surgery. Serum and cerebrospinal fluid (CSF) LDH estimation was carried out and the observations were analysed statistically.

Results: There was no significant difference of mean serum LDH level in patients with cerebral malaria or encephalitis but a significantly higher value was observed in both cases compared to controls. Mean serum LDH value was not significant among survivors and nonsurvivors of both the groups. CSF LDH was significantly high in viral encephalitis compared to cerebral malaria ($P< 0.0004$) and controls ($P< 0.001$). However CSF LDH values in cerebral malaria was significantly high compared to controls ($P<0.001$). Mean CSF LDH level in viral encephalitis was significantly high in non survivor compared to survivor. No such difference was observed in cerebral malaria.

Conclusion: CSF LDH has prognostic significance in viral encephalitis but not in cerebral malaria. Serum LDH is raised both in cerebral malaria and viral encephalitis but having no significant difference between them and it has no prognostic value.

KEYWORDS

Serum LDH, CSF LDH, Encephalitis, Cerebral Malaria

Introduction:

Malaria is a massive global health problem and fifth leading cause of death due to infectious disease worldwide. It is endemic mostly in tropics with high death rate. Most of the deaths have occurred in African region followed by south East Asia region. In India, malaria is one of the most important cause of direct or indirect infant, child and adult mortality rate. encephalitis is another disease of viral aetiology simulates cerebral malaria in its presentation. The incidence of clinically diagnosable encephalitis is between 3.5-7.4/100,000 population/ year[1].Herpes simplex virus (HSV) is the most common cause of acute sporadic encephalitis worldwide, accounting for 10-20% of all case[2,3]

Lactate dehydrogenase (LDH) is an intracellular enzyme of anaerobic glycolysis pathway. Increased LDH level in serum or any body fluid like pleural, pericardial fluid indicate cellular injury. Previous studies on raised LDH level in CSF indicates CNS bacterial infection[4, 5]. In viral encephalitis also LDH is increased compared to control. There is only one study on LDH, level in cerebral malaria by Jakka et al in 2006[6]. This study shows that serum and CSF LDH level increased in cerebral malaria in comparison to control but lower in encephalitis but it's association with progression is not studied yet. Earlier there is a study by Jakka et al [6] in paediatric age group in 2006 where CSF LDH has prognostic and diagnostic significance in these cases.

MATERIALS AND METHODS:

The study was conducted in the Department of Medicine, SCB Medical College, Cuttack, Odisha from September 2011 to September 2012 .Cerebral malaria cases were diagnosed clinically and by demonstration of parasite in peripheral smear and RDT. Viral encephalitis patients were diagnosed clinically and by serological tests (HSV-1 and HSV-2).Patients having neurological disorders like stroke, trauma and intracranial space occupying lesion (ICSOL), liver, kidney , cardiac or muscle diseases, on antipsychotics and antiepileptic drugs were excluded from the study, also excluded pregnant females and females on oral contraceptives .Controls were the individuals to be operated under spinal anaesthesia for minor surgical problems like hernia or hydrocoele having no evidence of neurological ,renal, cardiac or liver diseases .All the selected cases were subjected to detail examination and laboratory investigations. Blood samples were collected for routine and biochemical, radiological tests and serum LDH estimation .CSF samples were collected by lumbar puncture and sent for cytological, biochemical and LDH study. Serum and CSF LDH level is determined by kinetic method by using VITRAS 5.1/FS. The observations were analysed using SPSS for windows version 16.

OBSERVATIONS:

In our study, out of 22 cerebral malaria cases we had12(54.54%) males and 10(45.45%) females and out of 35 encephalitis patients , 22(62.8%) males and13(37.2%) females .All age groups from 15 to 65 years were equally affected in cerebral malaria. In viral encephalitis 23(48.56%) cases were in the age group of 35-65 years.

Out of 22 patients of cerebral malaria,the most common symptoms were fever and altered sensorium . Jaundice was present in 7 patients observed (31.08%) and convulsion in 6 patients (27.27%) In cerebral malaria, oliguria was seen in 2(9.09%), hepatomegaly in 5(22.72%) and spleenomegaly seen in 4(18.18%) cases . Interestingly meningeal sign and decerebrate rigidity were present in 2(9.09%) patients. The symptoms and signs observed were similar to other studies reported from India.

In viral encephalitis, altered sensorium was present in 100% cases and fever in 97.14% cases , 15(40%) cases had convulsion .But meningeal sign was present in 4(11.04%) patients . With the exception of jaundice and oliguria the symptoms were similar to patients of cerebral malaria. However, more patients had meningeal sign which is importantly observed in encephalitis.

On assessment of haematological parameters, hemoglobin ranged from 6.8-13 gm% with a mean value of 9.89±1.8 in cerebral malaria which was significantly lower than the Encephalitis group 11.3±1.60(p=0.0028) . This is a distinct difference between the two groups. Anaemia is common in severe malaria, may be due to increased destruction of red blood cells intravascularily and by sequestration in the spleen and other parts of circulation and loss of deformability leading to haemolysis[7] .Besides this Clark IA et al (1988)[8] and Wenish C et al(1995)[9] had observed that dyserythropoiesis was an important factor for anaemia of malarial origin . It also observed that hypersplenism is the another important cause for anaemia in malaria patients.[10,11]

Plasma glucose levels have been found to be low in patients of severe malaria. In the present study fasting plasma glucose in cerebral malaria was (87.5±11.82) which was significantly lower than viral encephalitis group 98.91±12.94(p<0.001) .

Severe malaria in adult is characterised by multiorgan failure . The commonly affected organ observed are CNS , kidney , liver .This is an important difference from viral encephalitis where CNS is primarily involved . Mean serum urea was 57.81±53.78 and creatinine value was 2.58±3.11 in cerebral malaria which were significantly higher than the viral encephalitis group.

Mean serum bilirubin was found to be significantly higher in cerebral malaria (3.53±4.03) than viral encephalitis (0.97±0.30) .Hepatopathy is an important observation reported in adult patients with falciparum malaria. It is characterised by high level conjugated serum bilirubin, aspartate amino transferase (AST) and alanine amino transferase (ALT) more than 3 times than normal value .Mean AST was observed to be 127.86±135.2., mean ALT was 137.31±165.5, and mean alkaline phosphatase 268.27±165.83 which are significantly higher than encephalitis group . Similar type of result also observed by Kocher DK et al 2003 [12] . Mishra SK et al (1999)[13] had also shown that there was significant rise in serum enzymes level in falciparum infection with jaundice. Our observations corroborate with observations published in other studies.

We assessed CSF for cytological and biochemical parameters and observed that cell count in viral encephalitis was 48.8±28.49 and which was significantly higher compared to cerebral malaria 4.04±2.76.

Similarly assessment of sugar level found to be within normal limit in both the group but lower in cerebral malaria (49±8.64) compared to viral encephalitis (60.4±8.46). Lower plasma glucose value could be the cause of low sugar. CSF protein was significantly high in viral encephalitis (46.68±11.46) compared to cerebral malaria (34.09±5.50)(p<001).

Table-1- Comparision on serum LDH level in between cerebral malaria , encephalitis and controls (figure-1).

	Serum LDH level (U/L) Mean ± SD	p value
Cerebral malaria (n=22)	486.31±152.01	Vs viral encephalitis >0.05 Vs control < 0.001
Viral encephalitis(n=35)	466.71±133.18	Vs control < 0.001
Control (n=25)	273.52±41.80	

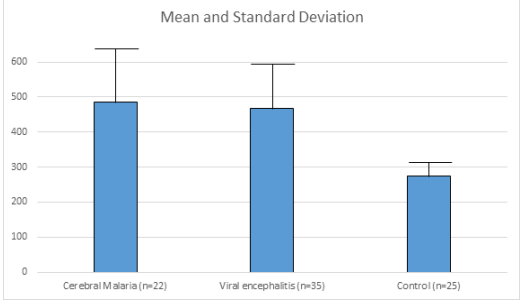

Fig -1

As indicated in TABLE 1, serum LDH levels in cerebral malaria was 486.31±152.01 which was higher than controls. In encephalitis it was 466.71±133.18 .Increase In Serum LDH level in cerebral malaria is due to hemolysis of RBC which is a source of LDH. Jakka et al (2006)[6] showed an insignificant increase in serum LDH levels in encephalitis compared to cerebral malaria. In our study this value is much higher in both encephalitis and cerebral malaria.

Table-2- Comparison of serum LDH level between survivor and non survivor in patients of cerebral malaria and viral encephalitis: (Figure-2)

	Survivor	Non survivor	p value
Cerebral malaria (n=22)	451.5±143.04	579.16±146.46	0.078
Viral encephalitis (n=35)	463.67±140.53	477.57±109.15	0.809

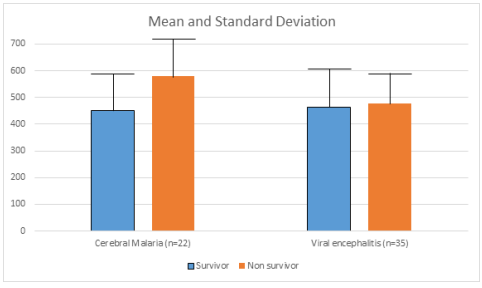

Fig-2

In cerebral malaria serum LDH in survivor was 451.5±143.04 and in non survivor was 579.16±146.46 which is not significant (p=0.078). It indicates serum LDH has no prognostic importance in cerebral malaria. Similarly in viral encephalitis serum LDH in survivor was 463.67±140.53 and in non survivor 477.57±109.15, showed no significant difference between them(p=809). So serum LDH also have no prognostic significance in viral encephalitis.

Table-3- Comparision of CSF LDH level in patients with cerebral malaria and viral encephalitis (figure-3) :

	CSF LDH level in (U/L) (Mean ±SD)	p value
Cerebral malaria (n=22)	36.7±11.60	Vs viral encephalitis = 0.0004
Viral encephalitis (n=35)	50.09±15.03	Vs control < 0.001
Control (n=22)	21.44±5.40	

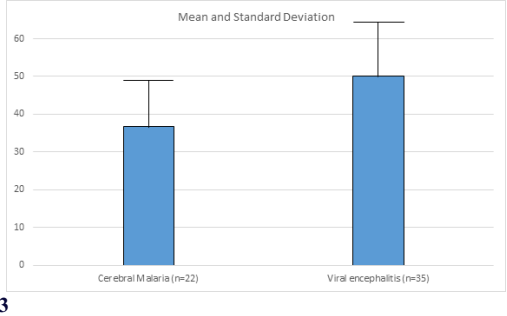

Fig-3

Mean LDH level in csf of patients with cerebral malaria was 36.7±11.60 which was significantly lower than viral encephalitis group(50.09±15.03)(p<0001) .CSF LDH level in control was 21.44±5.40 . There are limited studies on CSF LDH level in encephalitis. Study by Jakka et al(2006)[6] compared CSF LDH levels in between cerebral malaria and encephalitis, found higher LDH levels in encephalitis which was statically not significant. Other studies by FAN xue-wen et al (2005)[14] demonstrated high values of CSF LDH in tubercular meningitis, purulent meningitis and viral encephalitis compared to controls. Highest value was observed in tubercular meningitis followed by pyogenic meningitis and viral encephalitis.

Table-4.Comparison of CSF LDH level between survivor and non-survivor in patients with cerebral malaria and viral encephalitis:

	Survivor	Non survivor	p value
Cerebral malaria (n=22)	35.22±12.29	40.63±9.32	0.342
Viral encephalitis (n=35)	47.32±13.03	65.57±13.11	0.0031

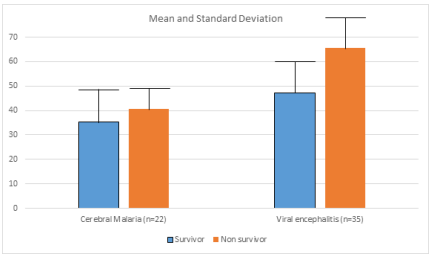

Fig-4

In non survivors of viral encephalitis mean CSF LDH level was 65.571±13.113 which was significantly higher compared to patients who survived(mean LDH value was 47.321±13.03) . In cerebral malaria mean CSF LDH level in non survivor was 40.63±9±32 which was not significantly higher from survivor group, where it was 35.22±12.29(p=0.342) . CSF LDH levels are contributed by granulocytes and lymphocytes present in CSF. Besides this, damage to neuronal cells also contribute in CSF LDH values. In viral encephalitis higher polymorphs CSF compared to cerebral malaria could be the reason for significant difference in CSF values. Besides this, neuronal damage is a significant feature of encephalitis while no injury has been observed in autopsy of brain of cerebral malaria patients. This could be another reason for significant difference in CSF LDH levels. However no significant difference in CSF LDH level in between survivor and non survivor.

CONCLUSION

1. CSF LDH is significantly higher in encephalitis than cerebral malaria patients and it has a prognostic value. CSF LDH has no prognostic significance in cerebral malaria.
2. Serum LDH is raised in both cerebral malaria and viral encephalitis but there was no significant difference between them. It has no prognostic value.

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