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# Function of serum markers in evaluating the seriousness and result of network procured pneumonia in Trinidadian populace

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Abstract

**Our aim was to determine whether the use of serum inflammatory markers such as erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and procalcitonin (PCT), either individually or in combination, is significantly associated with community-acquired pneumonia and to determine the role in assessment of the severity and outcome. This study was a prospective cohort study, included forty Trinidadian patients diagnosed with community acquired pneumonia. Blood samples were collected to measure inflammatory markers. Patients were classified according to the pneumonia severity index (PSI) scoring where after serum marker levels were compared among respective groups. Proportions test for positive predictive value of the serum marker indicated that CRP (P=0.001) and ESR (P=0.001) had higher sensitivities to community acquired pneumonia than PCT (P=0.05). There was no association between each of the serum markers and PSI. Eighty three percent low risks had a length of stay of two weeks, while only 18% of high risk stayed for the same duration. The combination of highly sensitive markers like CRP and ESR and a specific marker such as PCT emphasize their importance in better risk assessment in community acquired pneumonia patients.**

**Keywords:** Community acquired pneumonia, inflammatory marker, pneumonia scoring index, procalcitonin.

## INTRODUCTION

Pneumonia is a major health problem throughout the world. It is the third leading cause of death in the world and contributing about 7% of all deaths (2008). In USA, it is the eighth leading cause of death (2007), whereas in Trinidad, it is the sixth leading cause of death, according to the 1999 report from the central statistical office (CSO) (1999). Common symptoms of pneumonia include pyrexia, productive cough, pleuritic chest pain, hypoxia and shortness of breath. In addition to being life threatening, pneumonia results in several debilitating complications such as respiratory failure, septicemia and multi-organ failure. Diagnosis of pneumonia is one of the most important challenges in clinical medicine and ma-king a decision to admit these patients is more difficult.

Now, more than ever, there is a considerable pressure to treat as many patients as possible at home to avoid unnecessary health care cost (Craven et al., 2004). In order to do this, it is important to know the factors that are predictive of complicated course in pneumonia. Several clinical rules were developed to predict the mortality and to guide the admission decision. Among them Pneumonia severity index (PSI), often known as the PORT (patient outcomes research team) score is the most popular one (Fine et al., 1997). It is a quantitative tool that assesses the severity of a patient's illnes hospitalization. Because of its complex nature and low positive predictive value, it may not be useful as a sole indicator for deciding the inappropriate hospitalizations (Forest et al., 2003) and attempts to strengthen these existing systems and /or to formulate new systems or parameters are still in trial phases (Fine et al., 1997; Lim et al., 2001). Therefore, the main aim of this study was to pros-pectively evaluate the erythrocyte sedimentation rate (ESR),

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**Table 1.** Patients demographics.

| Demographics | Number (%) |
|---|---|
| **Age group** | |
| 18-37 | 10 (25) |
| 38-56 | 17 (42.5) |
| 57-75 | 13 (32.5) |
| **Gender** | |
| Male | 15 (37.5) |
| Female | 25 (62.5) |
| **Ethnicity** | |
| African | 16 (40) |
| East Indian | 19 (47.5) |
| Mixed | 5.0 (12.5) |
| **Occupation** | |
| Employed | 26 (65) |
| Unemployed | 14 (35) |
| **Living condition** | |
| Poor | 4.0 (10) |
| Average | 29 (72) |
| Good | 7.0 (18) |

erythrocyte sedimentation rate (ESR), C - reactive protein (CRP) and procalcitonin (PCT) levels in community acquired pneumonia patients and assess these levels with a clinical outcome.

## MATERIALS AND METHODS

### Study population and samples

An observational prospective cohort study was chosen. The study was approved by Ethics Committee, Faculty of Medical Sciences, the University of the West Indies (EC 83: 12/07-07/08). Patients with acute infection of the pulmonary parenchyma who acquired this infection in the community and associated with radiographic shadowing were considered as community acquired pneumonia (CAP) patients and selected for this study. Patients with symptoms of lower respiratory tract infection such as cough with or without expectoration, fever, chest pain and shortness of breath with radiological features such as lobar consolidation with air bronchogram and patchy bronchopneumonic shadows in chest x-ray and/or chest computerized tomography scan were considered for this study. Pneumonia in these patients was also confirmed with bacteriological culture. After applying the strict selection criteria, blood samples were collected from 40 patients among the 72 patients diagnosed with community acquired pneumonia at the Eric Williams Medical Sciences Complex and San Fernando government hospitals, Trinidad and Tobago during the period April to August 2007. The blood was tested for three serum markers for which validity was assessed by using pneumonia severity index (PSI) and outcome measures like mortality and morbidity in the initial one month, length of stay in hospital, intensive care unit (ICU) admission and subsequent hospitalization due to recurrence of pneumonia or because of its sequel. All these patients received pneumonia management according to the latest infectious diseases society of America/American thoracic society consensus guidelines on the management of community-acquired pneumonia in adults (Mandell, 2007). The target population was adults, 18-75 years of age, suffering from community acquired pneumonia in Trinidad. The inclusion criteria include both male and female patients, all ethnicities and all pneumonia severity classes (I-V). The patients with less than 18 or more than 75 years age, with hospital acquired pneumonia, with previous history of pneumonia, pneumonia with terminal event or was distal to a bronchial obstruction, with known preexisting lung disease, with previous cardiac surgery and with liver disease, tuberculosis and lung cancer were excluded from the study. Patients with a solid organ or hematological malignancy and those with immunological and hematological disorders, co-existing infections and coronary artery disease were not used. Finally, the patients who were on corticosteroids or other immunosuppressive drugs were also excluded. In our study, we used three serum markers erythrocyte sedimentation rate (ESR), C- reactive protein (CRP) and procalcitonin (PCT). ESR is an easy and inexpensive test used to diagnose conditions associated with acute and chronic inflammation. C- reactive protein (CRP) is used in the diagnosis and monitoring of different acute inflammatory processes. Serum procalcitonin (PCT) is relatively a new marker and its levels found to be significantly elevated in bacterial infections (Harrison, 1987).

The sampling method used was a consecutive convenience sample technique and demographic data was also collected. The informed consent was taken from all the participants. The subjects were classified according to their severity status which was the basis for the project. The blood samples were collected from patients within 24 h of admission. Samples were kept in different vials and marked with different codes to avoid bias. These samples were used for the determination of serum markers, cell counts, liver and renal function tests including electrolytes. Patients were regularly monitored in the hospital wards and in clinics until their clinical and radiological features had normalized. ESR was done using random access auto-analyzer (HUMASED 40). The serum sample was stored at -70°C to analyse CRP and lipid profile by a fully automated analyzer (Johnson and Johnson Vitros 250, Ortho-Clinical Diagnostics Inc., Rochester NY 14626, USA). Finally the procalcitonin was measured by monoclonal immunoluminometric assay (Liaison Brahms PCT; Berlin, Germany; limit of detection, 0.1 µ/l) (Masia et al., 2005).

### Statistics and calculations

Results were expressed as mean ± standard deviation. Data were analyzed using the SPSS (version 12.0, Inc., Chicago, Illinois). The comparisons within and among different parameters were done using chi squared t- test and one sample t-test. The p value $< 0.05$ was taken as the cut off level for significance.

## RESULTS

The studied population was between 18-75 years of age and most of them (68%) were between 18 - 56 years of age. Majority of the studied subjects were females and of African and East Indian ethnic groups. The chi-square test showed that there is no association between age, gender, ethnicity and living conditions of community

**Table 2.** Serum marker levels: normal, low risk and high risk classes.

| Serum marker | Low risk(PSI*Class 1-3) (n= 29, 73%) | High risk (PSI*Class 4,5) (n=11, 27%) |
|---|---|---|
| CRP (mg/l) | 35.0 ± 1.43** | 40.5 ± 3.90** |
| ESR (1st hour) | 46.51 ± 1.92** | 53.7 ± 1.10** |
| PCT (ng/dl) | 0.38 ± 0.027* | 0.43 ± 0.015* |

Values are expressed as mean ± SD**P= 001, * P= 0.05.

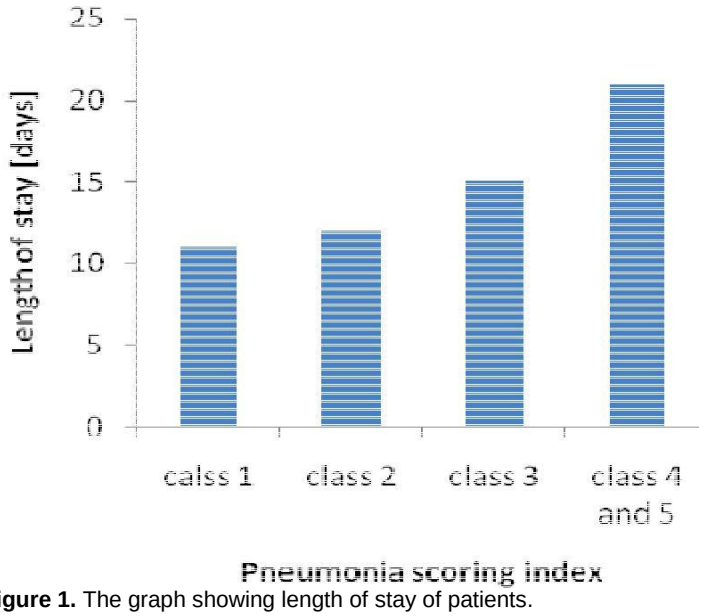


**Figure 1.** The graph showing length of stay of patients.

acquired pneumonia subjects. Among the study population 47% (19) were smokers while 25% (10) either had diabetes, hypertension or both (Table 1). These patients were grouped into low risk (classes 1, 2 and 3) and high risk (classes 4 and 5) groups. Seventy three percent (29) fell into the low risk class leaving 27% (11) in the more severe classes 4 and 5 according to the PSI scoring. Of the patients tested for PCT, 12 (30%) showed concentrations <0.1. All these patients were classified by PSI as a low risk group. Of the 13 patients (32%) who had PCT concentrations >0.5, four of them fell into the high risk group. Thirty patients had elevated CRP, 73% (n=22) of these had values ≥ 30 and 15% (n=5) had values ≥ 50. Table 2 shows the mean and standard deviation of serum marker levels of low risk and high risk class patients.

Of the 29 patients in the low risk class, 83% (n=24) were hospitalized for a duration of 1-14 days, whereas 78% (n=9) of the high risk group patients (n=11) were hospitalized for 15 to 21 days (Figure 1). Five percent (n=2) of the patients died were classified as high risk class. Mean and SD values of CRP, ESR and PCT for low risk patients are 35.0 ± 1.43 mg/L, 46.51 ± 1.92 in 1st hour and 0.38 ± 0.027 ng/dl, respectively (Table 2) . Whereas patient in high risk group showed values of 40.5 ± 3.90 mg/L, 53.7 ± 1.10 in 1st hour and 0.43 ± 0.015 ng/dL for CRP, ESR and PCT respectively (Table 2). In all high risk patients, PCT levels were >0.1 ng/dl. On the contrary only 5% of low risk group PCT levels showed elevated >0.1 ng/dl. The combination of CRP and ESR showed high positive predictive value. The PCT showed negative predictive value in assessing the severity of pneumonia in patients (Figure 2).

## DISCUSSION

Our study revealed many important and significant diagnostic implications of community acquired pneumonia. Numerous studies on independent serum markers have shown that a relationship exists between serum marker level and the severity of community acquired pneumonia (Masia et al., 2005; Jose et al., 2004). In the attempt to discover more efficient ways of community acquired pneumonia diagnosis, our aim was to establish whether the use of multiple serum markers (ESR, CRP and

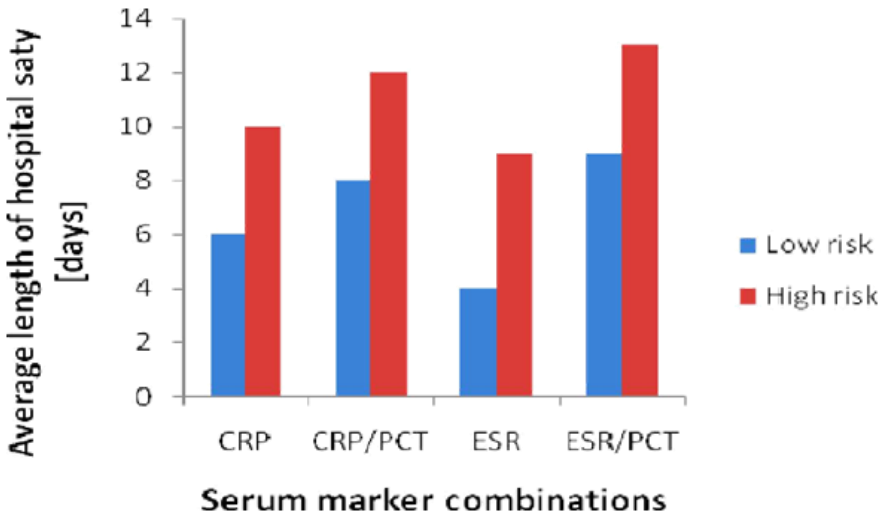


**Figure 2.** Graph showing the outcome for those with elevated CRP or ESR, oppose to elevated CRP/ESR and PCT.

PCT) individually and in combinations would be a better aid in the diagnosis and assessing the outcome of community acquired pneumonia.

In our study community acquired pneumonia was not associated with gender or ethnicity. In addition, it also showed that age plays a vital role in the incidence and out-\come as the majority of patients were of 18 - 56 years age (68%). This age bracket also represents the majority of the working class of the study population, as 65% of patients were employed. The one sample t test done to test the significance of each respective serum marker confirmed the positive predictive value of CRP and ESR to community acquired pneumonia, for high and low risk classes. Previous studies showed that although PCT have a low sensitivity, it shows admirable negative predictive value to community acquired pneumonia infection (Hedlund et al., 2000; Jose et al., 2004). Although PCT revealed lower sensitivity, almost half of the patients had increased PCT level when diagnosed with pneumonia. This indicated a promising partiality of procalcitonin as a potential adjunct test for community acquired pneumonia as described before (Masia et al., 2005; Hedlund et al., 2000; Polzin et al., 2003; Haufaster et al., 2002).

In low risk and high risk classes, there was a positive relation for ESR and CRP as in both classes, over 70% of patient showed a significant increase in these marker levels. In the low risk class, 83% of patients had increase in ESR and CRP, 33% of which also had increase in PCT. Those with increase in ESR and/or CRP had an average hospitalization period of 4 days. The patients with high PCT in this group had on average 2-3 days longer period of hospitalization. For the high risk class (classes 4 and 5), no clear cut point for severity risk criteria could be established. The 72% of high risk class patients showed increase for CRP and ESR. Forty percent were also positive for PCT increase. Of those who showed increased ESR and/or CRP, 67% had hospitalization averaging 7.5 days. Those patients with increased PCT had on an average 1-3 days longer hospitalization. There were eight re- admissions within six months of discharge. Among these six were initially classified as high risk PSI group with elevated ESR, CRP and PCT The remaining 2 were of low risk and showed no increase in these markers initially. Two of our high risk patients were admitted to the ICU and showed values ESR: 90mm/hr; CRP: 80mg/l, PCT: 0.58 ng/dl and these patients eventually died. Patients, who showed high PCT levels, had a slightly longer hospital stay, higher rate of readmission and ICU admission indicating the existing relationship with PCT. Therefore, high levels of PCT can shows the patients in need of further hospitalization and ICU admission.

One of the aims of our study was to see whether combinations of different serum markers could aid in the outcome assessment. Presently ESR, CRP and complete blood count (CBCs) are the only routine blood tests requested for pneumonia patients. Adding PCT may improve the overall assessment and helps in the treat-ment of community acquired pneumonia patients. Our study has shown that a combination of high CRP or ESR with PCT estimates the length of hospital stay, better than the individual markers in patients with community acquired pneumonia (Figure 2). Based on these results, patients can be better classified and therefore outcome can be better predicted. Therefore, doctors would be adequately prepared, now having the foresight of the community acquired pneumonia cases and judicious for antimicrobial therapy. The tests done and found to be of significant importance (ESR, CRP) are inexpensive,

standardized and widely used laboratory tests. PCT test, although not as common and fairly expensive, does have clinical worth in patients with in-creased severity. Our study has ultimately demonstrated that serum markers have great potential for risk assessment of patient with community acquired pneu-monia. The mean values of the serum markers showed reasonable difference from the normal for both risk groups (high and low risk) and could therefore be used as a guide. Significant findings of our study require further large scale studies to uncover serum markers full potential in community acquired pneumonia diagnosis and management.

## Conclusion

CRP and ESR are effective indicators in predicting the community acquired pneumonia outcome. PCT also showed a great potential as a diagnostic tool, despite our study limitations. The combination of PCT with ESR and CRP emphasized their importance in better risk assess-ment. Further comprehensive testing and research should be done to confirm our findings.

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