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The Diagnostic Role of Procalcitonin in Bacterial Pneumonia in Patients with Heart Failure

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ABSTRACT

Background: Recently, procalcitonin (PCT) has been identified as a useful biomarker to identify heart failure with bacterial pneumonia in clinical trials.

Objective: This study aimed to assess the role of procalcitonin in diagnosis of bacterial pneumonia in patients with congestive heart failure.

Patients and methods: The study was conducted in Chest Department, Cardiology Department and Cardiology Outpatient Clinic, Zagazig University Hospitals as a case control study. This study included sixty participants who were classified into 3 groups. Group 1 included 20 chronic stable heart failure patients, Group 2 comprised 20 diagnosed bacterial community-acquired pneumonia on top of chronic heart failure patients. Group 3 consisted of 20 healthy individuals as control group. All participants were subjected to full medical history, clinical examination, chest radiography, CT scan of the chest, ECG, echocardiography, microbiological investigations, general investigations (TLC, ESR, CRP, electrolytes, LFT, KFT, random and fasting blood sugar levels) and specific laboratory investigations (serum PCT level).

Results: Procalcitonin levels differed significantly among the groups studied. There was a substantial difference between the groups when comparing them pairwise. The best cut-off of PCT in diagnosis of bacterial pneumonia in CHF patients was ≥ 0.555 ng/ml with area under curve of 0.994, sensitivity of 95%, specificity of 97.5%, positive predictive value (PPV) of 95%, negative predictive value of 97.5% and accuracy of 96.7% ($p < 0.001$).

Conclusion: Procalcitonin measurement is useful in differentiating bacterial pneumonia in patients with heart failure from heart failure patients without pneumonia, hoping for better patient care.

Keywords: Procalcitonin, Heart failure, Pneumonia.

INTRODUCTION

There are several respiratory tract infections, like community-acquired pneumonia (CAP), as well as bronchitis that necessitate antibiotic therapy and contribute to the rise in antibiotic multi-resistant infections. Clinical criteria (like fever, dyspnea as well as cough) and chest radiography are the primary diagnostic tools for respiratory infections. However, despite the fact that PCR and culture procedures have low sensitivity and hence cannot rule out bacterial infection, various research and interventional trials have found that PCT is effective in patients with respiratory infections [(1)]. Pneumonia continues to be a primary cause of health issues and death worldwide, with its high mortality rate and widespread prevalence making it a substantial contributor to the use of antibiotics. [(2)].

Emergency medicine is plagued by acute dyspnea, which is associated with a high fatality rate. Dyspnea can have a variety of underlying reasons, the most common of which are cardiac or pulmonary causes. It's vital to rule out acute heart failure (AHF) as a possibility in these people [(3)]. The non-specific chest X-ray abnormalities in cardiogenic pulmonary edema make it challenging to diagnose pneumonia in patients with acute heart failure. Misdiagnosis has the side effect of delayed treatment, which could lead to worse consequences [(4)].

Pneumonia has been successfully diagnosed with the help of procalcitonin (PCT), a promising biomarker discovered in recent years. Viral, bacterial and nonspecific inflammatory diseases are all associated with high levels [(5)].

During a bacterial infection, the level of procalcitonin, a precursor peptide to the calcitonin hormone, rises dramatically. As a result, new research suggests that PCT can be used to guide antibiotic therapy in patients with heart failure by identifying those with concurrent bacterial infections [(6)].

We aimed at this study to assess the role of procalcitonin in diagnosis of bacterial pneumonia in patients with chronic heart failure.

PATIENTS AND METHODS

From November 2020 to April 2021, in Chest Department, Cardiology Department and Cardiology Outpatient Clinic, Zagazig University Hospitals, our case-control trial was conducted. Sixty participants were classified into:

Group (A): Included 20 cases with chronic stable heart failure, which is a clinical disease characterized by an impaired ability to fill or eject blood from the ventricles. Myocardial structural and functional abnormalities can induce chronic heart failure [(7)].

Group (B): Included 20 cases with definite diagnosis of bacterial community-acquired pneumonia on top of chronic heart failure, which is defined as an acute lung infection affecting the alveoli [(8)].

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Group (C): Included 20 healthy individuals as control group.

Inclusion Criteria:

Patients with heart failure and patients who developed symptoms and signs of bacterial community-acquired pneumonia on top of chronic heart failure.

Exclusion Criteria: patients with: Other causes of infection, use of anti-inflammatory or systemic steroid drugs, cardiogenic shock, chronic inflammatory conditions like chronic arthritis, malignancy, and confirmed myocardial infarction in the past two weeks prior to the study

All participants of the study were subjected to the following:

A) Complete history taking.

B) Complete clinical (general as well as local heart and chest) examination.

C) Radiology: Plain chest x-ray (lateral and postero-anterior views) as well as CT scan of the chest if indicated.

D) Electrocardiogram (ECG).

E) Echocardiography study: A Sono scape SSI 4000 US system was used to obtain standard transthoracic M-mode and two-dimensional echocardiograms.

F) Laboratory investigations*:*

- Microbiological investigations: Respiratory sample (sputum)) for Gram stain, culture and sensitivity using standard microbiological methods.
- CBC containing total and differential leucocytic count.
- Erythrocyte sedimentation rate (ESR).
- C-reactive protein (CRP)
- 5 -Electrolytes (sodium & potassium)
- Liver function tests including hepatic serum enzymes (ALT and AST)
- Kidney function including both serum urea and creatinine levels.
- Random, fasting and post prandial blood sugar levels.
- Serum PCT level.

Ethical consent:

All participants completed informed permission papers and submitted them to The Research Ethics Committee, Zagazig University and the study was permitted (ZU-IRB#6725). Ethics guidelines for human experimentation were adhered in line with the Helsinki Declaration of the World Medical Association.

Statistical analysis

Using SPSS software (USA) version 16. Numbers and percentages are used to represent data (percent) or mean ± SD. Different qualitative factors were examined using the Chi square (X^2) test or fisher. ANOVA test was used. Mann Whitney test was used in addition to Roc curve analysis with assessment of sensitivity as well as specificity. If the significant probability was less than 0.05, the threshold for statistical significance, the results were considered statistically significant and highly significant when P value $\leq$ 0.05 was considered significant.

RESULTS

There were statistically significant differences between the groups regarding special habits. Smokers represented 25%, 45% and 0% within CHF with pneumonia, CHF without pneumonia and control groups respectively. Mean ages for studied groups were 56.55, 56.25 and 51.8 years for CHF with pneumonia, CHF without pneumonia and control groups respectively. In addition, Female represented 55%, 40% and 50% of those within CHF with pneumonia, CHF without pneumonia and control groups respectively. Regarding related co-morbidities, no statistically significant differences between the studied groups were found (Table 1).

Table (1): demographic data comparisons between the studied groups

Parameter	Groups			Test	
	CHF with pneumonia group	**CHF without pneumonia**	**Control group**	**F/χ^2**	**P**
	N=20	**N=20**	**N=20**		
Age (year):					
Mean ± SD	56.55 ± 10.57	56.25 ± 13.57	51.8 ± 14.33	0.847	0.434
Gender:					
Female	11 (55%)	8 (40%)	10 (50%)	Fisher	0.627
Male	9 (45%)	12 (60%)	10 (50%)		
Occupation:					
Farmer	2 (10%)	5 (25%)	0 (0%)		
Housewife	11(55%)	8 (40%)	10 (50%)	6.661	0.133
Worker	7 (35%)	7 (35%)	10 (50%)		
Special habits:					
No	15 (75%)	9 (45%)	20 (100%)		
Ex-smoker	0 (0%)	1 (5%)	0 (0%)		
Bird breeder	0 (0%)	1 (5%)	0 (0%)	16.851	<0.001**
Smoker	5 (25%)	9 (45%)	0 (0%)		
Comorbidity:					
No	8 (40%)	4 (20%)			
Diabetes	4 (20%)	3 (15%)			
Hypertension	6 (30%)	7 (35%)			
Hepatitis C	0 (0%)	2 (10%)			
Hypothyroidism	0 (0%)	1 (5%)		9.553	0.215
IHD*	0 (0%)	3 (15%)			
CKD*	1 (5%)	0 (0%)			
Controlled AF*	1 (5%)	0 (0%)			

Concerning TLC, table (2) showed that there was a significant difference between the groups that were examined. On doing Tukey's HSD test, the difference was significant between CHF patients with pneumonia and each of the other groups. A significant statistical difference exists between the groups when looking at oxygen saturation levels. On doing Tukey's HSD test, the difference was significant between CHF patients with pneumonia and control group. Regarding LDH and ESR, on doing pairwise comparison. The difference between the control group and the other groups was statistically significant. The CRP levels of the studied groups were significantly different. On doing pairwise comparison, the difference was significant between CHF patients with pneumonia and each of the other groups.

Table (2): Comparison between the studied groups regarding some laboratory data

Parameter	**Groups**			Test	
	CHF with pneumonia	**CHF without pneumonia**	**Control group**	**F/KW**	**P**
	Mean ± SD	**Mean ± SD**	**Mean ± SD**		
TLC(*10^9/L)*	16.97 ± 3.57	8.31 ± 1.19	6.62 ± 1.64	F=72.244	<0.001**
Post hoc	P_1 <0.001**	P_2 0.17	P_3 <0.001**		
O_2 saturation (%)	94.2 ± 3.24	95.53± 3.79	96.9±1.48	F=4.177	0.021*
Post hoc	P_1 0.367	P_2 0.345	P_3 0.015*		
LDH (unit/L)*	262.75±6.68	279.35±9.19	183.60±6.87	KW=15.139	0.001**
Pairwise	P_1 >0.999	P_2 <0.001**	P_3 0.005*		
ESR(mm/hr) first hour*	56.59±6.06	30.14±3.18	9.45±2.07	KW=27.367	<0.001**
Pairwise	P_1 0.05	P_2 0.014*	P_3 <0.001**		
CRP(mg/L)*	72.80±8.18	16.05±1.65	5.46±1.16	KW=36.638	<0.001**
Pairwise	P_1 <0.001**	P_2 0.156	P_3 <0.001**		

Table (3) showed that procalcitonin differed significantly between the studied groups. Pairwise comparisons revealed a significant difference between the studied groups.

Table (3): Comparison between the studied groups regarding procalcitonin level

Parameter	Groups			Test	
	CHF with pneumonia group (Mean±SD)	CHF without pneumonia (Mean±SD)	Control group (Mean±SD)	KW	P
PCT(µg/L)	0.5 ± 0.17	0.26±0.04	0.07 ± 0.02	51.786	<0.001**
Pairwise	P_1 <0.001**	P_2 0.001**	P_3 <0.001**		

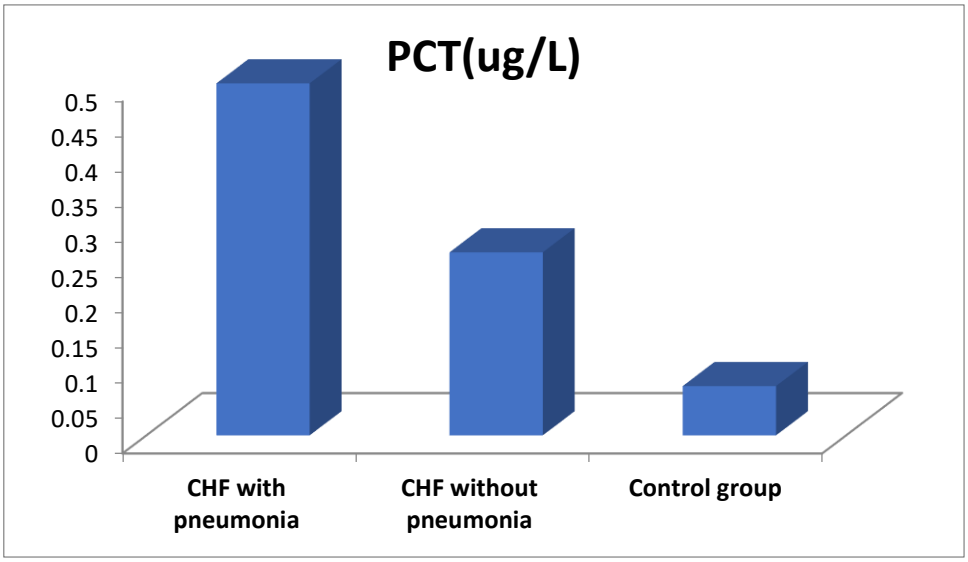

Figure (1): Bar chart showing Comparison between the studied groups regarding procalcitonin

Table (4) showed that the best cutoff of PCT in diagnosis of pneumonia in CHF patients was ≥ 0.555 µg/l with area under curve of 0.994, sensitivity of 95%, specificity of 97.5%, positive predictive value (PPV) of 95%, negative predictive value of 97.5% and accuracy of 96.7% (p < 0.001).

Table (4): Performance of PCT in diagnosis of pneumonia among studied patients with congestive heart failure

PCT	Cutoff	AUC	Sensitivity	Specificity	PPV	NPV	Accuracy	P
	≥0.555	0.994	95%	97.5%	95%	97.5%	96.7%	<0.001**

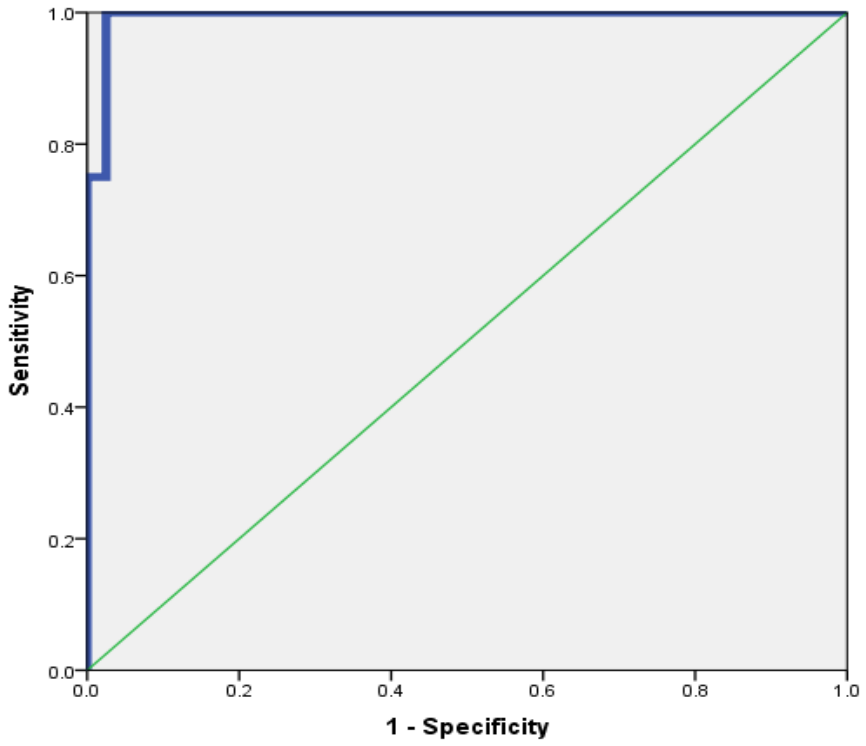

Figure (2): ROC curve showing Performance of PCT in diagnosis of pneumonia among patients with congestive heart failure among the studied patients.

DISCUSSION

In the emergency room, acute dyspnea is the leading cause of admission. Patients with heart failure must be treated for this primary symptom. An important diagnostic difficulty for doctors dealing with acute shortness of breath is how to distinguish it from other possible causes of dyspnea so that the patient can receive the proper treatment [9].

Regarding demographic data, statistically significant differences existed between groups regarding special habits only. Regarding related co-morbidities, age, gender and occupation, no differences between the studied groups were found statistically. **Shebl and Moety** [10] studied 50 patients with chronic ILD to see how well serum PCT performed in the diagnosis of bacterial pneumonia on top of chronic ILD. Demographic differences between patients with and without bacterial infection were shown to be non-significant.

Regarding laboratory data in this study, TLC, oxygen saturation, LDH, ESR, and CRP differed significantly between the studied groups. These results agree with that reported by **Tatar *et al.*** [11]. According to **Castro-Guardiola *et al.*** [12]**,** those with pneumonia had a mean serum CRP level of 18.1 mg/dl, which was significantly greater than that of patients without the illness. Also, in **Abdel Aziz *et al.*** [9] study, 60 people with acute dyspnea were tested to see if C-reactive protein and procalcitonin levels could be used to discriminate between acute decompensated heart failure and community-acquired pneumonia, [heart failure (group A) and pneumonia (group B) each comprised 30 individuals]. They found that the levels of Hs-CRP, ESR, and TLC in heart failure group and pneumonia group were significantly different.

In this study, regarding procalcitonin levels, pairwise comparisons revealed a significant difference between the studied groups. **Loncar *et al.*** [16] reported that people with cardiovascular disease are known to be more susceptible to PCT secretion because their digestive tracts are less permeable, which allows bacteria to enter and infect them. A study by **Niebauer and colleagues** [13] examined PCT and found that the concentrations of endotoxin and inflammatory cytokines rose when the patient had HF-induced edema. Compared to patients with compensated heart failure and healthy controls, PCT was shown to be greater in patients with oedematous heart failure. **Wang *et al.*** [14] selected 4,698 cases, including those with congestive heart failure, bacterial infection, heart failure-related bacterial infection and healthy persons to assess the value of PCT in diagnosis of bacterial infection. There was a significant variation in PCT expression between the four groups. In patients with simple heart failure, the level of PCT was much greater than in the control group, showing that PCT levels are up in patients with cardiac failure. It's possible that congestive heart failure influences PCT-based diagnosis of infection, as it was much higher in patients with concomitant bacterial infections than in those without.

In this study, the best cut-off value of PCT in diagnosis of pneumonia in CHF patients with pneumonia was ≥ 0.555 ng/ml with area under curve of 0.994, sensitivity of 95%, specificity of 97.5%, PPV of 95%, negative predictive value of 97.5% and accuracy of 96.7% ($p < 0.001$). **Cinar *et al.*** [15] to identify an infectious cause of dyspnea, they used a threshold level of 0.25 ng/ml for pneumonia. An accuracy rate of 48.8% was achieved with PCT in 154 patients who had a primary symptom of shortness of breath and an ambiguous diagnosis, while sensitivity was at 0.25 ng/ml and specificity was at 96.5%. Also, **Maisel and colleagues** [4] in a large number of patients with dyspnea, 155 had pneumonia, with a median PCT concentration of 0.18 ng/ml, while those without pneumonia had a median PCT concentration of 0.07 ng/ml.

PCT was employed by **Abdel Aziz *et al.*** [9] to detect acutely dyspneic patients with heart failure or community-acquired pneumonia with a PCT < 0.2 ng/ml and a PCT > 0.2 ng/ml respectively, with 100% and 93.33% sensitivity and specificity, respectively, using PCT. **Wang *et al.*** [14] used PCT value of 0.1 µg/L as the cutoff threshold for their study. There was no difference in the diagnostic value of PCT for infectious diseases in patients with uncomplicated bacterial infection and those with congestive heart failure. While PCT's diagnostic sensitivity was substantially higher when dealing with infections worsened by heart failure where it had a much lower positive predictive value when dealing with uncomplicated infections. Positive prognostic value for PCT dropped considerably as heart failure progressed. PCT can still be useful in the diagnosis of a mild bacterial disease or an infection exacerbated by heart failure. Patients with bacterial infections and severe heart failure were theorized to have greater PCT concentrations.

CONCLUSION

The findings in this study indicated that patients with heart failure and bacterial pneumonia had increased PCT level compared to those with heart failure without bacterial pneumonia. The procalcitonin test can be used to distinguish individuals with heart failure and bacterial pneumonia from those with heart failure only from day one allowing for better patient management.

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