



UTILITY OF CRP IN DIFFERENTIAL DIAGNOSIS OF ACUTE FEBRILE ILLNESS: AN OBSERVATIONAL STUDY.

Biochemistry

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ABSTRACT

BACKGROUND: Acute Febrile illness remains the leading cause of hospitalisation among adults and children in urban and rural regions of Southeast Asia (1). Infectious diseases like dengue, enteric fever, leptospirosis, and scrub typhus are the common causes of Acute Febrile Illness. The symptoms of such tropical diseases overlap during the initial period of infection. CRP, an acute phase reactant, is gaining focus recently in delineating bacterial from viral infections.

OBJECTIVE: To emphasize the usefulness of CRP in delineating bacterial from viral infections, in cases of acute febrile illness.

METHODOLOGY: An observational study is conducted in a diagnostic lab of an NGO, **Helping Hand Foundation**, in Hyderabad. A total of 76 Patients were included in the study. The samples were received at the lab for analysing fever profile, during a period of 2 months i.e. of September 2021 to October 2021.

RESULTS: Out of 76 patients included in the study, 21 (28%) patients were diagnosed as having typhoid. 15 (20%) were diagnosed with positive dengue serology and remaining 40 (52%) patients were included as having Acute Undifferentiated fever (AUF) with undetermined etiology and needs further evaluation. The p value for CRP levels, was calculated between the groups with significant widal titres and positive dengue serology, which came as ($p=0.0024$) (C.I 95%), which is considered statistically significant by conventional criteria.

CONCLUSION: CRP levels are significantly elevated in enteric fever cases when compared to the patients with positive dengue serology. Thus CRP can be a useful tool along with other blood investigations in differentiating bacterial and viral causes of Acute febrile illness.

KEYWORDS

INTRODUCTION

Every year, with the onset of the monsoon, the number of AUF cases increases significantly and this trend persists through the winter months. The term acute undifferentiated febrile illness (AUF) includes fever of less than 14 days duration without any evidence of organ or system specific aetiology [2]. These AUF that includes scrub typhus, dengue fever, malaria, enteric fever, and leptospirosis are the leading causes of morbidity and mortality in India [3]. It is difficult to distinguish these infections clinically, in the initial stages of the disease, as the early symptoms like high-grade fever, generalized body pains, and maculopapular rashes, can be seen in any of the above mentioned tropical infectious diseases. Similar clinical presentations with diverse etiologies, often confounds the diagnosis of febrile illness and delays the initiation of preferred appropriate treatment. Moreover diseases like enteric fever, malaria and chikungunya are prevalent in the area where dengue is endemic. Biomarkers have been gaining recognition as an important tool in the diagnosis of bacterial infection. An ideal biomarker would aid the physician in rapidly and reliably, making the diagnosis of bacterial infection in patients with Acute febrile illness. In this context we conducted an observational study to identify the role of CRP in differential diagnosis of AUF and rationale the use of antibiotics.

MATERIALS AND METHODS

Study setting: The study was conducted in a diagnostic laboratory of an NGO, **Helping Hand Foundation**, in Hyderabad.

Duration: The study was carried out during post monsoon period for a period of 2 months i.e. from September 2021 to October 2021.

Type of the study: Laboratory based observational study.

Sampling method and Test procedures: A total of 76 patients were included in the study. The samples were received at the lab for analysing fever profile, which includes Complete blood count (CBC), Complete urine examination (CUE), Smear for malaria parasite (MP), Slide Widal test, Dengue NS1, IgG, IgM and quantitative C reactive protein (CRP) using upconverting phosphor technology with sandwich immunochromatography.

DATA ANALYSIS: Statistical analysis was performed using Graph Pad Prism statistical software. MS Excel 2010 was used to analyse the data.

RESULTS

Out of 76 patients included in the study, 21 (28%) patients were diagnosed as having typhoid with significant widal titres ($\geq 1:160$). 15 (20%) were diagnosed with positive dengue serology and remaining 40 (52%) patients, who were tested as non-significant widal titres ($\leq 1:80$) and negative dengue serology with no correlation with other blood parameters, labeled as Acute Undifferentiated fever (AUF) with undetermined etiology (fig.1)

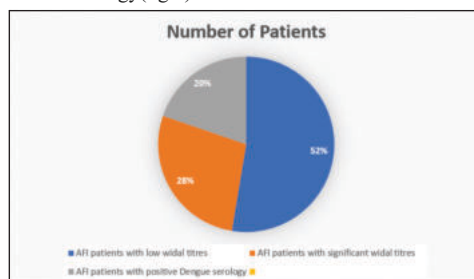


Figure 1

There was a significant difference in Mean CRP levels in the patients with significant widal titres (25.73 ± 22.79) and the patients with positive dengue serology (6.32 ± 1.99). While the patients with Acute undifferentiated fever showing mean CRP (12.44 ± 14.56) stating discrete data with median CRP value as 6.45 mg/L (fig.2).

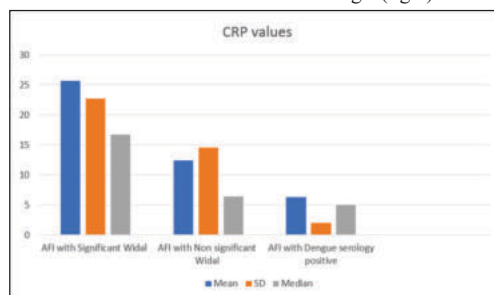


Figure 2

The p value was calculated between the groups with significant widal titres and positive dengue serology, which came as ($p=0.0024$) (C.I 95%), which is considered statistically significant by conventional criteria.

DISCUSSION

A rapid point-of-care test (POCT) to detect bacterial infection and to differentiate them from viral infections is of a great need in resource-constrained settings, where other laboratory diagnostics such as blood culture and radiology are not always available. CRP, first identified as a substance in the serum of patients with acute inflammation that reacted with the capsular polysaccharide capsular polysaccharide (C-polysaccharide) of pneumococcus[4]. It is a pentameric acute phase protein that is synthesized from the liver, due to increasing concentration of IL-6 which is produced by macrophages and adipocytes in response to inflammation[5]. CRP binds to the phosphocholine expressed on the surface of dead or dying cells and bacteria. This activates the complement system, promoting phagocytosis by macrophages, which clears necrotic and apoptotic cells and bacteria[6], as shown in figure.3.

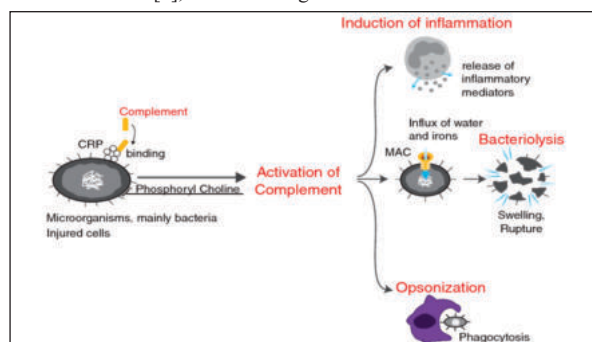


Figure3

In our study a significant correlation between elevated CRP levels and the presence of bacterial infections in febrile patients was confirmed. The mean CRP in patients with significant widal titres was more (25.73 ± 22.79) compared to the mean CRP in patients with positive dengue serology (6.32 ± 1.99). Thus, Our data demonstrated that a CRP level of less than 10 makes the diagnosis of bacterial infection extremely unlikely, whereas a CRP level greater than 20 should signal an active bacterial process and need of further evaluation and antibiotic administration.

CRP secretion starts within 4–6 h after stimulation and the assay for determining CRP levels is easy to perform, often automated, and comparatively low cost and less time consuming. Making it any easily accessible point of care testing (POCT), aiding in differential diagnosis of various causes of Acute febrile illness and thus helping in rational use of antibiotics in low resource settings.

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