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General Medicine

ROLE OF CRP AND PRO-CALCITONIN LEVELS IN DIFFERENTIATING COMMUNITY ACQUIRED PNEUMONIA (CAP) AND PULMONARY TUBERCULOSIS(PTB)- A CASE SERIES

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ABSTRACT **Background:** The varying clinical and radiographic presentation of CAP and TB and low sensitivity of AFB microscopy make it more difficulty to distinguish CAP from TB. Therefore, an adjunct diagnostic method that can determine whether CAP is caused by PTB or other Bacterial pathogen can help in isolating patients with TB and administering appropriate Anti TB or antibiotics at an early stage.

Aim & Objectives:

- To check CRP and Procalcitonin levels of patients with CAP and PTB.
- To investigate the utility of CRP and PCT levels for differentiating pulmonary tuberculosis from CAP.

Methodology - This was a Retrospective Observational Study of 20 of patients of LRTI, admitted in hospitals affiliated with Smt. NHLMMC. Their clinical manifestations, laboratory investigations were studied. **Result -** Out of total patients,13 had bacterial CAP, 7 had pulmonary TB. The median CRP concentration was 16.25 mg/dL (range, 0.30 to 36.61) in patients with bacterial CAP and 5.27 mg/dL (range, 0.24 to 13.22) in those with pulmonary TB ($p<0.001$). The median PCT level was 0.366 ng/mL (range, 0.01 to 0.636) with bacterial CAP and 0.044 ng/mL (range, 0.01 to 0.080) with pulmonary TB ($p<0.001$). No difference was detected in the discriminative values of CRP and PCT ($p=0.733$). **Conclusion-** The concentrations of CRP and PCT differed significantly in patients with PTB and bacterial CAP. The high sensitivity and negative predictive value for differentiating PTB from bacterial CAP suggest a supplementary role of CRP and PCT in the diagnostic exclusion of PTB from bacterial CAP in areas with high prevalence of PTB.

KEYWORDS : C-Reactive protein level, Pro-calcitonin levels, Community acquired pneumonia, Tuberculosis

Introduction:

Procalcitonin is a peptide precursor of the hormone calcitonin, which is produced by the thyroid's para-follicular C cells and is crucial in maintaining calcium homeostasis. The protein pro-calcitonin (PCT) has 116 amino acids in it. [1,2] It results from the cleavage of pre-pro-calcitonin by endo-peptidase. The neuro-endocrine cells of the lung and intestines also manufacture PCT, which is then released as an acute phase reactant in response to inflammatory stimuli, particularly those of bacterial origin. [3] There is substantially less of a noticeable increase in serum procalcitonin levels in response to viral infections, non-infectious inflammatory stimuli, and chronic inflammatory processes. Higher procalcitonin levels are linked to a higher risk of sepsis progression to severe sepsis in sepsis patients. [4]

Procalcitonin can be used for Bacterial sepsis diagnosis and it could assist in identifying renal involvement in kids with UTIs, also for identification of meningitis from other viral and bacterial diseases as well as to keep track of the therapeutic impact of antibiotic treatment and decreased antibiotic exposure. [5]

Acute phase reactant CRP serves as a stand-in for the pro-inflammatory cytokine IL-6. In addition to being made in the liver, CRP is also made by adipose tissue, endothelial cells, smooth muscle cells, and cells in the vascular wall. Sequential CRP may offer a more precise evaluation of inflammatory changes brought on by therapy. [6]

Aims & Objectives:

- To assess the CRP and Procalcitonin levels of patients with community acquired pneumonias and pulmonary tuberculosis.
- To investigate the utility of serum C- Reactive Protein(CRP) and serum Pro-Calcitonin(PCT) levels for differentiating pulmonary tuberculosis from community acquired pneumonia in Ahmedabad, a city with high TB burden.

Materials & Methodology:

A Retrospective Observational study was conducted among 20 patients of lower respiratory tract infection,during October 2019, admitted at Department of General Medicine, SVPIMSR, Ahmedabad. All patients of Lower respiratory tract infection aged more than 18 years were included. Patients with other infections, such as urinary tract infection, meningitis and infectious endocarditis, were excluded. The Institutional Ethical Committee permission was taken prior to the study. The written informed consent was taken from all study participants.

Operational Definition:

- Pulmonary Tuberculosis was defined by sputum smear-positive or culture-positive Mycobacterium tuberculosis in the presence of new radiographic pulmonary infiltration. All PTB patients were initially treated with a standard four-drug regimen of isoniazid, rifampin, pyrazinamide, and ethambutol or streptomycin.
- Pneumonia was diagnosed by the presence of new radiographic pulmonary infiltration and the following clinical findings: 1) axillary temperature >37.5C; and 2) a cough, purulent sputum, pleuritic chest pain or shortness of breath. CAP was defined if pneumonia had occurred at home.
- Venous blood samples were drawn from PTB and CAP patients on admission. Serum PCT and C-reactive protein (CRP) were measured within 24 h of admission. The normal range of PCT is 0.5 ng/mL and the lower limit of detection is 0.1 ng/mL. CRP normal value is Less than 10 mg/L and CRP increased when Equal to or greater than 10 mg/L.

Data entry & analysis:

Data were entered into MS Excel sheet and analyzed sing SPSS software version 24. Quantitative data were described as Frequency and Percentages as well as median. Differences between categorical groups were tested Fisher's exact test and between continuous data Mann-whitney test was applied. The p-value less than 0.05 considered as significant results.

Results:

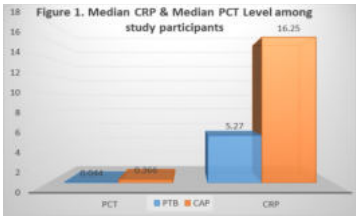
Total 20 patients of lower respiratory tract infection were included in the study, in which 7 had diagnosed PTB and 13 had diagnosed CAP.

Table 1. Comparison between Various complaints among study participants

Patient characteristics	PTB (n=7)	CAP (n=13)	P value
Fever	5 (71.4%)	13 (100%)	<0.001
Cough or Sputum	4 (57.1%)	9 (69.2%)	0.021
Dyspnea	2 (28.6%)	7 (53.8%)	<0.001

Weight loss	6 (85.7%)	2 (15.3%)	0.003
Cavitatory lesion	5 (71.4%)	2 (15.3%)	0.001

Among the study participants of PTB, 85.7% cases had complained of weight loss, followed by 71.4% had complained of fever as well as cavitation lesions. Only 2 patient's suffered from Dyspnea. While in patients of CAP disease, all suffered from fever as well as in 69.2% cases had complained of Cough. There was a significant association found between various characteristics like, fever, Cough, Dyspnea, Weight loss, Cavitatory lesion among both groups. [Table 1]



The median CRP concentration was 16.25 mg/dL (range, 0.30 to 36.61) in patients with bacterial CAP and 5.27 mg/dL (range, 0.24 to 13.22) in those with pulmonary TB ($p<0.001$). The median PCT level was 0.366 ng/mL (range, 0.01 to 0.636) with bacterial CAP and 0.044 ng/mL (range, 0.01 to 0.080) with pulmonary TB ($p<0.001$). No difference was detected in the discriminative values of CRP and PCT ($p=0.733$). [Figure 1]

Discussion:

Compared to other inflammatory markers including white blood cell count, erythrocyte sedimentation rate, and C-reactive protein, procalcitonin is more selective for bacterial infections. Though, false positives may still occur. Procalcitonin levels can be raised by significant stressors that result in systemic inflammation, including severe trauma, cardiac arrest or circulatory shock, surgery, burns, pancreatitis, and intracranial haemorrhage. [7] This may be because of gut translocation of lipopolysaccharide or other bacterial products, as well as other major stressors that result in systemic inflammation.

In the study of Kang YA et al [8] of the 87 patients, 57 had bacterial CAP and 30 had pulmonary TB. The median CRP concentration was 14.58 mg/dL (range, 0.30 to 36.61) in patients with bacterial CAP and 5.27 mg/dL (range, 0.24 to 13.22) in those with pulmonary TB ($p<0.001$). The median PCT level was 0.514 ng/mL (range, 0.01 to 27.75) with bacterial CAP and 0.029 ng/mL (range, 0.01 to 0.87) with pulmonary TB ($p<0.001$). No difference was detected in the discriminative values of CRP and PCT ($p=0.733$).

A research done by M. Ugajin et al [9] among total 102 PTB patients, 62 CAP patients, and 34 healthy volunteers were enrolled. Serum PCT in PTB patients was significantly lower than in CAP patients (mean±sd 0.21±0.49 versus 4.10±8.68 ng·mL−1; $p<0.0001$). By receiver-operating characteristic curve analysis, serum PCT was an appropriate discrimination marker for PTB and CAP (area under the curve 0.866). PTB patients with ≥0.5 ng·mL−1 (normal cut-off) had significantly shorter survival than those with <0.5 ng·mL−1 ($p<0.0001$).

Conclusion:

Patients with pulmonary TB and bacterial CAP had significantly different CRP and PCT values. In locations with a high prevalence of pulmonary TB, CRP and PCT may have an additional role in the diagnostic exclusion of pulmonary TB from bacterial CAP due to their high sensitivity and negative predictive value for separating pulmonary TB from bacterial CAP.

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