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ORIGINAL RESEARCH

Hematological and biochemical markers in prediction of severity of sepsis

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ABSTRACT

Introduction-Given the gravity of sepsis and emerging regulatory mandates, prompt diagnosis and intervention have been a primary priority in the healthcare sector. Consequently, researchers have focused on examining clusters of clinical tests to accurately detect or anticipate the beginning of sepsis. The present study was conducted to assess the hematological and biochemical markers in prediction of severity of sepsis.

Material and methods-The present prospective observational study was conducted at department of pathology in a tertiary care hospital among patients depicting symptoms of sepsis. Through consecutive sampling a total of 50 patients suspected of sepsis were taken for the study on the basis of inclusion and exclusion criteria. The parameters recorded were hematologic parameters (including WBC, RBC, platelets, ANC and IG), procalcitonin (PCT), and CRP for predicting sepsis.

Results –35 patients were under the category of prediction of sepsis, while 15 patients were under the category of prediction of severe sepsis. In both the group maximum patients were male (25/10; 10/5). The baseline SAPS-II score was significantly lower in sepsis patients(39.34±11.23) than in severe sepsis (45.32±10.23) and results were significant with p value 0.004.The area under the ROC curve (AUC) for predicting sepsis using solely haematology markers varied between 0.50 to 0.65. Upon examining procalcitonin and C-reactive protein exclusively, the AUC rose to 0.71 and 0.72, respectively. The combination of the absolute neutrophil count (ANC) and immunoglobulin (IG) count with inflammatory indicators resulted in an area under the curve (AUC) of 0.74. In predicting whether patients will progress to severe sepsis or septic shock, the identical combination of haematologic and inflammatory indicators yielded an AUC of 0.78

Conclusion-This study demonstrates that bedside physical examination, combined with laboratory testing (including haematologic and inflammatory biomarkers), constitutes the most effective parameters for clinicians to rapidly and accurately predict or diagnose sepsis in critically ill patients.

Keywords- biochemical, Hematological , immature granulocyte, sepsis, shock,white blood cells

INTRODUCTION

Sepsis is an atypical systemic response to what can occasionally be a commonplace infection. Historically acknowledged as a dangerous threat, sepsis remains a potentially fatal consequence. In the last ten years, numerous hospitals have implemented the Surviving Sepsis Campaign's suggestions for managing septic patients, resulting in a decrease in fatality rates from roughly 37% to 30%. Nonetheless, this remains excessively elevated. The frequency of sepsis among hospitalised patients has nearly doubled within the same timeframe, and it is now often identified in outpatient departments seeking care. [1,2]Therefore, it is important to recognize it early, so that supportive measures which have been shown to be successful may be implemented as soon as possible.

Numerous research have endeavoured to develop biomarkers capable of reliably diagnosing sepsis. Despite extensive research on numerous indicators, only a limited number are sufficiently reliable for regular clinical application in sepsis therapy. Complicating testing, no singular biomarker has yet demonstrated the ability to accurately diagnose sepsis in patients. Consequently, researchers have focused on examining clusters of clinical tests to accurately detect or anticipate the beginning of sepsis.[3]

Various biochemical and hemocytometric markers have been utilised in everyday practice, as alterations in these markers have been documented in numerous research and may function as predictive indicators of disease severity. Furthermore, patients with haematological disorders face an elevated risk of several infections and other comorbidities. [4]A full blood count is the most accessible, effective, and readily available test, as most regular laboratories own haematology analysers. Routine haematological and

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biochemical measures have demonstrated alterations in sepsis patients, as illustrated in numerous investigations. Numerous haematological markers in a full blood count exhibit alterations as the disease progresses. Sepsis infection exhibited leukocytosis, leukopenia, lymphocytopenia, eosinopenia, neutrophilia, thrombocytopenia, and elevated levels of D-Dimers, Ferritin, CRP, LDH, pro-calcitonin, ALT, AST, PT, and APTT, which are extensively utilised for risk classification [5-7]. Therefore, understanding the prognosis of infection and its association with comorbidities may offer critical insights for risk classification and decision-making in severely impacted sepsis patients [8].

Hence the present study was conducted to assess the hematological and biochemical markers in prediction of severity of sepsis.

MATERIAL AND METHODS

The present prospective observational study was conducted at department of pathologyin a tertiary care hospitalamong patients depicting symptoms of sepsis. Writteninformed consent was taken from patients after explaining them the complete procedure of the study.

Through consecutive sampling a total of 50 patients suspected of sepsis were taken for the study on the basis of inclusion and exclusion criteria.

Inclusion criteria: Sepsis is defined by the presence of infection and the fulfilment of more than two of the following criteria: temperature above 38ºC or below 36ºC, heart rate surpassing 90 beats per minute, respiration rate exceeding 20 breaths per minute or PaCO2 below 32 mm Hg, and white blood cell count over 12 k/mL or below 4 k/mL or comprising more than 10% immature (band) forms. Severe sepsis is characterised by sepsis accompanied by organ failure, hypoperfusion, or hypotension, with inclusion criteria necessitating the presence of at least one of the following: (1) Hypotension (systolic blood pressure ≤90 mm Hg or mean arterial pressure ≤75 mm Hg, rectified within 1 hour via fluid resuscitation), (2) arterial hypoxaemia (PaO2 ≤75 mm Hg in the absence of preexisting pulmonary pathology), (3) metabolic acidosis (pH ≤7.3 or base deficit ≥5 meq/L), (4) oliguria (urine output ≤30 mL/h for a minimum of 2 hours despite fluid resuscitation), (5) acute alteration of mental status, (6) diffuse intravascular coagulation (DIC) (INR >1.2 times plus d-dimers ≥500 or platelets ≤100,000/mL). Septic shock is characterised by significant hypotension, despite sufficient fluid resuscitation and administration of vasopressor medications. Changes in mental status were assessed using the Glasgow Coma Score (GCS), while the severity of the patient's condition was quantified according to the Simplified Acute Physiology Score (SAPS) II approach.[9]

Exclusion criteria: Individuals with significant comorbidities (such as cirrhosis, chronic renal failure, diabetes mellitus, COPD, malignancies, etc.), those undergoing any sort of immunosuppressive therapy, patients with hospital-acquired infections, or those exhibiting low performance status were excluded from the study.

Blood and other site cultures were collected upon admission and during hospitalisation as necessary, while other diagnostic techniques (chest X-rays, ultrasound, computed tomography, gallium scan, etc.) were conducted to ascertain the cause of infection. The parameters recorded were hematologic parameters (including WBC, RBC, platelets, ANC and IG), procalcitonin (PCT), and CRP for predicting sepsis.

All patients received an empirical antibiotic regimen in accordance with hospital standards, overseen by infectious disease specialists (e.g., third-generation cephalosporins or quinolones combined with an aminoglycoside, while vancomycin, teicoplanin, or clindamycin were administered when needed). Antimicrobial therapy was modified based on culture results, where necessary. Patients were meticulously observed during their hospitalisation, and critically ill patients were relocated to the ICU.

All statistical analyses were performed using software (SPSS, version 25.0, SPSS; Chicago, IL). Parametric data were analysed by using a two-tailed Student’s t-test. The data are reported as mean ± SD. Categorical data were analysed by x2 analysis with Fisher’s Exact test where appropriate.Receiver operator characteristic (ROC) curves were generated to evaluate various sepsis diagnostic models.A p value of <0.05 was considered significant.

RESULTS

35 patients were under the category of prediction of sepsis, while 15 patients were under the category of prediction of severe sepsis. In both the group maximum patients were male (25/10; 10/5). The baseline SAPS-II score was significantly lower in sepsis patients(39.34±11.23) than in severe sepsis (45.32±10.23) and results were significant with p value 0.004. Serum lactic acid, white blood count and Glasgow Coma Scale (GCS) scoring were similar in both groups, while pH and PO2 levels were significantly lower in severe sepsis patients as shown in Table 1.

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Table: 1 Demographic and clinical data of patient with prediction of sepsis and severe sepsis

Characteristics	Prediction of sepsis (n=35)	Prediction of severe sepsis (n=15)	P value
Age, year	70.34±13.12	74.32±11.25	0.345
Male/female	25/10	10/5	0.125
SAPS II	39.34±11.23	45.32±10.23	0.004
GCS	10.34±1.23	10.21±1.24	0.765
Lactic acid	25.43±11.23	34.32±18.90	0.231
pH	7.34±0.04	7.30±0.02	0.010
pO2	68.35±16.23	56.67±19.03	0.024
WBC	15.67±6.23	19.34±9.25	0.167

Receiver operator characteristic (ROC) curves were constructed to assess multiple sepsis diagnostic models utilising haematological and biomarker data obtained from patients (Table 2). The area under the ROC curve (AUC) for predicting sepsis using solely haematology markers varied between 0.50 to 0.65. Upon examining procalcitonin and C-reactive protein exclusively, the AUC rose to 0.71 and 0.72, respectively. The combination of the absolute neutrophil count (ANC) and immunoglobulin (IG) count with inflammatory indicators resulted in an area under the curve (AUC) of 0.74, indicating a strong predictive capacity for identifying sepsis in individuals prior to the manifestation of inflammatory symptoms. Furthermore, in predicting whether patients will progress to severe sepsis or septic shock, the identical combination of haematologic and inflammatory indicators yielded an AUC of 0.78 (Table 3).

Table 2:Areas under the ROC curves for individual biomarkers and hematological parameters to predict between patients with sepsis and severe sepsis

Parameter	Prediction of sepsis			Prediction of severe sepsis		
	AUC	95% CI	P value	AUC	95% CI	P value
PCT	0.71	0.62-0.78	<0.001	0.74	0.65-0.80	<0.001
CRP	0.72	0.65-0.80	<0.001	0.71	0.67-0.81	<0.001
WBC	0.65	0.55-0.74	0.003	0.63	0.55-0.75	0.004
IGC	0.56	0.48-0.70	0.129	0.60	0.50-0.70	0.055
ANC	0.67	0.55-0.74	0.003	0.59	0.56-0.72	0.004
Platelet	0.50	0.43-0.60	0.134	0.65	0.40-0.3	0.145
RBC	0.50	0.43-0.60	0.145	0.54	0.43-0.65	0.178

Table3:Area under the curve values for several models to predict patients with severe sepsis

Predictor	AUC	P value
ANC & IG	0.67	0.015
PCT & CRP	0.75	<0.001
All heme- leucocytosis	0.68	0.029
All heme- leukopenia	0.68	0.028
ANC+IG+PCT+CRP	0.78	<0.001

DISCUSSION

Sepsis syndrome has gained prominence, and despite advancements in antimicrobial therapy and intensive care unit support, it continues to exhibit high mortality rates. [10] The majority of patients who develop sepsis in tertiary hospitals possess chronic underlying conditions, such as diabetes, chronic pulmonary disease, renal failure, cancer, and leukaemia, rendering them susceptible to infection. [11] The presence of acute underlying disease has been extensively documented as a significant pre-treatment prognostic factor in sepsis. Numerous studies have identified central venous catheters, granulocytopenia, prior antibiotic use, and hospital-acquired infections as major predictors of mortality. [12-14] Due to the diverse underlying conditions present in septic patients and their influence on outcomes, assessing the role of organ dysfunction as an independent prognostic marker in sepsis proves challenging.[15]

The present study was conducted to assess the hematological and biochemical markers in prediction of severity of sepsis. The parameters recorded were hematologic parameters (including WBC, RBC, platelets, ANC and IG), procalcitonin (PCT), and CRP for predicting sepsis. We discovered that the combination of laboratory markers yielded more satisfactory findings than their solo use.No singular biomarker for sepsis is optimal; rather, numerous biomarkers are beneficial for detecting critically ill patients requiring enhanced monitoring to facilitate prompt diagnosis and treatment.

In 2010, Yu et al conducted a meta-analysis that compared PCT and CRP for diagnosing late-onset newborn sepsis. Four trials necessitated verification of

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infection, and in these, the pooled sensitivity for PCT exceeded that of CRP (72% versus 55%, p=0.05); the authors noted that this may be due to PCT levels likely increasing earlier than CRP in neonatal infections.

In five trials assessing the two biomarkers that did not necessitate evidence of infection, the overall accuracy for PCT was superior. A 2011 meta-analysis of a limited number of studies comparing the two biomarkers in burn patients failed to demonstrate the superiority of one over the other.[16,17]

In 2007, Kofoed et al indicated that the amalgamation of three or six pro-inflammatory biomarkers more precisely diagnosed patients with bacterial infections compared to any singular biomarker. In 2009, Shapiro et al. utilised similar methodology for the diagnosis of severe sepsis125. Samples from about 1000 patients presenting in the emergency department were utilised to predict outcomes 72 hours later. The incidence of severe sepsis was 52%, and the mortality rate among septic patients was 12%, as contrast to 0.9% for those who did not have sepsis. The researchers employed multivariate logistic regression to reduce an original list of more than 150 biomarkers to a panel of nine, ultimately identifying three that, when combined into a "sepsis score," most accurately predicted the onset of severe sepsis.[18,19]

The optimal panel of biomarkers for diagnosing sepsis or assessing the risk of progressing to severe sepsis will likely encompass both haematological and biochemical markers. Recently, a minimum of two research have endeavoured to integrate pro-inflammatory and anti-inflammatory indicators. Andaluz Ojeda et al employed an automated multiplexed immunoassay technique to concurrently quantify over 20 distinct cytokines in around 30 individuals suffering from acute sepsis. Gouel-Cheron et alintegrated monocyte HLA-DR. An alternate model for the progression of sepsis to severe sepsis posits that the compensatory anti-inflammatory response syndrome (CARS) initiates while the pro-inflammatory systemic inflammatory response syndrome (SIRS) remains evident. Comprehending the interaction of these contrasting characteristics may assist researchers in elucidating the pathophysiology of organ dysfunction in patients who experience severe sepsis.[20,21]

CONCLUSION

Patients with sepsis frequently have nonspecific inflammatory symptoms that can swiftly escalate to a more critical state if left untreated. Due of this swift advancement, it is imperative that patients receive prompt diagnosis and treatment. The study demonstrated that bedside physical examination, combined with laboratory testing—including haematologic and inflammatory biomarkers—constitutes the most effective parameters for clinicians to rapidly and accurately predict or diagnose sepsis in critically ill patients.

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