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ORIGINAL RESEARCH

Analysis of Oral Albumin Use and Factors Affecting the Success of its Therapy

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ABSTRACT

Hypoalbuminemia in a risk factor for medical treatment. Albumin has been shown to be a predictor in a number of studies in various settings. This research was conducted observationally to analyze the use of oral albumin and the factors that influence the success of therapy in the Lung Inpatient Room. This research was carried out by collecting secondary data via e-medical records. From the research results, the number of samples was 87 patients, 66 male patients (75.86%) were 21 female (24.14%), the largest age range was 51 - 60 years, 21 patients (24.14%). The highest body weight ranged from 61-70 kg for 50 patients (57.47%), the longest length of stay (*Length of Stay*) was 10-20 days for 45 patients (51.72%). The highest use of oral albumin was more than 100 capsules, as many as 20 patients (22.99%) with the highest duration of use being 10-19 days, namely 38 patients (43.68%). The statistical results show that there is no significant difference between before receiving oral albumin and after receiving oral albumin with a value of $P = 0.541$. Factors that influence the success of oral albumin therapy are length of stay with a value of $P = 0.001$ *. The conclusion is that there is a significant relationship between the effectiveness of oral albumin administration and length of stay.

Keywords: Oral albumin, length of stay, albumin data, effectiveness of oral albumin administration

Introduction

Albumin is a water-soluble 65kD protein (Igarashi, 2016), which is synthesized by the liver (Pratt, 2018). Albumin is the most abundant blood protein in humans, constituting about half of serum proteins, so it is responsible for blood oncotic pressure. Albumin is a major protein that has several physiological roles. Albumin accounts for approximately 80% of the colloid osmotic pressure of blood. Apart from that, albumin also functions as a transporter for various substances such as enzymes, hormones (thyroxine, cortisol, testosterone), bilirubin, drugs (Putri TD , *et a*, 2016; Gounden V , et al 2020) , Albumin forms around 50- 60% of total plasma proteins, of which 40% is found in plasma and 60% in the extracellular space. One of the most important is its role in helping maintain oncotic pressure in the vascular compartment which prevents fluid leakage in the extravascular space. The serum half-life of this molecule is approximately 20 days. Some of the main functions of albumin are binding to insoluble molecules in serum and transporting drugs and hormones. The albumin level that is considered normal varies depending on the study. Most consider hypoalbuminemia to be a serum albumin level lower than 34 or 35 g/L. Several processes control plasma albumin concentration, including the absolute rate of albumin synthesis, the rate of body catabolism, the distribution of albumin between vascular and extravascular compartments, and exogenous loss of albumin. The rate of albumin synthesis is influenced by nutrition and inflammation.

Hypoalbuminemia can be found in malnutrition (poor intake), advanced liver disease (impaired synthesis), kidney disease (increased losses), and in extreme catabolic conditions (increased damage) such as septicemia and metastatic carcinoma. Hypoalbuminemia is a abnormal conditions indicated with low levels of albumin in the blood, where albumin is the main protein that is important in the body (Mulyana et al, 2017). Associated hypoalbuminemia with poor functional status, longer duration of hospitalization as well higher morbidity and mortality (Mulyana et al, 2017; Hsu Hy, 2015). Hypoalbuminemia is known as a marker of energy malnutrition protein, but also related to infection, trauma, inflammation, liver disease,

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kidney disease and post stress surgery. Factors that associated with the risk of hypoalbuminemia (blood albumin level <3.5 g/dL) based on research, namely old age, smoking >20 cigarettes/day, stay in Nursing homes, there are two or more limitations on daily living activities - days, anemia, and diagnosed as well undergoing treatment for cancer (Kurniawan W, et al, 2014). Low albumin levels associated with improvement short-term and long-term mortality long (Akirov A , 2017). Any decrease in levels albumin in blood 0.25 g/dL associated with improvement motrality 24-56%. Rate internal albumin low blood pressure is directly proportional with an increase in the duration of patient stay. The prevalence of sufferers of hypoalbuminemia due to malnutrition in Indonesia is as big as 40-50% of patients experience or risk of hypoalbuminemia, where 12% experienced severe hypoalbuminemia .

Albumin capsules are a food supplement product that contains Ophiocephalus striatus or snakehead fish extract. This supplement is used to increase endurance in the elderly, children and pregnant women. It is an over-the-counter medication containing *Ophiocephalus striatus (snakehead fish)* extract 500 mg . The body's nutritional needs must always be met properly so as not to result in malnutrition. Nutritional adequacy may not be met solely from food consumption and support from supplement products is needed. Albumin capsules are a herbal supplement choice that is safe for consumption by all ages. This supplement contains snakehead fish extract which is rich in albumin. This supplement will help optimize the distribution of vitamins, enzymes and other important substances throughout the body. Albumin capsules can be consumed by children, pregnant women and the elderly. Albumin capsules are useful for increasing body endurance. Nutritional needs are well met because the distribution runs optimally. Apart from that, this supplement product is also useful for speeding up the wound healing process after surgery. Another benefit of this herbal supplement is that it helps build muscle mass. This product will also overcome malnutrition conditions in children and adults. Pregnant women can also feel the benefits of this supplement product, namely meeting their nutritional needs during pregnancy. This supplement can be purchased freely and must be consumed according to the dosage. Following are the dosages and how to consume supplements 1-4 capsules 3 times a day . There are several side effects that occur as a result of using this supplement , namely digestive disorders and hypersensitivity reactions Oral albumin is a drug that is not included in the National Formulary (FORNAS) so its use requires effectiveness and efficiency studies. So with the explanation above, researchers are interested in conducting research about Analysis of the use of oral albumin and the factors that influence the success of therapy. Albumin levels in the blood are influenced by several factors, namely: 1) Food Nutrients or nutritional components contained in the food eaten are used to form albumin, namely iron and protein. Intake of dietary protein and other essential nutrients must also be sufficient so that liver cells can form large amounts of albumin. 2) Liver and kidney function. Liver cells will release large amounts of albumin to meet the body's albumin needs. Poor liver function will interfere with the albumin synthesis process. Kidneys have 3 important functions, namely, filtration, reabsorption and excretion. If one or all of its functions are disrupted, the body's need for albumin will also be disrupted. 3) Disease Albumin synthesis will decrease in various diseases, especially liver disease. Plasma of patients with liver disease often shows a decreased ratio of albumin to 11 globulin. Albumin formation decreases relatively early in conditions of protein malnutrition, for example kwashiorkor.

Materials and Methode

Materials

The population in this study were patients hospitalized in soetomo hospital in the pulmonary ward who received oral albumin. Sampling was carried out within a total sampling in time limit from 1 January – 31 October 2022. The data collection method in this research was prospective. Data collection in this study used secondary data, namely from e-prescriptions from inpatients in the pulmonary inpatient room at Dokter Soetomo Hospital, Surabaya. Sampling was carried out within a time limit from January – October 2022

Methods

This research is a prospective, descriptive study to analyze the use of oral albumin and the factors that influence the success of therapy and is cross sectional by analyzing the correlation or relationship between independent variables (gender, age, weight, length of stay, main diagnosis) and dependent variable (increased albumin levels). The population in this study were patients hospitalized in the pulmonary ward who received oral albumin. Sampling was carried out within a time limit from January – October 2022. The data collection method in this research was prospective. Data collection in this study used secondary data, namely from e-prescriptions from inpatients in the pulmonary inpatient room at Dokter Soetomo Hospital, Surabaya. The variables that will be described in this study are the total number of patients, gender, body weight, age, length of stay and main diagnosis.

Data Analysis

Descriptive analysis using statistics and testing before and after administering oral albumin were analyzed using the T-Test and factors that influenced the success of therapy administering oral albumin using Chi-Square statistical analysis.

Result and Discussion

From the research results, it was found that the total number of patients who received oral albumin in the pulmonary inpatient room at Dr. Soetomo Surabaya with a sample size during the inpatient period from January to October 2022 of 87 patients, with details of 66 male patients (75.86%) and 21 female patients (24.14%) as in Figure 1.

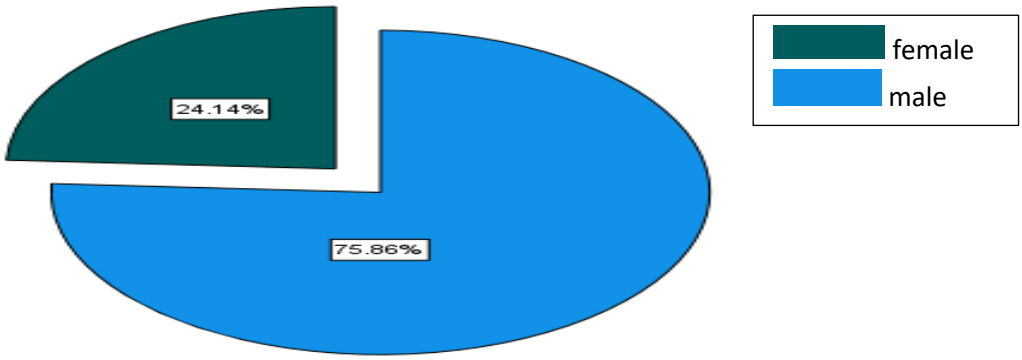

Figure 1. Gender characteristics

Based on gender characteristics, it was found that male patients had a greater risk of developing lung disease compared to female patients. This can be caused by male patients having many habits that can affect health, including smoking and drinking (alcohol) which can trigger systemic disease which can cause a decrease in kidney function and impact the quality of life (Septiwi, 2011). One behavior that has serious risks to health is smoking, which can put a person at risk of suffering from lung cancer and pulmonary tuberculosis 2 times higher than individuals who do not smoke (Benedict, et al, 2003). In general, people who smoke have a 73 percent higher risk of being infected with TB and have more than twice the potential to develop active TB (Christine, et al, 2022)

From the research results, it was found that the distribution of the highest patient weight ranged from 61-70 kg for 50 patients (57.47%), then 51-60 kg for 24 patients (27.59%), while 40-50 kg for 9 patients. (10.34%) and the remainder with body weight > 70 kg were 4 patients (4.60%) as in Figure 2.

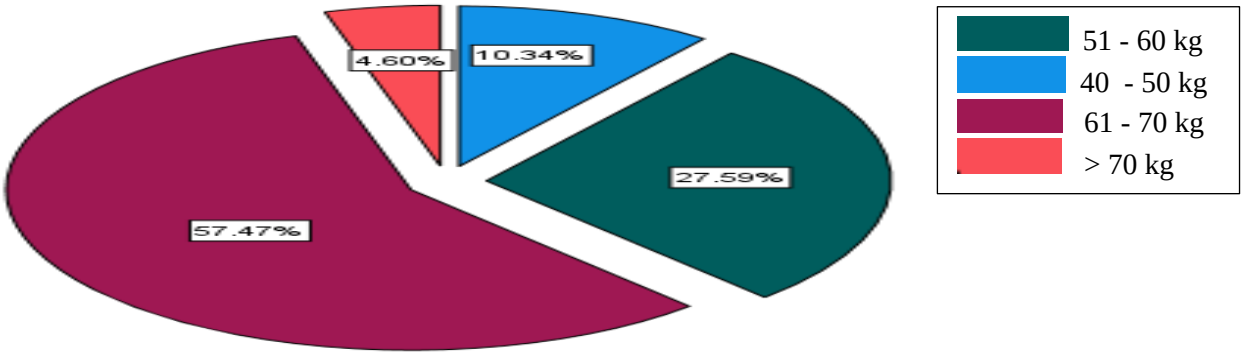

Figure 2. Patient weight distribution

In older adults aged ≥75 years a weight loss of ≥5% from the previous year (5–10% weight loss), a weight loss of ≥10% and underclassification of BMI (<18.5 kg/m2) were associated with low albumin levels. Characteristics based on patient age in the <20 years age group were 2 patients (2.30%), 9 patients aged 20 -30 years (10.34%), 16 patients aged 31 - 40 years (18.39%), 13 patients aged 41-50 years (14.94%), 21 patients aged 51-60 years (24.14%), 20 patients aged 61-70 years (22.99%) and > 70 years old as many 6 patients (6.90%) as in Figure 3.

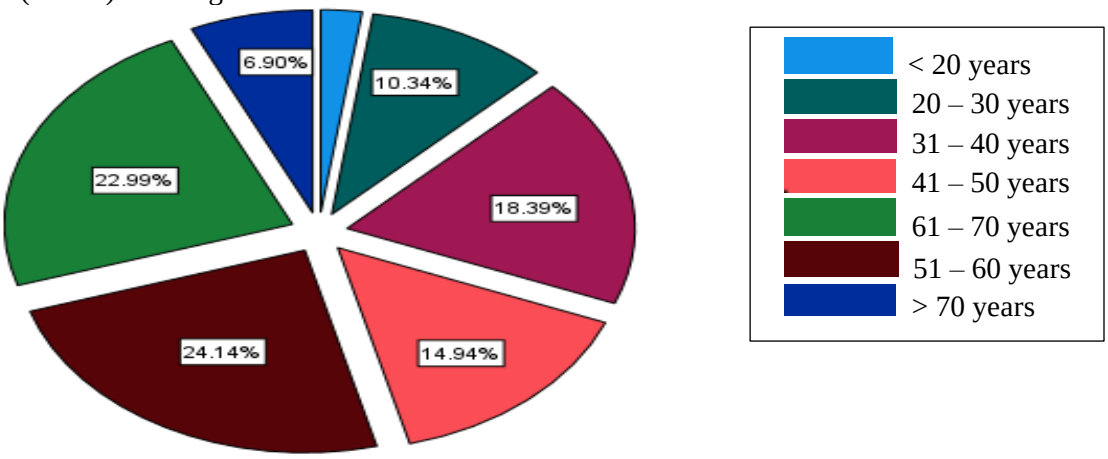

Figure 3. Patient age characteristics

At this age, age is closely related to the decline in organ function. Based on research results, the largest age groups are 51-60 years and 61-70 years based on diagnoses of lung cancer, tuberculosis and community-acquired pneumonia. With complex medical problems that are commonly found in elderly patients, this age group is vulnerable to problems that arise. related with drugs (*Drug Related Problems*) (Pramantara, 2007). A problem that elderly people often face over time is that there will be various declines in body organs. The decline in function is caused by an anatomical reduction in the number of cells as well as reduced activity, insufficient nutritional intake, pollution and free radicals, which result in all organs during the aging process experiencing structural and physiological changes

The length of stay or LOS (*Length Of Stay*) varies greatly. Patients with length of stay < 5 days were 5 people (5.75%), 5 – 10 days were 15 patients (17.24%), 10-20 days were 45 patients (51.72%), 20 – 30 days as many as 14 patients (16.09%), > 30 days as many as 8 patients (9.20%) as in Figure 4.

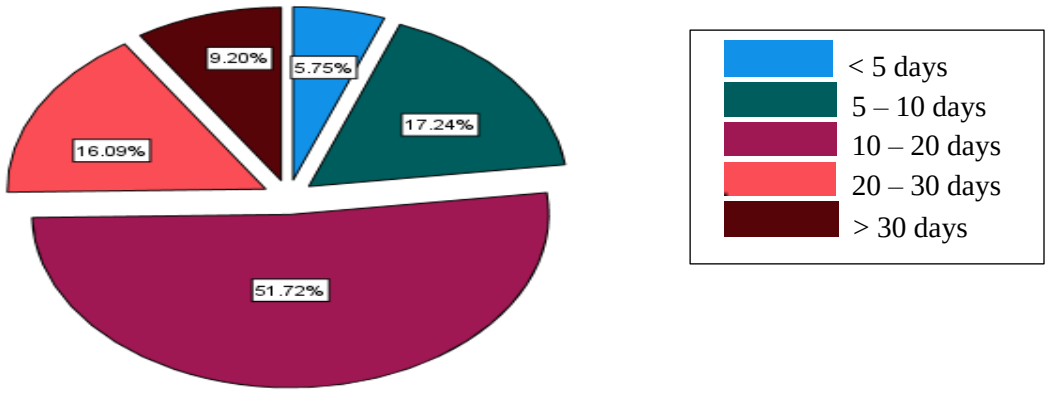

Figure 4. Long LOS (*Length Of Stay*)

From the research results, it was found that the highest length of stay (*LOS*) was 10–20 days for 45 patients (51.72%). Length of Hospitalization which describes the length of time the patient is treated. A hospital stay that is too long will cause losses, including increasing the burden of care costs for the patient or the patient's family, reducing the coverage of hospital health services, increasing *the BOR* (*Bed Occupancy Rate*) and becoming a waste for the hospital (hospital operational costs will be greater Length of hospitalization is related to initial nutritional status based on SGA (Subjective Global Assessment), BMI (Body Mass Index), nutritional intake (energy, protein, fat and carbohydrates), age, gender, treatment class, type of disease, number of disease diagnoses. , day of admission, day of discharge, and sources of costs, both related to the patient's clinical condition, medical procedures, patient management in the room and hospital administration problems can influence the delay in the patient's discharge. This will affect the length of stay (Tedja, 2012).

A prospective study conducted by *the British United Provident Association* suggests that decreased serum albumin levels may be a manifestation of preclinical cancer disease processes. In other cohort studies, investigators have reported additional examples of the prognostic role of serum albumin levels in various types of malignancies. Espinosa E et al. also reported that in patients with advanced NSCLC, low serum albumin levels correlated with poor survival. Low albumin levels also contribute to the complications associated with pulmonary TB patients because albumin is an important component of blood plasma with antioxidant activity, especially in binding free fatty acids. Pro-oxidants (free radicals) can attack cell membranes resulting in tissue damage in TB patients (Akiibinu, 2007). Apart from that, low albumin levels also indicate a poor prognosis in the treatment of TB patients (Puspitasari, 2013). Hypoalbuminemia is known to be associated with an increased risk of infection. Decreased albumin levels in pneumonia patients can occur due to a severe inflammatory reaction which causes pro-inflammatory cytokines such as interleukin 6 and 2 (IL-6 and IL-2), interferon alpha (IFN alpha) to become excessive. This situation causes capillary permeability to increase resulting in extravasation of albunin from intravascular to extravascular

The highest number of oral albumin uses during the inpatient period was 87 patients, with details of 20 patients (22.99%) using 100 or more oral albumin, then 10 patients (11.49%) using 90-99 oral albumin. -39 oral albumin in 10 patients (11.49%) and so on as in Figure 5.

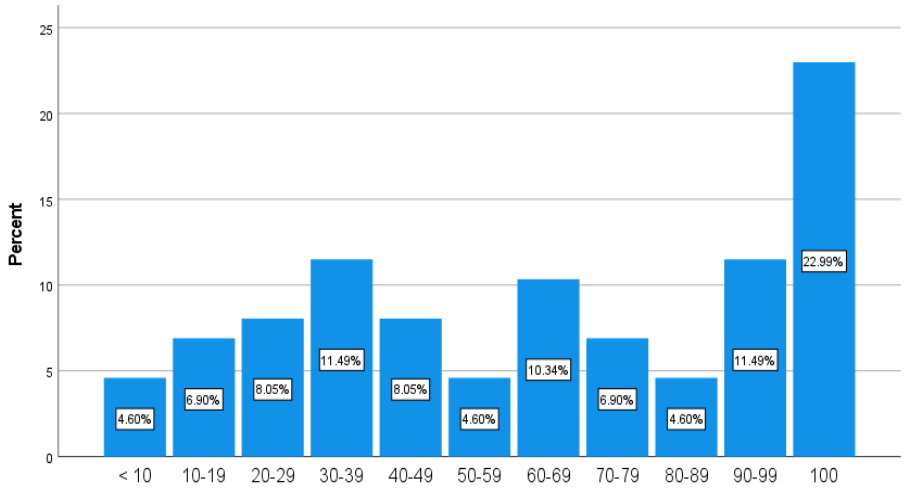

Figure 5. Number of oral albumin uses

Epidemiological data shows that the prevalence of hypoalbuminemia is influenced by age, gender, and the disease causing hypoalbuminemia. Hypoalbuminemia can occur at any age, but the prevalence increases at ages over 65 years. Several studies report a decrease in serum albumin levels in elderly women. Hypoalbuminemia is also often found in patients with critical illnesses such as Systemic Inflammation Responses Syndrome (SIRS), sepsis, and cancer. Serum albumin levels can predict morbidity, prognosis and mortality from acute illnesses, chronic illnesses or critical illnesses. (Akirov et al, 2017). Albumin is a colloidal protein, a plasma expander which plays an important role in regulating circulating blood volume. Albumin is used as a supplement therapy for hypoproteinemia, due to decreased synthesis or increased destruction/loss of albumin which endangers the sufferer's life. Albumin is also used as therapy due to disturbances in the balance of oncotic pressure and the resulting series of diseases/disorders (RSU Dr Soetomo, 2003). Albumin is an expensive drug due to market limitations and difficulties in the production process. In several studies regarding the evaluation of albumin use, discrepancies in albumin prescribing were reported.

From the research results, it was found that the highest amount of albumin consumed by patients > 100 capsules was 20 patients (22.99%). The difference in use for each patient is very different depending on the level of albumin examination. Albumin is an expensive drug due to market limitations and difficulties in the production process. In several studies regarding the evaluation of albumin use, discrepancies in albumin prescribing were reported. Until now, the use of albumin is still controversial. Its use may be based more on habit than scientific reasons. Due to its limited availability and high cost, it is important that the use of albumin is limited to indications that will clearly provide efficacy (Boldt, 2010). Albumin synthesis is stimulated by several things such as nutritional intake, insulin and oncotic pressure. Hypoalbuminemia is common in patients with heart failure, and its prevalence increases with age. Hypoalbumin can occur due to malnutrition, inflammation or other causes such as hemodilution, liver damage, protein-loss nephropathy in kidney damage, increased transcapillary escape rate, and nephrotic syndrome. The mechanism of hypoalbuminemia in cases of heart failure (HF) has not been specifically studied in HF patients. Malnutrition is a possible cause that can result from incorrect dietary habits or systemic infections. Mild hypoalbuminemia may occur due to hemodilution which is usually indicated in cases of fluid overload . Pulmonary TB patients are vulnerable to malnutrition due to poor appetite. Apart from that, infection also greatly influences the incidence of hypoalbuminemia in TB patients. (Arques and Ambrosi, 2011).

The length of time each patient uses oral albumin varies greatly. The longest duration of use was 10-19 days as many as 38 patients (43.68%) then 5 – 9 days as many as 19 patients (21.84%), < 5 days as many as 13 patients (14.94%), 20 – 29 days as many 10 patients (11.49%) and so on can be seen in Figure 6.

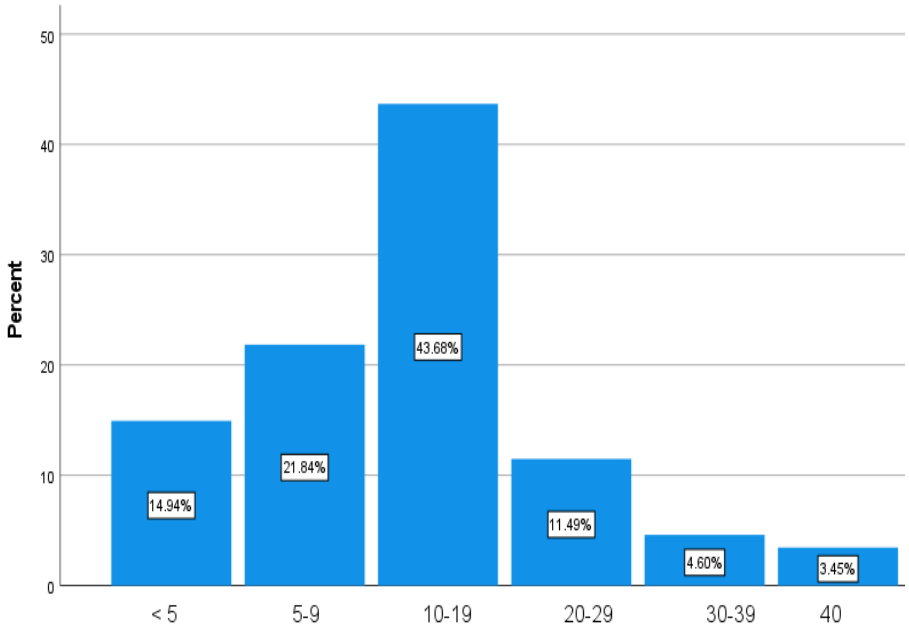

Figure 6. Duration of oral albumin use

The administration of albumin is adjusted to the patient's clinical condition, namely if the serum albumin is <2.5 g/dl up to a level of 3.5 g/dl. The effectiveness of albumin administration was assessed based on the increase in serum albumin after albumin administration. In this study, the oral albumin given had the same levels for each patient.

Evaluate the use of oral albumin by comparing the labamine levels before administering oral albumin and after administering oral albumin. The results of statistical analysis using the *T-Test* show that the value is not significant, namely $P = 0.541$. This shows that there is no significant difference between before receiving oral albumin and after as in table 1.

Table 1. Albumin data before and after receiving oral albumin

Category	*P*
Albumin data before administration of oral albumin Albumin data after oral administration of albumin	0.541

Note: *significant, P value <0.05

Oral albumin is a supplement made from snakehead fish (Ophiocephalus stiratus) extract which has a high albumin content which is useful for developing new cells (Dwijayanti et al., 2016). The high albumin content of snakehead fish extract can be useful as a source of amino acids needed in albumin synthesis. According to Nugroho (2016), administering snakehead fish extract albumin capsules is effective in increasing albumin levels in hypoalbuminemic patients and reducing the length of treatment and costs incurred in hypoalbuminemic patients.

The results of this study indicate that oral administration of albumin did not show significant results in increasing albumin levels. This is very different from previous research which showed that giving oral albumin therapy has been proven to be effective in increasing blood albumin levels at a more affordable price compared to albumin injections (Asfar et al., 2014; Nugroho, 2016). The insignificant results between before getting albumin and after getting albumin could be caused by various factors, including firstly the dose given was inadequate. On average, patients receive oral albumin at a dose of 3x1 capsule, whereas based on the literature the dose given is 3x2 capsules with a minimum administration time of 14 days or 2 weeks. Another study conducted by Heru, et al in 2019 at a hospital in Central Java found that supplementation with snakehead fish (Channa Striata) extract of 3x500 mg/day for 21 days was effective in increasing albumin levels and significantly speeding up the time of remission in children with the syndrome. nephrotic. Nephrotic syndrome is characterized by proteinuria, which is the loss of protein through urine.

Albumin is a type of protein that is often involved in proteinuria in patients with nephrotic syndrome (Herumuryawan & Hardaningsih, 2017). Research conducted by Mulyana, et al in 2017 regarding the effect of giving snakehead fish extract on albumin levels in hypoalbuminemia patients, proved that giving snakehead fish extract for 14 days can increase albumin levels in hypoalbuminemia patients. (Mulyana, Setiati, Maritini, Harimurti, & Dwimartutie, 2017). Similar to research conducted by Fadhilah TM and Sari EM in 2021, treatment with snakehead fish and egg whites for 15 days can increase albumin levels (Fadhilah & Sari, 2021). The second factor is that the most common symptoms of disease in the pulmonary inpatient room are coughing, weakness, lack of appetite, weight loss, this is highly correlated with decreased appetite, causing patients to experience malnutrition. Fourth, patients with chronic diseases are susceptible to hypoalbuminemia. The five abnormal albumin levels in this study can be influenced by several factors such as age, consumption of tuberculosis drugs for a long period of time which causes problems with liver function which affects the synthesis of albumin itself, poor diet and consumption of less nutritious food. Sixth, consumption of drugs that are bound to protein causes albumin levels in the body to decrease.

Snakehead fish extract can be a source of high protein oral nutrition, contains high levels of fatty acids, amino acids, vitamins and minerals so it has various benefits such as being a source of nutrition with high protein intake to synthesize albumin, antioxidant and anti-inflammatory functions (Radjatadoe, Suwondo, & Sumarni , 2021). Consuming snakehead fish which is rich in protein can provide an additional source of protein to replace protein lost through proteinuria, thereby increasing albumin levels in the blood. Snakehead fish is a good source of protein. Although proteins consumed from snakehead fish may not directly address proteinuria, they may contribute to an increase in overall albumin levels. (Herumuryawan & Hardaningsih, 2017)

To see what factors can influence the success of therapy using oral albumin, statistical analysis was carried out using the *Chi-Square test* . From the results of this analysis, a P value was obtained that was less than 0.05, namely length of stay, namely p=0.001, where the independent variables contributed 21.7% to changes in albumin levels as in table 2

Table 2. Factors that influence the success of oral albumin therapy

Category	*P*
Gender	0.714
Age	0.964
Weight	0.331
Length of hospitalization	0.001 *
Amount of albumin taken	0.182
Taking albumin for a long time	0.066
Adjust R square	0.217

Note: *significant, P value <0.05

Corti *et al* ., examined more than 4000 outpatients and found that a decrease in serum albumin levels had a close correlation with increased mortality, especially in women. Meanwhile, Herrman *et al* . found that low serum albumin levels were a predictor of death in 50% of internal medicine patients whose albumin levels were measured. In critical illness, the acute physiologic risk and chronic health evaluation (APACHE III) score including serum albumin levels shows a strong inverse correlation between serum albumin and mortality in critically ill patients. Owen *et al* ., have shown that low serum albumin concentrations in hemodialysis patients are a strong predictor of mortality. However, not everyone agrees with the results of the study. Law *et al* ., found no correlation of serum albumin levels with mortality in more than 21,000 men at a medical center in London, and a study in the Netherlands also showed no significant association of serum albumin levels with the risk of cardiovascular disease or all-cause mortality. Djousee found that low serum albumin levels correlated with increased mortality only in women. Several studies examined the dynamics of albumin levels over time. Changes in albumin from pre- to post-surgery in patients with Crohn's disease are useful, changes during the first six months of peritoneal dialysis were also significant, but in the above study from the Netherlands examining changes in albumin over three years, there was no effect on cardiovascular disease or mortality (Oster, *et al* ., 2022).

Conclusion

From results study Analysis of the use of oral albumin and the factors that influence the success of therapy can be concluded that: The total sample was 87 patients. Of the 87 patients, 66 male patients (75.86%) were 21 female patients (24.14%), the largest age range was 51 - 60 years, 21 patients (24.14%). The highest body weight ranged from 61-70 kg for 50 patients (57.47%), the longest length of stay (*Length of Stay*) was 10-20 days for 45 patients (51.72%). The highest use of oral albumin was more than 100 capsules, as many as 20 patients (22.99%) with the highest duration of use being 10-19 days, namely 38 patients (43.68%). The statistical results show that there is no significant difference between before receiving oral albumin and after receiving oral albumin with a value of $P = 0.541$. Factors that influence the success of oral albumin therapy are length of stay with a value of $P = 0.001$

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