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Original Research

Study of serum procalcitonin as a predictor of bacterial infection in patients with acute febrile illness

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ABSTRACT:
Aim: The aim of this study to determine the serum procalcitonin as a predictor of bacterial infection in patients with acute febrile illness. **Materials and Methods:** 100 adults (aged 20 and above) with a recent-onset fever (less than 2 weeks) were enrolled. Urine, sputum, and blood were submitted for bacterial culture and sensitivity based on the preliminary diagnosis and clinical suspicion. The Fine care PCT quick quantitative test was used to determine the concentration of procalcitonin in the blood. This test is a fluorescence immunoassay that measures PCT in human plasma, serum, or whole blood. The range of 0-0.5ng/ml was considered normal. Serum PCT levels over 0.5ng/ml were deemed high. Leucopenia was diagnosed when the total leucocyte count was less than 4000 cells/mm3, while normal was between 4000 and 11,000 cells/mm3, and high was over 11,000. (leucocytosis). **Results:** The sensitivity and specificity of serum PCT as a diagnostic test of bacterial infection was 62% and 93% respectively within 96% confidence interval. The positive predictive value of serum PCT was 46% whereas the negative predictive value was 96%.The diagnostic accuracy of serum PCT in detecting bacterial infection was 95%. TLC had a sensitivity of 56% and a specificity of 66% in identifying bacterial illness, whereas an increased leucocyte count had a diagnostic accuracy of 59%. **Conclusion:** In individuals presenting with acute febrile illness, serum PCT is a helpful test for diagnosing bacterial infection. In the emergency room, a serum PCT level below 0.5ng/ml may rule out bacterial infection. When it comes to predicting bacterial infection, leucocytosis is a less accurate indication than serum PCT.
Keywords: Procalcitonin, leucocyte count, bacterial infection

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INTRODUCTION

There is a substantial strain placed on the public health care system by infectious illnesses, which account for a large percentage of deaths globally. In infectious infections, the effects of tardy treatment commencement may be catastrophic. It is best to start antibiotics when there is sufficient proof that the infection is bacterial, even if there are cases when starting antibiotics early in the course of an acute febrile sickness might save a patient's life.[1-3] Total leucocyte count (TLC) is an easily accessible test that may be higher in bacterial infections. A positive culture for bacteria is the gold standard test for definite identification of bacterial infections, but it takes at least three days before results are available. However, it is not infectious disease specific, since it may be increased in the absence of infection due to factors such as trauma, mental stress, surgery, medicine, and smoking. Furthermore, a normal or low leucocyte count does not rule out bacterial infection.[4] Thus, a readily accessible test with appropriate sensitivity and specificity is necessary to identify

bacterial infections and distinguish them from viral infections in the emergency context. Before culture results are available, such a test will help with crucial decisions like starting broad-spectrum antibiotics. The serum protein procalcitonin (PCT) has only recently been identified as a diagnostic indicator of bacterial infection.[5]

Serum procalcitonin is a suitable marker for early detection of bacterial infection and to rule out viral infection. Procalcitonin is a 116-amino acid peptide whose production is increased in all parenchymal tissues in response to a bacterial infection and suppressed in viral infections.[6] Procalcitonin is detectable as early as 3-4 hours following infection, and its degree of rise correlates with the severity of infection. Antibiotic treatment in infectious diseases is increasingly being guided by serum procalcitonin levels. The purpose of this research is to determine whether serum procalcitonin is useful in identifying bacterial infection in individuals with acute febrile illness. The purpose of this research is to evaluate the sensitivity, specificity, and accuracy of serum procalcitonin in comparison to total leucocyte count in predicting bacterial infection, as well as to determine whether or not there is a correlation between serum procalcotonin level and bacterial culture.

MATERIALS AND METHODS

100 adults (aged 20 and above) with a recent-onset fever (less than 2 weeks) were enrolled. Antibiotic-treated subjects, those with trauma, burns, recent major surgery, shock, a deficiency in Vitamin B12/folic acid, those with a history of malignancy, and those with connective tissue diseases were not included in the study. The research was conducted in accordance with the guidelines set forth by the institution's ethical committee. Each participant in the research had a thorough medical history and physical assessment. Complete blood count, peripheral smear, ESR, C reactive proteins, serum procalcitonin levels, dengue serology, renal function test, and liver function test were all performed on the patient's blood upon admission. Urine, sputum, and blood were submitted for bacterial culture and sensitivity based on the preliminary diagnosis and clinical suspicion. Other than the regular collection of urine, imaging examinations including a chest x-ray and an ultrasound of the abdomen and pelvis were collected.

The Fine care PCT quick quantitative test was used to determine the concentration of procalcitonin in the blood. This test is a fluorescence immunoassay that measures PCT in human plasma, serum, or whole blood. The range of 0-0.5ng/ml was considered normal. Serum PCT levels over 0.5ng/ml were deemed high. Leucopenia was diagnosed when the total leucocyte count was less than 4000 cells/mm3, while normal was between 4000 and 11,000 cells/mm3, and high was over 11,000.

RESULTS

Positive blood, urine, or sputum culture results were found from 45 (45%) of the 100 patients investigated, suggesting a bacterial infection. The other 55(55%) participants who had a negative blood/urine/sputum culture were identified as having a viral infection. The most common type of bacterial infection was urinary tract infection, which was seen in 30 (66.67%) of the 45 subjects with bacterial infection, while 11 (24.44%) had a positive sputum culture (indicating lower respiratory tract infection) and 4 (8.89%) had a positive blood culture (indicating sepsis). The range of procalcitonin levels was measured, and the results were categorised as either below 0.5ng/ml or over 0.5ng/ml. Out of the 45 participants with a positive culture, 38(84.44%) had a serum procalcitonin level >0.5ng/ml while the remaining 7(15.56%) subjects had a value of ≤0.5ng/ml. Only 5 (9.10%) of the 55 participants suspected of having a viral infection (based on a negative culture report) had a procalcitonin value of >0.5ng/ml, whereas 50 (90.90%) of the subjects had a value 0.5ng/ml. The p value for the correlation between a positive culture and elevated serum procalcitonin levels of >0.5 was less than 0.0001. This demonstrates a statistically significant connection between bacterial infection and a higher blood procalcitonin level. The correlation between blood, urine, and sputum culture and serum PCT levels are shown in Table 1.

Table 1: Association between Serum Procalcitonin and Blood/urine/sputum culture.

	Serum Procalcitonin			Chi-square	P value
Blood/urine/sputum culture	≤0.5	>0.5	Total	43.58	<0.0001
Positive	7	38	45		
Negative	50	5	55		
Total	57	43	100		

The procalcitonin levels in 25 of the 30 patients (83.33%) with a positive urine culture were more than 0.5ng/ml, whereas the procalcitonin levels in just 5 (16.67%) were below that threshold. Sixty-two (74.28%) of the 70 patients with a negative urine culture had a serum PCT value of 0.5ng/ml, whereas just eighteen (25.72%) did. According to Table 2, there is a statistically significant correlation between a positive urine culture and a serum procalcitonin concentration of >0.5ng/ml (P = 0.00011).

Table 2: Association between Serum PCT and Urine culture

	Serum Procalcitonin			Chi-square	P value
Urine culture	≤0.5	>0.5	Total		
Positive	5	25	30		
Negative	52	18	70	16.87	0.00011
Total	57	43	100		

Serum procalcitonin levels >0.5ng/ml were seen in all 11 individuals with a positive sputum culture. Of the 89 instances where a sputum culture result was negative, 64.04 percent had a serum PCT level 0.5ng/ml, whereas 35.96 percent had a PCT level >0.5ng/ml. An link between a positive sputum culture and serum PCT levels >0.5ng/ml was identified (P = 0.0012). The correlation between sputum culture and serum PCT levels is seen in Table 3.

Table 3: Association between serum PCT and Sputum culture

	Serum procalcitonin			Chi-square	P value
Sputum culture	≤0.5	>0.5	Total		
Positive	0	11	11	12.87	0.0012
Negative	57	32	89		
Total	57	43	100		

Among the 4 cases with sepsis as indicated by a positive blood culture report, all 4(100%) had a serum PCT value of >0.5ng/ml. Out of the 96 subjects with a negative blood culture, 57(59.38%) had a PCT level of ≤0.5ng/ml and 39(40.62%) had a level of >0.5ng/ml. A statistically significant association was found between a positive blood culture and serum PCT level >0.5ng/ml, as the P value obtained for this association was 0.04. Table 4 shows the association between blood culture and serum PCT levels.

Table 4: Association between Serum PCT and blood culture

	Serum Procalcitonin			Chi square	P value
Blood c/s	≤0.5	>0.5	Total	**5.62**	
Positive	0	4	4		0.04
Negative	57	39	96		
Total	57	43	100		

The sensitivity and specificity of serum PCT as a diagnostic test of bacterial infection was 62% and 93% respectively within 96% confidence interval. The positive predictive value of serum PCT was 46% whereas the negative predictive value was 96%.The diagnostic accuracy of serum PCT in detecting bacterial infection was 95%.Table 5 shows the sensitivity, specificity and accuracy of serum PCT for diagnosing bacterial infection.

Table 5: Evaluation of Serum Procalcitonin as a marker of bacterial infection

Statistic	%
Sensitivity	62
Specificity	93
Area under curve	82
Positive Predictive value	46
Negative Predictive value	96
Accuracy	95

Among the 45 subjects with a bacterial infection (as indicated by a positive blood/urine/sputum culture), only 15(33.33%) had an elevated total leucocyte count of >11,000 cells/mm^3 whereas the remaining 30(66.67%) subjects had a TLC of ≤11,000 cells/mm^3.Among 55 subjects with a negative culture, 13(23.64%) had a TLC of >11,000 cells/mm^3 and 42 had a TLC of ≤11,000 cells/mm^3.The association between elevated total leucocyte count and a positive culture was not statistically significant as the P value obtained was 0.33(Table 6).

Table 6: Association between Total leucocyte count and bacterial culture

	Total leucocyte count			Chi-square	P value
Culture	≤11000	>11000	Total		
Positive	30	15	45	1.52	0.33
Negative	42	13	55		
Total	72	28	100		

TLC had a sensitivity of 56% and a specificity of 66% in identifying bacterial illness, whereas an increased leucocyte count had a diagnostic accuracy of 59%. The diagnostic sensitivity, specificity, and accuracy of TLC for bacterial infection are shown in Table 7.

Table 7: Evaluation of Total Leucocyte count as a diagnostic marker of bacterial infection

Statistic	%
Sensitivity	56
Specificity	66
Area Under Curve	60
Positive Predictive Value	23
Negative Predictive Value	89
Accuracy	59

Table 8: Association between total leucocyte count and serum PCT

	Serum procalcitonin			Chi -square	P value
Total leucocyte count	≤0.5	>0.5	Total		
≤11000	35	37	72	0.02	0.55
>11000	22	6	28		
Total	57	43	100		

DISCUSSION

Acute febrile illnesses are very common but difficult to diagnose and treat. Even though viruses often cause acute febrile symptoms, early diagnosis of bacterial infections is crucial. When a bacterial infection is identified quickly, antibiotic treatment may begin right once, avoiding potentially fatal consequences like sepsis. In contrast, antibiotics shouldn't be used haphazardly or routinely if there's no proof of a bacterial infection. Under normal physiological settings, pre-procalcitonin is secreted by the C cells of the thyroid glands. This marker of bacterial infection may be detected early in the course of an infection and so meets an urgent requirement. The enzyme cleavage of this precursor produces the active hormone procalcitonin. Procalcitonin is converted into calcitonin by pro-hormone convertase, the hormone responsible for controlling blood calcium levels. The content of procalcitonin in the blood is very low under normal circumstances (usually less than 0.05 ng/mL). Procalcitonin is normally synthesised in the thyroid gland. However, in patients with severe bacterial infections, extra-thyroidal synthesis of procalcitonin in several organs, including the liver, lung, pancreas, kidney, and intestine, as well as in leukocytes, can increase serum procalcitonin concentration by 100- to 1000-fold.[7,8] This increased extra-thyroidal production of procalcitonin is due to the stimulation of the calc Increased synthesis of PCT occurs within 2–4 hours after the commencement of severe bacterial infection, peaks at 6–8 hours postinfection, and is elevated throughout the duration of the inflammatory response because IFN- produced during viral infections inhibits calcitonin m-RNA induction. Considering these factors, PCT is an appropriate biomarker of bacterial infection in patients presenting with an acute febrile illness in a tertiary care centre. The purpose of this research was to assess the use of PCT as a biomarker of bacterial infection. The purpose of this research was to assess how well serum PCT predicts bacterial infection in comparison to a commonly used marker, such as leucocytosis.

The results of our research show that increased serum PCT levels (PCT >0.5ng/ml) are significantly correlated with a positive sputum culture for bacteria, suggesting a bacterial respiratory tract illness and also discovered a statistically significant correlation between a positive culture of lower respiratory tract secretions and high serum PCT levels. There were 110 patients with CA-P admitted to the ICU and studied by Boussekey et al.[9] Positive sputum cultures were associated with increased PCT levels (Mean PCT =0.24ng/ml) in a study of patients with acute exacerbation of COPD done by Chang C et al.[10] Researchers Yanhui Zhu et al.[11] observed a statistically significant correlation between bacterial growth in sputum and elevated PCT levels of 0.42ng/ml.

In our research, we discovered that a higher PCT level was linked to a positive urine culture for bacteria. Patients with ureteral calculi have a higher risk of a positive urine culture result if their serum PCT levels are high, as indicated by research by Papagiannopoulos D et al.[12] Similarly, Patil HV et al.[13] found that individuals with bacterial growth on urine culture had higher serum procalcitonin (range, 2.12-100 ng/ml). Similarly, Leng et al.[14] discovered an increased PCT level (mean value 11.25ng/ml) in individuals with urinary tract infections, with PCT levels being substantially greater for gram-negative bacteria infection than for gram-positive bacteria infection.

Having a positive blood culture was linked to higher serum PCT levels in a statistically meaningful way in our research. Similarly, Webb A L et al.[15] showed a strong connection between increased serum PCT levels (>2ng/ml) and a positive blood culture among emergency department patients with an admission diagnosis of severe sepsis. In a separate investigation of adults with acute febrile illness, Chirouze C. et al.[16] likewise discovered substantially greater PCT levels

in bacteremic patients compared to nonbacteremic individuals. Patients with acute pyelonephritis were more likely to have a positive blood culture if their serum PCT levels were high (mean PCT=4.89ng/ml), as shown by research by Lee G H et al.[17]

A positive blood, urine, or sputum culture was associated with an increased serum PCT level in our research. Therefore, our research shown that serum PCT accurately predicts bacterial infection in febrile individuals. We discovered no statistically significant link between leucocytosis and bacterial infection, contrary to the findings of studies by Qu J et al.[18] and Singh G et al.[19] Similarly, U P Dior et al.[20] could not find a consistent relationship between leucocytosis and bacterial infection in their study of feverish parturients. P. Leucocyte count was not observed to be independently linked with systemic bacterial infection, as reported by Hausfater et al.[21] Our research found that a serum procalcitonin cutoff of 0.5ng/ml had a sensitivity of 62%, specificity of 93%, positive predictive value of 46%, negative predictive value of 96%, and accuracy of 95% in diagnosing bacterial infection. A A El-Azeem et al.[22] showed that serum PCT (at a cut-off of 0.5ng/ml) gave a sensitivity of 94.1%, specificity of 88.4%, positive predictive value (PPV) of 91.4%, negative predictive value (NPV) of 92%, and diagnostic accuracy (Accuracy) of 91.6% for diagnosis of respiratory tract bacterial infections. Our study found similar results, except for lower sensitivity and positive predictive Delèvaux I et al.[23] observed that serum PCT >0.5ng/ml is a marker of bacterial infection with a sensitivity of 65%, a specificity of 96%, and an area under the ROC curve of 0.84. Thus, our results are consistent with those of Delevaux I et al.[23] which we have just discussed. Our research found that a leucocytic increase was 56% sensitive, 66% specific, and 59% accurate in predicting bacterial infection. Specifically, TLC had an AUC of 0.58. Leucocyte count >12,000 cell/mm3 was shown to have a comparable sensitivity (59.4%) and specificity (82.2%) in predicting bacterial infection by Charles-Eric Lavoignet et al.[24] but a higher AUC (0.77). WBC count at a cut-off level of 11,000 cells/mm3 exhibited a sensitivity of 65% and specificity of 70% for diagnosing bacterial infection in a research done by Wasserman et al.[25] among elderly individuals. These results are consistent with those of our investigation. From this it may be concluded that serum PCT is a more accurate indicator of bacterial infection than leucocytosis. Serum PCT 0.5 ng/ml may be helpful in ruling out bacterial infections, since its specificity and negative predictive value are better than its sensitivity and positive predictive value.

CONCLUSION

In individuals presenting with acute febrile illness, serum PCT is a helpful test for diagnosing bacterial infection. In the emergency room, a serum PCT level below 0.5ng/ml may rule out bacterial infection. When it comes to predicting bacterial infection, leucocytosis is a less accurate indication than serum PCT.

REFERENCES

1. Menéndez R, Torres A, Reyes S, Zalacain R, Capelastegui A, Aspa J, et al. Initial management of pneumonia and sepsis: factors associated with improved outcome, Eur Respir J. 2012;39:156-62.
2. Bronzwaer SL, Cars O, Buchholz U, et al. The Relationship between Antimicrobial Use and Antimicrobial Resistance in Europe. Emerging Infectious Diseases. 2002;8:278-282.
3. Klouche M, Schröder U. Rapid methods for diagnosis of bloodstream infections.Clin Chem Lab Med. 2008;46(7):888- 908.
4. Korppi M, Kröger L, Laitinen M.White blood cell and differential counts in acute respiratory viral and bacterial infections in children. Scand J Infect Dis. 1993;25(4):435-40.
5. Samsudin I, Vasikaran SD. Clinical Utility and Measurement of Procalcitonin. Clin Biochem Rev. 2017;38(2):59–68.
6. Becker KL, Snider R, Nylen ES. Procalcitonin in sepsis and systemic inflammation: a harmful biomarker and a therapeutic target. Br J Pharmacol. 2010; 159:253–64.
7. Lippi G,Sanchis-Gomar F.Procalcitonin in inflammatory bowel disease: Drawbacks and opportunities. World J Gastroenterol. 2017; 23(47):8283-8290.
8. Muller B,White JC,Nylen ES, Snider RH,Becker KL, Habener JF. Ubiquitous expression of the calcitonin-i gene in multiple tissues in response to sepsis. J Clin Endocrinol Metab. 2001; 86:396–404.
9. Boussekey N, Leroy O, Georges H, Devos P, d'Escrivan T, Guery B. Diagnostic and prognostic values of admission procalcitonin levels in community-acquired pneumonia in an intensive care unit. Infection. 2005;33(4):257-63.
10. Chang C,Yao WZ,Chen YH,Liu ZY, Zhang XW. The changes and clinical implications of serum procalcitonin in acute exacerbations of chronic obstructive pulmonary disease. Chinese journal of tuberculosis and respiratory diseases.2006 ; 29(7):444-7.
11. Zhu Y, Yuan Y, Huang H. Comparison of serum procalcitonin in respiratory infections and bloodstream infections. Int J Clin Exp Med.2015; 8(11):21586-21592.
12. Papagiannopoulos D,Whelan P,Ahmad W, et al. Procalcitonin is a strong predictor of urine culture results in patients with obstructing ureteral stones: A prospective, pilot study. Urol Ann. 2016;8(3):277-280
13. atil HV, Patil VC. Comparative study of procalcitonin and C-reactive protein in patients with sepsis. J Nat Sc Biol Med. 2020; 11:93-9.
14. Leng, Y.,Chen, C.,Zhang,Y., Luo, C., Liu, B.Ability of serum procalcitonin to distinguish focus of infection and pathogen types in patients with bloodstream infection. Ann Transl Med. 2019; 7(7):135
15. Webb A, Kramer N, Stead T, Mangal R, Lebowitz D, Dub L et al. Serum Procalcitonin Level Is Associated with Positive Blood Cultures, In-hospital Mortality, and Septic Shock in Emergency Department Sepsis Patients. Cureus 2020;12(4): e7812.

16. Chirouze C, Schuhmacher H, Rabaud C, Gil H, Khayat N, Estavoyer J et al. Low Serum Procalcitonin Level Accurately Predicts the Absence of Bacteremia in Adult Patients with Acute Fever. Clinical Infectious Diseases. 2002; 35(2):156- 161.
17. Lee G, Lee Y, Kim Y, Park S, Park J, Park K et al. A study of the effectiveness of using the serum procalcitonin level as a predictive test for bacteremia in acute pyelonephritis. Kosin Medical Journal. 2018;33(3):337.
18. Qu J, L X, Liu Y,Wang X.Evaluation of procalcitonin, C- reactive protein,interleukin-6 & serum amyloid A as diagnostic biomarkers of bacterial infection in febrile patients. Indian J Med Res. 2015 ; 141(3):315-21.
19. Singh G, Sharma S, Kaur J. Evaluation of Triple Biomarker Algorithm for Identification of Bacterial Sepsis in Critical Care Patients of a Tertiary Care Hospital. Curr Trends Diagn Treat. 2018; 2(1):9-14.
20. Dior U, Kogan L, Elchalal U, Goldschmidt N, Burger A, Nir- Paz R et al. Leukocyte blood count during early puerperium and its relation to puerperal infection. The Journal of Maternal-Fetal & Neonatal Medicine. 2013;27(1):18-23.
21. Hausfater P, Garric S, Ayed SB, Rosenheim M, Bernard M, Riou B.Usefulness of procalcitonin as a marker of systemic infection in emergency department patients: a prospective study.Clin Infect Dis. 2002 ; 34(7):895-901.
22. El-Azeem A, Hamdy G, Saraya M, Fawzy E, Anwar E, Abdulattif S. The role of procalcitonin as a guide for the diagnosis, prognosis, and decision of antibiotic therapy for lower respiratory tract infections. Egyptian Journal of Chest Diseases and Tuberculosis. 2013; 62(4):687-695.
23. Delèvaux I, André M, Colombier M, Albuisson E,Meylheuc F,Bègue RJ,Aumaître O.Can procalcitonin measurement help in differentiating between bacterial infection and other kinds of inflammatory processes?Ann Rheum Dis. 2003; 62(4):337- 40.
24. Lavoignet C, Le Borgne P, Chabrier S, Bidoire J, Slimani H, Chevrolet-Lavoignet J et al. White blood cell count and eosinopenia as valuable tools for the diagnosis of bacterial infections in the ED. European Journal of Clinical Microbiology & Infectious Diseases. 2019; 38(8):1523-1532.
25. Wasserman M, Levinstein M, Keller E, Lee S, Yoshikawa T. Utility of Fever, White Blood Cells, and Differential Count in Predicting Bacterial Infections in the Elderly. Journal of the American Geriatrics Society. 1989; 37(6):537-543.