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Diagnostic Value of Procalcitonin versus C-Reactive Protein among Infected Adults in The Intensive Care Unit

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Abstract

Background:*Infection is a major challenge in emergency departments and intensive care units (ICUs), causing high mortality and morbidity. Early diagnosis and timely intervention are essential to improve the prognosis of infected patients. Serum procalcitonin (PCT) is a biological marker of increasing interest for detecting bacterial infections including sepsis . It has been widely investigated that an increase in serum PCT correlates closely with the inflammatory response to microbial infections. CRP is acute phase reactant which is produced not only during infection but also in many types of inflammation. The study aimed to assess the diagnostic accuracy of procalcitonin versus CRP for sepsis in adults.****Methods:****This study was performed in The Intensive Care Unit Of Internal Medicine Department and medical microbiology and immunology department , Zagazig University Hospitals from the period between December 2019 and May 2020.All participants were submitted to the following:investigations:(Evaluation of Serum procalcitonin level and CRP).* ***Results:****There is no statistically significant difference between the studied groups as regard age, sex, and anthropometric measures. Our results revealed that Positive cases were significantly higher regard all markers. All markers with significant area under curve and cutoffs Higher validity regard detection of positive culture was CRP then PCT. Our results showed that Septic shock group was significantly higher regard CRP with no sig difference between infection and sepsis , regard PCT septic shock group was sig higher than other group and sepsis group was sig higher than infection . regard detection of sepsis, All markers with significant area under curve and cutoffs Higher validity was PCT and finally CRP.* ***Conclusion:*** *PCT and CRP are a promising markers for diagnosis of infection and sepsis. CRP is superior than PCT in detection of infection.*

Key words: metabolic syndrome- Uric acid- Evaluation

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I. Introduction:

Infection is a major challenge in emergency departments and intensive care units (ICUs), causing high mortality and morbidity. Early diagnosis and timely intervention are essential to improve the prognosis of infected patients. Bacterial culture is generally regarded as the gold standard for the diagnosis of sepsis, but it is time-consuming, frequently yields false-negative results, and microbial contamination can greatly affect its diagnostic value.[(1)]

Infectionif left untreated may lead to sepsis .Sepsis is a type of systematic inflammatory response syndrome (SIRS) caused by the invasion of pathogens or conditional pathogenic bacteria into the blood circulation. It can develop into severe sepsis, septic shock, and multiple organ failure. Sepsis occurs in 1%–2% of all hospitalized patients and accounts for as much as 25% of intensive care unit (ICU) cases. Its clinical manifestations vary with a rapid progression. As a costly disease, sepsis not only lowers patient's living quality, but also increases the mortality significantly.[(2)]

Various biomarkers have been reported useful in sepsis diagnosis, such as procalcitonin and C-reactive protein(CRP). However, these biomarkers may also be elevated in nonseptic conditions such as trauma, burn, and postoperative settings, and some are slow to rise after the onset of sepsis. **It** thus remains necessary to find reliable biomarkers to replace or improve those that are currently available.[(3)]

Recently, several immunologic biomarkers have been assessed in order to develop the best indicator of infections. Soluble CD14 subtype(sCD14-ST), known as presepsin, is a biomarker which has been demonstrated as a new, emerging, early indicator for the detection of different infections. Presepsin is elevated in response to bacterial infections and is decreased after healing or efficient treatment. [(4)]

Serum procalcitonin (PCT) is a biological marker of increasing interest for detecting bacterial infections including sepsis. It has been widely investigated that an increase in serum PCT correlates closely with the inflammatory response to microbial infections.[(5)]

CRP is acute phase reactant which is produced not only during infection but also in many types of inflammation and binds to polysaccharides in pathogens , activating the classical complement pathway. [(6)]

The study aimed toassess the diagnostic accuracy of procalcitoninversus CRP for sepsis in adults.

II. Patients and Methods

A)Site of study: This study was performedin The Intensive Care Unit Of Internal Medicine Department and medical microbiology and immunology department , Zagazig University Hospitals from the period between December 2019 and May 2020.

B)Study design :A cross-sectional study

C)Patient :

- **Sample size:**Using OPEN_EPI , This study included a total number of 96 subjects subdivided into three groups patients by using the most commonly used scoring system in medical ICU (SOFA

and qSOFA) score on admission for Severity assessment after suspicion of infection .

Group (I): infection including 65 patients

Group (II): sepsis including 23 patients

Group (III): septic shock including 8 patients

❖ **Inclusioncriteria:**

Any suspected case of infection among adultswith age group 18-60 years old, of both sex, in the intensive care unit according to clinical examination and routine investigations

IVMethods:

All participants were submitted to the following:

Thorough history taking:

1- **Full clinical examination**

2- **investigations:**

A- Routine investigations

B- Special investigations including

1- Evaluation of Serum procalcitonin level by ELISA technique.

2- CRP

3-Identification of micobes revealed from Blood culture at least two blood cultures from different sites, and other cultures from any suspected site of infection such as ; sputum ,wound ,urine,…….etc

Ethical clearance:

Written informed and oral consent were taken from relatives of patients who were participated in the study .in addition to approval for performing the study was obtained from internal medicine and medical ICU department, zagazig university hospitals after taking Institutional Review Board (IRB)approval.

Statistical analysis

Data collected throughout history, basic clinical examination, laboratory investigations and outcome measures coded, entered and analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) **(Statistical Package for the Social Sciences)** software for analysis. According to the type of data qualitative represent as number and percentage , quantitative continues group represent by mean ± SD , the following tests were used to test differences for significance;. difference and association of qualitative variable by Chi square test (X^2) . Differences between quantitative independent groups by t test or Mann Whitney, multiple by ANOVA or KruskalWalis, correlation by Spearman's correlation. P value was set at <0.05 for significant results &<0.001 for high significant result.

III. Results:

– Age was distributed as **51.93±10.74** with minimum 19 years and maximum 60 years, SBP, DBP, MAP and HR were distributed as **114.25±12.52**, **71.65±13.25, 83.5±11.36 and 88.69±9.58**, regard sex male were 54.2% and female 45.8% , 52.1% had HTN and 27.1% had DM regard smoking 51% were smoker, majority had Pneumonia **(Table 1).**

– CRP was distributed as **89.93±65.8** and PCT as **11.54±18.52(Table 2).**

– 75% had positive result in culture**(Table 3).**

– Positive cases were significantly higher regarding all markers**(Table 4).**

– All markers with significant area under curve and cutoffs higher validity (performance of CRP, PCT regard detection of positive culture) was CRP then PCT**(Table 5).**

– Septic shock group was significantly higher regard CRP with no sig difference between infection and sepsis by LSD, regard PCT septic shock group was sig higher than other group and sepsis group was sig higher than infection **(Table 6).**

– PCT was not significant AUC and cutoff with sensitivity 63.3% and specificity 58.8%**(Table 7).**

– All markers with significant area under curve and cutoffs higher validity was PCT then CRP **(Table 8).**

Table1: basic demographic and clinical data distribution among studied group (N=96)

Age	**Mean± SD**	**51.93±10.74**	
	Median (Range)	**56.5 (19-60)**	
SBP	**Mean± SD**	**114.25±12.52**	
	Median (Range)	**110.0 (85-145)**	
DBP	**Mean± SD**	**71.65±13.25**	
	Median (Range)	**70.0 (55-90)**	
MAP	**Mean± SD**	**83.5±11.36**	
	Median (Range)	**82.0 (55-108)**	
HR	**Mean± SD**	**88.69±9.58**	
	Median (Range)	**85.0 (70-110)**	
		N	**%**

Sex	**Female**	**44**	**45.8**
	Male	**52**	**54.2**
HTN	**-VE**	**46**	**47.9**
	+VE	**50**	**52.1**
DM	**-VE**	**70**	**72.9**
	+VE	**26**	**27.1**
Smoking	**-VE**	**47**	**49.0**
	+VE	**49**	**51.0**
Suggested sources of infection	**Pneumonia**	**55**	**57.2**
	UTI	**23**	**23.9**
	Dermal	**6**	**6.2**
	abdominal	**4**	**4.2**
	endocarditis	**4**	**4.2**
	others	**4**	**4.2**
	Total	**96**	**100.0**

SBP: systolic blood pressure, DBP: diastolic blood pressure, MAP: mean arterial blood pressure,HR: heart rate

Table 2: CRP and PCT distribution among studied group

	CRP	**PCT**
Mean± SD	**89.93±65.8**	**11.54±18.52**
Median (Range)	**62.5 (3-363)**	**1.7 (0.15-85.6)**

Table 3: culture result distribution among studied group

		N	%
Culture	**-VE**	**24**	**25.0**
	+VE	**72**	**75.0**
	Total	**96**	**100.0**

Table 4: comparison between positive and negative culture regard CRP, PCT.

		-VE culture	+VE culture	Mann Whitney	P
CRP	**Mean ±SD**	**6.92±5.21**	**117.6±82.26**	**-6.562**	**0.00****
	Median (Range)	**5.0 (3-34)**	**108.0 (5-363)**		
PCT	**Mean ±SD**	**3.75±8.52**	**14.14±18.65**	**-2.120**	**0.037***
	Median (Range)	**0.76 (0.15-41.97)**	**3.13 (0.15-100.0)**		

Table 5: AUC, cutoff and validity of CRP, PCT regard detection of positive culture

Test Result Variable(s)	Area	Cutoff	P	95% Confidence Interval		Sensitivity	Specificity
				Lower Bound	Upper Bound		
CRP	**0.984**	**>9.5**	**0.00****	**0.963**	**1.000**	**99.0%**	**98.0%**
PCT	**0.684**	**>1.58**	**0.007***	**0.569**	**0.799**	**78.5%**	**68.0%**

Table 6: comparison between bacteremia , sepsis and septic shock regard CRP, PCT.

	Infection	Sepsis	Septic shock	KruskalWallis	P
CRP	**111.2±84.7**	**101.25±55.13**	**188.75±85.29***	**3.718**	**0.029***

	102.5 (5-363)	**100.5 (5-195)**	**233.5 (35-278)**		
PCT	**8.64±16.25**	**18.51±20.54**	**38.37±25.13**	**6.897**	**0.002***
	1.75 (0.15-48.6)	**8.17 (0.19-68.6)**	**37.7 (1.9-85.6)**		

Table 7: AUC, cutoff and validity of PCT regard detection of sepsis

Test Result Variable(s)	Area	Cutoff	P	95% Confidence Interval		Sensitivity	Specificity
				Lower Bound	Upper Bound		
PCT	**0.632**	**>9.5**	**0.110**	**0.481**	**0.782**	**63.3%**	**58.8%**

Table 8: AUC, cutoff and validity of CRP, PCT regard detection of septic shock

Test Result Variable(s)	Area	Std. Error[a]	P	95% Confidence Interval		**Sensitivity**	**Specificity**
				Lower Bound	Upper Bound		
CRP	**0.766**	**>120.5**	**0.015***	**.567**	**.965**	**83.3%**	**62.0%**
PCT	**0.854**	**>20.5**	**0.001****	**.726**	**.981**	**87.0%**	**88.0%**

IV. Discussion

Regarding demographic and risk factors data, Age was distributed as 51.93±10.74 with minimum 19 years and maximum 60 years, regard sex male was 54.2% and female 45.8%.

52.1% had HTN and 27.1% had DM regard smoking 51% were smoker,with no significant difference or association on comparison between positive and negative culture.

On the other hand, Factors responsible for increasing the risk of infection are mainly dependent on patient factors like age, gender, co-morbidities i.e. diabetes, cardiovascular diseases, hypertension, immunocompromised state, smoking, alcohol, obesity, stress, malnutrition enhance the risk of infection[7].

regard distribution of (INR) was 1.85±0.45 **,** that interprets the condition of coagulopathy associated with sepsis.this was in accordance with a study showed that Acute vascular endothelial dysfunction is a central

event in the pathogenesis of sepsis, increasing vascular permeability, promoting activation of the coagulation cascade, tissue edema and compromising perfusion of vital organs. [8]

In our study, distribution among all studied group as following: PCT as 11.54±18.52 and PSP was 3.81±3.65 .but, on comparison between positive and negative culture regard PCT, Positive cases were significantly higher regard all markers: PCT as 14.14±18.65. on regard to detection of positive culture, all markers with significant area under curve and cutoffs Higher validity were CRP (with Sensitivity 99%, Specificity 98%) then PCT (with Sensitivity 78.5%, Specificity 68%).

Positive result in culture was 75% at a rate of 72 from 96 patient. Inside this positive percentage 66.7% had infection only and 22.2% had sepsis and 11.1% had septic shock.

With agreement of our study for cultures may not to be positive in all cases .Bacteria are by far the most common causative microorganisms in sepsis, and cultures are positive in about 50% of cases . It is known that cultures lack the sensitivity to identify all bacteria. Postulated reasons include prior antibiotic exposure, sampling error, insufficient volume for blood cultures, poor transport conditions, and slow-growing or fastidious bacteria [9].

Culture finding distribution among studied group as following , Majority were Klebsilla pneumonia, E. coli and Staphylococcus aureus with 27.8%, 20.8% and 18.1%.on the other hand, results from previous study showed that most prevalent bacteria causing infections are Pseudomonas aeruginosa, Klebsiella spp., and E. coli [10].

Similar results were reported from a prospective study of severe sepsis and septic shock in ICU patients in Thailand conducted between 2004 and 2006. Out of 390 patients, 241 patients had microorganisms isolated from any site, and 106 had positive blood cultures. The main pathogens were Klebsiellapneumoniae (19.9%) and E. coli (14%).[11]

Our findings were consistent with another study showed that In developed countries, Gram positive bacteria were the most frequently identified in patients with sepsis. In different studies conducted in High income countries (HICs), the leading Gram positive organisms isolated were S. aureus, Enterococcus species, S. pneumoniae while organisms such as E.coli, K. pneumoniae, Acinetobacterbaumannii and Pseudomonas species constituted the most common Gram negative species[12].

Our results regard Suggested sources of infection were distributed as following , Pneumonia 57.2%,UTI 23.9%,Dermal 6.2%,abdominal 4.2%,endocarditis 4.2%,others 4.2%.on the other hand ,another study showed The most common sites of infection were the lungs (31.0%), followed by intra-abdominal sites (26.3%), the urinary tract (18.4%), and soft tissue (10.9%).[13]

In our study, septic shock group was significantly higher regard CRP with no significant difference between infection and sepsis, regard PCT. septic shock group was significantly higher than other group and sepsis group was significantly higher than infection but regard to sepsis. Accordingly, our findings indicate that CRP is superior than PCT in detection of infection.

In agreement with our study, In Yamamoto et al. 2019 study, PCT and CRP was found to have the highest diagnostic accuracy for discriminating non-sepsis from sepsis and septic shock group as well as between sepsis groups.[14]

In disagreement ***Aliu-Bejta et al.*** [15] found revealed that There were no significant differences in CRP levels on admission between patients with sepsis and septic shock, mean ± SD, 201.6±97.0mg/L vs. 219.8±146.3mg/L, respectively (p=0.824). Baseline PCT levels did not differ between patients with sepsis and those with septic shock; mean ± SD, 20.0±28.5ng/mL vs. 32.9±39.2ng/mL (p=0.099), respectively. [15]

de GuadianaRomualdo et al., [16]foundCRP was not found to have any discriminating value in relation to sepsis severity groups.

However, different to our results, some studies ***Shozushima et al.,*** [17] found PCT to perform a good diagnostic value, even though when compared to CRP, the latter showed a better diagnostic accuracy.

V. Conclusion:

PCT and CRP are promising markers for diagnosis of infection and sepsis. CRP is superior than PCT in detection of infection.

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