Original Article

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# Assessment of Serum Procalcitonin as a Biomarker of Bloodstream Infection & Focal Bacterial Infection in Febrile Patients

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## Abstract

**Background:** To assess serum procalcitonin as a biomarker of bloodstream infection & focal bacterial infection in febrile patients. **Subjects and Methods:** Seventy- six adult patients presenting with fever (temperature >38 degree) were selected for the study. Imaging such as chest radiograph, ultrasonography (USG) of abdomen, computed tomography (CT) and magnetic resonance imaging were performa. Serum PCT levels were measured. **Results:** Aetiological diagnosis was evident focus of infection without bacteraemia in 24, dengue in 3, malaria in 3, scrub typhus in 1, leptospirosis in 6, bacteraemia in 8, other causes (non-infectious) in 1 and undiagnosed in 40 cases. Cause for evident focus of infection without bacteraemia was cellulitis in 3, UTI in 4, pneumonia in 7, TB in 3, pylonephritis in 2, bacterial in 1, viral in 1, acute meningitis in 1, acute gastroenteritis in 1 and swine flu in 1 patient. The difference was significant (P< 0.05). The mean PCT level in malaria patients was 5.7 ng/ml, in bacteremia was 8.2 ng/ml, in leptospirosis was 0.9 ng/ml, in dengue was 0.5 ng/ml, in scrup typhus was 0.7 ng/ml and in evident cause of infection cases was 3.4 ng/ml. The difference was significant (P< 0.05). **Conclusion:** Serum PCT level might be a useful biomarker for identifying bacteraemia as well as predicting mortality in patients with acute fever requiring admission to hospital.

**Keywords:** Fever, PCT, bacterial.

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## Introduction

Dengue is an acute infection characterized by fever, headache, muscle and joint pains, rash, nausea and vomiting.1 Dengue infections may also be asymptomatic or may lead to "classical" Dengue fever (DF), or Dengue hemorrhagic fever (DHF) without shock, or Dengue hemorrhagic fever (DHF) with shock. It is caused by an arbovirus and spread by Aedes mosquitoes.2 Dengue is caused by one of the four serotypes of the dengue virus (DEN-1, DEN-2, DEN-3 and DEN-4) also referred to as an arbovirus (arthropod-borne viruses) that belongs to the genus Flavivirus of the family Flaviviridae. Transmission to humans occurs by the bite of the female Aedes aegypti mosquito infected by one of four serotypes of the virus. This mosquito, a domestic species adapted to urban conditions, is the main vector.3

Approximately half of the world's population is at risk, especially people residing in tropical and subtropical climates.4 Dengue infection is a major challenge to public health, especially in South-East Asia for several years. Rapid urbanization, globalization, increasing population, poor solid waste, and water management have given rise to new habitats for mosquito breeding thereby increasing the number of cases and deaths.5 The identification of dengue cases is possible by distinct clinical features. Studies describe that atypical manifestations in dengue fever are multisystemic and multifaceted with organ involvement, such as liver, brain, heart, kidney, and central nervous system.6 Considering this, we planned this study to assess clinical profile and management of dengue cases in a tertiary care centre.

## Subjects and Methods

Seventy- six adult patients presenting with fever (temperature >38 degree) were selected for the study. Ethical clearance was obtained from institutional ethical clearance committee. All gave their valid written consent in vernacular language.

Data such as name, age, gender etc. was entered in case sheet. After thorough clinical examination, all underwent assessment of complete haemogram, peripheral blood smear and/or quantitative buffy coat method, serum biochemistry, urinalysis, urine culture, serological testing for dengue fever, scrub typhus, leptospirosis, HIV, anti-nuclear antibodies; blood cultures.

Imaging such as chest radiograph, ultrasonography (USG) of abdomen, computed tomography (CT) and magnetic resonance imaging were performa. Serum PCT levels were

measured using QDx Instacheck™ PCT as per the manufacturer's instructions. In patients with hospital-acquired infections (HAIs), appropriate laboratory investigations were done. Results were tabulated and assessed statistically. P value less than 0.05 was considered significant.

## Results

**Table I Distribution of patients**

| Total- 86 | | |
|---|---|---|
| Gender | Male | Female |
| Number | 56 | 30 |

Out of eighty- six patients, males were 56 and females were 30 (Table I).

**Table II Assessment of parameters**

| Parameters | Variables | Number | P value |
|---|---|---|---|
| Aetiological diagnosis | Evident focus of infection without bacteraemia | 24 | 0.01 |
| | Dengue | 3 | |
| | Malaria | 3 | |
| | Scrub typhus | 1 | |
| | Leptospirosis | 6 | |
| | Bacteraemia | 8 | |
| | Other causes (non-infectious) | 1 | |
| | Undiagnosed | 40 | |
| Cause for Evident focus of infection without bacteraemia (24) | Cellulitis | 3 | 0.04 |
| | UTI | 4 | |
| | Pneumonia | 7 | |
| | TB | 3 | |
| | Pylonephritis | 2 | |
| | Bacterial | 1 | |
| | Viral | 1 | |
| | Acute meningitis | 1 | |
| | Acute gastroenteritis | 1 | |
| | Swine flu | 1 | |

Aetiological diagnosis was evident focus of infection without bacteraemia in 24, dengue in 3, malaria in 3, scrub typhus in 1, leptospirosis in 6, bacteraemia in 8, other causes (non-infectious) in 1 and undiagnosed in 40 cases. Cause for evident focus of infection without bacteraemia was cellulitis in 3, UTI in 4, pneumonia in 7, TB in 3, pylonephritis in 2, bacterial in 1, viral in 1, acute meningitis in 1, acute gastroenteritis in 1 and swine flu in 1 patient. The difference was significant (P< 0.05) (Table II).

**Table III Comparison of serum procalcitonin levels in patients presenting with acute febrile illness**

| Acute febrile illness | Mean PCT | P value |
|---|---|---|
| Malaria | 5.7 | 0.01 |
| Bacteraemia | 8.2 | |
| Leptospirosis | 0.9 | |
| Dengue | 0.5 | |
| Scrub Typhus | 0.7 | |
| Evident cause of infection | 3.4 | |

The mean PCT level in malaria patients was 5.7 ng/ml, in bacteremia was 8.2 ng/ml, in leptospirosis was 0.9 ng/ml, in dengue was 0.5 ng/ml, in scrup typhus was 0.7 ng/ml and in evident cause of infection cases was 3.4 ng/ml. The difference was significant (P< 0.05) (Table III) (Table III).

## Discussion

Fever is the most frequent sign of infection and microbiologic data are always needed for a definitive diagnosis of bacteremia.8 Blood culture results take at least 24 to 48 hours; therefore, a rapid laboratory test that is able to identify severe bacterial infections would be very useful in the initial management of febrile patients and in a more appropriate use of antibacterial agents.9 Physicians often prescribe useless antibiotics or prolong hospital stays unnecessarily rather than assume the risk of fatal consequences.10 The present study assessed serum procalcitonin as a biomarker of bloodstream infection & focal bacterial infection in febrile patients.

Our results showed that Out of eighty- six patients, males were 56 and females were 30. Munoz et al11 determined the procalcitonin level in 103 unselected febrile hospitalized patients. Most of them had a proven (39) or probable bacterial infection (44). Procalcitonin was more frequently positive in bacteremic patients, in patients with a proven bacterial infection and in those with a high sepsis score,however; when cases with proven bacterial infection were considered as a reference, the sensitivity of the test was only 54% and the specificity 70%. Procalcitonin determination should not be included systematically in the screening of febrile hospitalized patients.

Our results showed that aetiological diagnosis was evident focus of infection without bacteraemia in 24, dengue in 3, malaria in 3, scrub typhus in 1, leptospirosis in 6, bacteraemia in 8, other causes (non-infectious) in 1 and undiagnosed in 40 cases. Cause for evident focus of infection without bacteraemia was cellulitis in 3, UTI in 4, pneumonia in 7, TB in 3, pylonephritis in 2, bacterial in 1, viral in 1, acute meningitis in 1, acute gastroenteritis in 1 and swine flu in 1 patient. Harikrishna et al12 measured the serum procalcitonin (PCT) levels at the time of initial presentation as a biomarker for identifying bacteraemia and as a predictor of mortality in patients admitted with acute fever. Four hundred and eighty patients were prospectively studied. Among patients with single infectious cause (n=275), significantly higher median serum PCT levels were evident in bacteraemia compared to leptospirosis

(P=0.002), dengue (P<0.001), scrub typhus (P<0.001) and evident focus of infection without bacteraemia (P=0.036). By receiver-operator characteristic curve analysis, at a cut-off value of >3.2 ng/ml, the sensitivity and specificity of serum PCT levels in predicting bacteraemia were 81.1 and 63.3 per cent, respectively. As per the worst-case scenario analysis, 91 (18.9%) patients had a poor outcome and these had significantly higher median serum PCT levels compared to survivors (n=389) [9.46 (2.03-44.4) vs. 1.23 (0.34-7.645); P<0.001]. At a cut-off value of >3.74 ng/ml, serum PCT levels at initial presentation predicted in-hospital mortality with a sensitivity and specificity of 67 and 67.5 per cent, respectively.

Our results showed that the mean PCT level in malaria patients was 5.7 ng/ml, in bacteremia was 8.2 ng/ml, in leptospirosis was 0.9 ng/ml, in dengue was 0.5 ng/ml, in scrup typhus was 0.7 ng/ml and in evident cause of infection cases was 3.4 ng/ml. Julián-Jiménez A et al13 evaluated the usefulness of PCT and CRP for predicting bacteraemia in urinary tract infections in the emergency department at a cut-off ≥1.16 ng/ml, serum PCT had a sensitivity of 100 per cent, a specificity of 97 per cent, a positive predictive value of 84 per cent and a negative predictive value of 100 per cent in detecting bacteraemia. Qu J et al14 in their study the median serum PCT level at the time of initial presentation with fever was 3.19 ng/ml (0.43-10.33). This difference may be due to the differences in the bacterial population type responsible for the fever since Gram-negative bacteraemias cause a higher elevation of PCT than those caused by Gram-positive pathogen.

## Conclusion

Serum PCT level might be a useful biomarker for identifying bacteraemia as well as predicting mortality in patients with acute fever requiring admission to hospital.

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