

# Effects of Serum Albumin Level in Lower vs Upper Extremity Surgery: A Hospital-based Retrospective Study

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## ABSTRACT

**Introduction:** Trauma and major surgery often lead to low serum albumin levels in patients. Several studies have reported depressed serum albumin levels in upper and lower extremity and other major surgeries. Metabolic stress response from major surgical interventions and prolonged immobility is primarily responsible for low serum albumin levels in these patients.

**Aim:** To investigate the preoperative and postoperative serum albumin levels in patients who underwent extremity surgery and compare the changes in albumin levels between those who underwent upper extremity surgery versus lower extremity surgery.

**Materials and Methods:** This was a hospital-based retrospective study. The study included 120 patients who presented to the Emergency Department of Surgery and Orthopaedics at Deben Mahata Government Medical College and Hospital, Purulia, West Bengal, India due to trauma. The study was conducted from November 30, 2018 to November 30, 2021. All patients underwent either lower or upper extremity surgery (Group 1 and Group 2, respectively) by orthopaedic surgeons and were consecutively selected regardless of their ages. The serum albumin levels at the time of admission and on the third day after surgery were obtained from the hospital patient records. Continuous variables were expressed as mean±standard deviation. The normality

test of the numerical variables was done using the Kolmogorov-Smirnov test.

**Results:** The mean age of the population in the upper extremity surgery group was 38.8 years vs 30.5 years in the lower extremity group. A statistically significant difference in the preoperative and postoperative serum albumin levels was found in both groups ( $p < 0.05$ ). Moreover, the mean difference between preoperative and postoperative serum albumin levels was found to be significantly higher in the lower extremity group ( $1.52 \pm 0.32$  g/dL) than in the upper extremity group ( $0.95 \pm 0.39$  g/dL) ( $p < 0.05$ ), and the coefficient of correlation between these two groups ( $r > 0.7$ ) indicated a significant difference between albumin levels in the two groups.

**Conclusion:** This study revealed that both upper and lower extremity surgeries caused hypoalbuminaemia. The study was novel in finding that lower extremity surgery caused more severe hypoalbuminaemia in the patients compared to those who underwent upper extremity surgery. A correlation study was done between the two groups, and it was found to be significant with a p-value of  $< 0.05$  and an r-value of  $> 0.7$ . The reason for this significant difference was the longer duration of lower extremity surgery, requiring more fluid support during the surgery and resulting in increased metabolic stress.

**Keywords:** Falls from height, Hypoalbuminaemia, Major surgery, Trauma surgery

## INTRODUCTION

Hypoalbuminaemia is a well-known marker of malnutrition and has prognostic and predictive value for many diseases or conditions, including major surgery, carcinomas, trauma, and colorectal or gastrointestinal disorders. Decreased serum albumin levels directly impact the length of hospital stay, surgery complications, morbidity, and mortality [1-4]. Hypoalbuminaemia is associated with poor tissue healing and collagen synthesis, and it is a good marker of traumatic, cardiac, colorectal, and general surgery. Major surgical interventions and traumas cause severe stress responses that lead to higher rates of complications, delays in recovery, and even mortality [5-8]. Inflammatory markers, such as C-Reactive Protein (CRP) and albumin help determine a patient's metabolic condition and predict their prognosis [8-11]. Studies have reported that hypoalbuminaemia is one of the markers of trauma and major surgery [10-12].

Albumin, a plasma protein synthesised in the liver, maintains colloid osmotic pressure that keeps body fluid in the intravascular space, shows antithrombotic effect, binds and transports some agents, scavenges free oxygen radicals, and plays a role in vascular permeability in shock and sepsis [12,13]. Serum albumin decreases in two ways: decreased synthesis of albumin in the liver due to chronic liver diseases, malnutrition, malabsorption, and carcinomas, and increased loss of albumin through traumas, nephrotic syndrome, major bleeding, fistulas, glomerulonephritis, pregnancy, and drug use [14,15].

Several studies have reported hypoalbuminaemia as a marker of trauma and major surgery. Sun J et al., demonstrated the consequences of hypoalbuminaemia in surgical septic patients [15]. Shin KH et al., found early postoperative hypoalbuminaemia as a risk factor for postoperative pneumonia following hip fracture surgery [16]. Althoff AD et al., observed postoperative hypoalbuminaemia following proximal humerus fracture surgery and found it to be a risk factor for postoperative complications [17]. Vora M et al., focused on upper extremity surgery due to trauma and resultant hypoalbuminaemia [18]. Most studies have focused on extremity surgery due to trauma and resultant hypoalbuminaemia, but only a few studies have reported the comparison between upper and lower extremity surgery patients in terms of hypoalbuminaemia.

Therefore, the present study aimed to investigate the preoperative and postoperative serum albumin levels in patients who underwent extremity surgery and compare the changes in albumin levels after upper extremity surgery with those after lower extremity surgery and it will be one of the few studies in the literature.

## MATERIALS AND METHODS

The study was a hospital-based retrospective study. It was carried out in the Department of surgery and Orthopaedics, Deben Mahata Government Medical College and Hospital, Purulia, West Bengal, India. A total of 120 patients who were referred to the Emergency Department of the tertiary care hospital with trauma such as traffic

accidents, falls, falls from a height between November 30, 2018 to November 30, 2021 were enrolled in the study, retrospectively and the data was collected from case registry and records of the Department of Surgery and Orthopaedics.

**Inclusion criteria:** All the patients included in the study underwent upper or lower extremity surgery by Department of Orthopaedics and Traumatology and were consecutively selected, regardless of their ages. In addition patients with only acute traumatic surgery and one extremity surgery were selected.

**Exclusion criteria:** Those who had multiple trauma or underwent multiple surgeries were excluded from study. Patients who underwent both upper and lower extremity surgeries were also excluded. Routine orthopaedic surgeries were excluded as well.

## Study Procedure

The patients were divided in two groups: upper extremity surgery (60 patients) and lower extremity surgery (60 patients). The serum albumin levels at the time of admission and on the third day after the surgery were obtained from the hospital patient records. They were analysed using a particle-enhanced turbimetric inhibition immunoassay method with an autoanalyser. The serum albumin level of the patients was tested each day during hospitalisation. All the patients in the present study stayed at hospital for atleast three days and most of them (64/120) stayed only for six days. Therefore, the albumin levels of the days 0, 3 were noted for a standardised interpretation.

## STATISTICAL ANALYSIS

Continuous variables were expressed as mean±standard deviation. The normality test of the numerical variables using Kolmogorov-Smirnov test. The Independent sample t-test was used to compare two independent groups. The paired sample t-test was used to compare pre- and postoperative albumin levels. In order to find out whether there is significant correlation between the serum albumin level (pre and postoperative) of the two groups (patients of upper extremity surgery and that of lower extremity surgery group) we have calculated coefficient of correlation which is represented by the symbol "r" and is given by the formula of coefficient of correlation. The correlation coefficient r tends to lie between -1.0 and+1.0, if r is near+1 it indicates a strong positive association. A value near-1 indicates a strong negative association. Data were statistically analysed using the software Jamovi Project (2018; Jamovi version 0.9.2.6; retrieved from <https://www.jamovi.org>, open source). The p-value less than 0.05 was considered as statistically significant.

## RESULTS

The upper extremity surgery group consisted of 34 (56.7%) male and 26 (43.3%) female patients and the lower extremity surgery group had 32 (53.3%) male and 28 (46.7%) female patients. No statistical significant gender variation between patients undergoing upper and lower extremity surgery is found ( $p=0.124$ ) [Table/Fig-1]. No statistically significant differences between the preoperative serum albumin levels were found ( $1.31\pm 0.43$  g/dL in males and  $1.14\pm 0.48$  g/dL in females;  $p=0.150$ ). The mean age of the

Demographic data	Lower extremity surgery (Group 1)	Upper extremity surgery (Group 2)	p-value
Gender distribution (Male:female)	1.14:1	1.3:1	0.124
Mean age (Mean±std. deviation)	43.20±22.05	42.76±20.97	$p>0.05$
Hospital stay in days (Arithmetic mean)	8	7	$p>0.05$
Hospital stay in days Mean±std.deviation	8.41±1.86	7.93±1.43	$p>0.05$
Hospital stay in days (Range)	6-10	6-9	$p>0.05$

**[Table/Fig-1]:** Demographic characteristics in upper and lower extremity surgery group.

patients who underwent upper and lower extremity surgeries was  $43.20\pm 22.05$  years (between 11 and 80 years) and  $42.76\pm 20.97$  years (between 6 and 76 years), respectively. No statistically significant correlation between ages of patients and differences in preoperative and postoperative serum albumin levels was found ( $r=-0.239$  and  $p=0.202$  in lower extremity surgery group;  $r=0.070$  and  $p=0.714$  in the upper extremity age surgery group).

The mean hospitalisation period was  $7.93\pm 1.43$  days (min: 6, max: 9) for the patients in the upper extremity surgery group and  $8.41\pm 1.86$  days (min: 6, max: 10) in the lower extremity surgery group. No significant difference in terms of hospital stay was observed between the two groups. The most common reason for the fractures was falls in both groups (28 patients for both groups) [Table/Fig-2]. The most common reason for the fractures was falls in both groups. The other common reasons were falls from height and out-car and in-car traffic accidents.

Type of trauma	Group 1 (Lower extremity) (Number of patients)	Group 2 (Upper extremity) (Number of patients)
Falls	28	28
Out-car traffic accidents	14	8
Falls from heights	4	12
In-car traffic accidents	4	6
Motorcycle accidents	4	4
Others	6	2

**[Table/Fig-2]:** Distribution of the patients according to the reasons of fractures. (Others=bicycle accident, auto/toto accident, injury by domestic cattle in rural areas)

Six patients in the upper extremity surgery group had open humerus shaft fractures: 4 of these had Gustli Anderson type 2 and two had type 3a. Among the 54 patients with closed fractures, 22 patients had humerus shaft fractures, 12 had humerus supracondylar fractures, eight had humerus proximal fractures, four had humerus medial epicondyle fractures, eight had clavicular, ulnar or radius fractures. In the lower extremity surgery group 4 patients had open femur shaft fractures. Among the 56 patients with closed fractures, 14 had multiple femur and/or tibia fractures, 10 had tibia shaft fractures, six had femur shaft fractures, four had tibia-fibula fracture, four had tibial plate fractures, 14 had single tibial fractures in various segments and four had single femur fractures.

The serum albumin levels were normal before the surgery but decreased after the surgery in both groups. A statistically significant difference in terms of preoperative and postoperative serum albumin levels was noted in both groups ( $p<0.05$ ) [Table/Fig-3]. Drop of mean value of serum albumin on postoperative (3<sup>rd</sup> day) from that of preoperative Serum albumin value in lower extremity group was more than that of upper extremity group in the present study. The mean difference between preoperative and postoperative serum albumin levels was found to be  $0.95\pm 0.39$  g/dL. In the upper

Parameters	Group 1 (Lower extremity)	Mean	Group 2 (Upper extremity)	Mean	p-value	r value (coefficient of correlation)
Preoperative albumin levels (gm/dL)	$3.76\pm 0.37$	3.72	$3.65\pm 0.38$	3.64	0.293 (a)	-
Postoperative albumin levels	$2.24\pm 0.28$	2.28	$2.71\pm 0.47$	2.85	$<0.05$ (a)	-
p-value (b)	$<0.05$ (b)		$<0.05$ (b)			-
Difference in albumin levels	$1.52\pm 0.32$		$0.95\pm 0.39$		$<0.05$ (a)	$>0.7$

**[Table/Fig-3]:** Comparison between the groups in terms of preoperative and postoperative albumin levels. Independent-samples test was used for comparisons between groups. Paired samples t-test was used for intragroup comparisons

extremity surgery group and  $1.52 \pm 0.32$  g/dL in the lower extremity surgery group. The mean difference between these two groups was statistically significant ( $p < 0.05$ ) indicating that the lower extremity surgery patients had a significantly higher decrease in albumin levels [Table/Fig-2]. The coefficient of correlation between these two groups  $r > 0.7$  indicated significant difference between albumin levels in two groups.

## DISCUSSION

Hypoalbuminaemia is a marker of malnourishment and is associated with higher rates of early complications in patients undergoing surgical treatment for major traumatic events. Alberti LR et al., showed in their study that there was hypoalbuminaemia following major surgeries in the 1<sup>st</sup> postoperative week and this was significantly correlated with duration of surgery ( $r \geq 0.7$ ) [9]. Sindgikar V et al., found significant postoperative hypoalbuminaemia in 48.5% cases in their study and it was associated with higher risk of complications [12]. Vora M et al., found that hypoalbuminaemia is associated with higher risk for complications and readmission after proximal humerus fracture surgery [18]. Sun J et al., found that preoperative and subsequently postoperative Serum level of albumin estimation will help to predict the prognosis of patients of both upper and lower extremity surgery as well as other major surgery [15]. The present study showed that upper and lower extremity surgeries were associated with postoperative hypoalbuminaemia. In addition, the study showed that the serum albumin levels were significantly decreased in the surgery of lower extremity compared with that of upper extremity.

Several studies reported an association between malnutrition and major surgery. Studies showed that hypoalbuminaemia was a marker of malnutrition in the patients who underwent major surgery [8-10,16]. However, in the present study all the patients of both groups had the same nutrition programme. In addition some studies showed that plasma albumin levels might decrease in spite of aggressive replacement therapy in some major trauma patients. They explained that the condition was due to altered endothelial permeability caused by cytokines such as interleukin 1 [8-11,17]. Thus, the study showed that hypoalbuminaemia occurred due to not only malnutrition but also some other factors.

Stress response after surgery and trauma has been a well-known entity, and it involved emerging metabolic, hormonal and electrolyte changes, and release of cytokines. It was stated that albumin showed an immediate response to surgical stress [2,9,14]. Hubner M et al., found that postoperative decrease in serum albumin reflected the magnitude of surgery and the associated stress response [8]. In major trauma and surgeries excessive fluid leaks into the interstitial and intravascular spaces as a result of systemic and tissue reactions, thereby decreasing the serum albumin levels [3,12]. Protein metabolism reported to be significantly disturbed after any kind of traumatic event such as surgery, sepsis and burn injuries. Albumin has been identified as a reliable marker of the process. Serum concentration of albumin showed a significant decrease as early as a few hours after the trauma or surgery [1,4,10]. In the study of Ryan S et al., serum albumin showed significant drop on the first postoperative day and the mean difference between preoperative and postoperative serum albumin levels was found to be  $1.54 \pm 0.34$  g/dL [13]. In the study of Althoff AD et al., there was significant fall of serum albumin concentration with the mean difference between preoperative and postoperative serum level of  $1.49 \pm 0.36$  gm/dL [17]. In the present study, it was accepted that all the patients had trauma and stress and all underwent a major surgery. This explained the cause of hyperalbuminemia in all patients, who participated in the study, however the significantly higher albuminemia in the lower extremity surgery patients was not clearly understood as it was not known which of the two surgeries caused more stress.

We have attempted to assess stress by measuring serum albumin concentration which is an important parameter of surgical stress.

One of the major differences between the patient groups in this study was immobility. Patients who underwent lower extremity surgery had much more immobility duration than the one who had upper extremity surgery. Despite the fact that, Afshinnia F et al., stated that immobility and hypoalbuminaemia are closely associated with osteoporosis, no evidence about an association between hypoalbuminaemia and immobility of the patients was found [14]. Immobility in the lower extremity surgery patients was considered to cause more severe hypoalbuminaemia in the present study although enough evidence was lacking. In the present study, six patients had open fractures in the upper extremity surgery group and four in the lower extremity surgery group. However, multiple close fractures were more in the lower extremity surgery group. This could be a reason for the difference between the groups causing a higher albumin decrease due to an effect on increasing metabolism as a result of trauma and injury [7, 18, 19].

The other major difference between the patient groups was the duration of the surgery. The lower extremity surgery took significantly more time compared with the upper extremity surgery. Therefore, more fluid support was given to the patients in the lower extremity surgery groups during the surgery. More liquid support results in the dilution of plasma and a hence decreased serum albumin level. In this context, the given excessive fluid was rapidly eliminated and the overload of sodium was slowly ejected resulting in further elongated extra fluid dilution of albumin. Studies have shown that the severity of the catabolic damage caused a proportional increase in vascular permeability [14-16]. Therefore, in the present study the duration of surgery of the lower extremities and the higher amount of fluid given during the surgery might explain the decrease in albumin.

Older patients who underwent surgery had more severe hypoalbuminaemia compared with the younger patients [9,15]. However in the present study, no association was found between the age of patients and serum albumin levels. In addition, no relationship was found between the serum albumin levels and the gender of patients.

## Limitation(s)

The patients were followed-up only for first seven days, not until the discharge. In addition, the serum level was observed only as laboratory finding the clinical reflection of hypoalbuminaemia was not recorded in the study.

## CONCLUSION(S)

In conclusion, the study found that both upper and lower extremity surgeries result in hypoalbuminaemia. Additionally, the study is novel in discovering that lower extremity surgery causes more severe hypoalbuminaemia in patients than upper extremity surgery, regardless of factors such as age, sex, nutrition, and stress. The significant difference in severity could be explained by the longer duration of lower extremity surgeries, which require more fluid support during the procedure.

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