Assessment of Albumin Usage Patterns and Appropriateness in a Comprehensive Cancer Centre

A retrospective study in Jordan

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Abstract

Objectives: Albumin is commonly used for various indications. However, conflicting data exists regarding its appropriate use in different clinical cases. In this study we aim to determine the pattern and appropriateness of albumin use among cancer patients treated at a comprehensive cancer center in Jordan. Methods: A retrospective analysis was conducted on adult cancer patients who were prescribed albumin between January 2019 and July 2020, in the outpatient and inpatient settings. Patient- and albumin-related data were collected, which included demographics, prescribing services, indications, and dosing regimens. We conducted thorough research using PubMed, and reviewed the related guidelines, drug information resources and the package insert to evaluate the appropriateness of albumin's indications and dosing regimens. Results: Albumin was prescribed to 1,361 patients during the study period. Each patient received an average of 74.4 ± 89 (SD) grams of albumin for an average of 2.6 ± 1.8 (SD) days. Albumin use was considered appropriate in 69% of the patients. The critical care service had the highest albumin consumption, with 37% of the prescribing being for the indication of septic shock.
Inappropriate use was observed among the medical solid tumor service (40.8 % of their prescriptions) and was most commonly prescribed for edema (28%). **Conclusion:** To our knowledge, this study represents the first to evaluate a large cohort of oncology patients. In about one third of the cases albumin prescribed indications were considered inappropriate. Continuous education on appropriate usage and regular evaluations of guideline implementation is necessary to ensure appropriate utilization.

**Keywords:** Albumins*/therapeutic use, drug utilization review, neoplasms, cancer care facilities, Jordan.

**Advances In Knowledge**
- This study assessed the usage patterns of albumin among cancer patients in a comprehensive cancer center, revealing that over a third of adult patients received albumin for purposes that did not align with international guidelines.

**Application To Patient Care**
- Considering albumin scarcity and expense, our suggestion is to create guidelines supported by consensus and evidence. Additionally, there should be ongoing education regarding proper usage and consistent evaluations to ensure guideline implementation.

**Introduction**
Human albumin, a physiological plasma expander, is commonly utilized for various indications such as septic shock, paracentesis-induced circulatory dysfunction, spontaneous bacterial peritonitis, and hepatorenal failure.\(^1\)\(^2\)\(^3\) However, there is conflicting data regarding the clinical effectiveness of albumin in various clinical scenarios. An example of this is the Saline versus Albumin Fluid Evaluation (SAFE) trial, which demonstrated that 4% albumin had comparable outcomes to normal saline when used for fluid resuscitation over a 28-day period.\(^4\) In addition, in a Cochrane review, authors concluded that there was insufficient evidence to establish the superiority of colloids over crystalloids in terms of reducing mortality when employed for fluid resuscitation.\(^5\)
Recent studies examined potential additional benefits of albumin, including its anti-inflammatory and antioxidant properties, binding capacity, modulation of hemostasis, vasodilatation, and acid-base homeostasis. This led to an increase in its global prescribing, with studies indicating its frequent use in unapproved indications lacking strong clinical evidence. The heterogeneity of patients' baseline characteristics and albumin levels contribute to the limited availability of clinical evidence for albumin use.

The existing literature described the use of albumin among cancer patients with various clinical conditions. It is well documented that cancer patients admitted to the intensive care unit (ICU) frequently exhibit hypoalbuminemia, defined by serum albumin levels falling below 2 gm/dL. Furthermore, albumin is commonly prescribed for paracentesis procedures following the occurrence of ascites, irrespective of whether the underlying cause is malignancy-related or not. Despite this, a comprehensive assessment of the appropriateness of albumin usage, along with its indications, remains largely absent within the existing literature. Notably, the only study available for evaluation involved only 53 patients.

In light of this literature gap, we conducted this study to examine the appropriateness of albumin utilization within the context of a comprehensive cancer center, which included an assessment of the indications as well as the dosing regimens.

**Methods**

This was a retrospective study conducted at the King Hussein cancer center in Amman, Jordan. King Hussein cancer center is a 350-bed comprehensive cancer center that treats adult and pediatric patients with various types of malignancies in the inpatient and outpatient settings. The study was approved by the institutional review board and was granted a waiver of informed consent due to the retrospective nature of the study.

Utilizing the pharmacy electronic system, we identified all patients who were prescribed albumin between January 2019 and July 2020. Eligible patients were adult patients, aged 18 and older, with a history of cancer, who received albumin in the inpatient or outpatient settings. Patients
who received albumin as a fluid expander for stem cell collection (for extracorporeal photopheresis procedure) were excluded from further assessment.

Each instance of albumin prescription during the study period was evaluated for the appropriateness of both the prescribing indication and the dosage regimen. The product available at our institution was the 20% albumin in 50 ml. To determine the appropriateness of the indications and dosing regimens for albumin, a team of 3 clinical pharmacists performed a thorough review of the literature and the available guidelines. Subsequently, the team formulated a list that included evidence-based indications and dosing regimens based on the most relevant literature, as outlined in Supplement 1.1,3,4,14 This list was used by the reviewers to determine the appropriateness of albumin use among the patients included in the study.

We utilized the American Society of Health-System Pharmacists (ASHP) guidelines for medication use evaluation to conduct this Drug Use Evaluation (DUE).12 Albumin use indications were determined based on the indications included in the physicians’ notes on the patient's electronic medical record. In cases where the indication for albumin prescribing was unclear, a second pharmacist reviewed the case. If there was any disagreement between the two reviewers, a third reviewer was consulted to examine the patient's profile.

We recorded patient characteristics, which included age, weight, gender, type of malignancy, and albumin serum levels, using the electronic patient medical record. In addition, we determined the albumin dose, indication, treatment duration, and number of albumin vials dispensed. To evaluate the services that most often prescribe albumin, we identified the clinical service that ordered albumin by reviewing the electronic prescriptions of albumin.

The evaluation of medication cost per service was determined utilizing the electronic billing system within the institution, with the associated expense based on the institutional selling price. The determination of vial quantity was made considering the availability of 50ml vials of 20% albumin, and the number of vials was rounded to a full vial.
Data analysis was conducted using Excel on Windows 10. Descriptive statistics were used, with average ± standard deviation (SD) for continuous data and numbers and percentages for nominal data.

Results

During the study period, 1,361 patients were included and a total of 2,399 albumin prescriptions were identified. Table (1) outlines the patient demographics and characteristics. Among the included patients, over half were male, the average age was 60±16 (SD) years, and the majority received albumin in the inpatient setting (83.6%). Each patient received an average of 74.4±90 grams of albumin, equivalent to 7.44 ± 8.9 (SD) vials of albumin. The average duration of albumin use was 2.6 ± 1.8 (SD) days.

The most frequent indications for prescribing albumin among our patients were paracentesis (22.8%), septic shock (13.3%), and renal failure (11.8%). A comprehensive distribution of the albumin prescriptions according to indication is outlined in Figure (1). The clinical service with the highest prescriptions of albumin was the medical solid service (n=733, 29.5%), followed by the nephrology service (n=537, 21.6%), and the critical care service (n=352, 18.2%), regardless of the appropriateness. (Table 2)

Most of the albumin consumption occurred in hospitalized patients (85.8%). Its usage in the outpatient settings constituted a smaller proportion (14.2%). In this group, the most common reason for albumin use was for fluid replacement following paracentesis (n=96, 27 %), with an average dose of 30 grams administered once after the procedure.

Among the patients included in the study, 69% were prescribed albumin for indications in alignment with the clinical evidence and internationally available guidelines.1,14 As summarized in Table (2). The solid tumor service was among the services with the highest percentage of inappropriate albumin prescriptions compared to its total number of prescriptions, with 299 cases (40.8% of their prescriptions). This was reported in the surgical service, with 128 cases (65.6%), and the palliative service. Among patients who had appropriate indications for the use of albumin, incorrect dosing regimens were reported in 23.1% (n = 385) of the prescriptions.
The total quantity of albumin used during the study period amounted to 183,290 grams, equivalent to 18,329 vials. Of this total, 136,070 grams were prescribed appropriately. The total cost of albumin consumption throughout the study amounted to 678,173 JD (equivalent to 955,173 USD). Notably, 174,714 JD (equivalent to 246,076 USD) was for cases that were considered inappropriate for indication and/or dosing regimen.

**Discussion**

In this study with a relatively large sample size, we reported inappropriate prescribing of albumin in about one third of the cases. The proportion of appropriate prescribing of albumin is higher than that reported by other studies.\(^{15-17}\) This may be attributed to several factors, which include the presence of clinical pharmacists in the inpatient setting on all clinical services to assess the necessity of albumin use and the implementation of a definite duration requirement for prescribing the medication.

The inappropriate utilization of albumin has been well documented in various studies conducted globally.\(^{8-9, 15-17}\) These findings emphasize the significance of establishing institutional consensus guidelines to regulate the use of albumin, minimize medication wastage, and prevent unintended adverse drug reactions.

Jahangard-Rafsanjani et al. evaluated the use of albumin use in a teaching hospital located in Iran. Their study included 135 patients and reported appropriate use in 34% of the patients.\(^{15}\) Similarly, Nafisi et al. conducted a study in Urmia, Iran, between 2014 and 2015, which included 202 patients. Their findings indicated a 39.1% rate of appropriate prescribing for albumin.\(^{16}\)

In a study conducted by Talasaz et al. in Tehran, Iran,\(^{17}\) hypoalbuminemia and nutritional supplementation were identified as the primary inappropriate indications for albumin use. Hypoalbuminemia accounted for 36.3% of the inappropriate use, while nutritional supplementation contributed to 24.4%. Similar findings were reported by Nafisi et al. with a total of 13.4% of albumin prescriptions in these categories.\(^{16}\) In our study, we also observed the significant presence of nutritional support and hypoalbuminemia as inappropriate indications for
albumin use, accounting for 10% (n = 89) of all inappropriate indications. It is important to note that our oncology patients often experience malnutrition and cachexia due to the disease itself and its treatment.\(^{18}\)

Though albumin is not recommended as a caloric protein source and not recommended to maintain serum albumin levels above 3 g/dL, prescribing albumin to increase the serum levels remains a common indication for its use. Hypoalbuminemia in many cases may be attributed to the impact of inflammatory processes on serum albumin levels, which leads to increased vascular permeability and leakage of albumin molecules.\(^{19-21}\) However, based on current evidence, albumin infusions cannot be recommended to increase serum albumin levels. Instead, it is crucial to identify and treat the underlying cause of hypoalbuminemia.\(^{18}\)

In our study, the intensive care unit accounted for the highest consumption of albumin vials, comprising 37% of the total number of vials dispensed. Within the ICU, albumin was commonly prescribed as a volume expander for conditions such as septic shock. It is noteworthy that the use of albumin in septic shock, as highlighted by Tigabu et al., did not demonstrate a reduction in the 28-day mortality rate and was not considered cost-effective in this indication.\(^{22-23}\) However, albumin could have a beneficial effect on patients receiving large volumes of crystalloids in light of the evidence showing higher blood pressure at early and later time points, higher static filling pressures, and lower net fluid balance.\(^1\)

In this study, paracentesis emerged as a common indication for appropriate albumin use. However, it is important to highlight the lack of uniformity among globally recognized guidelines concerning the exact volume of fluid extraction necessitating albumin administration.\(^3\) Our analysis revealed that a significant portion of patients' medical records lacked detailed information regarding the precise quantity of fluid withdrawn during paracentesis. Consequently, all patients receiving albumin for paracentesis were deemed to be treated appropriately. Nonetheless, this aspect presents a limitation in our study as we were unable to ascertain whether the drained fluid volume aligns with the prescribed albumin dose for replenishment and the suitability of its prescription.
Patients with chronic renal disease typically exhibit low levels of serum albumin, primarily due to reduced synthesis. There are multiple potential causes for this reduced synthesis, including malnutrition resulting from both anorexia related to uremia and protein restriction imposed during advanced stages of renal insufficiency. Additionally, patients with nephrotic syndrome may experience significant albumin loss in the urine. In our study, we observed that the nephrology service accounted for around 21% of albumin prescriptions. Among these prescriptions, only 5.8% were reported to be used inappropriately, mostly prescribed for edema especially in case of diuretic resistance. Based on findings from Lee et al., the utilization of albumin in cases of diuretic resistance lacks a solid foundation due to the varied data available and the absence of clear benefits in enhancing diuresis. These observations underscore the necessity for additional education to tackle this issue and mitigate inappropriate usage.

Buckley et al. reported a significant reduction (50.9%) in inappropriate albumin prescribing through the implementation of pharmacist-led interventions and medication prescribing reviews. These findings highlight the crucial need for developing guidelines and establishing strict criteria to control the prescribing patterns of albumin in hospitals and prevent resource waste. Considering the findings of this study, our objective is to develop local consensus guidelines for albumin use in our center and conduct additional educational sessions to enhance and standardize albumin utilization.

The results of our study, along with other studies documented in the literature, collectively indicate a consensus regarding the inappropriate use of albumin. DUEs will play a significant role in fostering discussions between physicians and pharmacists to obtain and develop evidence-based guidelines for the appropriate use and optimal utilization of albumin.

Our study has several limitations that should be acknowledged. Firstly, the retrospective design and reliance on patient medical records and physician notes as the sole source of information introduce potential biases and incomplete documentation. In addition, the retrospective nature of the study limited our ability to evaluate the clinical outcomes or complications associated with the use of albumin. Secondly, the presence of multiple reported indications for albumin use posed a challenge in determining the appropriateness of these indications and identifying the
primary indication for use. To mitigate this limitation, patients with unclear indications were subjected to a second and third review of clinical notes and medication profiles to enhance the accuracy of determining the most likely primary indications and their appropriateness. Another limitation of our study is the absence of a comprehensive pharmacoeconomic analysis regarding the use of albumin. Our analysis did not encompass the effect on patient outcomes (e.g., length of stay, mortality) or the indirect cost associated with the preparation and administration of albumin or with the potential adverse events associated with its use. Our analysis was confined to the direct costs of albumin use.

Conclusion
This study revealed inappropriate use of albumin in about one-third of the cases at a comprehensive cancer center. Given its limited availability and cost, we recommend the development of evidence-based guidelines that incorporate the major indications for the use of albumin. Continuous education on appropriate usage and regular evaluations of guideline implementation should also be considered. Future studies should concentrate on evaluating the impact of interventions on evidence-based prescribing of albumin, as well as assessing the use of albumin on patient outcomes (e.g., 28-day mortality and ICU length of stay) and adverse events.

Conflicts of Interest
The authors declare no conflict of interests.

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No funding was received for this study.

Author Contributions
All of the authors mentioned above made substantial contributions to the conception and design, data collection and analysis. They all reviewed the article, approved the content, and agreed to be accountable for all aspects of the study, including the accuracy and integrity of the work.

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References


Figure 1: Distribution of albumin prescriptions according to the indications (%).

*ARDS: acute respiratory distress syndrome; SBP: spontaneous bacterial peritonitis.

Table 1: Baseline Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Gender, n (%)</th>
<th>Patient status at the time of albumin order, n(%)</th>
<th>Type of Malignancy, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male, n (%)</td>
<td>Inpatient</td>
<td>Breast cancer</td>
</tr>
<tr>
<td></td>
<td>Female, n (%)</td>
<td>Outpatient</td>
<td>Lung cancer</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Colorectal cancer</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Gynecological malignancies</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>pancreas cancer</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Others</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>743 (54.6)</td>
<td>2,078 (83.6)</td>
<td>155 (11.3%)</td>
</tr>
<tr>
<td></td>
<td>618 (45.6)</td>
<td>407 (16.4)</td>
<td>117 (8.5%)</td>
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<td></td>
<td></td>
<td></td>
<td>84 (6.1%)</td>
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<td></td>
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<td>112 (8.3%)</td>
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<td></td>
<td></td>
<td></td>
<td>53 (3.9%)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>840 (61.7%)</td>
</tr>
</tbody>
</table>

Age (years), mean ± SD: 60 ± 16
<table>
<thead>
<tr>
<th>Serum albumin at the time of prescription (g/dl), mean ± SD</th>
<th>2.62 ±0.6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of vials per patient, mean ± SD</td>
<td>7.44 ± 8.9</td>
</tr>
<tr>
<td>Duration of albumin use (Days), mean ± SD</td>
<td>2.6±1.8</td>
</tr>
<tr>
<td>Total number of albumin vials dispensed (n)</td>
<td>18,329</td>
</tr>
<tr>
<td>Total cost of used albumin vials (USD)</td>
<td>960,471</td>
</tr>
</tbody>
</table>

Table 2: Albumin prescriptions across various services and the number of prescriptions considered inappropriate within each service.

<table>
<thead>
<tr>
<th>Service*</th>
<th>Albumin prescriptions per service, n (%)</th>
<th>Inappropriate prescriptions n (%***)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solid tumors</td>
<td>733 (29.5%)</td>
<td>299 (40.8 %)</td>
</tr>
<tr>
<td>Nephrology</td>
<td>537 (21.6%)</td>
<td>31 (5.8 %)</td>
</tr>
<tr>
<td>Critical care</td>
<td>452 (18.2%)</td>
<td>58 (12.8 %)</td>
</tr>
<tr>
<td>Outpatient</td>
<td>354 (14.2%)</td>
<td>189 (53.3 %)</td>
</tr>
<tr>
<td>Palliative</td>
<td>134 (5.4%)</td>
<td>58 (43.2 %)</td>
</tr>
<tr>
<td>Surgical</td>
<td>128 (5.2%)</td>
<td>84 (65.6 %)</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>38 (1.5%)</td>
<td>13 (34.2%)</td>
</tr>
<tr>
<td>Leukemia</td>
<td>23 (0.9%)</td>
<td>9 (39.1 %)</td>
</tr>
</tbody>
</table>

*Refers to the clinical service that prescribed albumin for the patient, regardless of the patient’s type of malignancy or hospital location.

**The percentage of inappropriate prescriptions compared to the total number of prescriptions within the same service.