Comparison of Serum Procalcitonin with Blood Culture (Gold Standard) for the Identification of Bacterial Infection in Critically Ill Patients

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ABSTRACT

Objective: To evaluate the determinative correctness of Procalcitonin (PCT) for identification of bacterial sepsis (gram positive and gram negative bacterial infection) in seriously morbid subjects who will get admission in ICU/emergency deptt. of Khyber teaching hospital and comparing it with blood cultures (gold standard)

Methodology: It was a cross-sectional study carried out in ICU /emergency deptt. of Khyber teaching hospital Peshawar from March 2019 to August 2019. A total of 75 patients including 51 patients having blood culture positive and 24 patients having blood culture negative were selected through non-probability consecutive sampling technique.

Results: In our study, mean PCT levels were significantly higher for blood culture positive than for blood culture negative cases (p value 0.000). Cut off level of serum PCT for identification of bacterial sepsis was ≥ 0.5ng/ml in critically ill patients. Plasma PCT levels have sensitivity, specificity, PPV and NPV of 92%, 80%, 90.2%, and 83.3% respectively in determining blood culture positive than blood culture negative patients. Furthermore it was revealed that PCT had an (AUC =0.97) for culture positive cases and had an (AUC= 0.025) for blood culture negative cases.

Conclusion: Sensitivity for PCT is greater than specificity, so serum PCT assay is a useful screening test and also a quick indicator of bacterial sepsis in critically ill patients.

Keywords: Blood culture, critically ill patient, Prolactin

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INTRODUCTION

Procalcitonin (PCT), pro hormone having 16 amino acids, is the precursor of the blood calcium regulating hormone secretion of chiefly thyroid gland, calcitonin. PCT is present in markedly decreased concentrations in standard plasma and is considered to be produced under physical circumstances by neuro endocrine tissue in the thyroid gland and lungs.[1] PCT is enormously produced by different kinds of tissues in sepsis described to be a systemic inflammatory response syndrome (SIRS).[2,3] PCT is a one hundred and sixteen. Amino acids protein unit that's greater concentrations are highly linked with septicaemia[4,5] and with the severity of disease.[6] This is formed as a result of toxic secretion of bacteria and multitude of inflammatory cytokines and may help in differentiating between sepsis due to bacteria or viruses[7]. and actual bacterial sepsis from polluted blood cultures[8,9]. Just1 hr. of postponement of sufficient anti-bacterial treatment enhance the death of infective subjects by five to ten percent.[10,11] PCT has been proved an indicator for starting or ending medical treatment in different clinics, including the casualty department,(ICU), and primary care[12]. If possible it will be better to mention the normal range of the PCT over here or somewhere appropriate. This research evaluated either PCT concentration in the cases of bacterial blood sepsis could act as a quick indicator for the presence and location of sepsis, and identified the use of PCT concentration for differentiating between(Gram negative bacteria) and Gram positive bacteria, respectively) in subjects of systemic infections or sepsis. Hence in this study we assesed the PCT blood levels in the samples taken from infected or septic patients and then we compared it with culture positive and negative patients. Increased levels of PCT were found in culture positive patients and low PCT levels were determined in culture negative subjects.

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METHODOLOGY

It was a cross sectional study conducted in the ICU/emergency deptt. of Khyber Teaching Hospital (KTH) from March 2019 to August 2019. A total of 75 patients were selected by non-probability consecutive sampling technique. All the patients, children and adult males or females in ICU or emergency deptt. with two or more signs and symptoms of infection i.e temperature more than or equal to 38 ^{0}C , heart rate more than 90 beats /min , white blood cell count< 4x 10^{9} / Lor> 12 x 10^{9}/ L were included in the study while the patients older than 70 yrs of age, patients who had blood transfusions before ICU stay ,patients with organ failure and those whose attendants refused for consent were excluded from study. Serum PCT levels were measured by electro chemiluminescence immunoassay ECLIA on Cobas e 411 analyzer at main Pathology laboratory Khyber teaching hospital Peshawar.

RESULTS

Out of total 75 patients were included in the study 60% subjects were females (n=45) while 40% were male gender (n=30). The median age of the category was 36 yrs. Fifty one (51) patients had bacterial growth on blood culture while there is no growth on blood culture in twenty four (24) patients for about five days . Mean PCT concentration for blood culture positive cases is 8.1 ng /ml while mean PCT level for culture negative cases was 0.4 ng/ml .n=55 i.e 52% subjects possess PCT concentration more than 0.5ng/ml. PCT levels less than 0.1 ng/ml had greater Negative predictive value (NPV) for excluding infection.

Sensitivity of PCT about 92% while specificity was about 80%. Positive predictive value was about 90.2% and Negative predictive value was 3.3%. PCT levels having median concentration of 11.2 ng/ml in the culture positive category were markedly greater than culture negative category i.e 0.1 ng / ml (p value 0.000). Fifty one patients (51) had bacterial growth on blood culture while there was no growth on culture in twenty four (24) patients for about five days .

About different microorganisms identified on blood culture the most frequent organism was the E.coli 24% (n= 18) and Streptococci 17% (n= 13). ROC curve was plotted to represent the specificity and sensitivity at various cut off values of PCT. For positive blood culture the result i.e AUC (area under curve) was .975 while for negative blood culture result the AUC was 0.025. In my study AUC for culture positive group was 0.9 , hence it has excellent diagnostic accuracy or the test is 90% valid and also the curve is closer to the left hand border then the top border of the ROC space .Hence AUC is a measure of how well PCT can distinguish between septic and non-infective groups of subjects. The PCT cut off decision should be on the basis of care settings, So I suggest a 0.5ng/ml cut off value of PCT in middle intensity settings like in ICU/ emergency deptt.

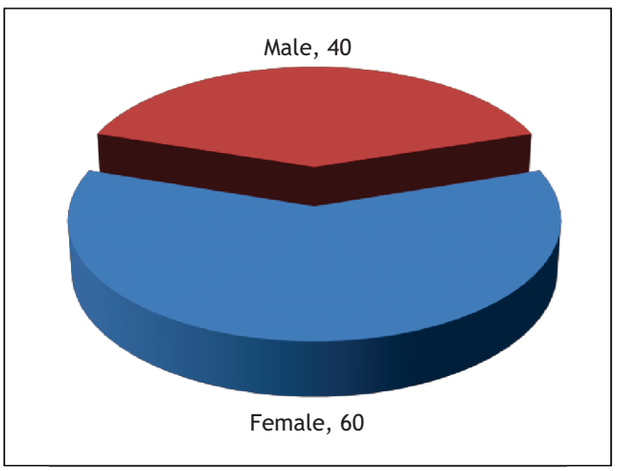

Fig.1: Male & Female Distribution

Table 1: Culture wise distribution

Blood Culture	Frequency	Percent
Negative	24	32.0
Positive	51	68.0
Total	75	100.0

Table 2: PCT Distribution Culture Wise

Parameters	Blood Culture		p.value
	Positive (mean+sd)	Negative (mean+sd)	
PCT	8.16+5.12	.429+.56	.000

Table 3: Age Distribution Culture Wise

Parameters	Blood Culture		p.value
	Positive (mean+sd)	Negative (mean+sd)	
Age	29.78+8.71	40.00+7.30	.000

DISCUSSION

In this research we determine about the function of PCT as a diagnostic and predictive test. My study demonstrates the PCT levels are raised in patients with bacterial infection and having blood culture positive than in blood culture negative patients. This reality is in concordance with other studies which also revealed raised PCT levels in culture positive

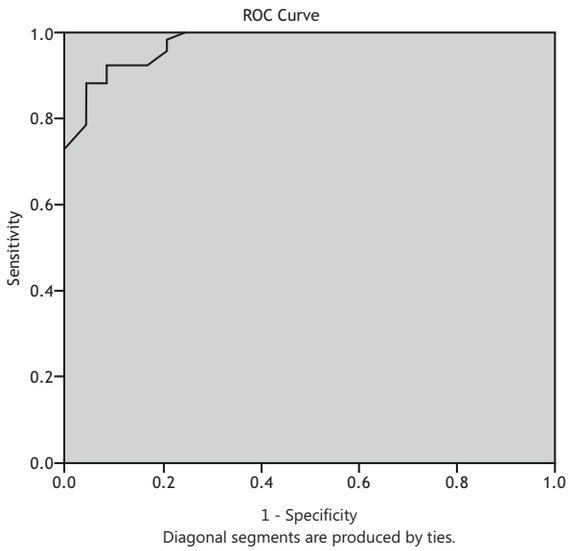

Fig. 2: ROC Curve

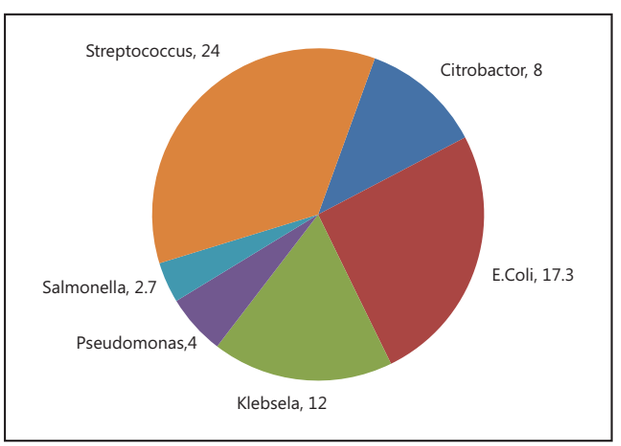

Fig. 3: Organism wise distribution

than culture negative patient's i.e in Pakistan (Karachi) [13], in U.K [14], in Japan[15].

Sensitivity and specificity of PCT for cut off value of0.5ng/mlis about 92%and80 %in my study, i.e sensitivity is greater than specificity, this finding is also demonstrated by other researches done having sensitivity and specificity of 93.75 % and 43.59% in Pakistan (Karachi)[13],sensitivity and specificity of88.90 %and80.40 % respectively in India [16],75% and 72% in USA [17], 76%and 69%[18], 86.7% and 85%in Kerala India [19].My research results about female preponderance of infection were (60%).Other studies from India documented greater frequency of infection in males as compared to females[20]. So this is contradictory report as compared to this study ,the reason for this contradiction in my study can be due to small sample size as compared to the studies in which there is male preponderance of infection.

On the basis of statistics obtained by the (EARS-Net), E. coli and Staph. aureus are the basic reason of septicaemia in man. [21] My research is also in agreement with this point but in my study streptococci and E-coli are the most frequent organisms. The PCT cut off value involved in ICUs / emergency deptt .throughout world for determination of infection changes exclusively. In my study PCT cut off value of more than and equal to 0.5 ng/ml is revealed for bacterial infection. This is in agreement with other researchers conducted which showed a PCT cut off level of 0.25 ng/ml in case of bacterial infection.[22] PCT cut off level of > 0.5ng/ml to indicate bacterial infection[19]and a PCT cut off level of more than and equal to 0.5 ng/ml.[23] On the whole, in my research it is revealed that PCT levels were markedly greater in subjects become septic with GNR (gram negative rods) as compared to GPC (gram positive cocci). The outcomes also indicate that procalcitonin can be used to distinguish between different kinds of bacteria. This reality is concordant with other studies which also revealed raised PCT levels to differentiate gram positive bactereamia from gram negative bacterial infection and this study was conducted in Turkey.[24]

My research also demonstrates higher levels of PCT in Gram negative bacteria ie >6ng/ml and for Gram positive bacteria 0.5 -3 ng/ml, this finding is also in favour with the researches done which revealed or gram negative bacteraemia PCT levels of 7.3 ng/ml and for gram positive bacteria PCT levels of about 0.46 ng/ml.[25] Different research projects also indicated PCT levels of >10.8 ng/ml suggesting gram negative bacterial infection and < or equal to 3ng/ml suggest gram positive bacterial infection.[26]

CONCLUSION

Sensitivity of PCT for bacterial infection is high while the specificity is low therefore serum PCT can be used as a. useful screening test especially in countries like Pakistan where bacterial infections are very common .

Cut off level for serum. PCT for identification of bacterial sepsis is equal to and >0.5 ng/ ml in critically ill patients. Serum. CT concentration is raised in Gram negative bacterial infection than Gram positive bacterial infection , ie levels of PCT for Gram negative bacterial infection are equal to and >6ng/ml while for Gram positive bacterial infection levels are 0.5 -3 ng / ml. This is an established fact worldwide that PCT level rises in bacterial infections. But in our country in very few health care set ups this marker is being used or identifying infection.

So my research provides a new information for the clinicians in the KP province . This study has not been conducted here before, and proves that PCT measurement should also be done in our province in health care set ups for early identification of bacterial infection.

REFERENCES

1. Becker KL, Snider R, Nylen ES. Procalcitonin in sepsis and systemic inflammation: a harmful biomarker and a therapeutic target. British journal of pharmacology. 2010; 159(2):253-64.
2. Lever A, Mackenzie I. Sepsis: definition, epidemiology, and diagnosis.BMJ.2007;335(7625):879-83.
3. Angus DC, Van der Poll T. Severe sepsis and septic shock. New England Journal of Medicine. 2013; 369(9):840-51
4. Cho SY, Choi JH. Biomarkers of sepsis. Infection & chemotherapy. 2014; 46(1):1-2
5. Christ-Crain M, Stolz D, Bingisser R, Muller C, Miedinger D, Huber PR, et al. Procalcitonin guidance of antibiotic therapy in community acquired pneumonia: a randomized trial. American journal of respiratory and critical care medicine. 2006; 174(1):84-93.
6. Schuetz P, Maurer P, Punjabi V, Desai A, Amin DN, Gluck E.Procalcitonin decrease over 72 hours in US critical care units predicts fatal outcome in sepsis patients. Critical Care. 2013; 17(3):R115.
7. Simon L, Gauvin F, Amre DK, Saint-Louis P, Lacroix J. Serum procalcitonin and C-reactive protein levels as markers of bacterial infection: a systematic review and meta-analysis. Clinical infectious diseases. 2004; 39(2):206-17
8. Schuetz P, Mueller B, Trampuz A. Serum procalcitonin for discrimination of blood contamination from bloodstream infection due to coagulase-negative staphylococci. Infection. 2007; 35(5):352.
9. Shomali W, Hachem R, Chaftari AM, Bahu R, El Helou G, Jiang Y, et al .Can procalcitoning differentiate Staphylococcus aureus from coagulase-negative staphylococci in clustered gram-positive bacteremia diagnostic microbiology and infectious disease. 2013; 76(2):158-61
10. Reinhart K, Meisner M. Biomarkers in the critically ill patient: procalcitonin. Critical care clinics. 2011; 27(2):253-63.
11. Mehanic S, Baljic R. The importance of serum procalcitonin in diagnosis and treatment of serious bacterial infections and sepsis. Materia socio-medica. 2013; 25(4):277.
12 Bouadma L, Luyt CE, Tubach F, Cracco C, Alvarez A, Schwebel C, et al . Use of procalcitonin to reduce patients' exposure to antibiotics in intensive care units (PRORATA trial): a multi centre and omised controlled trial. The Lancet. 2010; 375(9713):463-74
13 Ahmed S, Siddiqui I, Jafri L, Hashmi M, Khan AH, Ghani F. Prospective evaluation of serum procalcitonin in critically ill patients with suspected sepsis-experience from a tertiary care hospital in Pakistan. Annals of medicine and surgery. 2018; 35:180-4
14. Caffarini EM, DeMott J, Patel G, Lat I. Determining the clinical utility of an absolute procalcitonin value for predicting a positive culture result. Antimicrobial agents and chemotherapy. 2017; 61(5):e02007-16.
15. Watanabe Y, Oikawa N, Hariu M, Fuke R, Seki M. Ability of procalcitonin to diagnose bacterial infection and bacteria types compared with blood culture findings. International journal of general medicine. 2016; 9:325.
16. Charles MV, Kalaivani R, Venkatesh S, Kali A, Seetha KS. Evaluation of procalcitonin as a diagnostic marker in neonatal sepsis. Indian Journal of Pathology and Microbiology. 2018 Jan 1; 61(1):81.
17. Caffarini EM, DeMott J, Patel G, Lat I. Determining the clinical utility of an absolute procalcitonin value for predicting a positive culture result. Antimicrobial agents and chemotherapy. 2017; 61(5):e02007-16.
18. Hoeboer SH, van der Geest PJ, Nieboer D, Groeneveld AJ. The diagnostic accuracy of procalcitonin for bacteraemia: a systematic review and meta-analysis. Clinical Microbiology and Infection. 2015 May 1; 21(5):474-81.
19. Vijayan AL, Ravindran S, Saikant R, Lakshmi S, Kartik R. Procalcitonin: a promising diagnostic marker for sepsis and antibiotic therapy. Journal of intensive care. 2017 Dec; 5(1):51.
20. Zhang D, Micek ST, Kollef MH. Time to appropriate antibiotic therapy is an independent determinant of postinfection ICU and hospital lengths of stay in patients with sepsis. Critical care medicine. 2015; 43(10):2133-40.
21. Cleland DA, Eranki AP. Procalcitonin. InStatPearls [Internet] 2019 May 1. StatPearls Publishing.
22. Ahmed S, Siddiqui I, Jafri L, Hashmi M, Khan AH, Ghani F. Prospective evaluation of serum procalcitonin in critically ill patients with suspected sepsis-experience from a tertiary care hospital in Pakistan. Annals of medicine and surgery. 2018; 35:180-4.
23. Kostic I, Gurrieri C, Piva E, Semenzato G, Plebani M,

Caputo I, e t al. Comparison of presepsin, procalcitonin, interleukin-8 and C-reactive protein in predicting bacteraemia in febrile neutropenic adult patients with haematological malignancies. Mediterranean journal of hematology and infectious diseases. 2019; 11(1).

24. Bilgili B, Haliloğlu M, Aslan MS, Sayan İ, Kasapoğlu US, Cinel I. Diagnostic accuracy of procalcitonin for differentiating bacteraemic gram-negative sepsis from gram-positive sepsis. Turkish journal of anaesthesiology and reanimation. 2018; 46(1):38.
25. Leli C, Ferranti M, Moretti A, Dhahab A, Salim Z, Cenci E, e t al. Procalcitonin levels in gram-positive, gram-negative, and fungal bloodstream infections. Disease markers. 2015; 2015.
26. Schuetz P, Briel M, Christ-Crain M, Stolz D, Bouadma L, Wolff M, et al . Procalcitonin to guide initiation and duration of antibiotic treatment in acute respiratory infections: an individual patient data meta-analysis. Clinical infectious diseases. 2012; 55(5):651-62.