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A STUDY ON THE ROLE OF SERUM AND CSF LACTATE IN CEREBRAL MALARIA AND VIRAL ENCEPHALITIS WITH DIAGNOSTIC AND PROGNOSTIC SIGNIFICANCE.

Medicine

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

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

Dr. Pravat Kumar Thatoi Assistant Professor, PG Department of Medicine, SCB Medical College, Cuttack

ABSTRACT

Background: Malaria remains a serious challenge with high morbidly and mortality in the developing countries despite availability of advanced diagnostic and treatment facilities. Encephalitis too simulates cerebral malaria in presentation and severity. Most of the time, it is difficult clinically to diagnose individual entity to start the specific treatment. Several studies on cerebral malaria shows increase in cerebrospinal fluid (CSF) lactate being the sign of bad prognosis but a few studies are there to establish the role of CSF lactate level in viral encephalitis.

Objective: To study the role of serum and CSF lactate In cerebral malaria and encephalitis and its prognostic significance.

Method: Out of 57 cases, 22 malaria and 35 viral encephalitis cases were identified clinically, by Rapid Diagnostic Test (RDT) and blood MP for malaria and serological tests for herpes simplex virus (HSV)1 and HSV2. Age and sex matched 25 control cases were included having no neurological disease who were to be operated for minor surgical ailments like hernia, hydrocoele, etc. under spinal anaesthesia .Blood samples and CSF were collected and subjected to serum lactate and CSF lactate estimation along with routine biochemical and cytological investigations and analysed.

Results: Serum lactate in cerebral malaria was significantly higher compared to viral encephalitis and control. Mean CSF lactate was significantly high in cerebral malaria compared to viral encephalitis and control. CSF lactate value is higher in nonsurvivors than survivors. Serum lactate in viral encephalitis and control did not show any significant difference, also no significant difference between survivor and non survivor.

Conclusion: Serum lactate is significantly high in cerebral malaria compared to viral encephalitis and it has prognostic significance. CSF lactate is significantly higher in patients of viral encephalitis than cerebral malaria and it has prognostic value.

KEYWORDS

Serum lactate, CSF lactate, cerebral malaria, encephalitis.

INTRODUCTION:

Malaria represents the leading parasitic disease in the present world[1]. Half of the global population is at risk and the death in malaria is approximately more than one million per year[2]. It is a major health problem in African and South East Asian countries. Out of infected population of South East Asia, 65% reside in India [3] and the largest number of deaths in India are reported from Odisha[4].

Cerebral malaria is the most severe complication of Plasmodium falciparum infection with a mortality rate of 15-20% , that rise up to 30% if associated with multi organ dysfunction (MOD).[5]

Encephalitis is the infection of central nervous system, suspected in a febrile patient presenting with altered consciousness and signs of diffuse cerebral dysfunction. Virus is the main aetiology among several others and Herpes simplex the most common acute sporadic encephalitis worldwide accounting for 10-20% of all cases. [6,7]

Lactate is a by-product of anaerobic glycolysis pathway and its concentration increases in blood of patients of severe malaria,mainly when associated with multi organ dysfunction (MOD). [8,9]

The present study aims at addressing the role of lactate in serum and CSF of adult cerebral malaria and viral encephalitis patients and to find out the prognostic significance.

Materials and methods:

The study was conducted on 22 admitted cases of cerebral malaria diagnosed clinically and by demonstration of parasite in peripheral smear and RDT and on 35 patients of viral encephalitis diagnosed clinically and by serological tests (HSV 1 and HSV 2).Patients suffering from liver, muscle, cardiac and renal diseases were excluded; so also patients of stroke, intracranial space occupying lesion (ICSOL), trauma and on antipsychotic or antiepileptic drugs. Pregnant females and females on oral contraceptive pills were not included in our study. We took age and sex matched 25 individuals without any evidence of neurological disease and with minor surgical ailments like hernia, hydrocele who are to be operated under spinal anaesthesia as controls and the CSF was collected during spinal anaesthesia.

All the selected cases were subjected to clinical examination and laboratory investigations. We collected CSF by lumbar puncture under aseptic measure and sent for cytological and biochemical examination including lactate. Blood samples were collected for estimation of routine and biochemical investigation like complete haemogram, peripheral smear for malaria parasite, radiological investigation , plasma glucose, blood urea, serum creatinine, liver function tests, renal function tests, serum sodium and potassium, HSV1 and HSV2 (Ig M and Ig G) Serum and CSF lactate level is determined by END POINT COLORIMETRIC method using SELECTRO PRO M instrument. . The statistical analysis was conducted by using SPSS for windows version 16.

Results:

In patients with cerebral malaria, fever and altered sensorium were the most common symptoms (100%) while convulsion (27%), oliguria (9.9%) and black water fever (4.5%) were other manifestations. Icterus (31.81%) and pallor (27.27%) were commonly observed signs. Hepatomegaly was seen in 22.72% cases and meningeal sign and decerebrate rigidity were found in 9.09% cases.

In patients with viral encephalitis, altered sensorium and fever were present in 100% and 97.14% of cases respectively. Convulsion was observed in 40% of cases and meningeal sign in 11.4% of cases. Haemoglobin and plasma glucose were significantly low in cerebral malaria compared to encephalitis group. Serum urea, creatinine, serum bilirubin, aspartate amino transferase (AST), alanine amino transferase (ALT), alkaline phosphatase (ALP) were significantly high in cerebral malaria compared to viral encephalitis .No significant difference in total leukocyte count, serum sodium and serum potassium was seen between the two groups.

Table-1.Mortality rate in cerebral malaria and viral encephalitis:

	Total	Non survivor	Survivor
Cerebral malaria	22	06(27.27%)	16(72.72%)
Viral encephalitis	35	07(20%)	28(80%)

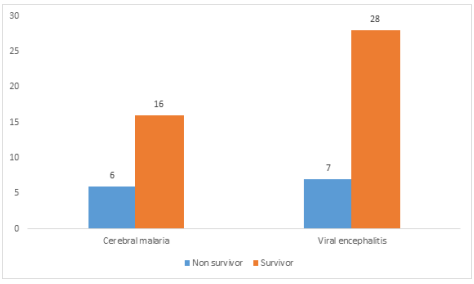

Figure-1 In cerebral malaria 6(27.27%) patients died and in viral encephalitis 7(20%) patients died.

Table-2.Comparison of serum lactate level in patients with cerebral malaria and viral encephalitis:

	Serum lactate level (mg/dl) (mean+-SD)	p value
Cerebral malaria	24.84±4.70	vs viral encephalitis <0.01; vs control <0.001
Viral encephalitis	20.50±3.11	vs control >0.131
Control	17.75±2.49	

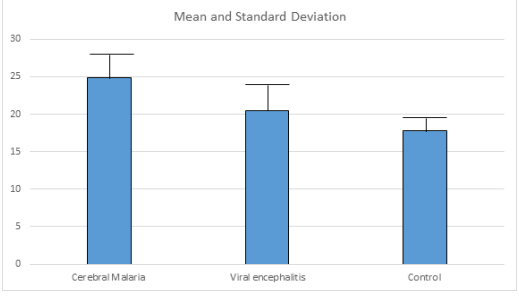

Figure-2 Mean CSF lactate values were not significantly different in cerebral malaria and encephalitis, but it was significantly high compared to controls.

Table-3. Comparison of CSF lactate level between cerebral malaria and viral encephalitis:

	CSF lactate (mg/dl) (mean±standard deviation)	p value
Cerebral malaria (n=22)	29.84± 12.10	Vs viral encephalitis=0.0012 Vs control<0.001
Viral Encephalitis (n=35)	22.49 ± 4.15	Vs control<0.001
Control (n=25)	14.55± 1.81	

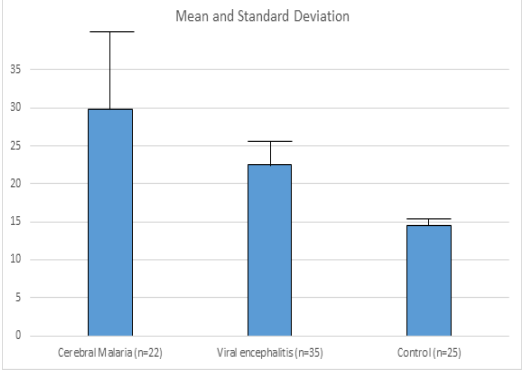

Figure-3 Mean CSF lactate values were not significantly different in cerebral malaria and encephalitis. But it was significantly high compared to controls.

Table-4. Comparison of serum lactate level between survivor and nonsurvivor in patients of cerebral malaria and viral encephalitis:

	Survivor	Non survivor	p value
Cerebral malaria (n=22)	22.63±3.13	30.30±2.25	<0.001
Viral encephalitis (n=35)	20.30±3.01	21.32±3.61	0.444

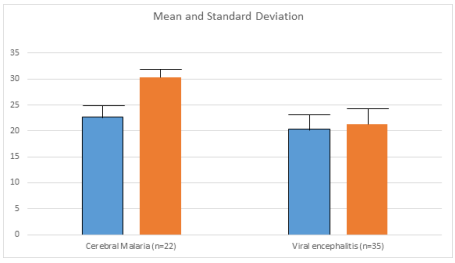

Figure-4 Mean serum lactate in patients who died of cerebral malaria was 30.30 ± 2.21 which was significantly high compared to survivors (p<0.001), highlighting its importance as a marker of prognosis in cerebral malaria. No difference was observed in the encephalitis group.

Table-5. Comparison of CSF lactate level between survivor and non-survivor in patients with cerebral malaria and viral encephalitis:

	Survivor (mean± SD)	Non survivor (mean±SD)	p value
Cerebral malaria	24.56±3.65	43.93±15.74	<0.0001
Encephalitis	21.08±3.34	27.14±2.28	<0.001

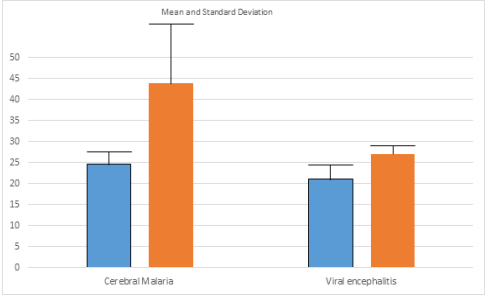

Figure-5

In patients of cerebral malaria who died, the CSF lactate value was significantly high compared to patients who survived (p<0.0001) signifying its importance in prognosis. There was also significantly high value in nonsurvivors compared to survivors (p<0.001) in encephalitis.

DISCUSSION:

Severe falciparum malaria and viral encephalitis are major public health concern in Odisha. The presentation can mimic each other leading to diagnostic dilemma. Although there are several diagnostic tools available for diagnosis of plasmodium falciparum infection, there is a problem in confirming viral encephalitis in the absence of virus isolation. Importantly, mortality is high if diagnosis and treatment is delayed. Besides this, there are limited tests to estimate prognostic outcome. In this context, an effort has been made in the present study to asses role of lactate that can be easily evaluated for its prognostic significance.

In cerebral malaria group males (54.54%) were more than females (45.45%). But this data does not reflect the incidence and gender distribution of disease in the community as the study was done in a tertiary care hospital. According to WHO malaria report males are more affected than females due to more exposure to mosquitoes bite for occupational reasons. In viral encephalitis group, there were total 62.8%males and 37.2% females. Out of 22 patients of cerebral malaria, the most common symptoms were fever and altered sensorium. Jaundice was present in 7 patients(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 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 patient of cerebral malaria.

Serum and CSF lactate have been reported to be a prognostic value in cerebral malaria. However there are a few studies on CSF lactate level in encephalitis. We assessed CSF lactate in both groups of patients and found that mean lactate value was29.84±12.10 in cerebral malaria group and 22.49±4.15 in viral encephalitis group. Both values are higher than control group 14.55±1.81($p<0.001$) .On further analysis CSF lactate was significantly higher in cerebral malaria compared to encephalitis ($p=0.0012$) .CSF biochemical parameter is linked to brain metabolic activity besides the systemic circulation. The origin of lactate in CSF in cerebral malaria could be attributed to tissue ischaemia due to occlusion of cerebral vasculature by parasitised and non parasitised RBC by phenomenon called cytoadherance and rosetting respectively. This lead to anaerobic metabolism leading to high lactate production. Although there is neuronal injury in viral encephalitis, anaerobic metabolism is not a feature of this disease. Analysing mortality, 6 out of 22 patients (27.27%) died in our study .They showed overall mortality rate is 20% in cerebral malaria. Mishra SK et al (2007)[10] showed mortality rate of 13.9% in pure cerebral malaria, 39.5% when associated with ARF, 59% with multiorgan failure. High mortality rate in our study may be due to multiorgan involvement.

CSF lactate level analysis between survivors and non survivors in cerebral malaria showed, those who died had significant higher value 43.99±15.74 compared to those who survived 24.56±3.65($p<0.0001$) .Our findings are consistent with the study published by Mandana IM et al(2002)[11] who demonstrated high CSF lactate value in patients who died compared to the survivors. A study on Ghanian children by Agbenyaga T et al (2003)[12] demonstrated high CSF lactate (8.2 mmol/litre) in non survivor compared to the survivors (3.4 mol/L). A similar study Nicolas J White et al (1985)[13] also demonstrated increase in CSF lactate levels in all patients of cerebral malaria with significantly higher levels (9.0±5.3mmol/L) in non survivors compared to survivors (3.4±1.1 mol/L) i.e. $p=0.0002$. All patients with CSF lactate >6mmol/litre is a poor prognostic indicator.

In present study 7 out of 35 patients died in viral encephalitis despite of adequate antiviral and supportive treatment. In viral encephalitis, mean CSF lactate value was 27.14±2.28 in non survivors compared to survivors which was 21.08±3.34. This difference was significant ($p<0.001$).Montain and Parret et al (1964)[14] showed CSF lactate depends upon infective organism and leukocytes present in CSF. Hansen et al (1974)[15] showed CSF lactic acidosis where CSF is normal due partly to inflamed tissue and partly due to decerebrate rigidity and convulsions.

Serum lactate levels were analysed and it was observed that in cerebral malaria it was 24.849±4.705 compared to 20.50±3.11 in encephalitis in control group. Similarly comparing lactate value in cerebral ($p<0.01$) and17.75± 2.49malaria between survivor and non survivors it was found that those who died had significantly higher value 30.30 ± 2.25 compared to those who survived 22.63 ± 3.13($p<0.001$) . Serum lactate in falciparum malaria infection results from tissue anoxia due to obstruction of blood vessels as discussed earlier.

Study in African children by Krishna S et al (1994)[8], Planche and Agbenyega T et al (2003[12], Allen SJ et al (1996)[16] showed lactic acidosis as a strong predictor of a fatal outcome in Falciparum malaria.

In encephalitis serum lactate level was almost equal in both survivors and non survivors. In patients who died, the level was 21.32±3.61 and in survivor it was 20.30±3.01.

Summary:

Total 22 Patients of Cerebral malaria and 35 patients of encephalitis were taken as cases. Age and sex matched 25 patients taken as controls.Males are more in number in compared to females in cerebral malaria and also in viral encephalitis. All age groups were equally affected in cerebral malaria group but 23(48.56%) cases were in the age group of 35-65 years in viral encephalitis.Most common presentation were fever and altered sensorium. Convulsion was seen in 27.27% cases in cerebral malaria. On CSF analysis mean total cell count, mean protein were significantly higher in oral encephalitis patients compared to cerebral malaria and Mean sugar was significantly low in cerebral malaria group.In cerebral malaria 6(27.27%) patients died and 7(20%) patients in viral encephalitis. Mean CSF lactate was significantly high in cerebral malaria compared to viral encephalitis and control. Patients who died of cerebral malaria significantly higher values than survivors.In viral encephalitis mean CSF lactate was also significantly high in non survivor compared to survivor.Serum lactate in cerebral malaria was significantly higher compared to viral encephalitis and control. There were also significant high values were seen in non survivor compared to survivor in cerebral malaria. Serum lactate In Encephalitis and control did not show any significant difference. There was no significant difference in serum lactate level between survivor and non survivor in viral encephalitis.

CONCLUSION:

1. Cerebral malaria and viral encephalitis are common diseases admitted to the tertiary care hospital whose clinical manifestations are alike.
2. High cell count, raised protein in CSF is more likely to be viral encephalitis.
3. High CSF lactate is common in cerebral malaria. It is significantly high in non survivor compared to survivor. Also in viral encephalitis, there is significant difference in CSF lactate level, indicating its prognostic significance in both cerebral malaria and viral encephalitis.
4. Serum lactate is significantly high in cerebral malaria compared to viral encephalitis and it has a prognostic significance.

A larger study involving more number of patients will help in establishing prognosis and supportive diagnosis in cerebral malaria and viral encephalitis.

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