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# PREOPERATIVE SERUM ALBUMIN LEVEL AS A PREDICTOR OF SURGICAL SITE INFECTION IN ELECTIVE SURGERY FOR GASTROINTESTINAL MALIGNANCY

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## ABSTRACT

**Background:** Surgical site infection (SSI) has a direct negative influence on patient outcome. To date, there are relatively few studies examining the influence of a patient's preoperative nutritional status (especially serum albumin) on the development of SSI. This study was aimed to identify demography of GI malignant cases operated in elective basis in gastrosurgery unit of Bir Hospital, study the rate of SSI in relation with preoperative serum albumin level, study relation between preoperative serum albumin level and length of post-op hospital stay. **Methods:** A prospective observational hospital based study performed at Bir Hospital, Mahaboudha Kathmandu during December 2015 to November 2016 over 56 cases who operated in elective basis for gastrointestinal malignancy. Patients were divided according to their serum albumin level into two groups. Group I: with serum albumin ≤3.5 gm/dl and Group II: with serum albumin >3.5 gm/dl. Postoperatively patients were observed for development of surgical site infection and length of hospital stay. **Results:** Postoperative surgical site infection was higher in number and percentage in group I (serum albumin ≤ 3.5 gm/dl) compared to group II (serum albumin > 3.5 gm/dl) with P-value 0.028. There was significant correlation between preoperative hypoalbuminemia and development of postoperative surgical site infection. Furthermore, the length of postoperative hospital stay was significantly longer in group I (serum albumin ≤ 3.5 gm/dl) (11.16±3.37 days) compared to group II (serum albumin > 3.5 gm/dl) (8.60±2.08 days) (P=0.002). **Conclusions:** The current study revealed that preoperative hypoalbuminemia is a predictor of development of postoperative surgical site infection and increases the length of postoperative hospital stay following surgery for gastrointestinal malignancy.

**KEYWORDS**: Surgical site infection, Serum albumin, Gastro-intestinal malignancy, length of hospital stay.

## INTRODCUTION

Surgical site infection (SSI) is defined as infection occurring in an incisional wound within 30 days of the procedure or within 1 year of procedure if prosthesis is implanted.[1] SSI can be superficial (involving only the skin and subcutaneous tissue of the incision), deep (involving fascial and muscle layers), or organ/space according to CDC definition.[2] SSI accounts for approximately 16% to 18% of all hospital infections. It also has a direct negative influence on patient outcome.

Previously described risk factors for the development of a SSI determined by the National Nosocomial Infection Surveillance (NNIS) include American Society of Anesthesiologist (ASA) grade III/IV, contaminated or dirty wounds, and the duration of procedure.[3] Other risk factors described include increased BMI, emergency surgery, surgeries involving a stoma, blood loss, frequency of glove changes, and the use of sub-cuticular sutures.[4,5] To date, there are relatively few studies examining the influence of a patient's preoperative nutritional status (especially serum albumin) on the development of SSI.

Malnutrition is a broad term that can be used to describe any imbalance in nutrition; from over-nutrition often seen in the developed world, to under-nutrition seen in many developing countries. Malnutrition can develop as a consequence of deficiency in dietary intake, increased requirements associated with a disease state, from complications of an underlying illness such as poor absorption and excessive nutrient losses, or from a combination of these aforementioned factors.[6]

Serum albumin is the main protein of human blood plasma.[7] Various studies in the past have noted that low preoperative serum albumin level is significantly related to postoperative septic morbidity and mortality, for many major surgical procedures.[3-5] Malnourishment is reported in 40% to 50% of hospitalized patients, with higher risk factor for postoperative infections and healing complications in patients who undergo major surgeries.[6]

The blood samples were collected in the previous and following day of the surgical procedure to dose serum albumin along with routine exams. The biuret method and bromocresol green were used, and serum albumin reference levels ranged from 3.5 g/dL to 5.5 g/dL.

Preoperative malnutrition is a major risk factor for increased postoperative morbidity and mortality Malnutrition is a common problem in surgical patients that adversely affects outcome.[1,7] Albumin is the most commonly used and reliable indicator of a patients nutritional status, it is also a negative acute phase protein.[8] In an acute illness or stress response there is a reduction in serum albumin due to alterations in hepatic metabolism and loss of albumin into the interstitium. Serum albumin is a reliable and reproducible predictor of surgical risk and has a close correlation with the degree of malnutrition.[9] Hypoalbuminemia is a predictor of death, hospital stay, and outcome and is strongly associated with postoperative complications.[3,10]

Although a variety of nutritional indices have been found to be valuable in predicting patient outcome, when used alone there is no consensus on the best method for assessing the nutritional status. The serum Albumin level is the most readily available and clinically useful parameter. A serum Albumin level greater than 3.5gm/dl suggests adequate protein stores. A serum Albumin level less than 3.5gm/dl raises concern for potential surgical complication.

Most of the surgeries for gastrointestinal malignancies done electively in our setup include carcinoma of stomach, carcinoma head of pancreas, peri-ampulary carcinoma, carcinoma of gall bladder and bile duct, bowel malignancies, gastrointestinal stromal tumor, carcinoma of esophagus and others. Also the patients with malignancies have impaired wound healing subsequently leading to wound related complications.

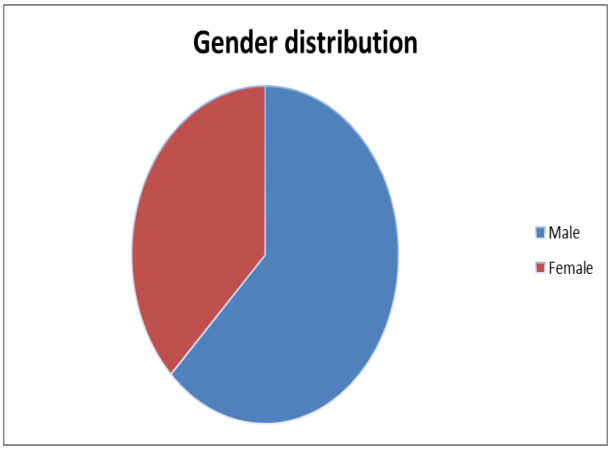
However, there is a relative dearth of information regarding the effect of hypoalbuminemia on the development of postoperative SSI. The aim of this study is to determine the relationship between preoperative albumin and the development of SSI in elective gastrointestinal malignant surgery.

## MATERIALS AND METHODS

This was a Observational Descriptive study done over one year from December 2015 to November 2016. It was done in gastrosurgery department of Bir Hospital, Kathmandu. All the patients with provisional diagnosis of gastrointestinal malignancy operated with final histopathological confirmation were included in this study. After Institutional Ethics Committee approval, 56 patients underwent elective major gastrointestinal oncological surgeries were included in the study. After fulfilling inclusion criteria, informed consent was taken. Serum albumin was sent within 1 week prior to surgery for all patient included. Preoperative serum albumin was measured and these patients were divided according to their serum albumin level into two groups. Group I: with serum albumin ≤3.5 gm/dl and Group II: with serum albumin >3.5 gm/dl. Prophylactic antibiotic, inj. Ceftriaxone 1gm and inj. metronidazole 500mg was given during induction of an anesthesia intravenously and repeated if surgery time was greater than 4 hours. Post-op antibiotic was given as per consultant decision. Duration of operation, inadvertent spillage of GI content, pre-op bowel preparation, drain placement and estimated blood loss was noted. All patients were observed for SSI during hospital stay and also during follow up in OPD after discharge for 30 days. Those not followed up in OPD, follow up was made over telephone and enquired for SSI. Working diagnosis of SSI was as follows

1. Purulent drainage.
2. Organisms isolated from an aseptically obtained culture of fluid or tissue from the incision.
3. Diagnosis of type of SSI by the consultant surgeon.
4. Diagnosis of type of SSI by ultrasound or CT abdomen and pelvis.

## RESULTS




**A**

**Fig 1: Demographic Distribution: Gender wise**

Total 56 patients were included in our study out of which 35(62.5%) were male and 21(37.5%) were female.

**Table 1: Patient's Personal characteristics.**

| | Group I Serum albumin level ≤ 3.5 mg/dl (n=31) | Group II Serum albumin level > 3.5 mg/dl (n=25) | P-value |
|---|---|---|---|
| Age (years) Mean±SD Range | 51.42±11.43 20.0 – 68.0 | 55.20±11.26 20.0 – 74.0 | 0.220 |
| Sex: No. (%) Male Female | 20 (64.6%) 11 (35.4%) | 15 (60%) 10 (40%) | 0.735 |
| BMI (kg/m$^2$) Mean±SD | 21.45±2.45 | 22.87±2.14 | 0.012 |

In my study from above mentioned table shows total number of patients in group I were 31 having serum albumin level ≤ 3.5 mg/dl and 25 patients in group II having serum albumin level >3.5 mg/dl. In group I, mean age of patient was 51.42, standard deviation of 11.43 with range of age from 20 years to 68 years and in group II, mean age of patient was 55.20, standard deviation of 11.26 with range of age from 20 years to 74 years having P-value 0.220 which is statistically not significant. In group I, total male patients were 20(64.6%), total female patients 11(35.4%) and in group II, total male patients 15(60%), total female patients 10(40%) having P-value 0.735 which is statistically not significant. Mean body mass index of patients in group I was 21.45 kg/m$^2$ with SD 2.45 and mean body mass index of patients in group II was 22.87 kg/m$^2$ with SD 2.14 having P-value 0.012 which is statistically significant.

**Table 2: Postoperative surgical site infection in group I and II.**

| | | Group I serum albumin ≤3.5 g/dl (N= 31) | Group II serum albumin >3.5 g/dl (N= 25) | P Value |
|---|---|---|---|---|
| Post-Op SSI | Yes [N (%)] | 15 (48.40) | 5 (20) | 0.028 |
| | No [N (%)] | 16 (51.60) | 20 (80) | |

In my study from above mentioned table shows in group I, total 15(48.4%) patients having postoperative surgical site infection whereas in group II, total 5(20%) patients having postoperative surgical site infection with P-value 0.028 which is statistically significant.

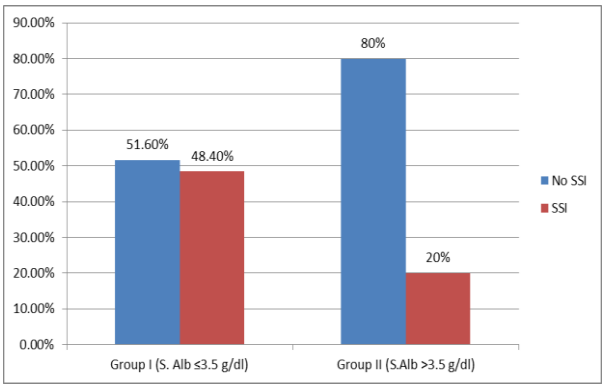



**Fig 2: Postoperative surgical site infection in group I and II.**

**Table 3: Postoperative surgical site infection in relation to BMI.**

| | Postoperative surgical site infection | | P-value |
|---|---|---|---|
| | Yes | No | |
| BMI of patient(kg/m$^2$) Mean±SD | 20.76±2.37 | 22.64±2.23 | 0.005 |

In my study from above mentioned table shows mean body mass index of patients having postoperative surgical site infection was 20.76 with standard deviation 2.37 and mean body mass index of patients not having postoperative surgical site infection was 22.64 with standard deviation 2.23. P-value was 0.005 which was statistically significant.

**Table 4: Distribution of length of hospital stay.**

| Mean length of postoperative hospital stay(days) | Group I Serum albumin ≤3.5gm/dl) | Group II Serum albumin >3.5gm/dl) | p-value |
|---|---|---|---|
| Mean±SD | 11.16±3.37 | 8.60 ±2.08 | 0.002 |
| Range (days) | 6-22 | 5-14 | |

This table shows in group I patients, mean length of postoperative hospital stay was 11.16 days, standard deviation 3.37, range from 6 days to 22 days and in group II, mean length of postoperative hospital stay was 8.60 days, standard deviation 2.08, range from 5 days to 14 days. P-value was 0.002 which was statistically significant.

**Table 5: Distribution of Malignancy organ and sex wise.**

| Organ of malignancy | Male | Female | Total | Percent |
|---|---|---|---|---|
| Bile duct | 2 | 0 | 2 | 3.6 |
| Colon | 9 | 5 | 14 | 25.0 |
| Duodenum | 0 | 1 | 1 | 1.8 |
| Gall Bladder | 3 | 5 | 8 | 14.3 |
| Pancreas | 12 | 3 | 15 | 26.8 |
| Rectum | 1 | 0 | 1 | 1.8 |
| Stomach | 8 | 7 | 15 | 26.8 |
| Total | 35 | 21 | 56 | 100.0 |

This table shows out of 56 patients 26.8% patients had malignancy of pancreas (12 male patients and 3 female patients), 26.8% patients had malignancy of stomach (8 male patients and 7 female patients), 25.0% patients had malignancy of colon (9 male patients and 5 female patients), 14.3% patients had malignancy of Gall Bladder (3 male patients and 5 female patients), 3.6% patients had malignancy of bile duct (2 male patients), 1.8% patients had rectal malignancy (one male patients), 1.8% patients had malignancy of duodenum (one male patient),

**Table 6: Type of surgical site infection.**

| Type of SSI | Frequency | Percent |
|---|---|---|
| superficial | 17 | 85 |
| deep | 1 | 5 |
| organ space | 1 | 5 |
| Total SSI | 20 | 100 |

This table shows among 20 patients having surgical site infection, 17 patients had superficial SSI, one patient had deep SSI and one patient had organ/space SSI.

## DISCUSSION

Serum albumin is a good and simple predictor of surgical risk and has a close correlation with the degree of malnutrition.[9] It has the highest positive predictive value of all the nutritional assessment methods for predicting associated complications and mortality.[11] Some researches has doubted reliability of albumin as an assessment of malnutrition as hypoalbuminemia is an acute phase reactant and is affected by systemic inflammation.[12] The increased demand for specific amino acids for acute phase protein synthesis degrades available body protein, including albumin.[13-15]

Preoperative hypoalbuminemia is significantly associated with the development of and is an independent risk factor for postoperative SSI. The incidence of SSI is not only important from an economic perspective but remains a negative influence on patient outcome, influencing mortality, duration of hospital stay, and quality of life.[16] Postoperative SSIs are due a combination of factors and the risks differ from patient to patient.[17] Accordingly, NNIS guidelines are being redefined to allow classification of surgical patients according to both intrinsic and extrinsic factors.[17] To date, there is an inadequate data in the literature regarding the effect of a patient's nutritional status on SSI development.

Hypoalbuminemia is associated with poor patient outcomes following surgery.[1, 7-9,18] A decrease in albumin from 45 to 21 g/L is associated with an increase of morbidity form 10% to 65%,[3] whereas Ryan et al demonstrated that serum albumin concentration on day 1 postoperatively is an independent predictor of poor surgical outcome following esophageal resection.[19] This may, however, be attributed to perioperative fluid overload and hemodilution, these factors also being associated with a poorer outcome.[20]

Surgical Site Infections (SSI) are responsible for 14%-16% of all hospital-acquired infections. In surgical patients, up to 38% of all hospital-acquired infections are SSI. In our study, the overall incidence of surgical site infection was 35.70%.

This study has highlighted the association of preoperative hypoalbuminemia as a risk factor for the development of SSI. Multivariate analysis of the relationship of serum albumin and SSI showed that a preoperative serum albumin ≤ 3.5 mg/dL increased the risk of SSI by 5.6 fold. Known determinants of SSI development are inoculation of bacteria, the virulence of the contaminant, the microenvironment of the wound, and the integrity of host defenses. It is likely that hypoalbuminemia increases the risk of SSI by modulating these factors.

Hypoalbuminemia is associated with poor tissue healing, decreased collagen synthesis and granuloma formation in surgical wounds.[21-23] Combined, these factors could cause delayed wound healing, increase wound dead space, and create an environment that predisposes to

infection. Hypoalbuminemia is also associated with impairment of the innate immune response; hypoalbuminemia is known to cause impairment of macrophage activation and induce macrophage apoptosis.[23,24] Furthermore, low serum albumin is known to cause tissue edema through a reduction in plasma colloid osmotic pressure and subsequent leak of interstitial fluid into the wound.[25] This fluid could provide a medium for bacterial propagation.[26] Together these factors could promote the development of SSI in the hypoalbuminemic patient.

In this study postoperative surgical site infections were higher in number and percentage in patient with serum albumin ≤ 3.5 gm/dl) compared to patient with serum albumin > 3.5 gm/dl which was statistically significant with P-value < 0.05. Also, serum albumin ≤ 3.5 gm/dl was associated with statistically significant increase in the mean length of post operation hospital stay (p < 0.05).

The result of our study was in agreement with, Lohsiriwat et al.[18] who demonstrated a higher rate of overall postoperative complications including surgical site infection and a longer hospital stay associated with hypoalbuminemia.

A more recent study was conducted by Hussein et al. showed a significant association between a low preoperative serum albumin of less than 3.5 gm/dl, with a postoperative complications including surgical site infection for patients undergoing surgery for gastrointestinal malignancy. Furthermore, the length of hospital stay was significantly longer in patient with serum albumin ≤ 3.5 gm/dl) (9.60±3.59 days) compared to patient with serum albumin > 3.5 gm/dl) (6.95±0.69 days) (P=0.002).

Hennessey et al.[27] who concluded Hypoalbuminemia is an independent risk factor for the development of SSI following gastrointestinal surgery and is associated with deeper SSI and prolonged inpatient stay. A total of 105 patients developed a SSI (20%). The median time to the development of SSI was 7 (5–10) days. On multivariate analysis, hypoalbuminemia was an independent risk factor for SSI development (relative risk, RR = 5.68, 95% confidence interval: 3.45–9.35, *P* < 0.001). Albumin < 3.0 mg/dL was associated with an increased rate of deep versus superficial SSI (*P*=0.002). The duration of inpatient stay was negatively correlated with preoperative albumin.

Cheng-Chou et al.[28] conducted a study to determine the relation of preoperative malnutrition and postoperative outcomes of cancer colon patients were reported that hypoalbuminemia is an independent risk factor for postoperative mortality, morbidity, as well as complications related to wounds, lungs, urinary system, and anastomosis. They concluded that hypoalbuminemia is a predictor of poor surgical outcomes of colon cancer patients. It is also a poor prognosis factor for long-term survival of colon cancer patients after curative operation. Hypoalbuminemia is associated with poor tissue healing, decreased collagen synthesis in surgical wounds or at anastomoses, and impairment of immune responses, such as macrophage activation and granuloma formation.[24] Therefore, wound infection, remote infections such as pneumonia, and anastomotic leakage are commonly observed in hypoalbuminaemic patients.[29]

Our results were in agreement with an early study conducted by Gibbs et al.[3] and demonstrated that hypoalbuminemia preoperatively or pretrauma is independently associated with the development postoperative complications, especially the development of infective complications.

A more recent study by Lohsiriwat et al.[30] found that in hypoalbuminemic patients; wound infection, remote infections such as pneumonia, and anastomotic leakage, were commonly found. In a large multi-center study by Hennessey et al.[27] the authors determined hypoalbuminemia (defined as albumin level 3.5 gm/dL) to be an independent predictor of surgical site infection in patients undergoing colorectal surgery which is applied to our work.

The mechanisms of increase in infectious etiologies in hypoalbuminemia are multifactorial and likely include impairment of tissue healing, decreased collagen synthesis and granuloma formation. The immune response in hypoalbuminemia is also compromised through impairment of macrophage activation and induction of macrophage apoptosis.[23,24] These factors together could explain the higher risk of surgical site infections in hypoalbuminemic patients.[31]

Patients at nutritional risk have higher complication rates after surgery for colorectal cancer. Especially, malnutrition increases the rate of anastomotic leakage and wound infection. Malnutrition was also a significant risk factor for the length of hospital stay.[32]

Shitanshu et al.[31] concluded that albumin level below 3.0 gm/dL help identify a high-risk surgical population. Although the causes of low albumin are multifactorial, identification of this subset of patients and aggressive optimization of nutritional status preoperatively or using alternative treatment strategies for patients who are extremely high risk for open surgery may improve surgical outcomes in this population.

In our study, lower BMI was significantly associated with postoperative surgical site infection with P-value <0.05. The study done by Watanabe A et al.[33] concluded that lower body mass index is a risk factor for postoperative surgical site infection.

However, there were no significant differences between the two groups in demographic data as regards age, sex (P>0.05) in our study.

Regarding the treatment of pre-existing hypoalbuminemia, no studies have shown any beneficial outcome with the administration of albumin infusions,[34-36] but a recent report discussed the administration of a supplemented diet before and after surgery and its beneficial effect on outcomes in malnourished patients with gastrointestinal cancer,[37] thus highlighting the detrimental effects of malnutrition. The use of prophylactic antibiotics in surgery has been shown to be effective in reducing the incidence of SSI.[3,16]

## CONCLUSION

The current study revealed that preoperative hypoalbuminemia significantly increases the risk of postoperative surgical site infection and length of postoperative hospital stay after major gastrointestinal cancer surgery.

Some limitations are present in this study, small number of patients studied in a single institution, limiting the globalization of the conclusions. We believe that the results of this study give reasons for raising attention about using serum albumin level as a simple and low cost prognostic tool to predict the risk of adverse surgical outcome and consequently, decreasing the incidence of postoperative surgical site infection and length of postoperative hospital stay.

### Limitations of the study

Considering the limited time frame of study, long term follow up of cases could not be done and the ultimate treatment opted by the patient and their effectiveness could not be followed in all the cases.

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## DECLARATIONS

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