



Albumin Use and Its Association with Nutritional Status in the Intensive Care Unit : A Narrative Review

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Abstract

Introduction: Albumin is the major protein in blood plasma that plays a pivotal role in the regulation of oncotic pressure and nutritional status, particularly in critically ill patients. Hypoalbuminemia is frequently observed in ICU patients and is associated with increased morbidity and mortality. This narrative review aims to assess the role and efficacy of albumin supplementation, administered both orally and intravenously, in supporting the nutritional status and prognosis of critically ill patients.

Methods: A literature search was conducted across the PubMed, Google Scholar, ScienceDirect, and ProQuest databases utilizing the keywords: "albumin", "critical illness", "nutrition", and "Intensive Care Unit". Articles included were those published within the last 10 years, available in English and Indonesian, and comprised review articles, clinical trials, and clinical practice guidelines. The selection process was performed through the screening of titles, abstracts, and subsequent full-text reviews. A total of 23 articles were included in this review.

Results: The literature indicates that albumin supplementation contributes to hemodynamic stability, a reduction in nosocomial infections, and improved prognosis in patients with conditions such as sepsis, ARDS, hepatic and renal dysfunction, and in post-operative states. Supplementation with snakehead fish (*Channa striata*) extract has also been reported to increase albumin levels. Accurate nutritional assessment, using tools like the Nutrition Focused Physical Exam (NFPE), Subjective Global Assessment (SGA), and biomarkers such as Total Lymphocyte Count (TLC) and Neutrophil to Lymphocyte Ratio (NLR) are essential for determining the nutritional status of critically ill patients. Specific recommendations from the ESPEN consensus and various hepatology and nephrology associations exist concerning the application of albumin in specific clinical conditions.

Conclusion: Albumin supplementation holds significant potential in supporting the nutritional status and improving the clinical outcomes of critically ill patients. Further studies are required to determine optimal protocols and the cost-effectiveness of albumin therapy in the critically ill patient population.

Keywords: Albumin, Critically ill patients, Hypoalbuminemia, Intensive Care Unit, Nutritional status

Abstrak

Pendahuluan: Albumin adalah protein utama dalam plasma darah yang memiliki peran penting dalam regulasi tekanan onkotik dan status nutrisi, terutama pada pasien sakit kritis. Hipoalbuminemia sering terjadi pada pasien ICU dan dikaitkan dengan peningkatan morbiditas serta mortalitas. Tinjauan naratif ini bertujuan untuk mengkaji peran dan efektivitas suplementasi albumin, baik secara oral maupun intravena, dalam mendukung status nutrisi dan prognosis pasien kritis.

Metode: Penelusuran literatur dilakukan melalui data basis PubMed, Google Scholar, ScienceDirect, dan ProQuest dengan kata kunci: "albumin", "critical illness", "nutrition", "ICU". Artikel yang dimasukkan merupakan publikasi dalam 10 tahun terakhir, tersedia dalam bahasa Inggris dan Indonesia, serta berupa artikel review, uji klinis, dan pedoman praktik klinis. Proses seleksi dilakukan melalui penyaringan judul, abstrak, dan pembacaan teks penuh. Sebanyak 23 artikel dimasukkan dalam tinjauan ini.

Hasil: Literatur menunjukkan bahwa suplementasi albumin berkontribusi pada stabilitas hemodinamik, pengurangan infeksi nosokomial, serta perbaikan prognosis pada pasien dengan sepsis, ARDS, gangguan fungsi hati dan ginjal, serta pascaoperasi. Suplementasi ekstrak ikan gabus juga dilaporkan meningkatkan kadar albumin. Penilaian nutrisi yang akurat, seperti NFPE, SGA, dan biomarker seperti TLC dan NLR, penting dalam menentukan status nutrisi pasien kritis. Terdapat rekomendasi spesifik dari konsensus ESPEN dan berbagai asosiasi hepatologi dan nefrologi mengenai penggunaan albumin dalam kondisi klinis tertentu.

Kesimpulan: Suplementasi albumin memiliki potensi besar dalam menunjang status nutrisi dan memperbaiki hasil klinis pasien kritis. Diperlukan studi lanjutan untuk menentukan protokol optimal dan kendala biaya dari terapi albumin pada populasi pasien kritis.

Kata kunci: Albumin, Pasien kritis, Hipoalbuminemia, Unit Terapi Intensif, Status nutrisi

Introduction

Albumin is the most abundant protein in plasma, accounting for approximately 60-75% of blood oncotic pressure. Beyond its influence on fluid distribution within body compartments, albumin also serves as a marker for malnutrition.¹ A decrease in blood albumin levels is a prognostic factor for patient morbidity and mortality. Historically, albumin has been used as a fluid therapy modality to increase intravascular volume, regulate oncotic pressure, and reduce nosocomial infections. Currently, the benefits of albumin use remain controversial, with some reports even suggesting an increase in patient mortality under certain conditions. This continues to be a subject of debate, particularly concerning the effectiveness, safety, and cost of albumin administration.^{2,3} This literature review aims to discuss the use of albumin in the management of critically ill patients, as well as the nutritional and metabolic aspects of albumin in critically ill patients.

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Methods

Literature search was conducted through the databases PubMed, Google Scholar, ScienceDirect, and ProQuest for literature reviews, clinical trials, and clinical practice guidelines using the keywords: "albumin", "critical illness", "nutrition", and "Intensive Care Unit". Included articles were published within the last 10 years and were available in English and Indonesian. The selection process was carried out by screening titles, abstracts, and full-text reading. A total of 23 articles were included in this literature review.

Results and Discussion

Albumin Physiology and Metabolism

Albumin is synthesized in the liver and secreted into the bloodstream. Approximately 30-40% of albumin in the bloodstream remains in the intravascular space, while the rest enters the interstitial space. The movement of albumin from the intravascular space to the interstitial space and vice versa is facilitated by the lymphatic system. Albumin has a large molecular weight and is negatively charged. These properties attract water from the extravascular compartment into the intravascular compartment.⁴

In normal conditions, intravascular albumin enters the interstitial space in limited amounts due to low vascular permeability. In the interstitial space, albumin functions as an antioxidant and serves as a source of amino acids for cell proliferation. Albumin that has been utilized by cells is degraded by cells in the liver.⁴

The etiology of hypoalbuminemia is multifactorial. During inflammation, pro-inflammatory cytokines increase vascular permeability to allow albumin, fibrinogen, immunoglobulins, electrolytes, and nutrients into injured tissues. Additionally, cellular utilization of albumin also increases as cells require more antioxidants and amino acids for proliferation. Consequently, albumin degradation is higher during inflammatory conditions, which can decrease blood albumin levels. For every 10 g/L decrease in serum albumin, the odds ratio (OR) of patient mortality increases by up to 137%, the risk of morbidity increases by up to 89%, and the length of hospital stay increases by up to 71%. Although blood albumin levels can be a prognostic factor for critically ill patients, the role of albumin supplementation in improving the condition of critically ill patients remains questionable to date.⁶

Nutritional Support in Critically Ill Patients

Patients admitted to the ICU for more than 48 hours should receive medical nutritional therapy. As shown in Figure 1, oral nutrition should be prioritized if the patient is able to

consume food. If oral consumption is not possible, early enteral nutrition (EEN) should be considered. Before initiating EEN, contraindications for enteral nutrition in the patient must be assessed.⁷

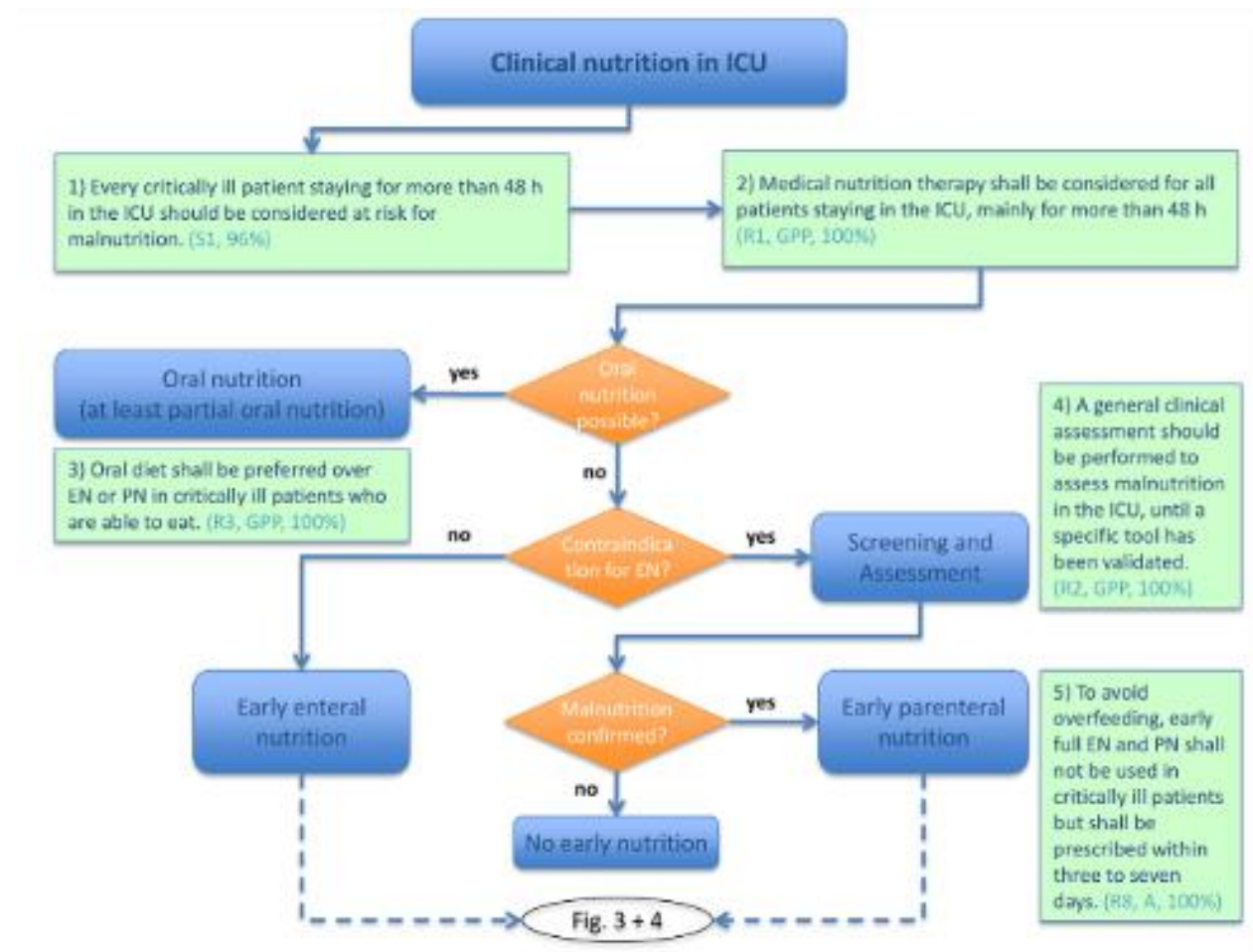


Figure 1. Nutritional Management in the ICU based on ESPEN Guidelines

Nutritional Support in Critically Ill Patients

If a patient has a contraindication for enteral nutrition, then early parenteral nutrition (EPN) should be given, provided the patient is confirmed to be malnourished. If malnutrition is not present, then early nutrition does not need to be provided. Guidance on early medical nutrition can be found in **Figure 1 and 2**.

Oral and Intravenous Albumin Supplementation

Several studies have investigated the supplementation of snakehead fish (*Ophiocephalus striatus*/Channa striatus) extract. Snakehead fish extract can increase albumin levels and may

help achieve disease remission compared to a placebo group.⁸ Administering snakehead fish extract for 14 days has been shown to increase both albumin and IGF-1 when compared to a placebo. Furthermore, snakehead fish extract has been observed to increase albumin to a higher mean value when compared to egg whites.⁹

Albumin Supplementation in Sepsis

In patients with sepsis, albumin can be utilized for fluid resuscitation and to mitigate hypoalbuminemia. The SAFE (Saline versus Albumin Fluid Evaluation) study indicated that while albumin use might lead to a reduction in

the OR of mortality, it did not demonstrate significant differences in the length of hospital stay, duration of mechanical ventilation, or the incidence of renal replacement therapy.¹⁰ The EARSS (Early Albumin Resuscitation during Septic Shock) study revealed that administering 100 mL of 20% albumin every 8 hours for 3 days significantly decreased the need for

catecholamines. Furthermore, a meta-analysis conducted by Wiedermann and Joannidis, which combined the results of the SAFE, ALBIOS (Albumin Italian Outcome Sepsis), and EARSS trials, concluded that albumin use was associated with a lower and statistically significant mortality rate.¹¹

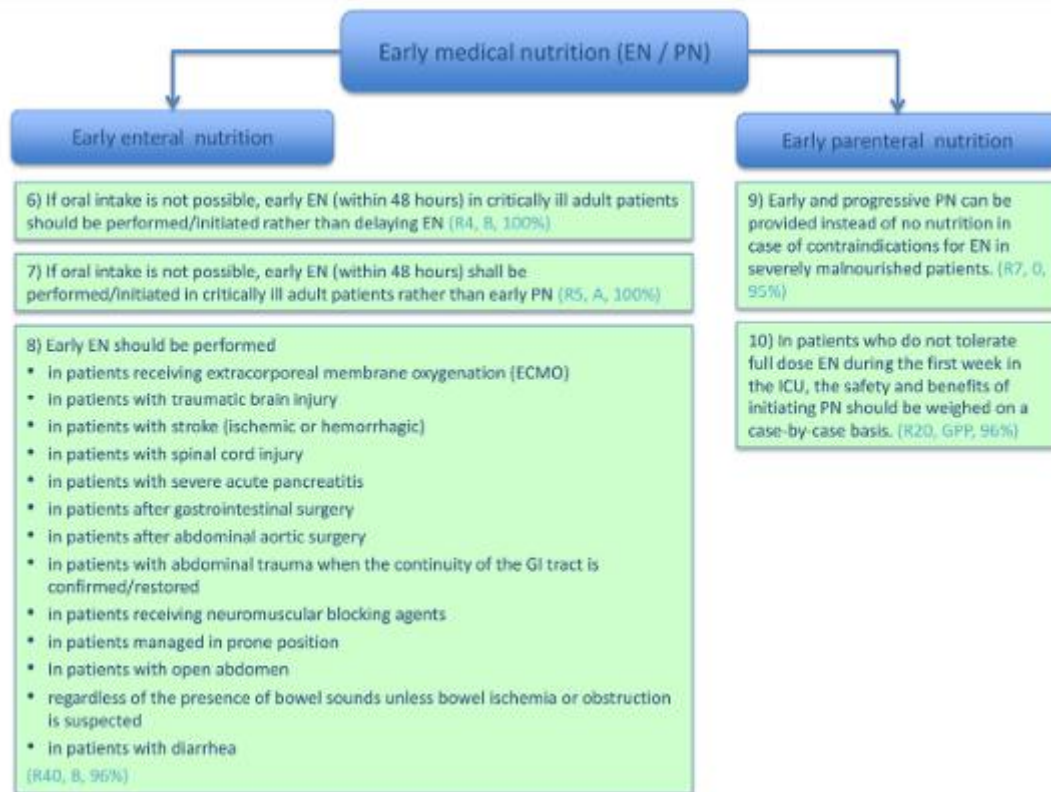


Figure 2. ESPEN Recommendations for Early Medical Nutrition

Albumin Supplementation in Acute Respiratory Distress Syndrome

In patients with acute respiratory distress syndrome (ARDS), increased alveolar-capillary barrier permeability can lead to high-protein fluid entering the alveoli. Fluid restriction, the use of furosemide, and albumin supplementation to achieve a negative fluid balance have demonstrated better oxygenation and a reduction in the need for mechanical ventilation in ARDS patients. The use of colloids can result in a decrease in alveolar-capillary permeability, tissue damage, and inflammatory cell infiltration. The combination of albumin administration with furosemide

provides better hemodynamic stability and a negative fluid balance.⁶

Albumin Supplementation in Patient with Liver Disease

In patients with hepatic cirrhosis, complications such as ascites requiring large-volume paracentesis, spontaneous bacterial peritonitis, and hepatorenal syndrome can occur. Large-volume paracentesis can lead to post-paracentesis circulatory dysfunction. However, a meta-analysis found that albumin administration did not provide a benefit in preventing the incidence of post-paracentesis circulatory dysfunction.²

Spontaneous bacterial peritonitis is generally treated with antibiotics. A study by Sort et al. investigated the combination of cefotaxime and albumin, finding that it could reduce mortality rates and the incidence of acute kidney injury (AKI) compared to cefotaxime alone.¹²

The British Society of Gastroenterology has issued recommendations regarding albumin use in patients with hepatic cirrhosis.¹³

1. For large-volume paracentesis (more than 5000 mL) performed in a single episode, plasma expansion should be given at the end of the procedure using albumin at 8 grams per liter of ascites fluid removed. This is equivalent to administering 100 mL of 20% Human Albumin Solution (HAS) for every 3 liters of ascitic fluid drained.
2. Patients with spontaneous bacterial peritonitis and elevated creatinine are advised to receive 1.5 mg/kg body weight of albumin within the first 6 hours, followed by 1 g/kg body weight on day 3.

Hepatorenal syndrome is a complication in patients with hepatic cirrhosis associated with high morbidity and mortality rates. A cumulative dose of 100 grams of albumin in patients with Type 1 hepatorenal syndrome (rapid decline in renal function, indicated by a twofold increase in serum creatinine or a minimum level of 2.5 mg/dL) can increase survival rates ($p = 0.023$).¹⁴ The German Society of Gastroenterology recommends administering 1 gram/kg body weight of albumin on the first day, followed by 20-40 g/day of albumin from day 2 to day 16.¹⁵

Albumin Supplementation in Patients Undergoing Renal Replacement Therapy

Administering 20-25% albumin can reduce the incidence of intradialytic hypotension (hypotension during hemodialysis). The RENAL RCT study, which included 1,508 critically ill patients with acute kidney injury

(AKI), showed that using 20% or 25% albumin was associated with more effective fluid removal.¹⁷

Albumin Supplementation in Abdominal Surgery

Patients undergoing abdominal surgery often experience an inflammatory reaction and the release of inflammatory mediators and cytokines, leading to increased vascular permeability. This results in the leakage of plasma albumin from capillaries and is linked to poor outcomes in surgical patients. The Chinese Society of Critical Care Medicine has issued several recommendations regarding the use of albumin in patients undergoing abdominal surgery.¹⁸

Albumin Supplementation in Cardiac Surgery

The use of a cardiopulmonary bypass machine during cardiac surgery leads to blood cell destruction, hemodilution, massive release of inflammatory mediators, increased capillary permeability, and ischemia-reperfusion injury. Patients frequently experience hemodynamic instability and hypoalbuminemia during the perioperative period of cardiac surgery, making fluid management a critical aspect to consider.¹⁸ Maintaining serum albumin levels above 4 g/L in cardiac surgery patients has also been shown to reduce the risk of acute kidney injury (AKI). A combination of albumin and crystalloids for fluid resuscitation in extracorporeal membrane oxygenation (ECMO) patients results in higher survival rates compared to using crystalloids alone.^{18,19} The fibrinogen-albumin ratio (FAR) is often used as a marker of disease severity during prothrombotic conditions. Two studies have indicated that ECMO use with a high FAR is associated with thromboembolic events. This highlights the importance of maintaining blood albumin levels while patients are on ECMO.²⁰

Nutritional Assessment in Critically Ill Patients

Critically ill patients in the ICU can experience significant weight loss, often 5-15% within the first week of admission. This weight loss and muscle wasting lead to metabolic and immune dysfunction, which can severely compromise the effectiveness of treatment, increase morbidity, prolong ICU stay, and escalate healthcare costs.⁸ A "nutrition-focused physical examination" (NFPE) is a vital component for diagnosing malnutrition. NFPE concentrates on general characteristics such as edema, muscle wasting, and subcutaneous fat loss, as well as specific micronutrient deficiencies. Another method for nutritional status assessment is the Subjective Global Assessment (SGA), a tool for evaluating malnutrition. The SGA utilizes a standardized questionnaire model for clinical history investigation and physical examination, offering a simple, inexpensive, and rapid method applicable at the patient's bedside.²¹ Other simple assessment methods include anthropometric variables: body weight, height, body mass index (BMI), triceps skinfold thickness, arm circumference, and arm muscle circumference.¹¹

Nutritional status can also be assessed using biomarkers such as TLC and NLR. TLC is recognized as a biomarker of a patient's nutritional status, as well as a prognostic factor in several clinical conditions. For this reason, TLC can be used as a single marker, and a decrease in TLC is recognized as an indicator of adverse effects and a predictor of prognosis. Lymphocyte maturation can be reduced in malnourished patients, leading to a decrease in the total circulating lymphocyte concentration to less than 1500/mm³. Interleukin and zinc are correlated with lymphocyte reduction. Therefore, adequate protein and nutrition are necessary for lymphocyte production, as protein energy malnutrition leads to decreased lymphocyte production. Furthermore, immune function is affected, increasing the risk of

infection due to impaired cell-mediated immunity and cytokine, complement, and phagocyte function. TLC levels have shown variations with the degree of malnutrition; for example, a TLC < 1,500/mm³ shows a strong correlation with malnutrition, and a TLC < 900/mm³ indicates severe malnutrition. The cut-off points used for classifying nutritional status (immunological impairment) according to TLC are: >2000 cells/mm³ (normal), 1,200 to 2,000 cells/mm³ (mild impairment), 800 to 1,199 cells/mm³ (moderate impairment), and < 800 cells/mm³ (severe impairment). Patients not at risk of malnutrition generally have a higher average TLC. TLC values correlate with upper arm circumference and triceps skinfold thickness but do not correlate with BMI, age, and calf circumference.²² In addition to TLC, the NLR is a new parameter for determining nutritional status that can be easily calculated from a complete blood count result and reflects systemic inflammation. A high NLR value in patients with malnutrition or at risk of malnutrition is caused by persistent low-grade systemic chronic inflammation.

Conclusion

Albumin is essential for maintaining fluid balance, and disturbances in its levels are common in critically ill patients due to increased capillary permeability during inflammation. Albumin supplementation should be tailored to the patient's condition, with evidence supporting its use in sepsis, hepatic cirrhosis, perioperative shock, and certain surgical settings. Nutritional support, both oral and intravenous, is important for malnourished patients as it can help restore albumin levels, improve hemodynamic stability, and reduce morbidity and mortality. Nutritional status assessment should integrate anthropometric, clinical, and laboratory parameters, including the NLR, which serves as both an inflammatory marker and a prognostic indicator, reflecting the interplay between malnutrition and systemic inflammation

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Conflicts of interest

There are no conflicts of interest.

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Daftar Pustaka

1. Allison SP, Lobo DN. The clinical significance of hypoalbuminaemia. *Clin Nutr*. 2024;43(4):909–14.
2. Melia D, Post B. Human albumin solutions in intensive care: A review. *J Intensive Care Soc*. 2021;22(3):248–54.
3. Schneider F, Dureau A, Helle S, Betscha C, Cremel G, Senger B. A Pilot Study on Continuous Infusion of 4% Albumin in Critically Ill Patients: Impact on Nosocomial Infection via a Reduction Mechanism for Oxidized Substrates. *Crit Care Explor*. 2019;1:9.
4. Soeters P, Wolfe R, Shenkin A. Hypoalbuminemia: Pathogenesis and Clinical Significance. *J Parenter Enter Nutr*. 2019;43(2):181–93.
5. Hryciw N, Joannidis M, Hiremath S. Intravenous Albumin for Mitigating Hypotension and Augmenting Ultrafiltration during Kidney Replacement Therapy. *CJASN*. 2021;16(5):820–8.
6. Saner F, Stueben B, Hoyer D, Broering D, Bezinover D. Use or Misuse of Albumin in Critical Ill Patients. *Diseases*. 2023;11(2):68.
7. Singer P, Blaser AR, Berger MM, Alhazzani W, Calder PC, Casaer MP, et al. ESPEN guideline on clinical nutrition in the intensive care unit. *Clin Nutr* [Internet]. 2019;38(1):48–79. Available from: <https://doi.org/10.1016/j.clnu.2018.08.037>
8. Muryawan MH, Soemantri A, Subagio HW, Sekarwana N. Pengaruh Suplementasi Ekstrak Ikan Gabus (*Channa Striata*) Terhadap Kadar Albumin, Kolesterol, Waktu Remisi Dan Kejadian Relaps Pada Anak Sindrom Nefrotik. *Medica Hosp J Clin Med*. 2019;6(1):7–12.
9. Mulyana R, Setiati S, Martini RD, Harimurti K. the Effect of *Ophiocephalus Striatus* Extract on Tnf-A and Tgf-B1 Levels, Dlco, and Qol in Stable Copd Patients With Muscle Wasting. *Respirology*. 2017;22(S3):175–6.
10. Finfer S, McEvoy S, Bellomo R, McArthur C, Myburgh J, Norton R, et al. Impact of albumin compared to saline on organ function and mortality of patients with severe sepsis. *Intensive Care Med*. 2011;37(1):86–96.
11. Joannidis M. Albumin Replacement in Severe Sepsis or Septic Shock. *N Engl J Med*. 2014;371(1):80–3.
12. Sort P, Navasa M, Arroyo V, Aldeguer X, Planas R, Ruiz-del-Arbol L. Effect of intravenous albumin on renal impairment and mortality in patients with cirrhosis and spontaneous bacterial peritonitis. 1999;403–9.
13. Moore KP, Aithal GP. Guidelines on the management of ascites in cirrhosis. *Gut*. 2006;55(SUPPL. 6):1–12.
14. Salerno F, Navickis RJ, Wilkes MM. Albumin treatment regimen for type 1 hepatorenal syndrome: A dose-response meta-analysis. *BMC Gastroenterol* [Internet]. 2015;15(1):1–11. Available from: <http://dx.doi.org/10.1186/s12876-015-0389-9>
15. Gerbes et al. Aktualisierte S2k-Leitlinie der Deutschen Gesellschaft für Gastroenterologie, Verdauungs- und Stoffwechselkrankheiten (DGVS). „Komplikationen der Leberzirrhose“. *Z Gastroenterol*. 2019;57(05):e168–e168.
16. Macedo E, Karl B, Lee E, Mehta RL. A randomized trial of albumin infusion to prevent intradialytic hypotension in hospitalized hypoalbuminemic patients. *Crit Care* [Internet]. 2021;25(1):1–8. Available from: <https://doi.org/10.1186/s13054-020-03441-0>
17. O'Brien Z, Finnis M, Gallagher M, Bellomo R. Early Treatment with Human Albumin Solution in Continuous Renal Replacement Patients. *Blood Purif*. 2021;50(2):205–13.
18. Yu YT, Liu J, Hu B, Wang RL, Yang XH, Shang XL, et al. Expert consensus on the use of human serum albumin in critically ill patients. *Chin Med J (Engl)*. 2021;134(14):1639–54.
19. Wengenmayer T, Schroth F, Biever PM, Duerschmied D, Benk C, Trummer G, et al. Albumin fluid resuscitation in patients on venoarterial extracorporeal membrane oxygenation (VA-ECMO) therapy is associated with improved survival. *Intensive Care Med* [Internet]. 2018;44(12):2312–4. Available from: <https://doi.org/10.1007/s00134-018-5443-y>
20. Acharya P, Jakobleff WA, Forest SJ, Chinnadurai T, Mellas N, Patel SR, et al. Fibrinogen Albumin Ratio and Ischemic Stroke during Venoarterial Extracorporeal Membrane Oxygenation. *ASAIO J*. 2020;66(3):277–82.

21. Rocha NP, Fortes RC. Total lymphocyte count and serum albumin as predictors of nutritional risk in surgical patients. *Arq Bras Cir Dig.* 2015;28(3):193–6.
22. Martin GS, Moss M, Wheeler AP, Mealer M, Morris JA, Bernard GR. A randomized, controlled trial of furosemide with or without albumin in hypoproteinemic patients with acute lung injury. *Crit Care Med.* 2005;33(8):1681–7.