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Original Article

Paediatrics Section

Role of Serum Lactate Clearance as a Predictor of Mortality and Morbidity in Neonatal Sepsis: A Prospective Cohort Study

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ABSTRACT

Introduction: Neonatal sepsis is a global healthcare concern, which is more prevalent in developing countries. However, surprisingly, biomarkers with good sensitivity and specificity to predict mortality and morbidity are lacking. Higher levels of serum lactate are observed in patients exposed to an inflammatory response, but its practical use remains limited. Therefore, the author aimed to investigate the relationship between serum lactate measurements and the severity of neonatal sepsis.

Aim: To assess the role of serum lactate clearance as a marker to predict mortality and morbidity in neonatal sepsis. Additionally, the secondary aim was to evaluate the demographic profile of neonatal sepsis and understand the relationship between C-reactive Protein (CRP), Procalcitonin, and lactate clearance in neonatal sepsis.

Materials and Methods: A prospective cohort study was conducted in the Sick Newborn Care Unit (SNCU) and Neonatal Intensive Care Unit (NICU) of Chittaranjan Seva Sadan, College of Obstetrics, Gynaecology, and Child Health in Kolkata, India, from June 2020 to May 2021. A total of 93 confirmed cases of neonatal sepsis were included in the study. Serum lactate levels were measured at the time of sepsis diagnosis and 48 hours after the first sample. Lactate clearance was calculated, and the neonates were followed till discharge or death. Various parameters, including complete blood count, CRP, Procalcitonin, culture, and Cerebrospinal Fluid (CSF), were assessed. The data obtained were statistically analysed using paired t-test, one-way Analysis of Variance (ANOVA), and Pearson's Chi-square test.

Results: A total of 93 neonates were included after meeting the inclusion and exclusion criteria. Among them, 10 neonates died, while 83 were successfully discharged. It was found that death was significantly associated ($p<0.0001$) with lactate clearance. Total 9 (90%) of the deceased neonates had negative lactate clearance, while only 21 (25.3%) discharged neonates had negative lactate clearance. Lactate clearance was also significantly associated with the duration of hypoglycaemia ($p=0.008$), duration of Nil Per Mouth (NPM) ($p=0.01$), and need for reintubation ($p=0.05$). However, no association was found with the duration of hospital stay, duration of fluid therapy, duration of oxygen requirement, and need for ventilation.

Conclusion: Lactate clearance showed a significant association with the risk of mortality in patients with neonatal sepsis. Therefore, lactate clearance can be used as a prognostic marker to identify sepsis. Early detection of sepsis can aid in proper management and subsequently reduce mortality.

Keywords: Death, Hypoglycaemia, Infection, Newborn, Reintubation, Shock

INTRODUCTION

While inside the mother's womb, a foetus is protected from infections by a variety of factors. Among them, the placenta and chorioamniotic membranes form a physical barrier, while a wide number of poorly described antibacterial substances present in the amniotic fluid provide an immunological shield to the developing embryo [1].

After childbirth, the natural barriers are shed off one by one, and the neonate becomes susceptible to pathogens present along the birth canal as well as in the external atmosphere. The poorly developed immune system adds to the vulnerability of the neonate to external pathogens [2]. Around 20% of neonates suffer from infections, and nearly 1% succumb to neonatal sepsis. The percentage is even higher (ranging from 30% to 40%) among lower gestational age babies or those suffering from severe sepsis [2,3]. Despite the prevalence of sepsis, there is a surprising lack of appropriate biomarkers with good sensitivity and specificity. Previous studies have shown that the well-established sepsis screen parameters have sensitivity and specificity as low as 30-40% [4,5].

Lactate is already established as a diagnostic marker in Systemic Inflammatory Response Syndrome (SIRS). When tissues are exposed to hypoxia, anaerobic metabolism sets in, replacing pyruvate, the normal end product of glycolysis, with lactate. As the hypoxic damage continues, there is a gradual build-up of lactate levels in the blood. Therefore, serial lactate measurement serves as a good indicator of the severity of the ongoing insult [6]. While normal blood lactate levels are approximately 0.5-2.5 mmol/L, blood lactate concentrations ≥4 mmol/L and impaired clearance have been independently associated with increased mortality in sepsis [7].

There has been controversy regarding the correct timing of lactate level testing, the interval between two successive tests, and even the interpretation of the test, which is also not devoid of controversies. The Surviving Sepsis Guidelines (2020) recommend using lactate levels to guide resuscitation in sepsis and sepsis-related organ dysfunctions, although the data is still inadequate and lacks clarity [8].

In a third-world country like India, the cost-effectiveness of any test plays an important role in policy formulation. Lactate clearance is easy to test and is almost universally available. The newer arterial blood gas analysers provide reliable results in a matter of minutes and are an integral part of almost every Paediatric Intensive Care Unit (PICU) and NICU. Therefore, it is prudent to utilise such a reliable and cost-effective biomarker to its full potential [9].

Although serum lactate is theoretically a good marker for an ongoing insult, its practical use in a systematic manner is quite limited to date. There have been very few studies conducted worldwide [10-12], and almost none in India [13], regarding the role of lactate clearance in neonatal sepsis. Hence, the present study was conducted to assess the role of serum lactate clearance as a predictive marker for determining patient outcomes in terms of mortality and morbidity in neonatal sepsis. The secondary aim was to study the demographic

profile of neonatal sepsis and understand the relationship between CRP, procalcitonin, and lactate clearance in neonatal sepsis.

MATERIALS AND METHODS

A prospective cohort study was conducted in the SNCU and NICU at Chittaranjan Seva Sadan, College of Obstetrics, Gynaecology, and Child Health hospital in Kolkata, India, over a period of 12 months from June 2020 to May 2021. Institutional Ethical Committee clearance (Ethical Clearance Number CSS/Estt/220/2020-Sl. No. 14) was obtained prior to commencing data collection. Written informed consent was obtained from the parents or guardians of the neonates enrolled in the study.

Inclusion criteria: All neonates with a confirmed diagnosis of neonatal sepsis, as proven by any or all of the following tests-positive sepsis screen, positive blood culture, positive urine culture, positive Procalcitonin, CSF positive for meningitis, and those admitted within the study period, were included.

Exclusion criteria: Neonates with severe birth asphyxia, diagnosed inborn errors of metabolism, or gross congenital anomalies were excluded from the study as they can have high lactate levels due to causes other than sepsis [14]. Additionally, samples were not taken if the neonate had a convulsion in the last two hours (lactate sample is to be taken atleast two hours after a convulsion, as lactate levels rise immediately after a convulsion and take some time to reach baseline) [15]. Neonates were also excluded if their guardians were unwilling to enroll their children in the present study.

Sample size: The total number of neonatal sepsis cases admitted in the SNCU and NICU during this time period was 112, of which 93 neonates were included through convenient sampling, while 19 were excluded after applying the inclusion and exclusion criteria.

Study Procedure

Two venous blood samples (approximately 0.2 mL) were drawn from peripheral veins of these patients to test for blood lactate levels (venous and arterial levels of lactate are highly correlated), once at the diagnosis of sepsis (referred to as the initial lactate level) and the second one taken 48 hours apart (referred to as the final lactate level) [14]. A tourniquet was not used (although there is no evidence to suggest that the application of a tourniquet would significantly alter serum lactate levels), and the sample was tested within 15 minutes of collection [14]. The samples were analysed using the Opti CCA Lactate Cassette, and lactate clearance was calculated from these values using the following formula.

Lactate clearance was calculated using the following formula: Lactate Clearance=(Initial lactate-final lactate)/final lactate×100% [16]. Based on whether these values were positive or negative (i.e., lactate clearance was greater than or less than zero), the neonates were divided into positive lactate clearance and negative lactate clearance cohorts [9,10]. Both cohorts were followed-up until discharge or death to track their clinical course during the hospital stay.

The outcome was defined by correlating serum lactate clearance with patient outcomes. A positive outcome was determined when patients with positive lactate clearance showed a better clinical course and fewer complications, or when patients with negative lactate clearance levels experienced an unfavorable clinical course with poor outcomes. The reverse was true for a negative outcome [10,13].

The major parameters studied were as follows:

- Patient particulars, including demographic parameters (age, gender, gestational age, birth weight, initial presentation, early/late onset sepsis-i.e., whether sepsis occurred within the first 72 hours of birth or not) [17].
- Results of conventional markers of sepsis, including:
- Sepsis screen (total leukocyte count [cells/mm^3], absolute neutrophil count [cells/mm^3], C-reactive protein [mg/L], micro erythrocyte sedimentation rate [mm/1st hour], immature: total neutrophil ratio. A sepsis screen was considered positive if two of these five parameters were abnormal [5].
- Blood culture along with antimicrobial sensitivity pattern.
- Serum procalcitonin (ng/mL).
- Cerebrospinal fluid studies (whenever necessary).
- Urine routine examination and culture sensitivity (wherever necessary).

Standard reference values were considered normal based on previous studies [17].

- Initial and final lactate levels and lactate clearance.
- Mortality rate (total number of deaths in a given population/total population, expressed as a percentage).
- Morbidity parameters (duration of oxygen requirement, duration of fluid support, duration of Nil Per Mouth (NPM), duration of hypoglycaemia, type of hypoglycaemia [persistent or not], duration of ventilation, mode of ventilation [highest support needed among continuous positive airway pressure, non invasive ventilation, and invasive ventilation], any incidence of reintubation or reventilation, duration of inotropes, and other complications. Hypoglycaemia lasting more than seven days was considered persistent [18].

STATISTICAL ANALYSIS

For statistical analysis, the data were entered into a Microsoft excel spreadsheet and then analysed using Statistical Package for Social Sciences (SPSS) (version 27.0; SPSS Inc., Chicago, IL, USA) and GraphPad Prism version 5. Paired t-test, one-way ANOVA, and Pearson's Chi-squared test were used to analyse the data as required. A p-value of ≤0.05 was considered statistically significant.

RESULTS

In the present study, lactate clearance was found to be positive in 63 (67.7%) patients and negative in 30 (32.3%) patients. In the lactate negative clearance group, 8 (26.7%) patients were female, and 22 (73.3%) patients were male. In the positive clearance group, 27 (42.9%) patients were female, and 36 (57.1%) patients were male. The association of gender with positive/negative clearance was not statistically significant (p=0.13). Other demographic parameters are summarised in [Table/Fig-1]. Although all the patients eventually developed sepsis, many were initially admitted for various other reasons. Even among those admitted with the clinical diagnosis of sepsis itself, the presentation varied. The most common indications

Parameters		Lactate clearance		Total	p-value
		Negative	Positive		
Gestational age	Early preterm (<35 weeks)	13 (43.3)	22 (34.9)	35 (37.6)	0.19
	Late preterm (35-37 weeks)	8 (26.7)	10 (15.9)	18 (19.4)	
	Term (>37 weeks)	9 (30)	31 (49.2)	40 (43.0)	
Birth weight	ELBW (<1000 g)	1 (3.3)	3 (4.8)	4 (4.3)	0.12
	VLBW (1000-1500 g)	13 (43.3)	20 (31.7)	33 (35.5)	
	LBW (1500-2500 g)	12 (40.0)	15 (23.8)	27 (29.0)	
	AGA (2500-4000 g)	4 (13.3)	23 (36.5)	27 (29.0)	
	LGA (>4000 g)	0 (0)	2 (3.2)	2 (2.2)	
Gender	Female	8 (26.7)	27 (42.9)	35 (37.6)	0.13
	Male	22 (73.3)	36 (57.1)	58 (62.4)	
EOS/LOS	EOS	15 (50.0)	16 (25.4)	31 (33.3)	0.01
	LOS	15 (50.0)	47 (74.6)	62 (66.7)	

[Table/Fig-1]: Demographic parameter distribution in positive and negative lactate clearance cohorts.
(Chi-square test); ELBW: Extremely low birth weight; VLBW: Very low birth weight; LBW: Low birth weight; NBW: Normal birth weight; EOS: Early-onset sepsis; LOS: Late-onset sepsis; AGA: Appropriate for gestational age; LGA: Large for gestational age

for admission were prematurity (29 neonates, 31.2%) and respiratory distress (25 neonates, 26.9%), followed by hypoglycaemia (8 neonates), intrauterine growth restriction (6 neonates), and seizures (6 neonates).

In the study, 46 (49.5%) patients had a negative sepsis screen, and 47 (50.5%) patients had a positive sepsis screen. Blood Culture and Sensitivity (C/S) was performed in all patients and yielded positive results in 47 patients. Four patients had more than one organism causing sepsis (2 in the positive lactate clearance group and 2 in the negative clearance cohort). In the lactate clearance positive group, 38 (60.3%) patients had a positive blood C/S, and 25 (39.7%) patients had a negative blood C/S. In the lactate clearance negative group, 19 (63.3%) patients had a positive blood C/S, and 11 (36.7%) patients had a negative blood C/S. The association between lactate clearance and blood culture positivity, urine examination, and CSF examination was not statistically significant [Table/Fig-2].

Parameters		Lactate clearance		Total {n (%)}	p-value
		Negative {n (%)}	Positive {n (%)}		
Gender	Female	8 (26.7)	27 (42.9)	35 (37.6)	0.13
	Male	22 (73.3)	36 (57.1)	58 (62.4)	
EOS/LOS	EOS	15 (50.0)	16 (25.4)	31 (33.3)	0.01
	LOS	15 (50.0)	47 (74.6)	62 (66.7)	
Sepsis screen	Negative	13 (43.3)	33 (52.4)	46 (49.5)	0.41
	Positive	17 (56.7)	30 (47.6)	47 (50.5)	
Blood C/S	Negative	11 (36.7)	25 (39.7)	46 (49.5)	0.18
	Positive	19 (63.3)	38 (60.3)	47 (50.5)	
Urine examination	Negative	29 (96.7)	60 (95.2)	89 (95.7)	0.75
	Positive	1 (3.3)	3 (4.8)	4 (4.3)	
Cerebrospinal fluid examination*	Negative	15 (60.0)	44 (77.2)	59 (72.0)	0.11
	Positive	10 (40.0)	13 (22.8)	23 (28.0)	

[Table/Fig-2]: Various investigative parameter distribution in positive and negative lactate clearance cohorts.
*CSF examination was not done in all cases as there was no clinical relevance
(Chi-square test)

Among the negative clearance cohort, 9 (30.0%) patients died, and 21 (70.0%) patients were discharged. Among the positive clearance cohort, 1 (1.6%) patient died, and 62 (98.4%) patients were discharged. Thus, the mortality rate in the negative clearance cohort was 30%, while in the positive clearance cohort, the mortality rate was only 1.6%, showing a major statistically significant difference (p<0.0001) [Table/Fig-3].

Outcome	Lactate clearance			p-value
	Negative (%)	Positive (%)	Total	
Dead	9 (30)	1 (1.6)	10	<0.0001
Discharged	21 (70)	62 (98.4)	83	
Total	30 (32.3)	63 (67.7)	93	

[Table/Fig-3]: Death in positive and negative lactate clearance cohorts.
(Chi-square test)

It was found that lactate clearance had a sensitivity of 0.74, specificity of 0.9, a Positive Predictive Value (PPV) of 98%, and a Negative Predictive Value (NPV) of 30% in determining the mortality rate in neonates with sepsis.

In the present study, 47 (50.5%) patients had normal procalcitonin levels, whereas 46 (49.5%) patients had increased procalcitonin levels (procalcitonin <0.1 ng/mL was considered normal). It was found that in the negative clearance cohort, 9 (30.0%) patients had normal procalcitonin levels, and 21 (70.0%) patients had increased procalcitonin levels. In the positive clearance cohort, 38 (60.3%) patients had normal procalcitonin levels, and 25 (39.7%) patients had increased procalcitonin levels, making the association of procalcitonin with positive/negative lactate clearance statistically significant (p=0.0062). However, the CRP values in the corresponding groups had no such clinical significance [Table/Fig-4].

Parameters	Procalcitonin category	Positive lactate clearance (%)	Negative lactate clearance (%)	Total	p-value
Procalcitonin	Normal	38 (80.9)	9 (19.1)	47	0.0062
	Increased	25 (54.3)	21 (45.7)	46	
	Total	63 (67.7)	30 (32.3)	93	
CRP	Normal	7 (0.11)	5 (16.7)	12	0.1564
	Increased	56 (88.9)	25 (83.3)	81	
	Total	63 (67.7)	30 (32.3)	93	

[Table/Fig-4]: Procalcitonin and CRP in positive and negative lactate clearance cohorts.
(Chi-square test)

The clinical courses of both cohorts were followed until their discharge or death, whichever came earlier. The following parameters were compared for both cohorts. The mean duration of hospital admission, fluid support, and inotrope support in the negative and positive lactate clearance cohorts were not statistically significant (p=0.78, 0.31, and 0.14, respectively). The association of the duration of ventilation (highest support required) with positive/negative clearance was statistically significant (p=0.042). The mean duration of Nasopharyngeal Mask (NPM) and hypoglycaemia in the negative and positive lactate clearance cohorts were statistically significant with p-values of 0.03 and 0.01, respectively. However, the mean duration of oxygen support in the negative and positive lactate clearance cohorts was not statistically significant (p=0.44) [Table/Fig-5].

Variables	Positive lactate clearance cohort (days±SD)	Negative lactate clearance cohort (days±SD)	p-value
Duration of fluid support	10.2±7.04	11.9±8.21	0.31
Duration of inotrope Support	2.1±3.8	3.4±4.4	0.14
Duration of ventilator support	3.5±4.9	5.8±7.9	0.042
Duration of hospital admission	20.3±8.6	20.8±9.2	0.78
Duration of NPM	2.4±3.5	4.3±4.4	0.03
Duration of O_2 support	6.2±7.8	7.6±8.3	0.44
Duration of hypoglycaemia	1.4±2.0	3.0±3.9	0.01

[Table/Fig-5]: Comparison between clinical course of positive and negative lactate clearance cohorts.
SD: Standard deviation; (Student's unpaired t-test)

In the negative lactate clearance cohort, 4 (13.3%) patients required reintubation, while in the positive clearance cohort, 2 (3.2%) patients required reintubation. The association of the need for reintubation with positive/negative clearance was not statistically significant (p=0.0585).

In the present study, 17 (35.4%) patients in the negative clearance group and 31 (64.6%) in the positive group had hypoglycaemia. In the negative lactate clearance cohort, 12 (70.6%) patients did not have persistent hypoglycaemia, while 5 (29.4%) patients had persistent hypoglycaemia. In the positive clearance cohort, 30 (96.8%) patients did not have persistent hypoglycaemia, and 1 (3.2%) patient had persistent hypoglycaemia, making the association of the type of hypoglycaemia with positive/negative clearance statistically significant (p=0.0087) [Table/Fig-6].

Hypoglycaemia type	Positive/negative clearance			p-value
	Negative (%)	Positive (%)	Total	
Not persistent	12 (28.6)	30 (71.4)	42 (100)	0.0087
Persistent	5 (83.3)	1 (16.7)	6 (100)	
Total	17 (35.4)	31 (64.6)	48 (100)	

[Table/Fig-6]: Duration of hypoglycaemia in positive and negative lactate clearance cohorts.
(Chi-square test)

The major complications that developed during the course of hospital stay were multiorgan failure (4 neonates), hydrocephalus (4 neonates), acute kidney injury (3 neonates), necrotising enterocolitis (3 neonates), etc. The complication rate was higher in the negative lactate clearance cohort than the positive lactate clearance cohort (p-value=0.55) [Table/Fig-7].

Complication	Negative lactate clearance (%)	Positive lactate clearance (%)	Total
Multiorgan failure	4 (40.0)	0 (0.0)	4 (25.0)
Hydrocephalus	2 (20.0)	2 (33.3)	4 (25.0)
Necrotising enterocolitis	2 (20.0)	1 (16.7)	3 (18.8)
Acute kidney injury	1 (10.0)	2 (33.3)	3 (18.8)
Bronchopulmonary dysplasia	1 (10.0)	1 (16.7)	2 (12.5)

[Table/Fig-7]: Complications in lactate positive and lactate negative cohorts.
*All patients not included in this table
(Chi-square test)

DISCUSSION

The measurement of lactate levels has become more frequent practice nowadays in all intensive care units. Many of the recent arterial blood gas analysers have incorporated lactate measurement, and lactate levels are automatically measured along with other parameters when performing a blood gas analysis. Therefore, we can use the same measurement for early detection as well as prognostication of sepsis.

In the present study, lactate clearance was found to be positive in 63 patients and negative in 30 patients. Among the patients who died, 90% had a negative lactate clearance, while 10% had a positive clearance. In the group that was successfully discharged, the rates were 25.3% and 74.7%, respectively, resulting in a significantly low clearance (p<0.0001) in the neonates who died. It was found that lactate clearance has a sensitivity of 0.74, specificity of 0.9, a Positive Predictive Value (PPV) of 98%, and a NPV of 30% in determining the mortality rate in neonates with sepsis. Thus, it can be concluded that a normalising or decreasing lactate trend after 48 hours can predict a chance of recovery with 98% accuracy. However, a falling lactate trend can only predict death in 30% of cases.

A study conducted by Nazir M et al., showed that lactate clearance at 24 hours had a sensitivity of 0.922 and specificity of 0.629 in predicting mortality in patients admitted to the Paediatric Intensive Care Unit (PICU) with septic shock [19]. Another study by Trisnadi F et al., also revealed similar findings in neonates with sepsis [11]. An article published by Scott HF et al., compared initial lactate levels in cases of sepsis and found that even a single initial lactate level had a sensitivity of 20% and specificity of 92% for predicting mortality [20]. A study conducted by Raksha SS et al., demonstrated that persistent hyperlactatemia was observed in non survivors, and serum lactate values persistently greater than 4 mmol/L within the first 24 hours of admission were associated with a greater risk of mortality [21].

Another interesting finding was that a higher incidence of negative lactate clearance was seen in Early-onset Sepsis (EOS) compared to Late-onset Sepsis (LOS) (48% vs. 24%), which corresponds well to the established idea that early-onset sepsis has a worse prognosis compared to late-onset sepsis [22].

Similarly, the percentages of negative clearance were higher in early preterm (37.1%) and late preterm (44.4%) neonates compared to term neonates (22.5%). It was also higher in the extremely low birth weight (25%), very low birth weight (39.4%), and low birth weight (44.4%) groups compared to normal birth weight (14.8%) neonates. There was no significant difference in lactate clearance between male and female neonates. These findings are evident considering that the chance of severe sepsis increases manifold as the gestational age and birth weight decrease, a fact that is well established in texts and studies [3,5].

The value of lactate clearance also corresponds well with the serum Procalcitonin level. The mean value of serum Procalcitonin in neonates with negative clearance was 7.08 ng/mL, while that in the positive clearance group was 1.07 ng/mL, which was statistically significant (p=0.0009). Similar results were seen in studies by Sofijanova A et al., and Hu Y et al., [23,24]. No such correlation was seen between mean Total Leukocyte Count (TLC), CRP, or Absolute Neutrophil Count (ANC) values, even when stratified according to gestational age or age of sample collection. Lactate clearance also did not vary significantly across neonates with blood culture positive or negative sepsis or normal or abnormal urine or Cerebrospinal Fluid (CSF) examination.

The mean duration of hospital stay was not found to be different in the positive and negative lactate clearance cohorts. Although there were differences in the mean values of the duration of fluid support, duration of oxygen support, duration of inotrope support, and duration of ventilation in preterm and term infants with negative and positive clearance, the differences were not statistically significant (p>0.05). These findings may be due to the fact that preterm neonates, even in the absence of sepsis or its co-morbidities, had a prolonged stay in the Neonatal Intensive Care Unit (NICU) due to various non infective complications. Studies with a larger sample size are more likely to overcome such bias. However, there was a significant percentage of persistent hypoglycaemia in the negative clearance group (29.4% vs. 3.2%, p=0.008), a statistically significant difference in the highest mode of ventilator support required (invasive vs. non invasive) (40.0% vs. 19.0%, p=0.042), and in the duration for which the neonate remained on Nil Per Mouth (NPM) (4.3 vs. 2.4 days, p=0.03).

Not many studies could be found on the role of lactate clearance in predicting the clinical course. A study conducted in Tibet on 67 ventilated neonates by Chen D et al., showed that lactate levels in neonates who died in the plateau group were significantly higher, and the lactate clearance rate was significantly lower than those in neonates who survived [25]. The cut-off points for the lactate clearance rate at six hours for predicting mortality were 6.09% in the plateau group. Another study by Mishra B et al., found that in the lactate clearance <10% group, inotropes (86.2% vs. 54.7%, p=0.0002) and ventilator support (89.6% vs. 66.6%, p=0.0015) were needed more than in the lactate clearance >20% group [26].

However, even after an extensive literature review, the authors failed to find any study correlating lactate clearance with the duration of hypoglycaemia, duration of NPM, mode of ventilation, or need for reintubation, etc. Therefore, there are practically no previous data to build on or compare these findings to. The present study helped the authors understand the importance of lactate clearance in early identification of sepsis and their subsequent prognosis, as well as the relationship between lactate clearance and many morbidity factors mentioned above (such as hypoglycaemia and duration of NPM). Therefore, lactate clearance can be incorporated in the future for early recognition of sepsis.

Limitation(s)

Being a hospital-based study with a limited time frame, the sample size was also limited. Hence, the data size was also small, and the resulting statistics might not accurately represent the population. Many neonates had clinical features suggestive of sepsis but could not be confirmed biochemically or microbiologically and had to be excluded from the study. Neonates with infections like meningitis had a prolonged duration of hospital stay due to their prolonged antimicrobial therapy, thereby skewing the distribution pattern. Severely ill neonates who died within a few days had a shorter duration of ventilation support, inotrope support, etc., thereby underestimating the severity of the aforementioned parameters.

CONCLUSION(S)

In conclusion, lactate clearance, being a simple and easily accessible test, can be utilised to provide important data regarding prognostication and early recognition of sepsis in neonatal care units, especially in nations with limited manpower and financial resources. However, unified guidelines are still lacking regarding this subject due to a lack of properly structured studies and meta-analyses. More studies need to be conducted to standardise the data and properly utilise this simple test, in order to reduce the overall burden of neonatal sepsis.

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