Delta Albumin a Game Changer in predicting Adverse Surgical Outcomes in Open Abdominal Surgeries

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Abstract- **Introduction: Albumin is an important protein; it is considered a negative active phase protein. In spite of other factors predicting surgical outcomes, little is known about the perioperative dynamics of Albumin and its effect on surgical outcome in abdominal surgeries. Delta albumin is calculated using Preoperative serum Albumin (PreOD) and Postoperative day 1 serum Albumin (POD1).**
Aim and Objective: This study is aimed to explore perioperative serum Albumin as a predictor of adverse outcome in open abdominal surgeries. To assess the effect of pre and post-operative serum Albumin on postoperative complications by calculating the percentage decrease in serum Albumin i.e. Delta Albumin.
Methods: Preoperative serum Albumin (PreOD) and Postoperative day 1 serum Albumin (POD1) of 60 patients undergoing Emergency open Abdominal surgery was analyzed and Delta albumin calculated. Cutoff for delta albumin (13.51%) was obtained by ROC curve analysis for the occurrence of postoperative complications. All patients were followed up for 30 days post-surgery for adverse surgical outcomes like: Surgical site infection, delayed wound healing, anastomotic leak, enterocutaneous fistula formation, need for reoperation, shock and death. These were graded with Clavien-Dindo classification.
Results: Delta albumin cutoff for post-operative complications was 13.51 % Patients with delta albumin below 13.51% did not develop post-operative complication (Specificity: 100%). Patients with delta albumin above 13.51% developed one or more of the mentioned complications within 30 days of surgery (Sensitivity 78.1%).
Conclusion: This study concluded that a percentage decrease of serum Albumin perioperatively i.e. Delta Albumin, is a better predictor of postoperative adverse outcomes in patients undergoing open abdominal surgeries than serum Albumin (both pre and post-operative).

Index Terms- **Serum Albumin, Delta Albumin, Adverse outcomes, Abdominal Surgery, Emergency Laparotomy, Postoperative complications, Predictor.**

I. INTRODUCTION:

Abdominal surgery is among the most frequently performed elective surgeries worldwide. Although postoperative mortality has decreased over the past few decades due to surgical and perioperative advancements, postoperative morbidity has remained high. While substantial efforts are being made to lower healthcare costs, postoperative complications pose a significant financial burden in addition to the associated morbidity[1]. Adverse events affect the patient and are untoward, undesired, or detrimental. The implications of postoperative wound infection include patient morbidity and suffering, additional use of resources, and delayed discharge in the presence of severe infection[2]. When compared to elective surgery, postoperative outcomes following emergency abdominal surgery are typically poorer.

Surgical procedures lead to well-understood metabolic, neuroendocrine, and immune responses, but the stress response to surgery contributes to increased postoperative complications. Pro-inflammatory cytokines will increase due to surgical stress, which leads to changes in circulating acute phase proteins, such as albumin and C-reactive protein (CRP)[2]. The magnitude of metabolic stress response mirrors the extent of surgical stress and presumably contributes to the risk of developing postoperative complications. Early identification of patients at risk may improve outcomes since measures to attenuate the surgical stress response and reduce morbidity[3]. A simple and reliable parameter is needed that represents surgical stress to identify patients at risk and to help tailor perioperative care[4]. Preoperative interventions can be used to control excessive stress response, and some of them have a significant positive effect on the clinical outcome. A reliable prediction of the surgical stress response is therefore highly desirable.Albumin is the most abundant protein in humans and is widely used as a nutrition marker. In addition, albumin shows an immediate response to surgical stress and could therefore qualify to measure surgical stress and to predict a complicated postoperative course as per a study by Hübner M. et al.[4] Serum albumin is known as a negative acute phase protein. A study noted that following surgery complications were linked to postoperative albumin levels. Low albumin levels are linked to postoperative complications[3]. Systemic inflammatory response syndrome (SIRS), which causes low plasma albumin levels in individuals after major abdominal surgery, is characterized by increased capillary albumin leakage. Although C reactive protein (CRP) and procalcitonin (PCT) have been proposed as predictors for adverse outcomes in colorectal surgery, they both display the critical limitation of slow kinetics[4].

For example, preoperative hypoalbuminemia can predict surgical site infections. Ryan et al.[5] found that postoperative hypoalbuminemia on postoperative day 1 (POD1) was associated with complications following esophagectomy. Sang et al.[6] also found that hypoalbuminemia on POD 2 was an independent risk factor for acute kidney injury in patients with living donor liver transplantation. However, these studies mainly focused on the impact of serum Albumin on the nutritional status of patients. Hypoalbuminemia is a predictor of delayed recovery of bowel function and is strongly associated with postoperative complications after right hemi colectomy for right-sided colon cancer, or following other major gastrointestinal surgeries[7]. Preliminary data suggested that Albumin levels rapidly dropped after surgery and correlated to outcomes in oesophageal, oral cancer, abdominal, pancreatic, liver resection, transplant and cardiac surgeries. However, prospective validation was missing, and Albumin was not used to assess surgical stress or to predict outcomes[1].
Recent studies revealed that the decrease of albumin following surgery was associated with the extent of surgical trauma and consequently with an elevated number of adverse events.1 Whether this is true for open abdominal surgeries is unknown. Thus, our study was designed to evaluate perioperative serum albumin dynamics with complication rates in patients undergoing open abdominal surgeries. Muller C et al. hypothesized that the decrease of serum albumin levels in the early postoperative period represented as Δ albumin was related to postoperative morbidity.8 Hence in the present study, we investigated the association between Delta albumin and postoperative complications after open abdominal surgeries.

II. AIM

To explore perioperative serum Albumin as a predictor of adverse outcomes in open abdominal surgeries.

III. OBJECTIVE

To assess the effect of pre and post-operative serum Albumin on postoperative complications by calculating the percentage decrease in serum Albumin i.e. Delta Albumin as mentioned in Equation 1.

$$\textit{Delta Albumin} = \frac{(PreOD - POD1)}{PreOD} \times 100. \qquad (1)$$

IV. METHODOLOGY

Source of data: All the patients who were admitted to the Department of General Surgery for Emergency Open abdominal surgeries during a period of one and a half years, i.e. January 2021 to July 2022, into Kempegowda Institute of Medical Sciences, Bengaluru.
Place of study: Kempegowda Institute Of Medical Sciences, Bengaluru.
Type of study: Comparative non-randomized prospective study.
Duration of the study: One and a half years (January 2021 to July 2022).
Sample size: 60 Patients satisfying Inclusion criteria.

Inclusion Criteria

All patients admitted to Dept. of General Surgery KIMS Hospital who underwent Emergency open abdominal surgery.

Exclusion Criteria

- Children below 18 years.
- Patients undergoing Elective open abdominal surgeries
- Patients with preoperative hypoalbuminemia (serum Albumin <3.5 g/dL).

Data Collection

Informed consent was taken to enroll the participants in the study. Data was collected from the case sheets of the patients participating in the study and recorded in the proforma. Delta albumin was calculated for each patient using Preoperative Serum Albumin (PreOD) and Postoperative day 1 S. Albumin (POD1). Patients were followed up at the Hospital till discharge and at home up to 30 days after the surgery, to look for complications as mentioned in **Fig. 1**. These complications were graded as per Clavien-Dindo Classification. ROC curve analysis of Delta Albumin values was done to identify the best predictive value and cut-off for the occurrence of adverse surgical outcomes.

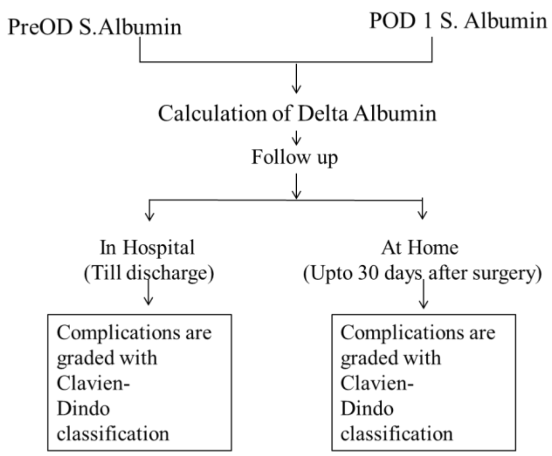

Figure 1 Algorithm of the study design

The patients were observed for the development of complications like
a) Surgical site infection
b) Wound dehiscence
c) GI bleeding
d) Intra-abdominal abscess
e) Anastomotic leak
f) Stoma complications
g) Early post-op bowel obstruction
h) Need for re-operation
i) Pneumonia
j) Sepsis, Septic shock
k) Single or Multi-organ dysfunction
l) Death

V. STATISTICAL ANALYSIS

Statistical Package for Social Sciences [SPSS] for Windows Version 22.0 Released 2013. Armonk, NY: IBM Corp., was used to perform statistical analyses. Descriptive analysis of all the explanatory and outcome parameters will be done using frequency and proportions for categorical variables, whereas Mean & SD for continuous variables. The Chi-Square test was used to compare the presence of postoperative complications based on patient characteristics. Independent Student t Test was used to compare the mean Albumin levels during the Pre-op & Post-op period & also the Delta Albumin levels based on the presence of Post-op complications. Mann-Whitney test was used to compare the mean values of Hematological Parameters based on the presence of post-op complications.

ROC Curve analysis was performed for Delta Albumin levels for determining the cut-off between patients with & without post-op complications. The level of significance was set at $P<0.05$.

VI. RESULT

In our study, most of the participants were male, 42 (70 percent) and 18 (30 percent) were female . The majority of the subjects were in the age group 18-30 years (35 percent), Range of Age distribution: 18 – 86 years, Mean age was: 43.87 years (SD 19.21), as depicted in **Table 1 and 2**. 42 of the study participants (70 percent) did not have any comorbidities, whereas 11 patients had single comorbidity like Diabetes mellitus, hypertension and hypothyroidism, and 7 patients had multiple comorbidities. The distribution of diagnosis and procedures done is detailed in **Tables 3 and 4**.

Table 1 Age distribution of study patients

Age	***n***	***%***
18-30 yrs.	21	35.0%
31-40 yrs.	8	13.3%
41-50 yrs.	6	10.0%
51-60 yrs.	11	18.4%
61-70 yrs.	12	20.0%
> 70 yrs.	2	3.3%
	Mean	SD
Mean	43.87	19.21
Range	18 – 86	

Table 2 Gender distribution of study patients

Category	***n***	***%***
Males	42	70.0%
Females	18	30.0%

Table 3 Distribution of study patients based on Diagnosis

Diagnosis	***n***	***%***
Hollow viscus perforation	12	20.0%
Appendicular Perforation	8	13.3%
Obstructed umbilical hernia	7	11.7%
Acute Appendicitis	5	8.3%
Acute Intestinal obstruction	5	8.3%
Stab injury to abdomen	5	8.3%
Small bowel obstruction	4	6.7%
Appendicular Abscess	2	3.3%
Penetrating injury to abdomen	2	3.3%
Appendicular Rupture	1	1.7%
Complete transection of pancreas	1	1.7%

CA Sigmoid colon	1	1.7%
Distal Ileal perforation	1	1.7%
Hemoperitoneum	1	1.7%
Perforated Mekel's diverticulum	1	1.7%
Jejunal perforation with Ileal stricture	1	1.7%
Perforated gallbladder	1	1.7%
Pre pyloric perforation	1	1.7%
Sigmoid volvulus	1	1.7%

Table 4 Distribution of study patients based on Procedure performed

Procedure	***n***	***%***
Exploratory laparotomy	28	46.7%
Exploratory laparotomy and resection anastomoses	12	20.0%
Exploratory laparotomy and Appendicectomy	5	8.3%
Exploratory laparotomy and Graham's patch repair	4	6.7%
Exploratory laparotomy and ileostomy	3	5.0%
Open Appendicectomy	3	5.0%
Mayos repair	2	3.3%
Exploratory laparotomy and distal pancreatectomy	1	1.7%
Exploratory laparotomy and peritoneal lavage	1	1.7%
Open umbilical hernioplasty	1	1.7%

Table 5 Distribution of study patients based on presence of comorbidity

Category	***n***	***%***
Type 2 Diabetes Mellitus	4	6.7%
Hypothyroidism	4	6.7%
Type 2 Diabetes + Hypertension	4	6.7%
Hypertension	3	5.0%
Hypertension + Hypothyroidism	2	3.3%
CLD + Portal hypertension	1	1.7%
Nil	42	70.0%

As depicted in **Table 6**, of the 60 patients included in our study, 41 (68.3 percent) of them developed one or more postoperative complications, whereas the remaining 19 (31.7 percent) of the patients did not develop any postoperative complications within 30 days of open abdominal surgery. The most common complications overall belonged to Grade I of Clavein-Dindo classification seen in 21 patients (35 percent) like delayed wound healing and surgical site infection. These were most frequently seen in the first five postoperative days with maximum incidence on a postoperative day POD 3 and 5 (45 and 46 percent respectively). Most Grade II complications like wound dehiscence, early post-op bowel obstruction and pneumonia were observed on POD 3 seen in 11 patients (18.3 percent). Grade III complications were noted in 7 patients (11.7 percent) were observed after POD 5. Grade IV and V complications were the least common, noted in 1 patient each as per **Table 7**.

Table 6 Distribution of study patients based on Post-op Complications

Post-op Complications	***n***	***%***
Present	41	68.3%
Absent	19	31.7%

Table 7 Distribution of Overall Post-operative Complications based on Clavien Dindo Classification among study patients

Post-op Complications Grades	***n***	***%***
Grade I	21	35.0%
Grade II	11	18.3%
Grade III	7	11.7%
Grade IVa	1	1.7%
Grade V	1	1.7%
Nil	19	31.7%

Table 8 indicates Univariate analysis of parameters like hemoglobin (Hb), total count (TC), differential count (DC), platelet count, and random blood sugar (RBS) etc was performed. Although only RBS showed a significant correlation was noted with postoperative

complications (p value 0.04). In our study, the age, gender, comorbidities and the type of OT procedure did not influence the incidence of postoperative complications.

Table 8 Comparison of presence of post-operative complications based on the patient characteristics using Chi Square Test

Variable	***Category***	***Present***		***Absent***		***p-value***
		n	***%***	***n***	***%***	
Age	≤ 45 yrs.	20	48.8%	11	57.9%	0.51
	> 45 yrs.	21	51.2%	8	42.1%	
Gender	Males	29	70.7%	13	68.4%	0.86
	Females	12	29.3%	6	31.6%	
Comorbidity	Present	14	34.1%	4	21.1%	0.30
	Absent	27	65.9%	15	78.9%	

In our study, the mean Preoperative Serum Albumin (PreOD) value in patients without postoperative complications was 4.2 (SD 0.32) and 4.07 (SD 0.44) in patients who developed postoperative complications. This difference was not statistically significant. The mean Postoperative day 1 Serum Albumin (POD1) value was 3.09 (SD 0.64) in patients who developed complications which was significantly lower than those who did not develop complications 3.9 (SD 0.36), p-value <0.01 **Table 9.**

Table 9 Comparison of mean Albumin levels during Pre-op & Post-op period based on the presence of Post-op complications using Independent Student t Test

Albumin	***Complications***	***N***	***Mean***	***SD***	***Mean Diff***	***p-value***
Pre-op	Present	41	4.070	0.439	-0.153	0.18
	Absent	19	4.223	0.320		
Post-op	Present	41	3.086	0.643	-0.825	<0.001*
	Absent	19	3.911	0.358		

Figure 2 depicts the Receiver Operator Curve (ROC) was plotted for the Delta albumin values of all patients and a cut-off value of 13.51 percent was achieved. The area under the curve (AUC) was 0.93 and the p-value was 0.001 indicating the cut-off value was statistically significant. Patients with delta albumin below 13.51 percent did not develop post-operative complications. (Specificity: 100%). And patients with delta albumin above 13.51% developed one or more of the mentioned complications within 30 days of surgery. (Sensitivity 78.1%) **Table 10,11**

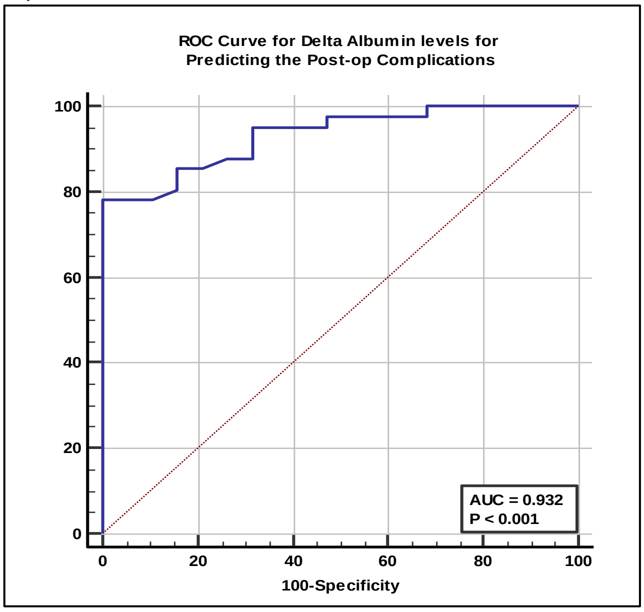

Fig 2 ROC Curve analysis for Delta Albumin levels for determining the cut-off between patients with & without post-op complications

Table 10 Comparison of mean Delta Albumin levels based on the presence of Post-op complications using Independent Student t Test

Albumin	*Complications*	*N*	*Mean*	*SD*	*Mean Diff*	*p-value*
Delta Albumin	Present	41	0.243	0.131	0.168	<0.001*
	Absent	19	0.075	0.035		

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Table 11 ROC Curve analysis for Delta Albumin levels for determining the cut-off between patients with & without post-op complications

Variable	*AUC*	*Std. Error*	*95% Conf. Interval*		*p-value*	*Cut off*	*Sn (%)*	*Sp (%)*
			Lower	Upper				
Delta Albumin	0.93	0.03	0.84	0.98	<0.001*	>13.514	78.05	100.00

VII. DISCUSSION

Despite technical improvements and advances in perioperative care, major abdominal operations are still associated with a high rate of severe complications, long-term disability, and health and social costs[9]. The morbidity and mortality rates are 30% and 2-5% respectively [10,11]. Markers that allow early detection of complications and prediction of their severity, ideally before patients become symptomatic, are an area of interest for many surgeons [12]. This study offers a thorough analysis of Delta Albumin's prognostic value for postoperative complications after open abdominal surgeries.

A similar study conducted by Dharap et al. concluded that postoperative complications were observed in 31.50%; minor complications (Grade I and II) in 19.75% and major complications (Grade III and IV) in 8.0% of patients. Postoperative mortality (Grade V) was 3.75%.13 According to a study conducted by Maitreyee et al. a total of 150 cases with abdominal operations were included in this study. Among them, 29 patients developed SSI. The incidence of SSI among them was 19.3% [14].

In our study, The mean Postoperative day 1 Serum Albumin (POD1) value was 3.09 (SD 0.64) in patients who developed complications which was significantly lower than those who did not develop complications 3.9 (SD 0.36), p-value <0.01. Poziomyck et al [15] examined mortality in patients who developed postoperative complications following foregut surgery. Lower serum albumin levels were associated with mortality and longer hospital stay. In 258 patients undergoing oesophagogastric excision for high-grade dysplasia, Noble et al. [16] looked at significant complications and anastomotic leak. The study discovered a strong correlation between low serum albumin levels and major complications on postoperative days 3 and 7, as well as the anastomotic leak. Furthermore, they discovered that a NUn score >10 was indicative of an anastomotic leak and death on postoperative day 4 when albumin was paired with C-reactive protein (CRP) and white cell count (WCC).

Ryan et al. [5] showed that decreased serum albumin concentration on the first postoperative day was also an independent predictor of poor surgical outcome following gastrointestinal cancer surgery. Delta Albumin on POD1 correlated to surgical stress (mE-PASS) (r=0.275, p=0.01) and to surrogates such as duration of surgery (r=0.562, p<0.001), blood loss (r=0.391, p<0.001) and surgical approach (p=0.55, p<0.001). Delta Albumin on POD1 was significantly associated with adverse outcomes, showing significant correlations with CCI (p=0.383, p<0.001) and LoS (p=0.468, p<0.001) [1].

In a study conducted by Hübner et all, the correlation of Albumin Drop with Clinical Outcome Measures. Delta Albumin values were estimated for all patient groups concerning postoperative complications (online appendix). There was a trend of higher Delta Albumin levels in patients with major complications ($P = 0.082$) and a significant difference comparing patients with no complication with the group with any complication (6.1 ± 5.2 versus 10.0 ± 5.4 g/L, $P = 0.005$). Albumin drop and length of hospital stay were statistically correlated (Pearson $\rho = 0.285$, $P < 0.020$) [4]. The Delta albumin cut-off value in our study was 13.51 percent which was comparable to 14.77 and 14.0 percent, values in studies conducted by Christian et al. [17] and Zhi Jian et al. [18]

VIII. CONCLUSION

This study concluded that a percentage decrease of serum albumin perioperatively i.e. Delta Albumin is a better predictor of postoperative adverse outcomes in patients undergoing open abdominal surgeries than Serum Albumin (both pre and post-operative). Hence Delta albumin can be used as a simple, low-cost prognostic tool to predict the risk of adverse surgical outcomes.

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