



ISSN: 0976-3031

Available Online at <http://www.recentscientific.com>

CODEN: IJRSFP (USA)

International Journal of Recent Scientific Research
Vol. 10, Issue, 06(D), pp. 32951-32953, June, 2019

**International Journal of
Recent Scientific
Research**

DOI: 10.24327/IJRSR

Research Article

USEFULNESS OF PROCALCITONIN IN GUIDING THERAPY PRIOR TO CULTURE AND SENSITIVITY REPORTS ANTIBIOTIC

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DOI: <http://dx.doi.org/10.24327/ijrsr.2019.1006.3574>

ARTICLE INFO

Article History:

Received 12th March, 2019

Received in revised form 23rd

April, 2019

Accepted 7th May, 2019

Published online 28th June, 2019

Key Words:

Procalcitonin, C - reactive protein,
Systemic inflammatory response
syndrome, antibiotics, sepsis

ABSTRACT

Background: Procalcitonin (PCT) is currently the most studied infection biomarker and it's blood levels seem to mirror the severity of illness and outcome. PCT is also widely used together with other biomarkers, such as white blood cells (WBC) count and C reactive protein (CRP) to guide antibiotic therapy. This study aims to verify the diagnostic and prognostic power of PCT to guide antibiotics therapy in the emergency department(ED), prior to obtaining culture and sensitivity reports, specifically in patients with suspected/proven sepsis.

Objectives: To determine the usefulness of sepsis biomarkers procalcitonin in guiding antibiotic therapy prior to obtaining culture and sensitivity reports, specifically in patients presenting to the Emergency department with suspected/proven sepsis.

Materials and Methods: PCT and Blood culture were simultaneously measured and compared in 113 patients who presented in emergency department with suspected/proven sepsis (2 positive criteria out of 4 for SIRS) according to the International consensus for sepsis. Other Necessary culture specimens were taken from appropriate suspected sources of infection, on case to case basis.

Results: In culture positive 31 patients Procalcitonin levels were >0.2 in 20 patients, whereas CRP values were >10 in all the 31 patients.

Conclusion: Antibiotic de-escalation strategy should not be employed solely based on procalcitonin and CRP levels. Lab culture reports and clinical judgement along with the sepsis biomarkers should also be taken into consideration, before de-escalation of antibiotics.

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INTRODUCTION

Procalcitonin is the prohormone of calcitonin and present in minute quantities in health. However during infection, its level rise considerably and correlated with the severity of infection. Many studies have demonstrated the value of procalcitonin levels for diagnosing sepsis and disease severity. Procalcitonin levels have also been successfully used to guide antibiotic administration, de-escalation and discontinuation.¹ In recent studies procalcitonin (PCT), a peptide consisting of 116 amino acids, was found to be elevated in patients with sepsis and severe infections². The concentrations of the prohormone seemed closely related to the severity of the bacterial infection guiding antibiotic therapy for the same.

Sepsis is the primary cause of death from infection especially if not recognized and treated promptly. Its early recognition mandates urgent attention. The 1991 Consensus Conference on sepsis³ developed initial definitions that focused on the then-

prevailing view that sepsis resulted from a host's systemic inflammatory response syndrome (SIRS) described as 2 or more out of 4 criteria: 1-Temperature >38°C or <36°C 2-Heart rate >90/min 3-Respiratory rate >20/min or P_{aco}₂ <32 mm Hg (4.3 kPa) 4-White blood cell count >12 000/mm³ or <4000/mm³ or >10% immature bands.

This may progress to septic shock. Septic shock is defined as "sepsis-induced hypotension persisting despite adequate fluid resuscitation", and requires vasopressors to keep MAP >65mmHg and elevated Lactate levels >4mmol. Organ dysfunction can be identified as an acute change in total SOFA score ≥2 points consequent to the infection. The baseline SOFA score can be assumed to be zero in patients not known to have pre-existing organ dysfunction. A SOFA score ≥2 reflects an overall mortality risk of approximately 10% in a general hospital population with suspected infection. Even patients presenting with modest dysfunction can deteriorate further, emphasizing the seriousness of this condition and the need for

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prompt and appropriate intervention, if not already being instituted.

MATERIALS AND METHODS

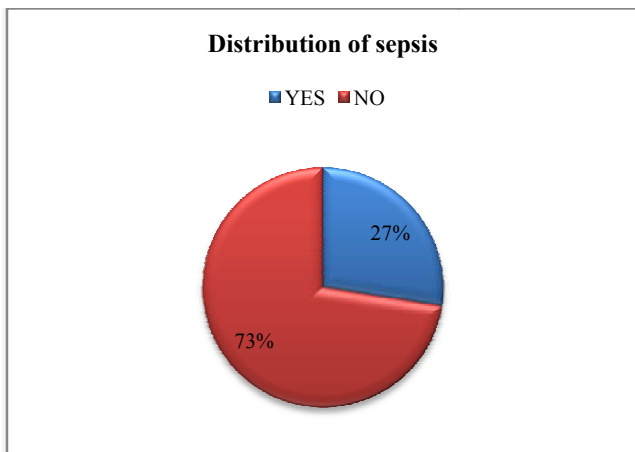
PCT and CRP were simultaneously measured and compared in 113 patients who presented to the Emergency Department with suspected/proven sepsis (2 positive criteria out of 4, according to the International Consensus for sepsis; according to site). Simultaneously appropriate cultures based on clinical judgement of the ER physician were obtained and sent to lab, before antibiotics and other supportive treatment were given based on patient’s clinical conditions PCT analysis was done on cobas8000 system based on the Electro chemiluminescence immunoassay “ECLIA” (based on the Sandwich Principle).

CRP test was done based on the Test principle, Particle enhanced immunoturbidimetric assay. Human CRP agglutinates with latex particles coated with monoclonal anti-CRP antibodies. The aggregates are determined turbidimetrically and the machine used was CRPL3: ACN 8210(cobas), Blood culture was done on BACTEC blood culture system. Urine, ET, ascitic, sputum culture was analysed using manual methods.

RESULTS

This study included a total of 113 cases, 75 (66.4%) males and 38 (33.6%) females. The mean age was 54.23 ± 19.83 years. Among them 31 (27.4%) were culture positive. The clinical specimens used for culture were – blood 98 (96.7%), urine 12 (10.6%), Sputum 2 (1.8%), and BAL aspirate 1 (0.9%). The major isolates were E.coli and Klebsiella Pneumonia.

In culture positive 31 patients PCT levels were >0.2 in 20 patients, whereas CRP values were >10 in all the 31 patients. De-escalation of antibiotics have been grossly based on PCT values in other studies conducted worldwide⁴. Antibiotics should have been deescalated in 11 patients (35%), as their procalcitonin values were low. On the contrary, if CRP values were taken into consideration, none of the patients will have to be de-escalated from existing antibiotic therapy. Thus, we reached a conclusion that antibiotic de-escalation strategy should not be employed solely based on procalcitonin and CRP levels. And that culture reports and clinical judgement along with the sepsis biomarkers should also be taken into consideration.

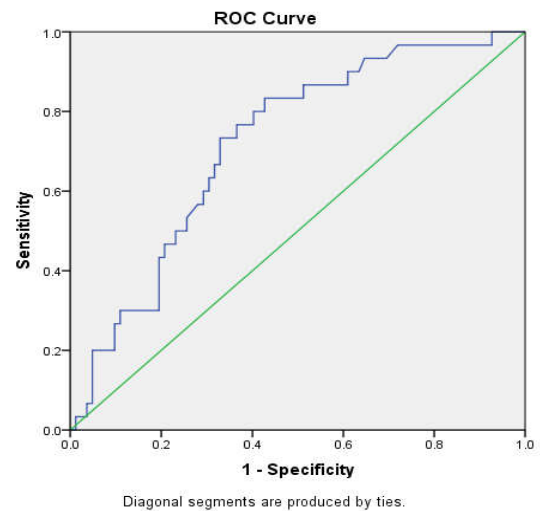


Comparison of mean PCT and CRP in culture positive sepsis patients

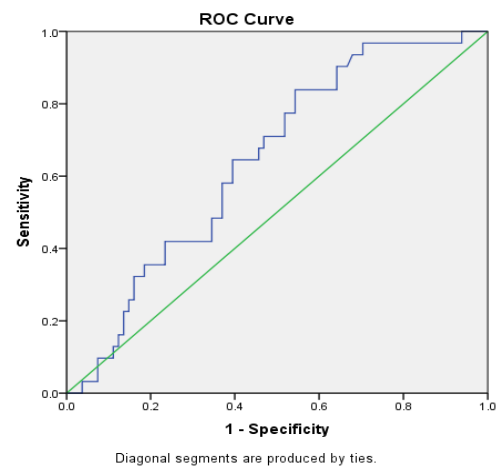
Variables	Culture positive	N	Mean	Std. Deviation	p value
Procalevel	Yes	31	16.47	25.53	0.458
	No	82	12.40	26.04	
CRP	Yes	31	164.11	79.10	0.001
	No	82	104.20	79.26	

The mean PCT was 13.52 ±25.85 ng/ml and CRP 120.25 ± 83.24 ng/ml. The mean PCT level in sepsis was 13.52 ±25.85 and in non-sepsis was 12.40 ±26.04. The results show that it is not statistically significant. The mean CRP was 164.11 ±79.10 ng/ml and CRP 104.20 ± 79.26 ng/ml. The mean PCT level in sepsis was 13.52 ±25.85 and in non sepsis was 12.40 ±26.04. The results show that it is statistically significant.

ROC curve of CRP



ROC curve of PCT



Out of 54 patients with PCT level > 0.2 ng/ml, 20 (37%) have sepsis compared to PCT level ≤ 2 ng/ml, 11 (19.3%). There is statistically significant association of PCT with sepsis (p value =0.037). Out of 49 patients with CRP level > 124 ng/ml, 22 (44.9%) have sepsis compared to CRP level ≤ 124 ng/ml, 12 (12.7%). There is statistically significant association of PCT with sepsis (p value =<0.001).

Variables	PCT	CRP
Sensitivity	64.5%	73.3%
Specificity	57.5%	67%
PVP	37%	44.9%
PVN	80.7%	12.7%
Accuracy	58%	68%

DISCUSSION

Several controlled clinical studies have evaluated the potential of the infection biomarker procalcitonin (PCT) to improve the diagnostic work-up of patients with infections and its influence on decisions regarding antibiotic therapy. Most research has focused on lower respiratory tract infections and critically ill sepsis patients. Although promising findings have been published in these different types of infections, there are a number of limitations regarding PCT, including suboptimal sensitivity and/or specificity, which make a careful interpretation of PCT in the clinical context mandatory. In previous study, PCT has been put forward as a promising candidate marker for diagnosis and for antibiotic stewardship in patients with systemic infections⁵. Limitations of every PCT measurement include false-positive and false-negative results⁶

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How to cite this article:

Indresh Kumar *et al.*, 2019, Usefulness of Procalcitonin in Guiding Therapy Prior to Culture and Sensitivity Reports Antibiotic. *Int J Recent Sci Res*. 10(06), pp. 32951-32953. DOI: <http://dx.doi.org/10.24327/ijrsr.2019.1006.3574>
