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Absolute Eosinophil Count versus C Reactive Protein as a Diagnostic and Prognostic Marker on Sepsis among in Patients of a Tertiary Care Centre in South Kerala

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Abstract
Introduction: *Sepsis exists on a continuum of severity, ranging from infection and bacteremia to sepsis and septic shock, which can lead to multiple organ dysfunction syndrome (MODS) and death. The clinical and biologic phenotype of sepsis is modified by pre existing illness, co morbid conditions, medications and interventions. Overall mortality among patients admitted with sepsis in the ICU will be around 62%. Since cultures are positive only in < 50% of the cases, various biochemical markers are evaluated to improve the diagnostic sensitivity and prognosis. This study compared the usefulness of Absolute Eosinophil Count (AEC) and C Reactive Protein (CRP)*
Materials and Methods: *A prospective case control study was done using 61 cases and controls. The cut off for AEC was 35 and the cut off of CRP was 6. The cases were followed up till their end point in the hospital, defined as cured or died. The sensitivity, specificity and predictive values of AEC and CRP in diagnosing sepsis at the defined cut off was calculated using ROC curve. The prognostic accuracy was also calculated.*
Observations: *The mortality rate of sepsis in our institution is 83.6%. The sensitivity, specificity, Positive and Negative Predictive Values of Absolute Eosinophil count in diagnosis of sepsis is 57.4%, 98.4%, 97.2% and 69.8% respectively.The sensitivity, specificity, Positive Predictive Value and Negative Predictive Value of C Reactive protein is 91.8%, 91.8%, 91.8% and 99.8% respectively.. Of the 51 deaths, 46 had CRP more than 6. Among the 10 cases cured, all had a CRP more than 6. Absolute Eosinophil Count of < 50 was seen in 29 of the 5eaths, and 6 of the 10 cases who were cured also had an AEC of < 50. So according to our study, both CRP and AEC are poor predictors of prognosis in sepsis.*

Introduction

Sepsis, a syndrome of physiologic, pathologic and biochemical abnormalities induced by infection, is a major public health concern(1). Sepsis exists on a continuum of severity, ranging from infection and bacteremia to sepsis and septic shock, which can lead to multiple organ dysfunction syndrome (MODS) and death. The clinical and biologic phenotype of sepsis is modified by pre existing illness, co morbid conditions, medications and interventions.(1)

The causative organism for sepsis can be virus, bacteria, fungus or even parasite. Host factors like alcoholism, diabetes mellitus, chronic kidney disease, malignancies, immunosuppressive treatment and advanced age are risk factors for developing sepsis.

The definitions of sepsis have rapidly evolved since the early 1990s. The Systemic Inflammatory

Response Syndrome is no longer included in the definition since it is not always caused by infection.

Overall mortality among patients admitted with sepsis in the ICU will be around 62%. Because of the high mortality, early detection is of utmost importance. Since cultures are positive only in < 50% of the cases, various biochemical markers are evaluated to improve the diagnostic sensitivity and prognosis.

The present study therefore compares the utility of Absolute Eosinophil Count (AEC) Vs C reactive protein(CRP) in the diagnosis and prognosis of Sepsis.

Aims and Objectives

1. To compare Absolute Eosinophil Count and CRP as a diagnostic and prognostic marker in sepsis.
2. To assess the validity of Absolute Eosinophil Count in sepsis as a diagnostic and prognostic marker in sepsis.

Materials and Methods

It is a prospective observational case control study. The sample size calculated was 60. The sample size decided was 65.

Patients admitted in a Tertiary care centre in South Kerala with suspected sepsis who satisfied the inclusion criteria were studied.

Cases

Inclusion Criteria

1. Patients > 18 years of age who satisfied the diagnostic criteria of sepsis by the qSOFA criteria.

Exclusion Criteria

1. Patients with HIV, TB and Malignancy.
2. Patients on long term immunosuppression.
3. Those not giving consent.

Controls

65 age and sex matched controls without any acute illness were taken as controls. They satisfied most of the exclusion criteria.

All the patients who satisfied the inclusion criteria were studied with a detailed clinical examination as well as CRP and Absolute Eosinophil Count.

Of the 65 patients who got enrolled, 4 were taken to other centres and hence were lost for follow up. Hence the sample size was 61 in both cases and controls.

Observations

Figure 1: Percentage Distribution of cases according to Age

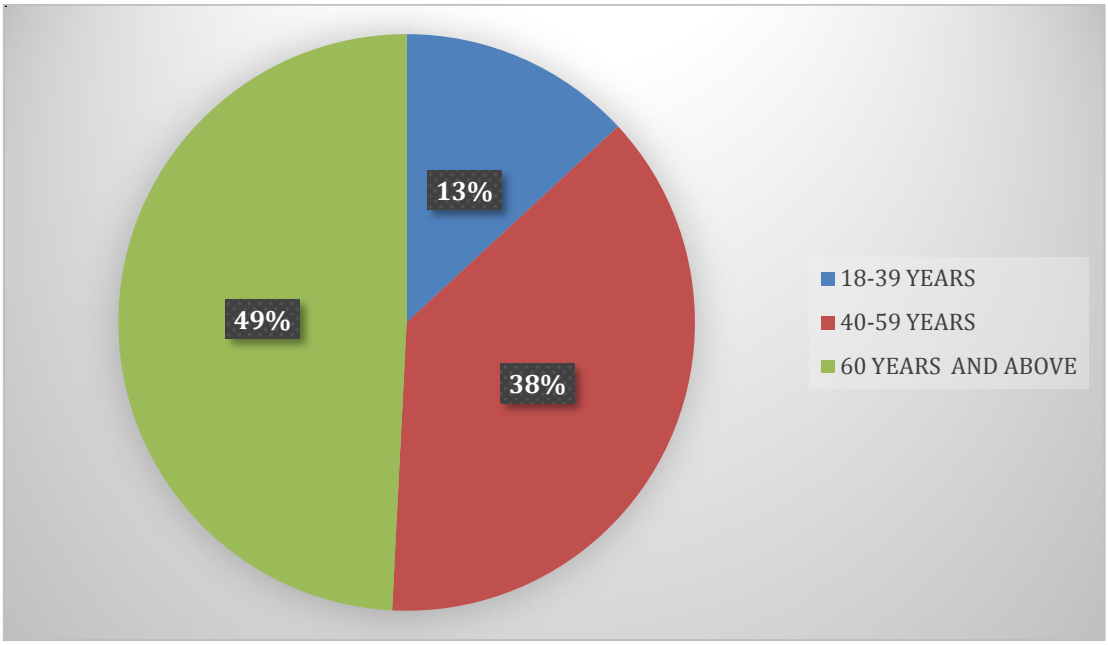


Figure 2: Percentage Distribution of Cases according to qSOFA Score:

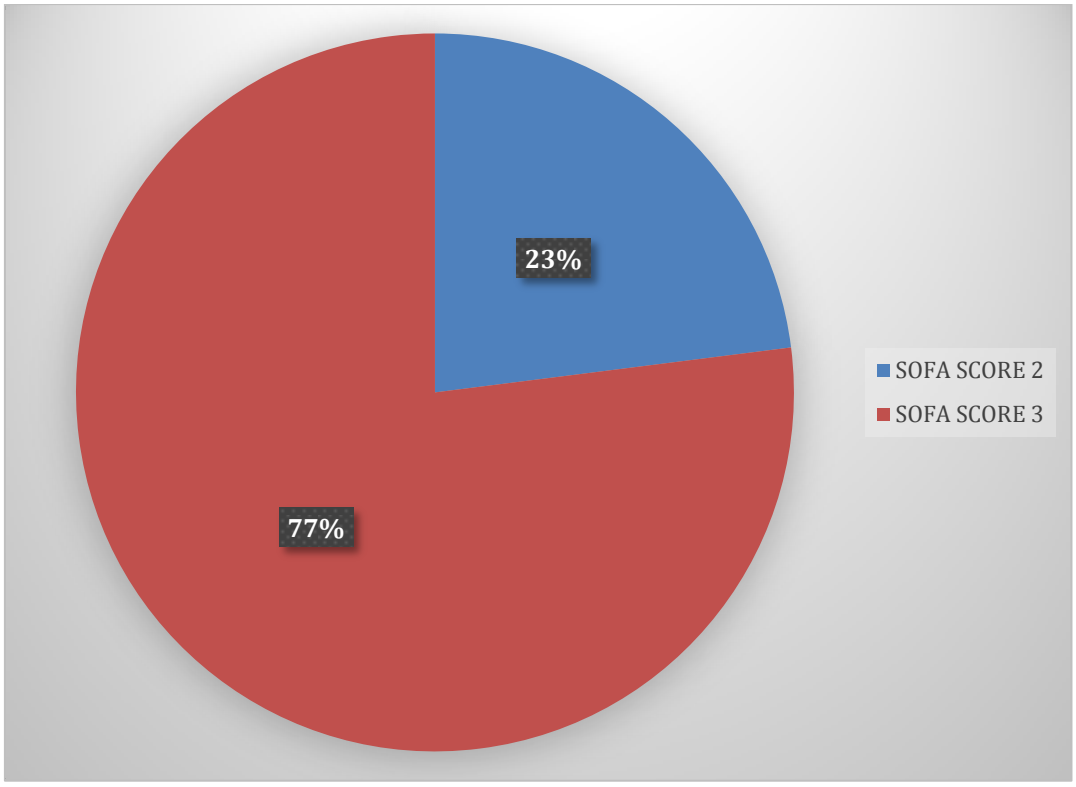


Figure 3: Percentage Distribution of Cases according to AEC

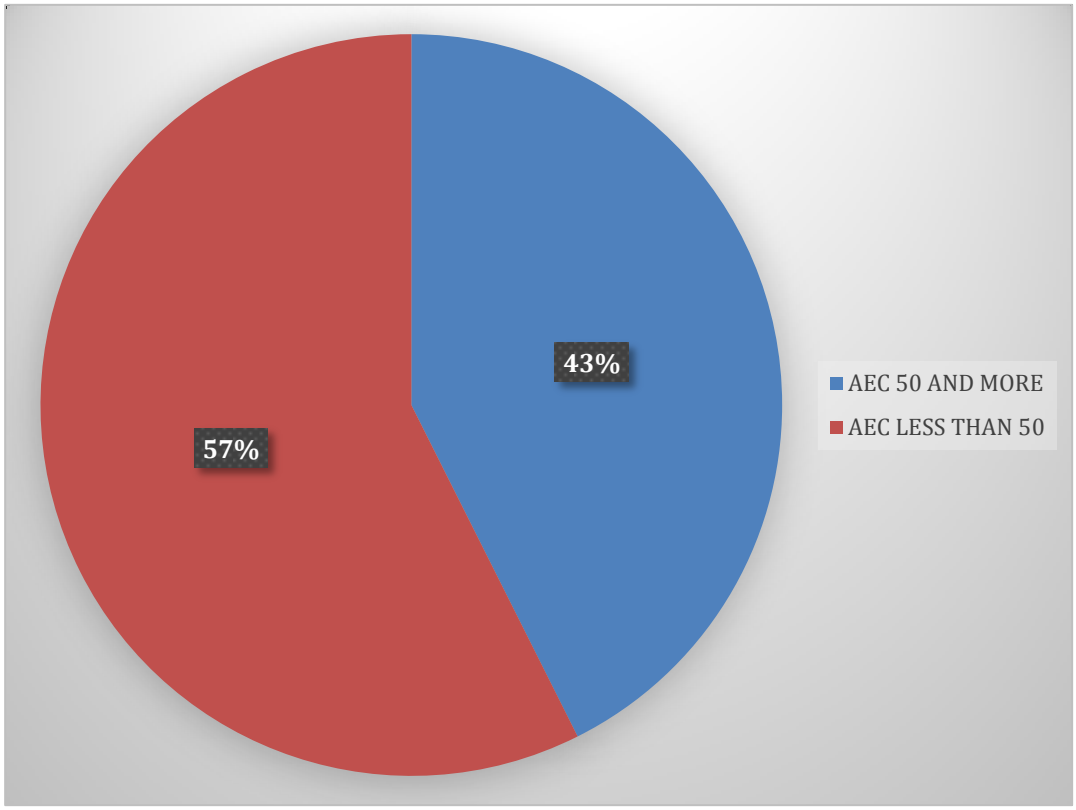


Figure 4: Percentage Distribution of Controls according to AEC

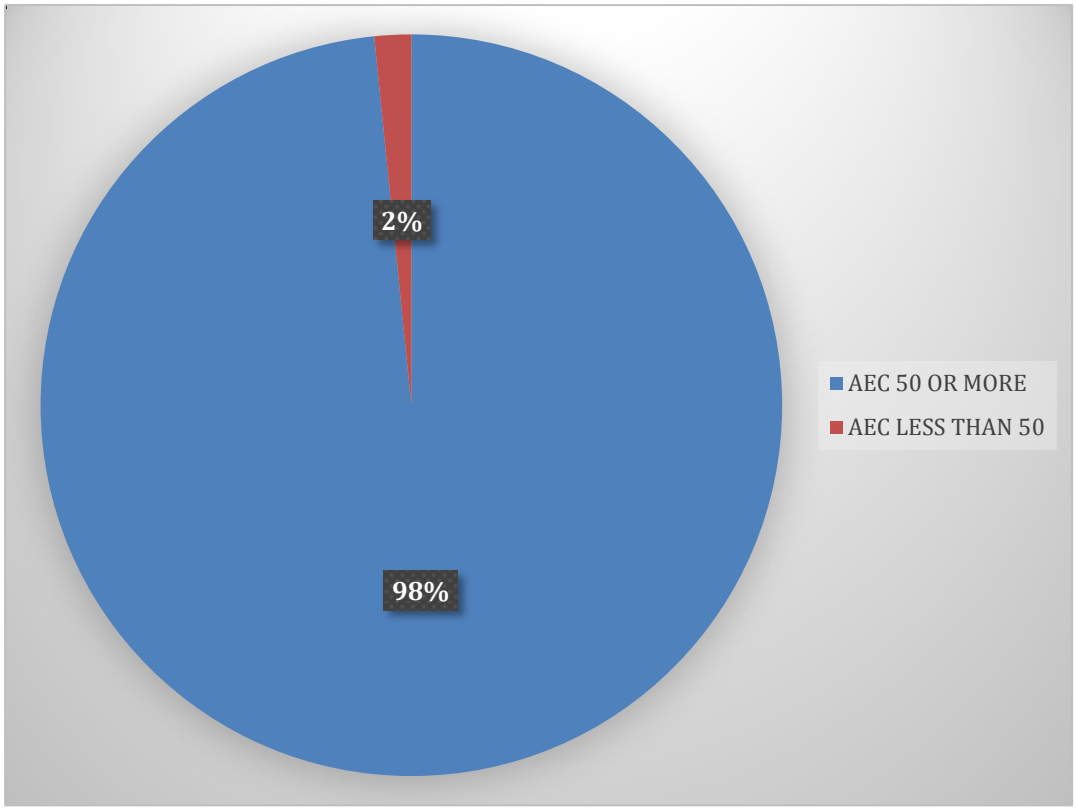


Figure 5: Percentage Distribution of cases According to CRP

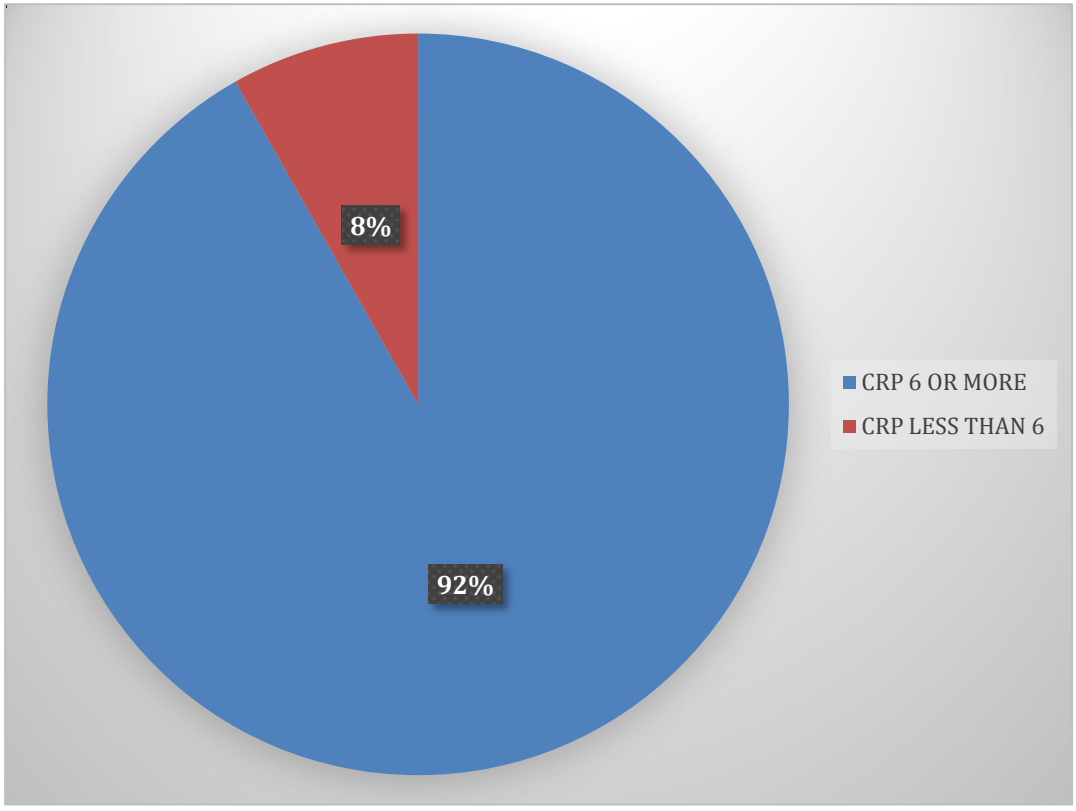


Figure 6: Percentage Distribution of Controls according to CRP

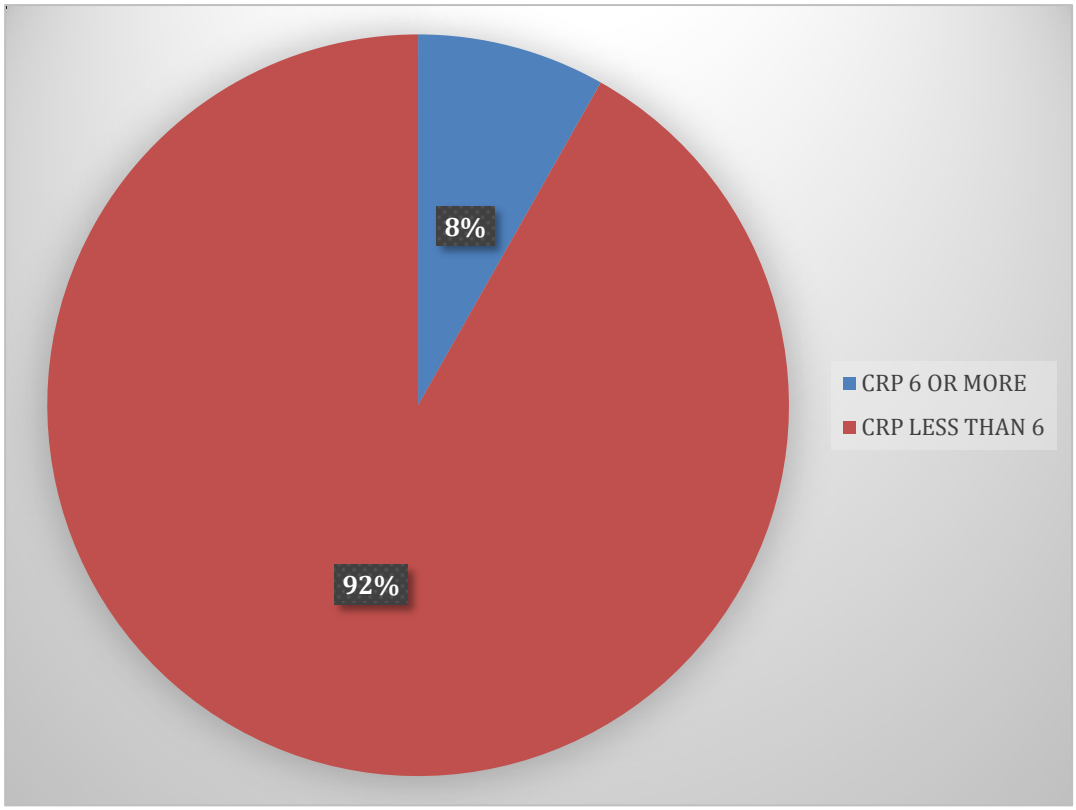


Table 1: Predictive Power of AEC as Diagnostic Marker in Sepsis

Absolute Eosinophil Count	Sepsis	
	Present	Absent
Less than 50	35	1
More than or equal To 50	26	60

Sensitivity 57.4%, Specificity 98.4%, Positive Predictive Value 97.2%, Negative Predictive Value 69.8%, Accuracy 77.9%

Table 2: Predictive Power of CRP as Diagnostic Marker in Sepsis

CRP	Sepsis	
	Present	Absent
Less than or Equal to 6	5	56
More Than 6	56	5

Sensitivity 91.8%, Specificity 91.8%, Positive Predictive Value 91.8%, Accuracy 91.8%.

Table 3: Comparison of AEC and CRP as a Diagnostic Marker in Sepsis

	AEC	CRP	Z	P VALUE
Sensitivity	57.4%	91.8%	6.176	<0.01
Specificity	98.4%	91.8%	2.368	0.018
Positive Predictive Value	97.2%	91.8%	1.858	0.064
Negative Predictive Value	69.8%	91.8%	4.368	<0.01
Accuracy	77.9%	91.8%	3.034	0.002

Best Cut Off For AEC as a Diagnostic Marker in Sepsis

The best cut off for AEC under the ROC curve is 245. Area under the curve = 0.897. (95% CI 0.836-0.959), p=0.000 with a sensitivity of 83.6%, specificity of 91.8% and a Positive Predictive Value of 91.8%.

Best Cut Off For CRP as a Diagnostic Marker in Sepsis

The best cut off value obtained for CRP as a diagnostic marker in sepsis using an ROC curve is 7. Area under the curve =0.938(95%CI 0.892-0.983), p=0.000, with a sensitivity of 91.8%,

specificity of 91.8% and a Positive predictive value of 91.8%.

Predictive Power of AEC as a Prognostic Marker in Sepsis

Kappa =-0.02, p=0.854. Poor agreement, with a sensitivity of 56.9%, specificity of 40% and accuracy of 54.1%

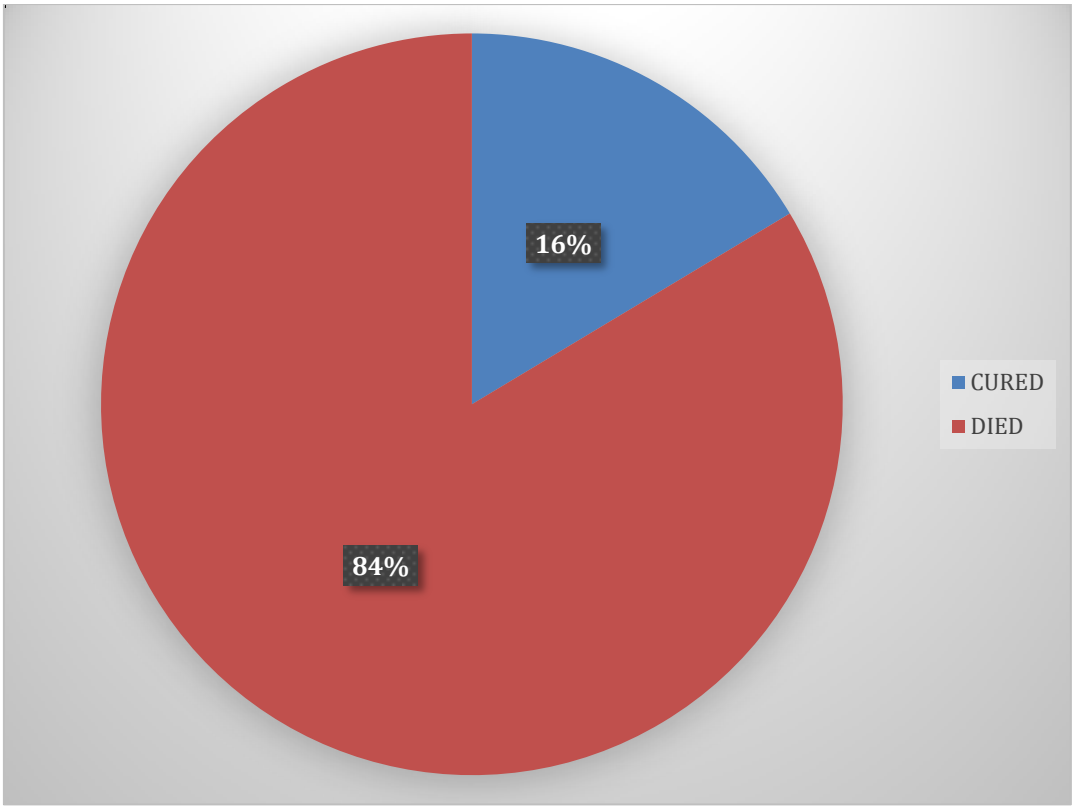
Predictive Power of CRP as a Prognostic Factor in Sepsis

Kappa=-0.12, p= 0.301. Poor agreement, with a sensitivity of 90.2%, 0% specificity and an accuracy of 75.4%

At the best cut off of 35, the sensitivity of AEC as a prognostic marker is 35.3%, specificity is 90%, accuracy of 44.3%. Area under the curve=0.539(95%CI 0.391-0.688) p=0.697.

At the best cut off of 39, the sensitivity of CRP is 41.2%, specificity is 60% and accuracy is 44%. Area under the curve =0.423(95%CI 0.248-0.597), p=0.442.

Figure 7: Percentage Distribution of Samples according to the end Point



Discussion

The early diagnosis of sepsis plays an integral role in the morbidity and mortality of sepsis. The clinical parameters that make up sepsis syndrome are not specific and frequently overlap with the presentation of a Systemic Inflammatory Response Syndrome secondary to non infectious causes[(2)].

Acute infections induce eosinopenia through several mechanisms, like sequestration of eosinophils at the site of inflammation, emergence of mature eosinophils from the bone marrow and suppression of eosinophil production[(3)]. Acute stress also involves eosinopenia, which is mediated by adrenal glucocorticoids and epinephrine.

An early diagnosis of sepsis before microbial cultures are available would certainly facilitate the choice of antibiotic therapy and reduce patient mortality[(4)].

This is a prospective observational case-control study to compare the accuracy of two biomarkers, Absolute Eosinophil Count and C Reactive Protein as diagnostic and prognostic markers. In

this study, C reactive protein of >6 and Absolute Eosinophil Count of < 50 is considered as a biomarker of sepsis.

64 cases were enrolled in the study of which 3 were lost for follow up. Hence the total number of cases were 61. 61 age and sex matched controls were taken from the bystanders of various patients.

Among the cases, 49.2% were in the age group of > 60 years. Only 13.1% cases of sepsis was seen in those less than 40 years of age. 77% of cases had a qSOFA score of 2 and 23% had a score of 3. 57.4% of the cases had an Absolute Eosinophil count of <50. Out of the controls, 98.4% had an absolute eosinophil count of >50. So, the sensitivity, specificity, Positive and Negative Predictive Values of Absolute Eosinophil count in diagnosis of sepsis is 57.4%, 98.4%, 97.2% and 69.8% respectively.

91.8% of the cases had C Reactive Protein of >6, whereas only 8.2% of the controls had a C reactive protein of >6. Hence, the sensitivity, specificity, Positive Predictive Value and Negative Predictive Value of C Reactive protein is 91.8%, 91.8%, 91.8% and 99.8% respectively.

Therefore, C Reactive Protein has greater sensitivity in diagnosis of sepsis and Absolute Eosinophil Count has a greater specificity.

In a study conducted by Khalid Abidi et al, the sensitivity of AEC is 80%, specificity is 91%[(5)]. Compared with the study done by Jose Garnacho-Montero et al, the sensitivity of C Reactive Protein is 90.6%, which is comparable to the present study. But our study shows a higher specificity of CRP compared to their study[(6)].

End point taken in our study was either cured or died. 83.6% cases of sepsis died in our study. Of the 51 deaths, 46 had CRP more than 6. Among the 10 cases cured, all had a CRP

More than 6. So CRP is a poor predictor of outcome in sepsis. Absolute Eosinophil Count of < 50 was seen in 29 of the 5eaths, and 6 of the 10 cases who were cured also had an AEC of < 50. So according to our study, AEC is also a poor predictor of prognosis in sepsis.

Best cut off of AEC as a prognostic marker is below 35. Area under the curve is 0.539, p value 0.697, with sensitivity of 35.4%, specificity of 90%, Positive Predictive Value of 97.4% and Negative Predictive Value of 21.4%.

Best cut of CRP as a prognostic marker is above 39. Area under the curve is 0.423, p value 0.697, with a sensitivity of 41.2%, specificity of 60%, Positive Predictive Value of 84% and Negative Predictive Value of 84%.

Our study concludes that CRP has greater sensitivity, whereas, AEC has greater specificity in diagnosing sepsis. Both AEC and CRP are poor predictors of outcome. A larger population and a sub group analysis of cause of sepsis may throw further light in this context.

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