## **Original Research Article**

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## A study to evaluate post operative drop in serum albumin level as marker for surgical stress and predictor for clinical outcome in laparotomy patients

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### ABSTRACT

**Background:** Surgical involvements trigger metabolic stress responses of different magnitude, contributing to delayed recovery, complication rate and length of hospital stay. Insulin resistance, serum albumin levels, cytokines such as interleukin-6, interleukin-10, and other cytokines are used in clinical studies as measure for surgical stress. Clinical practitioners routinely measure C-reactive protein (CRP) levels in the blood after surgery to assess postoperative inflammation and predict the likelihood of postsurgical side effects. The slow kinetics of CRP, which makes it a poor predictor of stress-related complications, is a significant drawback. Albumin is widely used as nutritional marker and predictor. It shows an immediate response to surgical stress and could therefore qualify to measure surgical stress and to predict a complicated postoperative course. The aim of the present study was therefore to evaluate post-operative drop in serum albumin as a marker for surgical stress and predictor for clinical outcome in laparotomy patients.

**Methods:** Patients admitted under surgical units from December 2020 to June 2022, at Mamata Medical College and Hospital, Khammam. A study was carried out on 50 patients admitted, undergoing Laparotomy electively and Emergency. All these patients have been assessed both preoperatively and postoperatively and their complications have been documented.

**Results:** Serum albumin levels were compared pre-operatively and postoperatively using analysis of variance (ANOVA) test. There is statistical significance between pre-operative serum albumin levels and postoperative serum albumin levels from post-operative day (POD) 1 to POD 5.

**Conclusions:** The serum albumin measurement is simple, cost effective and easy to perform. Using the serum albumin as a marker, reliable predictions can be made regarding the surgical complications, duration of stay in the hospital and the severity of surgical stress.

Keywords: Serum albumin, Surgical stress, Emergency, Laparotomy, Marker

#### **INTRODUCTION**

Surgical involvements trigger metabolic stress responses of different magnitude, contributing to delayed recovery, complication rate and length of hospital stay. Mainly, the term "major abdominal surgery" remains ill-defined and includes procedure-related factors, like the type of surgical approach (laparoscopy versus laparotomy), type and extent of organ resection, operative time, and blood loss; but secondarily also patient factors, for example, underlying disease (benign versus malignant), nutritional status and pre-existing comorbidities, are subsumed.

Recent improvements in perioperative care aiming to modulate a tremendous stress response have been proven to be successful. Application of improved recovery pathways has shown a decreasing effect on surgical stress and subsequently reducing hospital stay, complications, and costs after colorectal surgery. A strict perioperative nutritional support and use of immune-modulating formulas proved to reduce both (infectious) complications after major surgery and hospital stay. Similarly, the perioperative use of corticosteroids is been used; and preliminary results for this simple intervention are promising with regard to postoperative outcomes.

A simple and reliable parameter representing surgical stress would be clinically important to identify patients at risk and to tailor perioperative care. Thorell suggested insulin resistance to quantify the stress response.<sup>1</sup> However, insulin resistance is difficult to measure and also costly and hence never been implemented routinely. For the same reasons, interleukins IL-6, IL-10 and other cytokines are used in clinical studies only.<sup>1</sup>

Postoperative serum C-reactive protein (CRP) levels are widely used in clinical practice to assess postoperative inflammation and to predict postoperative complications. A major drawback of CRP as predictor for stress-related complications is its slow kinetics. Peak values are measured only at postoperative day 2 or 3, which may be too late for early preventive interventions. Albumin is the most abundant protein in humans and widely used as nutritional marker and predictor for outcomes. 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. This particular aspect has not yet been considered for clinical use.

The aim of the present study was therefore to evaluate postoperative drop in serum albumin as a marker for surgical stress and predictor for clinical outcome in laparotomy patients.

#### Aim and objectives

To study the serum albumin levels as a marker for surgical stress; and to study the serum albumin levels as a potential predictor of adverse outcomes like delayed wound healing, increased hospital stay and organ dysfunction.

#### **METHODS**

#### Study area

The study was conducted at the department of general surgery, Mamata Medical College, Khammam. The study was approved by ethical committee for research studies of Mamata Medical College.

#### Study population

Patients undergoing laparotomy electively and emergency were a part of the study population.

#### Study design

The design of the study was cross-sectional.

#### Study period

The study was conducted from December 2020 to June 2022.

#### Sample size

50 patients were included in the study.

#### Inclusion criteria

Patients of age 16-70 years undergoing laparotomies in elective and emergencies were included in the study.

#### Exclusion criteria

Patients with age <16 years or >70 years, patients with known decompensated liver disease, human immunedeficiency virus (HIV) patients and CD count <200 were excluded from the study.

#### Methodology

Permission from the institutional ethical committee was taken for the study prior to data collection. A proper informed consent was taken from the subjects regarding the study. Serum albumin (g/l) levels were measured in preoperative period at 7 o'clock in the morning before breakfast in a state of fasting. First sample was taken 4–6 hours postoperatively. Subsequent samples of albumin level were monitored up to post-operative day-5 (POD–5).

The duration of surgery was determined from the time of incision to the closure of skin. This was done by the anaesthetist. The decision to measure blood loss intraoperatively was done collaboratively by the surgeon and the anaesthetist. The blood loss was ascertained by the measurement of the aspiration fluids and the gauze materials that were soaked. Based on the surgery and the complications that developed after that, Dindo-Clavien method was used to assess and grade the severity of the complications.

#### Dindo-Clavien system

Grades I and II- measured as minor complications, grades III and IV- measured as major complications, and grade V- mortality.

The following surgeries were performed: laparoscopic cholecystectomy, extraperitoneal incisional hernia repair, open colectomy, upper gastrointestinal resections, gastrectomy, bowel resection and anastomosis, adhesiolysis, Graham's patch repair, right salphingectomy, and GI resections.

Table 1: Dindo-Clavien system of grading.

Grade	Implications
1	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic and radiological intervention; acceptable therapeutic regimens are: drugs as antiemetics, antipyretics, analgesics, diuretics and electrolytes and physiotherapy
2	Requiring pharmacological treatment with drugs other than such allowed for grade I complications; blood transfusion, antibiotics and total parenteral nutrition are also included
3	Requiring surgical, endoscopic or radiological intervention
3a	Intervention under regional/local anaesthesia
3b	Intervention under general anaesthesia
4	Life threatening complication requiring intensive care/intensive care unit management
4a	Single organ dysfunction
4b	Multi organ dysfunction
5	Patient demise

#### Statistical analysis

Data entry was done using Microsoft (MS) excel and statistically analysed using statistical package for social sciences (SPSS) version 16 for MS Windows. Analysis of variance (ANOVA) was used to show the difference between two or more means or components through significance tests. P value less than 0.05 considered to be statistically significant.

#### RESULTS

Majority of the patients belonged to the age group of 41-50 years (44%) followed by 51-60 years (18%), 21-30 years (14%), 61-70 years (12%), <20 years (6%) and 31-40 years (6%). Mean age was 44.06+14.07 years (Table 2).

Most common indication of surgery was duodenal perforation (18%) followed by ruptured ectopic pregnancy (6%), sigmoid volvulus (6%), acute intestinal obstruction (4%), hollow viscous perforation (4%), obstructed incisional hernia (4%), obstructed left inguinal hernia (4%), obstructed umblical hernia (4%), right ovarian cyst torsion (4%), right blunt injury abdomen (4%), ruptured liver abscess (4%), superior mesentric vein thrombosis (4%), acute abdomen appendicular perforation (2%), acute abdomen torsion ovarian (2%), appendicular perforation (2%), assault stab injury (2%), assault stab injury abdomen

(illeal perforation) (2%), carcinoma rectum (2%), carcinoma stomach antropyloric growth stage II (2%), fall from height (2%), gastric perforation (2%), ileocecaltb with perforation query (2%), internal hernia with pain abdomen (2%), intestinal obstruction (adhesions) (2%), intususseption (2%), left torsion ovarian cyst (2%), obstructed right inguinal hernia (2%) and stab injury abdomen (2%).

## Table 2: Distribution of patients based on the age<br/>group.

Age group (years)	Frequency	Percent (%)	Mean+SD
<20	3	6.0	
21-30	7	14.0	
31-40	3	6.0	
41-50	22	44.0	44.06+14.07
51-60	9	18.0	
61-70	6	12.0	
Total	50	100.0	

#### Table 3: Distribution of patients based on the gender.

Gender	Frequency	Percent
Male	32	64.0
Female	18	36.0
Total	50	100.0

#### Table 4: Distribution of patient based on indication of surgery.

Indication of surgery	Frequency	Percentage
Acute abdomen appendicular perforation	1	2.0
Acute abdomen ruptured ectopic pregnancy	1	2.0
Acute abdomen torsion ovary	1	2.0
Acute intestinal obstruction	2	
Appendicular perforation	1	2.0
Assault stab injury	1	2.0
Assault stab injury (ileal perforation)	1	2.0
Carcinoma rectum	1	2.0

Continued.

Indication of surgery	Frequency	Percentage
Carinoma stomach antropyloric growth stage II	1	2.0
Duodenal perforation	9	18.0
Fall from height	1	2.0
Gastric perforation	1	2.0
Hollow viscous perforation	2	4.0
Ileocecal TB with perforation query	1	2.0
Internal hernia with pain abdomen	1	2.0
Intestinal obstruction (adhesions)	1	2.0
Intususseption	1	2.0
Left torsion ovarian cyst	1	2.0
Obstructed incisional hernia	2	4.0
Obstructed left inguinal hernia	2	4.0
Obstructed right inguinal hernia	1	2.0
Obstructed umbilical hernia	2	4.0
Right ovarian cyst torsion	2	4.0
Right blunt injury abdomen	2	4.0
Ruptured ectopic pregnancy	3	6.0
Ruptured liver abscess	2	4.0
Sigmoid volvulus	3	6.0
Stab injury abdomen	1	2.0
Superior mesenteric vein thrombosis	2	4.0
Total	50	100.0

### Table 5: Distribution of patient based on indication of surgery.

Surgery procedure done	Frequency	Percentage
Diversion colostomy	1	2.0
Exploratory laparotomy	1	2.0
Exploratory laparotomy + wash given	2	4.0
Exploratory laparotomy and proceed	2	4.0
Grahams omental patch closure	12	24.0
Jejunostomy with resection	1	2.0
Jejunostomy with resection of gangrene bowel of 100cm	1	2.0
Jejunostomy with resection of gangrene bowel up to terminal ileum	1	2.0
Laparotomy left oopherectomy	2	4.0
Laparotomy right salphingectomy	1	2.0
Laparotomy right oopherectomy	5	10.0
Laparotomy + adhesinolysis	4	8.0
Laparotomy + appendicectomy	1	2.0
Laparotomy + Jejunostomy	1	2.0
Laparotomy + left salphingectomy	1	2.0
Laparotomy + packing done	1	2.0
Laparotomy + resection anastomosis	2	4.0
Polytrauma transverse colon	1	2.0
Resection and anastomosis	7	14.0
Right herniorraphy	1	2.0
Segmental ileal resection	1	2.0
Subtotal gastrectomy with D2	1	2.0
Total	50	100.0

Most common procedure done was grahams omental patch closure (24%) followed by resection and anastamosis (14%), laparotomy + right oophorectomy (10%), laparotomy + adhesinolysis (8%), exploratory laparotomy + wash given (4%), exploratory laparotomy and proceed (4%), laparotomy left oophorectomy (4%), laparotomy + resection anastomosis (4%), diversion colostomy (2%), exploratory laparotomy (2%), jejunostomy with resection

(2%), jejunostomy with resection of 100 cm gangrene bowel (2%), laparotomy and resection of gangrene bowel up to terminal ileum (2%), laparotomy right salphingectomy (2%), laparotomy + appendicectomy (2%), laparotomy + jejunostomy (2%), laparotomy + ltsalphingectomy (2%), laparotomy + packing done (2%), polytrauma transverse colon (2%), right herniorapphy (2%), segmental ileal resection (2%) and subtotal gastrectomy with d2 (2%) (Table 5).

## Table 6: Distribution of patient based on the Dindo-Clavein classification.

Grading as per Dindo- Clavein classificaton	Frequency	Percent
Grade 1	23	46.0
Grade 2	12	24.0
Grade 3a	8	16.0
Grade 4a	2	4.0
Grade 4b	4	8.0
Grade 5	1	2.0
Total	50	100.0

# Table 7: Distribution of patient based on the postoperative complication.

Post operative complication	Frequency	Percent
Acute kidney injury	1	2.0
Acute kidney injury + dialysis done	1	2.0
AKI with wound gaping	1	2.0
AKI wound infection	1	2.0
Blood transfusion	6	12.0
Burst abdomen secondary suturing done	1	2.0
Elevated renal parameters	1	2.0
Elevated renal parameter wound infection	1	2.0
Mild fever	1	2.0
MODS	3	6.0
MODS with ventilator	1	2.0
Post op fever	4	8.0
Wound gaping	3	6.0
Wound gaping and secondary suturing done	4	8.0
Wound infection	3	6.0
No complication	18	36.0
Total	50	100.0

According to Dindo-Clavein classification, 46% patients belonged to grade 1, 24% patients belonged to grade 2, 16% patients belonged to grade 3a, 4% patients belonged to grade 4a, 8% patients belonged to grade 4b and 2% patients belonged to grade 5.

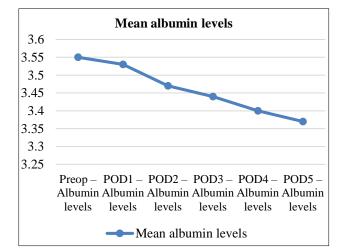
Most common post operative complication was blood transfusion (12%) followed by post operative fever (8%), wound gaping and secondary suturing done (8%), MODS (6%), wound gaping (6%), wound infection (6%), acute kidney injury (2%), acute kidney injury + dialysis done (2%), AKI with wound gaping (2%), AKI wound infection (2%), burst abdomen secondary suturing done (2%), elevated renal parameters (2%), elevated renal parameter wound infection (2%), mild fever (2%) and MODS with ventilator (2%) (Table 7).

Mean preoperative serum albumin levels were 3.55+0.47 g/dl. Post-operatively, serum albumin levels decreased from 3.53 to 3.37 from day 1 to day 5.

There is albumin drop of 4.5% from POD 1 to POD 5 due to surgical stress (Table 8).

#### Table 8: Mean serum albumin levels- preoperatively and postoperatively.

Parameters	Mean	Standard deviation
<b>Preop</b> – albumin levels	3.55	0.47
POD1 – albumin levels	3.53	0.49
POD2 – albumin levels	3.47	0.48
POD3 – albumin levels	3.44	0.49
POD4 – albumin levels	3.40	0.50
POD5 – albumin levels	3.37	0.52



## Figure 1: Mean serum albumin levels- preoperatively and postoperatively.

Serum albumin levels were compared pre-operatively and postoperatively using ANOVA test.

There is statistical significance between pre-operative serum albumin levels and postoperative serum albumin levels from POD 1 to POD 5 (Table 9).

Albumin levels	ANOVA			
	Sum of squares	Mean square	F	P value
POD1 – albumin levels				
Between groups	12.064	0.804	337.793	0.001
Within groups	0.081	0.002		
Total	12.145			
POD2 – albumin levels				
Between groups	11.355	0.757	91.585	0.001
Within groups	0.281	0.008		
Total	11.636			
POD3 – albumin levels				
Between groups	11.815	0.788	86.449	0.001
Within groups	0.310	0.009		
Total	12.125			
POD4 – albumin levels				
Between groups	12.197	0.813	65.456	0.001
Within groups	0.422	0.012		
Total	12.619			
POD5 – albumin levels				
Between groups	12.808	0.854	52.078	0.001
Within groups	0.557	0.016		
Total	13.366			

# Table 9: ANOVA test between preoperative mean serum albumin levels and postoperative mean serum albumin levels (day 1 to day 5).

### Table 10: Mean duration of hospital stay.

Parameter	Mean	Standard deviation
<b>Duration of hospital</b> stay (days)	7.56	2.56

### DISCUSSION

Major surgery is followed by a significant metabolic stress response, which is linked with a higher risk of adverse outcomes in the long run. Many perioperative interventions are available to help patients manage an excessive stress response, with some of these interventions having a significant positive impact on clinical outcome. It is therefore of great importance to be able to predict the surgical stress response with accuracy.

The marker should be easy to use, inexpensive, and widely available early in the postoperative period. It should be strongly correlated with surgical trauma and a reliable good indicator of postoperative complications and prolonged hospital stay. As of now, there is no such parameter available.<sup>16</sup> Following surgery or trauma, the stress response has been studied extensively, and it has been demonstrated to involve significant electrolytic, hormonal, and metabolic changes, and the production of cytokines. An increase in the proinflammatory cytokine IL-6 has been linked to postoperative insulin resistance and the severity of(surgical) injury, and it appears to occur within hours of receiving a physical injury. The fact is that

it is not practical for regular use due to the requirement of expensive and sophisticated measuring equipment.<sup>16</sup>

#### Post operative complications

In this study, most common post operative complication was blood transfusion (12%) followed by post operative fever (8%), wound gaping and secondary suturing done (8%), MODS (6%), wound gaping (6%), wound infection (6%), acute kidney injury (2%), acute kidney injury + dialysis done (2%), AKI with wound gaping (2%), AKI wound infection (2%), burst abdomen secondary suturing done (2%), elevated renal parameters (2%), elevate drenal parameter wound infection (2%), mild fever (2%) and MODS with ventilator (2%).

Hypoalbuminemia was the most significant risk factor that delayed wound healing and hence predisposing to wound dehiscence.

There was statistically significant positive correlation between hypoalbuminemia and wound dehiscence in studies done by Fleck et al and Hoye et al.<sup>17,18</sup>

#### Duration of stay

In the present study, mean duration of stay in hospital was 7.56+2.56 days. In a study conducted by Hubner et al<sup>12</sup>, albumin drop and length of hospital stay were found to be statistically related. In Arun et al, mean length of hospital stay in hypoalbumin patients was found to be 10.8 days with a standard deviation of 4.245 and that of normal

albumin patients was found to be 9.03 days with a standard deviation of 3.765.<sup>16</sup> In hypoalbumin patients, 50% were discharged within 10 days and 50% after 10 days. Truong et al mentioned that hypoalbuminemia significantly influences the length of hospital stay.<sup>3</sup>

#### Serum albumin levels

In the present study, mean preoperative serum albumin levels were 3.55+0.47 g/dl. Post operatively, serum albumin levels decreased from 3.53 to 3.37 from day 1 to day 5. There is albumin drop of 4.5% from POD 1 to POD 5 due to surgical stress. There is statistical significance between pre-operative serum albumin levels and postoperative serum albumin levels from POD 1 to POD 5. According to Lohsiriwat et al, the mean albumin level was 2.6 g/dl in patients of right sided colon cancer.<sup>19</sup> Cochrane study put this at 2.2 g/dl in different emergency surgeries.<sup>6</sup>

Specifically, Gibbs et al stated that preoperative serum albumin level as a surgical 2 mortality and morbidity predictor is a valid hypothesis.<sup>20</sup>

The serum albumin level had the strongest and most consistent relationship with stress response and clinical outcome. Immediately following surgery, albumin dropped precipitously and then stabilized until POD 3.

#### Limitations

There were also several limitations in this study where only a single set of surgical procedures were evaluated. The other surgical procedures were not considered as a part of this study.

The smaller sample size leaves us with only a hypothesis.

#### CONCLUSION

The serum albumin measurement is simple, easy and cost effective. It is also easy to perform anywhere unlike like other methods that require state of the art care. Using the serum albumin as a marker, reliable predictions can be made regarding the surgical complications, duration of stay in the hospital and the severity of surgical stress.

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