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Evaluation of Human Albumin Use Pattern in a Referral Teaching Hospital

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ABSTRACT

Background: Albumin is generally used in hypovolemic conditions and due to its high cost and complicated manufacturing process, its appropriate use is a vital issue to be considered. The aim of this study was to evaluate the pattern of Albumin prescription in Imam Khomeini teaching hospital in Urmia, Iran.country.

Methods: This study was carried out between December 2014 to December 2015 in the Imam Khomeini hospital, affiliated to Urmia University of Medical Sciences, using pre-designed forms covering demographic data and clinical and laboratory information that was completed by the educated pharmacist on a daily observational basis.

Results: A total of 202 patients were selected with the mean age of 55.9±20.5 years, including 53% male patients. The highest prescription percentages were for patients with the diagnosis of Gastrointestinal Cancers (10.9%) while most of the patients were admitted in burn ward (16.3%). Overall 2755 Albumin 20% vials equal to almost 3030 million Rials were used while only 79 (39.1%) of the prescriptions were appropriate. Hypoalbuminemia was responsible for the highest number of inappropriate indications.

Conclusion: Our results showed a low percentage of acceptable prescriptions which highlights the necessity for reviewing and supervising the utilization of Albumin in this hospital.

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Introduction

DSerum albumin is the most predominant protein in human blood plasma produced mainly in the liver. It increases intravascular oncotic pressure and mobilizes the fluids from interstitial into intravascular space. Albumin transports different endogenous substances including hormones, fatty acids, and exogenous compounds like drugs. Besides, it is an important buffer in the plasma of humans (1, 2).

Generally, Albumin is approved for use in hypovolemic conditions as a plasma volume expander and maintaining cardiac output in the treatment of certain types of the shock especially when other non-protein colloids cannot be used (1). Its manufacturing process is complicated and costly, some part due to purification and viral assurance (3, 4).

Clinical considerations and suitable guidelines are the basis of the proper use of medications (3). Drug Utilization Evaluation (DUE) is one of the most effective studies for assessment of drugs especially those with high-cost, narrow therapeutic index, and broad-spectrum activity. DUE ensures the rational use of drugs at the individual patient level and assess the actual process of prescribing, dispensing or administering a drug (indications, dose, drug interactions, etc.) (5).

On the other hand one of the most important factors

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on the overall cost of the treatment is an appropriate prescription of the drug (3). As reported, consideration of reliable guidelines in the prescription of costly drugs like Albumin could result in a 56% reduction in overall treatment cost (6). According to the high price of this drug, its pattern of use may influence the health resources burden largely, as same as the patients' outcomes (7). The reported irrational prescription of Albumin varies from 18 % to even 91% in different studies (2, 8–11).

A study in China showed that 50% of adverse drug reactions (ADRs) caused by Albumin is due to its irrational use and following the guidelines in the hospitals will be a help in reducing the ADRs (12).

A few studies have been done in different parts of Iran and all of them signify the necessity to reconsider the appropriate use of Albumin for hospitalized patients (3, 4, 9, 13).

Yet in 2011 and 2017 still, 50% and 57.5% of Albumin prescriptions consecutively were reported as irrational in two large teaching hospitals in Iran (3, 14).

Studies have shown that concurrent use of furosemide as a loop diuretic with albumin would positively affect the outcome of diuresis in patients. Moreover, albumin enhances the delivery of furosemide to its effective site which consequently improves the overall diuresis (15).

The aim of this study is to evaluate the rational use of Albumin in Imam Khomeini, a teaching hospital in Urmia-Iran.

Table 1. Appropriate indications for Albumin use

Indication	Notes	GoR*
Appropriate indications (for which there is a widespread consensus)		
Paracentesis	5 g of albumin/L ascitic fluid removed, after paracentesis of volumes > 5 L.	1C+
Therapeutic plasmapheresis	For exchanges of > 20 mL/kg in one session or > 20 mL/kg/week in more than one session.	2C+
Spontaneous bacterial peritonitis	In association with antibiotics.	1C+
Occasionally appropriate indications (when other criteria are fulfilled)		
Heart surgery	Last-choice treatment after crystalloids and non-protein colloids.	2C+
Major surgery	Albumin should not be used in the immediate post-operative period. The only indication for use: serum albumin <2 g/dL after normalization of circulatory volume.	2C+
Cirrhosis of the liver with refractory ascites	Generally ineffective, except in patients with serum albumin < 2 g/dL.	2C
Contraindications to the use of non-protein colloids	- pregnancy and breastfeeding;	2C
	- perinatal period and early infancy; - acute liver failure; - moderate-severe renal failure (particularly when anuria/oliguria); -dialysis treatment in the presence of severe abnormalities of hemostasis and baseline albumin < 2 – 2.5 g/dL; - intracranial haemorrhage; - hypersensitivity.	
Hemorrhagic shock	Only in the case of: - lack of response to crystalloids or colloids; - contraindication to the use of non-protein colloids	1A
Hepatorenal syndrome	In association with vasoconstricting drugs.	2B
Nephrotic syndrome	Only in patients with albumin < 2 g/dL with hypovolemia and/or pulmonary edema.	2C
Organ transplantation	In the post-operative period after liver transplantation to control ascites and peripheral edema to replace the loss of ascitic fluid from the drainage tubes, if albumin < 2.5 g/dL with a hematocrit > 30%.	1C
Burns	In the case of burns of > 30% body surface area, after the first 24 hours.	2C+
Dose		
The dose needed to obtain a serum albumin ≥ 2.5 g/dL is calculated using the following formula: Dose (g) = [desired albumin concentration (2.5 g/dL) – actual albumin concentration (g/dL)] x plasma volume (0.8 x kg)		

*GoR: Grade of Recommendation

Methods

This cross-sectional prospective study was carried out during December 2014 to December 2015 in the 17 wards in Imam Khomeini teaching Hospital affiliated to Urmia University of Medical Sciences. All the hospitalized patients who received human Albumin solution 20% with signed consent form were assessed for eligibility. Patients with incomplete data were excluded from further assessment. If a patient died during the study, the date of death was considered as the date for the end of observation. Other dosage forms of Albumin were not available in Iran, so they are not included in this study.

Data collection including demographic data (age, sex) and clinical and laboratory information (ward, Indications, the number of Albumin prescriptions, the number of used Albumin vials per patient, duration of albumin prescription, duration of hospitalization, and the level of serum Albumin) was recorded on predesigned forms (Table 3). An educated pharmacist conducted the daily chart review using pharmacy medication files, patients' files, laboratory results and nursing files.

Rational prescription of Albumin was evaluated according to ASHP (American Society of Health-System Pharmacists) guidelines (1, 12, 16). The appropriate indications were shown in Table 1.

Analysis of the data was done by SPSS 25. Quantitative results are reported as mean ± SD and qualitative results as a number and percentages.

Results

During the one-year study, 217 hospitalized patients were enrolled. Fifteen patients were excluded due to incomplete data and the analysis was done on the remained 202 patients.

The mean age was 55.91 ± 20.5 years old and about half of them were male (53 %). Other demographic and clinical data can be found in Table 2. Most of the enrolled patients were from the burn ward (16.3%), followed by the Nephrology (11.9%) and Neurology ward (11.4%) (Figure 2). These patients were diagnosed mostly with burning (16.3%), gastrointestinal cancers (10.9%), and edema (9.9%) consecutively (Figure 1).

Table 2. Demographic characteristics and clinical data of the study population, N (%) or (mean ± SD).

Characteristic	N=202
Age (years)	55.91 ± 20.49
Sex Male Female	 107 (53) 95 (47)
Serum albumin at the time of prescription (g/dl)	2.87 ± 2.51
Number of vials per patient	14.89 ± 14.02 (1-75)
Albumin use duration (Days)	6.4 ± 5.3 (1-31)
Hospitalization duration (Days)	12.6 ± 8.9 (2-49)
Albumin use duration to Hospitalization duration ratio	0.54 ± 0.28 (0.03-1)
Total number of used albumin vials	2775
Total cost of used albumin vials (Dollars)	26000

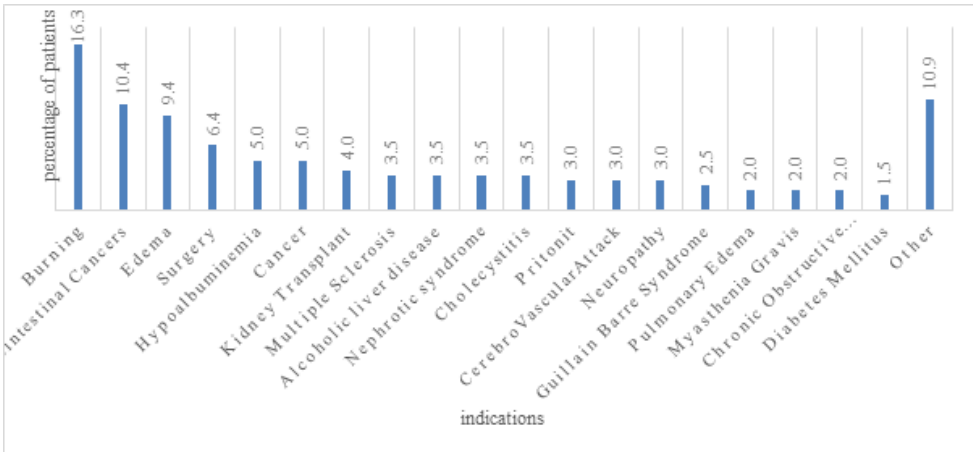

Figure 1. Distribution of Albumin prescriptions according to the Indications (%)., Other indications with frequencies ≤1% including Paresthesia, Idiopathic Myelofibrosis, Epilepsy, Deep Venous Thrombosis, Hypertriglyceridemia, Hydrocephalus, Thrombotic Thrombocytopenic Purpura,

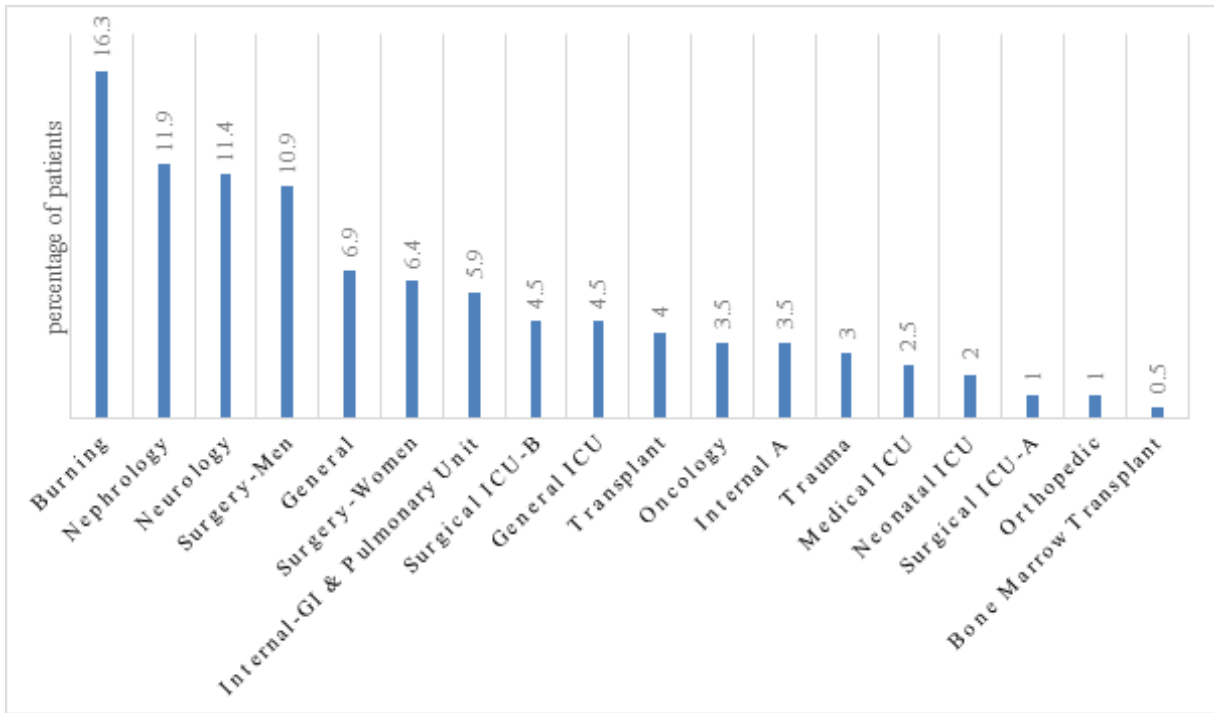

Figure 2. Distribution of Albumin prescriptions according to the wards (%).

When come up to the number of used Albumin vials, the total number of 202 patients used 2755 vials of Albumin 20%. Burn ward with 555 vials (21.15%) had the most consumption of the albumin, followed by Neurology (N=435, 15.79%) and Nephrology wards (N=415, 15.06%) (Figure 3). Accordingly Burning (N=555, 20.15 %), Gastrointestinal cancers (N=287, 10.42 %), and edema (N=273, 9.91 %) make the top three of the most common diagnoses. (Figure 4).About 90 patients (44.6 %) took furosemide and albumin concurrently.

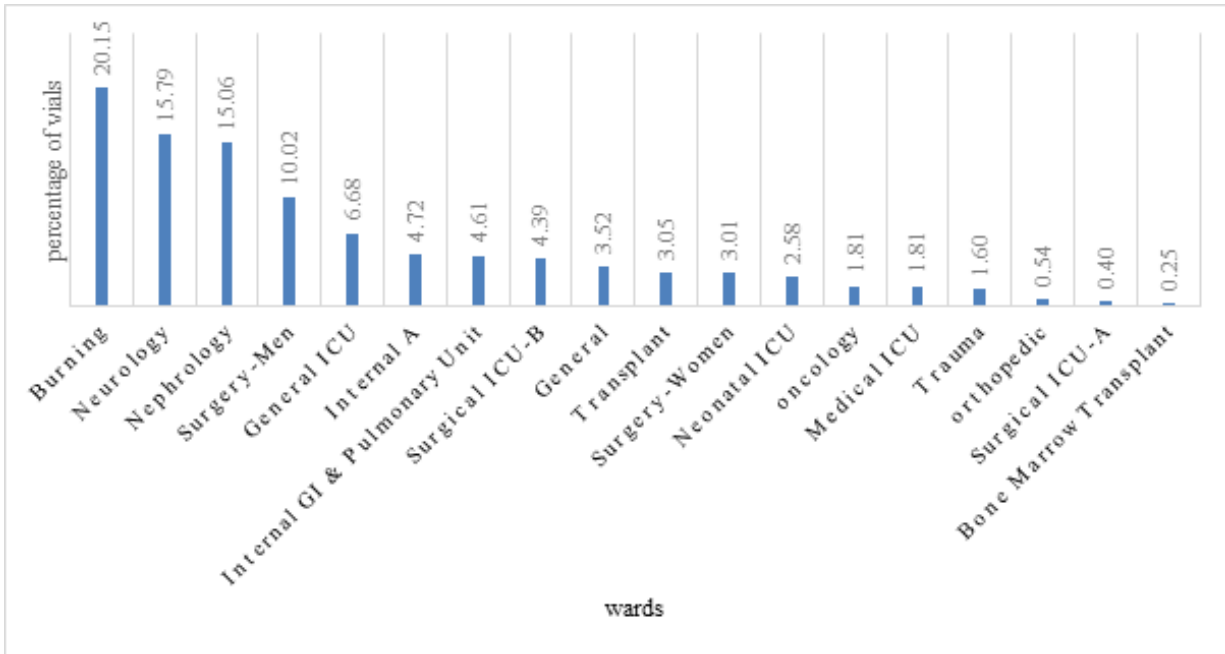

Figure 3. Distribution of used Albumin vials according to the wards (%).

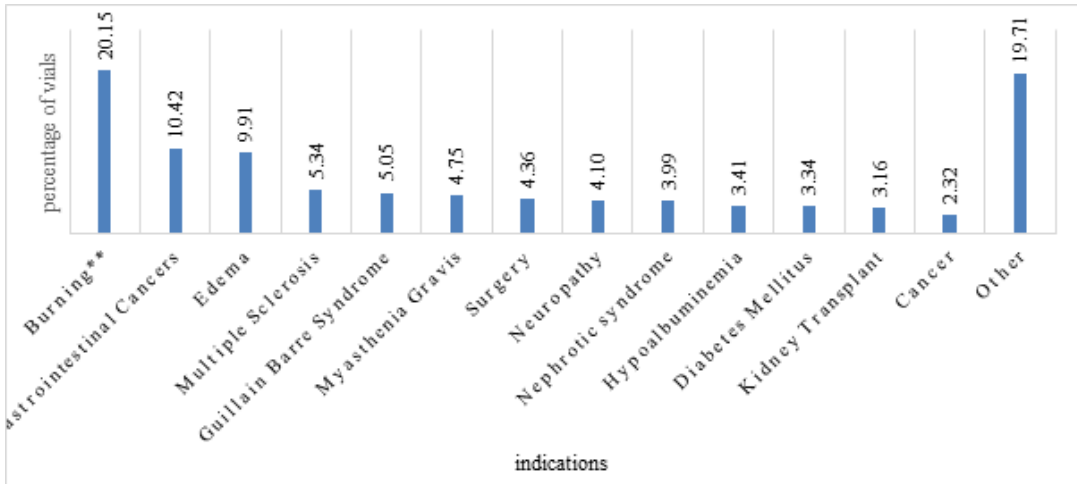

Figure 4. Distribution of used Albumin vials according to the Diagnosis (%); Other diagnosis includes: Cholecystitis(2.14), Cerebrovascular Attack(2.11), Peritonitis(1.89), Infection(1.42), Hydrocephalus(1.38), Alcoholic liver disease(1.31), Paresthesia(1.31), Lupus(1.23), Hypertriglyceridemia(1.09), Pulmonary Edema(1.02), Carolisyndrome(0.87), Gallbladder surgery(0.80), Epilepsy(0.58), Chronic Obstructive Pulmonary Disease(0.54), pancreatitis(0.47), Pneumothorax(0.44), Thrombotic Thrombocytopenic Purpura(0.40), Intestine Ischemia(0.36), Deep Venous Thrombosis(0.25), Idiopathic Myelofibrosis(0.11).

**Including burning with body surface area involvement of 50%(4.61 vials), 30% (11.03 vials), 10%(1.56 vials) and 60%(2.94 vials).

The level of Albumin was not measured in 22 (11%) of patients despite receiving Albumin, while studies state the association between the low level of serum albumin (<2g/dL) and the post-surgery complications as well as morbidity in hospitalized patient. So measuring serum albumin is an important factor in decision making for Albumin prescription (13, 17, 18). The average level of albumin in enrolled patients was 2.87 ± 2.51 g/dL and 34 patients had albumin level of less than 2g/dL.

Among all prescriptions according to ASHP guidelines, only 79 (39.1%) of them were appropriate while considering the number of vials which were used appropriately, this percentage is equal to 34.8% (N=959). Hypoalbuminemia and Burning had the highest number of inappropriate and appropriate indications (5% and 12.9% respectively). In 89% of the cases, the electrolyte levels were measured.

During the study period, the cost of one vial of the 20% human albumin solution was 1.1 million Rials (10 dollars) on average. Therefore, this number of vials resulted in a significant cost for the hospital which equals almost 3030 million Rials (86500 dollars).The 1796 vials which were related to inappropriate prescriptions have burdened the hospital with almost 1976 million Rials (56400 dollars) which is 65.2% of total albumin cost during this study.

Table 3. A sample of pre-designed forms

Patient information		**Date:** …… /...../……				
Name:		Record NO:				
Age:		Ward:				
Sex:						
Present illness:						
Patient CC:						
Pharmacist Note:						
Albumin Information						
Albumin level:		Duration & number of used Albumin vials:				
Number of Albumin vials:		Appropriate /Inappropriate indication				
Furosemide prescription:						
Lab data						
Date	/ /	/ /	/ /	/ /	/ /	/ /
Albumin						

Discussion

Drug Use Evaluation studies result in a proper report of the prescription process in hospitals and give a reasonable view of available standard guidelines. Different studies have reported a significant range of improper prescription of Albumin from 35 % to even 90% (Table 4) (2, 8-11, 14) which was notable. Meanwhile, applying controversial guidelines and other clinical considerations in these studies could not be ignored as a reason for this wide range (14).

Table 4. Summary of studies of investigating Albumin utilization pattern carried out in Iran

First author (year)	Sample Size	Applied guideline	Appropriate Prescriptions (%)	The most Inappropriate Indication	Ward with the most Prescription
Nafisi (Present study)	202	ASHP[£] 2015	39.1	Hypoalbuminemia	Burn
Talasaz (2012) (19)	69	ASHP 1996	63.8	Hypoalbuminemia	ICU[¥]
Kazemi (2013) (24)	120	ASHP 1996	4	Intractable Edema	ICU
Zolfagharian (2017) (14)	100	AHFS [€] 2009	38-42.5	Nutritional Supplementation	Burn ward
Mahmoudi (2015) (6)	12680	ASHP	48.8 (pre)	Hypo-Albuminemia	General surgery
Ala (2015) (4)	100	ASHP	63	Hypo-Albuminemia	ICU
Jahangard (2011) (3)	135	Guidelines for Albumin use in: -Medical University South Carolina2009 -The University of North Carolina and Chapel Hill2000 -West Penn Allegheny Health system2009	25.2%	Volume Expansion After the Cardiac Surgery	ICU-open heart
Hamishehkar (2016) (9)	210	ASHP	23.8	Hypoalbuminemia	ICU & surgery
Foroughinia (2017) (13)	110	ASHP	12.7%	Nephrotic syndrome without hypoalbuminemia	Internal
Farsad (2016) (20)	300	ASHP	6.3%	Incorrect indication of prescription without checking serum albumin level	Cardiovascular
Dastan (2018) (23)	90	Other Papers	21.6%	Critical care medicine	Critical care ward

[£] American Society of Health-System Pharmacists, [¥] Intensive care unit, [€] American Hospital Formulary Service

Our results showed a low percentage of appropriate prescriptions. The high rate of unnecessary use of Albumin highlights the need for reviewing and supervising its use. This study was the first study to investigate the use of Albumin in Urmia city and provided a valuable view of the need for reconsideration of using the current evidence-based guidelines in practice. The necessity for this issue becomes more important when the results were compared with other parts of the world.

In 2012 the appropriate prescriptions of Albumin were reported 63.8% in a large hospital in Tehran (19) while in this study we had just 39% proper prescription in the largest hospital in Urmia. This rate also was higher in 2015 in a hospital in Mazandaran with 63% justifiable

prescriptions (4). Moreover, in 2016 in Shaheed Rajaei, 93.7% of prescriptions were reported as improper which is extremely high (20).

In this study, we recruited 202 patients which were more than most of the studies that have been done in Iran except for the one carried out in Shiraz with 12680 patients (6) and another study in Tehran in 2016 with 300 patients (20). We found that about 39% of the Albumin prescriptions were appropriate while it was reported to be in a range of 4-63% in other studies in Iran. Like most of the other studies, we also used ASHP guidelines for the assessment of the prescriptions. In this study, most of the patients who received Albumin were from the burn ward like the study by Zolfagharian et al., (14). But in the other studies, ICU, internal and general surgery wards have the most patients with inappropriate Albumin prescriptions. Hypoalbuminemia was the main inappropriate indication in Urmia, as in Tehran (19), Tabriz (9), Shiraz (6) and Qaemshahr (4) studies, while in 2011 it has been shown that there is not enough evidence in favor of using albumin for hypovolemia, burns, and hypoalbuminemia (20).

Other inappropriate indications in other studies were intractable edema (7), nephrotic syndrome without hypoalbuminemia (13), nutritional supplementation (14), albumin administration without checking serum albumin level (19), and volume expansion (3). The total cost of albumin for the duration of the study was reported 369268$ by Hamishehkar et al., (9), and 48500$ by Foroughinia et al., (13), for 210 and 110 patients respectively. In our study, this cost was 86500$ for 202 patients. All these data show a considerably high cost of albumin in the health care system.

In 2004 a study in Thailand showed that 35.6% of prescriptions are inappropriate and 14% of them were prescribed for contraindicated cases. Similar to most of the studies that have been done in Iran (4, 6, 9, 19), hypoalbuminemia was the reason with the highest number of prescriptions in this study as well. These results were reported while the sample size was lower compared to our study with 74 inpatients (2). A study in 2013 showed that 50% of adverse drug reactions caused by Albumin are due to its irrational use and mostly off-label use and following the guidelines in the hospitals will be a help in reducing the ADRs. This study provided reliable data since it assessed data from 22 years of albumin ADR case reports. According to their data, malignant tumor, liver diseases, and trauma were the most frequent diagnosis of the patients that were included in this retrospective study (12). In 2016, Hamishehkar et al., showed that almost 76% of Albumin prescriptions are inappropriate (9). In 1997 a study showed only 8.1% of an appropriate prescription for Albumin. In this study, internal and gastroenterology wards had the most frequent use of albumin as well as the paracentesis and hypoalbuminemia as the two indications with the highest number of albumin prescriptions (8).

Kishk et al. in 2013 showed only 9.6% of rational Albumin prescriptions in medical intensive care unit with non-hemorrhagic shock as the main reason for the inappropriate use of albumin (10). In 2002 a study in Belgium showed only 18.3% of inappropriate prescriptions and mentioned a 50% decrease in Albumin consumption resulted from obeying the guidelines. It has been stated that most of the cases were considered inappropriate due to starting the treatment procedure too early (11).

In a study in Spain which evaluated the use of albumin in 22 public hospitals, only 23% of prescriptions were considered appropriate with nutritional support as the major cause of improper use of albumin (21).

The effect of an intervention in prescriptions has been shown in multiple studies. In 2016 intervention resulted in a 37% decrease in the inappropriate prescription of albumin (22). Moreover, in Tehran, an interventional study was performed in which 79.3% reduction in the inappropriate prescription of albumin was seen which presents the positive effect of interventions by a clinical pharmacist in hospital settings (23).

Excluding the incomplete and missed information due to the lack of an organized and comprehensive internal network, and also handwritten prescriptions may affect the results. When come to the conclusion it should be noted that the results of the DUE studies may be expressed as the number of used vials, or the number of the prescriptions. As the different diagnoses, may need various number of vials, it may not surprising if a ward with fewer patients on Albumin, spend more vials of Albumin. Another issue is the lack of a national guideline (7) for the use of Albumin which makes it more complicated to decide on the appropriate use of the Albumin. As we did not discuss the rationale of prescriptions directly with physicians, our results could be biased in this way.

This study shows a low percentage of rational Albumin utilization in the hospital setting and emphasizes the need for supervising drug utilization patterns via various policies to target cost and outcomes. Further research with a more consistent method in obtaining patient data along with performing interventions, will give even better conclusions in this area.

References

1. Liumbruno G, Bennardello F, Lattanzio A, Piccoli P, Rossettias G. Recommendations for the use of albumin and immunoglobulins. Blood Transfuse 2009;7(3):216-34.

2. Aramwit P, Kasettratat N. Evaluation of serum albumin utilization in inpatient at a private hospital in Bangkok. Yakugaku Zasshi 2004;124(9):631-4.

3. Jahangard-Rafsanjani Z, Javadi MR, Torkamandi H, Alahyari S, Talasaz A, Gholami K. The evaluation of albumin utilization in a teaching university hospital in Iran. Iran J Pharm Res 2011;10(2):385-90.

4. Ala S, Salehifar E, Chalaki V. Evaluation of Albumin Use in a Teaching Hospital. Journal of Mazandaran University of Medical Sciences 2015;

25(129):137-41.

5. Holloway K, Green T. Tools to investigate the use of medicines. Drug and therapeutics committees: A practical guide. France: World Health Organization (WHO) 2003;71-94.

6. Mahmoudi L, Karamikhah R, Mahdavinia A, Samiei H, Petramfar P, Niknam R. Implementation of pharmaceutical practice guidelines by a project model based: clinical and economic impact. Medicine (Baltimore) 2015; 94(42):e1744 .

7. Farasatinasab M, Amouzegar A, Safari S, et al. Albumin utilization evaluation in a major teaching hospital in Iran: Recommendations for guideline development. J Res Pharm Pract 2018;7(3): 157–63.

8. Vargas E, De Miguel V, Portolés A, et al. Use of albumin in two Spanish university hospitals. Eur J Clin Pharmacol 1997;52(6):465-70.

9. Shafiee E, Rezaee H, Entezari-Maleki T, Hamishehkar H. The evaluation of albumin use in an Iranian university hospital. Pharmaceutical Sciences 2016; 22(3):186-9.

10. Kishk O, Yeung SY, Gonzales J. 928: Evaluation of Albumin Use in a Medical Intensive Care Unit. J Crit Care Med 2013;41(12):A233.

11. Somers A, Bauters T, Robays H, Bogaert M, Colardyn F. Evaluation of human albumin use in a university hospital in Belgium. Pharm World Sci 2002;24(3):111-6.

12. Zhou T, Lu S, Liu X, Zhang Y, Xu F. Review of the rational use and adverse reactions to human serum albumin in the People's Republic of China. Patient Prefer Adherence 2013;28(7):1207-12.

13. Foroughinia F, Mazraie S. Investigating the use of human albumin in a non-teaching hospital in Iran. Iran J Pharm Res 2017;16(2):817-22.

14. Zolfagharian F, Ghazanfari S, Elyasi S, et al. Drug utilization evaluation of albumin in a teaching hospital of Mashhad, Iran: an interventional pre–post design study. Int J Clin Pharm 2017;39(4):704-11.

15. Duffy M, Jain S, Harrell N, Kothari N, Reddi AS. Albumin and furosemide combination for management of edema in nephrotic syndrome: a review of clinical studies. Cells 2015;4(4):622-30.

16. Service AHF, Snow EK. AHFS Drug Information 2009: American Society of Health-System Pharmacists; 2009.

17. Levitt DG, Levitt MD. Human serum albumin homeostasis: a new look at the roles of synthesis, catabolism, renal and gastrointestinal excretion, and the clinical value of serum albumin measurements. Int J Gen Med 2016;15(9):229-55.

18. Gounden V, Jialal I. Hypoalbuminemia. StatPearls. Treasure Island (FL): StatPearls Publishing; 2019.

19. Talasaz AH, 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):85-7.

20. Farsad BF, Hadavand N, Masumi S, Salehi H. 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(3):1469-77.

21. Remohí MJ, Arcos AS, Ramos BS, Paloma JB, Aznar MD. Costs related to inappropriate use of albumin in Spain. Ann Pharmacother 2000;34(10):1198-205.

22. Lyu PF, Hockenberry JM, Gaydos LM, Howard DH, Buchman TG, Murphy DJ. Impact of a sequential intervention on albumin utilization in critical care. Crit Care Med 2016;44(7):1307-13.

23. Dastan F, Jamaati H, Emami H, et al. Reducing inappropriate utilization of albumin: the value of pharmacist-led intervention model. Iran J Pharm Res 2018;17(3):1125-29.

24. Kazemi Y, Hadavand N, Hayatshahi A, et al. Albumin Utilization in a Teaching Hospital in Tehran: Time to Revise the Prescribing Strategies. J Pharm Care 2013;1(4):127-32.