



## PATTERN OF ALBUMIN USE AT A MAJOR TERTIARY HOSPITAL IN RIYADH

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### ABSTRACT

**Background:** Albumin is a colloidal solution that counters the major part of human plasma protein. Since use of Albumin for hospitalized patients were based on observational studies, there were a need to evaluate the unjustifiable use of albumin which may have a negative impact on both patient's clinical outcomes and health care cost.

**Method:** This is an observational retrospective and prospective study. It was conducted for a two month period to assess the use of Albumin by using a regular follow-up for albumin prescription at a major tertiary hospital in Riyadh.

**Results:** In this study which was conducted in 2019 for two month period, one thousand albumins prescriptions were reviewed retrospectively and prospectively to the implementation of the institutional guideline. Data showed that, albumin 20% was the most common prescribed concentration, majority of for albumin prescriptions were received from general medicine and emergency physicians, whereas nephrology and intensive care units physicians have the highest percentage of re-prescribing albumin. The most common indication for albumin use was under the category "others (O)" by 30% in the retrospective phase and almost by 50% in the prospective phase. A total of 40% prescriptions were not validated as per the institutional guideline. There was a significant correlation between category (O) use and inappropriate implementation of the institutional guideline between age groups in terms of the duration and indications ( $P = 0.016$ ). There was also a significant association between the ward use of albumin, specifically intensive care units and oncology, and a lack of implementation of the guideline ( $P < 0.0001$ ). The estimated cost due to unjustified use of albumin was almost 200000 SR between 5% and 20% of albumin concentrations.

**Conclusion:** Unjustified albumin use and improper implementation of institutional guideline is prevalent and correlated mainly with category (O).

**Keywords:** Albumin, Military hospital, Adult, Drug utilizations

### INTRODUCTION

Human albumin is a physiological plasma-expander and the main factor for determining the oncotic pressure of blood, and, therefore, the regulation of plasma volume and tissue

fluid balance. Albumin is also involved in the transport of numerous endogenous substances, such as unconjugated bilirubin and hormones, as well as exogenous substances, including drugs. The body content of albumin is 4-5 g/kg,

distributed predominantly in the extracellular space; 30-40% is found in the intravascular compartment (40-50 g/L of plasma) and is responsible for about 80% of the osmotic pressure of the plasma. It is not yet clear whether there is a threshold concentration of albumin below which its oncotic function compromised to a clinically relevant degree. However, there is a consensus that oncotic activity remains physiologically adequate at values of albumin  $\geq 2$  g/dL and total proteins  $\geq 3.5$  g/dL. The half-life of endogenous albumin is about three weeks, while that of blood-derived albumin is only 12–16 hours, and it is notably reduced in conditions of increased capillary permeability [1].

The solution of albumin is commonly used in clinical practice, although precise indications for albumin are not defined. The theoretical and pharmacological benefits of using human albumin solution (HAS) concomitant with a minority of reporting adverse reactions have led to an increased willingness to use HAS, and preparations of 5%, 20%, and 25% have been registered. Albumin is considered to be one of the most expensive medications, and there are often difficulties with its supply and production. Although there is considerable research regarding the use and administration of albumin, controversial indications remain [2,3]. The definition of justified use of albumin is based on the applicable local guidelines and clinical needs of patients in different institutions. However, unjustified albumin use has been reported and is considered to be a significant problem in health care systems, although the definition of unjustifiable albumin use might vary according to the institutional guideline [4]. Generally, the widespread and unjustified use of albumin has led to healthcare costs increasing; therefore, assessing and evaluating the current practice of albumin prescribing is important to improve health care outcomes, funding, and reduce the gap between both practice- and evidence-based recommendations [5]. To provide an optimal guideline for prescribing and use, a drug utilization evaluation and a comprehensive review of patients' prescription and administration processes for albumin will help to improve decision-making and patient outcomes, as well as control of health system funding. In our institution, the prevalence of unjustifiable albumin use and the detrimental cost are not well defined.

Therefore, an evaluation for albumin will take place, considering that it should only be used when indicated, and the selected concentration should be administered according to the institutional guideline refer to definition 2.2.

## MATERIALS AND METHODS

This is a biphasic observational study that took place in a tertiary hospital over two months in Saudi Arabia in Riyadh.

A standard albumin data sheet format was created and used to collect the required information. The assigned pharmacist reviewed albumin prescriptions retrospectively for one month using the standard datasheet. Retrospective prescriptions were conducted using a pharmacy pyxis report for all patients who received albumin and were randomly selected. The collected data included demographic information; gender; co-morbidities (hypertension, diabetes, dyslipidemia, coronary artery disease, atrial fibrillation, and other conditions); prescriber specialty, indication for use; and dose, concentration, and quantity of albumin administered.

Albumin administration was classified as justifiable or unjustifiable by the reviewers according to the institutional applicant guideline.

For both phases, the patient information identified by using the hospital and pharmacy System. Assessments were handled according to the hospital guideline, and any element not prescribed accordingly considered to have failed for implementation and considered unjustified.

Unfortunately, during the retrospective phase, the credibility of use cannot be achieved as per the nature of the hospital record system; due to that prospective phase was established, were additionally patient's file chart and condition can be reviewed on daily bases. Therefore the exact indication written in the pharmacy and hospital system can be reviewed for matching with the exactly written indication in the patient file and reviewing patient condition. This process was carried out by a trained pharmacist or clinical pharmacist in order to ensure consistency of the indication. The pharmacist examined the collected data and subsequently determined the justification of the data according to the hospital guideline. This study received approval from the Ethical and Research Committee.

### Data analysis

Data were encoded manually using SPSS program Version 22 for analysis. Fisher exact test or Chi-square was used to compare between qualitative independent variable. Student T-test and ANOVA were used in cases of quantitative independent variables to compare between the two groups or several groups, depending on the device used respectively other statistical tests may have been used depending on the emerging result. A P-value  $<0.05$  was used as a marker to point for significant results.

### Definitions

Albumin indications were categorized as "justifiable" or "unjustifiable" or "not available" According to the indications approved by local hospital guideline. The following indications for albumin were considered "justifiable": hepatorenal syndrome, spontaneous bacterial

peritonitis large-volume paracentesis (>5 L) and fluid resuscitation for hypovolemia and shock syndromes, intradialytic hypotension (IDH), hypoalbuminemia defined as serum <20 g/L, burn injury after 24 hours of burn and >50% TBSA, and others. Other indications, not mentioned in the hospital guideline, were considered to be unjustifiable after they were thoroughly evaluated during the prospective phase. In the event that the indication was not mentioned in the prescriptions, it was also considered to be unjustifiable after a thorough evaluation by the pharmacist using the patient's record for clarification. The dose, frequency, and concentration of albumin use, as well as completion of the prescription, were classified as "implemented" or "not-implemented" or "not available" according to the institutional guideline, if the prescription was incomplete then this was considered as "not available" and was considered to be "unjustifiable".

## RESULTS

### Baseline characteristics

At a tertiary hospital, a total of 1000 prescriptions were screened over two months. A total of 997 prescriptions were finally included and reviewed in a biphasic manner. These prescriptions were approached randomly and enrolled. Consent for approval was obtained from the Institutional

Review Board of the hospital. In the retrospective phase, a total of 500 prescriptions were reviewed by pharmacists and included, while, in the prospective phase, a total of 500 prescriptions were reviewed, and four were excluded due to a lack of data following review of the patients' charts to identify the match indications and implementation of the hospital guideline. The baseline characteristics of the admitted patients who received albumin during the retrospective and prospective phase are shown in **Table 1**. The characteristics of prescribing albumin are summarized in **Table 2**.

### Albumin use

During the retrospective phase, 500 prescriptions were reviewed for albumin use, and the most common indication was for the category "others (O)" followed by spontaneous bacterial peritonitis (SBP), hypovolemia and shock (V) (**Table 2**). The highest use of albumin was for the 20% albumin concentration. Unfortunately, assessing the validation of prescription cannot be achieved as all of these indications approved by the institutional guideline and patient file for actual use cannot be tracked retrospectively. General medicine and emergency prescribers were in the front line for albumin use, followed by nephrology and intensive care units.

**Table 1:** The baseline characteristics of the admitted patients who received albumin during the retrospective and prospective phase.

Characteristics	Prospective Phase	Retrospective Phase
Age (Years)	66 (<1 -99) <sup>a</sup>	69 (0 -102) <sup>a</sup>
Weight (kg)	65 (3 -160) <sup>a</sup>	60 (3 -160) <sup>a</sup>
<b>Gender<sup>b</sup></b>		
Male	287 (57.9)	287 (57.3)
Female	209 (42.1)	214 (42.7)
<b>Total</b>	496 (100)	501 (100)
Average use (Days) <sup>a</sup>	1 (1-29) <sup>a</sup>	287 (57.3)
Average time for prescribing Albumin	N/A	0 (0 – 5 Days) <sup>a</sup>
Average time of hospital stay (Days)*	N/A	63 (1 – 469) <sup>a</sup>

<sup>a</sup> Median (minimum-maximum), <sup>b</sup>n (%)  
\* (n = 442/501)

**Table 2:** The characteristics of prescribing albumin.

Variables	Prospective		Retrospective	
	N	(%)	N	(%)
<b>Wards</b>				
Emergency	37	7.5	24	4.8
Intensive care unit	77	15.5	78	15.6
Oncology	139	28	31	6.2
Gynecology	7	1.4	3	0.6
Surgery	31	6.3	30	6
Pediatric intensive care unit	34	6.9	3	0.6
All specialties	37	34.5	331	66
<b>Total</b>	496	-100	501	-100
<b>Intake Frequencies</b>				
- Once	117	-23.6	122	-24.4
- Twice a day	206	-69	237	-47.3
- Once a day	129	-43.5	54	-10.8
- PRN- as needed	37	-7.5	72	-14.4
- TSD- three times A day	7	-1.2	2	-0.4
<b>Total</b>	496	-100	501	-100

<b>Indications</b>				
- Hypovolemia and shock	112	-22.6	102	21
- IDH	28	-5.6	59	-11.8
- Nephrotic syndrome	15	-3	35	-7
- Burn Injury	-	-	8	-1.6
- No Indication	53	-10.7	-	-
- Plasma Exchange	3	-0.6	-	-
- Spontaneous bacterial Peritonitis	5	-1	117	-23.4
- Other, hypovolemia and shock	5	-1	-	-
- Other	275	-55.4	133	-26.5
<b>Total</b>	496	-100	501	-100
<b>Other category</b>				
- Ascitis	5	-1	-	-
- Bowel injury	1	-0.2	-	-
- Dialysis	2	-0.4	-	-
- Drain replacement	15	-3	-	-
- Hepatoctomy	2	-0.4	-	-
- Liver transplant	1	-0.2	-	-
- Low albumin	162	-32.7	-	-
- Malignancy	55	-11.1	-	-
- Obstructive jaundice	8	-1.6	-	-
- Other indication	244	-49.2	-	-
- Post dialysis	1	-0.2	-	-
<b>Total</b>	496	-100	-	-
<b>Prescriber Specialty</b>				
- Clinical hematology	5	-1	23	-4.6
- Adult cardiology	24	-4.8	8	-1.6
- Department of anesthesia	9	-1.8	-	-
- Emergency department	2	-0.4	181	-36.1
- General medicine	6	-1.2	111	-22.2
- Intensive care services	24	-4.8	22	-4.4
- Multi organ transplant center	10	-3.3	19	-3.8
- Oncology	105	-21.2	14	-2.8
- Orthopedics	2	-0.4	-	-
- Pulmonary medicine	17	-5.7	-	-
- General surgery	77	-26	79	-15.8
- Not available	203	-68	2	-0.4
<b>Total</b>	496	-100	501	-100

Following the retrospective phase, the implementation of albumin guideline for actual use was done prospectively. The highest category used were "others (O)" by 55%, followed by hypovolemia and shock (V) at 22%, whereas 11% of prescriptions were submitted without a clear indication.

All of these indications were extensively reviewed by checking patients conditions and charts to assess the credibility of actual albumin use as one of the indications allowed in hospital guideline is category O which consider to be out of context and depend on the prescriber preference. Therefore, following the review of a "category (O)" indication to identify the actual use, the majority of indications under this category were for low albumin (33%) and malignancy (11%). Assessing the implementation of the institutional guideline for appropriateness for low albumin use was as follows: 40% of indications were unjustifiable as per the hospital guideline because there were no albumin level readings in the form of patient records, and

only 30% were considered to be justified. With regards to malignancy, 16% were unjustified indications, and only up to 10% as an average was justified in terms of dosing, the correct concentration, and duration and considered to be implemented as per guideline **Table 3, Figure 1**.

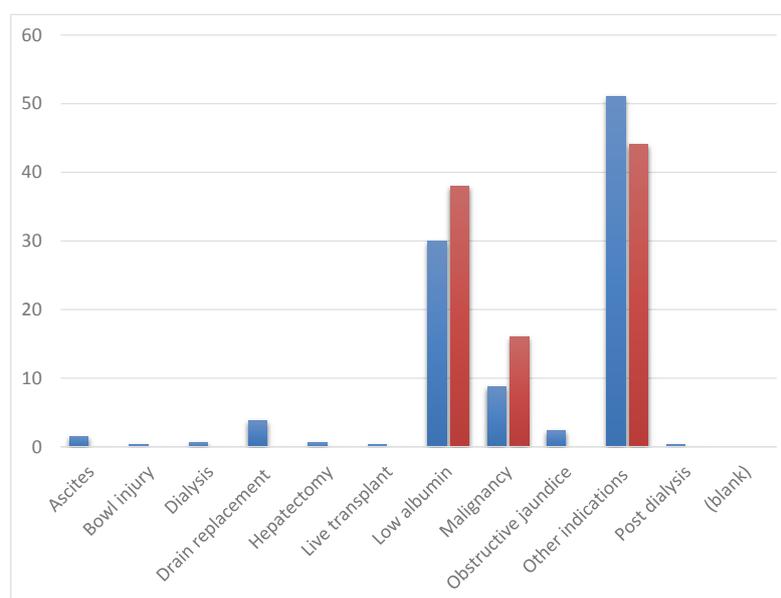
Overall, the implementation of the guideline was 70% in terms of dosing and duration for albumin use. On the other hand, it reached up to 60% in choosing the appropriate concentration and indications. The most common albumin concentrations used were similar to the retrospective phase, which is the (20%). In terms of prescribers, 30% were from general medicine, 20% were from oncology, and 14% were accepted without a prescriber code.

#### **Clinical outcomes**

There was a significant association between category (O) and inappropriate implementation of the guideline (**Appendix A; Tables 4 and 5**).

**Table 3:** Shows unjustified and justified indications in terms of dosing, the correct concentration, and duration and considered to be implemented as per guideline.

Other category	Dose*		Concentration*		Duration*	
	Implemented	Not Implemented	Implemented	Not Implemented	Implemented	Not Implemented
Ascites	5 (1.4)	0 (0.0)	5 (1.7)	0 (0.0)	5 (1.6)	0 (0.0)
Bowl injury	1 (0.3)	0 (0.0)	1 (0.3)	0 (0.0)	1 (0.3)	0 (0.0)
Dialysis	2 (0.6)	0 (0.0)	2 (0.7)	0 (0.0)	2 (0.6)	0 (0.0)
Drain replacement	15 (4.2)	0 (0.0)	15 (5.0)	0 (0.0)	15 (4.7)	0 (0.0)
Hepatectomy	2 (0.6)	0 (0.0)	2 (0.7)	0 (0.0)	2 (0.6)	0 (0.0)
Live transplant	1 (0.3)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.6)
Low albumin	100 (28.2)	62 (43.7)	54 (17.8)	108 (56.0)	88 (27.7)	74 (41.6)
Malignancy	39 (11.0)	16 (11.3)	39 (12.9)	16 (8.3)	41 (12.9)	14 (7.9)
Obstructive jaundice	8 (2.3)	0 (0.0)	7 (2.3)	1 (0.5)	8 (2.5)	0 (0.0)
Post dialysis	1 (0.3)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.6)
Other indications	180 (50.8)	64 (45.1)	176 (58.1)	68 (35.2)	156 (49.1)	88 (49.4)
<b>Total</b>	<b>354 (100)</b>	<b>142 (100)</b>	<b>303 (100)</b>	<b>193 (100)</b>	<b>318 (100)</b>	<b>178 (100)</b>

**Figure 1:** Indication of albumin in prospective phase as blue represent the justifiable use were orange color represent the unjustified use.

### Economics

The overall albumin cost during the study period for a 20% albumin concentration was 220,779 SR, and 309,270 SR for an albumin concentration of 5%. For category (O) indication albumin 20%, the cost was 220000 SR, while for albumin 5% of the cost was 219000 SR. For inappropriate use of category others (O) it cost almost 210000 SR for albumin 20% and 117000 SR for albumin 5%.

### DISCUSSION

The main goal of this study is to evaluate the use of albumin in a tertiary hospital in Saudi Arabia. The institutional guideline has been used for an extended period of time and has allowed different indications to be utilized by providing the open option of the category “other (O)”. It should be emphasized that the result of this study is a call to update the guideline and reassess the use of albumin consistently annually.

A cross-sectional study was performed in 2011 in Shariati Hospital that found among 1281 vials of albumin prescribed

for 135 patients during the study period, only 32.1% were prescribed, 25% of which were utilized appropriately according to the guidelines. Another retrospective was done in a cross-sectional design performed in a teaching hospital in Iran and assessed 320 albumin prescriptions, in which 50% were considered to be for inappropriate indications, which led to \$97,398 wastage [6]. The wastage is consistent with our study result emphasizing that developing an institutional protocol or guideline and audit with feedback or educational activities alone will not provide achievable targeted long-term results. Validation and use of albumin have varied among studies relying on institutional or international guidelines. In a research center of Cardiovascular and Medical, a prospective cross-sectional study was performed to evaluate the use of albumin prescription for a total of 6 months. It included 300 patients who were prescribed albumin. The prescriptions were assumed inappropriately for 90% patients; the most common reason was an incorrect indication of prescription without checking the serum albumin level (56.39%).

Based on this study, the majority of albumin prescriptions were used for ascites and edema (60%), followed by hypoalbuminemia and hypoproteinemia (30%) ([7]. The default prescription for low albumin was prevalence also in our study; unfortunately, there is no standard definition for hypoproteinemia or low albumin to be replenished; no definition for specific dose or concentration was established. Another study at a university-affiliated hospital evaluated a total of 63.8% of the albumin administrations in concordance with the ASHP protocol, among which, the most reported usage of albumin by up to (40%) were cardiac surgery. Other indications were nephritic syndrome, septic shock, transplantation, plasmapheresis, and cirrhosis. In 36.2% of cases, the albumin indication was not clear; however, hypoalbuminemia (36.2%) and nutritional supplementation (24.4%) were the two most frequent reasons for inappropriate albumin use. Furthermore, there was a significant association between mortality rate and an increased number of used albumin vial [8]. A different approach to control the use of albumin has been raised by several studies, including the interventional study and other studies that used an established organizational protocol and guidelines. Back in 2000, a study provided an educational program to improve the quality of albumin prescribing by assessing the adaptation of the guideline for albumin use. The authors demonstrated that during the observational period, nearly 76% of prescriptions for albumin were found to be inappropriate, and during the intervention phase, the percentage of inappropriate albumin prescribing decreased to 38.8% [9,10]. Together, these results highlight that it is essential to establish a comprehensive educational campaign over a period of time to facilitate a paradigm shift in organizational prescribing patterns with an effective strategy that will allow a sustainable cost saving and an overall reduction in albumin use.

## LIMITATIONS

The institutional guideline has been developed by a multidisciplinary team, including the medical and surgical department to aid minimization of bias and include any indications that might be missed otherwise at an evidence-based level. There are several limitations to this study that should be discussed. First, the definition of inappropriate and appropriate use for albumin in our institutional guideline may contrast with those of other institutions. Second, this is an observational study in which evaluations of the intended use of albumin in the retrospective phase were lacking. Third, this study did not include cost-effectiveness analysis, as several required factors not been evaluated, including safety efficacy for each indication, target populations, and the severity of illness. Finally, we did not evaluate the clinical outcomes as this was out with the scope of this study.

## CONCLUSION

Unjustified use of albumin is increasing and these results indicate the need for the guideline to be reviewed and updated. The adjustment for prescribing and dispensing albumin process needs to be reevaluated.

## CONFLICT OF INTEREST

The authors have no financial or other potential conflicts of interest to declare.

## AUTHOR CONTRIBUTIONS

All authors contributed equally to writing and reviewing the manuscript, and all authors agree to be accountable for the content of the work.

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## REFERENCES

1. Rafsanjani, Z., Javadi, M., Torkamandi, H., Alahyari, S., Talasaz, A., et al. The evaluation of albumin utilization in a teaching university hospital in Iran. *IJPR*. 2011;10(2):385-390.
2. Delaney, A.P., Dan, A., McCaffrey, J., Finfer, S. The role of albumin as a resuscitation fluid for patients with sepsis: A systematic review and meta-analysis. *Crit Care Med*. 2011;39:386-391.
3. Dellinger, R.P., Levy, M.M., Rhodes, A., Annane, D., Gerlach, H., et al. Surviving sepsis campaign: International guidelines for management of severe sepsis and septic shock: 2012. *Crit Care Med*. 2013;41:580-637.
4. Vargas, E., De Miguel, V., Portole, A., Avendano, C., Ambit, M., et al. Use of albumin in two Spanish university hospitals. *Eur J Clin Pharmacol*. 1997;52:465-470.
5. Veronica, D., Vargas, E., Portoles, A., Puerro, M., Terleira, A., et al. Modification of albumin use pattern after an educational intervention. *Dis Manage Health Outcomes* 2000;8(1):43-50.
6. Jahangard-Rafsanjani, Z., Javadi, M., Torkamandi, H., Alahyari, S., Talasaz, A., et al. The evaluation of albumin utilization in a teaching university hospital in Iran. *IJPR* 2011;10(2):385-390.
7. Farsad, B.F., Hadavand, N., Masumi, S. Albumin utilization review to evaluate the efficacy and cost, perform as a

- qualitative study in special wards in Shaheed Rajaei cardiovascular, medical & research center. Biosciences, Biotechnology Research Asia. 2016;13:1469-1477.
8. Talasaz, A.H., Jahangard-Rafsanjani, Z., Ziaie, S., Fahimi, F. Evaluation of the pattern of human albumin utilization at a university affiliated hospital. Arch Iran Med. 2012;15(2):85-87.
  9. Farasatinasab, M., Amouzegar, A., Safari, S., Ghanbari, B., Darkahian, M., et al. Albumin utilization evaluation in a major teaching hospital in Iran: Recommendations for Guideline Development. J Res Pharm Pract. 2018;7(3):157-163.
  10. Tucker, C. The impact of criteria for use and a prescriber order form on albumin utilization. J Basic Clin Pharma. 2017;8:255-258.