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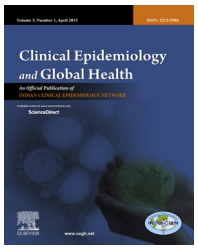

Procalcitonin and C-reactive protein in WHO defined severe and very severe community acquired pneumonia: A hospital based cross-sectional study

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ABSTRACT

Objectives: To correlate and compare serum levels of procalcitonin (PCT) and C-reactive protein (CRP) in children with severe and very severe community acquired pneumonia (CAP), as defined by World Health Organization (WHO) and also had radiological abnormalities consistent with pneumonia.

Methods: This was a cross-sectional study, done in a tertiary care teaching hospital in north India. Included were children aged between 2 months and 5 years, hospitalized for CAP. Definitions of WHO for diagnosing severe and very severe pneumonia have been used as gold standard. Written informed consent was obtained from parents. Those, who have wheeze, fever more than 14 days, and severe malnutrition, were excluded. For estimations of serum PCT and CRP levels, commercially available enzymes linked fluorescent assay and enzymes linked immune-sorbent assay kits were used, respectively.

Results: From June 2013 to September 2013, fifty cases were recruited, among which 56% ($n = 28/50$) and 44% ($n = 22/50$) were very severe pneumonia and severe pneumonia, respectively. In cases of very severe pneumonia and severe pneumonia, mean serum PCT levels were 17.65 $\pm$ 18.9 ng/ml and 0.93 $\pm$ 2.91 ng/ml ($p = 0.01$) and mean serum CRP levels were 85.25 $\pm$ 17.83 mg/dl and 56.50 $\pm$ 23.13 mg/dl ($p \leq 0.01$), respectively. Serum PCT and CRP levels were positively linearly correlated ($r = 0.45$). Using serum PCT levels >2 ng/ml and serum CRP levels >60 mg/dl, cut-off for differentiating very severe and severe pneumonia, the sensitivity was same (92.9%), but specificity of PCT was higher (86.4%) than CRP (63.6%). Area under receiver operating characteristics (ROC) curves was 0.923 and 0.837 for serum PCT and CRP, respectively.

Conclusion: Serum PCT and CRP are positively linearly correlating with each other and PCT has better differentiating ability between very severe and severe pneumonia than CRP.

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1. Introduction

According to World Health Organization (WHO), there are 156 million new cases of the community acquired pneumonia (CAP) in children less than 5 years of age, worldwide annually.[1] In India, 43 million new cases occur annually with an incidence of 0.37 episodes per child-year in this age group. This results in India, 1.8 million under-five deaths, which account 18% of global under five mortality.[1,2]

To recognize CAP in community settings, under the integrated management of neonatal and childhood illness (IMNCI) program, age specific cut-offs of respiratory rate (RR) have been used. In children with difficult breathing and/or cough, for the age of 2–12 months and more than 12 months to 5 years, ≥50 breaths per minute and ≥40 breaths per minute cut -offs have been used, respectively.[3] Among such cases, presence of lower chest indrawing (LCI) alone categorizes them as severe CAP, while the presence of central cyanosis or unable to drink along with LCI categorizes them as very severe CAP.[3] However, there are studies suggesting either overestimation or underestimation of severity of pneumonia, if assessed on these clinical parameters only.[4–6]

Since assessment of severity of CAP based on clinical parameters only can either underestimate or overestimate, the severity and isolation of organism is relatively difficult. Hence, we did this study with primary objective to correlate and compare serum PCT and CRP levels in very severe and severe CAP. Secondary objectives were to assess, if there was difference in the levels of these biomarkers among those who developed complications such as empyema, pneumothorax, acute respiratory distress syndrome (ARDS), or septic shock when compared to those did not.

2. Materials and methods

This was a cross-sectional study, conducted in Department of Pediatrics, King George's Medical University, a tertiary care teaching hospital in north India, between June and September 2013, after approval from institutional ethics committee. Included were hospitalized children who fulfilled WHO criteria of pneumonia, aged 2 months to 5 years and digital X-ray chest, posterior-anterior (PA) view showing abnormalities consistent with the diagnosis of pneumonia.[7] Written informed consent was obtained for participation in the study from parents or legal guardians. Excluded were those, who have wheeze on admission, fever more than 14 days, congenital heart disease, and severe malnutrition as defined by WHO.[8]

All cases were followed till final outcome, which could be discharge, death, or parents left against medical advice. The clinical improvement was defined as decrease in RR below age specific cut-offs (nontachypneic range), decreased work of breathing as defined by absence of nasal flaring and LCI, and maintaining saturation of peripheral oxygen (SpO_2) >92% at room air. Complications included were septic shock,[9] empyema, pneumothorax, and/or ARDS[10] at admission or during hospitalization. Digital X-ray chest PA view repeated on advice of treating physician. Findings of X-ray chest were classified into 3 groups as per WHO guidelines for interpretation of chest X-ray, nonend point infiltrates, end point consolidation, and pleural effusion.[7] End point consolidation is as a dense opacity that may be a fluffy consolidation of a portion or whole of a lobe or of the entire lung, often containing air bronchograms and sometimes associated with pleural effusion, while non-end-point infiltrates are linear and patchy densities (interstitial infiltrate) in a lacy pattern involving both lungs, featuring peri-bronchial thickening, and multiple areas of atelectasis.[7]

Data were collected on demographic variables including anthropometry and clinical variables including severity of CAP at admission, RR, heart rate (HR), chest indrawing, sensorium, need of oxygen therapy with duration, duration of hospital stay, and complications. Sample size was calculated for a correlation coefficient ($r = 0.4$) between PCT and CRP, a two-sided test, 5% significance level test ($\alpha = 0.05$) with 80% power ($\beta = 0.2$), the required sample size was approximate 47.[11]

From all recruited cases, 2 ml of blood sample was withdrawn on admission through venepuncture aseptically in plain eppendorf and transported to translational unit of Department of Pediatrics. Samples were centrifuged at 2000 rpm for 5 min and separated serum stored at −20 °C till further processing for estimation of PCT and CRP levels. For estimation of PCT and CRP levels, commercially available enzymes linked fluorescent assay (ELFA) and enzymes linked immune-sorbent assay (ELISA) kits (Vidas B.R.A.H.M.S. Biomerieux, Durham, USA and Vitros 250 chemistry system, Johnson and Johnson, USA) were used, respectively. Manufacturers' instructions were strictly followed during process. The above PCT kits needed 200 μL serum and measuring range is 0.05–200 ng/ml.

Data were recorded in preformed questionnaires, entered in MS excel and analyzed by SPSS Vs16 software. Continuous variables are presented as mean ± standard deviation (SD) and compared by using Student *t*-test. Categorical variables are presented as proportions and compared by using chi-square test. Pearson's correlation coefficient is used to see, whether serum PCT and CRP levels were related linearly. Results are reported with 95% confidence interval (CI) and level of statistical significance is less than 0.05 by using 2-tailed *p*-value. Receiver operating characteristic (ROC) curves were drawn for serum PCT and CRP levels by SPSS software. An AUC <0.75 is regarded as non-contributive.[12] Sensitivities, specificities, and predictive values were also calculated for best possible cut-offs.

3. Results

From June 2013 to September 2013, 50 cases were recruited from 63 admitted children with CAP, who fulfill the inclusion criteria, among which 56% ($n = 28/50$) and 44% ($n = 22/50$) children were with very severe pneumonia and severe pneumonia, respectively. Baseline characteristics of cases with very severe and severe pneumonia are compared in Table 1. Mean serum PCT levels were 17.65 ± 18.9 ng/ml and 0.93 ± 2.91 ng/ml ($p = 0.01$), and mean serum CRP levels were 85.25 ± 17.83 mg/dl and 56.50 ± 23.13 mg/dl ($p \leq 0.01$) in children with very severe pneumonia and severe pneumonia, respectively. Using Pearson's correlation coefficient, serum PCT and CRP levels showed linear correlation ($r = 0.45$, $p < 0.01$,