

**THE ASSOCIATION BETWEEN PROTEIN BINDING
PROPERTY OF ANTIBIOTIC AND THE PREDICTION
OF 28-DAY MORTALITY & LENGTH OF STAY FOR
HYPOALBUMINEMIA PATIENTS**

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**DISERTASI YANG DIKEMUKAKAN UNTUK
MEMPEROLEH IJAZAH
DOKTOR PAKAR PERUBATAN KECEMASAN**

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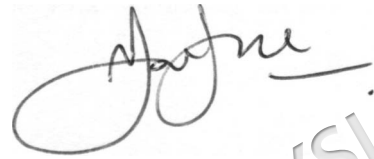
DECLARATION

I hereby declare that the work of this thesis is my own except for the quotation and summaries which have been duly acknowledge.

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ABSTRACT

INTRODUCTION: Infections are commonly seen these days in every ER. Not recognizing an infection may lead to a more sinister issue known as sepsis. Along with it, more are seen with hypoalbuminemia and the study of its implication has been very limited. According to the Surviving sepsis Campaign, antibiotic should be served within an hour once an infection it is recognized. Generally, there two groups of antibiotics, high bound and low bound group and research on this in hypoalbuminemia patients is very limited. The objective of this study is to determine the association of the type of protein bound antibiotic prescribe Emergency Department and mortality in patient with sepsis. **METHODS:** A retrospective review of medical records of 168 patients attended at the Emergency Department of HCTM, was performed. The review included patients aged 12 and above, who were diagnosed with any infection and had albumin counts less than 30 upon treatment from January 2019 till December 2019. Review of the type of antibiotic prescribed was made and each patient's 28 days outcome was documented. This study was also done to determine if the length of admission had any association to the type of antibiotic prescribed. **RESULTS:** A total of 168 patients were included in this study (n=168) [77 female (n=45.8%) and 91 males (n=54.2%)]. Of this, 125 patients were prescribed with low-protein-binding-antibiotics and 43 were prescribed high-protein-binding-antibiotic. In terms of mortality, the patients whom received low-protein-binding-antibiotic showed to have better 28 days outcome with a significant p value of 0.05. In term of length of stay, showed no significance between these two types of antibiotics, as the p value was 0.63. **CONCLUSION:** According to this study, the usage of low-protein-binding-antibiotics in hypoalbuminemia patient has shown to have greater impact in improving mortality. Despite lack of data in improving the length of stay, but the overall improvement in mortality shows there is association between mortality and type of protein-binding-antibiotic that is prescribed.

KEYWORDS

Infection, Sepsis, Hypoalbuminemia, Low-protein-binding-antibiotic, High-protein-binding-antibiotic, Mortality.

ABSTRAK

PENGENALAN: Pada masa kini, kes-kes infeksi makin kerap dilihat di kebanyakan Jabatan Kecemasan. Tidak mengenali infeksi pada awal akan menyebabkan kesan serious seperti ‘sepsis’. Seiring dengan itu, lebih banyak yang dilihat dengan hypoalbuminemia dan kajian implikasinya dalam kes “sepsis” adalah sangat terhad. Menurut Kempen Surviving Sepsis, antibiotik harus diberikan dalam masa satu jam setelah dikenalipasti. Secara amnya, terdapat dua kumpulan antibiotik, kumpulan antibiotik yang mempunyai affinity terhadap protein tinggi dan kumpulan yang memiliki affiniti rendah. Dapat diperhatikan, penyelidikan mengenai implikasi kumpulan antibiotic yang berbeza ini ke atas pesakit yang mengalami infeksi yang turut mengalami hypoalbuminemia adalah sangat terhad. Objektif kajian ini adalah untuk mengetahui kaitan antara, jika ada, di antara kumpulan antibiotic yang diberikan di Jabatan Kecemasan dan kadar kematian pada pesakit seperti di atas.

KAEDAH: Ulasan retrospektif terhadap rekod perubatan 168 pesakit yang hadir di Jabatan Kecemasan HCTM, telah dilakukan. Kajian ini merangkumi pesakit berusia 12 tahun ke atas, yang berada dalam mengalami sebarang infeksi dan mempunyai jumlah albumin kurang dari 30 semasa rawatan dari Januari 2019 hingga Disember 2019. Jenis antibiotik yang diberikan dinilai mengikut kumpulannya dan 28 hari “mortality” bagi setiap pesakit didokumentasikan. Kajian ini juga dilakukan untuk mengetahui jika tempoh kemasukan wad juga dipengaruhi oleh jenis antibiotic yang telah diberikan.

KEPUTUSAN: Sebanyak 168 pesakit dimasukkan dalam kajian ini ($n = 168$) [77 wanita ($n = 45.8\%$) dan 91 lelaki ($n = 54.2\%$)]. Dari jumlah tersebut, 125 pesakit diberi antibiotik yang mempunyai affinity protein rendah dan 43 pesakit diberi antibiotik yang mempunyai affinity protein tinggi. Dari aspek 28 hari kematian, pesakit yang mendapat kumpulan antibiotic affinity protein rendah menunjukkan hasil yang lebih baik dan juga signifikansi, dengan nilai $P < 0.05$. Dari segi jangka masa di wad, ia tidak menunjukkan kepentingan antara kedua-dua jenis antibiotik ini, kerana nilai P adalah 0.63.

KESIMPULAN: Menurut kajian ini, penggunaan antibiotic affinity protein rendah pada pesakit hypoalbuminemia telah menunjukkan kesan yang lebih besar dalam mengurangkan kadar kematian selepas 28 hari. Walaupun kekurangan data untuk menyokong implikasi kumpulan antibiotic terhadap tempoh kemasukan wad, ia adalah jelas pengurangan keseluruhan kadar kematian selepas 28 hari, menunjukkan ada kaitan antara kadar kematian dan kumpulan antibiotic yang diberikan kepada pesakit.

KATA KUNCI

Sepsis, Hypoalbuminemia, Antibiotik affiniti protein rendah, Antibiotik affinity protein tinggi, Kematian.m



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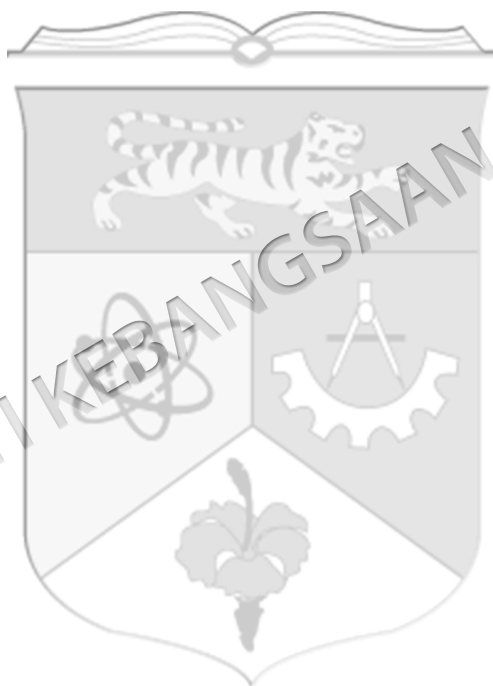
Data Collection Sheet

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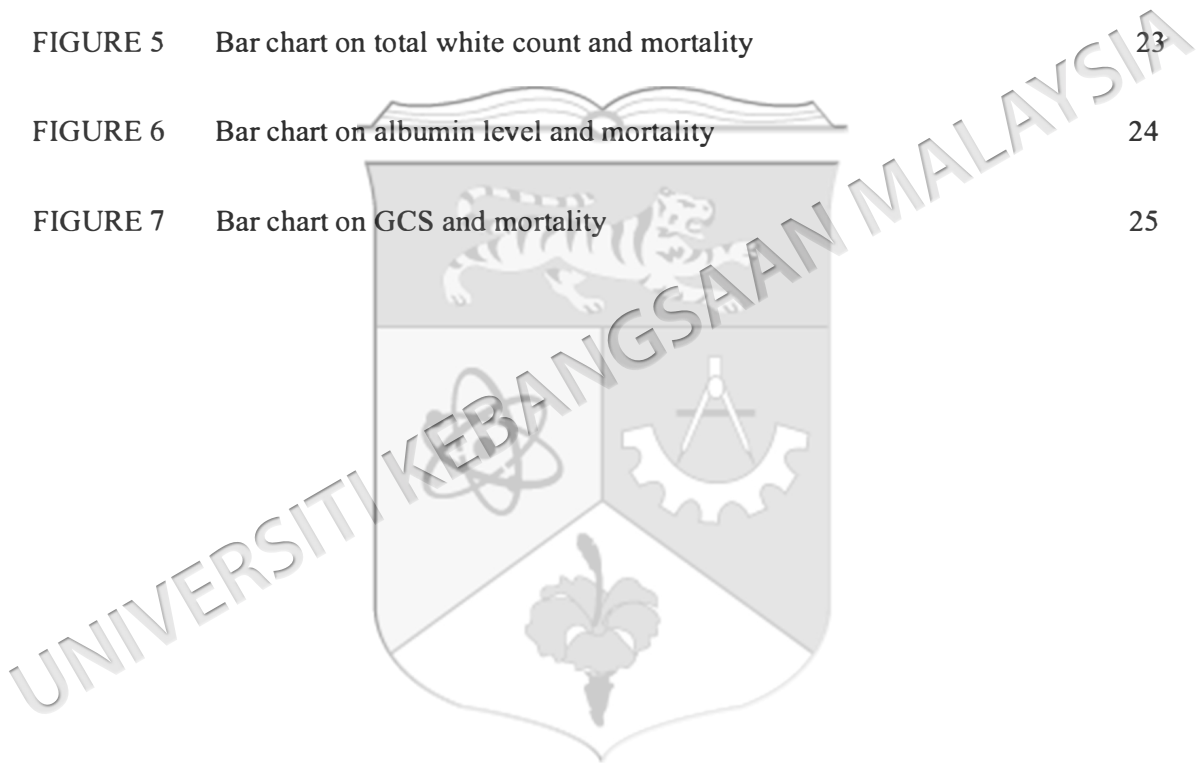
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CHAPTER 1

INTRODUCTION

Infections are seen commonly in the Emergency Department recently. Early detection of infection is needed to prevent the more serious complication such as sepsis. Years of research have dedicated in building the right tools and scores to ensure that infections are detected early and treated. Mortality increases when a patient with infection has multiple co-morbidities. This was shown in the study on Charlson Index, which shown that the one-year mortality in ED with patients with infections rose with multiple co-morbidities (Murray et al. 2006).

Amongst all the co-morbidities, hypoalbuminemia is the most studied currently. One of particular reason being, it is often seen but under-recognized in critically ill patients. Human serum albumin is mainly synthesized in the liver and it is an acute phase protein. It plays an important role as ligand-binding, transport proteins and also as antioxidants. Aside that, it maintains colloid osmotic pressure, modulates inflammatory response and may influence oxidative damage. In infections, hypoalbuminemia is commonly seen. This could be due to reduced synthesis by the liver itself or due to increased losses/proteolysis, which are all contributed by the infection itself. Recent study on hypoalbuminemia predicting mortality in Covid-19 patients, shown that hypoalbuminemia, independent of the patients Charlson index criteria, poses a greater mortality rate (Viana-Llamas et al. 2021).

In managing any infection or sepsis, the Surviving Sepsis Campaign (SSC) has advised that the administration of antibiotics should be done within an hour. Often, in the Emergency Department, a broad-spectrum antibiotic is prescribed first. Question arises if the type of protein-binding-antibiotic prescribed affects the mortality in patients? It is known that a drug

may exist in two forms, bound and unbound to proteins. The unbound drug is understood to exhibit the pharmacokinetic effect and along it is the division that can be metabolized and excreted. Protein binding of a drug may also affect its' half-life. In this case those highly protein bound drug may act as a reservoir and be slowly released to the system once the unbounded drug is fully metabolized. In sepsis, with hypoalbuminemia, one would expect to have higher fraction of unbound drugs and ideally would lead to better outcome if low bound antibiotics is prescribed in sepsis. However, with hypoalbuminemia, there would be a lost in maintaining the oncotic pressure, which usually results in plasma leakage, a fairly common complication seen in sepsis. In such cases, would type of protein-binding-antibiotic affect the mortality?



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