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TO STUDY THE CORRELATION OF SERUM LACTATE CLEARANCE AND OUTCOME IN NEONATAL SEPSIS

Paediatrics

Dr. Pallavi Mohan* Post graduate resident, Dept of paediatrics, Maharishi Markandeshwar Institute of medical sciences & Research, MMDU,Mullana, Ambala, Haryana, India. *Corresponding Author

Dr. Harita Kirpal Assistant professor, Dept of paediatrics, Maharishi Markandeshwar Institute of medical sciences & research,MMDU, Mullana, Ambala,Haryana, India

Dr. Kusum Mahajan Prof.& Head, Dept of paediatrics, Maharishi Markandeshwar Institute of Medical Sciences & Research, MMDU,Mullana,Ambala, Haryana, India.

Dr. Praveen Kumar Reddy Mopuri Senior Resident, Dept of paediatrics, Maharishi Markandeshwar Institute of Medical Sciences & Research, MMDU, Mullana, Ambala, Haryana, India.

Dr. Jaswir Singh Professor , Dept of paediatrics, Maharishi Markandeshwar Institute of Medical Sciences & Research, MMDU, Mullana, Ambala, Haryana, India.

ABSTRACT

Introduction: The mechanism for hyperlactatemia in sepsis, an increased lactate level represents the increased glycolytic flux due to hypermetabolism. If hyperlactatemia cannot be corrected in time, it can cause damage to multiple organs perinatally and increase the mortality and disability rate of neonate. An increase in blood lactate concentrations during hospitalization is considered to represent a significant prognostic indicator for neonates **Aim and Objectives:** To Study the correlation of Serum Lactate clearance and outcome in Neonatal Sepsis **Material and methods:** This longitudinal study was conducted in the Division of Neonatology, Department of Pediatrics, at Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana, Haryana and its associated Hospital. One ml of venous blood will be collected under aseptic precautions for plasma lactate just before administering 1st dose of antibiotic using a heparinized syringe and lactate will be estimated by an automated analyser. Sample for plasma lactate will be taken again 6 hours after administration of 1st antibiotic dose and analysed in a similar manner. **Results:** In the present study 88% study subjects were discharged, whereas 12 % subjects died. In the present study associations of abnormal lactate level immediate after admission to CRP level of the study subjects to diagnose sepsis. The sensitivity of lactate level to diagnose sepsis considering CRP as diagnostic modality of sepsis, sensitivity is 66.67%, specificity is 17.15%, PPV is 25.64% and NPV is 54.54%. In the present study associations of abnormal lactate level immediate after admission to CRP level of the study subjects to diagnose sepsis. The sensitivity of lactate level to diagnose sepsis considering CRP as diagnostic modality of sepsis, sensitivity is 66.67%, specificity is 17.15%, PPV is 25.64% and NPV is 54.54% **Conclusions:** The sensitivity of lactate clearance to diagnose sepsis considering blood culture as diagnostic modality of sepsis, sensitivity is 75%, specificity is 47.62%, PPV is 21.43% and NPV is 90.9%. In the present study the area under the curve for lactate clearance was 0.515, with significant association with outcome of study subjects

KEYWORDS

Lactate clearance, sepsis, blood culture, CRP

INTRODUCTION

The incidence of neonatal sepsis according to National Neonatal Perinatal Database (NNPD, 2002-03) is 30 per 1000 live births. The NNPD network in India found sepsis to be one of the commonest causes of neonatal mortality contributing to 19% of all neonatal deaths (1). Neonates with sepsis may present in or progress to septic shock, exemplified initially by cardiovascular dysfunction requiring fluid resuscitation or inotropic support. The clinical presentation of early onset sepsis in the newborn is variable. Typically, cold shock is characterized by peripheral vasoconstriction, cool peripheries, and tachycardia; hypotension is often a pre-terminal event. Warm shock is characterized by peripheral vasodilation and hypotension secondary to endotoxin release. These clinically different presentations may benefit from different therapeutic interventions.(2)

Hyperlactatemia is defined as lactate levels between 18 and 45 mg/dl without metabolic acidosis whereas lactic acidosis is defined as lactate levels greater than 45 mg/dl and pH below 7.35.Multiple conditions resulting in inadequate oxygen delivery, disproportionate oxygen demand, and diminished oxygen use may lead to elevated lactate levels. Hyperlactatemia is a cardinal finding of sepsis and septic shock.(3)

The mechanism for hyperlactatemia in sepsis, an increased lactate level represents the increased glycolytic flux due to hypermetabolism. If hyperlactatemia cannot be corrected in time, it can cause damage to multiple organs perinatally and increase the mortality and disability rate of neonates. An increase in blood lactate concentrations during hospitalization is considered to represent a significant prognostic indicator for neonates(4). Moreover, continual measurement of blood lactate concentrations is more useful than a single measurement and can provide more accurate prognostic evaluation. Dynamic monitoring of blood lactate levels in asphyxiated neonates can lead to a dynamic understanding of the internal environment and provide a basis for judging the prognosis of neonates and formulating measures for rescue and treatment.(5)

Immunometabolism is an emerging field recognizing the complex interactions between the metabolism and the immune system both in infections and other diseases. Recent studies suggest that sepsis simultaneously induces both hyper- and hypo-inflammatory responses. Moreover, some studies report a correlation between early deaths and an acute hyper-inflammatory phase, whereas late deaths are associated with a prolonged immunosuppression and recurrent infection (6) The main cause of death in sepsis is organ system failure initiated by cellular hypoxia. This condition is caused by the formation of micro thrombi in small blood vessels which impair the blood flow. Disruption of tissue perfusion and cellular hypoxia can occur before cardiovascular responses emerge. Therefore, tissues increasingly need anaerobic metabolism to meet their energy requirements, resulting in production and accumulation of lactate in the blood.(5)

Lactate clearance is the reduction of lactate concentrations with interventional strategies, therapeutic strategies that can potentially decrease arterial lactate may be associated with improved clinical outcomes. However, Lactate clearance studies to predict mortality and prognosis in neonatal sepsis patients have never been done. Six-hour lactate clearance may be useful as a predictive indicator of mortality in critically ill neonates and those who suffer from severe asphyxia.(7)

This study was conducted to determine the usefulness of lactate clearance as a predictor of mortality in neonatal sepsis patients and themain objective of this study was to determine whether the initial venous lactate level in the emergency care of suspected sepsis in neonates is associated with mortality.

This longitudinal study was conducted in the Division of Neonatology,

Department of Paediatrics, at Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana , Haryana and its associated Hospital.. An approval from the Ethical Committee of the Institute was obtained. Written informed consent was obtained from the parents/guardian or the surrogate for participation. The duration of the study was 18 months.

Study Design:

Hospital based observational longitudinal study.

Sample Size:

A minimum of 50 neonates with suspected neonatal septicemia.

Participants

Inclusion Criteria:

NEONATES with two or more of the following risk factors from different variables were enrolled in this study (7)

Exclusion Criteria:

1. Neonates who had received antibiotics
2. Neonates with severe congenital abnormalities/twins/Infants of diabetic mother(IDM)or those with suspected IEM.
3. Those who received blood transfusion or infusion Ringer lactate prior to examination.
4. Those who have suffered from shock due to cause other than sepsis.
5. Those who did not give the consent for the study.
6. Babies born through meconium stained liquor

Detailed Methodology:

Neonates having 2 or more risk factors for sepsis were enrolled in the study.Neonates on the basis of clinical and laboratory parameters were divided into two groups-those with Proven Sepsis and those with Probable Sepsis. One ml of venous blood was collected under aseptic precautions for plasma lactate just before administering 1st dose of antibiotic using a heparinized syringe and lactate was estimated by an automated analyser. Sample for plasma lactate was taken again 6 hours after administration of 1st antibiotic dose and analysed in a similar manner.

Procedure

- Consent was taken (from the parents) prior to taking the sample.
- Venous blood samples were taken from recruited neonates, prior to administration of 1st antibiotic dose for the succeeding investigations.
- Blood culture(1-2ml), complete blood count (0.5 ml), CRP and Serum lactate (1 ml).
- EDTA blood was taken on a clean dry slide and a thin tongue shaped smear was made after air drying and staining with Leishman's stain. The Total leucocyte count, differential leucocyte count, Absolute Neutrophil count, Band cell count, I/T Ratio, and platelet count were calculated as per standard hematological method.
- Blood sample for serum lactate was taken again after 6 hours of antibiotic therapy and the clearance was estimated.

RESULT

Out of 50 children studied, 22 (44.0%) children were in pre term i.e. less than 37 weeks, 17 children (34.0%) were in term i.e. between 37 weeks to 42 weeks, 11 children (22.0 %) were in post term i.e. greater than 42 weeks. Among the study population, 32(64%) were male children and 18 (36%) were female children. In the 50 study population, normal ANC level was observed in 35 (70%) cases whereas abnormal ANC level was observed in 15 (30%) cases. Among the 50 study population, normal TLC level was observed in 16 (32%) cases whereas Increase TLC level was observed in 32 (64%) cases.

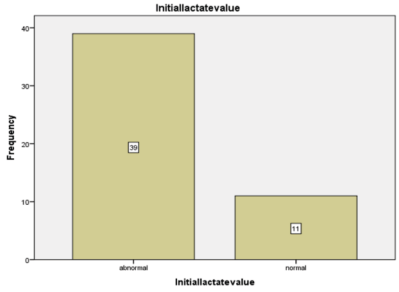

Figure 1: Figure showing percentage of initial Lactate level

Out of the 50 study population, normal CRP level was observed in 37 (74%) cases whereas abnormal CRP level was observed in 13 (26%) cases.

Table 17: Association between Lactate clearance and CRP level

		CRP LEVEL		Total
		POSITIVE	Positive	
Lactate clearance	abnormal	10	30	40
	normal	5	5	10
Total		15	35	50

Sensitivity- 10/15- 66.67%, specificity- 5/35- 14.29%, PPV- 10/40- 25%, NPV- 5/10- 50%

Above table describes the associations of abnormal lactate level immediate after admission to CRP level of the study subjects to diagnose sepsis. The sensitivity of lactate level to diagnose sepsis considering CRP as diagnostic modality of sepsis, sensitivity is 66.67%, specificity is 17.15%, PPV is 25.64% and NPV is 54.54%

Table 22: Area under the curve of ROC curve of lactate clearance with blood culture

Area Under the Curve				
Test Result Variable(s): Lactate clearance				
Area	Std. Error[a]	Asymptotic Sig .[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.503	.133	.979	.241	.765

Tab 22 shows the area under the curve for lactate clearance was 0.503, with significant association with blood culture,

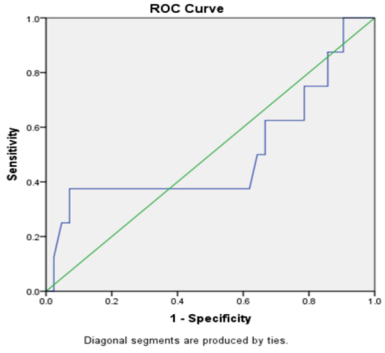

Fig 22: ROC curve of lactate clearance with blood culture

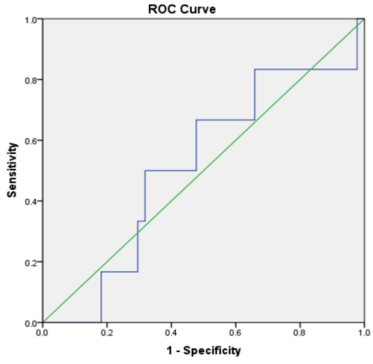

Fig 23: ROC curve of lactate clearance with outcome of study subjects

DISCUSSION

An increased lactate level represents the increased glycolytic flux due to hypermetabolism in septic shock, an increased glycolytic flux is due to tissue hypoxia. This suggests that there are two varieties of lactate, namely, the "stress lactate" and the "shock lactate." Blood lactate levels of up to 18 mg/dl (2 mmol/l) are usually defined to be normal for critically ill patients. Hyperlactatemia is defined as lactate levels between 18 and 45 mg/dl without metabolic acidosis whereas lactic acidosis is defined as lactate levels greater than 45 mg/dl and pH below 7.35. Increased lactate levels may be considered an early marker of a potentially reversible state, e.g., early septic shock, possibly indicating that "there is still room" to boost fast intervention.

Gestational Age

In the present study Out of 50 children studied, 30 (60.0%) babies were

pre term i.e. less than 37 weeks, 20 babies (40.0%) were term i.e. between 37 weeks to 42 weeks. **Kondle V.K et al.**(8) Study shows gestational age 37 weeks (32 to 40 weeks). **Helal N F et al.**(9) study shows the mean gestational age of the enrolled neonates was 34.95 weeks (28-40 weeks). **Chen D et al.**(5) Study showed the mean gestational age (weeks) 31.9 + 3.5 weeks in neonates who died whereas 34.4 + 4.0 weeks in neonates who survived and gestational age and birth weight in the group of neonates who died were significantly lower than those in the group of neonates who survived (both $P < 0.05$). **Dr Satish Kumar Sethi et al.**(2) in their study showed majority of study subjects in survivor group were term i.e more than 37 weeks gestational age whereas in died group majority of study subjects were preterm. **Luis Kanhiti Oharomari Junior et al**(10) in their study showed Overall, the mean gestational age was 29 weeks and 1 day (median of 29 weeks, standard deviation (SD) of 3.1 weeks)

Sex

In the present study the study population, 32(64%) were male children and 18 (36%) were female children. **Kondle V.K et al.**(8) Study displayed female neonates 88 whereas male neonates 100 in their study. **Choudhary et al.** (11) study shows male: female ratio 1.6:1 in study subjects. **Zanak K et al.**(12) Study showed lactate clearance group 50% was male and 50% were female and in non-lactate clearance group 34.2% were female and 65.8% were males. **Chen D et al.** (9) Study shows Sex (male/female) 18/7 in neonates who died whereas 32/10 in neonates who survived. The study by **Aramburo A et al.**(13) 46% were female, so it is in accordance of our study to have male preponderance. Study by **Dr Satish Kumar Sethi et al.** (2) in their study also shows male preponderance in both survivor and died group, This male preponderance was similar to our present study which also shows male preponderance. **Dedi K. Saputra, et al.**(14) shows in their study majority of subjects were male (24/45).

Lactate Clearance

In the present study,Out of the 50 study population, abnormal lactate clearance was observed in 40 (80.0%) cases whereas normal lactate clearance was observed in 10 (20%) cases, lactate clearance less than 30% was considered abnormal. **Kondle V.K et al.** (8)Study shows there were 23 neonates with more than 9mmol/dl of lactate at admission. 6 neonates had clearance value of less than 30% at 24 hours. All 6 babies had prolonged stay of more than 15 days and their outcome was negative. In 21 neonates SNAP II score was more than 60 at admission but, lactate clearance were less than 30% in 69 neonates (41%). LAC24 and SNAP II score had significant correlation. **Hatheril et al.**(15) showed that persistent hyper-lactatemia >2 mmol/L after 24 hours was associated with 93% mortality, as compared to 30% in those children whose lactate level had normalized. **Saputra DK, et al**(14)**.** study shows the outcome between patients with lactate clearance of less than or equal to 34.7% and more than 34.7% was statistically significant. **Nguyen et al.**(16) found that the 6-hour lactate clearance rate at 10% as a threshold for assessing mortality during hospitalization had good specificity and sensitivity.

Outcome of Study Population

In the present study,in the 50 study population, the death was seen in 6 (12.0%) cases whereas, recovered/discharge 44 (88.0%) cases. **Zanak K et al.**(12) Study shows the incidence of death among the lactate non-clearance group was 84.2% compared to 9.6% among the lactate clearance group. This association was found to be statistically significant ($p<0.05$).

Study by **Felix Nathan Trisnadi et al.**(6) shows that a greater proportion of deaths occurred in the group of neonates with low lactate clearance at six hours (48%) than in those with high lactate clearance at six hours (7%). Logistic regression analysis showed that lactate clearance at six hours was a significant predictor of mortality (RR15.1; 95%CI 1.7 to 133). Similarly, other studies, found that the mortality of critically ill neonates with low lactate clearance at six hours was significantly higher than that of the high lactate clearance group (50% vs. 9.4%,15 respectively, and 68% vs. 13.1%,16 respectively). A higher proportion of deaths in the low lactate clearance group in previous studies compared with our study were likely due to their subjects being recruited later in the course of their illness, compared to our subjects who were recruited at the time of diagnosis.

CONCLUSIONS

REFERENCES

1. Wattal C, Kler N, Oberoi JK, Fursule A, Kumar A, Thakur A. Neonatal sepsis: mortality and morbidity in neonatal sepsis due to multidrug-resistant (MDR) organisms: part 1. Indian J Pediatr. 2020;87(2):117–21.
2. Sethi SK, Mohapatra JP. Lactate Clearance in Neonates withSeptic Shock as a Predictor of Outcome. 2021;3(2):13–8.
3. Jat KR, Jhamb U, Gupta VK. Serum lactate levels as the predictor of outcome in pediatric septic shock. Indian J Crit care Med peer-reviewed, Off Publ Indian Soc Crit Care Med. 2011;15(2):102.
4. Luft FC. Lactic acidosis update for critical care clinicians. J Am Soc Nephrol. 2001;12(suppl 1):S15–9.
5. Chen D, Liu X, Li J. Lactate levels and clearance rate in neonates undergoing mechanical ventilation in Tibet. J Int Med Res. 2020;48(10):0300060520962388.
6. Trisnadi FN, Haksari EL, Wibowo T. Lactate clearance as a predictor of mortality in neonatal sepsis. Paediatr Indones. 2016;56(4):193–8.
7. LEE D CADY JR, WEIL MAXH, AFIFI AA, MICHAELS SF, LIU VY, SHUBIN H. Quantization of severity of critical illness with special reference to blood lactate. Crit Care Med. 1973;1(2):75–80.
8. Kondle DVK, P DG. A comparison study of blood lactate and lactate clearance with SNAP II score as predictors of outcome in sick neonates. Pediatr Rev Int J Pediatr Res. 2017;4(6):388–96.
9. Helal NF, Samra NM, Ghany EAGA, Said EA. Can the Score for Neonatal Acute Physiology II (SNAPII) Predict Morbidity and Mortality in Neonates with Sepsis? J Neonatal Biol. 2013;02(02).
10. Junior LKO, Carmona F, Aragon DC, Gonçalves-Ferri WA. Evaluation of urine output, lactate levels and lactate clearance in the transitional period in very low birth weight preterm infants. Eur J Pediatr. 2021;180(1):91–7.
11. Choudhary R, Sitaraman S, Choudhary A. Lactate clearance as the predictor of outcome in pediatric septic shock. J Emerg Trauma Shock. 2017;10(2):55.
12. Zanak K, Saikia D, Sharma S, Chattopadhya A. Lactate clearance at 6 hours after admission as a predictor of mortality in children with clinically suspected sepsis. Sri Lanka J Child Heal. 2022;51(1):34–8.
13. Aramburo A, Todd J, George EC, Kiguli S, Olupot-Olupot P, Opoka RO, et al. Lactate clearance as a prognostic marker of mortality in severely ill febrile children in East Africa. BMC Med. 2018;16(1):1–12.
14. Saputra DK, Runtunuwu AL, Tatura SNN, Manoppo JIC, Lolombulan JH. Lactate clearance and mortality in pediatric sepsis. Paediatr Indones. 2016;56(4):215.
15. Hatherill M, Sajjanhar T, Tibby SM, Champion MP, Anderson D, Marsh MJ, et al. Serum lactate as a predictor of mortality after paediatric cardiac surgery. Arch Dis Child. 1997;77(3):235–8.
16. Nguyen HB, Rivers EP, Knoblich BP, Jacobsen G, Muzzin A, Ressler JA, et al. Early lactate clearance is associated with improved outcome in severe sepsis and septic shock. Crit Care Med. 2004;32(8):1637–42.