PREALBUMIN AS A PREDICTOR OF MORTALITY IN COMMUNITY-ACQUIRED PNEUMONIA

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ABSTRACT

Background: Community-acquired pneumonia is an acute infection of the lung parenchyma transmitted from the community with a high mortality rate. Predictors of mortality include the Pneumonia Severity Index (PSI) and CURB-65, and the biomarkers procalcitonin and D-dimers. Prealbumin (also known as transthyretin) is a biomarker for protein calorie malnutrition and has shown a positive correlation to negative patient outcomes in several different conditions. This study aims to study how prealbumin can be used as a predictor of mortality in CAP.

Method: Articles were identified by searching 4 databases and screened for eligibility; 2 articles were eligible for this study. Assessment was done using the Quality in Prognosis Studies (QUIPS) tools and the Prognosis Critical Appraisal form.

Result: The two articles assessed in this study have found that prealbumin is correlated with negative outcomes, particularly mortality. The studies have found that the patients who died had low serum prealbumin levels at admission.

Conclusion: Serum prealbumin concentration is the preferred biomarker for protein calorie malnutrition as it is more sensitive compared to other biomarkers. There is a strong correlation between low serum prealbumin concentration upon admission with negative patient outcomes for patients with CAP. Further studies should include a wider range of subjects, specifically in age, and investigate the role of prealbumin as a predictor of malnutrition or inflammation and how it correlates to negative patient outcomes.

Keyword: prealbumin, transthyretin, community-acquired pneumonia, mortality

ABSTRAK

Latar Belakang: *Community-acquired* pneumonia adalah infeksi akut parenkim paru yang ditularkan dari komunitas dengan angka mortalitas yang tinggi. Beberapa prediktor mortalitas CAP termasuk Pneumonia Severity Index (PSI) dan CURB-65, dan biomarker prokalsitonin, dan D-dimer. Prealbumin (atau transthyretin) adalah biomarker untuk malnutrisi kalori protein dan telah menunjukkan korelasi positif dengan prognosis buruk pasien dalam beberapa kondisi yang berbeda. Penelitian ini bertujuan untuk mempelajari bagaimana prealbumin dapat digunakan sebagai prediktor mortalitas pada CAP.

Metode: Artikel diidentifikasi dengan mencari 4 database dan disaring untuk kelayakan; 2 artikel memenuhi syarat untuk penelitian ini. Assessmen dilakukan sesuai *Quality in Prognosis Studies* (QUIPS) dan formulir *Prognosis Critical Appraisal*.

Hasil: Dua artikel yang dinilai dalam penelitian ini telah menemukan bahwa prealbumin berkorelasi dengan prognosis buruk, terutama mortalitas. Kedua penelitian telah menemukan bahwa pasien yang meninggal memiliki kadar serum prealbumin yang rendah saat masuk rumah sakit.

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Kesimpulan: Kadar serum prealbumin adalah biomarker sering digunakan untuk malnutrisi protein kalori karena merupakan biomarker yang lebih sensitif dibanding biomarker yang lain. Ada korelasi kuat antara konsentrasi prealbumin serum rendah saat masuk rumah sakit dengan mortalitas untuk pasien dengan CAP. Penelitian selanjutnya harus mencakup tipe subyek yang lebih luas, khususnya usia, dan menyelidiki peran prealbumin sebagai biomarker untuk malnutrisi atau inflamasi dan korelasinya dengan mortalitas pasien.

Kata Kunci: prealbumin, transthyretin, pneumonia komunitas, mortalitas

BACKGROUND

Community-acquired pneumonia

Community-acquired pneumonia (CAP) is an acute infection of the lung parenchyma that is transmitted from the community. It is a common illness that needs to be taken seriously due to its mortality rate (2% in outpatient care, 5-20% in hospitalized patients, and at least 50% in patients in intensive care), especially in elderly patients and patients with comorbidities. In Indonesia, CAP is one of the top 10 illnesses found in inpatient care with a crude fatality rate of 7,6%.[1] Guidelines on the diagnosis and treatment of CAP were made by the Indonesian Lung Doctors Association (*Perhimpunan Dokter Paru Indonesia*) in 2014, British Thoracic Society (BTS) in 2009, and Infectious Diseases Society of America (IDSA) in 2007.[1-3]

Determining the severity of CAP in a patient is helpful in determining where and how the patient should be treated. The Pneumonia Severity Index (PSI) and CURB-65 tools were designed to predict mortality, however they are often used by clinicians to help determine if the patient should be hospitalized or not.[4-5] The PSI is recommended by IDSA guidelines while the BTS guideline recommends using the CURB-65 tool. [6] The risk factors the PSI take into account include demographic characteristics, comorbidities, physical examination findings, as well as laboratory and radiographic findings.[4] The CURB-65 is much easier to use as it only takes into account 5 factors: confusion, blood urea nitrogen, respiratory rate, blood pressure, and age.[5]

There has been increasing interest in the role of biomarkers and how it can be used for CAP. The biomarkers that have been studied include procalcitonin and C-reactive, copeptin, pro-atrial natriuretic peptide, adrenomedullin, cortisol, and D-dimers.[7-9] The biomarker that is most often used are procalcitonin as it can predict treatment failure in CAP patients, help in the differential diagnosis of bacterial and viral pneumonia, and help distinguish cases according to their severity.[8-9] The most predictive factor for mortality was found to be pro-vasopressin, although other biomarkers such as procalcitonin, pro-atrial natriuretic peptide, and D-dimers also showed a correlation to increased mortality.[7]

Prealbumin as a biomarker for patient outcome

Prealbumin, also known as transthyretin, is a plasma protein produced by the choroid plexus, liver, and enterochromaffin cells in the gastrointestinal mucosa. It is the preferred marker for protein calorie malnutrition as it can be evaluated using laboratory instruments available in all hospitals and the production of prealbumin is not affected until late stage liver disease. Prealbumin has a high ratio of essential to nonessential amino acids in the body, making it a unique marker for protein synthesis.[10] The half-life of prealbumin in plasma is approximately 2 days (compared to the 10- and 20-day half-life of transferrin and albumin, respectfully) thus it is more sensitive to changes in protein-energy status and its reflects recent dietary intake rather than overall nutritional status.[10-11]

Several studies have shown the correlation between serum prealbumin levels and patient's outcome.[10] In a study of elderly patients with dementia and aspiration pneumonia, although there was a weak correlation between levels and mortality during hospitalization, the study demonstrated that prealbumin levels were associated with six-month mortality.[12] A study of patients with heart failure found that patients with a low prealbumin level at discharge had a higher risk of six-month morbidity and mortality.[13] In a study evaluating prealbumin as a prognostic factor in elderly patients in intensive care, low levels of prealbumin were found in patients at high risk of metabolic losses associated with stress hypermetabolism.[14]

Case Illustration

A 60-year-old woman was admitted in the emergency room with chief complaint of pain on her right foot due to dropping part of her bed on it. The patient also complained of general weakness, urine that was slightly foamy and cloudy, and a fever, with an uncertain pattern of high temperatures followed by a lower temperature that felt slightly above than normal. The patient's right foot was swollen with a bulla on the dorsal side, the foot was visibly red and warm to the touch. Pain was felt with and without movement with VAS 3. The patient has a history of diabetes mellitus type 2, hypertension, as well as congestive heart failure. It was determined that she had diabetic foot with cellulitis on her right foot.

The patient was also determined to have community-acquired pneumonia CURB-65 0 due to the following findings. On physical examination, the patient was *compos mentis*, oriented to person, place, and time. Her blood pressure was 150/70, heart rate 82 bpm, respiration rate 20x/minute, temperature 37,6^{o}C, and BMI 26,67 kg/m^{2}. An incidental finding was bilateral basal coarse moist rales. Laboratory findings showed that she had a serum urea level of 26 mg/dL.

Clinical Question

In a patient with community-acquired pneumonia, what is the efficacy of prealbumin as a predictor of mortality?

METHOD

Search strategy

Databases used in this study were CINAHL plus (through EBSCOhost), ProQuest, Scopus, and Trip. The following search term was used for this study:

("community-acquired infections" AND "pneumonia") AND ("prediction" OR "prognostic factors") AND ("death" OR "mortality") AND ("prealbumin" OR "transthyretin")

The inclusion criteria were articles available in English, articles with full-text availability, studies with human subjects, and studies with adult subjects. The exclusion criteria were articles that were not available in English, articles without full-text availability, studies that used animal subjects, studies where the subjects were children, systematic reviews, meta-analyses, literature reviews, case reports and series, editorials, treatment effect modification studies, average/overall prognosis model studies, and prognostic model or risk prediction studies.

Assessment

One reviewer independently conducted the risk of bias assessment of the selected studies.[15] Risk of bias assessment was done using the Quality in Prognosis Studies (QUIPS) tool from the Prognosis Methods Group of Cochrane.[16] One reviewer independently conducted the critical appraisal of the selected studies. Critical appraisal was done according to the Prognosis Critical Appraisal form available from The Centre for Evidence-Based Medicine of the University of Oxford.

RESULT

Twelve records were found through database searching with 0 duplicates found. Twelve records were screened and 2 full-text articles were assessed for eligibility. Two articles were found to be eligible for this study. The two articles assessed in this study was "Prognosis of community acquired pneumonia (CAP): Value of triggering receptor expressed on myeloid cells-1 (TREM-1) and other mediators of the inflammatory response" by Tejera et al. in 2007 and "Hypoalbuminemia in hospitalized patients with community-acquired pneumonia" by Hedlund, JU. In 1995. The risk of bias assessment has shown that both studies had a low risk of bias. Upon critical appraisal, results of both studies can be applied to the patient in the case illustration as both the patient and the subjects in each study were relatively older and also had different comorbidities similar to the patient. The results of the studies when applied in this patient could be a strong predictor of the patient's mortality

DISCUSSION

The study by Tejera, et al. studied the usefulness of TREM-1 in the diagnosis and prognosis of patients with CAP. The study collected data during

admission of the patient while the outcome that was being investigated was whether the patient had died or was alive at discharge. One of the other prognostic values that it investigated was prealbumin, where 195 patients who were alive at discharge had a median prealbumin level of 12 mg/dL while the 21 patients who died had a median prealbumin level of 7 mg/dL. Statistical analysis was done with Mann-Whitney's *U* test; the study found a strong correlation between low serum prealbumin levels and patient death (p <0,001).[17]

The study by Hedlund did not directly study the correlation between serum prealbumin levels and mortality; the study was investigating the reasons for hypoalbuminemia in patients with CAP, with the assumption that hypoalbuminemia upon admission was correlated with acute mortality, morbidity, and later recurrences. Data was collected during admission, day-3, day-6, day-9, week-8, and month-6 after admission. The study found that there was a significant positive correlation between serum albumin and serum prealbumin levels (p <0,001). From these results, we can infer that there is a significant positive correlation between serum prealbumin levels and negative patient outcomes which include acute mortality, morbidity, and later recurrences.[18]

Prealbumin has been shown to be a sensitive marker for protein calorie malnutrition, which also makes it a useful biomarker for negative outcomes in several conditions.[10-14] The two articles assessed in this study have found that prealbumin is correlated with negative outcomes, particularly mortality. The study by Tejera, et al. have found that the patients who died had poor nutrition markers at admission such as a lower BMI, low serum albumin levels, and low serum prealbumin levels. However, the study by Hedlund found that the low serum albumin levels were a result of the inflammatory reaction and did not recommend nutritional supplementation to alter the clinical outcome of the patients. In both studies, the subjects are relatively older (all subjects in both studies were over 50 years old). While these patient characteristics are similar to that of the patient in the case illustration, the findings of these studies may not apply in younger patients.[17-18]

CONCLUSION

Serum prealbumin concentration is the preferred biomarker for protein calorie malnutrition that is more sensitive compared to other biomarkers. Previous studies have shown a positive correlation between serum prealbumin levels and negative patient outcomes, particularly mortality, in conditions such as aspiration pneumonia in elderly patients with pneumonia, patients with heart failure, and elderly patients in intensive care. There is a strong correlation between low serum prealbumin concentration upon admission with negative patient outcomes for patients with CAP. Further studies should include a wider range of subjects, specifically in age, and investigate the role of prealbumin as a predictor of malnutrition or inflammation and how it correlates to negative patient outcomes.

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