

## Serum procalcitonin as diagnostic marker for postoperative surgical wound infection

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**Background:** Early diagnosis and treatment of postoperative infections is important to curtail the morbidity and economic burden associated with them. Currently there is no reliable diagnostic markers to differentiate infectious cause of postoperative fever from non-infectious one. The effectiveness of serum procalcitonin in establishing the same was investigated. **Method:** It was a cross-sectional study in which 100 consecutive patients who had onset of fever within seven days of the surgery were evaluated. These patients were divided into two groups of 50 each. Group A comprised of 50 patients having fever and elevated TLC (total leukocyte count) & ANC (absolute neutrophil count). Group B had 50 patients having fever but with normal TLC and ANC. All patients were assessed for C-reactive protein level, and serum procalcitonin and wound condition. Patients who had unhealthy wounds, their wound swabs were sent for microbiological work up. **Results:** 11/50 patients had raised serum procalcitonin levels in group A whereas in group B none had abnormal PCT levels. The statistical analysis showed that this difference was statistically significant as p value was <0.05. There was also statistically significant relation between PCT and wound condition. All patients with unhealthy wound were culture positive and also had raised raised serum procalcitonin levels. However, CRP was raise in patients in both the groups (96/100) which was found to be statistically insignificant with P value =0.307. **Conclusion:** Serum procalcitonin is a helpful biomarker marker in differentiating infectious from noninfectious causes of postoperative fever and can be used as an adjunct with clinical and microbiological findings.

**Keywords:** Post-operative fever, Serum procalcitonin, C-reactive protein

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## Introduction

Postoperative fever is one of the most common complications after surgery. Its cause can be infectious or non-infectious [1]. Among infectious causes, surgical site infections/postoperative wound infections are the most frequent, accounting for almost 38% of the total [2]. Surgical site wound infections usually appear after five days, but sometimes they may appear as early as first post-operative day. Therefore, post-operative fever requires inspection of the surgical site wound.

Since postoperative infection greatly impacts mortality and morbidity in patients therefore establishing the cause of fever is crucial for correct treatment. It also saves unnecessary use of antibiotics in the patients without an infection and thus preventing the development of antimicrobial resistance.

Besides microbiological testing, C-reactive protein (CRP) and procalcitonin (PCT) are two markers useful to establish infectious cause of fever. Of the two, CRP is the most widely used. It is an acute phase reactant whose plasma concentration increases rapidly in inflammatory disorders therefore it is used to monitor the postoperative course in surgical trauma [3,4].

PCT is a good marker of infection which has been shown by previous studies [5,6]. In healthy individuals, blood level of procalcitonin, is below detectable limits but its level rises in pro-inflammatory response to bacterial infections [7]. Level does not rise significantly with viral or non-infectious inflammations.

The aim of this study was to investigate the effectiveness of serum procalcitonin levels in differentiating infectious aetiology of fever after surgery from non-infectious causes.

## Material and Methods

**Ethical approval:** This study was carried out after obtaining ethical approval from the institutional ethics committee and informed consent from the patients.

**Settings:** The study was designed and carried out in the department of Biochemistry in collaboration with department of Microbiology, Sri Guru Ram Das Institute of Medical Sciences and Research, Amritsar.

**Study design:** It was a cross-sectional study conducted on 100 patients complaining of postoperative fever (>18 years of age).

For the present study postoperative fever was taken as a temperature greater than 38 C (or greater than 100.4 F) on 2 consecutive post-operative days or greater than 39 C (or greater than 102.2 F) on any postoperative day [8].

These patients were assessed for White blood-cell count, C-reactive protein level, and serum procalcitonin and were divided into two groups of 50 each, as follows:

**Group A:** 50 patients having fever and elevated TLC (total leukocyte count) & ANC (absolute neutrophil count).

**Group B:** 50 patients having fever but with normal TLC and ANC

**Inclusion criteria:** All patients, more than 18 years of age and complaining of fever within seven days of surgery.

**Exclusion criteria:** Patients having fever on the day of surgery.

### Method

**Sample collection:** Blood samples were collected as per order of draw, from the patients by performing phlebotomy aseptically after disinfection of vein puncture site with 70% alcohol followed by 2% tincture iodine [9]. For every patient, 3 ml of blood sample was collected in red cap and 2ml in lavender (EDTA) cap vacutainers and was sent to laboratory within 60 minutes for serum procalcitonin assay, CRP and TLC & ANC. Wound swabs were taken from the patients who had unhealthy wounds and were sent for microbiological work up.

**Sample processing:** PCT assay: The samples in red cap were subjected to ELISA sandwich enzyme immunoassay for quantitative measurement of human procalcitonin. C-reactive protein test was measured by Turbidimeter. Reference range for C-reactive protein was taken as <5 mg/l.

TLC: EDTA blood sample in purple cap vacutainer were subjected to total leukocyte count measured by Automated Cell Counter. Normal reference range 4000 to 11000 mm

ANC: Absolute neutrophil count was calculated by formula: ANC= (Absolute-Polymorphs + Absolute-Bands)

The reference range for ANC in adults is 1500-8000 cells per micro litre.

All wound swabs were processed in the department of Microbiology as per standard bacteriological techniques for aerobic cultures [10]. Antimicrobial sensitivity testing was determined by Kirby Bauer method and results were interpreted as per CLSI guidelines [11]

## Results

A total of 100 patients were enrolled in the study. Table 1 shows age and sex wise distribution of the patients. There was preponderance of male patients over females and maximum number of patients were in the age group of 51-70 years

**Table-1: Age & Sex wise distribution of patients.**

Age in years	Males	Females	Total
<30	17	8	25
31-50	20	11	31
51-70	31	5	36
>70	5	3	8
Total	73	27	100

**Table-2: Serum Procalcitonin Levels**

Serum PCT	Group A	Group B	Total
Within normal limits (<0.5 ng/ml)	39	50	89
Raised (>0.5 ng/ml)	11	0	11
Total	50	50	100

Among of 50 patients in the study group A 11 patients had raised serum procalcitonin levels and 39 patients had normal serum procalcitonin levels. Whereas in group B none had abnormal PCT levels. The statistical analysis showed that this difference was significant as p value was <0.05

**Table-3: C-Reactive Protein Levels**

Serum CRP	Group A	Group B	Total
Within normal limits (<5 mg/ml)	3	1	4
Raised (>5 mg/ml)	47	49	96
Total	50	50	100

C-Reactive Protein was raised in 96/100 patients, out of which 47 were in study group A and 49 in the group B. P value 0.307 (statistically insignificant)

**Table-4: Wound condition.**

Wound	Group A	Group B	Total
Not healthy	8	0	8
Healthy	42	50	92
Total	50	50	100

Unhealthy wound condition was taken as marker of infection and wound swabs were sent for microbiological work up. 8/50 patients in the study group A had unhealthy wounds and their cultures also came out to be positive. Table 5 shows the comparison of two ie. wound condition and serum procalcitonin and the results were statistically significant as p value was <0.05

**Table-5: Comparison of Serum procalcitonin with wound condition in study group A.**

	Healthy wounds	Unhealthy wounds	Total
Normal PCT (<0.5 ng/ml)	38	1	39
Raised (>0.5 ng/ml)	4	7	11
Total	42	8	50

P value is <0.05 (statistically significant)

Sensitivity of PCT: 87.5%%

Specificity: 90.4%%

Positive predictive value: 63.6%

Negative predictive value: 97.4%

## Discussion

Postoperative fever is a common problem encountered after a surgery and incidence varies between 13-14% [12]. The cause of fever can be a pyretic response to surgery i.e. due to postoperative healing process leading to the production of pro-inflammatory response or sometime infectious aetiology [13,14].

Earlier, tests like TLC and C-reactive proteins were used to rule out infectious aetiology of the fever but now a days serum procalcitonin is considered a better biomarker to rule out an infectious cause of fever. In a healthy individual, blood level of procalcitonin is below the detectable limits of a diagnostic assay [15]. A multi centric study published in Lancet in 2010 states that the value of serum procalcitonin > 0.25 ng/ml is suggestive of a bacterial infection and antibiotics are usually advised when serum procalcitonin are > 0.5 ng/ml which is suggestive of sepsis [16].

In the present study, serum procalcitonin levels were raised in 39/50 patients with fever who also had raised TLC (group A) and none in the group B in which TLC was also normal (table 2).

The comparison of serum procalcitonin with raised TLC proved statistically significant with p value <0.05.

These findings were in concordance with a study by Grace M. Lee & Harper which showed that raised TLC and absolute neutrophil count were good predictor of bacteraemia [17].

However, comparison of C-reactive protein with TLC was statistically insignificant with a p value=0.305 (Table 3). C-reactive protein levels were raised in both groups A as well as B ie in 96/100 both groups combined.

Similar findings had been reported by Clayton N Kraft et al who also observed in their study that serum C-reactive protein levels were high in all patients postoperatively for 14 days after spinal surgery even in the absence of infection [18].

In a systemic review and met-analysis by Lan Hu; they observed that the sensitivity of serum procalcitonin for differentiating bacterial infections from nonbacterial infections was higher compared to CRP, however there was no significant difference in specificity [19].

Comparison was also made between serum procalcitonin levels and condition of the wound at the surgical site. The p value obtained was <0.05 (statistically significant) means there was a correlation between the two (Table 5).

Unhealthy wound condition was taken as marker of infection. Wound was unhealthy in 8/50 patients in the study group A and their wound swabs were sent for microbiological work up which came out to be culture positive. Their serum procalcitonin was also raised as shown in table 5. There was only one patient who's wound was unhealthy but serum procalcitonin levels were normal. Wound condition was taken as gold standard and with this data the sensitivity of serum procalcitonin as biomarker in diagnosing infection was 87.5%, specificity 90.4%, with a positive predictive value of 63.6% and negative predictive value of 97.4% respectively.

These findings were in concordance with the study by Sabina Hunziker et al who also reported that serum procalcitonin values were significantly higher in patients with infection compared with patients without infection [1]. In another study by Catherine Chirouze et al, they demonstrated that serum procalcitonin findings can accurately predict bacteraemia in hospitalized patients with with 0.4 ng/mL as cutoff value [20].

**Limitations:** Limitation of the present study was a moderate sample size, it requires validation in a larger study group.

## Conclusion

Early establishment of the cause of postoperative fever is important for an effective treatment. It is concluded from this study that serum procalcitonin levels may be used as a diagnostic marker along with clinical and microbiological parameters to differentiate infectious cause from non-infectious cause of fever in patients who have recently undergone a surgical procedure.

This will help in cutting down the economic burden on the patient as well as curtailing the emergence of antimicrobial resistance.

## What the study adds in the existing knowledge?

This study showed that serum procalcitonin is a good biomarker of infection, better than standard biomarker, CRP, which was nonspecifically raised in both the groups. Therefore, PCT can be used as an adjunct to other parameters to rule out infectious causes of postoperative fever.

## Author's contribution

- **Manmeet Kaur Gill:** Research work, Data analysis, Scientific paper writing
- **Dr. Sahiba Kukreja:** Research Question framing, Study design, Research work, Data analysis

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