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Evaluation of Procalcitonin, CRP and Blood culture in diagnosis of sepsis and their correlation with WBC counts.

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Abstract
Background: *Procalcitonin , C Reactive protein and blood culture methods are used as diagnostic marker of sepsis.*
Objective: *To evaluate diagnostic markers of infection in patients admitted with features of sepsis, comparing role of procalcitonin and CRP with WBC counts in all clinically suspected cases of sepsis.*
Methods: *We conducted retrospective study of 50 patients admitted with clinical features of sepsis, evaluated diagnostic role of Procalcitonin and CRP in 50 clinically suspected cases of sepsis and correlated them with WBC counts by dividing the patients on the basis of WBC counts into three catagories-low, normal and high.*
Result: *The study comprised of 50 patients , out of these cases only 5 were culture positive. All 50 cases were catagorised into 3 groups on the basis of WBC counts, less than 4000/cumm : 3cases(6%), 4000-10000/cumm: 15 cases(30%) and cases number >10000/cumm: 32 cases(64%). CRP was elevated in 46(92%) patients among these cases majority 30 had elevated WBC counts, 13 had normal and 03 had below normal counts. PCT was <0.5ng/ml in 17(34%) of cases, number of cases with elevated PCT value 18(36%) had values between (0.5-2.0ng/ml), 07(14%) between 2.0-10.0ng/ml and 08 had values more than 10ng/ml. We calculated coefficient of correlation between WBC counts and with CRP and PCT ,CRP has weak correlation with both low and high WBC count and PCT also shown weak correlation with both low and high WBC counts.*
Conclusion: *It was concluded that although CRP and PCT have role as a sepsis marker but their correlation with WBC was found insignificant. Procalcitonin and CRP is good prognostic markers of infection but not definitive marker of sepsis, as it could raise in others non bacterial cause of infections and inflammatory conditions, blood culture is still gold standard method to diagnose sepsis.*
Keywords*: CRP,PCT, Sepsis*
Abbreviations: *CRP:- C Reactive protein ,PCT:- Procalcitonin, SIRS:-Systemic inflammatory response.*

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I. Introduction

The early detection of infection has clinical importance as it could lead to timely detection and lead to better clinical outcome. The gold standard remain culture method but the diagnostic delay and contaminants pose the major impedance to quick reliable diagnosis. Now a days CRP, WBC , tumor necrosis factor-alpha, interleukins are emerging as non specific markers for diagnosing sepsis but procalcitonin a member of calcitonin super family can be better tool for diagnosing sepsis and to distinguish between bacterial and viral infections, procalcitonin is a discriminator as viral infections trigger alpha-interpheron by macrophages which inhibit TNF synthesis ,hence PCT level does not enhance in viral infection as it raise in bacterial infections[(1)]. All types of microbes can causes sepsis but bacteria cause the most[(2,3,4)]. During sepsis the microbes invade the blood stream and release various virulent factors these evokes the release of endogenous mediators from endothelial cells, macrophages, neutrophils and plasma cells[(5)], sepsis related inflammatory response arise when body attempts to neutralize pathogenic infection which in turn leads to tissue damage and organs of hosts[(6,7)].Clinical symptoms of sepsis include tachycardia, tachypnea ,fever, leucocytosis/leucopenia. Usually severe sepsis associated with multiple organ dysfunction or hypotension is known as septic shock[(8)].The serum level of procalcitonin rises rapidly than CRP and peaks within short time and also when patients respond to antimicrobial therapy, PCT level returns to normal faster than CRP which makes it better marker for sepsis[(9)]. But procalcitonin also have some limitations like CRP as its increased level not always associated with infection, it can raise after severe fungal infection, acute infection with plasmodium falciparum, after major trauma or surgery, after severe cardiogenic shock, prolonged organ perfusion anomalies, medullary carcinoma

thyroid etc and decreased level can not exclude the presence of bacterial infection, it might be obtained during early course of infection.

`Range of procalcitonin and its interpretation:-
<0.1ng/ml = No systemic inflammatory response.
0.1-0.49ng/ml = Minor or no significant inflammatory response.
0.50-1.99ng/ml = Moderate risk for progression to SIRS.
2-9.99ng/ml = Severe SIRS, most likely due to sepsis.
>10ng/ml = High likelihood of severe sepsis or septic shock (due to severe bacterial infection).
CRP is synthesized by hepatocytes and vascular endothelial cells and its secretion mediated by IL-6, IL-1 and TNF-alpha[10].It binds to polysaccharides in presence of calcium on surface of microorganisms to trigger classical compliment pathway[11].It is elevated in rheumatoid arthritis, cardiogenic shock ,other inflammatory disorders and in some bacterial infection, it exponentially decreases over 18-20 hour period[12],tissue damage like trauma and cancer increases it from 1mg/lit to 500mg/lit within 24-72hours[13,14].

II. Material And Methods

The retrospective study was conducted in the department of pathology in Cygnus hospital, Kurukshetra (Haryana). All patients were adults admitted in hospital in the year 2019, their blood counts, CRP, PCT and blood culture reports taken into this study. Total WBC counts was obtained using Norma, PCT by GP machine(Getein Bio tech) and CRP by ERBA CHEM-5Plus V2.The study cases were divided into three three groups on the basis of WBC groups.

III. Results

The study comprised of 50 patients, 36 (72%) males and 14(28%) females aged from 21 to 83 years . Out of these, 5 cases were culture positive and 45 cases came negative. All cases were catagorised into 3 groups on the basis of WBC counts, less than 4000/cumm : 3 cases(6%), 4000-10000/cumm: 15 cases(30%) and cases number >10000/cumm: 32 cases(64%). CRP was elevated in 46(92%) cases among these patients majority 30 had elevated WBC counts, 13 had normal and 03 had below normal counts shown in Table 2. PCT was <0.5ng/ml in 17(34%) of cases and cases with elevated PCT value 18(36%) had values between (0.5-2.0ng/ml), 07(14%) between 2.0-10.0ng/ml and 08 had values more than 10ng/ml (Table 3). We calculated coefficient of correlation between WBC counts and with CRP and PCT. The results as shown in Table 4 indicate that CRP has weak correlation with both low and high WBC count. PCT also shown weak correlation with both low and high WBC counts. Overall correlation of CRP with WBC count was 0.141 and of PCT 0.064 which are low values.

Table1 : Showing stratification of cases on the basis of WBC counts

WBC count in /cumm	Number of patients	Percentage
<4000	03	06
4000-10,000	15	30
>10,000	32	64

Table2: CRP in patients with infection

WBC count/cumm	<3mg/lit	>3mg/lit	
<4000	00	03	03
4000-10,000	01	13	14
>10,000	03	30	33
	04(8%)	46(92%)	50(100%)

Table 3: PCT in patients with infection.

WBC count/cumm	<0.5	0.5-2.0	2.0-10	>10	
<4000	01	00	00	02	03
4000-10,000	05	08	01	00	14
>10,000	11	10	06	06	33
	17(34%)	18(36%)	07(14%)	08(16%)	50(100%)

Table 4:Correlation coefficient

WBC	CRP	PCT
Low	-0.172	-0.269
Normal	0.265	0.050
High	-0.237	-0.117
Total WBC	0.141	- 0.064

IV. Discussion

The diagnosis of sepsis prior to culture is very helpful in early initiation of treatment. In our study only 5 cases out of 50 cases came blood culture positive with high WBC counts, CRP values and PCT values. 33 cases had elevated PCT values out of which 18 cases had PCT value in range 0.5-2.0ng/ml, 7 cases had 2.0-10ng/ml and 8 cases had >10ng/ml . However 28 cases shown false positive PCT values but majority of them had PCT values between 0.5 to 2.0ng/ml and 15 cases showed significant high PCT values that is more than >2.0ng/ml. Similarly CRP was raised in 46 cases out of which 30 cases had elevated WBC count that is more than 10,000/cumm and 3 cases with WBC count <4000/cumm. However 41 cases which were blood culture negative gave a positively high CRP values. In present study we have not found any advantage of PCT over CRP which is comparable with other study[15].CRP when compared to PCT is affordable specially in resource limited set ups. Our study clearly indicates that of these three parameters for sepsis, none of the index can confidently rule out presence or absence of sepsis. In spite of novel new marker like PCT ,it has high probability to miss sepsis therefore it is essential for clinician not to rely on any single laboratory parameters . It's a multidisciplinary approach where sole reliance on any single parameter can miss sepsis may lead to an unfavourable outcome for patients.

V. Conclusion

Our study conclude that not a single method is reliable to diagnose sepsis, blood culture considered as gold standard method to diagnose sepsis but it can come false negative due to administration of antibiotics prior to sampling ,PCT and CRP aid in diagnosis of sepsis. Ideally combination of these methods should be taken into consideration to diagnose sepsis.

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