Journal of Chemical Health Risks

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JCHR (2024) 14(3), 432-440 | ISSN:2251-6727

Procalcitonin as a Biomarker for Predicting Infectious Diseases

Ashok Kumar Sah[1]*, Rabab Hassan Elshaikh[2], Anuradha Rajput[3], Suresh Jaiswal[4], Darla Srinivas Rao[1], Kajal Arora[1], Rohit Rathore[5], Ankur Vashishtha[6], Nisha Bhardwaj[1], Savari Silvester Y[1] Ranjay Kumar Choudhary[6]*

[1]Department of Medical Laboratory Technology, School of Allied Science, Galgotias University, Greater Noida, Uttar Pradesh, India

[2]Department of Medical Laboratory Science, College of Applied and Health Sciences, A 'Sharqiyah University, Ibra, Oman

3Department of Medical Laboratory Technology, School of Allied Health Sciences, IIMT University, Meerut, Uttar Pradesh, India

[4]School of Health & Allied Sciences, Pokhara University, Nepal

[5]Department of Physiotherapy, Faculty of Allied Health Sciences, PDM University, Bahadurgarh, HR, India

[6]Department of Medical Laboratory Technology, School of Allied Science, Sharda University, Gr Noida, Uttar Pradesh, India

[7]Department of Medical Laboratory Technology, Amity Medical School, Amity University Haryana, Gurugram, HR, India

***Corresponding author:**

Ashok Kumar Sah

Professor, Department of medical Laboratory Technology, School of Allied Science, Galgotias University, Uttar Pradesh, India,

Prof (Dr) Ranjay Kumar Choudhary, Amity Medical School, Amity University Haryana, Gurugram, HR,

(Received: 04 February 2024 Revised: 11 March 2024 Accepted: 08 April 2024)

KEYWORDS

Procalcitonin

Biomarker Sepsis

Bacterial infections

Aspergillus

ABSTRACT:

Introduction: It's still difficult to diagnose bacterial and fungal infections in a timely manner. Most often, there is a paucity of trustworthy clinical and microbiological criteria from accessible specimens that may be used to identify bacterial infections and rule out other infections.

Objectives: The objective of the study was to diagnose bacterial and fungal infections based on Procalcitonin level.

Methods: PCT levels were measured in sera using the automatic analyzer VIDAS B.R.A.H.M.S PCT assay. The lower limit of detection of the assay was 0.05 ng/ml and the functional assay sensitivity was 0.09 ng/ml. For each sample, an aliquot of 5 to 10 ml whole blood was inoculated into BACTEC aerobic and anaerobic bottles. The bottles were incubated for 5 days. Identification of microorganisms was performed with the VITEK-2 system.

Results: The main findings of this study are that, in patients with suspected sepsis, the PCT mean value of 48.12 ng/ml could be of help in predicting an infection caused by Gram-negatives, the mean value of 33.05 ng/ml could be of help in predicting an infection caused by Gram-positives, and the mean value of 11.59 ng/ml could be of help in predicting an infection caused by Fungi. In this study, the value of PCT for patients infected with Fungi did not exceed 50 ng/ml, the value of PCT for patients infected with Gram Positive bacteria did not exceed 100 ng/ml and in the case of Gram Negative, the value of PCT reached up to 200 ng/ml which is the maximum detection level.

Conclusions: This study suggests that PCT may be of value in distinguishing Gram Negative from Gram Positive and fungal bloodstream infections. Nevertheless, its utility in predicting different microorganisms needs to be assessed in further studies.

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JCHR (2024) 14(3), 432-440 | ISSN:2251-6727

1. Introduction

Sepsis is a systemic immune response to infection by microbial organisms. Sepsis is defined as the presence (probable or documented) of infection together with systemic manifestations of infection. The most common primary source of infection resulting in sepsis is the lungs, accounting for about half of all cases, followed by the abdomen, and the urinary tract. No definitive source is found in one third of the cases [1]. Sepsis encompasses a spectrum of illness that ranges from minor signs and symptoms to organ dysfunction (severe sepsis) and shock. Increasing severity correlates with increasing mortality, which rises from 25-30% for severe sepsis to 40-70% for septic shock [2]. Approximately, 25-35% of patients with severe sepsis and 40-55% of patients with septic shock die within 30 days [3].

Sepsis and its complication have a significant and increasing impact on health factor and are one of the leading causes of mortality. The incidence of sepsis is increasing worldwide. In general, sepsis accounts for approximately 2% of all hospitalizations in developed countries. Severe sepsis is a common, frequently fatal, and expensive condition [4]. Mortality rate in sepsis remains high despite the current advances in medical science, technologies, and practice. Timely diagnosis and treatment are highly important in reducing the morbidity and mortality associated with sepsis. At times, the diagnostic uncertainty remains high despite the available clinical information. Thus, a laboratory test with more specificity is essential. Serum biomarkers like PCT may aid in the early diagnosis of sepsis and therapeutic interventions.

Sepsis is Systemic Inflammatory Response Syndrome (SIRS) due to bacterial infection and this condition requires prompt initiation of antibiotic therapy [5]. On the other hand, indiscriminate use of antibiotics in critically ill patients with SIRS due to other causes leads to overuse of antibiotics with risk of rise in antibiotic resistance. Search for a biomarker for sepsis which is highly specific and sensitive with minimum turnaround time that can reliably distinguish bacterial infection from other infections, such as, viral, fungal, or protozoal infection as well as non-infectious causes of SIRS is underway. It has also been felt that the biomarker should also be able to determine the severity of the infection and response to treatment, thus acting as an effective prognostic indicator [6].

Traditional markers of sepsis like C reactive protein (CRP), erythrocytes sedimentation rate (ESR) and leucocyte count have been widely used worldwide but all these lack specificity. Novel biomarkers which hold promise include PCT, interleukins, low eosinophil count, adrenomedullin, interferon resisting, natriuretic peptides, and copeptin; and the list is ever expanding [7]. However, during the last two decades, PCT has attracted universal attention and is the most studied biomarker for sepsis.

2. Methods

A retrospective study was carried out on 149 patients and the study was carried out at the department of microbiology. Procalcitonin, bacterial culture and fungal culture were carried out by using different techniques.

PCT (procalcitonin) estimation was carried out by VIDAS PCT kit on the principle of sandwich immunoassay method with a final fluorescent detection on serum. The solid phase receptacle (SPR) served as the solid phase as well as the pipetting device. The sample was transferred into the wells containing anti-PCT antibodies labelled with alkaline phosphatase (conjugate). The sample mixture was cycled in an out of the SPR several times. This operation enabled the antigen to bind with the immunoglobulin fixed to the interior wall of the SPR and the conjugate to form a sandwich. Unbound sample components were eliminated during the washing steps. During the final step the substrate was cycled in and out of the SPR and hydrolysis of the substrate occurred into a fluorescent product that was measured by the optical scanner in the instrument.

Once the assay was completed, results were analyzed automatically by the analyzer. The concentrations were expressed in ng/ml. Values which were <0.05 ng/ml were considered positive and value >2.0 ng/ml was critical value and was reported as per protocol.

The BacT-ALERT microbial detection system utilized a colorimetric sensor and reflected light to monitor the presence and production of CO2 that was dissolved in the culture medium. If microorganisms were present in the test sample, CO2 was produced as the organisms

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JCHR (2024) 14(3), 432-440 | ISSN:2251-6727

metabolized the substrates in the culture medium when growth of the microorganisms produced CO2, the color of the gas permeable sensor installed in the bottom of each culture bottom changed from blue green to yellow.

No interpretation was required as positive or negative culture bottles were determined by decision making software contained in the BacT-ALERT microbial detection system. Final identification and sensitivity were done using appropriate card on VITEK 2 system. In case of any problem with identification, specimen was processed as given in SOP of manual identification. Manual antibiotic sensitivity testing was done by Kirby Bauer method and interpretation of results was done following the CLSI guidelines.

Culture of various specimens for isolation of fungus: The diagnosis of fungal infection was dependent entirely on the selection and collection of an appropriate clinical specimen for culture in Sabroud's Dextrose Agar (SDA). Growth of fungus and identification was done by different morphology and biochemical procedure and AST was done to determine the susceptibility.

Culture of various specimens for isolation of bacteria from body fluids/blood:

Pleural, pericardial, peritoneal, CSF, blood and synovial fluids are normally sterile. The fluid from affected body cavity was aspirated by clinicians and was investigated in microbiology lab for identification of the etiological agent and antibiotic susceptibility. Culture of these fluids was done on different microbiological medias to detect and confirm clinically suspected infection. Organisms isolated were processed for identification and antibiotic susceptibility testing using the Bact-Alert 3D automated system and VITEK 2 system, respectively for the purpose.

All data were statistically analyzed by using SPSS Ver. 2020 software. The Chi-square test was used to check the association between the variables and P value less than 0.05 was considered statically significant.

3. Results

All the 149 samples of PCT had critical values i.e., > 2 and showing the growth of bacteria and fungus were only included in the study. The highest age of the participant was 94 and lowest age 19 with mean age of 60.69 with std. deviation of 60.69±14.58 as shown in table 1.

	N	Minimum	Maximum	Mean	Std. Deviation
AGE GROUP	149	19	94	60.69	14.58

Table 1: Descriptive statistics of the participants whose samples showed growth.

Variables	**Frequency**	**Percentage (%)**
Gender		
Female	49	32.9
Male	100	67.1
Age category		
less than 25 years	4	2.7
25 to 50 years	34	22.8
above 50 years	111	74.5
Type of specimen		
Blood	117	78.6
Broncho alveolar lavage (BAL)	1	.7
Body fluid	2	1.3
Pus	3	2.0
Sputum	2	1.3
Urine	24	16.1
Type of organism		
FG	30	20.2
GNB	61	40.9

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JCHR (2024) 14(3), 432-440 | ISSN:2251-6727

GPC	58	38.9
Total	149	100.0

Table 2: Distribution of socio demographic variables of those whose samples showed growth.

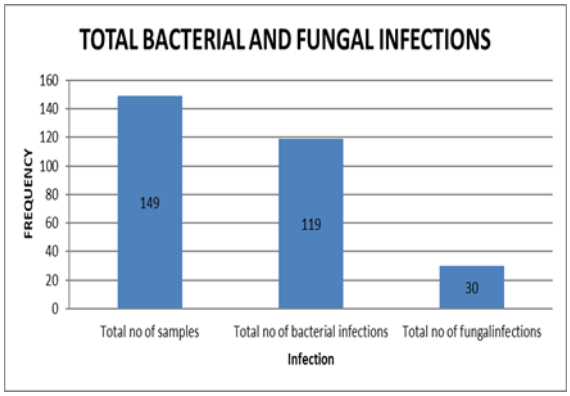

Figure 1: Bacterial and fungal infections**.**

Out of total 149 selected samples that had shown growth, 119 samples showed bacterial growth and the remaining 30 samples showed fungal growth, i.e., 79.87% patients were having bacterial infection and remaining 20.13 % patients were having fungal infection.

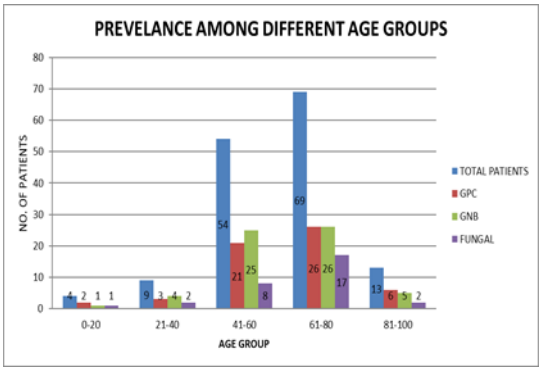

Figure 2: Prevalence of the infections among different age groups.

The prevalence of sepsis among the age group of 0-20 was 4, out of which, the growth of GPC, GNB and fungus was 2, 1 and 1 respectively. The prevalence of sepsis among the age group of 21-40 was 9. Out of those, the growth of GPC, GNB and Fungal was 3, 4 and 2 respectively. The prevalence of sepsis among the age group of 41-60 was 54. Out of those, the growth of GPC, GNB and fungus was 21, 25 and 8 respectively. The prevalence of sepsis among the age group of 61-80 was 69. Of those, the growth of GPC, GNB and Fungal was 26, 26 and 17 respectively. The prevalence of sepsis among the age group of 81-100 was 13 and the growth of GPC, GNB and fungus was 6, 5 and 2 respectively.

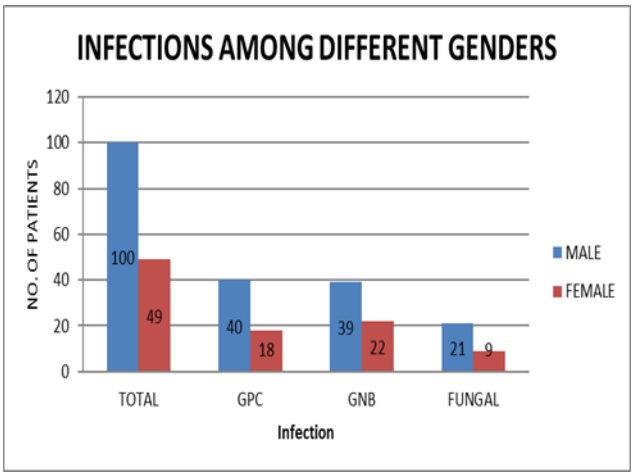

Figure 4: Number of patients according to Procalcitonin ranges.

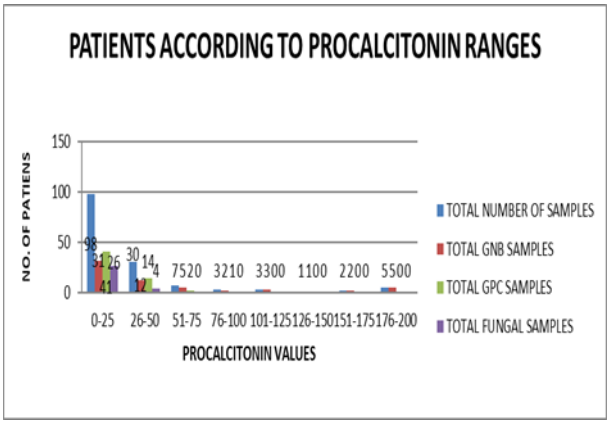

Figure 1: Infections among different genders

Out of total 149 patients, 100 patients were found to be male while, 49 were female. Out of the 100 male patients, the prevalence of GPC, GNB and fungal growth was 40, 39 and 21 respectively. Out of the 49 female patients, the prevalence of GPC, GNB and fungal growth was 18, 22 and 9 respectively.

The graph shows the different ranges of PCT and corresponding growth. Out of total 149 samples that have shown growth, 98 samples are found to be between the PCT ranges of 0-25, i.e. 49% samples have PCT range of

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JCHR (2024) 14(3), 432-440 | ISSN:2251-6727

0-25. Out of these 98 samples, 31 samples have shown growth of GPC, mainly *Streptococcus*, *Staphylococcus* and *Enterococcus*. Forty-one samples have shown growth of GNB, mainly *K. pneumoniae* and *E. coli*. The remaining 26 samples have shown fungal growth, mainly *Candida*.

Out of the total 149 samples, 4 samples were positive between the PCT ranges of 76-100. All the 5 samples showed bacterial growth only. Out of these 4 samples, 1 sample has shown growth of GPC and only the remaining 3 samples have shown growth of GNB. Out of the 149 positive samples, 3 samples were found positive between the PCT ranges of 101-125. All the 3 samples showed GNB growth only.

Of the total 149 samples, 1 sample was found positive between the PCT ranges of 126-150. The sample showed GNB growth only, while 2 samples were found positive between the PCT ranges of 151-175. Both the samples showed GNB growth only. Out of total of 149 samples, 5 samples were found positive between the PCT ranges of 176-200. All the 5 samples showed GNB growth only. There is no fungal growth found in PCT values above 50 and no GPC was found above 100.

Variables	**PCT interpretation**		**Chi square value**	**P value**
	2.00 to 9.99 ng/ml (severe systemic infection)	**more than 10 ng/ml (severe sepsis or septic shock)**		
Sex				
Female	26 (35.6%)	23 (30.3%)	0.483	0.301
Male	47 (64.4%)	53 (69.7%)		
Age category (yrs)				
less than 25	1 (1.4%)	3 (3.9%)	1.636	0.441
25 to 50	19 (26.0%)	15 (19.7%)		
more than 50	53 (72.6%)	58 (76.3%)		
Total	73 (100.0%)	76 (100.0%)		

Table 3. Association of different PCT levels with socio demographic variables.

Variables	**PCT interpretation**		**Chi square value**	**P value**
	2.00 to 9.99 ng/ml (severe systemic infection)	**more than 10 ng/ml (severe sepsis or septic shock)**		
Type of specimen				
Blood	55 (75.4%)	62 (81.6%)	4.993	0.545
Bal	1 (1.4%)	0 (0.0%)		
Body fluid	1 (1.4%)	1 (1.3%)		
Pus	1 (1.4%)	2 (2.6%)		
Sputum	2 (2.7%)	0 (0.0%)		
Urine	13 (17.8%)	11 (14.5%)		
Total	73(100.0 %)	76 (100.0%)		

Figure 2: Association of different PCT levels with type of specimen.

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Variables	PCT interpretation		Chi square value	P value
	2.00 to 9.99 ng/ml (severe systemic infection)	more than 10 ng/ml (severe sepsis or septic shock)		
Type of infection				
Bacterial	56 (76.7%)	63 (82.9%)	0.885	0.347
Fungal	17 (23.3%)	13 (17.1%)		
Total	73 (100.0%)	76 (100.0%)		

Figure 3: Association of different PCT levels with type of infection.

Variables	Types of infection		Chi square value	P value
	Bacterial	Fungal		
Gender				
Female	40 (33.6%)	9 (30.0%)	0.142	0.707
Male	79 (66.4%)	21 (70.0%)		
Age category				
less than 25 years	3 (2.5%)	1 (3.3%)	12.966	0.05*
25 to 50 years	27 (22.7%)	7 (23.3%)		
above 50 years	89 (74.8%)	22 (73.3%)		
Total	119 (100.0%)	30 (100.0%)		

Figure 4: Association of type of infection with type of gender and age.

***=Significant**

4. Discussion

The study evaluated the diagnostic accuracy of PCT in bacterial and fungal infections. The PCT is a reliable marker that contributes to the early diagnosis of invasive bacterial and fungal infection and also for the evaluation of their severity and prognosis.

The present study was carried out in a population of 149 patients mainly from internal medicine wards, for which blood cultures were collected together with sera for PCT determination.

The age distribution is similar to studies done around the world. A western study reported a higher incidence of sepsis in patients aged above 57 years [8]. The mean age in an epidemiological study of sepsis in India was 54.9 years. It is found that males (67.1%) are more affected with sepsis compared to females (32.9%) in the present study. Studies by previous workers also indicated a higher incidence among men. Martin et al., in 2000 studied the demography, temporal incidence and changes in incidence and outcome of sepsis over 20 years in the United States and reported that sepsis was more common in men, accounting for 48.1% of cases on average per year and men were more likely to have sepsis than women with a mean annual relative risk of 1.28 [8]. Todi et al. [9] reported from a multicenter trial done at 12 centers in India that sepsis was more common in males. The ability of PCT to discriminate infections by Gram-positive or Gram-negative organisms has been recently described. Charles et al. in 2008 in a retrospective study on 97 bacteremia episodes, found that serum PCT levels were markedly greater for Gram-negatives than for Gram-positives [10]. Similarly, Koivula et al. in 2011 predicted the elevated levels of PCT within 24 hours after the onset of fever as an infection of Gram-negative bacteremia in haematological patients [11]. Brodská et al. in 2013, in a retrospective study evaluating 166 patients, found that PCT cut-off of 15 ng/ml can

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discriminate between sepsis caused by Gram-negative bacteria or by Gram-positives and fungi, with a specificity of 87.8%. In that study, infections caused by Gram Negatives were the most prevalent (61 out of total 149 samples or 40.9%). In this study, it was observed that the patients infected with GNB were most prevalent in the age group of above 40 years. The maximum samples were from age the group of 41 to 80years, i.e. 51 out of 61 samples [12]. Only 1 sample was observed in the age group of 0 to 20 years. It was also observed that the Maximum PCT value of 200 ng/ ml was seen only in GNB. Maximum infection among GNB was caused by Enterobacteriaceae family which included E. coli with 28 cases K. pneumoniae with 27 cases contributing 90.1 % of total infection caused by Gram Negatives. Similarly, Shuhua et al. (2014) observed that E. coli and K. pneumoniae were the most common causative pathogens of Gram-negative bacterial infections. Similarly, they also observed that PCT levels in patients with E. coli or K. pneumoniae sepsis were significantly higher than in patients with other Gram-negative, Gram-positive or fungal sepsis.

In the present study, infections caused by fungi were the least prevalent (30 out of total 149 samples of 20%). According to Leli et al. (2015), low concentrations of PCT in critically ill patients might suggest fungal infection. Similarly in this study also, it was observed that PCT levels in fungal cases did not exceed more than 50 ng/ml which exceed up to 100 ng/ml in GPC and up to 200 ng/ml in GNB [13]. PCT levels might be used as a surrogate marker to distinguish Gram-negative sepsis from Gram-positive or fungal sepsis. Similarly, Shuhua et al. (2014), observed that serum PCT [14] levels were significantly higher in patients with Gram-negative sepsis than in patients with Gram-positive or fungal sepsis [15, 16]. LPS binding to TLR4 activates the classical MyD88-dependent signaling pathway and induces the production of cytokines, such as tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6) (Takeuchi et al., 1999). Oberhoffer et al. in 1999, demonstrated that both LPS and sepsis-related cytokines increased PCT expression in human peripheral blood mononuclear cells (PBMCs). In PBMCs cultured with LPS, TNF-α, or IL-6, PCT mRNA was detected at levels 4- to 230-fold, 2- to 90-fold, or 2- to 35-fold, [17] respectively, higher than in control cultures. In addition, Gram-positive pathogens induce relatively poor cytokine levels (TNF-α and IL-6) than Gram-positive ones do, owing to TLR2-dependent simulation [18,19]. These factors might mediate the expression of serum PCT concentrations in response to Gram-negative bacterial infections.

Serum PCT concentrations were moderately elevated in fungal and Gram-positive sepsis, mechanisms of PCT expression were different. TLRs were sensed by both Gram-positive bacteria and fungi, but the major receptors recognizing fungi are CLRs [20]. In addition, serum interferon-gamma (IFN-γ) levels are markedly elevated in patients with fungal infections [21]. IFN-γ is a critical factor for defense against fungal infections. In vitro, PCT secretion has been found to be inhibited by IFN-γ [22]. Thus, PCT concentrations in fungal sepsis might be regulated by IFN-γ levels [23]. Similarly [24] observed that out of total 171 patients, the number of patients who had BC-negative results, gram-positive cocci (GPC), and gram-negative rods (GNRs) were 124, 28, and 19, respectively.

5. Conclusion:

The present study demonstrates serum PCT to be among the most promising sepsis markers in critically ill patients, capable of complementing clinical signs and routine lab. parameters suggestive of severe infection. Serum PCT levels were significantly higher in patients with Gram-negative sepsis than in patients with Gram-positive and higher in Gram Positive sepsis than in Fungal sepsis. It should be noted that the importance of microbiological examinations remains unchanged. Blood culture and antimicrobial susceptibility testing are required in clinical applications to positively identify causative microorganisms and assess their sensitivity to different antibiotics. In this study, it is concluded that, in patients with suspected sepsis, the PCT mean value of 48.12 ng/ml could be of help in predicting an infection caused by Gram-negatives, the PCT mean value of 33.05 ng/ml could be of help in predicting an infection caused by Gram-positives, the PCT mean value of 11.59 ng/ml could be of help in predicting an infection caused by fungi. In this study, the value of PCT for patients infected with fungi did not exceed 50 ng/ml, the value of PCT for patients infected with Gram Positive bacteria did not exceed 100 ng/ml and in case of Gram Negative, the value of PCT reached up to 200 ng/ml which is the

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maximum detection level of the VIDAS B.R.A.H.M.S PCT. These results suggest that PCT could be of some help to clinicians in evaluating the more appropriate initial antimicrobial therapy in the cases in which, even if informed of the presence of Gram-negative bacilli in patients' Blood Culture, they have to wait further 24–48 hours for species identification. The ability of PCT to discriminate infections by Gram-positive or Gram-negative organisms has been recently described.

Acknowledgements:

The helping hand extended by Dr Rabab Hassan Elshaikh of A 'Sharqiyah University Oman, Prof (Dr) Ranjay Kumar Choudhary, Amity University Haryana and Dr Shagun Agrawal, Galgotias University are highly acknowledged. Laboratory facilities provided by the Galgotias University is acknowledged here with thanks.

Conflict of interest:

The authors declare that there is no conflict of interest regarding the publication of the manuscript.

Authors' Contribution:

Ashok K Sah, Shagun Agrawal, and Rabab Hassan Elshaikh, Ranjay Kumar Choudhary conceptualized the manuscript, Darla Srinivas Rao, Kajal Arora, Rohit Rathore, Ankur Vashishtha, Anuradha Rajput, Nisha Bhardwaj gathered the data with regard to this work. Suresh Jaiswal and Savari Silvester Y analyzed these data, Ankur Vashishtha, Suresh Jaiswal, Shagun Agrawal and Ashok K Sah necessary inputs were given towards the designing of the manuscript. Ashok K Sah, Shagun Agrawal, and Rabab Hassan Elshaikh, Suresh Jaiswal, Ranjay Kumar Choudhary supervised and executed the entire study, critically revised and edited and communicated the manuscript. All authors discussed the methodology and results and contributed to the final manuscript.

Data availability:

All datasets generated or analysed during this study are included in the manuscript.

Ethics Statement:

The authors are responsible for all parts of the work, including ensuring that any questions about the accuracy or integrity of any portion of the work are thoroughly examined and resolved. All study protocols were authorized by Onco Biomedical and Research (Approval ID. 2023-185). All study participants agreed to the use of their samples for research purposes and provided written informed consent.

Source of Funding: No

References:

1. Munford Robert S, Suffredini Anthony F. Sepsis, Severe Sepsis and Septic Shoc. In: Bennett John E, Dolin Raphael, Blaser Martin J, Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases (8th ed). Elsevier Health Sciences, Philadelphia, 2014, 914-934.
2. Shiferaw B, Bekele E. The Role of PCT as a Biomarker in Sepsis. J Infect Dis Epidemiol, 2016, 2(1):1-5.
3. Chaudhury A, Rao TV. Bacteraemia in a tertiary care urban hospital in south India. Indian J Pathol Microbiol, 1999, 42:317–20.
4. Martini A, Gottin L, Menestrina N, Schweiger V, Simion D, Vincent JL. PCT levels in surgical patients at risk of candidemia. J Infect. 2010, 60:425–30.
5. Borc RC. Sepsis, the sepsis syndrome, multi-organ failure: a plea for comparable definitions. Ann Intern Med;1991, 114:332-3.
6. Pavoa P, Salluh JI. Biomarker guided antibiotic therapy in adult critically ill patients: a critical review. Ann Intensive Care, 2012, 2:32.
7. Kibe S, Adams K, Barlow G. Diagnostic and prognostic biomarkers of sepsis in critical care. J Antimicrob Chemother, 2011, 66(2):i33-40.
8. Martin GS, Mannino DM, Eaton S, Moss M. The epidemiology of sepsis in the United States from 1979 through 2000. N Engl J Med. 2003;348:1546–54.
9. Todi S, Chatterjee S, Bhattacharyya M. Epidemiology of severe sepsis in India. Crit Care Med. 2007;11:65.
10. Charles PE, Ladoire S, Aho S, Quenot JP, Doise JM, Prin S. Serum PCT elevation in critically ill patients at the onset of bacteremia caused by either Gram

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www.jchr.org

JCHR (2024) 14(3), 432-440 | ISSN:2251-6727

negative or Gram positive bacteria. BMC Infect Dis 2008;8:38.

11. Koivula, S. Hämäläinen, E. Jantunen et al., "Elevated PCT predicts Gram-negative sepsis in haematological patients with febrile neutropenia," Scandinavian Journal of Infectious Diseases, 2011, 43:471–478.
12. H Brodská, K Malíčková, V Adámková, H Benáková, M M Šåastná, and T Zima, "Significantly higher PCT levels could differentiate Gram-negative sepsis from Gram-positive and fungal sepsis," Clinical & Experimental Medicine, 2013, 13(3): 165–170.
13. Leli C, Ferranti M, Moretti A, Al Dhahab ZS, Cenci E, Mencacci A. PCT levels in gram-positive, gram-negative, and fungal bloodstream infections. Dis Markers, 2015:701480.
14. Shuhua Li, Hengmo Rong, Qinliang Guo, Yifei Chen, Guqing Zhang,and Jiong Yang. Serum PCT levels distinguish Gram-negative bacterial sepsis from Gram-positive bacterial and fungal sepsis, Journal of Research in Medical Sciences, 2016, 21:39.
15. Allison J, Hall L, MacIntyre I, Craig RK. The construction and partial characterisation of plasmid containing complimentary DNA sequences to human calcitonin precursor poly protein. Biochem J. 1981;199:725–31.
16. Takeuchi O, Hoshino K, Kawai T, Sanjo H, Takada H, Ogawa T, et al., Differential roles of TLR2 and TLR4 in recognition of gram-negative and gram-positive bacterial cell wall components. Immunity. 1999;11:443–51.
17. Oberhoffer M, Stonans I, Russwurm S, Stonane E, Vogelsang H, Junker U, et al., PCT expression in human peripheral blood mononuclear cells and its modulation by lipopolysaccharides and sepsis-related cytokines in vitro. J Lab Clin Med 1999;134 :49-55
18. Beran O, Potmešil R, Holub M. Differences in Toll-like receptor expression and cytokine production after stimulation with heat-killed gram-positive and gram-negative bacteria. Folia Microbiol (Praha) 2011;56:138–42.
19. Tavares E, Maldonado R, Ojeda ML, Miñano FJ. Circulating inflammatory mediators during start of fever in differential diagnosis of gram-negative and gram-positive infections in leukopenic rats. Clin Diagn Lab Immunol. 2005;12:1085–93.
20. Plato A, Hardison SE, Brown GD. Pattern recognition receptors in antifungal immunity. Semin Immunopathol. 2015;37:97–106.
21. Bouzani M, Ok M, McCormick A, Ebel F, Kurzai O, Morton CO, et al., Human NK cells display important antifungal activity against Aspergillus fumigatus, which is directly mediated by IFN-gamma release. J Immunol. 2011;187:1369–76.
22. Linscheid P, Seboek D, Nylen ES, Langer I, Schlatter M, Becker KL, et al., In vitro and in vivo calcitonin I gene expression in parenchymal cells: A novel product of human adipose tissue. Endocrinology. 2003;144:5578–84.
23. Dou YH, Du JK, Liu HL, Shong XD. The role of PCT in the identification of invasive fungal infection-a systemic review and meta-analysis. Diagn Microbiol Infect Dis. 2013;76:464–9.
24. Takao Arai, Shoichi Ohta, Junya Tsurukiri, Kenichiro Kumasaka, Katsuhiro Nagata, Taihei Okita, Taishi Oomura, Akira Hoshiai, Masaharu Koyama, Tetsuo Yukioka,. 2016, PCT levels predict to identify bacterial strains in blood cultures of septic patients, The American Journal of Emergency Medicine, 34(11):(2150-2153).