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Original Article

Predictive value of Admission Serum Cortisol for Mechanical Ventilation in Community-Acquired Pneumonia: A Prospective Study

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Abstract

Background: *Early identification of patients requiring mechanical ventilation (MV) either invasive or non invasive is critical to reduce morbidity and mortality in community-acquired pneumonia (CAP). Cortisol, a primary stress hormone, may serve as a prognostic marker in CAP.*

Objective: *To evaluate the association between admission serum cortisol levels and the need for MV in patients with CAP.*

Methods: *This prospective study enrolled 92 adults with CAP admitted to Dhaka Medical College Hospital over 12 months. Serum cortisol was measured at 9:00 AM on the first available morning after admission using ELISA. All participants were categorized into high cortisol (>23 mcg/dL) and normal cortisol (≤23 mcg/dL) groups. The primary outcome was the requirement for MV. Logistic regression and receiver operating characteristic (ROC) analysis were applied to assess predictive value.*

Results: *Patients with high cortisol had a significantly greater need for MV compared with those with normal levels (31.8% vs 4.2%, p = 0.001). High cortisol independently predicted MV (OR = 10.7, 95% CI: 2.28–50.6, p = 0.030). ROC analysis showed good discriminative ability for cortisol (AUC = 0.831), while CURB-65 (AUC = 0.972) and CRP (AUC = 0.947) performed better.*

Conclusion: *Admission serum cortisol is independently associated with the need for MV in CAP patients and provides additional prognostic information beyond conventional severity scores. Incorporating cortisol measurement into early assessment may improve risk stratification and help guide timely escalation of care, especially in resource-limited settings.*

Keywords: *Community-acquired pneumonia, serum cortisol, mechanical ventilation, CURB-65, risk stratification*

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Introduction

Despite advances in antimicrobial therapy, globally, up to 42% of CAP patients require hospital admission, among them 10%–14% are admitted to intensive care units (ICUs) for Community-acquired pneumonia (CAP).[1,2] Among those requiring ICU care, mortality rates can reach as high as 35%.[3] In addition to its clinical consequences, CAP leads to prolonged hospital stays, increased need for invasive support such as mechanical ventilation (MV), and elevated healthcare costs.[4] Accurate and early risk stratification of CAP patients is essential to guide decisions about hospital admission, ICU transfer, and the need for mechanical ventilation. The CURB-

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65 and Pneumonia Severity Index (PSI), well-known clinical scoring systems, can predict outcomes like mortality and ICU admission.[5] However, these tools may lack specificity in forecasting which patients will deteriorate rapidly and require respiratory support. In this context, reliable predictors could improve prognostic accuracy and help allocate critical care resources more effectively.

Cortisol, the principal glucocorticoid hormone released in response to physiological stress, plays a central role in modulating immune and inflammatory responses.

In critical illness, the hypothalamic-pituitary-adrenal (HPA) axis is activated, and as a result, serum cortisol levels are raised. Prior studies have demonstrated that cortisol elevation is associated with adverse outcomes in conditions of severe pneumonia sepsis, acute respiratory distress syndrome (ARDS).[6–9] The connection between cortisol levels and the severity of pneumonia has already been established in different studies. Specifically, higher cortisol levels are associated with more severe pneumonia scores and greater rates of ICU admission. This highlights the critical role cortisol plays in our body's response to severe infection.[10-13] However, the association between admission serum cortisol levels and the specific need for mechanical ventilation in CAP patients remains insufficiently explored. The connection between cortisol levels and the severity of pneumonia has already been established in different studies. Specifically, higher cortisol levels are associated with more severe pneumonia scores and greater rates of ICU admission.[14,15] Recent research also supports the prognostic role of cortisol in viral and non-viral respiratory failure, including COVID-19 and CAP.[16-18] However, the association between admission serum cortisol levels and the specific need for mechanical ventilation in CAP patients remains insufficiently explored.

Addressing this gap, the present study aims to find out whether elevated serum cortisol levels measured on the first day of hospitalization are independently associated with an increased need for mechanical ventilation among patients with community-acquired pneumonia. The findings may improve the early identification of high-risk patients and inform resource allocation in resource-limited, high-burden healthcare settings.

Materials and Methods

Study Design

This was a prospective observational study design to establish the association between serum cortisol levels and need for mechanical ventilation among patients admitted to Dhaka Medical College Hospital with community-acquired pneumonia (CAP). The study was carried out over 12 months at Dhaka Medical College Hospital (DMCH), a tertiary care center in Dhaka, Bangladesh, following Institutional Review Board (IRB) approval.

Study Population

The study population was all adult patients (aged e"18 years) admitted with a diagnosis of community-acquired pneumonia (CAP) to the Departments of Internal Medicine, Respiratory Medicine, and Intensive Care Unit (ICU) at Dhaka Medical College Hospital during the designated study period. A consecutive sampling technique was employed. The sample size was calculated based on the findings of a study (5), which reported a 35% incidence of mechanical ventilation among CAP patients with high serum cortisol levels compared to 10% in those with normal levels. Using a two-sided test with a 95% confidence level (Zá/2 = 1.96) and 80% power (Zâ = 0.84) and adjusting for an estimated 15% loss to follow-up, the final sample size was determined to be 92 patients. Inclusion criteria encompassed a confirmed diagnosis of CAP based on clinical and radiological findings, and willingness to provide written informed consent. Patients were excluded if they had a history of adrenal insufficiency or adrenal tumor, recent or current use of systemic corticosteroids, active or recent malignancy, severe immunocompromisation (e.g., HIV or chemotherapy), advanced liver or renal dysfunction, severe psychiatric illness, were pregnant or lactating, or were unwilling to provide informed consent.

Study Procedure

After obtaining IRB approval, eligible patients were enrolled at the time of hospital admission. Informed written consent was obtained from each participant or their legal representative.

Data were collected using a semi-structured questionnaire, including demographic details, clinical presentation, comorbidities, laboratory findings, and clinical outcomes. On the first post-admission morning at 9:00 AM, a 3 mL venous blood sample was collected from each participant to measure serum cortisol levels. The timing was standardized to reduce the effect of diurnal variation.

Samples were drawn using sterile venipuncture into serum-separating tubes (SST) containing clot activator and gel. After allowing the blood to clot for 15–30 minutes at room temperature, samples were centrifuged at 1,500–2,000 RPM for 10–15 minutes. The separated serum was stored at "20°C or lower until analyzed.

Serum total cortisol levels were measured using a commercially available **ELISA kit** in the Dhaka Medical College Biochemistry Department. to minimize inter-assay

variability, all samples were processed in a single batch. The assay measured **total serum cortisol**, which includes both free and protein-bound fractions. Measurements were performed at 9:00 AM to reduce diurnal variation. Moreover, results were interpreted based on predefined cut-offs:

- **High cortisol**: >23 mcg/dL (>635 nmol/L)
- **Normal/low cortisol**: ≤23 mcg/dL (≤635 nmol/L)

Patients were followed throughout hospitalization to document relevant outcomes, including mechanical ventilation requirement.

Outcome:

Mechanical ventilation (MV) was defined as the initiation of either invasive ventilation via endotracheal intubation or non-invasive positive pressure ventilation (NIPPV) during hospitalization. Patients already receiving any form of oxygen supplementation before serum cortisol measurement were eligible; however, only those not yet on MV at the time of blood sampling were included in the analysis.

Data Analysis

SPSS version 26.0 (IBM Corp., Armonk, NY, USA) for Data analysis. For normally distributed data reported as mean ± standard deviation (SD) and median with interquartile range (IQR) for skewed data. Categorical variables were presented as frequencies and percentages.

Comparisons between groups were made using the independent t-test or Mann–Whitney U test for continuous variables and the chi-square or Fisher's exact test for categorical variables. To explore the independent predictors of mechanical ventilation, Multivariable logistic regression analysis was applied. Variables included in the model were selected based on biological plausibility, literature support, and those showing a univariate association ($p < 0.10$) with the outcome. The following covariates were adjusted for: CURB-65 score, Blood pressure (hypotension), CRP level, Timing of hospitalization, Presence of comorbidities (hypertension, diabetes), Age, and sex.

The final model was refined using **stepwise forward selection**. Receiver operating characteristic (ROC) curve analysis was employed to assess the diagnostic performance of cortisol levels. A two-tailed p-value <0.05 was considered statistically significant.

Ethical Consideration

The study received ethical approval from the Institutional Review Board (IRB) of Dhaka Medical College before commencement (memo No. ERC-DMC/ECC/2024/180). Written informed consent was obtained from all participants or their legal representatives. Participant confidentiality was strictly maintained, and all data were anonymized during analysis to ensure privacy and compliance with ethical research standards.

Results

A total of 92 patients with community-acquired pneumonia (CAP) were included in the study.

Serum Cortisol and Mechanical Ventilation

There was a statistically significant association between admission serum cortisol levels and the need for mechanical ventilation. Patients with high cortisol levels (>23 mcg/dL) had a markedly higher requirement for ventilation (14/44; 31.8%) compared to those with normal cortisol (2/48; 4.2%) ($p = 0.001$) (Table I).

Table I. Association of Serum Cortisol Levels with Requirement for Mechanical Ventilation (N = 92)

Mechanical Ventilation	Normal Cortisol (≤23 mcg/dL)	High Cortisol (>23mcg/dL)	Total	p-value\
Required	2 (4.2%)	14 (31.8%)	16 (17.4%)	0.001
Not Required	46 (95.8%)	30 (68.2%)	76 (82.6%)	
Total	48 (100%)	44 (100%)	92 (100%)	

Socio-Demographic and Clinical Variables

Timing of hospitalization was strongly associated with ventilation status. Patients admitted late (≥48 hours after symptom onset) were significantly more likely to require ventilation ($p < 0.001$). No significant associations were observed with age, sex, education level, socioeconomic status, smoking, or comorbidities. However, a trend toward higher ventilation requirements was noted among patients with hypertension and diabetes (Table II).

Table II

Socio-Demographic and Clinical History Variables by Mechanical Ventilation Status (N = 92)

Variable	Category	Mechanical Ventilation (n=16)	No Mechanical Ventilation (n=76)	Total (n=92)	p-value
Age (years)	18–40	4 (25.0%)	27 (35.5%)	31(33.7%)	0.363
	41–65	9 (56.3%)	43 (56.6%)	52 (56.5%)	
	>65	3 (18.7%)	6 (7.9%)	9 (9.8%)	
Sex	Male	6 (37.5%)	43 (56.6%)	49 (53.3%)	0.164
	Female	10 (62.5%)	33 (43.4%)	43 (46.7%)	
Education Level	Illiterate	2 (12.5%)	17 (22.4%)	19 (20.7%)	0.160
	Primary	8 (50.0%)	20 (26.3%)	28 (30.4%)	
	SSC	6 (37.5%)	29 (38.2%)	35 (38.0%)	
	HSC and above	0 (0.0%)	10 (13.2%)	10 (10.9%)	
Socioeconomic Status	Lower	15 (93.7%)	59 (77.6%)	74 (80.4%)	0.160
	Middle/Upper	1 (6.3%)	17 (22.4%)	18 (19.6%)	
Time Hospitalization	Early (<48 hrs)	0 (0.0%)	53 (69.7%)	53 (57.6%)	**<0.001**
	Late (≤48 hrs)	16 (100%)	23 (30.3%)	39 (42.4%)	
Comorbidities	None	3 (18.7%)	36 (47.4%)	39 (42.4%)	0.099
	Hypertension	8 (50.0%)	27 (35.5%)	35 (38.0%)	
	Diabetes Mellitus	5 (31.3%)	13 (17.1%)	18 (19.6%)	
Smoking Status	Yes	6 (37.5%)	38 (50.0%)	44 (47.8%)	0.363

Note: Bold p-value indicates statistically significant association ($p < 0.05$). Chi-square or Fisher's exact test was used where appropriate

Clinical Characteristics

Several clinical features were significantly associated with the need for mechanical ventilation, including tachypnea ($p < 0.001$), hypoxemia ($p < 0.001$), malaise ($p = 0.004$), confusion ($p < 0.001$), respiratory rate ≥30/min ($p < 0.001$), and hypotension (SBP <90 mmHg or DBP ≤60 mmHg; $p < 0.001$). In contrast, shortness of breath, pleuritic chest pain, pulse rate, and mean systolic/diastolic blood pressure did not differ significantly between groups (Table 3).

Table III

Association of Clinical and Examination Characteristics with need for mechanical ventilation (N = 92)

Variable	MV (N=16)%	No MV(N=76)%	Total (N=92)%	p-value
Shortness of breath	16 (100)	75 (98.7)	91 (98.9)	0.645
Pleuritic chest pain	15 (93.8)	64 (84.2)	79 (85.9)	0.319
Tachypnea	15 (93.8)	29 (38.2)	44 (47.8)	**<0.001**
Hypoxemia	15 (93.8)	8 (10.5)	23 (25.0)	**<0.001**
Malaise	9 (56.3)	16 (21.1)	25 (27.2)	0.004
Confusion	16 (100)	22 (28.9)	38 (41.3)	**<0.001**
Respiratory rate ≥30/min	14 (87.5)	16 (21.1)	30 (32.6)	**<0.001**
SBP <90 mmHg or DBP ≤60 mmHg	10 (62.5)	5 (6.6)	15 (16.3)	**<0.001**
Systolic BP (mmHg) (mean ± SD)	92.2 ± 23.6	115.0 ± 18.1	–	0.567
Diastolic BP (mmHg) (mean ± SD)	60.0 ± 15.5	79.8 ± 29.5	–	0.389

Laboratory Parameters

Patients requiring ventilation showed significantly elevated markers of inflammation and tissue injury, including total WBC count ($p = 0.042$), CRP ($p < 0.001$), LDH ($p = 0.002$), and lactate ($p = 0.002$). No significant differences were observed in serum creatinine, SGPT, SGOT, or ESR (Table IV).

Table IV

Comparison of Laboratory Parameters by Mechanical Ventilation Requirement (N = 92)

Laboratory Parameter	Ventilated (N=16) Mean ± SD	Not Ventilated (N=76) Mean ± SD	p-value
WBC (cells/ìL)	22,856 ± 2,497	16,462 ± 4,269	0.042
S. Creatinine (mg/dL)	1.46 ± 0.30	1.06 ± 0.25	0.956
SGPT (U/L)	45.0 ± 14.8	34.4 ± 17.0	0.489
SGOT (U/L)	47.8 ± 29.8	32.7 ± 21.5	0.069
CRP (mg/L)	168.4 ± 50.8	40.4 ± 52.9	**<0.001**
ESR (mm/hr)	57.9 ± 16.5	39.0 ± 18.3	0.775
LDH (U/L)	245.6 ± 133.5	157.4 ± 67.8	0.002
Lactate (mmol/L)	2.13 ± 1.12	1.18 ± 0.77	0.002

Multivariable Predictors need for mechanical ventilation

The final logistic regression model identified multiple predictors need for mechanical ventilation. CURB-65 score was the strongest predictor: compared with low-risk patients (score 0–1), those with a score of 2 had 3.7-fold increased odds, while patients with scores 3–5 had nearly 15-fold higher odds need for mechanical ventilation. High admission serum cortisol was an independent predictor, conferring more than a tenfold increase in odds compared with normal cortisol (OR = 10.733; 95% CI: 2.275–50.638; $p = 0.030$). Normal blood pressure was associated with a 90% reduction in odds compared to low blood pressure (OR = 0.099; $p = 0.012$). CRP (OR = 1.021 per unit increase; $p = 0.001$) and LDH (OR = 1.241; $p = 0.029$) were also significant predictors. The model constant was not significant ($p = 0.996$) (Table V).

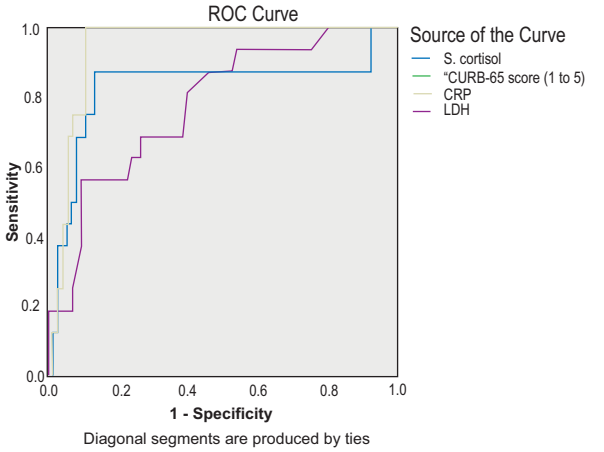
Predictive Performance (ROC Analysis)

Receiver operating characteristic (ROC) analysis demonstrated excellent predictive performance of the studied variables. CURB-65 had the highest discriminative ability for need for mechanical ventilation (AUC = 0.972), followed by CRP (AUC = 0.947), serum cortisol (AUC = 0.831), and LDH (AUC = 0.781) (Figure 1).

Table V

Final Logistic Regression Model (Stepwise Forward Selection) for Predictors of need for mechanical ventilation (N = 92)

Variable	Category	OR	95% CI	p-value
CURB-65 Score (0–5)	0–1 (Low risk) (ref)	1.00	–	–
	2 (Moderate risk)	3.68	0.99 – 5.89	0.04
	3–5 (High risk)	14.52	6.12 – 21.97	0.05
Serum Cortisol	Normal (ref)	1.00	–	–
	High (>23 mcg/dL)	10.73	2.28 – 50.63	0.03
Blood Pressure	Low systolic & diastolic (ref)	1.00	–	–
	Normal	0.09	0.02 – 0.49	0.01
CRP	Continuous (per unit ↑)	1.02	1.01 – 1.03	0.00
LDH	Continuous (per unit ↑)	1.24	0.97 – 1.31	0.03
Constant	–	73.23	–	0.10



Area Under the Curve

Test Result Variable(s)	Area
S. Cortisol	.831
"CURB-65 score (1 to 5)	.972
CRP	.947
LDH	.781

Figure 1. *Receiver Operating Characteristic (ROC) Curves for Predictors of Mechanical Ventilation*

The log-rank test demonstrated a statistically significant difference in survival distributions between the two groups ($p < 0.001$), confirming that elevated admission serum cortisol was associated with poorer in-hospital survival. Fig 2

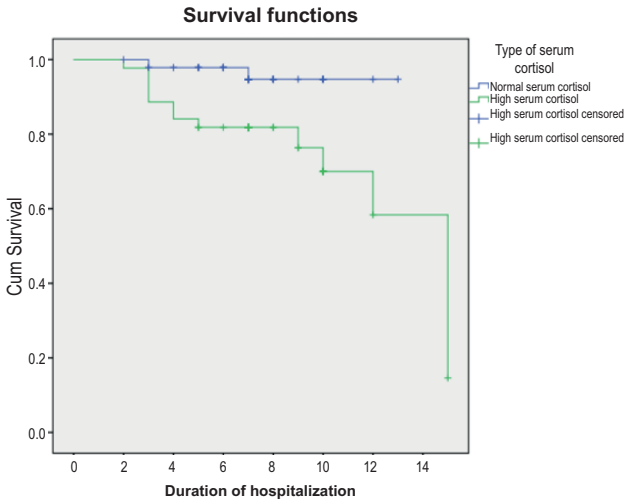


Figure 2. *Kaplan–Meier survival analysis comparing in-hospital survival between patients with normal and high admission serum cortisol levels. Patients with high cortisol had significantly lower survival compared with those with normal cortisol (log-rank test, $p < 0.001$).*

Discussion:

This prospective study demonstrates that community-acquired pneumonia (CAP) patients with elevated admission serum cortisol levels are at significantly higher risk of requiring mechanical ventilation (MV). Patients with high cortisol (>23 mcg/dL) had a much greater likelihood of MV compared to those with normal cortisol (31.8% vs 4.2%, $p = 0.001$). These findings support the role of serum cortisol as a prognostic biomarker for respiratory failure in CAP.

Cortisol is a central stress hormone, secreted in response to systemic inflammation and hypoxia through hypothalamic–pituitary–adrenal (HPA) axis activation. In CAP, the inflammatory burden and hypoxemic stress stimulate this axis, leading to increased cortisol levels that correlate with disease severity.[1,2] Prior research has shown that elevated cortisol is associated with adverse outcomes, including increased mortality, ICU admission, and greater need for organ support.[3,5,13] More recently, studies in mechanically ventilated cohorts, COVID-19 patients, and ICU populations have confirmed the association between cortisol and poor outcomes.[16,17,19,20]

In our cohort, high cortisol was an important predictor of the need for mechanical ventilation even after adjusting for CURB-65, CRP, and LDH in logistic regression. Cortisol provided good discriminative value (AUC = 0.831), complementing traditional clinical predictors such as CURB-65 (AUC = 0.972) and CRP (AUC = 0.947) in receiver operating characteristic (ROC) analysis. These findings align with other studies that admission cortisol thresholds around >23–25 mcg/dL are associated with adverse outcomes in severe CAP.[21,22] The Kaplan–Meier survival analysis further confirmed that patients with elevated cortisol had significantly poorer in-hospital survival. Together, these findings suggest that cortisol adds incremental prognostic information beyond conventional clinical scores.

Another key finding was the relationship between late hospitalization (e"48 hours after symptom onset) and the need for MV. Delayed hospitalization may exacerbate the inflammatory cascade, increase systemic stress, and further elevate cortisol levels, thereby compounding the risk of deterioration. This is consistent with prior studies emphasizing the prognostic importance of early treatment and recognition in pneumonia.[7]

Interestingly, most demographic variables, such as age, sex, and socioeconomic status, were not significantly associated with the need for mechanical ventilation. Compared to other baseline demographic risk factors, cortisol may be a more sensitive and specific indicator of impending respiratory distress.[19,20]

From a clinical perspective, routine measurement of admission cortisol could improve risk stratification in CAP. Identifying patients at risk of early decompensation would allow clinicians to prioritize intensive monitoring, timely escalation of therapy, and appropriate allocation of critical care resources—particularly valuable in resource-limited healthcare settings. In parallel, evidence from NIV studies underscores that patients predicted early for decompensation could benefit from timely ventilatory support trials.[8,9]

Conclusion

Serum cortisol is an independent predictor of mechanical ventilation and ICU admission in patients with community-acquired pneumonia. Elevated admission cortisol reflects disease severity and systemic stress, providing prognostic information that complements established scoring systems such as CURB-65 and CRP.

Limitations

This study has several limitations. First, there was a lack of generalizability as it was conducted at a single center with a modest sample size. Second, cortisol was measured only once at admission, which does not account for diurnal variation or dynamic changes over the disease course. Third, although patients with confounding conditions (e.g., steroid therapy, adrenal disorders) were excluded, other unmeasured factors may have influenced cortisol levels.

Recommendation:

Future studies should include larger, multicenter cohorts with serial cortisol measurements to capture dynamic patterns better and validate the prognostic role of cortisol in CAP. Comparative analyses of cortisol with other emerging biomarkers (e.g., procalcitonin, IL-6) may also strengthen its utility in guiding patient management.

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