



Original Article

# Clinical utility of serum procalcitonin in adult patients admitted with community-acquired pneumonia in Ilorin, Nigeria

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## ABSTRACT

**Objectives:** The usefulness of biomarkers in community acquired pneumonia (CAP) has been under the research light with limited reports from Africa. This study aimed at evaluating the clinical usefulness of serum procalcitonin (PCT) in patients admitted with CAP in a tertiary hospital in Ilorin, Nigeria.

**Materials and Methods:** This was prospective single center observational study of 102 admitted patients with clinical and radiologic features of CAP. All the patients had serum PCT assay, complete blood count, blood culture, sputum microbiology, and serological evaluation for atypical pathogens. Repeat PCT assay was done following 1 week of antibiotic therapy. The patients were classified into one of two diagnostic groups: Those with microbiologically confirmed bacterial CAP and those without bacterial CAP.

**Results:** Over half (58/102; 56.8%) of the patients had microbiologically confirmed bacterial CAP. The baseline serum PCT concentrations were significantly higher in patients with bacterial CAP when compared to the non-bacterial CAP group ( $2.55 \pm 0.14$  vs.  $0.94 \pm 0.61$  ng/ml;  $P < 0.001$ ). There was also a statistically significant difference between the pre- and post-treatment serum PCT concentrations in the bacterial CAP group ( $P < 0.001$ ) and the non-bacterial CAP group ( $P = 0.006$ ). The area under the receiver operating characteristic (AUC) for pre-treatment PCT in diagnosing bacterial CAP was 0.795 (95% confidence level [CI]: 0.709–0.881) with a sensitivity of 67.2% and specificity of 79.5% at an optimal cutoff of 1.5 ng/ml. Overall, the biomarker was independently associated with white cell counts  $>10 \times 10^9/L$  (AOR = 6.28; 95% CI: 1.30–30.32,  $P = 0.02$ ). The baseline mean serum PCT levels were also significantly higher in patients admitted for 7 or more days ( $P = 0.010$ ).

**Conclusion:** Serum PCT had good diagnostic strength in patients admitted with bacterial CAP in Ilorin. The biomarker can also assist clinicians with predicting the pathogenic group and monitoring clinical progress of CAP.

**Keywords:** Community-acquired pneumonia, Ilorin, Nigeria, Procalcitonin

## INTRODUCTION

Community acquired pneumonia (CAP) is prevalent in Nigeria with the disease responsible for 2.5–5.7% of medical admissions<sup>[1,2]</sup> and about 15–25% of hospital admissions related to respiratory illnesses.<sup>[3,4]</sup> The disease also remains a cause of significant mortality with intra hospital mortality figures in Nigeria ranging from 7.4% to 26%.<sup>[1,3-7]</sup>

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Regarding the diagnosis of CAP, the symptoms, and signs as well as plain chest radiograph though critical to it, do not always provide a clue to the etiologic agent.<sup>[8]</sup> This is because of a broad range of clinical features associated with the disease and the fact that chest radiography is not 100% sensitive or specific for CAP especially in the very early stages of the disease.<sup>[9]</sup> Furthermore, sputum and blood cultures which are useful for identification of the pathogenic agent(s) are associated with the risk of contamination in the process of specimen collection and may take several days to give positive results, thereby delaying definite diagnosis and treatment. Furthermore, polymerase chain reaction (PCR) despite its high sensitivity and specificity is very costly and is generally unavailable in low- and middle-income settings. These factors preclude their use in the routine day-to-day clinical practice for CAP diagnosis particularly in developing countries such as Nigeria. Hence, there is a need to evaluate the usefulness of other modalities such as serum biomarkers in facilitating early diagnosis, determining the likely class of etiologic agent as well as aiding severity assessment and prognostication. Although these biomarkers are not readily available in low- and middle-income settings like Nigeria, their clinical use may potentially guide reduce irrational antibiotic use, guide therapy, and improve the quality of care given to patients with CAP.

Procalcitonin (PCT) is a 116 amino acid peptide produced mainly by the parafollicular cells of the thyroid gland and belongs to the calcitonin superfamily.<sup>[10]</sup> In sepsis, PCT is also secreted from the lungs, liver, and intestines.<sup>[10]</sup> Normal PCT levels in adults are <0.15 ng/ml, rising within 6–12 h of bacterial infection and reaching a peak in 22–35 h.<sup>[11]</sup> The serum levels are known to reduce by half daily when infection is controlled.<sup>[11]</sup> This peptide has been identified in previous surveys to be a more reliable parameter when compared to C-reactive protein and other biomarkers in patients with bacterial infections including CAP.<sup>[12,13]</sup> Clinical studies in developed nations have demonstrated the usefulness of serum PCT levels in CAP using different cutoff values.<sup>[12,14-16]</sup> Interestingly, a recent systematic review of 12 studies and 2804 patients with CAP by Kamat *et al.*<sup>[17]</sup> concluded that serum PCT is unlikely to differentiate between bacterial and non-bacterial infections in CAP patients. Hence, it would be necessary to evaluate for possible regional differences in the value of using PCT to predict the etiology of CAP.

This study aimed at evaluating the clinical usefulness of serum PCT in patients admitted with CAP in Ilorin, Nigeria, and potentially explores the possibility of including PCT as part of the initial laboratory assessment of patients with CAP in the country where there is a paucity of information regarding the clinical utility of PCT.

## MATERIALS AND METHODS

### Study design and location

This prospective single center observational study was carried out at the Emergency Medical Unit and medical wards of the University of Ilorin Teaching Hospital between January and December 2017. The hospital is a 600-bed tertiary health facility located in Ilorin, the capital of Kwara state in the North-Central geopolitical zone of Nigeria and serves as a referral center for patients in the state as well as other adjoining states of Osun, Oyo, Ekiti, Kogi, and Niger.

### Study subjects

Consecutive consenting adult patients, 18 years or more diagnosed with CAP on presentation at the medical emergency unit and medical wards of UITH, Ilorin based on clinical and radiologic evidence. Recruited subjects were followed up from admission to the point of discharge or death.

### Exclusion criteria

The following criteria were excluded from the study:

- Patients with prior hospitalization within the preceding 2 weeks of diagnosis and those with prior antibiotic use for the index illness based on information provided by the patient.
- Patients with other causes of bacterial sepsis such as meningitis and urinary tract infection as well as patients with severe non-infectious inflammatory stimuli such as major burns or severe trauma; all of which can also cause a rise in serum PCT levels.<sup>[7]</sup>

### Sample size determination

The required sample size was obtained using the Fisher's statistical formula for estimating minimum sample size in descriptive health studies in populations >10,000.<sup>[18]</sup> The formula;  $n = Z^2pq/d^2$  was used where  $n$  = the desired sample size when target population is >10,000,  $Z$  = standard normal deviate which was set at 1.96 (corresponding to 95% confidence level [CI]) and  $P$  = proportion in the target population estimated to have a particular characteristic. The initial minimum sample size calculated was 83. The minimum sample size calculation was based on a previous prevalence figure of 5.7%<sup>[2]</sup> with 5% margin of error. However, to ensure better statistical deductions from the analysis of data generated, the consenting 102 patients with CAP within the 1-year study period were recruited.

### Procedures

A structured questionnaire adapted from the modified Medical Research Council respiratory questionnaire was administered

by the researchers to obtain the patient's demographics and reported symptoms of CAP. A detailed physical examination was also carried out and findings were documented. All patients had plain chest radiographs (posterior anterior view) to assess for evidence of infiltrates or opacities. A 15-ml sample of each subject's venous blood was obtained by venepuncture at admission using aseptic techniques. The blood samples were used for serum PCT estimation (Elabscience Human PCT Enzyme Linked Immunosorbent Assay [ELISA] kit; Texas, USA), complete blood count, blood culture, and serum urea levels. There was also serological evaluation for *Mycoplasma pneumoniae* (Calbiotech *M. pneumoniae* IgM ELISA Kit; California, USA), *Chlamydia pneumoniae* (Calbiotech *C. pneumoniae* IgM ELISA Kit; California, USA), *Legionella pneumophila* (Trinity Biotech *L. pneumophila* IgM ELISA Kit; New York, USA), Influenza virus (My BioSource Influenza A virus IgM ELISA Kit; California, USA), and Respiratory syncytial virus (Genway Biotech Respiratory Syncytial Virus IgM ELISA Kit; California, USA). The quantitative assessments for serum PCT and the serological evaluation for atypical bacterial and viral pathogens were carried out using ELISA techniques with strict adherence to the manufacturer's instructions. A 2-ml sample of venous blood for repeat serum PCT levels was also taken 7 days after commencement of antibiotic therapy for subjects not lost to departure against medical advice and death.

Sputum samples were also collected in universal sterile containers before commencement of the first dose of empirical antibiotics in all the patients who had productive cough. The sputum samples were first inspected macroscopically at the microbiology unit and then subsequently under a microscope. This was followed by an initial Gram staining following which culture was performed if the specimen contained at least 25 neutrophils and less than ten epithelial cells per high power field. Sputum samples were subsequently liquefied and inoculated into blood, MacConkey, and chocolate agars. Thereafter, incubation was done aerobically at 37°C.

Venous blood (5 ml) was also inoculated into the brain heart infusion broth containing 0.05% sodium polyanetholesulfonate. A minimum of blood to broth ratio of 1:10 was used. This was incubated at 37°C and checked for bacterial growth for up to 7 days. Bottles that show growth were sub-cultured on chocolate and MacConkey agar plates. Those with no growth after 7 days were sub-cultured before being labeled negative.

The complete blood counts were carried out to obtain the white blood cell (WBC) counts using the Sysmex XE 2100 automated hematology analyzer (Sysmex Corporation Inc., Kobe, Japan). The cutoff for WBC count used was  $10 \times 10^9/L$ . The severity of the disease was assessed at admission using the British Thoracic Society recommended CURB-65 scoring

method.<sup>[19]</sup> The serum urea levels were used in the calculation of the CURB-65 scores.

### Primary outcomes

Based on the clinical and microbiological results, these patients were assigned to two diagnostics outcomes: bacterial CAP and non-bacterial CAP. Bacterial CAP was defined as microbiologically confirmed CAP for bacterial infection while non-bacterial CAP was defined as patients having CAP due to other pathogens (viral or fungal).

### Data analysis

All data obtained were analyzed using Statistical Package for the Social Science, IBM SPSS statistics® 2018 version 24.0 for Windows by IBM, Chicago, IL, USA. The sensitivity, specificity, positive predictive, and negative predictive values of serum PCT for microbiologically confirmed bacterial CAP were determined by the area under curve (AUC) at various cutoff levels using the receiver operating characteristic (ROC) curve analysis. The optimal cutoff point for serum PCT on the ROC was determined using the Youden index. The cutoff levels that were evaluated in the methods ranged from 0.4 to 2.5. Positive and negative likelihood ratios were also determined for CAP using the formula: Sensitivity/(1-specificity) and (1-sensitivity)/specificity respectively. Patient characteristics were compared using the Chi-square test or Fisher's exact test, as appropriate, for categorical variables and continuous variables with the Student's *t*-test for normally distributed variables and the Mann-Whitney U-test for non-normally distributed variables.  $P < 0.05$  was statistically significant.

### Ethical considerations

Ethical approval for the study was obtained from the Ethical Review Committee of the University of Ilorin Teaching Hospital. Informed consent was obtained from every subject using a consent form which stated in clear terms the purpose of the study and the investigations to be undertaken. All procedures done were in accordance with the ethical standards of the responsible committee on human experimentation.

## RESULTS

### Baseline clinical and laboratory characteristics of patients

One hundred and two consecutive patients with CAP were recruited consisting 46 males giving a male to female ratio of 1:1.2. The highest frequency in terms of the age group was observed in subjects aged  $\geq 70$  years (20/102; 19.6%). Ninety-five (93.1%) were managed on the medical ward while 6.9% (7/102) were managed in the Intensive Care Unit. The percentage mortality was 17.6% (95% CI: 9.49–25.78) while 5.9% of the subjects departed against medical advice.

The pre-treatment serum PCT concentrations were significantly higher in patients with bacterial CAP when compared to patients with non-bacterial CAP ( $P < 0.001$ ) [Table 1]. In addition, there was statistically significant difference between the pre- and post-treatment serum PCT concentrations in the bacterial CAP group ( $P < 0.001$ ) as well as the non-bacterial CAP group ( $P = 0.006$ ).

### Classes of pathogens detected

There was microbiological confirmation of CAP in 69.6% (71/102) of the patients as shown in [Table 2]. Out of the 102 consecutive patients, 58 (58.9%) had microbiologically confirmed bacterial CAP. Majority of the pathogens isolated were solely typical bacterial pathogens (33/102; 32.3%). There was serological evidence of viral and atypical bacterial pathogens in 11.8% (12/102) and 10.7% (11/102) of the patients, respectively.

### Diagnostic strength of PCT in bacterial CAP

The area under the ROC curve (AUC) for pre-treatment PCT in diagnosing bacterial CAP as shown in [Figure 1] was 0.795 (95% CI: 0.709–0.881), indicating a good overall diagnostic ability of the PCT in detecting those with bacterial CAP alone irrespective of the various cutoff concentrations.

As shown in [Table 3], the sensitivity was highest at a PCT cutoff point of 0.4 ng/ml (100%) while the specificity was highest at a PCT cutoff point of 2.0 ng/ml (95.4%). However, the best overall diagnostic accuracy was at a cutoff of 1.5 ng/ml with a Youden index of 0.47. The sensitivity of pre-treatment PCT for bacterial CAP alone at this cutoff point

**Table 1:** Baseline mean clinical and laboratory characteristics of patients ( $n=102$ ).

Patient characteristics	Bacterial CAP ( $n=58$ )	Non-bacterial CAP ( $n=44$ )	P values
Mean age (years)	49±22	50±22	0.681*
Mean temperature (in degrees Celsius)	38±0.8	38±0.9	0.773*
Mean oxygen saturation (%)	91±6	91±8	0.823*
Mean respiratory rate (cpm)	34±5	34±6	0.759*
Mean WBC count ( $10 \times 10^9/L$ )	10.95±6.31	11.31±5.95	0.769*
Mean pre-treatment PCT (ng/ml)	2.55±0.14	0.94±0.61	<0.001*
Mean post-treatment PCT (ng/ml)	0.67±0.42	0.53±0.48	0.255*
Median length of hospital stay (days)	6 (3–10)	5 (3–6)	0.288*

WBC: White bloods cell, cpm: Cycles per minute, bpm: Beats per minute, CAP: Community acquired pneumonia, PCT: Procalcitonin, \*Independent samples *t*-test, \*Mann–Whitney U-test

was 67.2% with a specificity of 79.5%, positive predictive value of 81.2%, and negative predictive value of 64.8%.

### Relationship between pre-treatment PCT levels and markers of severity of CAP/prognostic indices

[Table 4] shows that the mean pre-treatment PCT levels were significantly higher amongst patients with bacteremia ( $P = 0.006$ ), presence of complications of CAP ( $P = 0.015$ ),

**Table 2:** Pathogens and mode of detection.

Organisms and mode of isolation	Frequency (%)
Sputum culture alone ( $n=21$ ; 20.6%)	
<i>K. pneumonia</i>	8 (7.8)
<i>S. pneumoniae</i>	6 (5.9)
<i>S. aureus</i>	2 (2.0)
<i>P. aeruginosa</i>	2 (2.0)
<i>K. oxytoca</i>	2 (2.0)
<i>Candida albicans</i>	1 (1.0)
Blood culture alone ( $n=11$ ; 10.8%)	
<i>K. pneumonia</i>	6 (5.9)
<i>S. aureus</i>	4 (3.9)
<i>P. aeruginosa</i>	1 (1.0)
Sputum and blood culture ( $n=2$ ; 2%)	
<i>K. pneumonia</i>	1 (1.0)
<i>S. aureus</i>	1 (1.0)
Serology alone ( $n=24$ ; 23.5%)	
<i>L. pneumophila</i>	8 (7.8)
<i>Mycoplasma pneumoniae</i>	3 (2.9)
RSV	12 (11.8)
<i>L. pneumophila</i> and RSV (double pathogens from serology)	1 (1.0)
Mixed/Double pathogens (Sputum and or blood culture+Serology)	
Typical bacteria isolated from blood culture in combination with atypical bacteria/viruses isolated from serology ( $n=3$ ; 2.9%)	
<i>S. aureus</i> and <i>L. pneumophila</i>	1 (1.0)
<i>S. aureus</i> and RSV	2 (2.0)
Typical bacteria isolated from sputum culture in combination with atypical bacteria/viruses isolated from serology ( $n=7$ ; 6.9%)	
<i>K. pneumoniae</i> and <i>L. pneumophila</i>	2 (2.0)
<i>K. pneumoniae</i> and RSV	1 (1.0)
<i>K. oxytoca</i> and <i>L. pneumophila</i>	1 (1.0)
<i>S. aureus</i> and Influenza A virus	1 (1.0)
<i>S. pneumoniae</i> and Influenza A virus	1 (1.0)
<i>S. pneumoniae</i> and RSV	1 (1.0)
Typical bacteria isolated from both sputum and blood culture in combination with atypical bacteria/viruses from serology ( $n=3$ ; 2.9%)	
<i>K. pneumoniae</i> and <i>Chlamydia pneumoniae</i>	1 (1.0)
<i>K. pneumoniae</i> and <i>L. pneumophila</i>	1 (1.0)
<i>S. aureus</i> and <i>L. pneumophila</i>	1 (1.0)
No organism isolated	31 (30.4)

*K. pneumonia*: *Klebsiella pneumoniae*, *S. pneumonia*: *Streptococcus pneumoniae*, *S. aureus*: *Staphylococcus aureus*, *P. aeruginosa*: *Pseudomonas aeruginosa*, *K. oxytoca*: *Klebsiella oxytoca*, *L. pneumophila*: *Legionella pneumophila*, RSV: Respiratory syncytial virus

**Table 3:** Diagnostic strength of pretreatment PCT in microbiologically confirmed cases of bacterial CAP.

Pre-treatment PCT level (ng/ml)	Sensitivity	Specificity	PPV	NPV	PLR	NLR	Youden index
0.4	1.000	0.136	0.601	1.000	1.157	0.000	0.14
0.5	0.948	0.318	0.647	0.823	1.390	0.164	0.27
1.0	0.741	0.659	0.741	0.659	2.173	0.393	0.40
1.5	0.672	0.795	0.812	0.648	3.278	0.413	0.47
2.0	0.396	0.954	0.920	0.545	8.608	0.633	0.35

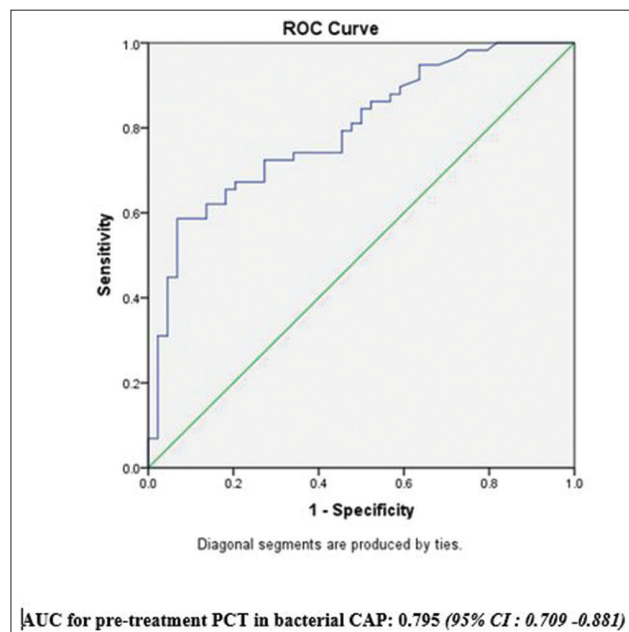
PPV: Positive predictive value, NPV: Negative predictive value, PLR: Positive likelihood ratio, NLR: Negative likelihood ratio, CAP: Community acquired pneumonia, PCT: Procalcitonin

**Table 4:** Relationship between pre-treatment PCT levels and markers of CAP severity.

Markers of CAP severity	Mean Pre-treatment PCT level (ng/ml)	Test-statistic	P-value
CURB-65 score			
0	0.75±0.28	0.850*	0.497
1	1.41±0.80		
2	1.41±0.85		
3	1.52±0.85		
4	1.40±1.03		
Presence of bacteremia			
Yes	1.84±0.62	2.985**	0.006
No	1.31±0.82		
Presence of complications			
Yes	1.63±0.79	2.464**	0.015
No	1.24±0.79		
Type of complication			
Hypoxemia	1.67±0.83	1.427*	0.212
Pleural effusion	1.57±0.85		
Empyema thoracis	1.30±0.49		
Septicemia	1.54±0.85		
Lung abscess	2.56*		
Hemoptysis	2.06±0.28		
No complication	1.24±0.79		
Number of lobes affected			
1	1.32±0.80	1.385*	0.252
2	1.43±0.79		
3	1.99±0.70		
4	1.55±1.24		
WBC count ( $\times 10^9/L$ )			
Less than or equal to 10	1.18±0.81	2.936**	0.004
Greater than 10	1.64±0.75		
Presence of hypoxemia			
Yes	1.48±0.87	0.711**	0.479
No	1.35±0.79		

CAP: Community acquired pneumonia, PCT: Procalcitonin, \*Analysis of variance (ANOVA), \*\*Independent samples *t*-test, \*Single entry

and WBC counts  $>10 \times 10^9/L$  ( $P = 0.004$ ). The mean pre-treatment PCT in subjects who died was greater than in those that survived ( $1.74 \pm 0.79$  vs.  $1.33 \pm 0.81$  ng/ml); however,



**Figure 1:** ROC curve to determine the diagnostic strength of pre-treatment PCT in microbiologically confirmed bacterial CAP. CAP: Community acquired pneumonia, PCT: Procalcitonin, ROC: Receiver operating characteristics, AUC: Area under curve.

the difference was not statistically significant ( $P = 0.057$ ). The mean serum PCT levels were also significantly higher in patients who spent 7 days or more on admission when compared to those who spent  $<7$  days ( $1.72 \pm 0.74$  vs.  $1.26 \pm 0.81$  ng/ml;  $P = 0.010$ ) [Table 5].

After multivariate logistic regression analysis, serum PCT concentrations  $>0.5$  ng/ml were independently associated with the white cell counts  $>10 \times 10^9/L$  (AOR = 6.28; 95% CI: 1.30–30.32).

## DISCUSSION

Our study demonstrates a good degree of accuracy of serum PCT in diagnosing patients with clinical, radiologic, and microbiologic confirmation of bacterial CAP irrespective of the varying PCT concentrations. This information is very germane given the paucity of information regarding this

**Table 5:** Relationship between mean pre-treatment PCT levels and prognostic indices.

Variable	Mean Pre-treatment PCT (ng/ml)	t-test*	P-value
Clinical outcome during admission period			
Alive (n=78)	1.33±0.81	1.931	0.057
Dead (n=18)	1.74±0.79		
Number of days on admission before discharge			
Less than 7 days	1.26±0.81	2.634	0.010
Greater than or equal to 7 days	1.72±0.74		
Place of treatment			
Wards (n=95)	1.39±0.81	0.153	0.878
ICU (n=7)	1.43±0.87		

\*Independent samples t-test, PCT: Procalcitonin

subject in sub-Saharan Africa. Although a previous study by Nyamande *et al.*<sup>[16]</sup> in South Africa demonstrated elevated PCT levels in bacterial CAP when compared to pulmonary tuberculosis and *Pneumocystis jirovecii* pneumonia, the overall diagnostic accuracy for the biomarker was not evaluated.

Furthermore, our finding of sensitivity and specificity values of 67.2% and 79.5%, respectively, at an optimal cutoff level of 1.5 ng/ml was lower than that reported by El-Azeem *et al.*<sup>[20]</sup> in Kuwait who reported a sensitivity and specificity of 94.1% and 88.4%, respectively, with a diagnostic accuracy of 91.6% at a cutoff point of 0.5 ng/ml. The diagnostic accuracy of PCT in their study was, however, for typical bacterial lower respiratory tract infections alone in contrast to our study which covered both typical and atypical bacterial pathogens. In addition, Kang *et al.*<sup>[21]</sup> also reported an accuracy of PCT for diagnosing bacterial CAP of 87.2% with a sensitivity of 93.1% and specificity of 59.6% at an optimal cutoff level of 0.25 ng/ml. The higher values obtained compared to ours may be related to the fact that only 57 patients were recruited, and the only atypical bacterial pathogen assayed for was *L. pneumoniae*.

Overall, the variability of the diagnostic accuracy and optimal cutoff points of PCT across several studies may be related to the varying number of subjects recruited, the different criteria used by the authors to define CAP at the entry point of patient recruitment, the diverse detection ranges, and sensitivity of the PCT serological assay kits used, the number of organisms assayed as well as whether the diagnostic discrimination was for typical bacterial CAP or CAP in its entirety. This may make comparison of various studies difficult and limit the standardization of the biomarker for use in patients with CAP.

The mean pre-treatment PCT was higher in patients with bacterial CAP when compared with those with non-bacterial

CAP. These findings were consistent with other reports by Hedlund *et al.*,<sup>[12]</sup> El-Dib *et al.*,<sup>[22]</sup> Piacentini *et al.*,<sup>[23]</sup> and Jereb and Kotar.<sup>[24]</sup> This may be explained by the fact that PCT production is principally stimulated by cytokines produced following exposure to endotoxins produced by typical bacterial organisms such as tumor necrosis factor as well as interleukins 1 and 6.<sup>[25]</sup> In addition, the insignificant increase in serum PCT levels in patients with viral CAP may be due to inhibition of PCT synthesis by interferon-gamma which is robustly produced in response to viral infections.<sup>[26,27]</sup> This observation further buttresses the strength of serum PCT in potentially determining the etiology of CAP even before microbiological confirmation of the disease by culture, serologic, or PCR techniques. Furthermore, our observation of a significant reduction in serum PCT levels following antibiotic therapy indicates the probable use of this biomarker for therapeutic monitoring of CAP.

The patients with bacteremia also had a higher pre-treatment PCT level when compared to those without bacteremia, exemplifying the link between rising PCT levels and increasing severity of disease. This is in tandem with the findings by Boussekey *et al.*<sup>[28]</sup> and Schuetz *et al.*<sup>[29]</sup> who reported higher levels of serum PCT in patients with CAP who had positive blood cultures. The finding of higher serum PCT levels in our patients who had complications of CAP is also consistent with a previous observation by Boussekey *et al.*<sup>[28]</sup> In addition, patients with elevated white cell counts also had higher mean serum PCT values than those with lower white cell counts. This may be related to the underlying systemic inflammatory response that governs both processes, particularly in response to bacterial infections. In general, the mean pre-treatment PCT values were higher in patients with severe CAP; particularly in subjects with bacteremia, leukocytosis, and those with complications of CAP. These findings indicate that elevated pre-treatment serum PCT levels may assist clinicians in early prediction of severe disease. We also observed that patients who spent 1 week or more on admission had higher mean serum PCT levels indicating its strength in indicating patients likely to have prolonged hospital stay.

Our study was not without limitations. First, the number of viruses assayed for was limited to two pathogens. However, these viral pathogens assayed for are the most common causes of viral CAP globally. Second, the self-reported history of non-antibiotic use before hospital presentation cannot be totally validated considering the fact that the antibiotics can easily be obtained without doctor's prescription in our settings. Consequently, participants reporting bias of prior antibiotic use may underestimate serum PCT concentrations. Third, limitations related to serological assessment of pathogens particularly with issues related to cross reactivity may have affected the frequency of the atypical pathogens

reported. It is also cardinal to note that there may be a need in the future for cross-validation and subsequent external validity testing of results in our setting using independent data sets to further ascertain the accuracy of the performance metrics.

However, despite these limitations, our study has provided cardinal and novel information regarding the usefulness of the biomarker in a black population. The findings will also serve as a template for further larger research regarding the clinical usefulness of serum PCT in patients with CAP in Nigeria and sub-Saharan Africa.

## CONCLUSION

Serum PCT assay can be a supportive investigatory modality in guiding clinicians during evaluation of persons admitted with CAP. The biomarker could aid prompt clinical diagnosis, help predict likely etiologic agent, assess severity, and monitor clinical progress. Hence, the semi quantitative/point of care forms of serum PCT assay may also be helpful for rapid assessment in the emergency room.

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## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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