MEDFARM: Jurnal Farmasi dan Kesehatan, Vol. 15, No. 1, 2026, Page 43-55
e-ISSN : 2715-9957
p-ISSN: 2354-8487

Rational Use of Human Serum Albumin and its Clinical Outcomes in Hospitalized Hypoalbuminemic Patients

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ABSTRACT

Hypoalbuminemia is defined as a serum albumin level <3.5 g/dL, with clinically significant levels <2.5 g/dL associated with increased morbidity and mortality. Human Serum Albumin (HSA) is administered to increase serum albumin levels; however, its use requires evaluation to ensure rational prescribing and optimal therapeutic outcomes. This study aimed to evaluate the pattern of HSA use, analyze changes in serum albumin levels, and determine the relationship between the rationality of HSA use and albumin level achievement in hospitalized patients with hypoalbuminemia at Bhayangkara Hospital Kediri. This observational retrospective study used medical records of patients hospitalized from January to December 2025. A total of 32 patients meeting the inclusion criteria were selected using total sampling. Data were analyzed using the Paired t-test and Chi-Square test. Most patients were male (59.37%), aged >60 years (65.63%), and hospitalized for <10 days (78.13%). Among patients receiving 20% HSA therapy, 28 patients (87.50%) received rational therapy, while 4 patients (12.50%) received irrational therapy based on the 2023 National Formulary criteria. Paired t-test analysis showed a significant increase in serum albumin levels after HSA administration ($p<0.05$). However, Chi-Square analysis showed no significant association between the rationality of HSA use and achievement of albumin level improvement ($p>0.05$). HSA therapy significantly increased serum albumin levels, although rationality of use was not significantly associated with albumin target achievement

Keyword : Evaluation, Hypoalbuminemia, Albumin

Introduction

Serum albumin is one of the essential proteins in blood plasma produced by the liver. This protein has many important roles in the body, particularly in maintaining oncotic pressure, which helps retain fluid within blood vessels. Albumin can bind free fatty acids and various toxic substances, thereby helping to prevent damage caused by oxidative stress and inflammation. Serum albumin levels are often used as indicators of nutritional status and organ function, as well as markers of the severity of acute conditions such as sepsis (Rabi et al., 2024). Low serum albumin levels are associated

with a poor prognosis in severely ill patients, including an increased risk of mortality. The decrease in albumin levels in critically ill patients is generally caused by endothelial damage and increased capillary permeability, which allows albumin to shift into the extravascular tissues. Critically ill patients often experience malnutrition, and the liver also reduces albumin synthesis during acute physiological stress, resulting in a significant decline in serum albumin levels (Jin et al., 2022).

Low albumin levels, or hypoalbuminemia, are conditions in which serum albumin levels decrease below the normal limit, generally defined as less than 3.5 g/dL. However, this condition is considered clinically significant when albumin levels fall below 2.5 g/dL. Hypoalbuminemia is commonly found in elderly patients, particularly those living in long-term care facilities or hospitalized patients. This condition is also frequently observed in patients with malnutrition or advanced chronic diseases. In certain conditions such as sepsis, severe infections, trauma, or after major surgery, albumin levels may decrease significantly by approximately 1.0–1.5 g/dL within one week. This decline occurs through several mechanisms, including decreased hepatic albumin synthesis, increased albumin loss into body tissues (interstitial space), and increased albumin catabolism. Furthermore, during inflammatory conditions, albumin production may further decrease due to the influence of inflammatory mediators such as interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor alpha (TNF-α). In many clinical cases, hypoalbuminemia results from a combination of these mechanisms (Gatta et al., 2012).

Human Serum Albumin (HSA) is one of the most expensive non-blood plasma substitute fluids compared to Hydroxyethyl Starch (HES) powder and crystalloid solutions such as sodium chloride and lactated Ringer's solution. In many hospitals, HSA is frequently administered to manage hypoalbuminemia and hypovolemia. However, the use of intravenous albumin in the management of hypoalbuminemia remains controversial because, in many cases, low albumin levels reflect a manifestation of an underlying disease rather than being the primary condition that should be directly treated (Boldt, 2010). The use of albumin remains controversial, particularly over the last two decades, as debates have intensified following the publication of a meta-analysis by the Cochrane Injuries Group Albumin Reviewers in 1998. The study demonstrated that albumin administration did not reduce mortality in critically ill patients compared with other, more economical plasma expanders such as hydroxyethyl starch (Zhou et al., 2013).The Guidelines for Albumin Use of Dr. Soetomo Regional General Hospital (PPARSDS), published in 2003, recommend albumin administration as supportive therapy in hypoalbuminemia. This condition may result from either decreased albumin production or increased albumin destruction/loss, which can endanger patients' lives due to disturbances in fluid balance, oncotic pressure, and the associated series of diseases or complications.

Based on a study conducted at Dr. Soetomo General Hospital in 2015 evaluating the use of intravenous Human Serum Albumin (HSA) vials prescribed to 100 patients

aged over 18 years, it was found that only 59% of HSA use complied with the guidelines, while the remaining 41% were considered inappropriate indications (Jatiningsih, Pramantara, & Rahmawati, 2015). Another study conducted in 2019 at dr. Zainoel Abidin Regional Hospital, Aceh, evaluated the use of Human Serum Albumin (HSA) infusion in 30 medical records of patients treated in the digestive surgery ward. The study found that only 10% of HSA administration was rational, whereas 90% was irrational based on dose appropriateness, and there was no correlation between the rationality of albumin infusion administration and the achievement of serum albumin levels (Maraiyuna et al., 2019). Another study conducted at Aceh Provincial Hospital in 2021 reported that 56.38% of patients treated with Human Serum Albumin (HSA) experienced improvement in albumin levels, as indicated by increased serum albumin levels before and after intervention (Desiyana et al., 2021).

Another study conducted in 2011 at a Teaching University Hospital in Iran evaluated 1,281 albumin vials prescribed to 135 patients and found that only 32.1% of the indications for albumin use were consistent with clinical guidelines (Jahangard-Rafsanjani et al., 2011). A similar study conducted in several hospitals in Rio de Janeiro, Brazil, reported that only one-third of albumin use met the criteria for rational use, accounting for 33.1%. Meanwhile, approximately 61.8% of albumin use did not comply with guidelines, 4.6% were considered controversial, and 0.4% could not be categorized (Matos & Rozenfeld, 2005). This study aimed to evaluate the pattern of use and albumin level outcomes of Human Serum Albumin (HSA) therapy in hospitalized hypoalbuminemia patients at Bhayangkara Hospital Kediri. The findings of this study are expected to provide information and input for healthcare practitioners in managing issues related to the use of HSA in hypoalbuminemia patients, thereby improving the quality of healthcare services. In addition, this study is expected to provide an overview of the utilization pattern of Human Serum Albumin (HSA) therapy in hypoalbuminemia patients, which may serve as a reference for future research.

Methodology

This study employed a descriptive research design with a retrospective approach. The study was conducted at Bhayangkara Hospital Kediri in January 2026. The study population consisted of all hospitalized patients diagnosed with hypoalbuminemia based on medical record data from January 2025 to December 2025, with a total sample of 32 patients. Data analysis was performed using the Paired t-test to compare changes in albumin levels before and after HSA administration and the Chi-Square test to determine the relationship between the rationality of HSA use and the achievement of serum albumin levels.

The inclusion criteria in this study were hospitalized patients diagnosed with hypoalbuminemia, patients who received Human Serum Albumin (HSA) therapy, and patients who had complete medical record data, including serum albumin laboratory results before and after HSA administration. The exclusion criteria were patients who

discontinued treatment or were discharged before completing HSA therapy, and patients who received concomitant therapies known to directly affect serum albumin levels, such as amino acid and zinc supplementation.

Result and Discussion

The evaluation of human serum albumin (HSA) use in hospitalized hypoalbuminemia patients at Bhayangkara Hospital Kediri was conducted during January 2026. The study used a retrospective design with a total sampling technique. Based on the results, the study population consisted of 108 patients diagnosed with hypoalbuminemia. Patients who met the inclusion criteria were 32 patients, who were then included as the study sample.The collected data were recorded in a Data Collection Sheet (DCS) and subsequently compiled into a master table. This study was approved by the Health Research Ethics Committee of the Institute of Health Sciences Bhakti Wiyata Kediri under ethical clearance number 1191/FF/EP/XII/2025, dated December 11, 2025. The study data were analyzed descriptively, including patient demographic characteristics, appropriateness of HSA use, and achievement of serum albumin levels.

Tabel 1. Demographic Characteris-tics of Patients

Patient Demographics	Number of Patients (n)	Percentage (%)
Gender		
Male	19	59.37%
Female	13	40.63%
Total	**32**	**100%**
Age (Years)		
18–44	5	15.62%
45–59	6	18.75%
≥60	21	65.63%
Total	**32**	**100%**
Length of Stay		
<10 Days	25	78.13%
>10 Days	7	21.87%
Total	**32**	**100%**

Hospitalized hypoalbuminemia patients at Bhayangkara Hospital Kediri were predominantly male (59.37%) compared to female patients (40.63%), with the majority aged ≥60 years (65.63%). Most patients had a length of hospital stay of less than 10 days (78.13%).Based on Table 1, male patients were more predominant (59.37%) compared to female patients (40.63%). From the data obtained, it can be seen that hypoalbuminemia was more frequently observed in male patients compared to female patients. This finding is consistent with a study conducted by Jatiningsih et al. (2015) at Dr. Soetomo General Hospital, which also reported a higher proportion of male patients (56%) compared to female patients (44%).However, a study by H. S. Oster et al. (2022) in a large observational cohort demonstrated that sex is not a predictive factor for serum albumin levels in hypoalbuminemic patients. Similarly, a large-scale observational study by Weaving et al. (2015), which analyzed more than one million albumin test results,

confirmed that the differences in serum albumin levels between males and females are relatively small and not clinically significant. Therefore, many hospitals use the same reference range for albumin levels for both sexes.The difference in the proportion of hypoalbuminemia cases based on sex in this study may be influenced by clinical conditions, comorbidities, and disease severity rather than sex itself.

Based on the age distribution data obtained, hypoalbuminemia was observed predominantly in elderly patients, accounting for 21 patients, compared to 5 patients aged 18–44 years and 6 patients aged 45–59 years. These findings indicate that older adults represent the most vulnerable group to hypoalbuminemia. Physiologically, the aging process leads to a decline in the liver's ability to synthesize albumin. A study conducted by Caso et al. (2007) demonstrated that the absolute albumin synthesis rate in elderly subjects was significantly lower, approximately 25%, compared to younger subjects, both during fasting conditions and after nutritional intake. This reduction in synthesis rate results in a smaller intravascular albumin reserve in older adults, making them more susceptible to decreased serum albumin levels.In addition to reduced albumin synthesis, elderly individuals also experience a decline in muscle mass (sarcopenia). In addition to decreased albumin synthesis, elderly individuals experience a reduction in muscle mass (sarcopenia), which serves as the body's protein reserve. Albumin plays an important role as an amino acid reservoir that can be mobilized during metabolic stress. In older adults, the reduction in muscle mass leads to diminished protein reserves. Consequently, during acute illness, inflammation, or catabolic conditions, the body is unable to maintain optimal serum albumin levels, making elderly patients more susceptible to hypoalbuminemia compared to younger age groups (Caso et al., 2007).The high incidence of hypoalbuminemia in elderly patients in this study is the result of an interaction between decreased albumin synthesis due to the aging process, reduced body protein reserves, increased comorbidities and chronic inflammation, as well as limited nutritional intake and utilization.

The majority of hypoalbuminemic patients at RS Bhayangkara Kediri had a length of hospital stay of less than 10 days.Most hypoalbuminemia patients (78.13%) at Bhayangkara Hospital Kediri who were hospitalized underwent a length of stay (LOS) of less than 10 days, while 21.87% had a LOS of more than 10 days. These results indicate that most hypoalbuminemia patients experienced relatively rapid clinical improvement after receiving intravenous albumin therapy. The predominance of hospital stays of less than 10 days may be explained by several clinical mechanisms, one of which is the improvement in serum albumin levels following HSA administration. This was demonstrated by 21 patients who experienced increased albumin levels after receiving HSA therapy. Improvement in albumin levels contributes to faster stabilization of the patient's clinical condition.Albumin plays an essential role in maintaining plasma oncotic pressure, transporting various substances, and modulating inflammatory responses. Increased albumin levels help improve fluid balance and tissue perfusion, thereby accelerating clinical recovery (Nicholson et al., 2000). This finding is supported by a study

conducted by Cuomo et al. (2025), which reported that higher albumin levels were associated with shorter hospital stays, whereas low albumin levels were related to prolonged hospitalization. However, the length of hospital stay is not solely influenced by HSA therapy, but may also be affected by factors such as disease severity, comorbidities, age, and response to other therapies. A study by Rhee et al. (2022) demonstrated that factors such as age and duration of intensive therapy significantly influenced hospital stay among hypoalbuminemia patients. Therefore, the predominance of hospitalization periods of less than 10 days may reflect that most patients had relatively mild clinical conditions or responded well to therapy.

In this study, seven patients had a length of hospital stay greater than 10 days. The dominant factor contributing to prolonged hospitalization in these patients was severe inflammation, which was experienced by all of them. Severe inflammation is a systemic immune response to trauma, infection, surgery, or chronic disease conditions, which physiologically increases the production of positive acute-phase proteins (such as CRP and fibrinogen) while simultaneously reducing hepatic albumin synthesis (Vincent et al., 2003; Soeters et al., 2019). Consequently, even though patients received human serum albumin (HSA), plasma albumin levels did not increase optimally because the liver prioritized protein synthesis for immune responses.Furthermore, severe inflammation increases capillary permeability, causing albumin leakage into the extravascular space. In critically ill patients, such as those with colonic perforation, sepsis, or post-traumatic conditions, albumin leakage becomes more pronounced, resulting in HSA therapy providing only temporary effects without significantly reducing hospitalization duration (Vincent et al., 2003). Severe inflammation also enhances protein catabolism, leading to accelerated albumin degradation. As a result, patients with tumors, diabetes mellitus, or postoperative conditions experienced persistent hypoalbuminemia.Another important factor contributing to prolonged hospitalization was advanced age (Farag et al., 2016). Elderly patients commonly experience sarcopenia, characterized by progressive loss of skeletal muscle mass and function, resulting in reduced body protein reserves. This condition makes it more difficult for the body to synthesize new albumin, causing serum albumin levels to decline more rapidly and limiting the response to HSA administration (Caso et al., 2007).In addition to these factors, the analysis identified irrational HSA administration in one patient. Inappropriate HSA use, including administration without proper indication or dosage and without addressing the underlying cause of hypoalbuminemia, has been shown to fail in improving clinical outcomes, including length of hospital stay (Vincent et al., 2003).

Table 2. Appropriateness of 20% HSA Use

Appropriateness of 20% HSA Use*	Number of Patients (n)	Percentage (%)
Rational	28	87.50%
Irrational	4	12.50%
Total	**32**	**100%**

*The appropriateness of HSA use was assessed based on the 2023 National Formulary criteria.

Observation of the utilization pattern of human serum albumin (HSA) was conducted based on the appropriateness of HSA indications according to the diagnosis of hypoalbuminemia and the National Formulary criteria. Data presented in Table 2 showed that, out of a total of 32 patients, the majority received 20% human serum albumin (HSA) therapy appropriately, with a rationality rate of 87.50%, while irrational use accounted for 12.50%.The high percentage of rational HSA use indicates that HSA administration in hospitalized hypoalbuminemia patients at Bhayangkara Hospital Kediri was generally in accordance with clinical guidelines and the applicable National Formulary policy. The irrational use of HSA observed in 5 patients was attributed to HSA administration in patients with serum albumin levels >2.5 g/dL without specific clinical conditions such as shock, pre-shock, or massive ascites. Administration of HSA at these albumin levels did not meet the indication criteria stated in the 2023 National Formulary.Albumin administration based solely on serum albumin values without considering clear clinical indications does not provide significant clinical benefit. Consequently, such therapy may be ineffective in improving patient prognosis and may increase the risk of adverse effects (Callum et al., 2024).

Tabel 3. Mean Albumin Level Before and After 20% HSA Administratition

Type of Therapy	Mean Albumin Level (g/dL)			
	Pre-Therapy Albumin Level	Post-Therapy Albumin Level	Albumin Increase	Albumin Decrease
20% HSA	2.12 ± 0.37	2.32 ± 0.38	0.20 ± 0.27	0.25 ± 0.17

The achievement of patient albumin levels in this study was assessed based on the increase in serum albumin levels. The increase in albumin levels was determined from the difference between pre- and post-HSA administration albumin values obtained from each patient’s laboratory results. The pre-albumin level refers to the last albumin measurement taken before albumin administration, while the post-albumin level refers to the first albumin measurement taken after administration of albumin, as presented in Table3, among the 32 patients who received 20% Human Serum Albumin (HSA) therapy, the majority experienced an increase in serum albumin levels after HSA administration, with a mean increase of 0.20 g/dL. This finding was lower than the results reported by Anggraini et al. (2025) at Rumah Sakit Paru Dr. H. A. Rotinsulu, which demonstrated a

mean increase in serum albumin levels of 0.473 g/dL following administration of 20% HSA.This difference may be attributed to the fact that the majority of hospitalized hypoalbuminemic patients at RS Bhayangkara Kediri were elderly patients who generally have lower albumin synthesis rates and reduced muscle mass (sarcopenia). Consequently, the body is less capable of maintaining optimal serum albumin levels, a condition that may be further aggravated by the patients' underlying clinical conditions (Caso et al., 2007).

The decrease in albumin levels shown in Table 3 was attributed to severe inflammatory conditions. During inflammation, there is an increased release of pro-inflammatory cytokines such as interleukin-6 and tumor necrosis factor-α, which suppress hepatic albumin synthesis and enhance protein catabolism (Soeters et al., 2019; Vincent et al., 2003). In addition, albumin is a negative acute-phase protein; therefore, its production decreases during an ongoing inflammatory response.As a result, although exogenous HSA is administered, it cannot be maintained in the circulation for a prolonged period because it continues to be degraded without a corresponding increase in endogenous synthesis. Furthermore, in severe inflammation, capillary permeability increases, causing albumin to shift from the intravascular compartment to the interstitial space (Farag & Ebrahim, 2016). This redistribution leads to a subsequent decrease in serum albumin levels even after an initial increase following HSA administration.Additionally, albumin distribution in the body is dynamic, with only a portion remaining in the intravascular space while the rest is located in the extravascular compartment. Therefore, the effect of HSA administration on increasing serum albumin levels tends to be temporary if not accompanied by improvement in the underlying clinical condition (Farag & Ebrahim, 2016; Vincent et al., 2003).This finding indicates that the success of albumin therapy is not solely determined by HSA administration, but is highly dependent on the management of the underlying cause of hypoalbuminemia as well as the patient's overall clinical condition.

Table 4. Results of Pre- and Post-HSA Albumin Level Analysis

Variable	Mean ± SD	n	p-value
Pre-Therapy Albumin Level	2.12 ± 0.37	32	0.000
Post-Therapy Albumin Level	2.32 ± 0.38	32	

A Paired t-test was performed to determine the difference between pre- and post-treatment albumin levels following HSA administration. The results of the Paired t-test, presented in Table 4, showed a statistically significant difference between albumin levels before and after administration of 20% Human Serum Albumin (HSA), with a p-value of <0.05.These findings indicate that administration of 20% HSA resulted in a statistically significant increase in serum albumin levels after therapy, with the mean albumin level rising from 2.12 ± 0.37 g/dL to 2.32 ± 0.38 g/dL. This result is consistent with a study conducted by Witha et al. (2024), which reported that the use of 20% human serum

albumin significantly increased serum albumin levels, with a p-value of 0.000 (<0.05). This consistency of findings strengthens the evidence that HSA therapy is effective in improving serum albumin biochemically.However, an increase in serum albumin levels does not always reflect overall clinical improvement. A study by Finfer et al. (2006) showed that albumin administration did not result in significant differences in major clinical outcomes, such as mortality or length of hospital stay, compared with crystalloid fluids in critically ill patients. The study also reported that resuscitation with either albumin or saline produced similar clinical outcomes, with no significant differences in 28-day mortality or other clinical parameters such as length of stay, organ failure incidence, or ventilator requirement (Finfer et al., 2006).

Tabel 5. Results of the Analysis of the Relationship Between the Rationality of HSA Use and Achievement of Albumin Levels

Rationality of HSA Use*	Achievement of Albumin Levels			p-Value
	Increased	Unchanged	Decreased	
Rational	23	4	1	0.203
Irrational	1	0	3	
Total	**24**	**4**	**4**	

*Rationality was assessed based on the appropriateness of 20% HSA administration according to the diagnosis of hypoalbuminemia and the criteria of the National Formulary

Analysis of the relationship between the rationality of HSA administration and albumin level achievement using the Chi-Square test showed a p-value of >0.05. These results indicate that there was no statistically significant association between the rationality of HSA use and the achievement of patients' albumin levels. These findings indicate that there was no statistically significant relationship between the rationality of human serum albumin (HSA) administration and the achievement of patient serum albumin levels. This result is consistent with a study conducted by Maraiyuna et al. (2019), which also reported no correlation between the rationality of HSA use and changes in serum albumin levels. The study showed that although rationality assessment was performed based on albumin usage guidelines, the changes in serum albumin after HSA administration were not statistically significant (p = 0.831 > 0.05).These similar findings suggest that improvement in serum albumin levels is not solely determined by the appropriateness of HSA administration. Instead, it may be influenced by various clinical factors such as underlying disease conditions, degree of inflammation, nutritional status, liver function, and altered albumin distribution due to increased capillary permeability.This can be further explained through several pathophysiological mechanisms affecting albumin distribution, metabolism, and loss in the body. In inflammatory conditions, increased capillary permeability leads to the movement of albumin from the intravascular space to the interstitial space (third spacing). This results in an expanded albumin distribution volume and a reduction in serum albumin levels, even when HSA is administered rationally. Inflammation significantly increases capillary leakage and albumin extravasation into tissues. Even in critically ill patients such as those

with sepsis, the capillary leak phenomenon persists despite intravenous albumin administration, making it difficult to achieve optimal increases in serum albumin levels (Soeters et al., 2019; Ren et al., 2026).

In addition, in critically ill patients there is an increased rate of albumin catabolism. Administered albumin is more rapidly degraded due to metabolic stress, infection, or trauma. Studies have shown that albumin half-life may be shortened and protein degradation increases during inflammatory conditions, resulting in a suboptimal response to albumin therapy (Soeters et al., 2019).Another contributing factor is ongoing albumin loss. In conditions such as sepsis, burns, or nephrotic syndrome, albumin can escape from the circulation in significant amounts. This is supported by a study by Selden et al. (2025), which demonstrated net albumin leakage into the interstitial space in ICU patients, even after albumin administration. On the other hand, hemodilution due to intravenous fluid administration may also reduce plasma albumin concentration. Although the total body albumin may increase after HSA administration, the measured serum concentration can remain low due to dilution effects (Vincent et al., 2003).Thus, the rationality of HSA use does not always correlate directly with an increase in serum albumin levels. This is because albumin levels are influenced by multiple complex factors such as inflammation, fluid distribution, catabolism, and albumin loss. Therefore, the evaluation of HSA therapy outcomes should not be based solely on serum albumin improvement but should also consider overall clinical outcomes, such as hemodynamic stability and patient clinical condition.

Based on these findings, stricter monitoring of HSA use should be implemented through more selective prescribing criteria, particularly in patients with severe inflammation or active sepsis. Clinical and laboratory parameters, including serum albumin levels, inflammatory markers, and the underlying disease condition, should be carefully evaluated before HSA administration is approved. In addition, periodic audits of HSA utilization may help identify prescriptions with limited clinical benefit, thereby reducing unnecessary healthcare expenditures. Optimization of the treatment of the underlying cause of hypoalbuminemia and adequate nutritional support should also be prioritized before considering HSA therapy, given its relatively high cost and the possibility that the increase in serum albumin levels may be only temporary in patients with severe inflammatory conditions.

Conclusion

The study showed that 87.50% of patients received rational 20% Human Serum Albumin (HSA) therapy, while 12.50% received irrational therapy based on the 2023 National Formulary criteria. The results of the Paired t-test comparing serum albumin levels before and after HSA administration demonstrated a p-value of <0.05, indicating a statistically significant difference following HSA therapy. However, the Chi-Square test analyzing the relationship between the rationality of HSA use and the achievement of

albumin levels produced a p-value of >0.05, indicating that there was no statistically significant association between the rationality of HSA use and albumin level achievement.

Declaration of Competing Interest

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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