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# ROLE OF PROCALCITONIN AS SURROGATE MARKER OF RENAL DAMAGE AMONG CASES OF SEPSIS IN A TERTIARY CARE HOSPITAL OF EASTERN INDIA

Clinical Biochemistry

**Susruta Sen** — Department of Lab Medicine, CK-Birla Hospitals-CMRI (The Calcutta Medical Research Institute) & BM Birla Heart Research Centre, Kolkata-700027, India

**Sharmistha Choudhuri*** — Department of Biochemistry, RG Kar Medical College & Hospital, Kolkata-700004, India *Corresponding Author

**Sudip Roy** — Department of Lab Medicine, CK-Birla Hospitals-CMRI (The Calcutta Medical Research Institute) & BM Birla Heart Research Centre, Kolkata-700027, India

**Nivedita Bhattacharjee** — Department of Lab Medicine, CK-Birla Hospitals-CMRI (The Calcutta Medical Research Institute) & BM Birla Heart Research Centre, Kolkata-700027, India

**Saumya Chandra** — Department of Neuroscience, Ballygunge Science College, Kolkata-700019, India

## ABSTRACT

**Introduction:** Procalcitonin is a popular biomarker for assessing severity in sepsis of bacterial origin. However, interpreting PCT levels in patients with renal impairment can be tricky, where irrespective of infection higher cut-offs are seen, as compared to those with normal renal status **Methods:** We conducted a retrospective, analytical, comparative audit utilizing 243 serum samples from patients, admitted with clinical symptoms and signs of sepsis, with or without renal dysfunction. Pre-treatment serum PCT and creatinine levels were compared as were the post treatment levels. Individual pre and post treatment levels of each biomarker were also compared. Concomitantly, the blood or urine culture results of these individuals were also taken into account, to ascertain microbiological evidence of bacterial infection in these individuals. **Results:** Pre-treatment serum levels of PCT showed a significant association with pre-treatment serum creatinine levels [P <0.0001], as did post-treatment serum PCT and creatinine values [P <0.0001]. Pre and post treatment values of individual markers also showed significant difference when compared amongst themselves [P <0.0001]. **Conclusions:** Procalcitonin, although a popular marker for bacterial sepsis, need cautious interpretation and simultaneous corroboration by other markers of bacteria induced inflammation, in individuals with pre-existing or concomitant renal dysfunction, so that appropriate antimicrobial therapy can be instituted judiciously, without imposing additional burden on already challenged kidneys.

## KEYWORDS

Procalcitonin, Sepsis, Creatinine

## INTRODUCTION

Procalcitonin [PCT], important laboratory tool for predicting the presence of a bacterial infection in patients presenting with sepsis; [1] its chief advantage being in its ability to reduce inappropriate antibiotic exposure by ruling out bacterial infection more reliably and accurately than previously used measures, including C-reactive protein or white blood cell count.[2, 3, 4] The molecule which is peptide precursor of calcitonin, produced in the parafollicular C cells of the thyroid gland, typically exhibits values less than 0.1 ng/mL, in absence of bacterial infections, with levels shooting beyond 0.25 ng/mL, in presence of bacterial infestation.[5] However, interpreting PCT levels in patients with comorbidities states can be tricky, considering that PCT levels may be elevated even in absence of bacterial infection, in disorders like present, such as massive stress, medullary thyroid carcinoma, small cell lung cancer, among others.[6] Additionally and most pertinent to our current study, PCT levels among patients with renal dysfunction are often elevated, even in the absence of infection, with half-life of PCT being very similar in patients with and without renal dysfunction; around 33 hours for those with renal impairment compared to 28.9 hours for those without.[7] The existence of higher level of PCT in individuals with renal impairment but without actual bacterial infection can have serious implications, chiefly in the form of undesirable, unnecessary and potentially nephrotoxic antibiotic therapy in such persons, who already have compromised renal function.[8] Previous studies have postulated renal impairment itself being a pro-inflammatory state, that acts as impetus for rise in PCT, irrespective of concomitant bacterial infection.[9,10]

Our present study was undertaken with the aim to establish the possible role of PCT in acting as a potential surrogate marker for renal status, in patients admitted with clinical symptoms and signs of sepsis, with or without renal dysfunction. We conducted study on serum samples such of patients with suspected sepsis that had come to lab for PCT assay. We recruited into the study, 243 such samples and also noted the serum creatinine values in such samples. The blood or urine culture results of these individuals were also taken into account, to ascertain microbiological evidence of bacterial infection in these individuals.

## MATERIALS AND METHODS

**Study Variables:** A retrospective, analytical, comparative audit was conducted in the Department of Laboratory Medicine of CK-Birla Hospitals, CMRI, Kolkata, from 1st February 2025 to 31st August 2025, utilizing 243 serum samples from patients, admitted with clinical symptoms and signs of sepsis, with or without renal dysfunction. Serum levels of PCT and creatinine were noted. Concomitantly, the blood or urine culture results of these individuals were also taken into account, to ascertain microbiological evidence of bacterial infection in these individuals.

**Case Selection and Sampling Details:** Briefly, 243 serum samples were selected, admitted with clinical symptoms and signs of sepsis, with or without renal dysfunction. Serum levels of PCT and creatinine were noted. Concomitantly, the blood or urine culture results of these individuals were also taken into account, to ascertain microbiological evidence of bacterial infection in these individuals.

**Ethical Considerations:** Since the entire study was conducted on samples of patients, coming to lab for routine investigations, hence ethical clearance was not required separately for the same.

**Assay of PCT and Creatinine:** Procalcitonin levels in serum was estimated by electrochemiluminescence immunoassay [ECLIA], in automated platform; the Roche COBAS e411. Cut-offs for clinical interpretation of the assay were; < 0.05 – 0.10 ng/mL: Normal / healthy baseline (bacterial infection unlikely).; 0.10 – 0.25 ng/mL: Low risk or low likelihood of a clinically relevant bacterial infection; 0.25 – 0.50 ng/mL: Moderate risk / intermediate likelihood of bacterial infection; clinical monitoring or serial testing recommended; > 0.50 ng/mL: High likelihood of a severe bacterial infection or systemic inflammation/sepsis, warranting active medical evaluation.

Serum creatinine [biological reference interval 0.70 -1.30 mg/dL (males); 0.55 -1.02 mg/dL (females)] was estimated by modified kinetic Jaffe method using auto-analyzer Roche Cobas 6000.

**Microbiological Confirmation of Sepsis:** The laboratory confirmation of sepsis was done using the BACTEC culture system for blood samples and standard MacConkey Agar medium for urine samples. Briefly, positive cultures were those which showed growth evidence within 24-48 hours of incubation; thereby confirming the sepsis.

**Statistical Analyses:** The data generated was analysed by MS Excel 2013 and Graph-Pad Prism v.8.4.3, using appropriate statistical tools. Normality of the sample distribution was tested by D'Agostino & Pearson omnibus normality test. For comparing, pre-treatment serum PCT and creatinine levels Mann Whitney Test was applied. The same test was applied for comparing the post-treatment serum PCT and creatinine levels. Additionally, comparison between pre and post treatment levels of serum PCT as well as pre and post treatment levels of serum creatinine, were done by Wilcoxon matched-pairs signed rank test. In all statistical analysis P value ≤0.05, was considered as statistically significant.

## RESULTS:

**1. Patient Profiles and Culture Status:** A total of 243 samples of individuals admitted with clinical symptoms and signs of sepsis, with or without renal dysfunction, which had come to the hospital laboratory for routine analysis was selected. Blood or urine culture was performed in designated culture media. Out of the total 243 samples; 185 [76.13%] showing growth within 24 to 48 hours of incubation, were designated as positive while the remaining 58 [23.87%] that did not show growth within 24 to 48 hours of incubation, were designated as negative. Figure 1 depicts percentages of samples showing positive or negative status on culture.

**2. Comparative Analyses Between Pre-treatment Level Serum PCT & Creatinine and Post-treatment Level Serum PCT & Creatinine:** Procalcitonin [PCT] and creatinine were both assayed in the 243 chosen samples, irresective of culture results. Pre-treatment serum levels of PCT showed a significant association with pre-treatment serum creatinine levels [P <0.0001; Fig 2A]. Likewise, post-treatment serum PCT levels showed significant association with post-treatment serum creatinine levels [P <0.0001; Fig 2B].

**3. Comparative Analyses Between Pre and Post-treatment Levels of Serum PCT & Pre and Post-treatment Levels of Serum Creatinine:** We also compared the pre-treatment PCT and creatinine levels with their respective post-treatment levels. A significant difference was observed in post-treatment levels of both parameters [P <0.0001; Fig 3A and P <0.0001; Fig 3B], when compared against their respective pre-treatment levels.

## DISCUSSION

Procalcitonin is a ubiquitous polypeptide rapidly released in the presence of bacterial toxins and proinflammatory mediators of which IL-1β and TNF-α are predominant. [11] The steeper elevations in serum levels are significantly more common in moderate-to-severe bacterial infections, especially those affecting the respiratory tract.[12, 13] Chronic kidney disease [CKD] is classically defined as gradual loss of renal function over a period of years or decades, with a very prolonged asymptomatic period, owning to the kidney's significant compensation mechanism, since the remaining renal nephrons are capable of removing toxins and maintaining homeostasis. [14]

Inflammation has been recognized as an integral part of CKD and is associated with cardiovascular disease, protein.energy wasting, and mortality among patients with CKD. The origin of inflammation in CKD patients is often attributable to impaired renal function.[15] Moreover, impaired renal function leads to the decreased excretion of proinflammatory cytokines and this impaired function is also responsible for the chronic inflammation observed in CKD patients. [16]

PCT which is a pro-inflammatory biomarker especially in bacterial infections, usually exhibits values < 0.01 ng/mL, in healthy individuals and is significantly elevated under the stimulation of pathogens. However, due to the pre.existing endogenous inflammation that occurs in CKD patients and the reference range that applies to the general population may not be appropriate for diagnosing infections in CKD patients.[1,7,17] Our present study which dealt with 243 samples of individuals who were admitted with clinically suspected sepsis and out of whom 185 also showed positive growth on culture [76.13%; Fig 1], exhibited pre-treatment serum PCT ranging from 0.02 ng/mL upto as high as 100 ng/mL. Furthermore, 146 out of the 243 samples [60.1%] taken into consideration for the study showed concomitant pre-treatment serum creatinine levels > 1.0 mg/dL, out of which again 12 showed levels exceeding the critical cut-off of 5.0 mg/mL. These pre-treatment serum creatinine levels showed a significant association with pre-treatment PCT levels [Fig 2A] as did the same pairing wrt post-treatment values [Fig 2B]

The major standpoint of the current study is to emphasize that therapy in sepsis should not be merely guided by PCT levels, as these may well be elevated in renal impairment and need corroboration by other sepsis markers such as CRP, in the absence of which there would only be resultant indiscriminate usage of antimicrobials and that too with increasing stress of excreting potentially nephrotoxic antimicrobials by an already weak renal machinery. [8, 14] In fact sensitivity cut-offs of 1.5 ng/mL, 0.1 ng/mL, and 1.75 ng/mL, have been established by one study, for acute kidney injury [AKI], CKD, and end-stage renal disease [ESRD], respectively, [6] while another study determined that the average PCT level in in CKD patients to be 1.82 ng/mL. [18] In our study the average pre-treatment serum PCT level was 6.712 ng/mL against an average pre-treatment serum creatinine level of 1.848 mg/dL. This higher average of serum PCT was due to vast majority of samples belonging to individuals with microbiologically proven case of sepsis [blood/urine culture positive for bacterial growth after 24 to 48 hours of incubation].

## CONCLUSION

Procalcitonin is one of the most in vogue biomarkers for assessing severity in sepsis of bacterial origin. However, cut-offs which are applicable to individuals with healthy kidneys are not so in those with pre-existing or concomitant renal impairment acute, chronic or end-stage. Hence in such individuals, PCT levels need cautious interpretation and simultaneous corroboration by other markers of bacteria induced inflammation, so that appropriate antimicrobial therapy can be instituted judiciously, without imposing additional burden on already challenged kidneys. Our future study aims to select certain biomarkers, to be studied alongwith serum PCT, these biomarkers characteristically although elevated due to infection, would be independent of renal status of the individual.

**FIG 1: Percentages of Culture Status of Blood or Urine Samples [%]; n=243; Culture Negative =58, Culture Positive = 185**

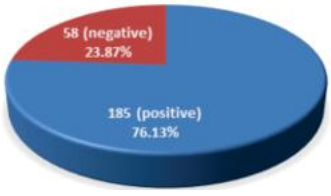



Fig 2A: Comparison of pre treatment serum PCT and pre treatment serum creatinine levels; n= 243; Mann-Whitney Test applied; P <0.0001

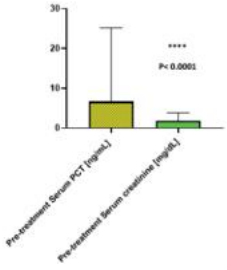



Fig 2B: Comparison of post treatment serum PCT and post treatment serum creatinine levels; n= 243; Mann-Whitney Test applied; P =0.0016

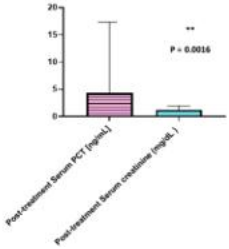



Fig 3A: Comparison between pre & post treatment serum PCT levels; n= 243; Wilcoxon matched-pairs signed rank test applied; P <0.0001

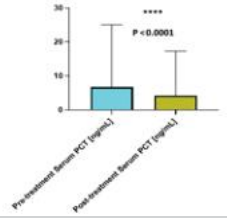
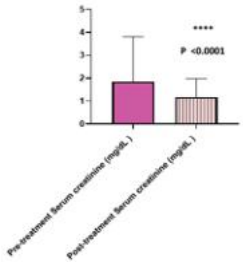


Fig 3B: Comparison between pre & post treatment serum creatinine levels; n= 243; Wilcoxon matched-pairs signed rank test applied; P <0.0001

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