

Original Research Article

Correlation of post-operative albumin level to the clinical outcome in patients undergoing abdominal (intra-peritoneal) surgery

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ABSTRACT

Background: Surgical interventions have become part and parcel of an individual's life. The average number of surgeries that a person undergoes in their lifetime is 9.2 (3.4 inpatient operations, 2.6 outpatient operations, and 3.2 non-operating room invasive procedures). So it is important to make sure that the patient undergoes surgery smoothly and gets out of hospital well at early days. There are many factors that help to predict the outcome post surgeries, in this study we have used albumin (pre and post op) and its difference for predicting the clinical outcome.

Methods: 80 patients who are undergoing abdominal (intra-peritoneal) surgeries from October 2019 to December 2020 was studied. Serum albumin was estimated by Randox albumin assay method. Serum albumin level was obtained pre-operatively, post-op after 6 hours and on POD-1 and their difference is found and compared with clinical outcome using Clavien-Dindo classification.

Results: It was observed that 81.5% (22 out of 27) of patients with albumin drop more than 10% by 6 hours post operatively are likely to develop complications of surgery. It was observed that 89% (16 out of 18) of patients with albumin drop more than 15% by POD1 are likely to develop complications of surgery.

Conclusions: In our study raised serum albumin drop post-operatively was associated with complications and so it can be concluded that serum albumin may be used as a marker for predicting the clinical outcome of the patients undergoing surgery.

Keywords: Serum albumin, Abdominal (intra-peritoneal) surgery

INTRODUCTION

Surgical interventions have become part and parcel of an individual's life. One United States study says that average number of surgeries that a person undergoes in his/her lifetime is 9.2.¹

Surgical complications such as surgical site infections continue to be a serious problem, despite developments in asepsis, antimicrobial medications, sanitation, and operating methods. They are to blame for the rising expense, morbidity, and mortality associated with surgical procedures, and they remain a big issue even in hospitals with the most sophisticated equipment and proper

preoperative preparation and antibiotic prophylaxis policies.²

There are several clinical, bio-chemical, and radiological methods available to help clinicians quickly diagnose postoperative problems.³

Acute-phase proteins (APPs) are a type of protein whose plasma levels rise (positive acute-phase proteins) or fall (negative acute-phase proteins) in response to inflammation. When an injury occurs, inflammatory cells release cytokines such as IL-1, IL-6, and TNF-ALPHA, which cause alterations in acute phase protein secretions in the liver.⁴⁻⁶

CRP, hepcidin, ferritin, ceruloplasmin, haptoglobin, fibrinogen, prothrombin, and platelet activating factor are examples of positive acute phase reactants. Albumin, transferrin, transthyretin, retinol binding protein, anticortin, and transcortin are the negative acute phase proteins. In the acute phase reaction to trauma, stress, inflammation, or sepsis, the rate of transcription of albumin mRNA and synthesis of albumin decreases, whereas the rate of gene transcription for positive acute phase proteins like CRP increases.⁷

Albumin is a protein and a biochemical marker that has an instantaneous reaction to surgical stress and is commonly utilised as a nutritional marker and outcome predictor. In the majority of major abdominal procedures, a drop in albumin level can be seen during the first few hours after surgery. Despite well-established pathophysiological fundamentals of albumin kinetics, albumin is rarely employed as a marker of problems in the early postoperative period. There is also a link between albumin levels and surgical trauma and postoperative stress response.⁸ Decreased plasma albumin concentration (P-alb) associated with surgical trauma is known and the mechanism is likely to be multifactorial, but increased capillary leakage is believed to be a major factor. This altered capillary leak can result from an inflammatory response evoked by surgical trauma.⁹

Since albumin is a negative phase protein, its synthesis and blood levels decrease after injury. Surgery is also a kind of man-made injury for the benefit of a person. Albumin levels decrease postoperatively and can be used as a predictor for finding clinical results.^{5,10,11} There is a plethora of studies in the literature looking at the level of albumin as a predictor of postoperative complications in abdominal surgeries. The present study was aimed to examine the level of albumin pre and post operatively in the context of predicting complications of surgeries in patients undergoing abdominal surgeries.

METHODS

Study setting

The study was carried out at Bharati Vidyapeeth Research Centre and Hospital, Pune.

Study design

The study was prospective observational type of study.

Study duration

Study was carried out from October 2019 to August 2021.

Study population

Patients admitted in general surgery department and undergoing any abdominal (intra-peritoneal) surgery in Bharati Hospital and research center, Pune from October

2019 to August 2021 were included in the study after giving informed consent and ethical clearance.

Study participants

110 patients admitted in general surgery department and undergoing any abdominal surgery in Bharati hospital and research center, Pune from October 2019 to August 2021 were included in the study after giving informed consent and ethical clearance.

Sample size estimation

The estimated sample size was 110.

Sampling technique

The sampling technique was convenience sampling.

Tool of data collection

A specially designed proforma was filled for each patient. These proforma have general information about the patients, pre and post-operative albumin and other variables.

Inclusion criteria

People undergoing abdominal (intra-peritoneal) surgeries between and those with age group of 18-70 years were included.

Exclusion criteria

People with underlying liver disease were excluded.

The study group comprised of patients above pediatric age group and both genders that undergo abdominal (intra-peritoneal) surgery at Bharati Hospital and Research Center, Pune. All included patients were admitted, initially subjected for detailed history taking which included symptoms and duration of the disease; general physical and systemic examination. A specially designed proforma was filled for each patient. These proforma have general information about the patients, pre and post-operative albumin and other variables. The data was then analyzed for correlation of the post-operative albumin drop with the clinical outcome of the abdominal (intra-peritoneal) surgeries using Clavien-Dindo scoring system.

Data analysis

The collected data was entered in Microsoft excel sheet and analyzed. The results were presented in tabular and graphic format. Post-operative albumin drop was compared with the post-operative complications using Clavien-Dindo scoring system. The amount of post-operative albumin drop was equated with the development of complication post-operatively.

RESULTS

The present study was done to study the correlation of postoperative changes in albumin to the clinical outcome in patients undergoing abdominal (intra-peritoneal) surgery. Total 110 patients (Table 1 shows age distribution) were included in the present study who underwent intra-peritoneal surgeries. Out of total patients included 59 (53.6%) were females and 51 (46.4%) were males (Figure 1). The albumin levels were measured before and 6-hour after surgery, the percentage difference change in the albumin level after 6-hour of surgery was calculated. The change was more than or equal to 10% among 36 patients, while it was <10% among 74 patients. The albumin levels were measured before and 24-hour after surgery, the percentage difference change in the albumin level after 24-hour of surgery was calculated. The change was more than or equal to 15% among 20 patients, while it was <15% among 90 patients. The patients were evaluated for the development of post-surgical complications. The distribution of complications is shown in Table 2. Grade 1 complications were the most prevalent, while 67 patients developed no any complications. The complications among patients in study population divided on the basis of percentage albumin change 6-hour after surgery. The distribution of patients was compared by means of chi-square test, there was a significantly high number of patients developed complications who had $\geq 10\%$ of albumin change (Table 3). Similarly, the complications among patients in study population divided on the basis of percentage albumin change 24-hour after surgery. The distribution of patients was compared by means of Chi square test, there was a significantly high number (18 out of 20) of patients developed complications who had $\geq 15\%$ of albumin change (Table 4). No any significant association between the complications

developed and the duration of surgery was noted in the present study (Table 5).

Table 1: Age distribution.

Age group (years)	N	%
<30	20	18.2
>50	49	44.5
30-50	41	37.3
Total	110	100.0

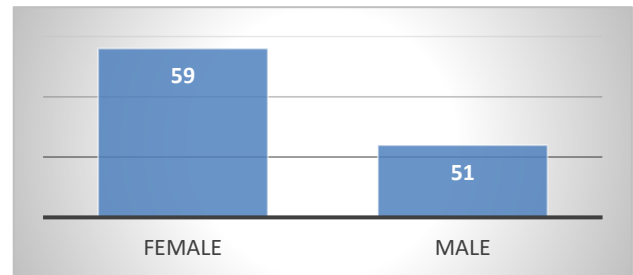


Figure 1: Gender distribution (n=110).

Table 2: Distribution of post-surgery complications among the study population according to Clavien-Dindo classification (n=110).

Grade	N	%
Grade 1	28	25.5
Grade 2	6	5.5
Grade 3a	2	1.8
Grade 3b	2	1.8
Grade 5	5	4.5
No complications	67	60.9
Total	110	100.0

Table 3: Association of the type of complications with percentage change in albumin at 6-hour post-surgery.

Type of complications	% albumin difference		Total	P value
	<10 (%)	≥ 10 (%)		
Grade 1	11 (15)	17 (47)	28	<0.0001
Grade 2	2 (2)	4 (11)	6	
Grade 3a	1 (1)	1 (3)	2	
Grade 3b	0	2 (5)	2	
Grade 5	0	5 (14)	5	
No complications	60 (81)	7 (19)	67	
Total	74	36	110	

Table 4: Association of the type of complications with percentage change in albumin at POD-1.

Type of complications	% albumin difference		Total	P value
	<15 (%)	≥ 15 (%)		
Grade 1	21 (23)	7 (35)	28	<0.0001
Grade 2	2 (2)	4 (20)	6	
Grade 3a	1 (1)	1 (5)	2	
Grade 3b	1 (1)	1 (5)	2	
Grade 5	0	5 (20)	5	
No complications	65 (72)	2 (10)	67	
Total	90 (100)	20 (100)	110	

Table 5: Association of outcome with duration of surgery.

Type of complications	Duration of study			Total	P value
	≤150	>300	150-300		
Grade 1	2	5	21	28	<0.354
Grade 2	0	0	6	6	
Grade 3a	1	0	1	2	
Grade 3b	0	0	2	2	
Grade 5	0	2	3	5	
No complications	4	12	51	67	
Total	7	19	84	110	

DISCUSSION

One of the most commonly performed elective surgeries are abdominal surgeries. Over the last few decades, the postoperative morbidity has remained high, in spite of reduced postoperative mortality due to surgical and perioperative improvements. The postoperative complications in patients lead to a significant financial burden, in addition to morbidity. For this purpose, to reduce healthcare expenditures, important efforts are currently pursued.¹² Increased vascular permeability for cells and plasma solutes is a universal reaction in trauma, critical illness, chronic disease, life events, multiple or isolated organ failure, and cancer. This response is evident in circumstances including edema in healing wounds and the necessity to maintain intravascular volume by 'overhydrating' traumatized or post-surgery patients.¹³

Due to inflammatory signals, a rapid decline in the level of albumin is seen which is a maintenance protein.¹⁴ Serum levels of albumin predict outcome in first-hit acute inflammatory conditions such as primary trauma, burns, or acute infections. Acute inflammation elicits an acute phase reaction characterized by changes of albumin and other markers of inflammation including CRP, which increases within hours after major surgery.¹⁵

The present study was aimed to examine the level of albumin pre-operatively and its use as a marker to complications in patients undergoing abdominal surgeries. The correlation of postoperative changes in albumin to the clinical outcome in patients undergoing abdominal (intra-peritoneal) surgery was studied. The mean age of the all patients studied was 47.63±17.45 years, and 53.6% were females and 46.4% were males.

Similar to present study Issangya et al studied 61 participants; with the mean age of 51.6±16.3, but in contrast to our finding 28 (45.9%) participants were experienced postoperative adverse outcomes and the majorities were males 40 (65.6%).¹⁶

Zhou et al tried to identify peri-operative variables associated with operative duration and determined their influence on clinical outcomes in pediatric patients.¹⁷ The operative time was often increased by excision difficulty caused by a larger choledochal cyst size, a greater BMI, and older age in the multivariate analysis. A long surgical

duration was associated with delayed gastrointestinal functional recovery, as measured using the time to first defecation and first bowel movement. Significantly lower levels of serum albumin were found in the long operative time group than in the short operative time group. The total length of postoperative hospital stay was longer in patients in the long operative time group than in those in the short operative time group. In the present study the duration of surgery was recorded, among 6.4% patients it was ≤150 minutes, in 76.4% patients it was between 150-300 minutes and in 17.3% it was >300 minutes. For perioperative morbidity and even in patients with normal preoperative levels, a negative acute-phase protein, albumin, is important.¹⁸

Labgaa et al reported the sudden drop in the levels of serum albumin after surgery.¹⁷ Serum albumin drop (ΔAlb) was found to be correlated with the mEPASS score and to CRP increase. ΔAlb was also correlated to overall complications, CCI and length of hospital stay. The efficacy of ΔAlb with sensitivity of 77.1% and a specificity of 67.2% to predict complications gave the value of ≥10 g/l. A threefold increased risk showed after overall post-operative complications in patients with ΔAlb≥10 g/l on POD-1.

The albumin levels pre and post-operatively were recorded by Issangya et al among the patients undergoing abdominal surgeries.¹⁶ In pre-operative serum albumin values, 67.8% patients had albumin level of lower than 3.4 g/l while similar to present study, lower than 3.4 g/l post-operative albumin values had in 91% patients. A high ΔAlb had in 27.3% patients with median percentage value of 14.77%. Also, an independent significant factor, ΔAlb, associated with adverse outcomes was reported in this study. The percentage difference in the albumin level after 6-hour of surgery was <10% among 67.3% of patients and ≥10% among 32.7% of patients. The percentage difference change in the albumin level after 24-hours of surgery was <15% among 81.8% of patients and ≥15% among 18.2% of patients.

Similar to present study Hübner et al studied albumin level drop as marker of surgical stress, a significant immediate decline by 10 g/l after surgery.¹⁰ Operation length, maximum CRP and estimated blood loss was correlated with maximal Albumin decrease. Pre-operative and post-operative hypoalbuminemia were identified in 15.4% and

51.2% of subjects, respectively. The decrease in plasma albumin concentration in association with surgical trauma is well known, and the mechanisms are probably multifactorial, but an increase in capillary leakage is thought to be a major component. This altered capillary leakage may be attributed to the inflammatory reaction elicited by the surgical trauma.⁹

The most prevalent types of complications recorded among the study population were grade I (25.5%), followed by grade 2 (5.5%), grade 5 (4.5%), grade 3a (wound gaping and 2 suturing) and grade 3b each present among 1.8% of patients. In a correlation analysis demonstrated positively correlation of postoperative exogenous albumin infusion with complication grade among the patients undergoing pancreaticoduodenectomy.¹⁹

The factors including, a high CRP on POD 3 or 4, the presence of Charcot's triad and a longer operating time predicted a high Δ Alb level which was explained by Liu Q et al in determining the perioperative factors related with the post-operative reduction in serum albumin. The high occurrence of postoperative complications with gastrointestinal functional recovery delay, reflected by the postoperative defecation and bowel movement delay was also related to a high Δ Alb level. Patients undergoing pancreatic surgery showed the lowest albumin values (34.7-5.3 g/l), followed by gastroesophageal (36.4-5.4 g/l), colorectal (37.8-5.1 g/l), and hepatic surgery (38.4-5.8 g/l) patients. The association between albumin levels and the type of surgery approached significance.¹⁹

When the association of percent difference change in albumin level after 6-hours of surgery was studied with type of complications, we found a significant association indicating if more the percent difference in albumin level, the number of complications also increases. Similar, results were obtained when the results were compared after 24-hours of surgery. While the comparison of type of complication with duration of surgery did not yield any significant association among these parameters.

In patients having complications and a longer hospital stay had significantly higher maximal decreased Albumin levels reported by Hübner et al.¹⁰ They concluded that a drop in albumin in early post-operative condition was correlated with adverse clinical outcomes and also reflect the magnitude of surgical trauma.

After gastric cancer resection short-term complications developed by 27.8% patients were reported in a study by Liu et al.¹¹ The serum albumin decline postoperatively was found to be an independent risk factor for complications. The cutoff value was reported to be 14.0%. After gastrectomy the likelihood of short-term complications were more in patients with postoperative decrease in serum albumin if $\geq 14.0\%$. The results of study by Nakano et al for predicting the prognosis of patients with curatively

resected PDAC reported potential markers being postoperative level and recovery rate of serum albumin.²⁰

Surgery in the abdominal cavity is followed by a larger decrease in serum albumin concentrations, as in other surgical procedures. Enhanced capillary permeability causes escape of fluid and albumins from the vessels, and returns to normal in 12-24 h after surgery; however, after extensive surgery, albumin was found in the extravascular compartment 7-10 days after surgery.²¹

Altered metabolism combines with the mechanisms of decrease at early postoperative phase, blood loss/dilution and most importantly due to capillary leakage redistribution into the third space. In the early postoperative phase, the latter accounts for >75% decrease in the level of albumin and appears to be related to the magnitude of systemic inflammatory response. Therefore, perioperative fluid management may affect decrease in albumin level, but it mainly reflects the extent of postsurgical stress response.¹²

Serum albumin is widely used as reliable indicator for nutritional status and as predictor for clinical outcomes. Protein metabolism is significantly disturbed after any kind of traumatic event, for example, surgery, sepsis, and burn injuries; albumin has been identified as a reliable indicator of this process. Plasma concentrations of albumin reveal an important decrease as early as a few hours after the hit.

The underlying pathophysiological mechanisms include: 1) the impairment in the albumin synthesis is seen during the early postoperative phase as an importance of acute phase proteins, in the host defense process these acute phase proteins are needed to facilitate the production of these acute phase molecules. However, the decrease observed at initial period is found to be transitory. In the early postoperative period the increase in the fractional albumin synthesis is proportionally to the degree of inflammation is seen; perioperative nutrition can further stimulate the production; 2) in the early postoperative phase, nearly 10 times basal energy expenditure increases, and within 10 days to favor gluconeogenesis up to 20% of protein from body store can be consumed; 3) however, sequestration into the third space is the most important postoperative losses of albumin. In the context of sepsis and (surgical) trauma, a well-known phenomenon is capillary leak.¹⁰

Even though our study shows the efficacy of post-operative albumin drop in abdominal (intra-peritoneal) surgeries in predicting the complications it had been done in small sample size and includes all types of intra-peritoneal surgeries. Our study had not brought out the association between the comorbidity (diabetes, hypertension) and the outcome. Our study had not discussed about the association of laparoscopic versus open surgery with post-operative albumin drop. In the near future a study with large sample size, including only

selective intra-peritoneal surgery could validate the efficacy of post-operative albumin drop in predicting outcome.

CONCLUSION

As per literature early perioperative decreases in serum albumin levels may be a good, simple and cost-effective tool to predict adverse outcomes in major abdominal surgeries. $\geq 10\%$ and $\geq 15\%$ decrease in albumin level after 6 hrs and 24 hrs of surgery respectively than before surgery in patients undergoing abdominal surgeries, has a better predictive value for prediction of surgical complications. Therefore, the estimation of albumin level after 6 hours of surgery can be recommended for the prediction of any adverse outcomes of surgery.

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