The association between the serum total cortisol as an adrenal response biomarker and severe community-acquired pneumonia

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Introduction The serum total cortisol is a biomarker to adrenal response in stressful conditions including infection. This study aims to estimate the serum total cortisol level in severe community-acquired pneumonia (CAP) and to study its relation to the severity of illness.

Patients and methods The study included 50 patients, who with severe CAP were admitted to the ICU of National Institute of Chest Diseases (Embaba), and 20 healthy adults as the control. Ethical approval done by ASU ethical approval team as the paper was taken from masters thesis. The severity of CAP was estimated using pneumonia severity index (PSI) and CURB65 scores. The two groups were subjected to the estimation of serum total cortisol level (8 a.m.) by electrochemiluminescence immunoassay.

Results Serum total cortisol level significantly increased in the patient group than in the control group (20.356±11.198 and 15.070±1.384 μg/dl, respectively). Serum total cortisol level was positively correlated with PSI but not with CURB65 score.

Conclusion Severe CAP is associated with increased serum total cortisol level compared to normal. Serum total cortisol level was positively correlated with the disease severity as estimated by PSI.

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Introduction

Community-acquired pneumonia (CAP) is accompanied by significant mortality and morbidity and is the most prevalent cause of infectious diseases mortality in cases with critical illness. Patients with severe CAP often require ICU admission [1].

Hypothalamic–pituitary–adrenal axis has an important role toward the immune response in microorganisms present in the patients with severe infections [2].

Cortisol is a major endogenous regulator of inflammation and the predominant corticosteroid is released by the adrenal cortex [3].

This study aims to estimate the serum total cortisol level in severe CAP and to study its relation to the severity of illness.

Patients and methods

This study was conducted on 50 patients with severe CAP who were admitted to the ICU. The diagnosis was based on appearance of the recent radiographical opacity, and at least two concordant clinical manifestations, such as body temperature more than or equal to 38°C, productive cough, chest pain, dyspnea, and crepitation on auscultation. The severity of CAP was categorized according to CURB65 [4] and pneumonia severity index (PSI) [5] scores. Patients who were excluded from the study were the following: under 18 years old, or having nosocomial pneumonia, immunosuppression including AIDS or recent chemotherapy, active tuberculosis, sarcoidosis, pregnant woman, concomitant therapy with steroid medication, history of adrenal, hypothalamic or pituitary illness, malignancy, malnutrition, and hypoalbuminemia.

Twenty healthy adults were included as the control.

The following parameters were required for diagnosis and assessment of severity: history of present illness and comorbidities, clinical examination, arterial blood gases by blood gases analyzer (GEM Premier 3000, Werfen, Bedford, England, with iQM), complete blood picture, liver function test, serum urea and creatinine, sputum culture and sensitivity, erythrocyte sedimentation rate (ESR), serum sodium and potassium, and serum total cortisol level (8 a.m. and within the first 72 h of ICU admission).

The two groups consented to participate in the study.

Statistical analysis

Collected information were coded, tabulated, and analyzed using IBM SPSS statistics (statistical package for the social sciences) software (version 22.0, 2013; IBM Corp., Chicago, Illinois, USA).

Statistical terms such as minimum and maximum (range) and mean±SD were used for quantitative information.

Inferential analysis was done for quantitative variables using independent *t* test in cases of two independent groups with normal distributed data. Inferential analyses in qualitative information, for independent variables were done using χ^2 test for differences between proportions. Whereas correlations were done using Pearson's correlation for numerical parametric information and using Spearman's rho test for numerical not normally distributed data. The level of significance estimated by *P* value less than 0.050 is significant, otherwise it is nonsignificant.

Results

This study included 50 patients, 27 (54%) males and 23 (46%) females with age range from 18 to 70 years, mean ±SD 50.88±15.192 years. Healthy adults (as control) were 11 (55%) males and nine (45%) females with age range from 19 to 70 years, mean±SD 51.600±13.308 years as shown in Tables 1 and 2.

The study found that the patients had a statistically significant increase in the mean±SD value of serum total cortisol 20.356±11.198 μg/dl compared with the mean±SD value of serum total cortisol of the control 15.070±1.384 μg/dl (Table 3). The serum total cortisol level was positively correlated ($P<0.001$) with PSI (Fig. 1). There was no such correlation with CURB65 score.

The current study found that there was no statistical significant difference in the serum total cortisol level in the patients with respect to comorbidities (Table 4).

The current study showed that there was an audible blood pressure in 40 (80%) patients and nonaudible blood pressure in 10 (20%) patients, and there was no significant difference in the serum total cortisol level in the patients with audible blood pressure compared to nonaudible blood pressure.

The mean±SD values of temperature 38.588±0.847, pulse 110.860±12.829, and respiratory rate 34.240 ±3.127 in severe CAP patients were compared with temperature 37.000±0.065, pulse 86.950±6.057, and respiratory rate 14.900±1.252 in the control.

Arterial oxygen tension (PaO_2) was 50.920±6.171 mmHg in severe CAP patients compared with 97.105±0.900 mmHg in the control. There was no correlation between the serum total cortisol level and PaO_2 among the patients.

The current study noted that there was a statistically significant increase in the mean±SD value of urea 94.840±40.407, creatinine 2.041±0.871, total leukocytic count 20.534±8.256, and ESR 'first hour' 103.500±26.654 in severe CAP patients compared with urea 31.450±9.248, creatinine 1.005±0.176, total leukocytic count 5.700 ±0.979, and ESR 'first hour' 17.750±6.584 in the control.

The study noted that there was no statistical significant difference in the serum total cortisol level in the patients with respect to sex and age.

Table 1 Comparison between statistical data of patients and the control with respect to age

Age	Groups		*t* test	
	Patients	Control	*t*	*P* value
Range	18–70	19–70	–0.185	0.854
Mean±SD	50.880±15.192	51.600±13.308		

Table 2 Comparison between the statistical data of patients and the control with respect to sex

Sex	Groups [*N* (%)]			χ^2	
	Patients	Control	Total	χ^2	*P* value
Male	27 (54.00)	11 (55.00)	38 (54.29)	0.006	0.940
Female	23 (46.00)	9 (45.00)	32 (45.71)		
Total	50 (100.00)	20 (100.00)	70 (100.00)		

Table 3 Comparison between the two groups with respect to the serum total cortisol (μg/dl)

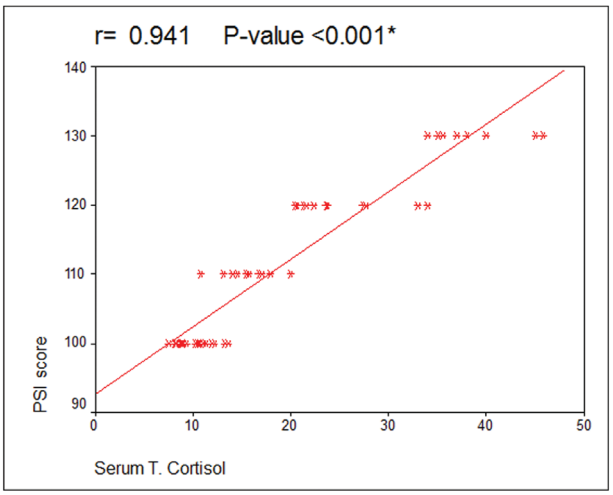
Serum total cortisol	Groups		*t* test	
	Patients	Controls	*t*	*P* value
Range	7.5–45.9	12.5–18	2.096	<0.050*
Mean±SD	20.356±11.198	15.070±1.384		

* means it is statistically significant.

When presenting the chest symptoms, dyspnea turned out to be the most prevalent symptom in 49 (98%) patients, followed by cough in 47 (94%) patients, chest pain in 11 (22%) patients, and hemoptysis in four (8%) patients.

In the bacterial etiology of pneumonia, there was no bacterial growth in one (2%) patient, *Streptococcus pneumoniae* in 26 (52%) patients, *Staphylococcus aureus* in 13 (26%) patients, *Haemophilu influenza* in seven (14%) patients, *Klebsiella* spp. in two (4%) patients, and *Acinetobacter* spp. in one (2%) patient. The viral swab for H1N1 influenza virus was carried out, in which 27 (54%) patients had positive results and 23 (46%) patients had negative results. On the basis of the above findings, 26 patients were diagnosed as having combined bacterial and viral pneumonia, 23 patients as bacterial pneumonia, and one patient as viral pneumonia without bacterial infection.

Figure 1



Correlation between serum total cortisol (μg/dl) and pneumonia severity index (PSI) score.

There was no significant difference in the serum total cortisol level in patients with combined etiology compared to absolute bacterial etiology (Table 4).

In patients who underwent computed tomography (CT), the findings were bronchopneumonia in 24 (48%) patients, lobar pneumonia in 13 (26%) patients, pneumonia with effusion in 10 (20%) patients, and interstitial pneumonia in three (6%) patients. There was no statistically significant difference in the serum total cortisol level between the CT patterns among the different types of pneumonia (Table 4).

With respect to mechanical ventilation, 16 (32%) patients needed mechanical ventilation, whereas 34 (68%) patients did not. There was no statistically significant difference in serum total cortisol level between the patients who were on mechanical ventilation and the patients who were not (Table 4).

Discussion

To evaluate the level of serum total cortisol in 50 cases suffering from severe CAP, the current study focused on the patients admitted in the ICU.

The study showed that there was no statistical significant difference in the serum total cortisol level

Table 4 Statistical study of the serum total cortisol (μg/dl) among patients with respect to other variables

	Serum total cortisol		*t* test	
	N	Mean±SD	*t*	*P* value
Sex				
Male	27	18.944±11.027	−0.965	0.339
Female	23	22.013±11.415		
Comorbidities				
No comorbidities	37	20.397±11.630	0.044	0.965
Comorbidities	13	20.239±10.309		
CT chest findings				
Bronchopneumonia	24	20.125±10.665	0.413	0.744
Lobar pneumonia	13	22.354±14.093		
Pneumonia with effusion	10	17.460±9.276		
Interstitial pneumonia	3	23.200±10.237		
Mechanical ventilation				
No	34	20.106±11.087	−0.228	0.821
Yes	16	20.888±11.781		
Etiology				
Bacterial	23	20.743±12.060	0.224	0.824
Combined viral H1N1and bacterial	26	20.026±10.631		

CT, computed tomography.

in the patients with respect to age and sex. The age range was 18–70 years with a mean±SD age of 50.88 ±15.192 years. There was no statistically significant correlation in our study between age and the serum total cortisol level in the patients. These results were in accordance with Kudielka *et al.* [6], who found that the response patterns of the serum total cortisol did not differ between age and sex .

We found that the patients had a statistically significant increase in the mean value of serum total cortisol when compared with the mean of serum total cortisol of the control. These results were in agreement with Salluh *et al.* [7], who found that there is highly statistically significant increase in the mean value of serum cortisol level in cases with different types of pneumonia (classified according to severity), with highest level in severe ones. He also stated that the serum cortisol level is a good indicator to understand CAP severity.

The study showed that there is no correlation between the serum total cortisol level andPaO_2in the patients. It does not match with the study of Fouda and Elatar [8], who found that the serum total cortisol level noted significantly negative correlation with PaO_2. This mismatch can be related to the study sample of Fouda and Elatar [8]. It was a small convenience sample that included a wide range of CAP severity (PSI classes I–V) and a wide range of PaO_2 values, whereas the current study included severe cases admitted to ICU with (PSI class IV) [8].

The study found that there was no correlation between the serum total cortisol level and total leukocytic count in the patients. The current study also found, there was a statistically significant increase in the mean value of the total leukocytic count in the patients when compared with the control. Our results matched with Mandell *et al.* [9], who found that leukocyte levels more than 14×10^9/l had been associated with pneumonia severity.

In the current study we found that there is statistically significant increase in ESR 'first hour' in the patients when compared with the control. There is no correlation between the serum total cortisol level and ESR first hour in the patients.

The study also noted that there is no significant difference in the serum total cortisol level in the patients with respect to the bacterial etiology and combined H1N1 influenza virus and bacterial etiology.

We also found that there is no statistically significant difference between the serum total cortisol level and the CT patterns of severe pneumonia in the patients.

The study noted that there was no statistically significant difference in serum total cortisol level between the patients who were on mechanical ventilation and the patients who were not.

We found that the serum total cortisol level positively correlated with the PSI of the patients when matched with the study by Mueller *et al.* [10], who found that the serum total cortisol level is significantly increased with increasing CAP severity, as assessed by PSI.

In the current study we found that there was no correlation between the serum total cortisol level and CURB65 score, which may be because the study included only high-risk patients, and most of these patients had CURB65 score 3.

In the blood pressure measurement, the current study found that there was nonaudible blood pressure in 10 patients and audible blood pressure in 40 patients. The study showed that there was no difference in cortisol level between audible and nonaudible blood pressure in patients. This is in agreement with Cooper and Stewart [11], who found that hypotension was inadequate to diagnose the adrenal function.

In the current study we found that there was a statistically significant decrease in the mean value of PaO_2 in the patients when compared with the mean value of PaO_2 of the control. These findings are in agreement with Charles *et al.* [12], who found that PaO_2 below 60 mmHg is one of the criteria for CAP severity.

The study noted that there was statistically significant increase in urea and creatinine in the patients when compared with the control. These findings are in accordance with Mongardon *et al.* [13], who found that acute kidney impairment is a common complication in patients with severe CAP and many of them presented renal impairment on ICU admission.

From this study we concluded that increased serum total cortisol is a good biomarker for severe CAP and there is positive correlation between the serum total cortisol level and the disease severity as assessed by PSI.

Limitations

There was only a single sample of serum cortisol that was evaluated in this study. The study did not evaluate sequent samples of serum total cortisol over the day or during the

course of illness, which can add to the prognostic information. We did not evaluate the working of the adrenal gland based on the response to injection of synthetic adrenocorticotropin, as used in other studies.

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Conflicts of interest
There are no conflict of interest.

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