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Original Article

Pre-operative Hypoalbuminemia is an Independent Predictor for the Development of Post-operative Surgical Site Infection in Gastrointestinal Surgeries: A Study in Rural Population of Central India

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Abstract

Background: Surgical site infection (SSI) is defined as an infection occurring in an incisional wound within 30 days of the procedure or within 1 year if a prosthesis is implanted.

Objective: To determine the correlation of pre-operative serum hypoalbuminemia with post-operative SSI in patients who underwent gastrointestinal surgeries.

Methods: A prospective cross-sectional study was performed which included 150 patients who had undergone gastrointestinal surgery. Each patient was evaluated for pre-operative serum albumin and followed postoperatively for SSI. Hypoalbuminemia was defined as serum albumin <3 g/dL. Univariate analysis was done and *P* value was calculated for each variable.

Results: Age of the patients varied from 19 to 70 years and a maximum number of patients were between 40 and 59 years (43.43%). The mean ± standard deviation for age in the study was 48.25 ± 15.16 years, and maximum rate of SSI was noted in the patients of age 60-70 years which was 13% ($P = 0.66$) which was higher among females than males (32.50% vs. 17.27%, $P = 0.04$). A total of 32 patients (21.33%) had developed SSI. There were 22 superficial infections (68.75% of all infections), 7 deep infections (21.8%), and 3 organ space infections (9.3%). The rate of complication was maximum in patients with serum albumin <2.1 g/dL (80%). A univariate analysis shows that pre-operative serum albumin (<3 g/dL) is a strong predictor for SSI ($P = 0.001$). Rate of SSI was most common in patients with basal metabolic index <18.5 kg/m^2 which was found to be 32.78% ($P = 0.011$) with increased length of hospital stay.

Conclusion: Pre-operative hypoalbuminemia <3.0 g/dL is a strong independent risk factor for post-operative SSI following gastrointestinal surgeries.

Key words: Albumin, Hypoalbuminemia, Surgical site infection

INTRODUCTION

Hypoalbuminemia has been shown to be associated with increased mortality and morbidity rates in both hospitalized patients and community-dwelling elderly persons. In surgery, an association between hypoalbuminemia and adverse outcome has been recognized for many years.[1-4] There is a substantial evidence to show that patients who have signs of malnutrition have a higher risk of complications and an increased risk of death in comparison with patients who have adequate nutritional reserves.[5] Nutritional assessment is essential for identifying patients who are at risk of developing complications related to significant malnutrition. A dietary history, physical examination (including anthropometric measurements), and relevant laboratory tests are the appropriate tools needed for an accurate evaluation of a patient's pre-operative nutritional

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status.[6] Albumin is the most commonly used and reliable indicator of a patient's nutritional status; it is also a negative acute phase protein.[7] 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.[8]

Surgical site infection (SSI) is defined as infection occurring in an incisional wound within 30 days of the procedure or within 1 year if a prosthesis is implanted.[9] SSI can be superficial (involving only the skin and subcutaneous tissue of the incision), deep (involving fascial and muscle layers), or organ space.[10] SSI is also important from an economic point of view, especially among the rural population. These patients can expect to spend additional days in the hospital and suffer significantly increased morbidity and mortality.

Previously described risk factors for the development of a SSI determined by the National Nosocomial Infection Surveillance include American Society of Anesthetics (ASA) Grade III/IV, contaminated or dirty wounds, and the duration of procedure.[11] Other risk factors described include increased body mass index (BMI), emergency surgery, surgeries involving a stoma, blood loss, frequency of glove changes, and the use of subcuticular sutures.[12,13]

The aim of this study was to determine the relationship between pre-operative albumin and the development of SSI.

MATERIALS AND METHODS

In a prospective study, we included 150 patients with hypoalbuminemia (serum albumin <3 g/dL) who had undergone gastrointestinal surgeries in a rural hospital in Central India. Post-operative diagnosis of SSI in each case was done by the attending surgeon. Infection was determined according to the Centers for Disease Control and Prevention definitions of wound infection and was confirmed with positive wound cultures. Nutritional assessment including mid-upper arm circumference and skin-fold thickness along with BMI was calculated for all the patients in the study. Other details were recorded including age, gender, operation type (gastric, hepatobiliary, small, or large bowel), operation class (elective or emergency), ASA Grade, type of anesthesia, duration of procedure, length of hospital stay (LOS), and wound classification (clean, clean/contaminated, contaminated, and dirty). SSI was also classified as superficial incisional, deep incisional, or organ space SSI. Routine post-operative care was provided to each patient and each patient was followed up for a minimum of 30 days. Patients were divided into three class based on the degree of hypoalbuminemia - Class I (2.8-3 g/dL), Class II (2.1-2.7 g/dL), and Class III (<2.1 g/dL). This study has been accepted and sanctioned by the Ethics Committee Board of the Institute where the study has been undertaken.

Inclusion Criteria

This included patients who consented for the study with age >18 years; patients having pre-operative serum albumin <3 g/dL among those who underwent emergency and elective gastrointestinal surgeries and ASA up to Grade III were included in the study.

Exclusion Criteria

All patients having pre-operative serum albumin ≥3.0 g/dL were excluded from the study; patients diagnosed for chronic liver disease and jaundice, sepsis (white blood cell >12,000 cells/mm^3), severe anemia (hemoglobin <8 g/dL); diabetes mellitus Type II and chronic renal disease; patients on steroids or chemotherapy for any oncological disease or any other hepatotoxic drugs; and clinically significant signs and symptoms of hypoalbuminemia. Obese patients and patients with BMI <12 and >40 were excluded from the study and especially prolonged addiction to alcohol and tobacco were excluded from the study; significant medical and family history pertaining to medical disease including cirrhosis of liver, protein-losing enteropathy, nephrotic syndrome, congenital analbuminemia, ulcerative colitis, cystic fibrosis, hepatitis, heart failure, renal failure, amyloidosis, and autoimmune diseases were ruled out.

Statistical Analysis

Statistical analysis was done using descriptive and inferential statistics using Chi-square test and multiple regression analysis and software used in the analysis were SPSS 17.0 version and GraphPad Prism 5.0. Data have been entered in excel sheet and has been analyzed using STATA software. Continuous variables are presented as mean ± standard deviation and compared using *t*-test. Categorical variables are presented as proportions and compared using Chi-square test. Multivariate analysis is used to determine risk factors associated with serum albumin and various clinical and biochemical parameters. $P < 0.05$ is regarded as being statistically significant.

OBSERVATIONS AND RESULTS

Patient Characteristics

Of the total 150 patients included in the study, a total of 32 patients (overall rate 21.33%) had developed SSI. The median duration to diagnosis of SSI was 7 (5-10) days. There were 22 superficial infections (68.75% of all infections), 7 deep infections (21.8%), and 3 organ space infections (9.3%). The mean age was 48.25 ± 15.16 years with maximum percentage of SSI in the age group of 60-70 years (32.65%; 13% with SSI), but no significance in age at the time of surgery and development of SSI ($P = 0.66$). Male to female ratio (M: F) was 2.8:1 and the complication rate was more in females than males (32.50% vs. 17.27%, $P = 0.04$). The rural population included in the study showed a wide range of nutritional deficiencies which were evaluated through various tools including BMI and 40.66% of patients had BMI <18.5 kg/m^2, 43.33% patients between 18.5 and 24.9 kg/m^2, and 16% having BMI between 25 and 30 kg/m^2. ASA Grade III was associated with an increased incidence of SSI (32.20%, $P = 0.032$, Chi-square test). Operation types were classified as gastric (closure of perforation, partial, or total gastrectomy; $n = 36$), hepatobiliary (open cholecystectomy, CBD exploration, hepaticojejunostomy, and Whipple's procedure; $n = 10$), small bowel (resection, wedge resection, adhesiolysis, and closure of perforation; $n = 48$), and colorectal (resection of colon or rectum, abdominoperineal resection and stoma formation, Hartmann's procedure, and fecal diversion; $n = 56$) (Table 1).

Hypoalbuminemia and SSI

Pre-operative evaluation of serum albumin showed that the maximum number of patients had hypoalbuminemia Class II (2.1-2.7 g/dL, 56.66%) which had an direct impact of the number SSI postoperatively (rate 24.09%) and highest rate was found in patients with hypoalbuminemia Class III (<2.1 g/dL, rate 80%, $P = 0.001$) (Table 2 and Figure 1). Rate of superficial wound infection increased with decrease in value of serum albumin and rates of deep wound infection (25%) and organ space infection (50%) was maximum for Class III hypoalbuminemia (Table 3 and Figure 2). Depth of infection of wound is inversely proportional to the class of hypoalbuminemia.

BMI and SSI

In our study, 40.66% of the total patients had pre-operative BMI <18.5 kg/m^2 which had a maximum impact on the development of SSI (8.33% Grade I; 15.38% Grade II; 32.78% Grade III; $P = 0.011$) (Table 2 and Figure 3). The rate of SSI increased as there is decrease in BMI which is quite prevalent in low socioeconomic background of the rural population. Involuntary weight loss (WL) >5% was found in 34.54% ($P = 0.01$) of significant WL within 6 months of post-operative period in patients who developed SSI. All these had a direct influence on increased LOS postoperatively in patients that developed SSI (overall rate 34.34%, $P = 0.04$).

Operative Variables and SSI

Those patients who had undergone an emergency surgery relative to an elective procedure had a higher incidence of SSI (29.48% vs. 12.50%; $P = 0.011$) (Table 1 and Figure 5). Moreover, the extent of intraoperative contamination

Table 1: Various operative variables and correlation with SSI

Parameters	Total *n* (%)	SSI (+) (%)	SSI (−) (%)	*P* value
Total	150	32 (21.33)	118 (78.67)	
Wound				
Clean	56 (37.33)	5 (8.92)	51 (91.08)	*P*=0.0007
Clean contaminated	46 (30.66)	10 (21.73)	36 (78.27)	
Contaminated	32 (21.33)	8 (25)	24 (75)	
Dirty	16 (10.66)	9 (56.25)	7 (43.75)	
Operation class				
Emergency	78 (52)	23 (29.48)	55 (70.52)	*P*=0.011
Elective	72 (48)	9 (12.50)	63 (87.50)	
Operation type				
Gastric	36 (24)	5 (13.88)	31 (86.12)	*P*=0.014
Hepatobiliary	10 (6.65)	6 (60)	4 (40)	
Small bowel	48 (32)	11 (22.91)	37 (77.09)	
Colorectal	56 (37.33)	10 (17.85)	46 (82.15)	

SSI: Surgical site infection

Table 2: Comparison of patient demographics and incidence of SSI

Parameters	Total (*n*) (%)	SSI (+) (%)	SSI (−) (%)	*P* value
Patients	150	32 (21.33)	118 (78.67)	
Age (years)				*P*=0.66
<20	3 (2)	1	2	
20-39	37 (24.66)	7	30	
40-59	61 (40.66)	11	50	
60-70	49 (32.65)	13	36	
Gender				
Male	110 (73.33)	19 (17.27)	91 (82.73)	*P*=0.04
Female	40 (26.66)	13 (32.50)	27 (67.50)	
Pre-operative serum albumin (g/dL)				
Class I (2.8-3)	62 (40.66)	8 (13.13)	54 (87.09)	*P*=0.001
Class II (2.1-2.7)	83 (56.66)	20 (24.09)	63 (75.90)	
Class III (<2.1)	5 (3.33)	4 (80)	1 (20)	
BMI (kg/m^2)				
Grade I (25-30)	24 (16)	2 (8.33)	22 (91.67)	*P*=0.011
Grade II (18.5-24.9)	65 (43.33)	10 (15.38)	55 (84.62)	
Grade III (<18.5)	61 (40.66)	20 (32.78)	41 (67.22)	
ASA grade				
Grade I	14 (9.33)	2 (14.28)	12 (85.72)	*P*=0.032
Grade II	77 (51.33)	11 (14.28)	66 (85.72)	
Grade III	59 (39.33)	19 (32.20)	40 (67.80)	

BMI: Body mass index, ASA: American society of anesthetics

Table 3: Distribution of depth of wound infection based on class of hypoalbuminemia

Hypoalbuminemia Class	SI (%)	DI (%)	OS infection (%)	Total SSI
Total	22 (68.75)	7 (21.8)	3 (9.3)	32
Class I	7 (87.5)	1 (12.50)	0	8
Class II	14 (70)	5 (20)	1 (5)	20
Class III	1 (25)	1 (25)	2 (50)	4

SI: Superficial infection, DI: Deep infection, OS: Organ space, SSI: Surgical site infection

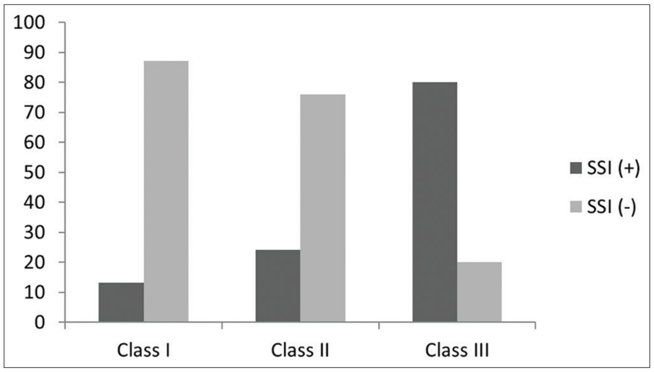

Figure 1: Presentation of distribution of surgical site infection and class of hypoalbuminemia

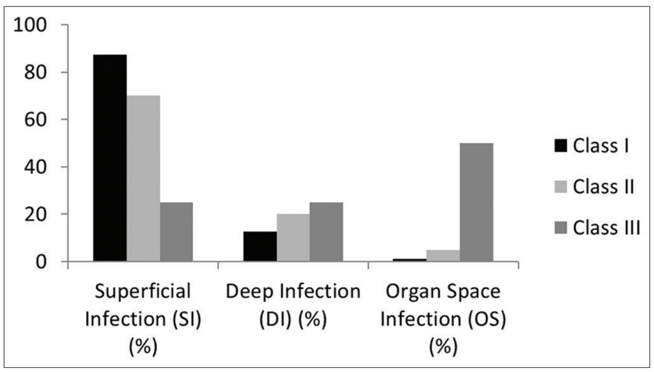

Figure 2: Distribution of depth of wound infection based on class of hypoalbuminemia

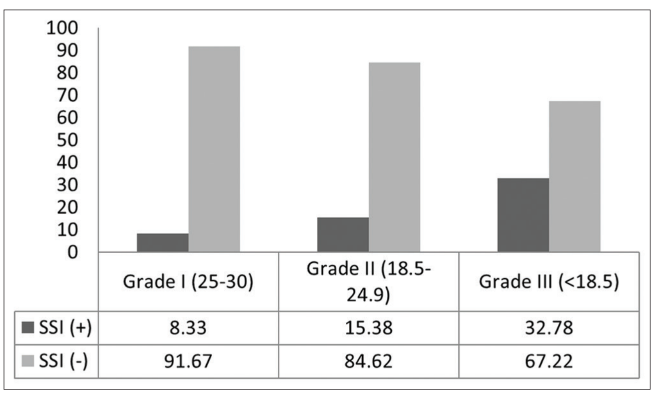

Figure 3: Distribution of surgical site infection based on grade of pre-operative body mass index (*P* = 0.011)

affected the rate of SSI with 8.92% of clean wounds, 21.73% of clean-contaminated wounds, 25% of contaminated, and 56.25% of dirty wounds developing SSI ($P = 0.0007$) (Table 1 and Figure 4). The incidence of SSI following gastric surgery was 13.88%, hepatobiliary was 60%, small bowel was 22.91%, and colorectal was 17.85% ($P = 0.014$) (Table 1 and Figure 6).

DISCUSSION

Malnutrition is a major problem in patients undergoing gastrointestinal surgeries for any reason. The potential contributors to malnutrition in these patients are multiple including insufficient food and nutrient intakes, impairment of nutrient absorption, and low socio-economic status of the patients where patients cannot afford good nutritive diet. There are many tools to assess patient's nutritional

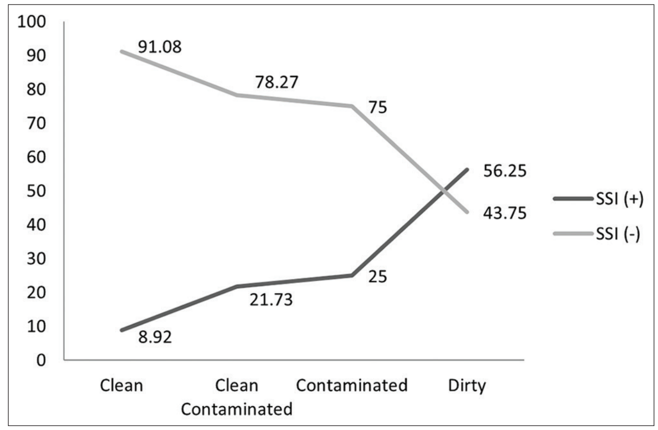

Figure 4: Effect of wound class on post-operative surgical site infection (*P* = 0.0007)

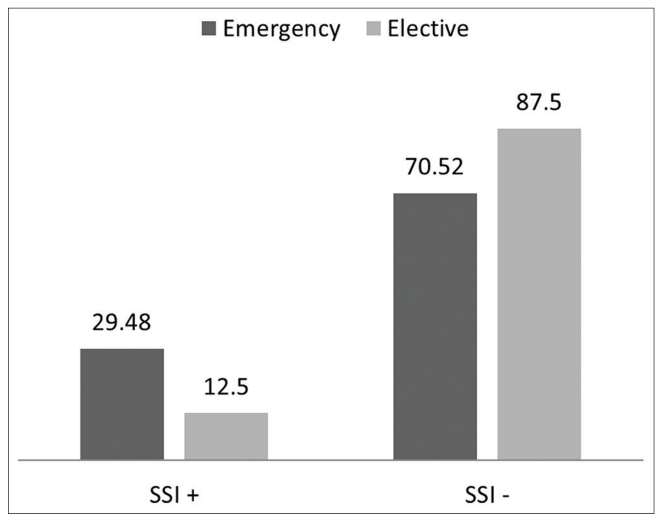

Figure 5: Effect of operation class on post-operative surgical site infection (*P* = 0.011)

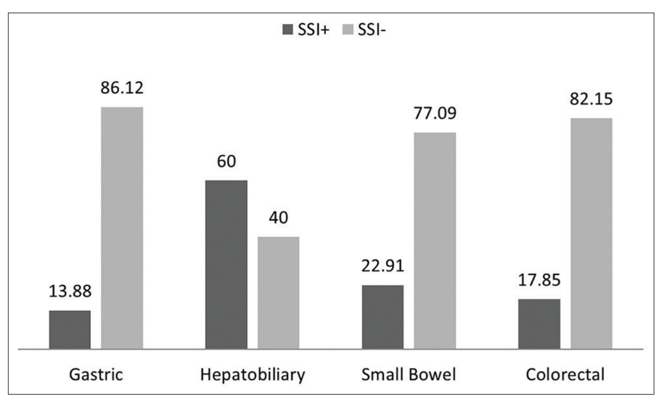

Figure 6: Effect of operation type on post-operative surgical site infection (*P* = 0.014)

status, ranging from clinical appraisal to anthropometric and various laboratory investigative measures. Serum albumin is a good and simple predictor of surgical risk and has a close correlation with the degree of malnutrition.[14] Pre-operative hypoalbuminemia, serum albumin level <3 g/dL was associated with the development of SSI and is an independent risk factor for other post-operative complications. Although serum albumin level may also be affected by acute factors such as trauma and surgical stress, it is predictive of operative outcome because it is a marker of disease and malnutrition as well as possibly conferring a direct protective effect through several biological mechanisms.[15] There are increased needs by the body due to stress of illness, injury, or infection which results in depletion of visceral protein sources leading to abnormal function in organ systems including gastrointestinal malabsorption, impaired immunologic response and impaired production of albumin, and other plasma proteins in the liver. Gibbs *et al.* reported that pneumonia (10.6%) and SSI (SSI, 10.3%) were the two most common complications in the patients who had hypoalbuminemia.[16] Similar results were observed by Hennessey *et al.* in their study of 524 patients where a total of 105 patients developed SSI (20%). They also concluded that there is a significant rise in the rate of post-operative complications as the age advances (P < 0.001 in both studies).[17]

Mullen *et al.* found that low BMI <18.5 kg/m^2 has a five-fold increased risk in resulting to post-operative complications.[18] Similarly, a study by Beghetto *et al.* concluded that serum albumin level was the strongest predictive parameter for death and hospital infection (<3.5 g/dL) and BMI <18.5 kg/m^2 was associated with death and post-operative infection and with increased LOS (P <0.01).[19]

However, albumin infusion is usually not effective because the albumin will degrade quickly, and infusion does not address the underlying causes of adverse operative outcome.[20] 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, thus highlighting the detrimental effects of malnutrition.[21] Surgeons should be aware of the implications of low pre-operative serum albumin and consider nutritional intervention in the malnourished patients undergoing surgery. The use of prophylactic antibiotics in surgery has been shown to be effective in reducing the incidence of SSI.[16] These patients should receive antibiotic prophylaxis within 60 minutes of surgery and they should be continued for 24 h.[22]

Patients' nutritional status has to be optimum to avoid the occurrence of post-operative SSI. It is obvious in our study that wherever serum albumin and BMI were low, the complication rates increased. Pre-operative improvement of nutritional status must be done before undertaking any surgery. However, this is possible only when the surgery is routine and patients can safely be kept in waiting till the improvement of nutritional status. However, this is not always possible in case of emergency surgeries.

CONCLUSION

Pre-operative hypoalbuminemia is a predictor of post-operative SSI and assessment of nutritional status with pre- and post-operative buildup of patients is of importance to prevent SSI, thus decreasing additional cost burden, LOS, and an overall better quality of life.

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