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EOSINOPENIA AS A DIAGNOSTIC MARKER IN PATIENTS WITH SEPSIS: A CASE CONTROL STUDY

Pathology

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ABSTRACT

Sepsis is a major cause leading to morbidity and mortality in intensive care unit (ICU).Eosinopenia is proposed as one potential biomarker in sepsis by various studies.The study was performed to look for absolute eosinophil count as an effective biomarker of sepsis, especially in cost constraint conditions like India. A prospective case control study where 50 patients with proven or suspicion of sepsis were taken as cases and 50 non-infected patients were taken as controls.The total leukocyte count and the eosinophil count were recorded on admission,not daily. Absolute eosinophil count was measured and eosinopenia was considered to be a value <50cells/mm3. Out of 50 cases with proven or suspicion of sepsis,34 patients(68%) of SIRS with sepsis and 16 patients(32%) were having severe sepsis with septic shock. Maximum patients in both category were in age group of 60-80 years. Eosinopenia (AEC<50cells/mm3) was present in all 34(100%) patients of SIRS with sepsis and 15(93.75%) patients of severe sepsis with septic shock. Eosinopenia showed a sensitivity of 84% and specificity of 96% in diagnosis of sepsis.It was found that Absolute Eosinophil Count (AEC) below 50 cells/cumm can be utilised for diagnosis of sepsis in patients admitted in critical condition with good sensitivity and high specificity however it should be taken into account that a normal eosinophil count does not exclude sepsis.

KEYWORDS

Absolute eosinophil count , Eosinopenia , Sepsis

INTRODUCTION

Sepsis is found to be a major cause leading to morbidity and mortality in the intensive care unit (ICU) [1]. Sepsis refers to unregulated immune activation due to severe systemic infection.Sepsis occurs when the infectious agent interact with the host and result in release of various biochemical mediators of inflammation.Definitions Task Force in 2016 formulated the Third International Consensus Definitions specifying that sepsis is an unregulated response of host to infectious agent culminating in acute organ dysfunction[2]. In acute infection,there is release of chemical mediators due to acute inflammation which causes circulating eosinophils to sequestrate at the site of infection and ultimately resulting in eosinopenia[3,4]. Other mechanisms causing eosinopenia include:acute stress due to epinephrine and adrenal glucorticoids, suppression of eosinophil production and also suppression of egress of eosinophils from bone marrow[3-8].Eosinopenia i.e. low eosinophil count in peripheral blood, was found to be a good diagnostic tool of infection in various studies[9].The low eosinophil count can be utilised as a prognostic factor at ICU admission as it is widely available,cheap and results can be obtained rapidly after taking sample. Eosinopenia can be utilised as effective tool for diagnosing sepsis in critically ill patients.Clinical and laboratory parameters can be misleading as they are not specific and often they can change in patients of severe sepsis with systemic inflammatory response syndrome(SIRS)[10,11].Various observational studies have shown that sepsis is associated with low eosinophil count and hence eosinopenia can be used as effective biomarker in sepsis.Eosinophil count is evaluated in routine blood investigations and it has more usefulness in cost constraint settings like India as it will not lead to additional cost. Eosinopenia can be utilised as an effective diagnostic and prognostic tool by clinician especially in patients of low socioeconomic strata if similar sensitivity and specificity can be obtained as with other accepted biomarkers of sepsis such as procalcitonin and CRP. Hence,the study was done to look for the utility of Absolute eosinophil count as a diagnostic marker for sepsis, especially in Indian conditions[12].

A biomarker which is cheap,rapid,easily available and having high specificity with good sensitivity, correlating well with the diagnosis and prognosis of sepsis,can be utilised as an ideal biomarker[13].

MATERIAL AND METHODS

Study design

This is a prospective study conducted in SGT medical college and university , gurugram over a duration of 1 year from August 2020 to July 2021. A total of 50 cases admitted in ICU, SGT Hospital with proven or suspicion of sepsis were included in study and 50 non-infected patients were taken as control.As eosinopenia is measured in routine clinical investigations and hence informed consent was not required.

Patients with high eosinophil count e.g. atopic dermatitis, bronchial asthma, allergic rhinitis, parasitic disease and patients of haematological malignancy, HIV infection, on chemotherapy were considered in exclusion criteria of the study.

Data Collection

Each patient was evaluated in terms of age, gender and main diagnosis.Vital signs were also recorded on admission in ICU which included pulse rate,temperature,respiratory rate,systolic and diastolic blood pressure and urine output.The total leukocyte count and eosinophil count were recorded once at the time of admission and not daily.

Blood culture were withdrawn if the patient was febrile or having signs of severe sepsis or requiring vasopressor support for suspected septic shock.

Patients were categorised into SIRS, sepsis, severe sepsis, or septic shock accordingly as per the crieteria of the American College of Chest Physicians/Society of Critical Care Medicine[2].SIRS is defined by the presence of two or more of the following criteria: respiratory rate >20/min or PaCO2 < 32 Torr, heart rate >90 beats/min, body temperature >38°C or <36°C and white blood cell count >12,000 cells/mm3, <4,000 cells/mm3, or >10% immature forms. Sepsis is a systemic infection which is associated with SIRS.If there is associated hypotension(systolic blood pressure<90mmHg or a reduction ≥ 40 mmHg from baseline),hypoperfusion or organ dysfunction then it is considered in category of severe sepsis.When severe sepsis is associated with persisting hypotension even after adequate fluid resuscitation then it is termed as septic shock[14]. Absolute eosinophil count was measured and eosinopenia was considered to be a value <50cells/mm3. We evaluated eosinopenia as marker of sepsis in SIRS with sepsis and severe sepsis patients.

RESULTS

This is a prospective observational study for evaluating the

effectiveness of eosinopenia as a diagnostic biomarker in sepsis which included 50 patients with proven or suspicion of sepsis as cases and 50, non infected patients as controls. Following observations and results were obtained from the study.

Out of 50 cases with proven or suspicion of sepsis,34 patients(68%) were having SIRS with sepsis and 16 patients(32%) with severe sepsis and septic shock(Table 1). Maximum patients in both category were in age group of 60-80 years(Table 2)(Fig. 2). Eosinopenia (<50cells/mm3) was present in all 34(100%) patients of SIRS with sepsis and 15(93.75%) patients of severe sepsis with septic shock(Table 1).

Table 1. Distribution Of Sepsis

	No. of patients	Percent	AEC <50cells/cumm	Percent
SIRS with Sepsis	34	68.00%	34	100.00%
Severe Sepsis with Septic Shock	16	32.00%	15	93.75%

Fig.1: Age group distribution in cases

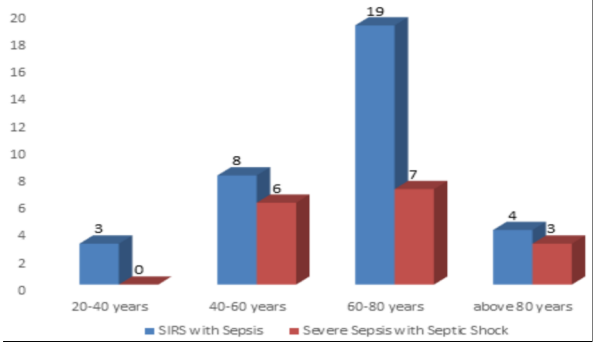

Table 2. Distribution Of Age Group According To The Sepsis

Age group	SIRS with Sepsis	%	Severe Sepsis with Septic Shock	%
20-40 years	3	100%	0	0.00%
40-60 years	8	57.14%	6	42.86%
60-80 years	19	73.08%	7	26.92%
above 80 years	4	57.14%	3	42.86%
Chi-square=2.86	Df=3	p-value=0.414 (NS)		

NS-Not Significant

Out of total 50 cases of sepsis,42 patients(84%) were having eosinopenia(AEC <50 cells/mm3) which was significant statistically(p value<0.001) whereas only 2 patients(4%) of non infective control group showed eosinopenia (Table 3).

Table 3. Distribution of AEC(Absolute Eosinophil Count)

AEC	No. of patients(Case)	Percent	No. of patients(Control)	Percent
<50	42	84.00%	2	4.00%
50-100	5	10.00%	12	24.00%
>100	3	6.00%	36	72.00%
Chi-square= 67.17	p-value<0.001**			

**p-value <0.01= significant

The Major source of infection in cases were pneumonia(52%), urosepsis(20%),meningitis(2%) and others(24%) including malaria, dengue shock syndrome, pulmonary Tuberculosis(Table 4) whereas control group included patients of ACS(Acute Coronary Syndrome), unstable angina, stroke, LVF(Left Ventricular Failure), SAH(Sub Arachnoid Haemmorhage).

Table 4. Distribution of diagnosis among number of patients

Diagnosis	No. of patients (Case)	Percent
Pneumonia	26	52.00%
Meningitis	2	4.00%
Urosepsis	10	20.00%
Others	12	24.00%

Eosinopenia(AEC<50cells/mm3) displayed a sensitivity of 84% and specificity of 96% in diagnosis of sepsis(Table 5).

Table 5. Distribution of Sensitivity and specificity according to AEC

	Sensitivity	Specificity
AEC < 50 cells/cumm	84%	96%

DISCUSSION:

Eosinopenia occurs as a result of acute infection because cytokines regulating production of eosinophil are not significantly activated in sepsis. This study focussed to asses the utility of eosinopenia as a tool to diagnose sepsis in patients with critical condition. A total of 50 cases were included in study along with 50 patients without sepsis were taken as control.This study shows that eosinopenia is a cheap,old and neglected marker of sepsis. The study undertaken by Gil and colleagues showed that bacterial infection is associated with an inflammatory syndrome and eosinophil count <40 cells/mm3.In our study, eosinopenia also showed significant association with parameters of sepsis. As an economical test, especially in our country, eosinopenia offers a high degree of certainity in the evaluation and diagnosis of sepsis in critically ill patients.This may help the clinicians in diagnosis and stepwise approach for the management of patients with critical condition.The present study has few limitations-1. The eosinophil count collected on the day of admission to ICU and not daily. So,eosinopenia cannot be used for evaluation of prognosis of the disease.

2. No surgical patients were enrolled in study as the patients admitted to medical ICU only taken as a part of the study. In present study, out of 50 cases with proven or suspicion of sepsis,34 patients(68%) were having SIRS with sepsis and 16 patients(32%) with severe sepsis and septic shock. Eosinopenia is considered with AEC<50 cells/mm3.Out of total 50 patients in sepsis arm,42 patients(84%) were having eosinopenia which was significant statistically(p value<0.001) whereas only 2 patients(4%) of non sepsis arm(control) group showed eosinopenia.Eosinopenia was found in all 34(100%) patients of SIRS with sepsis and 15(93.75%) patients of severe sepsis with septic shock Whereas in a prospective study done by Hussain et al, 98.5% patients who had eosinopenia (AEC<50cells/cu.mm),had sepsis. In another study done by karakonstantis et al in general hospital of heraklion(Greece), eosinopenia(AEC<50cells/cumm) at the time of admission was present in 71% of patients of infectious group compared to 32% in the non infectious group[15].In our study, majority of cases were having pneumonia accounting 26 cases(52%).Next common cause of infection in cases were others(malaria,Dengue shock syndrome, Acute gastroenteritis) accounting 12 cases(24%),followed by 10 cases(20%) of urosepsis and 2 cases of meningitis(4%) whereas in a study performed by Abidi et al in Morocco,the major source of infection in cases was also found to be respiratory tract(60%),followed by urinary tract(21%), meningitis(13%) and others(6%)[16].In our study, eosinopenia at <50 cells/cumm was found to have 84% sensitivity and 96% specificity in predicting diagnosis of sepsis whereas it was observed to have 79.3% sensitivity and 76.2% specificity in a study carried out by Reddy et al with eosinopenia <40cells/cumm.In a study done at Ibn sina university hospital(Morocco),Eosinopenia <50 cells/cumm yielded sensitivity of 80% and specificity of 91%.In another study performed by Hussain et al,sensitivity of eosinopenia(AEC<50cells/cumm) in the diagnosis of sepsis was 65% and specificity 97%.

CONCLUSION

Our study has a considerable implication for physicians in the Indian scenario.It is found that Absolute eosinophil count below 50 cells/cumm can be utilised as a marker for diagnosing sepsis in patients admitted to ICU in critical condition with good sensitivity and high specificity however it should be taken into account that sepsis can also be a possibility in presence of normal eosinophil count. Further studies are required for assessing eosinopenia as a prognostic marker in sepsis, for analysing the evolution of eosinopenia with the severity of sepsis and for establishment of ideal cutoff values of this marker.So it can be concluded that physician should keep in mind the possibility of sepsis when there is eosinopenia in patients with SIRS and should make treatment plan according to that.

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