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Original Research Article

STUDY ON ROLE OF SERUM LACTATE LEVELS AND LACTATE CLEARANCE TO PREDICT THE OUTCOME OF PATIENTS WITH PAEDIATRIC SHOCK IN RURAL TERTIARY CARE TEACHING HOSPITAL

Article History:

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Abstract: ***Background***: Shock remains a leading cause of morbidity and mortality in Paediatric Intensive Care Units (PICU). Serum lactate levels serve as a biomarker for tissue hypoxia and hypo perfusion, with serial monitoring potentially predicting patient outcomes. ***Objective:*** To assess the correlation between serial lactate level monitoring and lactate clearance with clinical outcomes in critically ill children with shock. ***Methods***: This prospective observational cohort study was conducted from December 2020 to November 2023 in two tertiary care teaching hospitals in rural Maharashtra, India. 144 critically ill children admitted to PICU with shock were enrolled. Serum lactate levels were measured at admission and 12-24 hours post-admission. Patients were excluded if they had suspected inborn errors of metabolism or died within 24 hours of admission. ***Results:*** Of 144 patients, 58 (40.6%) died. While initial lactate levels >4 mmol/L showed a mortality rate of 37.8%, the second lactate level >4 mmol/L (measured 12-24 hours post-admission) was associated with significantly higher mortality at 68.7%. The mean change in lactate levels among patients who died was -4.19 mmol/L, indicating worsening hyperlactatemia. Cardiogenic and septic shock had the highest mortality rates. Decreased lactate clearance was strongly associated with poor outcomes. *Conclusions:* Serial lactate monitoring is superior to single measurements for predicting outcomes in paediatric shock. Early identification and correction of tissue hypoperfusion are critical to preventing multi-organ dysfunction syndrome (MODS) and reducing mortality. Persistent or worsening hyperlactatemia (>4 mmol/L at 12-24 hours) is a strong predictor of mortality, emphasizing the importance of lactate clearance assessment in guiding clinical management.

Keywords: Paediatric Intensive Care Unit, Shock, Lactate levels, Lactate clearance, PICU Outcome.

INTRODUCTION

In thePaediatric Intensive Care Unit (PICU), though shock is one of the most commonly diagnosed etiology, it is still poorly understood. Academic definitions of shock include an acute state that results from cardiovascular malfunction and the circulatory system's inability to effectively supply nutrients and oxygen to fulfil the metabolic demands of essential organs. (1) The diagnosis is still based on the clinical element of the criteria, and hypotension is not a requirement. Septic shock is the most prevalent life-threatening illness affecting children globally.

Because it provides 90% of the body's energy requirements, aerobic metabolism requires oxygen. When there is tissue-level hypoxia, cells switch to anaerobic metabolism, which is less effective since it is unable to maintain normal aerobic cellular metabolism. Lactic acid is a by-product of anaerobic metabolism, which occurs when the body's cells are not easily accessible to oxygen. (2)

Lactate is the end product of anaerobic glycolysis, the final step of which is the conversion of pyruvate into lactate by the enzyme lactate dehydrogenase (LDH). Lactic acid is produced by various cells in the body, including muscle cells, red blood cells and neurons. Lactic acid is often considered the waste product of glycolysis. But as always with metabolism, there is no such thing as waste. In a fasted state, lactate can be taken up by other organs and continue its way to the tricarboxylic acid (TCA) cycle. In addition, lactate can serve as a substrate in signalling pathways.(3,4)

Oxygen debt, which results in lactic acidosis and gradual clinical deterioration, is caused when there is an imbalance between the amount of oxygen delivered to the tissue and the amount of oxygen that is needed. The estimation of the blood's lactic acid content makes the serum lactate level a relatively sensitive and reliable biomarker of tissue hypoxia and hypoperfusion. (5,6)Various underlying disease processes commonly result in reduced tissue perfusion in sick children. The development of Multi-Organ Dysfunction Syndrome (MODS) may result from delayed identification of tissue hypoperfusion.If not promptly identified and rectified, this has an adverse effect on mortality and morbidity rates. (7)
Regardless of whether the primary underlying pathophysiologic change is hypovolemic, cardiogenic, obstructive, or distributive, lactate concentrations rise in all types of shock.(8)

The purpose of the current study was to assess the serial lactate levels in children experiencing septic shock and to link such levels with the outcome.

Objectives:
To assess the relationship between serial lactate levels monitoring and lactate clearance and correlate the outcome in the children with shock.

MATERIAL AND METHODS

Study design: Prospective observational cohort study
Setting:AcharyaVinobaBhave Rural Hospital (AVBRH), Sawangi and Jawaharlal Nehru Medical College (JNMC), Wardhaare tertiary care teaching hospitals in rural Maharashtra. The Pediatrics Department in AVBRH and JNMC are well-equipped with 20-bedded PICU. From December 2020 to November 2023, this study was carried out at the Pediatric Intensive Care Units (PICU) at the Jawaharlal Nehru Medical College, Wardha and AVBRH Hospital in Sawangi, Wardha by DrMesharam RJ. The data analysis, draft preparation, review and critical inputs were done by DrAnupamBaheBapan, Associate Professor, Indira Medial College and Hospital, Pandur, Tamil Nadu and DrSwarnaLatha J, Team Lead, PICU and Paediatric Emergencies, Tx Children’s Hospital, Banjara Hills, Hyderabad.
Inclusion Criteria:
oAll critically ill children in PICU who are in shock

Exclusion Criteria:
Suspected or confirmed cases of Inborn Errors of Metabolism
Death within 24 hours after admission to the PICU
Sample size calculation:
The result is derived using the formula for sample size in a one-sample proportion hypothesis test with specified power and significance level.
Step 1:Defining Parameters and Critical Values
The following parameters are provided or derived:
Hypothesized population percentage (Null Hypothesis, p_0):0.23
Alternative percentage (p_a):0.35
Significance level (α): 0.05 (two-sided), which gives a Z-score ($Z\alpha/2$) of approximately 1.96.
Power ($1-\beta$): 0.90 (90%), which means β=0.10. The Z-score for β ($Z\beta$)is approximately 1.282.
Difference to detect (d): $pa-p0=0.35-0.23=\mathbf{0.12}$
Step 2: Applying the Sample Size Formula
The formula used to calculate the sample size (n) for a one-sample proportion test with power is:
n=((Z_(α/2) √(p_0 (1-p_0))+Z_β √(p_a (1-p_a)))^2)/((p_a-p_0)^2)
Step 3: Calculation of Sample Size
Substitute the values into the formula:
$Z\alpha/2 = 1.96$
$Z\beta = 1.282$
$p0 = 0.23$
$1-p0 = 0.77$
$pa = 0.35$
$1-pa = 0.65$
$pa-p0 = 0.12$
n=((1.96√(0.23(0.77))+1.282√(0.35(0.65)))^2)/((0.12)^2)
Intermediate Calculations:
√(0.23(0.77))≈0.42178
√(0.35(0.65))≈0.4770
1.96×0.42178≈0.82669
1.282×0.4770≈0.6114
0.82669+0.61145≈1.43814
(1.43814)^2≈2.06836
(0.12)^2=0.0144
n≈2.06836/0.0144≈143.63

The result is typically rounded up to the nearest whole number to ensure sufficient power, so n=**144** using these standard Z-values.

Ethical Approval

The approval of the institutional ethical committee of the University of DMIMS was taken. IEC no: DMIMS (DU)/IEC/2020-21/9275.

Methodology:

The study was carried out from October 2020 to November 2022 in the Paediatric Intensive Care Unit (PICU) at the AVBRH hospital in Sawangi and Jawaharlal Nehru Medical College, Wardha. Based on the inclusion criteria and non-randomized purposive sampling, 144 critically sick children admitted to the Paediatric Intensive Care Unit were selected. Based on the medical history, physical examination and investigations, patients were categorised according to the type of shock they were experiencing: Septic Shock, Cardiogenic Shock, Warm Shock, Obstructive Shock and Neurogenic Shock. When treating shock victims, the calculation of serum lactate levels is often done to direct therapy.

Data Collection:

The patients admitted at AVBRH and JNMC, fulfilling the inclusion criteria were included in the study.The intension of the study was explained to the parents in detail and their children were enrolled in the study after obtaining a written informed consent from them. Relevant demographic essentials like age, gender, admission, diagnosis and associated risk factors like malnutrition were collected.

The cases were transferred from the regular paediatric ward to the PICU or admitted through casualty during emergency hours. All subjects underwent an anthropometric evaluation after initial stabilization. When a patient was admitted to the PICU, the clinical history, general and systemic examination were once again performed and a tentative diagnosis was made. All routine and specialised investigations were sent for the cases as was deemed necessary.

The calculation and evaluation of 1st and 2nd lactate levels and change in lactate levels was done as follows. The negative change in lactate level indicates that the 2nd lactate level was more than the 1st lactate level and there is decreased lactate clearance. Positive value of change in lactate levels indicate that the 2nd lactate level was less than the 1st lactate level and there was increased lactate clearance.

Treatment was started in accordance with the child's condition as the examination progresses. SOFA score was used to categorise the child's severity, as shown in the table below. The SOFA score demonstrated fair to good accuracy for predicting in-hospital mortality when applied to patients with severe sepsis with evidence of hypoperfusion at the time of ED presentation. (9)The clinical state was determined by evaluating the vital signs,organ manifestations, existence of associated comorbiditiesand the patient's progress during the hospital stay. Anynecessary surgical, medical, and therapeutic interventions were documented in the case record form. According to the Surviving Sepsis Campaign (SSC) guidelines,(10)care was considered correctly initiated if the child developed Multi-Organ Dysfunction Syndrome (MODS) while already undergoing treatment for sepsis. On institutional procedures for the care of paediatric shock, all evaluations and actions were predicated.

RESULTS

SOFA SCORE: Sequential Organ Failure Assessment Score (11)

Definitions

- **Critically Ill Children:**

Children admitted in PICU requiring continuous monitoring due to various medical and surgical pathophysiologies. (1)

- **Shock**:

Is an acute process characterised by the body's inability to provide enough oxygento meet the metabolic demands of vital organs and tissues. (1)

- **Sepsis**:

Sepsis is defined as SIRS (Systemic Inflammatory Response Syndrome) that has an infectious origin that is either suspected or confirmed.(10)

Criteria for PICU admission:

- ✓ Shock
- ✓ GCS < 8
- ✓ Hypoxia
- ✓ Respiratory distress
- ✓ Hepatic failure

- ✓ Post GI surgery
- ✓ Requiring mechanical ventilation
- ✓ Requiring Non-Invasive Ventilation
- ✓ Requiring Post Op care

Investigations:

After a complete clinical examination, investigations viz.,Complete Blood Count (CBC), Liver Function Test, Kidney Function Test, Blood Gas were sent. Serum lactate levels at the time of presentation of shock and 12-24 hours after the initial presentation were done.

SOFA score was measured by taking platelet count, bilirubin, sr. creatinine and PaO2/FiO2 ratio into account.Chest radiograph was done wherever indicated.

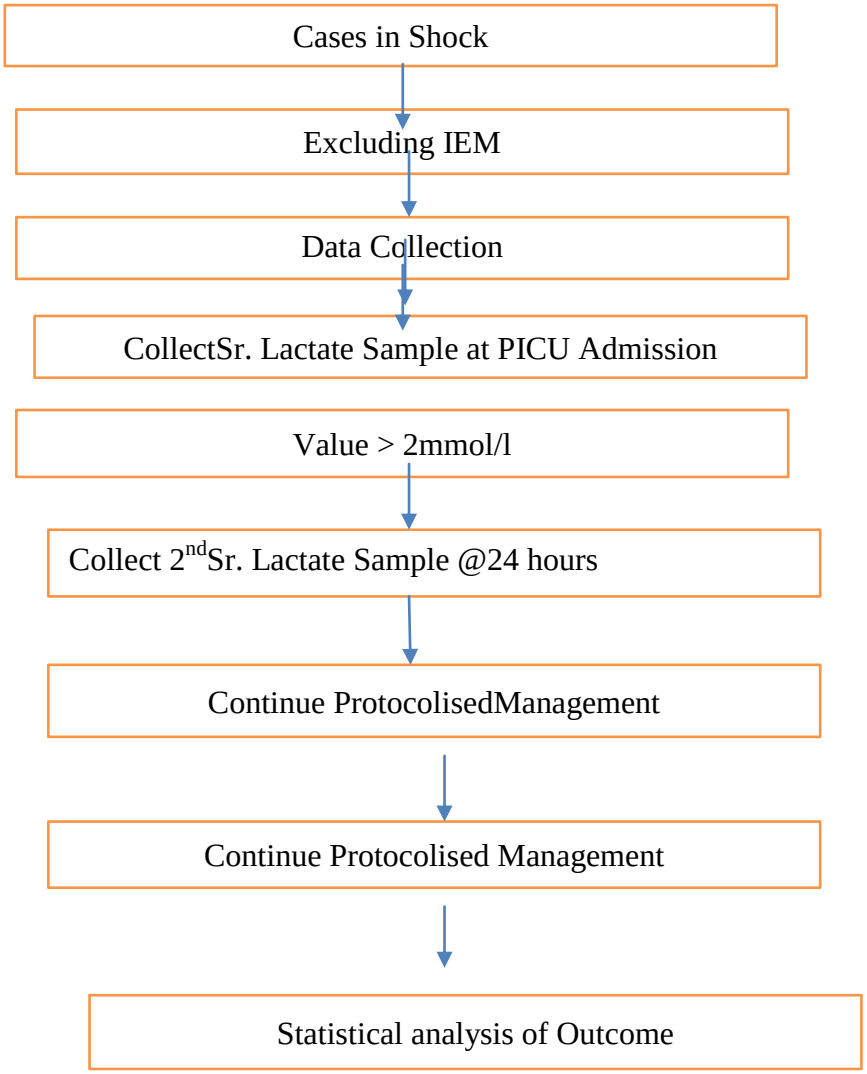
Instrumentation:

1. The results were obtained using ABX-Pentra XL 80. The levels of hemoglobin, total and differential leucocyte count, total platelet count were recorded.
2. LFT, KFT and Serum lactate levels were determined using VITROS 5600 integrated system and manufactured by Ortho Clinical Diagnostics.
3. The normal values were taken as:

Sr Albumin- 3.5 to 5.5 g/dl
Sr Creatinine- < 1 mg/dl
SrLactate- 0 to 4 mmol/L

4. Chest radiogram was done and abnormal findingsrecorded.
5. The duration of stay of each child was recorded

Flow chart:



Statistical analysis:

Data was entered into Microsoft Excel sheet and statistical analysis was done. Relationship of various demographic, clinical characteristics and etiology with outcome were evaluated employing Chi- square test, Fischer's exact test for categorical data and independent T test for continuous data with normal distribution. p value was considered significant if less than 0.05.

OBSERVATION AND RESULTS:

In the present study of 144 cases, 1st serum lactate levels were sent at the time of admission and 2nd lactate levels were sent 12-24 hours after admission. The relation between lactate levels, lactate clearance and clinical outcome is as mentioned below.There were 83 males and 60 females. 32.17% were in the age group of 1 month to 1 year, 27.97% were between 10-18 years of age, 22.38% were in the age group of 5-10 years of age and 17.49% were between 1-5 years of age.Majority of the patients had cardiogenic shock and maximum number of deaths were among the patients with cardiogenic shock followed by septic shock.

Majority of the patients with poor prognosis had septic shock and cardiogenic shock.There was significant decrease in the clearance of lactate in the presence of hepatic dysfunction in presence of shock. Majority of patients with higher duration of complaints had higher lactate levels comparatively than those with less duration of complaints.58 study cases died and all the cases had elevated lactate levels.The most common causes were systemic illnesses like pneumonia, congenital heart disease, gastroenteritis, seizures etc.Malnutrition and multi organ dysfunction syndrome were highly associated in patients who died.The mean change in lactate levels in those patients that died was -4.19 which indicates that the 2nd lactate levels were more than the initial levels on admission.Patients with 2nd lactate levels > 4 mmol/L had higher mortality rate.

DISCUSSION

In the present study, out of 144 patients, 61 patients had a lactate level < 4mmol/L, among which 27 (44.27%) died. 82 patients had initial lactate value > 4 mmol/L, among which 31 (37.8%) died. 76 patients (53.14%) had 2nd lactate level < 4 mmol/L, among which 12 patients (15.79%) died. 67 patients (46.86%) had lactate values > 4 mmol/L, among which 46 (68.65%) died.

Majority of the patients who died had initial lactate levels < 4 mmol/L which is within the normal limits. These patients were admitted in PICU during the initial stages of shock and 1st lactate level was sent immediately after admission. 7 patients that died had diagnosis of pneumonia, leukemia, heart failure and chronic kidney disease. All these patients were started on ionotropic support but did not improve and their condition deteriorated over a period of time and the mean lactate clearance was - 7.6 mmol/L which indicates that the 2nd lactate level was elevated indicating the bad prognosis of the patient.

The lactate levels in shock usually may take as late as 3-6 hours to increase. This may also depend on the severity of the illness, prognosis to treatment and presence of MODS. This explains the increased death rates when the 1st lactate level at admission was normal. The 2nd lactate level sent 12-24 hours after admission was associated with higher mortality rates.

The mean of 2nd lactate levelwas more than 1st lactate level among those that died and the negative mean value of change in lactate levels among those dead indicates that the lactate clearance was less among the dead.

Based on serial blood gas readings, increased mortality was associated with lactate and unidentified anions (Strong Ion Gap = SIG). Metabolic acidosis (both lactic and non-lactic) seemed to be associated with high mortality and increased length of stay in hospital and in the ICU. (12)

In a study done by **Rocha A et al**(13), 93 patients (37.3%) with a maximal lactate level of more than 2.0 mmol/L on D1 were profiled. In this patient group (n = 93), there were 11 deaths (11.8%) while in the PICU and one additional patient passed away after 28 days, for a total mortality rate of 12.9%. When lactate concentrations either rose or slightly reduced (less than 0.05 mmol/L) from D1 to D2, mortality was predicted with the highest sensitivity (0.636) and specificity (0.890). Higher serum lactate readings (L 0.05 mmol/L) from D1 to D2 were linked to higher mortality during PICU stays (L 0.05 mmol/L).

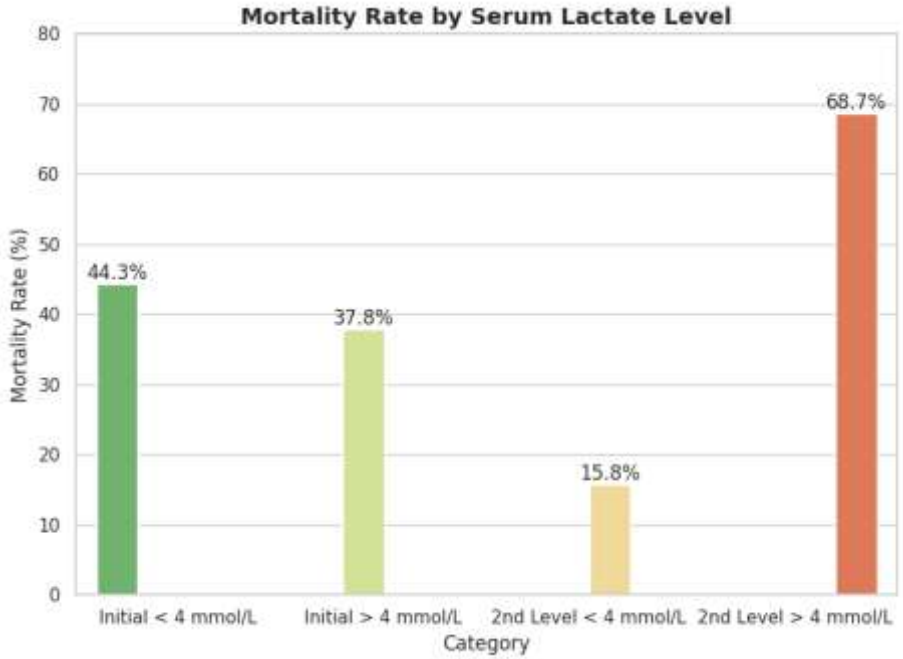
In a study by**Jat K et al** (14), 3 lactate levels at 0-3 hours, 12 hours and 24 hours of admission were considered. In their study, lactate value of > 5 mmol/L was taken as elevated lactate and all three lactate levels were elevated in patients with mortality and all the lactate levels had significant values in patients with mortality.

A study done by **Patriawati KA et al**(15) also had taken 3 lactate values into consideration, 1st at admission, 2nd at

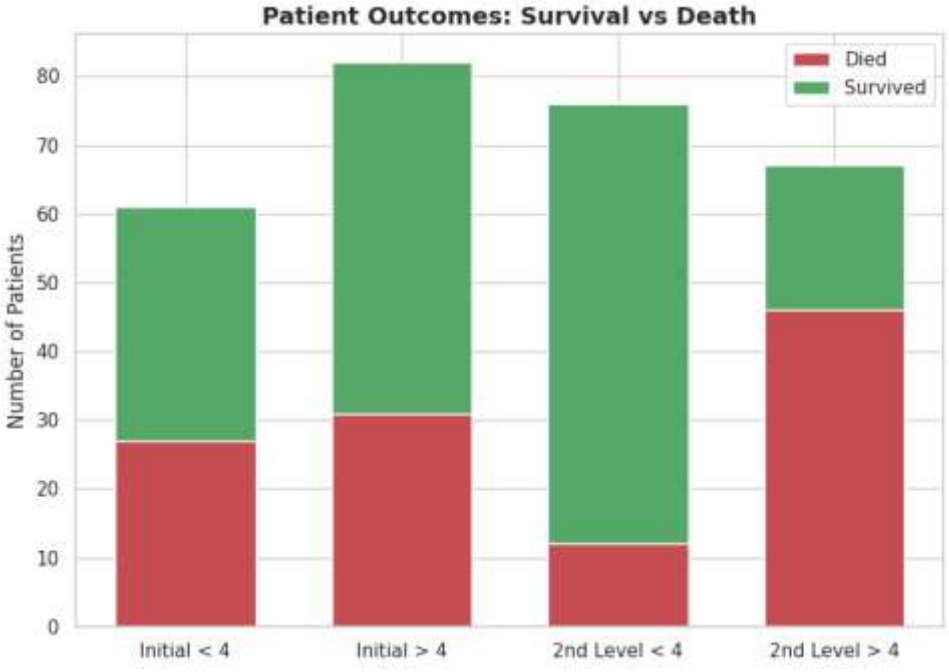
6 hours and 3rd at 24 hours of admission. In their study, the 1st and 3rd lactate values had significant association with mortality i.e, the patients with high (> 4mmol/L) initial and third lactate levels had higher mortality rates. 2nd lactate level at 6 hours of admission did not have much significance with the outcome. The lactate clearance rate is more important than the single serum lactate value.

Distribution of Study Population by Age: The study predominantly involved infants (1 month - 1 year) comprising 32.17% of the cohort, followed by adolescents (10-18 years).

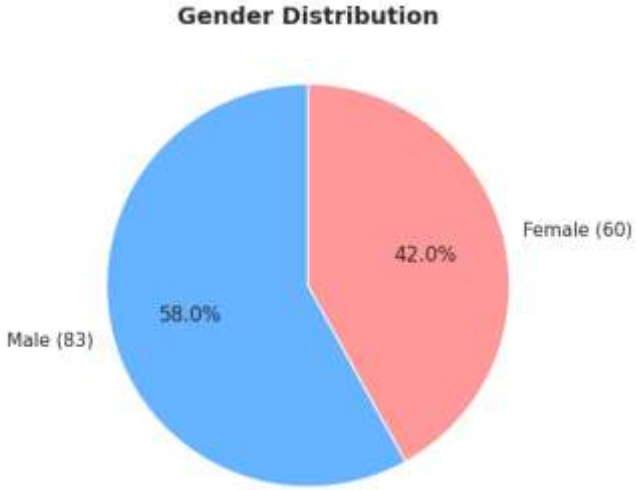
Mortality Rate by Serum Lactate Level: This chart highlights the study's central finding. While initial lactate levels > 4 mmol/L had a mortality rate of 37.8%, the 2nd lactate level > 4 mmol/L (taken 12-24 hours post-admission) was associated with a significantly higher mortality rate of 68.7%. This supports the conclusion that persistent hyperlactatemia is a stronger predictor of death than the initial level.



Patient Outcomes: Survival vs Death: This stacked bar chart visualizes the absolute numbers. Notice the dramatic shift in the "2nd Level > 4" column, where the number of deaths (red) exceeds survivors (green), unlike the "2nd Level < 4" group where survival is very high. This visually reinforces the importance of lactate clearance.



Gender Distribution: The study included a higher proportion of males (58.0%) compared to females (42.0%).



CONCLUSIONS: This study posits that both lactate level estimation for prognostic purposes and early shock recognition for timely intervention are critical factors in preventing negative patient outcomes.Multiple lactate levels estimation is better than single lactate values in determining the outcome of the patients in shock.

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