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THE ROLE OF SERUM LACTATE AND LACTATE CLEARANCE AS A SURROGATE MARKER FOR PEDIATRIC SEPSIS

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Abstract

Introduction: Sepsis is an important cause of mortality and morbidity in children. Paediatric sepsis in India has a high mortality rate of 40%, which necessitates early risk stratification and timely escalation of level of care for improving survival. Biochemical markers such as serum lactate are helpful in such cases. Lactate is frequently measured to estimate the extent of hypoxia at cellular level, and it correlates well with indices of end organ perfusion. Serum lactate level can be measured at bed side with rapid turn around time. Lactate testing is simple, inexpensive and reasonably sensitive tool for prognostication. Very few studies regarding lactate and lactate clearance have been done in paediatric population.

Materials and Methods: 46 children aged between 1 month and 14 years of age were studied. Arterial blood sample was collected, and lactate levels were measured bedside using Abbott i-STAT. 300 handheld blood analyser at admission, 6 hours, 12 hours, 18 hours, 24 hours, 36 hours and 48 hours. Lactate clearance was calculated. PRISM III score (Pediatric severity index) was done on all patients on admission. Chi-square test was applied to check the dependency of different parameters on outcome (survival or non-survival) of the patients. Unpaired t-test is used to compare the means of different parameters since the standard deviation of the population is unknown. Spearman's correlation coefficient between blood lactate on admission and PRISM III score was obtained. Sensitivity, specificity for diagnostic tests were obtained. Receiver's operative curve was also obtained to get the area under the curve and cut off point for prediction.

Results: Out of 46 cases, 45.7% were males and 54.3% were females. Majority (45.7%) cases were in the age groups of 1 to 5 years and 21.7% belonged to age <1 year. Mean age was 5.3 years in non-survivors and 4.9 years in survivors group. Lower respiratory tract infection was the major cause of PICU admission (43.47%). Majority (78.3%) had PRISM III score of 1 to 5. Majority of study participants had PRISM III score ranging between 1-5, followed by 11-15. Among 46 cases 91.3%

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had hyperlactatemia (>2mmol/L) on admission. Among 46 cases, 19.6% were non-survivors. Inotropes usage was 18.9% in survivors and 66.7% in non-survivors. This difference was found to be statistically significant (P value <0.05).

Conclusion: Mean lactate levels were always higher in non-survivors as compared to survivors at all points of time from admission till 48 hours. Area under the curve for lactate levels was significant at all time points for predicting mortality. The best cut off values of lactate for predicting mortality with maximum sensitivity and specificity were 4.94 mmol/l at admission, 4.15 mmol/l at 6 hours, 4 mmol/l at 12 hours, 3.75 mmol/l at 18 hours, 3.22 mmol/l at 24 hours, 2.85 mmol/l at 36 hours and 2.55 mmol/l at 48 hours. Mean PRISM III score was more in non-survivors (15.00) as compared to survivors (2.51) and this difference was found to be statistically significant.

Key Words: Sepsis, Lactate, Sensitivity, specificity, paediatric population.

INTRODUCTION

Sepsis is an important cause of mortality and morbidity in children.[1] WHO estimated that 80% of deaths in children below 4 years of age was sepsis related. Pediatric sepsis in India has a high mortality rate of 40%, which necessitates early risk stratification and timely intervention for improving survival.[2] Biochemical markers such as serum lactate, C-Reactive protein, procalcitonin are helpful in such cases.[3]

Lactate is produced by the tissues in body. It is produced maximum by muscles in the body. Under normal conditions, the liver rapidly clears lactate with a small amount being cleared by the kidneys.[4] In sepsis, systemic inflammation leads to impaired tissue oxygenation which increases production of serum lactate by anaerobic metabolism. Lactate is formed through reduction of pyruvate (product of glycolysis) by enzyme lactate dehydrogenase. In aerobic conditions pyruvate is oxidized to acetyl CoA by the enzyme pyruvate dehydrogenase (PDH). If action of PDH is inhibited as occurs in anaerobic conditions like hypoperfusion, pyruvate is converted to lactate. Lactate structurally exists in two isomers L-lactate and D- lactate.5 Lactate measured usually include only L-lactate (the primary isomer produced in humans).

Lactate is frequently measured to estimate the extent of hypoxia at cellular level, and it correlates well with indices of end organ perfusion. Elevation of serum lactate is an important marker of impaired tissue perfusion in children with sepsis. It can also be elevated even in the absence of arterial hypotension.

In early phase of shock resuscitation, lactate levels are more closely related to outcome when compared to parameters such as blood pressure.8 Sepsis patients who respond to treatment have higher level of lactate clearance.9 Serum lactate can be measured bedside with rapid turnaround time. Lactate testing is simple, reasonably sensitive, and an inexpensive tool for prognostication in a child with severe sepsis.

Very few studies were done to investigate the association of hyperlactatemia at admission and lactate clearance rate with mortality. This study was undertaken to determine

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if hyperlactatemia at admission and the lactate clearance can be used as a prognostic markers in critically ill children.

AIMS & OBJECTIVES

AIM: To explore the predictive ability of serum lactate and lactate clearance as prognostic markers of severity in children with sepsis.

Primary Objectives:

- To study the potential clinical utility of serum lactate levels as prognostic indicator in children with sepsis.
- To study the potential clinical utility of serum lactate clearance as a prognostic indicator in children with sepsis.

Secondary objective:

To study whether serum lactate clearance is superior to initial serum lactate levels for prognostication in children with sepsis.

MATERIALS AND METHODS

Ethical clearance: Prior to the commencement of study ethical clearance was obtained from institutional ethical review board the of ESIC Hospital, Sanathnagar.

Informed consent: Parents whose Children fulfilled the inclusive criteria were briefed about the nature of the study and a written informed consent was obtained from them and confidentiality was assured.

Study area: ESIC Medical College hospital and Super Speciality Hospital, Sanathnagar.

Study Duration: December 2020 – May 2021.

Sample Size: All children admitted with sepsis during study period were included in the study.

Taking OpenEpi info and using mean and SD of study by Kana Ram Jat et al minimum required sample size calculated was 38. Sample size was obtained by standard formula, Where “n” is sample size, “z” is confidence interval, “σ” is standard deviation, “e”is allowable error.

Study Population: All children between ages of 1 month to 14 years.

Inclusion Criteria: Children aged from 1 month to 14 years, admitted into PICU with diagnosis of sepsis were included. Sepsis was defined as per Surviving Sepsis Campaign.

Exclusion Criteria: Inborn error of metabolism, Chronic Liver Disease, Chronic kidney disease,

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Trauma, burns.

Study Design: Prospective cohort study

Method of measurement of outcome of interest: After an informed consent detailed history and physical examination was done. Demographic Data: age, gender, weight, comorbid conditions, nutritional status were collected. Arterial blood sample was collected, and lactate levels were measured bedside using Abbott i-STAT 300 handheld blood analyser, which was labelled as blood lactate on admission, other samples that were sent include serum electrolytes, RFT, CBC, APTT & PT. Repeat blood lactate was done at 6 hours, 12 hours, 18 hours, 24 hours, 36 hours and 48 hours. Equipment used for Blood lactate estimation was Abbott i-STAT 300 handheld blood analyser using CG4+ cartridge. Lactate clearance was calculated as –

Lactate clearance = (Initial lactate — Current lactate) x 100 / Initial lactate.

PRISM III score (Pediatric severity index) was done on all patients on admission. PRISM III score based on age-related physiological parameters were collected during the first 24 hours after admission. Parameters assessed were as follows systolic blood pressure, heart rate, temperature, pupillary reflexes, mental status, acidosis (pH and total CO2), pCO2, pO2, glucose, potassium, creatinine, blood urea, white blood cell count, platelet count and prothrombin or partial thromboplastin time. All patients were managed according to existing protocol of PICU. All patients were followed up till transfer from PICU or death. A favourable outcome being child discharged to home or shifted to ward.

Need for inotropes, mechanical ventilation and death considered as unfavourable outcome. Parameters like mechanical ventilation support, inotropic effect, death and duration of PICU stay were included in the data. Prognosis of patient in terms of survivors and non survivors and time taken for recovery from shock was determined and correlated with serum lactate and lactate clearance.

Statistical methods: Proportion and percentages were obtained for qualitative data, and mean, standard deviation was obtained for quantitative data. Chi-square test was applied to check the dependency of different parameters on outcome (survival or non-survival) of the patients. Unpaired t-test is used to compare the means of different parameters since the standard deviation of the population is unknown. Spearman's correlation coefficient between blood lactate on admission and PRISM III score was obtained. Sensitivity, specificity for diagnostic tests were obtained. Receiver's operative curve was also obtained to get the area under the curve and cut off point for prediction Analysis was done by using Microsoft office Excel and SPSS-22, with the help of a statistician.

RESULTS

Age	Frequency (n)	Percent (%)
<1 year	10	21.7
1-5 years	21	45.7
6-10 years	7	15.2
>10 years	8	17.4
Total	46	100.0

Table 1: Distribution according to age

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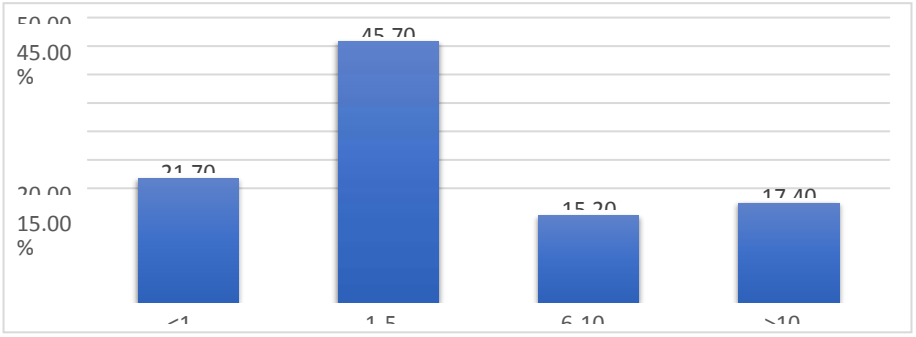

Fig 1: Distribution according to age

Majority of study participants belong to age group of 1-5 years, followed by less than one year and 6-10 years age group.

Sex	Frequency (n)	Percent (%)
Female	25	54.3
Male	21	45.7
Total	46	100.0

Table 2: Distribution according to sex

In the present study, female participants were more as compared to male participants.

Disease	Frequency (n)	Percent (%)
Lower Respiratory tract infections	20	43.4
Gut-associated sepsis	8	17.3
Central Nervous system associated sepsis	5	10.8
Tropical fevers (dengue /enteric /scrub with secondary infection)	9	19.5
Cardiac associated sepsis	2	4.3
Others	2	4.3
Total	46	100

Table 3: Distribution according to Etiology

Majority of the cause of sepsis was LRTI related (43.4%) followed by tropical fever (dengue /enteric /scrub with secondary infection) (19.5%).

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Lactate Level	Frequency (n)	Percent (%)
Normal (<2mmol/L)	4	8.7
Hyperlactatemia (>2mmol/L)	42	91.3
Total	46	100.0

Table 4: Distribution according to lactate levels on admission

Lactate levels at admission were below 2 mmol/L in 8.7% and above 2 mmol/L in 91.3% participants.

Outcome	Frequency (n)	Percent (%)
Survivors	37	80.4
Non-Survivors	9	19.6
Total	46	100.0

Table 5: Distribution according to outcome

In the present study, 19.6% were non-survivors.

	Non-Survivors		Survivors		p-Value
	Mean	SD	Mean	SD	
On Admission	5.12099	2.083063	3.38318	1.250280	.002
At 6 hours	4.600	2.0922	3.019	1.1158	.003
At 12 hours	4.20988	2.186127	2.75976	1.071361	.006
At 18 hours	3.571	1.1572	2.481	.8888	.007
At 24 hours	3.58730	1.177139	2.29730	.885043	.002
At 36 hours	3.371	1.3732	2.097	.7418	.001
At 48 hours	3.26984	1.672652	1.90090	.676260	.001

Table 6: Distribution according to mean lactate levels between survivors and non-survivors

As shown in the above table, mean lactate levels were always higher in non-survivors as compared to survivors at all points of time from admission till 48 hours. The difference was found to be statistically significant at all time intervals (P value <0.05). This shows that high lactate levels were associated with high chances of mortality.

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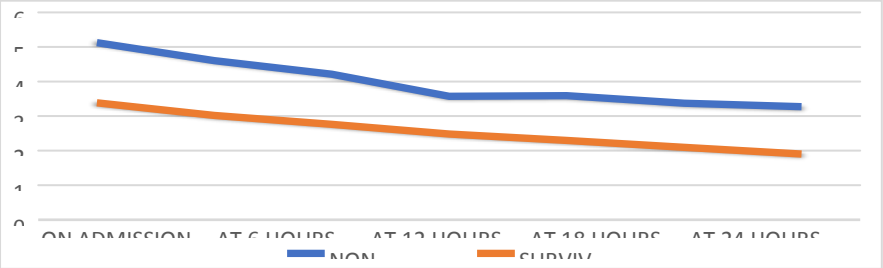
Fig 2: Distribution according to mean lactate levels between survivors and non-survivors



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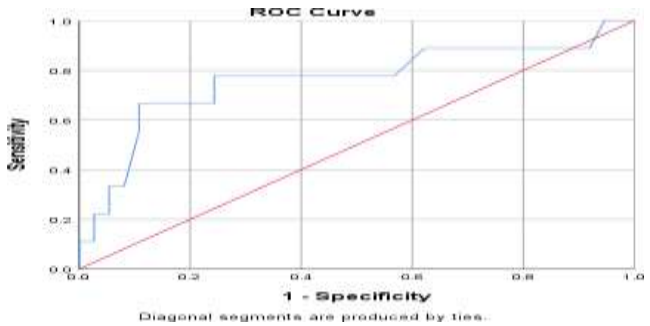

Fig 3: ROC curve for lactate levels at admission

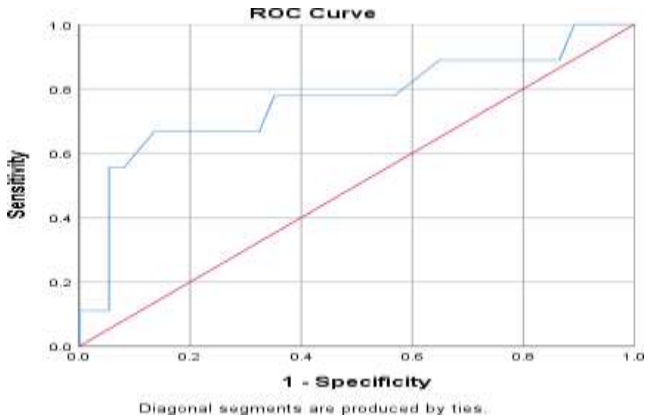

Fig 4: ROC curve for lactate levels at 6 hours

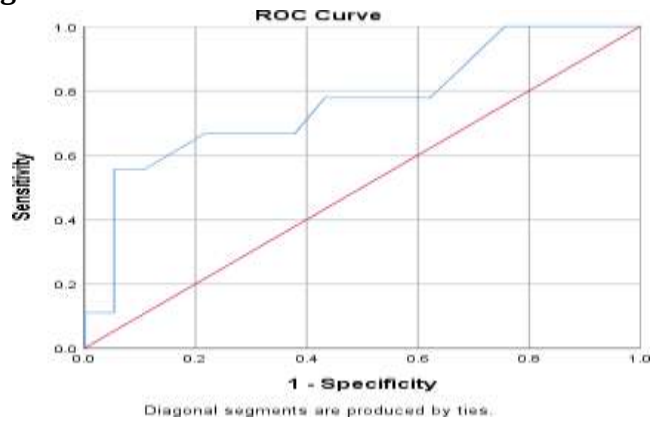

Fig 5: ROC curve for lactate levels at 12 hours

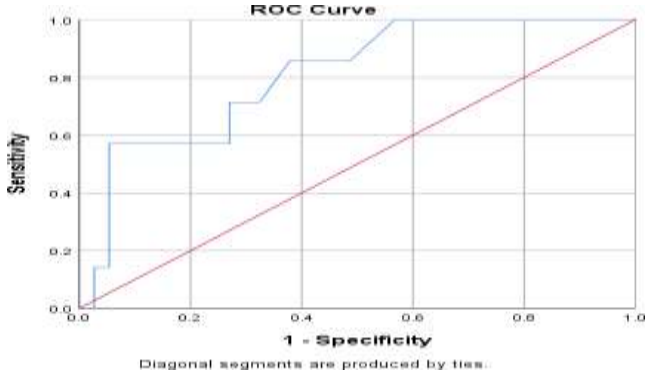

Fig 6: ROC curve for lactate levels at 18 hours

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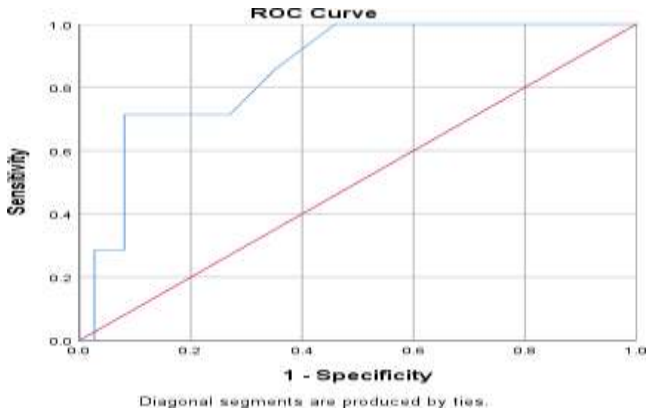

Fig 7: ROC curve for lactate levels at 24 hours

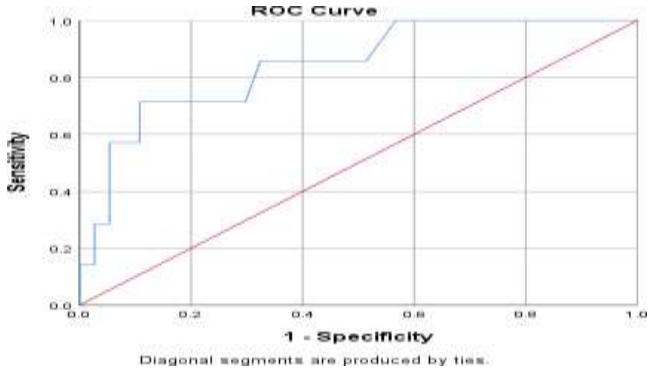

Fig 8: ROC curve for lactate levels at 36 hours

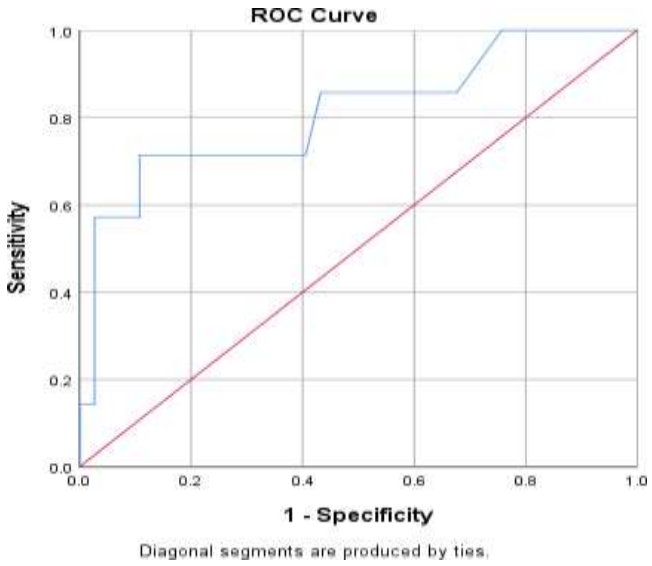

Fig 9: ROC curve for lactate levels at 48 hours

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	Area under curve	Std. Error	p-value	95% CI	
				Lower bound	Upper Bound
At admission	.761	.105	.016	.555	.968
At 6 hours	.761	.103	.016	.559	.964
At 12 hours	.760	.096	.017	.571	.949
At 18 hours	.809	.081	.010	.651	.967
At 24 hours	.855	.067	.003	.725	.986
At 36 hours	.844	.078	.004	.690	.997
At 48 hours	.811	.101	.010	.612	1.000

Table 7: According to area under the curve of lactate levels (ROC curve)

Area under the curve for lactate levels was significant at all time points for predicting mortality as shown in the above table.

	Lactate cut off	Sensitivity	Specificity
At admission	4.944	66.7%	89.2%
At 6 hours	4.15	66.7%	86.5%
At 12 hours	4.00	55.6%	94.6%
At 18 hours	3.75	57.1%	94.6%
At 24 hours	3.222	71.4%	91.9%
At 36 hours	2.85	71.4%	89.2%
At 48 hours	2.555	71.4%	89.2%

Table 8: According to lactate levels (ROC curve) and its sensitivity and specificity

The best cut off values of lactate for predicting mortality with maximum sensitivity and specificity were 4.94 mmol/l at admission, 4.15 mmol/l at 6 hours, 4 mmol/l at 12 hours, 3.75 mmol/l at 18 hours, 3.22 mmol/l at 24 hours, 2.85 mmol/l at 36 hours and 2.55 mmol/l at 48 hours.

	Non-Survivors		Survivors		p-Value
	Mean	SD	Mean	SD	
At 6 hours	4.769	3.068	10.765	18.960	.353
At 12 hours	3.684	18.832	19.726	35.083	.194
At 18 hours	8.499	16.045	32.219	24.010	.017
At 24 hours	16.0344	13.181	42.320	20.593	.002
At 36 hours	18.197	11.622	52.583	18.615	.001

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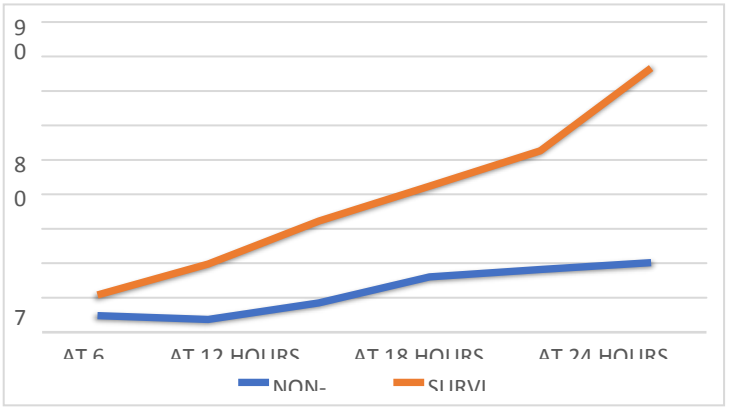
At 48 hours	20.158	10.987	76.613	12.709	.001

Table 9: Distribution according to mean lactate clearance levels between survivorsand non-survivors

As shown in the above table, mean lactate clearance levels were always lower in non-survivors as compared to survivors at all points of time from admission till 48 hours. The difference was found to be statistically significant at all time intervals (P value <0.05) except at 6 hours and 12 hours. This shows that low lactate clearance levels were associated with high chances of mortality.

Fig 10: Distribution according to mean lactate clearance levels between survivorsand non-survivors



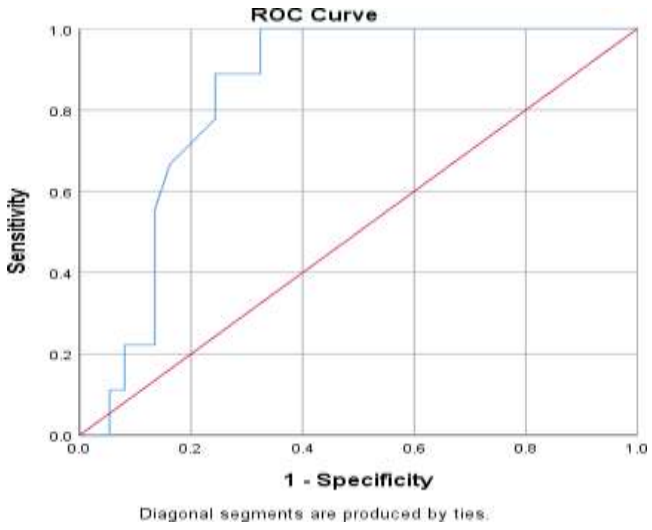


Fig 11: ROC curve for lactate clearance at 6 hours

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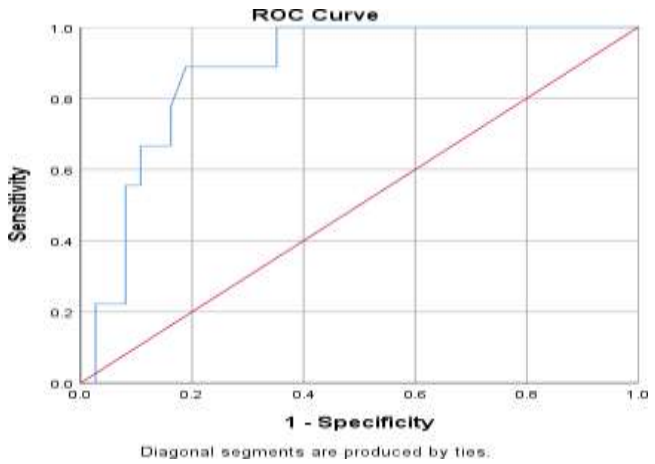

Fig 12: ROC curve for lactate clearance at 12 hours

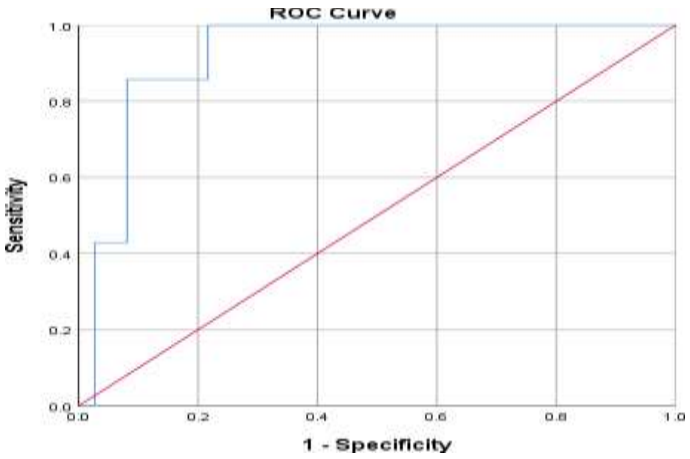

Fig 13: ROC curve for lactate clearance at 18 hours

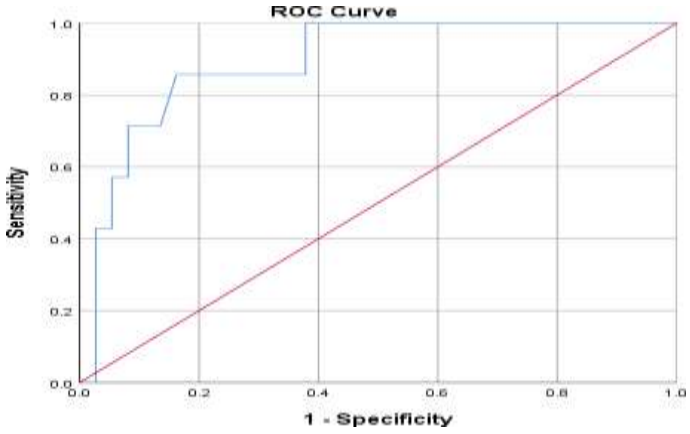

Fig 14: ROC curve for lactate clearance at 24 hours

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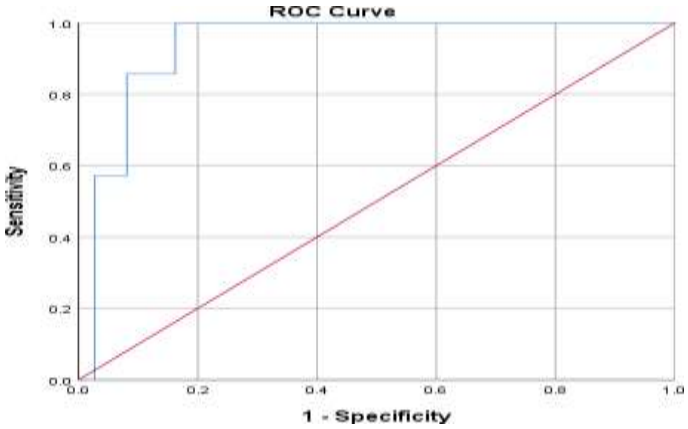

Fig 15: ROC curve for lactate clearance at 36 hours

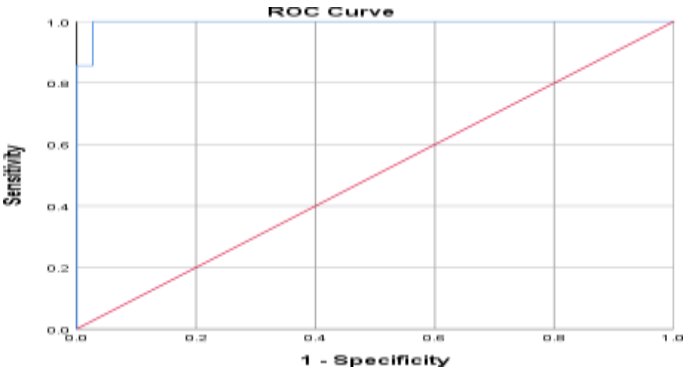

Fig 16: ROC curve for lactate clearance at 48 hours

	Area under curve	Std. Error	P value	95% CI	
				Lower bound	Upper Bound
At 6 hours	.838	.058	.002	.725	.951
At 12 hours	.878	.052	.000	.776	.980
At 18 hours	.923	.042	.000	.840	1.000
At 24 hours	.892	.057	.001	.780	1.000
At 36 hours	.938	.037	.000	.866	1.000
At 48 hours	.996	.006	.000	.984	1.000

Table 10: According to area under the curve of lactate clearance levels (ROC curve)

Area under the curve for lactate clearance levels was significant at all time points for predicting mortality as shown in the above table.

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	Lactate clearance % cut off	Sensitivity	Specificity
At 6 hours	7.41%	100%	67.6%
At 12 hours	14.95%	88.9%	81.1%
At 18 hours	24.44%	100%	78.4%
At 24 hours	25.83%	85.7%	83.8%
At 36 hours	38.58%	100%	83.8%
At 48 hours	40.94%	100%	97.3%

Table 11: According to lactate clearance levels (ROC curve) and its sensitivity and specificity

The best cut off values of lactate clearance for predicting mortality with maximum sensitivity and specificity were 7.41% at 6 hours, 14.95% at 12 hours, 24.44% at 18 hours, 25.83% at 24 hours, 38.58% at 36 hours and 40.94% at 48 hours.

PRISM III score	Frequency (n)	Percent (%)
0	1	2.2
1-5	36	78.3
6-10	0	0.0
11-15	6	13.0
16-20	3	6.5
Total	46	100.0

Table 12: Distribution according to PRISM III score

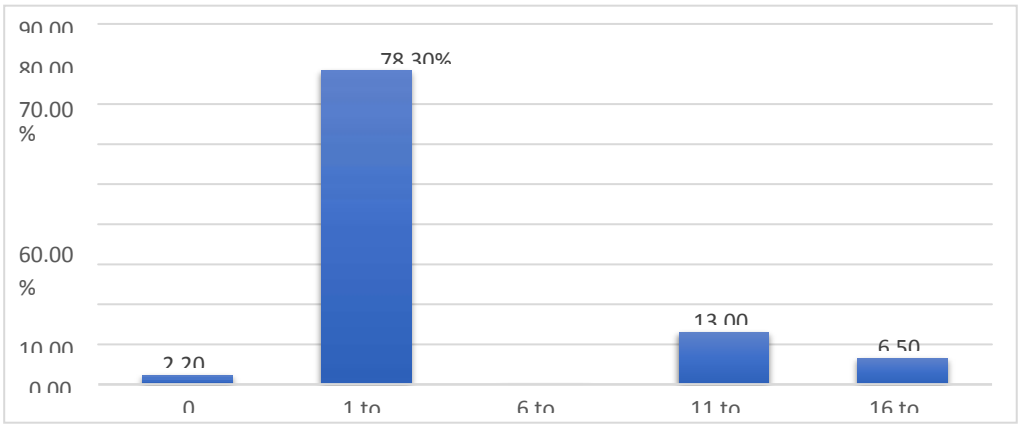

Fig 17: Distribution according to PRISM III score

Majority of study participants had PRISM III score ranging between 1-5, followed by 11-15.

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		Lactate On Admission
PRISM III Total	Pearson Correlation	.469
	p Value	.001
	N	46

Table 13: Pearson Correlation between PRISM III score and Lactate on admission

Positive correlation was observed between lactate on admission and PRISM III score.

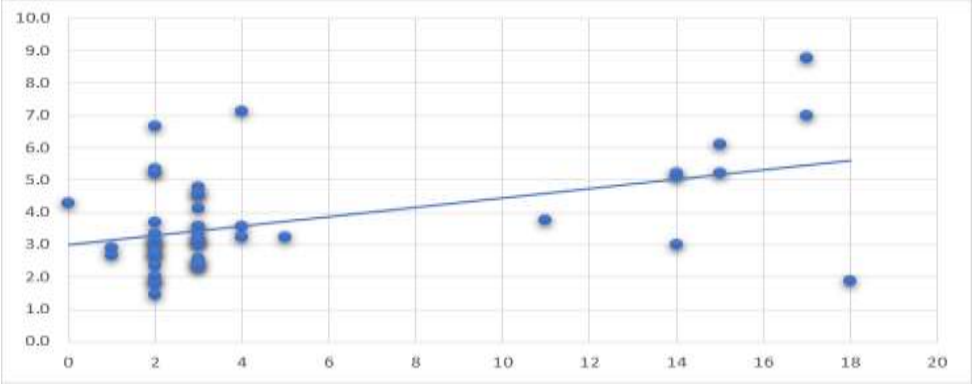

Fig 18: Pearson Correlation between PRISM III score and Lactate on admission

	Non-Survivors		Survivors		p-Value
	Mean	SD	Mean	SD	
Age (years)	5.367	5.2877	4.951	4.7752	.820
PRISM III	15.00	2.121	2.51	.932	.001
Inotropes Duration	4.333	3.0768	3.857	1.0690	.707
No. of inotropes	1.833	.7528	1.714	.7559	.782
Duration of PICU stay	4.3056	3.03567	5.6757	2.40433	.152

Table 14: Interventions amongst survivors and non-survivors

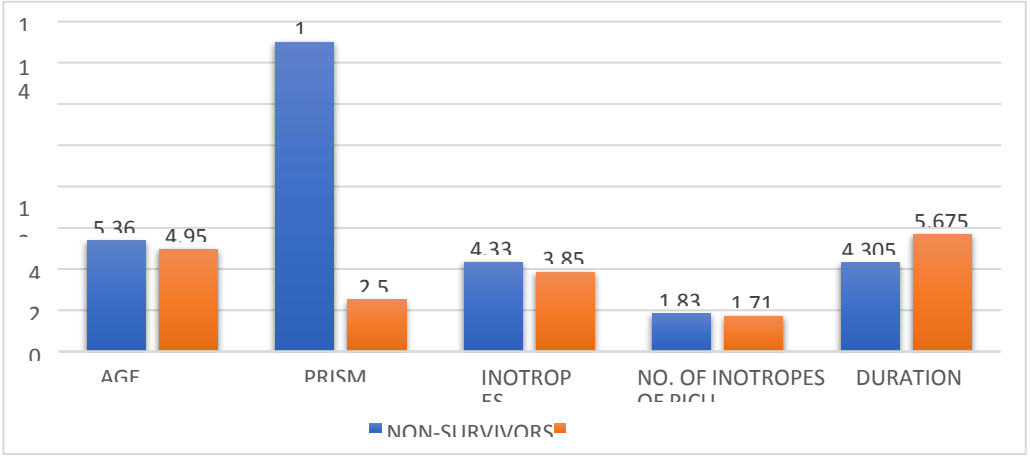

Fig 19: Interventions amongst survivors and non-survivors

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Mean age was 5.3 years in non-survivors and 4.9 years in survivors group. The difference was not found to be statistically significant (P value >0.05). Mean PRISM III score was more in non-survivors (15.00) as compared to survivors (2.51) and this difference was found to be statistically significant (P value <0.05). Mean duration of inotropes was more in non-survivors as compared to survivors but the difference was not found to be statistically significant (P value >0.05). There is no significant difference between number of inotropes between non-survivors and survivors (P value >0.05). There is no significant difference between duration of PICU stay between non-survivors andsurvivors (P value >0.05).

			Outcome		Total
			Survivors	Non-Survivors	
Sex	Female	Count	20	5	25
		%	54.1%	55.6%	54.3%
	Male	Count	17	4	21
		%	45.9%	44.4%	45.7%
Total		Count	37	9	46
		%	100.0%	100.0%	100.0%

Table 15: Comparison between sex and outcome (Chi Square = 0.085, p Value =0.770)

As shown in the above table, there is no significant difference of sex distribution between survivors and non-survivors (p value >0.05).

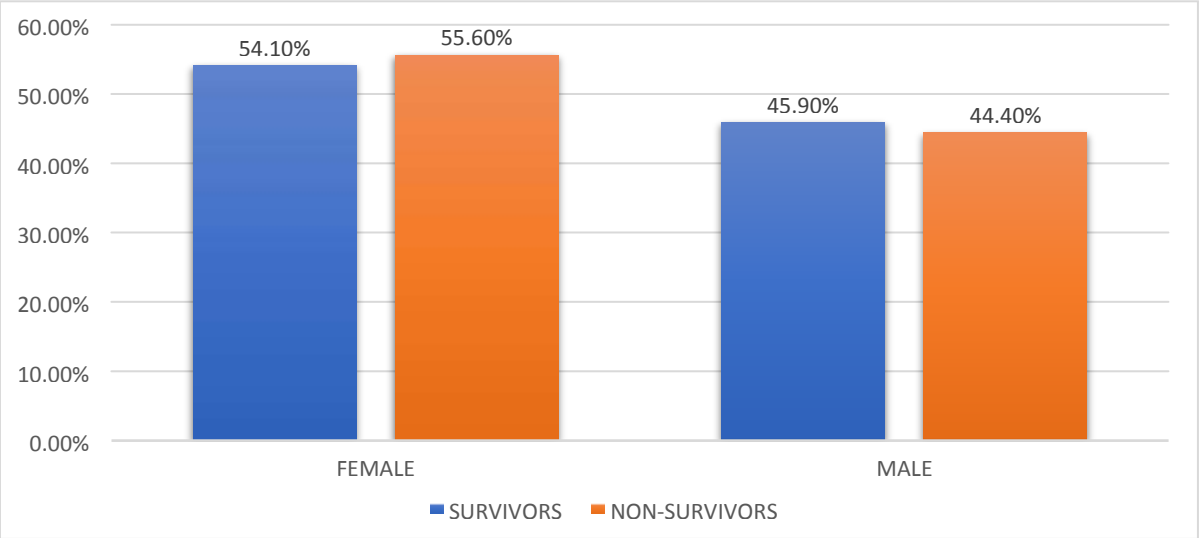

Fig 20: Comparison between sex and outcome

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			Outcome		Total
			Survivors	Non-Survivors	
Inotropes	No	Count	30	3	33
		%	81.1%	33.3%	71.7%
	Yes	Count	7	6	13
		%	18.9%	66.7%	28.3%
Total		Count	37	9	46
		%	100.0%	100.0%	100.0%

Table 16: Relation of outcome with initiation of inotrope support within 6 hours of admission (Chi Square = 5.956, p Value = 0.015)

Inotropes usage was 18.9% in survivors and 66.7% in non-survivors. This difference was foundto be statistically significant (P value <0.05).

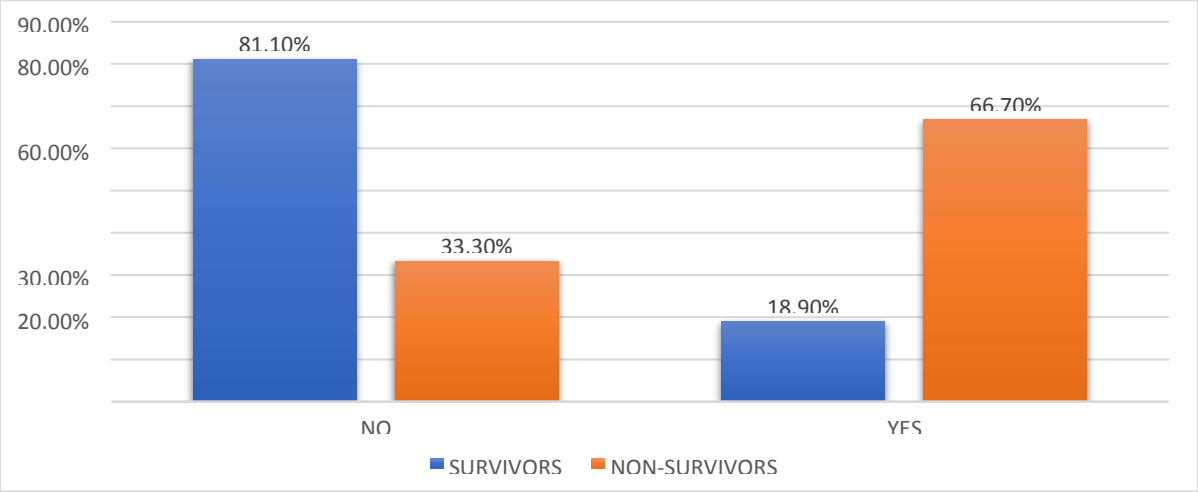

Fig 21: Relation of outcome with initiation of inotrope support within 6 hours ofadmission

DISCUSSION

Baseline characteristics: Among 46 children in our study, 10 (21.7%) were infants, 21 (45.7%) in the age group of 1-5 years. Patients above 5 years of age were 15 (32.6%) out of 46 patients. In a previous study by Umashankar infants were the largest group. In their study 47.3 % were infants, 38.2 % were between 1 to 5 years of age group. In infants and younger children, the incidence of sepsis and associated mortality is higher. Most of the cases in our study were infants and children between 1 to 5 years of age, which was similar to a study done by Jat etal.[6]

In our study, out of 46 cases we observed that 21 were males and 25 were females, with a female preponderance of 54.3%. A study published in 2016 by Umashankar showed male predominance (54.5%) as compared to females (45.5%), but Choudhury J et al. found female predominance (male:female -1:2) in their study.

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Hyperlactatemia has been detected in critically ill patients and several clinical studies have shown an association between its levels and outcome, with higher levels in those patients who will eventually die. In our study population the mean blood lactate level of patients who died (5.12 ±2.08 mmol/L) was higher than who survived (3.38 ±1.25 mmol/L). Only 8.7% patients were with normal lactate levels at admission and majority (91.3%) were with hyperlactatemia. Bai et al observed similar findings as 77% patients were with a high level of lactate at admission (>2 mmol/l). Broder and Weil noted that only 11% of those with lactate level >4mmol/L survived. Smith et al also observed higher lactate levels at admission. Moreover Smith et al. suggest that hyperlactatemia can identify patients at risk of deaths and can also be used as indicator of ICU admission. Trials have demonstrated the prognostic value of lactate levels in post cardiac surgery patients, surgical patients, in infections/sepsisand septic shock.[7]

In our study, we have taken second lactate sample after 6 hours of admission to allow adequate time for the lactate to be cleared from the liver and kidney. A study done by Areesha et al, showed that lactate levels done after six hours showed best results of lactate clearance, and lactate levels done before didn't allow adequate time for its clearance.[8]

In our study, all seven lactate levels at - admission, 6hours, 12 hours, 18 hours, 24 hours, 36 hours, and 48 hours were significantly higher among non survivors than survivors. Similar results were found in a study by Choudhury J et al. where lactate levels were significantly higher in non-survivors in comparison to survivors. Sanz et al. found out that PIM (Pediatric Index Mortality) and lactate have a prognostic value in critically ill children. Siegel et al. observed that, in children admitted to the ICU after a cardiac surgery, high levels of lactate had a positive predictive value of 100% and a negative predictive value of 97% for death. By using univariate logistic regression, Duke et al. found that lactate allowed distinguishing survivors from non-survivors among children with sepsis at 12 and 24 hours of admission. Hatherill et al. suggest that hyperlactatemia can indicate death on admission andif it persists after 24 hours of treatment.

In our study, the best cut off values of lactate for predicting mortality with maximum sensitivity and specificity were 4.94 mmol/l at admission, 4.15 mmol/l at 6 hours, 4 mmol/l at 12 hours, 3.75 mmol/l at 18 hours, 3.22 mmol/l at 24 hours, 2.85 mmol/l at 36 hours and 2.55mmol/l at 48 hours.

In the present study serial blood lactate measurements at admission (p=0.016), 6 hours (p=0.016), 12 hours (p=0.017), 18 hours (p=0.010), 24 hours (p=0.003), 36 hours (p=0.004), and 48 hours (p=0.000) was significantly higher in patients who died. The area under ROC curve for lactate level at admission was 0.761 (CI=0.555 to 0.968), at 6 hours was 0.761 (CI=0.559 to 0.964), at 12 hours was 0.760 (CI=0.571 to 0.949), at 18 hours was 0.760 (CI=0.651 to 0.967), at 24 hours was 0.855 (CI=0.725 to 0.986), at 36 hours was 0.844 (CI=0.690 to 0.997) and at 48 hours was 0.811 (CI=0.612 to 1.000). The area under ROC curve for lactate of 4.94, 4.15, 4.00, 3.75, 3.22, 2.85, and 2.55 mmol/L at admission, 6 hours, 12 hours, 18 hours, 24 hours, 36 hours, and 48 hours was significant for prediction of mortality. In our study, the best sensitivity (71.4%) and specificity (91.9%) was with lactatelevels at 24 hours with significant area under ROC curve (AUC=0.855).

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Serial lactate estimation: In our study, admission lactate levels of 4.99mmol/L produced best sensitivity (66.7%) and specificity (89.2%). At 6 hours best sensitivity (66.7%) and specificity (86.5%) were obtained for blood lactate levels greater than 4.15mmol/L. At 12 hours best sensitivity (55.6%) and specificity (94.6%) were obtained for blood lactate levels greater than 4.0mmol/L. The best sensitivity (57.1%) and specificity (94.6%) for lactate level of 3.75 mmol/L were obtained at 18 hours. Best sensitivity (71.4%) and specificity (91.9%) at 24 hours were obtained for lactate levels at 3.22mmol/L. Best sensitivity (71.40%) and specificity (89.2%) at 48 hours for lactate levels at 2.55mmol/L. In a study by Koliski et al. 3mmol/L had the best sensitivity and specificity at 24 hours of lactate estimation, which was almost similar to our study. In previous studies by Duke et al. and Koliski et al a lactate level >3 mmol/l significantly predicted mortality which was 5 mmol/l in a study by Jat et al. The reason for this difference may be patient selection as Duke et al. included patients with sepsis with or without shock while Kana Ram Jat et al. included only patients with septic shock where high lactate levels was expected.

PRISM III score and admission lactate: The PRISM III score is the most accepted as a valid measure of illness severity in the first 24 hours after admission and reflects the clinical picture of a child during the early admission Period. Previous studies suggest that PRISM III is an important tool in predicting mortality and clinical outcomes in the paediatric population, the association of admission blood lactate with in-hospital mortality in this study was independent of age, gender. In previous study by Bai et al. multivariate regression analysis showed that high blood lactate level and high prism score were independent risk factors for mortality. In our study Spearman's Correlation Coefficient between blood lactate on admission and PRISM III score is r= 0.469 (p=0.001). There is positive correlation between blood lactate on admission and PRISM III score. Similarly in a study by Jat et al. Spearman's Correlation Coefficient between blood lactate on admission and PRISM III score was used and was found to be highly positive (p=0.003).

Lactate clearance: Lactate clearance is rate of fall in lactate after resuscitation is started. This has shown some promise in predicting mortality in patients with sepsis. In the present study lactate levels were estimated at admission, 6 hours, 12 hours, 18 hours, 24 hours, 36 hours and 48 hours and the clearance was calculated as follows —

Lactate clearance = (Initial lactate - Current lactate) x 100 / Initial lactate.

The best cut off values of lactate clearance for predicting mortality with maximum sensitivity and specificity were 7.41% at 6 hours, 14.95% at 12 hours, 24.44% at 18 hours, 83% at 24 hours, 38.58% at 36 hours and 40.94% at 48 hours.

Several studies in severe septic patients pointed out values of lactate clearance in 6 hours but no data is available for longer duration. In a study by Munde et al. lactate clearance of <30% at 6 hours for prediction of mortality in PICU admitted children had a sensitivity of 75% and specificity of 97%, area under ROC curve was 0.977 (CI=0.943 to 1.012) for prediction of mortality.[86] The area under ROC Curve is high in their study because of high cut off value of lactate clearance (<30%) and high mortality (90%) among delayed on non- lactate clearance group.

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From our study we found out that high lactate levels at admission correlated well with severity of sepsis. Lactate clearance even though was high in survivors when compared to non-survivors, the clearance was not significant till 12 hours of resuscitation. So, in the initial period of resuscitation, lactate levels can be used as a marker for prognostication in sepsis, and as time progresses lactate clearance can also be used as a marker of prognostication.[9]

In our study relationship between survivors and non-survivors which are statistically significant are patient with shock, PRISM III score, mean blood lactate value on admission, and duration of PICU stay. But age, sex, need of mechanical ventilation and inotropic support are not statistically significant. Choudhury et al. in his study found similar results about age of the patient. Similarly in a study by Jat et al. found significant difference in PRISM III Score and mean lactate levels in survivors and non-survivors.[10]

In our study 80.4% were survivors while 19.6% died. In a study by Koliski et al. mortality was 24%, mortality was 26.66% in a study by Munde et al., 10.4% in a study byBai et al and 10% in a Study Kana Ram Jat et al.

CONCLUSION

Mean lactate levels were always higher in non-survivors as compared to survivors at all points of time from admission till 48 hours. Area under the curve for lactate levels was significant at all time points for predicting mortality. The best cut off values of lactate for predicting mortality with maximum sensitivity and specificity were 4.94 mmol/l at admission, 4.15 mmol/l at 6 hours, 4 mmol/l at 12 hours, 3.75 mmol/l at 18 hours, 3.22 mmol/l at 24 hours, 2.85 mmol/l at 36 hours and 2.55 mmol/l at 48 hours. Mean PRISM III score was more in non-survivors (15.00) as compared to survivors (2.51) and this difference was found to be statistically significant. In our study, blood lactate and PRISM III score on admission had a positive correlation. Mortality was 23.5% in patients with hyperlactatemia on admission. Mean lactate clearance levels were always lower in non-survivors as compared to survivors at all points of time from admission till 48 hours. Area under the curve for lactate clearance levels was significant at all time points for predicting mortality.

Lactate clearance even though was high in survivors when compared to non-survivors, the clearance was not significant till 12 hours of resuscitation. So, in the initial period of resuscitation, lactate levels can be used as a marker for prognostication in sepsis, and as time progresses lactate clearance can also be used as a marker of prognostication. The best cut off values of lactate clearance for predicting mortality with maximum sensitivity and specificity were 7.41% at 6 hours, 14.95% at 12 hours, 24.44% at 18 hours, 25.83% at 24 hours, 38.58% at 36 hours and 40.94% at 48 hours.

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