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ORIGINAL RESEARCH

Study of Lactate, Lactate Albumin Ratio (LAR), Procalcitonin (PCT) and Immature Platelet Fraction (IPF) on admission in comparison to APACHE II as a marker of severity in patients admitted with sepsis in tertiary care hospital

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ABSTRACT

Aim: To assess the association of Lactate, Lactate Albumin Ratio, Procalcitonin and Immature Platelet Fractionin comparison to APACHE IIon admission as marker of severity in sepsis patients

Objectives

- To assess Lactate / Albumin Ratio (LAR) in patients with sepsis.
- To assess Lactate value in patients with sepsis .
- To assess Procalcitonin (PCT) value in patients with sepsis.
- To assess Immature Platelet Function (IPF) value in patients with sepsis.
- To compare Lactate, LAR, PCT and IPF with APACHE II score on admission in patients with sepsis for prognostication

Material and methods: Hospital based Observational Cross-Sectional Study was conducted at Mahatma Gandhi Hospital , Jaipur between September 2022 to December 2023. Data of 180 patients was collected according to inclusion criteria. Sepsis biomarkers that is Lactate , LAR , IPF , PCT were calculated and were compared to APACHE II score at the time of admission for the purpose of prognostication. **Result:** Comparing these biomarkers, the Lacto-albumin ratio and Procalcitonin appear to demonstrate stronger associations with disease severity as reflected by APACHE II scores compared to Lactate and IPF. This underscores the importance of multi-parameter assessment in sepsis management to enhance prognostic accuracy and guide therapeutic decisions tailored to individual patient needs. **Conclusion:** In this study all four markers positively correlated with APACHE II score, that is the level of markers increased along with severity of sepsis. But our study particularly identifies significant associations: APACHE II scores correlate significantly with Procalcitonin and Lacto-albumin ratio. The biomarkers of sepsis used in our study that is Lactate, Lactate Albumin Ratio (LAR) , Immature Platelet Fraction (IPF), Procalcitonin (PCT) can be used to enhance early risk stratification and guide more tailored therapeutic interventions for septic patients .

Keywords : Sepsis , Septic Shock , IPF , PCT , LAR , APACHE II , SOFA , MAP

conflicting. patients.

INTRODUCTION

Sepsis continues to stand as a significant and pervasive global health challenge, contributing substantially to morbidity and mortality on a worldwide scale. It is life-threatening organ

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dysfunction caused by a dysregulated host responseto infection.[1] Sepsis and septic shock are major healthcare problems, impacting millions of people around the world each year and killing betweenone in three and one in six of those it affects. As of 2017, research findings indicated that sepsis accounted for a staggering 20% of all deaths across the globe, shedding light on the urgency of understanding and addressing this critical issue.[2] In order to better comprehend the complexities of sepsis, International Guidelines for the Management of Sepsis and Septic Shock in 2021 are a crucial set of recommendations developed by experts in the field of critical care medicine. These guidelines provide evidence-based strategies and protocols for the diagnosis and treatment of sepsis and septic shock, two life-threatening conditions characterized by the body's severe response to infection.

Early diagnosis and the prompt initiation of antimicrobial therapy are of paramount importance in effectively treating sepsis and, in doing so, saving lives. The identification of serum biomarkers plays a pivotal role in aiding the diagnosis of sepsis, guiding clinical decision-making, and predicting outcomes.

Several studies have highlighted the advantages of procalcitonin (PCT) as a biomarker for sepsis. PCT exhibits distinct characteristics that make it a valuable tool for sepsis diagnosis and management. PCT levels rise more rapidly than CRP levels in response to infection and peak within a shorter timeframe.

Serum lactate, serving as a surrogate marker for tissue perfusion, is integral in assessing the severity of the condition. As a result, it is currently recommended that serum lactate levels be measured within the first hour of presentation in all patients with suspected sepsis, with a repeat measurement within 2 to 4 hours if the initial lactate level exceeds 2 mmol/L. [3] The monitoring of serum lactate levels aids in both diagnosis and the ongoing assessment of sepsis patients, facilitating timely intervention and patient management.

One emerging sepsis biomarker is the lactate to albumin (L/A) ratio. This innovative approach, which considers both lactate and albumin levels, takes into account the nutritional status of septic patients. It has the potential to address a limitation in current major scoring systems, such as the SOFA score.[4] Serum albumin, in particular, has been found to correlate with morbidity and mortality among critically ill patients. [5] Given the constraints associated with lactate as a standalone marker and the need for an effective surrogate of disease severity, a growing body of literature supports the use of the L/A ratio as a predictive tool for mortality and multiple organ failure in critically ill patients with sepsis. One potentially useful marker is the percentage immature platelet fraction (IPF), which is an often-overlooked but valuable tool. IPF measurement provides information about platelet production and distinguishes between thrombocytopenia due to increased peripheral platelet destruction and thrombocytopenia linked to bone marrow failure resulting from toxic agents or persistent infections. [6] IPF is reflective of reticulated platelet numbers and directly correlates with the thrombopoietic rate. This measurement has shown promise as a prognostic marker for conditions like disseminated intravascular coagulation and is commonly used in neonatal ICUs to investigate the cause of thrombocytopenia in newborns.[7] The ease of calculating IPF with readily available blood cell counters makes it a practical tool for clinical use.

This study aims to compare the efficacy of lactate, lactate-to-albumin ratio (LAR), procalcitonin (PCT), and immature platelet fraction (IPF) with established scoring system such as the Acute Physiology and Chronic Health Evaluation II (APACHE II) score. The APACHE II scoreevaluates disease severity based on acute physiological derangements and chronic health conditions, are widely used in clinical practice for risk stratification and prognostication in sepsis (Vincent et al., 1996; Knaus et al., 1985).

MATERIAL AND METHODS

- **Type of Study**: Hospital based Observational Cross-Sectional Study.
- **Study population**: All patients age between 18 to 65 years admitted in ICU and Emergency Department with Septic shock or Sepsis, Mahatma Gandhi Hospital, Jaipur from August 2022 to December 2023.
- **Place of Study**: Mahatma Gandhi Medical Hospital, Jaipur.
- **Duration of Study**: September 2022 to December 2023.
- Detailed history and necessary investigations will be undertaken. The purpose of the study will be explained to the patient/guardians and informed consent obtained.
- Patients are selected for study that satisfy all inclusion and exclusion criteria.
- Institute Ethics Committee approval will be taken before undertaking the study.
- Written and inform consent will be taken from all participants before enrolment into the study.
- **Inclusion criteria**: All patients > 18 years of age admitted with sepsis (according to sepsis 3 definition).[2]
- **Exclusion criteria**:
- All patients who are not willing to give consent.
- Cardiac arrest on presentation
- Pregnancy
- Trauma patients
- Liver failure on presentation
- **Sample size:** All patients age 18- 65 years admitted in ICU diagnosed as Sepsis/ Septic shock, Mahatma Gandhi Hospital, Jaipur from September 2022 to December 2023.
- **Plan of Study:**
- **Intended intervention**: No

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- **Dosages of drugs**: Drugs will be administered as per set protocol and patients' requirement
- **Route of administration**: No new drug will be administered
- **Duration of treatment**: As per patients' disease
- **Details of invasive procedures (if any):** As per patients' disease, no invasive procedure for the study
- **Duration of study**: 1.5 years Duration of study: from September 2022 to December 2023 at Mahatma Gandhi Hospital, Jaipur.
- **Potential risk**: There is no risk related to study involved.

OBSERVATION

Apache: 2 Scoring System

Physiologic Variable	Points								
	+4	+3	+2	+1	0	+1	+2	+3	+4
1. Temperature (°C)	≥41	39-40.9		38.5-38.9	36-38.4	34-35.9	32-33.9	30-31.9	≤29.9
2. Mean arterial pressure (mmHg)	≥160	130-159	110-129		70-109		50-69		≤49
3. Heart rate (/min)	≥180	140-179	110-139		70-109		55-69	40-54	≤39
4. Respiratory rate (/min)	≥50	35-49		25-34	12-24	10-11	6-9		≤5
5. Oxygenation (mmHg) a. A-aDO_2 if FiO_2 ≥0.5 b. PaO_2 if FiO_2 <0.5	500	350-499	200-349		<200 >70	61-70		55-60	<55
6. Acid-base balance a. Arterial pH b. Serum HCO_3 (mEq/l) if no arterial blood gas	≥7.7 ≥52	7.6-7.69 41-51.9		7.5-7.59 32-40.9	7.33-7.49 22-31.9		7.25-7.32 18-21.9	7.15-7.24 15-17.9	<7.15 <15
7. Sodium (mEq/l)	≥180	160-179	155-159	150-154	130-149		120-129	111-119	≤110
8. Potassium (mEq/l)	≥7	6-6.9		5.5-5.9	3.5-5.4	3-3.4	2.5-2.9		<2.5
9. Creatinine (mg/dl)	≥3.5	2-3.4	1.5-1.9		0.6-1.4		<0.6		
10. Hematocirt (%)	≥60		50-59.9	46-49.9	30-45.9		20-29.9		<2.5
11. White blood count (×1000/mm^3)	≥40		20-39.9	15.19.9	3-14.9		1-2.9		<1
12. Glasgow Coma Score (GCS)	Score = 15 minus actual GCS								
A. Total Acute Physiology Score (sum of 12 above points)									
B. Age points (years) ≤44=0; 45 to 54=2; 55 to 64=3; 65 to 74=5; ≥75=6									
C. Chronic Health Points*									
Total APACHE II Score (add together the points from A+B+C)									

* Chronic Health Points: If the patient has a history of severe organ system insufficiency or is immune-compromised as defined below, assign points as follows:
5 points for non-operative or emergency post-operative patients
2 points for elective post-operative patinets

Table 18: APACHE II score in study population

APACHE II Score	No of cases	Percentage
0-4	27	15.0
5-9	30	16.7
10-14	35	19.4
15-19	29	16.1
20-24	20	11.1
25-29	18	10.0
30-34	13	7.2
>34	8	4.4
Mean±SD	13.39±8.96	

The Acute Physiology and Chronic Health Evaluation (APACHE II) scores in this study cohort reflect the severity of illness and prognostic implications among the subjects. Scores ranging from 10 to 14 were the most prevalent, observed in 19.4% of cases, indicating moderate severity of illness. Categories encompassing scores from 15 to 19 and 5 to 9 were also notable, comprising 16.1% and 16.7% of the cohort, respectively, highlighting a spectrum of disease severity from moderate to mild. Higher scores, indicative of more severe illness, were less frequent; scores from 20 to 24 and 25 to 29 were observed in 11.1% and 10.0% of cases, respectively. Scores exceeding 30, including categories from 30 to 34 and >34, were less common, collectively representing 11.6% of the cohort. The mean APACHE II score for the study population was 13.39 ± 8.96, indicating a moderate overall severity of illness.

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Table 29: Comparison of APACHE II Score and various Inflammatory parameters and predicted Mortality

APACHE II score	Lactate (mg/dL)	Lacto-albumin ratio	Procalcitonin (ng/ml)	Immature platelets fractions (%)	Predicted mortality
	Mean± SD	Mean± SD	Mean± SD	Mean± SD	
0-4	2.4 ± 1.3	2.1 ± 0.5	0.5 ± 0.4	2.5 ± 1.1	~4%
5-9	2.5 ± 1.8	2.3 ± 0.8	0.7 ± 0.1	2.4 ± 0.5	~8%
10-14	2.5 ± 1.5	2.6 ± 0.2	1.0 ± 0.3	2.2 ± 1.3	~15%
15-19	2.6 ± 1.3	3.0 ± 0.8	1.5 ± 0.6	2.6 ± 0.6	~25%
20-24	2.9 ± 2.5	3.4 ± 0.4	2.0 ± 0.5	3.0 ± 1.9	~40%
25-29	2.8 ± 2.8	3.8 ± 1.1	2.5 ± 0.2	3.0 ± 1.8	~55%
30-34	3.0 ± 3.1	4.2 ± 1.3	3.0 ± 0.7	3.0 ± 1.2	~75%
>34	3.5 ± 3.0	4.6 ± 1.2	3.5 ± 0.4	3.1 ± 1.9	~85%
p-Value	**0.329**	**0.003**	**0.021**	**0.438**	

The association between APACHE II scores and biomarkers provides valuable insights into the severity of illness and prognostic indicators among critically ill patients. Lactate levels showed no significant variation across APACHE II score categories (p = 0.329), with mean values ranging from 2.4 ± 1.3 mg/dL in the lowest score group (0-4) to 3.5 ± 3.0 mg/dL in the highest (>34). In contrast, the Lacto-albumin ratio demonstrated significant differences (p = 0.003), increasing from 2.1 ± 0.5 in the lowest score group to 4.6 ± 1.2 in the highest, indicating escalating metabolic imbalance and inflammatory response with increasing APACHE II scores. Procalcitonin levels also varied significantly (p = 0.021), rising from 0.5 ± 0.4 ng/ml in the lowest score group to 3.5 ± 0.4 ng/ml in the highest, reflecting heightened systemic inflammatory activity. Immature platelet fractions displayed no significant change across APACHE II scores (p = 0.438), with mean percentages ranging narrowly from 2.2% to 3.1%. Predicted mortality rates increased progressively with higher APACHE II scores, from approximately 4% in the lowest score group to 85% in the highest, underscoring the clinical relevance of APACHE II scores in predicting outcomes in critically ill patients based on these biomarkers.

DISCUSSION

The analysis of biomarkers in sepsis patients across different APACHE II score ranges provides valuable insights into the relationship between biomarker levels and disease severity, as well as their prognostic value. The APACHE II score is a widely used severity-of-disease classification system, and higher scores are associated with increased predicted mortality in critically ill patients (Knaus et al., 1985).[8]

Lactate levels showed a non-significant increase across the APACHE II score ranges, with a mean of 2.4 ± 1.3 mg/dL in the 0-4 score range, rising to 3.5 ± 3.0 mg/dL in the >34 score range (p=0.329). Although the increase was not statistically significant, elevated lactate levels are well-documented as a marker of tissue hypoxia and metabolic stress, commonly observed in severe sepsis and septic shock (Casserly et al., 2015).[9]

The Lactate-Albumin Ratio (LAR) exhibited a significant increase with higher APACHE II scores, from 2.1 ± 0.5 in the 0-4 score range to 4.6 ± 1.2 in the >34 score range (p=0.003). This finding underscores the potential of LAR as a prognostic biomarker, reflecting both metabolic derangement and hypoalbuminemia in severe sepsis and septic shock (Artero et al., 2017).[10] The strong correlation with APACHE II scores suggests that LAR could be integrated into clinical practice to improve the prediction of sepsis outcomes.

Procalcitonin (PCT) levels also increased significantly with higher APACHE II scores, from 0.5 ± 0.4 ng/ml in the 0-4 score range to 3.5 ± 0.4 ng/ml in the >34 score range (p=0.021). PCT is a well-established marker of bacterial infection and sepsis, with higher levels indicating more severe infection and systemic inflammatory response (Mussap et al., 2012).[11] The significant rise in PCT levels with increasing APACHE II scores supports its role in assessing sepsis severity and guiding antibiotic therapy.

Immature Platelet Fraction (IPF) showed a non-significant increase from 2.5 ± 1.1% in the 0-4 score range to 3.1 ± 1.9% in the >34 score range (p=0.438). While IPF has been suggested as a marker of platelet production and turnover in response to infection and inflammation, the non-significant trend in our study may reflect the complex interplay of factors affecting platelet dynamics in sepsis (Stratz et al., 2012).[12]

The predicted mortality increased markedly with higher APACHE II scores, from approximately 4% in the 0-4 score range to 85% in the >34 score range. This trend emphasizes the prognostic power of the APACHE II score in predicting outcomes in sepsis patients. The integration of biomarker levels with APACHE II scores could enhance risk stratification and guide clinical management decisions.

Comparing these biomarkers, the Lacto-albumin ratio and Procalcitonin appear to demonstrate stronger associations with disease severity as reflected by APACHE II scores compared to Lactate and IPF. This underscores the importance of multi-parameter

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assessment in sepsis management to enhance prognostic accuracy and guide therapeutic decisions tailored to individual patient needs.

CONCLUSION

Sepsis is the life-threatening organ dysfunction caused by dysregulated host response to infection, representing urgent medical emergency. Despite the considerable progress in medical care, sepsis continues to represent a substantial burden on healthcare systems, impacting millions of people around the world each year, contributing significantly to both morbidity and mortality. Early diagnosis and the prompt initiation of antimicrobial therapy are of paramount importance in effectively treating sepsis and, in doing so, saving lives.

The identification of serum biomarkers plays a pivotal role in aiding the diagnosis of sepsis, guiding clinical decision-making, and predicting outcomes. By comparing these biomarkers with APACHE II score upon admission we can make a more robust assessment of sepsis severity. Combination of biomarkers and scoring systems can help us in early risk stratification and prognostication of sepsis at the time of hospital admission. The APACHE II score, which evaluates disease severity based on acute physiological derangements and chronic health conditions, IS widely used in clinical practice, with higher values corresponding to increased predicted mortality rates across different score ranges.

Our study offers valuable insights into the clinical characteristics and prognostic indicators among patients hospitalized with sepsis. The research underscores the intricate interplay of demographic variables, infection sources, microbiological causes, and concurrent health conditions in determining disease severity. Stratification based on the severity of sepsis and the examination of biomarkers such as Serum Lactate, Serum Lacto-albumin ratio, Procalcitonin, and Immature Platelet Fraction (IPF) in relation to APACHE II score highlight their crucial role in predicting clinical outcomes and guiding therapeutic interventions at the time of hospital admission.

In this study all four markers positively correlated with APACHE II score, that is the level of markers increased along with severity of sepsis. But our study particularly identifies significant associations: APACHE II scores correlate significantly with Procalcitonin and Lacto-albumin ratio.The biomarkers of sepsis used in our study that is Lactate, Lactate Albumin Ratio (LAR) , Immature Platelet Fraction (IPF), Procalcitonin (PCT) can be used to enhance early risk stratification and guide more tailored therapeutic interventions for septic patients .

Future studies using a larger sample size from multiple sites are recommended to confirm the generalizability of our findings.

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