ORIGINAL RESEARCH PAPER

Medical Science

CORRELATION BETWEEN SERUM CORTISOL LEVEL WITH CURB-65 SCORE AT HOSPITAL ADMISSION IN COMMUNITY-ACQUIRED PNEUMONIA PATIENTS IN HAJI ADAM MALIK GENERAL HOSPITAL MEDAN

KEY WORDS: community-acquired pneumonia, cortisol , CURB-65

Gusti Nugroho* Division of Pulmonology and Allergy Internal Medicine Department Medical Faculty, University of Sumatera Utara/ Adam Malik Hospital, Jl. Bunga Lau Medan Indonesia * Corresponding Author

Alwinsyah Abidin Division of Pulmonology and Allergy Internal Medicine Department Medical Faculty, University of Sumatera Utara/ Adam Malik Hospital, Jl. Bunga Lau Medan Indonesia

Santi Syafril Division of Pulmonology and Allergy Internal Medicine Department Medical Faculty, University of Sumatera Utara/ Adam Malik Hospital, Jl. Bunga Lau Medan Indonesia

ABSTRACT

Background : Community-acquired pneumonia (CAP) is one of the most common infectious disease and remains associated with high rates of morbidity and mortality worldwide. Optimal risk stratification remains to be evaluated. Currently, several biomarkers and prognostic scores have been evaluated to predict pognosis in CAP. The cortisol level on admission can be a useful biomarker for CAP prognosis.
Method : The study design is cross sectional correlation analytic study that involved 40 patients with signs and symptoms of CAP.
Result: From 40 samples, 23 male (57.5%) and 17 female (42.5%). There was significant difference of serum cortisol level between mild and high risk CAP ($p < 0.001$). Serum cortisol level and CURB-65 score are strongly positive correlated with correlation cefficient (r) 0.919, $p < 0.001$. A total 40 isolates were successfully isolated from blood samples with highest prevalence of Klebsiella pneumonia (22.5%), Acinetobacter baumannii (15%) followed by E.coli (10%), Burkhlderia cepacia (5%).
Conclusion: Serum cortisol level correlates to severity of CAP patients assessed by CURB-65 score.

1. INTRODUCTION

Community-acquired pneumonia (CAP) are defined as a lung parenchym infection that acquired from community with acute infection sign and symptomps and infiltrat appearance in thorax rontgen in patients with absance hospitality history in 2 weeks.1,2 Nosocomial infections cause morbidity, mortality and increased health costs. Urinary tract infection (UTI) is the most common cause of nosocomial infections2,3 and accounts for 35% - 50% of all nosocomial infections 4-7and are often associated with the use of urinary catheters in 80% of cases.[7,8]

The high mortality rate of pneumonia is often associated with improper therapy, the level of virulence of causative microorganisms, resistance to antibiotics, inaccuracy of diagnosis, and the condition of comorbidities that patients have7. Various attempts have been made to reduce the CAP mortality rate. One approach is to assess the degree of disease of the patient at the time of admission as soon as the diagnosis of CAP is established. Various predictors have been developed and tested in various countries. PSI (Pneumonia severity index) and CURB-65 (Confusion, Blood urea nitrogen, Respiratory rate, Blood pressure, Age ≥ 65 years) are validated predictors and are widely known in determining the degree of CAP disease in various countries. because the assessment of the degree of CAP that has been carried out subjectively at the time of initial entry can result in inappropriate therapy (under-estimate or over-estimate) so as to provide a worse prognosis for patients.[8-10]

In CAP patients, high serum cortisol levels at admission to the hospital are associated with a poor prognosis. The use of circulating cortisol levels as a prognostic predictor has been widely reported in various critical illnesses. A cohort study of 64 CAP patients reported a significant association between cortisol levels and Pneumonia Patient Outcome Research Team (PORT) scoring which was one type of pneumonia severity score, and the risk of death and length of hospital stay. These findings are also in accordance with a larger cohort study that identified total basal cortisol as the best independent predictor in predicting the prognosis of mild to severe CAP patients 11-13. 45 For this reason, cortisol can be used as a biomarker that is useful in predicting CAP patients [14.]

2. METHOD

This type of research was observational analytic with cross-sectional design. The number of samples obtained by 50 people with sampling is done by consecutive sampling method until the number of samples is met according to inclusion and exclusion criteria. Krteria inclusion in this study patients who had just entered the diagnosis of community pneumonia, aged over 18 years, and agreed to participate in informed consent to undergo the examination. While the exclusion criteria were recorded hospitalization in the past 10 days, patients with cystic fibrosis and active pulmonary tuberculosis, severely immunosuppressed patients, patients received steroid therapy or antifungal therapy for 14 days, patients were dehydrated at the time of admission.

Taking blood samples through the mediana cubital vein before eating in the morning at 08.00 WIB as much as 5ml was put in a sterile tube containing heparin. Examination of serum cortisol levels using the Elecsys Cortisol Reagent Kit device using the Electro Chemiluminescence Immunoassay (ECLIA) examination system performed at the Clinical Pathology laboratory at Adam Malik Hospital, Medan. Examination of sputum culture was carried out by the direct smear method where the sputum material obtained was planted into the blood agar and McConkey media.

Data will be analyzed descriptively to the frequency distribution of subjects based research on characteristics. To see the difference in mean variables between groups, an independent T-comparison test is used if it is normally distributed and if the data are not normally distributed the Mann-Whitney test is used. Furthermore, to find relationships between variables used the correlation coefficient test. Data processing and statistical tests were carried out using the SPSS program.

3. RESULT

This study was conducted during December 2017 to March 2018 and was followed by 50 patients who met the inclusion criteria. Male subjects were 23 people (57.5%) and women as many as 17 people (42.5%) with an age range between 37 to 87 years with an average age of 57.28 ± 11,728 years. On examination of sputum culture obtained as many as 26 people (65%) positive culture and 14 people (35%) negative culture results. From the results of the examination, there were 8 types of pathogens identified with the most pathogenic characteristics, respectively, were 9 people (22.5%), followed by Acinobacter baumani with 6 people (15%), Escherichia coli with 4 people (10%), B cepacia and S. haemolyticus were 2 people (5%), and the remaining one person

(2.5%) were E. cloacea, P. aeruginosa, and S. aureus. (Table 1).

Table1.Frequency distribution based on the characteristic of patients

Variable	Value
Sex (n) Male Female	 23 (57.5%) 17 (42.5%)
Age (years) (± SD)	57.28 ± 11.728
Awareness (n) Compos Mentis Confussion	23 (57.5%) 17 (42.5%)
Vital Sign(± SD) Sistolic Blood Pressure (mmHg) Diastolic Blood Pressure (mmHg) HR (x/minute) RR (x/minute) Temperature (Celcius)	107.75 ± 16.716 69.75 ± 10.739 94.35 ± 9.074 30.03 ± 2.516 37.520 ± 0.765
Laboratorium (± SD) Leukocyte (gr/dl) Ureum (mg/dl) Creatinin (mg/dl)	11.357 ± 5.377 44.88 ± 28.621 2.55 ± 3.376
Sputum Culture (n) Positive Negative	26 (65%) 14 (35%)

Examination of serum cortisol levels in the subjects of this study gave an average value of 18.08 ± 7.95 mcg / dL, with 21 people (52.5%) having serum cortisol levels in the normal range (3.2-19.4 mcg / dL) and 19 people (47.5%) having levels high cortisol (> 19.4 mcg / dL).

Descriptive analysis of the distribution of CURB-65 scores based on serum cortisol levels showed subjects having a score of 0-1 with normal cortisol levels (3.2-19.4) as many as 10 people, score 2 as many as 7 people (17.5%) and scores 3-5 as many as 4 people (10%). Whereas in the group of subjects with increased cortisol levels (> 19.4) who had a score of 0-1 as many as 0 (0%), a score of 2 (0%), and a score of 3-5 as many as 19 people(72.4%). (Table 2).

Table 2. Distribution of Serum Cortisol Levels Based on CURB-65 Score

CURB-65 Score	Serum Cortisol	
	3.2-19.4	> 19.4
0	5 (12.5%)	0 (0%)
1	5 (12.5%)	0 (0%)
2	7 (17.5%)	0 (0%)
3	4 (10.0%)	2 (5.0%)
4	0 (0%)	8 (20.0%)
5	0 (0%)	9 (22.5%)
Total	21 (52.5%)	19 (47.5%)

The mean cortisol value in subjects with a mild degree (score <2) was 8.78 ± 1,996 and at moderate to severe (score ≥ 2) was 21.18 ± 6.639. The results of the analysis with the independent T test showed a significant difference in the amount of cortisol along with the increase in the CURB-65 score (p <0.001). The relationship between serum cortisol and CURB-65 score was obtained from the Pearson correlation test with a correlation coefficient (r) value of 0.919 and p <0.001. This shows that the higher serum cortisol levels will increase the CURB-65 score. (Table 3). (table 4)

Table 3. Cortisol Mean Based on CURB-65 Score

CURB-65 Score	Mean Cortisol			
	n	Mean ± SD		p
< 2 ≥ 2	10 30	8.78 ± 1.996 21.18 ± 6.639	< 0.001	

Table 4. Relationship between Serum Cortisol and CURB-65 Score

	p	r	r^2
Cortisol with CURB-65 score	< 0.001	0.919	0.852

4. DISCUSSION

The results of this study showed that there were differences in mean cortisol values in subjects with mild degrees (CURB score <2), namely 8.78 ± 1,996 and at moderate to severe levels (CURB score ≥ 2), ie 21.18 ± 6.639. This is in accordance with the research of Martin et al. And Suresh et al .'s study in which serum cortisol levels at initial admission increased significantly in CAP compared to mild to moderate degrees (p <0.001). This study also showed a strong association between serum cortisol and the severity of CAP. Previously Remmelts et al. Also stated that there was a significant relationship between serum cortisol levels and CAP severity assessed from CURB-65 and PSI scores (p <0.05). Suresh et al. Also got the same results with a value of p <0.001.15

Cortisol is a biomarker that describes stress and cardiovascular responses. Many studies have reported an association of cortisol with CAP prognosis. In one study cortisol was found to significantly improve CURB-65 performance and was better at predicting CAP prognosis than inflammatory biomarkers of C-reactive protein (CRP) and Procalcitonin (PCT). Measurements of total cortisol and free cortisol levels are almost as good considering the measurement of free cortisol is more difficult to obtain. Another study also states that cortisol can be a biomarker that can identify the prognosis of both low and high risk patients. It is often debated about the timing of blood sampling which is associated with diurnal changes in blood cortisol concentration. However, some studies say during infectious diseases, the body often loses the circadian rhythm of cortisol 16,17.

A review study by Kolditz et al although the international guidelines recommend a clinical scoring system to determine the severity of CAP, this scoring system still has weaknesses. CURB-65 and PSI state that both are weak in predicting high-risk patients. In addition, these two systems cannot always accurately identify patients who are in a deep degree or who need intensive treatment. CURB-65 can provide good results in the elderly patient group when adding assessment of comorbid factors and patient functional status.18,19

5. CONCLUSION

In conclussion, the mean difference cortisol levels in this study shows that in mild CURB-65 scores (score 0-1) was 8.78 ± 1,996 with mean cortisol levels in moderate-severe CURB-65 scores (score 3-5) which was 21.18 ± 6.639 which was significant significantly (p <0.01). The average score of the CURB-65 score in this study was 2.85 ± 1.718, with the highest proportion of groups with severe degrees (score 3-5) as many as 23 people (57.5%), followed by mild degrees (scores 0-1) as many as 10 people (25%) , and moderate degrees (score 2) as many as 7 people (17.5%). There was a mean difference in cortisol levels in mild CURB-65 scores (score 0-1), which was 8.78 ± 1,996 with mean cortisol levels in moderate-severe CURB-65 scores (score 3-5) which was 21.18 ± 6.639 which was significantly significant (p <0.01). There is a strong positive relationship between serum cortisol levels and CURB-65 scores, with the correlation coefficient (r) being 0.919 which is significantly (p <0.01).

REFERENCE

1. Anna F, Wibisono MJ. Manajemen sepsis pada pneumonia. Majalah kedokteran respirasi. 2010; 1(2): 52-5.
2. Brown SM, Jones JP, Aronsky D, et al. Relationships among initial hospital triage, disease progression, and mortality in community acquired pneumonia. Respirology. 2012; 17(8): 1207-13.
3. Rostrepo MI, Faverio P, Anzueto A. Long term prognosis in community acquired pneumonia. Curr Opin Infect Dis. 2013; 26(2): 151-8.
4. Peto L, Nadjm Behzad. The bacterial aetiology of adult community-acquired pneumonia in Asia: a systematic review. Trans R Soc Trop Med Hyg. 2014; 108(6): 326-37.
5. Perhimpunan Dokter Paru Indonesia. Pedoman Diagnosis dan Penatalaksanaan Pneumonia Komuniti di Indonesia. 2003.
6. Marrie TJ, File TM. Epidemiology, pathogenesis and microbiology of community acquired pneumonia in adults. Uptodate. 2012.
7. Thomas M, John B. Epidemiology, pathogenesis, microbiology, and diagnosis of hospital-acquired, ventilator-associated, and health-care associated pneumonia in

adult. Uptodate. 2012.
8. Centers for Disease Control and Prevention. Pneumonia. 2016. Available at: http://www.cdc.gov/nchs/FASTATS/pneumonia.htm [Accessed May 2017]
9. Nieman LK. Adrenal Steroid Biosynthesis. Uptodate. 2013. Available at: https://www.uptodate.com/contents/adrenal-steroid-biosynthesis [Accessed May 2017]
10. Broulette J, Yu H, Pyenson B, et al. The incidence rate and economic burden of community-acquired pneumonia in working-age population. American Health and Drug. 2013; 6(8): 494-8.
11. Moghaddam MA, Bakhshi H, Rezaei B, et al. Pneumonia severity index compared to CURB-65 in predicting the outcome of community acquired pneumonia among patients referred to an Iranian emergency department: a prospective study. The Brazilian J of Infect Dis. 2012; 17(2): 179-83.
12. Rahmawati FS, Sugiri YJ, Santoso S, et al. Validitas sistem skoring tingkat keparahan dan mortalitas pneumonia komunitas dengan menggunakan PSI dan CURB-65 di Rumah Sakit Dr. Saiful Anwar Malang. Jurnal Respirologi Indonesia. 2013; 33: 26-9.
13. Mbata, GJ, Chukwuka CJ, Onyedum, C, Onwubere, BJ. The CURB-65 scoring system in severity assesment of eastern nigerian patients with community-acquired pneumonia: a prospective observational study. Primary Care Respiratory Journal. 2013; 22(2): 175-180.
14. Steel HC, Cockeran R, Anderson R, Feldman C. Overview od community-acquired pneumonia and the role of inflammatory mechanisms in the immunopathogenesis of severe pneumococcal disease. J Mediators of Inflammation. 2013. Available at: http://dx.doi.org/10.1155/2013/490346 [Accessed May 2017]
15. Chandravanshi S, Patel RK, Fala L, et al. Serum cortisol level as a predictor of severity and outcome in community acquired pneumonia. J of Evol Med Dent Scie. 2015; 4(69): 12006-9.
16. Fouda OM, Elatar SL. The association of serum total cortisol and pneumonia severity index. Saudi Med J. 2010; 31(8): 887-9.
17. Chandravanshi S, Patel RK, Fala L, et al. Serum cortisol level as a predictor of severity and outcome in community acquired pneumonia. J of Evol Med Dent Scie. 2015; 4(69): 12006-9.
18. Kolditz M, Hoffken G, Martus P, et al. Serum cortisol predicts death and critical disease independently of CRB-65 score in community-acquired pneumonia: a prospective observational cohort study. BMC Infectious Dis. 2012; 12: 90.
19. Kolditz M, Ewig S, Hoffken G. Management-based risk prediction in community-acquired pneumonia by scores and biomarkers. Eur Respir J. 2013; 41: 974-80.