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Original Research Article

Role of Hypocholesterolemia and Hypoalbuminemia as a predictor of Surgical Site Infection

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ABSTRACT

Background: Surgical site infections (SSIs) contribute significantly to morbidity, mortality, prolonged hospital stays, and increased healthcare costs. Various patient-related factors, such as age, nutritional status, pre-existing infections, and comorbid conditions, influence the likelihood of developing SSIs. This study aims to investigate the role of hypocholesterolemia and hypoalbuminemia as potential risk factors for SSIs following elective surgeries.

Materials and Methods: A prospective observational study was conducted involving 100 patients undergoing elective surgery at Department of Surgery, SAIMS & PG Institute, Indore (M.P). Preoperative serum albumin and cholesterol levels, along with variables such as length of hospital stay and duration of surgery, were recorded. The relationship between these factors and the development of SSIs was analyzed using SPSS software version 21.0.

Results: The study population consisted of 58% males with a mean age of 38.72 ± 10.56 years. The majority of patients (65%) had hypoalbuminemia whereas 24% exhibited low cholesterol levels. A total of 28% of patients developed SSIs. The mean albumin levels were significantly lower in patients who developed SSIs ($p<0.01$). However, the mean cholesterol levels showed no significant difference between patients with and without SSIs ($p>0.05$). Additionally, patients who developed SSIs had a significantly longer hospital stay ($p<0.01$). The ROC curve analysis identified a serum albumin level below 3.0 mg% as a significant predictor of SSIs, with a sensitivity of 81.6% and specificity of 41.2%

Conclusion: The findings of this study suggest that preoperative serum albumin levels are a significant prognostic indicator for the development of SSIs following elective surgery. In contrast, no significant association was found between serum cholesterol levels and the occurrence of SSIs. It is recommended that serum albumin levels be routinely measured before surgery as part of the preoperative assessment to predict and mitigate the risk of SSIs.

Keywords: Hypoalbuminemia, Hypercholesterolemia, Surgical Site Infections, Elective Surgeries.

Study Design: Prospective Study.

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INTRODUCTION

Surgical site infection (SSI) is defined as an infection related to an operative procedure that occurs at or near the surgical incision within 30 days post-operation if no prosthetic is used, and up to 1 year if a prosthetic is implanted [1].

According to the US Centers for Disease Control and Prevention (CDC) National Nosocomial Infections Surveillance (NNIS) system, SSIs are the third most common nosocomial infection, accounting for 14-16% of all hospital-acquired infections and 38% of infections among surgical patients [2]. Laparotomy procedures, in particular, have reported higher SSI rates, reaching up to 20%, with a range of 3.4% to 36.1% across various studies [3].

In India, tertiary care hospitals report an SSI incidence of 2.06% for minimal invasive surgery (MIS) and 16.16% for open surgery (OS) [4]. Additional research indicates an SSI incidence range of 2% to 23% across all surgical procedures from 1995 to 2010 [5]. The CDC categorizes SSIs into three main types: superficial, deep, and organ/space infections [6]. Additionally, the SSI risk varies based on the type of procedure (elective or emergency) and wound contamination level, which the CDC classifies into four categories: clean, clean-contaminated, contaminated, and dirty-infected wounds [7].

- **Clean wounds** are uninfected and free from inflammation, without entry into the respiratory, alimentary, genital, or urinary tracts.
- **Clean-Contaminated wounds** involve controlled entry into these tracts without unusual contamination, as in procedures on the biliary tract, appendix, vagina, and oropharynx, provided there is no infection or major technique breach.
- **Contaminated wounds** include open, fresh accidental wounds, cases with major sterile breaches, or significant spillage from the gastrointestinal tract; this also includes incisions with non-purulent inflammation or necrotic tissue.
- **Dirty-Infected wounds**, the highest risk category, consist of old traumatic wounds with retained devitalized tissue, existing infections, or perforated viscera where infectious organisms are present in the operative area prior to surgery. [7]

Surgical site infections (SSI) lead to substantial morbidity and mortality, often resulting in prolonged hospital stays and increased healthcare costs [8]. The extended hospitalization associated with SSI impacts not only patient quality of life but also efficiency and productivity. SSIs typically arise from exogenous or endogenous microorganisms that infiltrate the wound either during surgery (primary infection) or afterward (secondary infection). Primary infections, which are generally more severe, tend to emerge within 5 to 7 days post-surgery [9]. While most SSIs are confined to the skin and subcutaneous tissue, some can progress to deep or necrotizing infections, commonly presenting with symptoms such as pain, tenderness, redness, localized heat, swelling, and pus discharge [10,11].

Both patient-related factors—such as advanced age, nutritional deficiencies, pre-existing infections, and comorbidities—and procedure-related factors—such as the choice of suture material, surgical technique, operation duration, preoperative preparation, and instrument sterilization—play significant roles in influencing SSI risk [2]. Additionally, research suggests that low serum albumin and cholesterol levels are associated with increased SSI risk, extended hospital stays, and mortality, highlighting these factors as major contributors to morbidity and mortality among hospitalized patients [12-15].

Hypolipidemia, defined as hypocholesterolemia with total cholesterol levels below 150 mg/dl, is recognized as an independent predictor of clinical outcomes in critically ill patients. Cholesterol plays a crucial role in gluconeogenesis and immune function, while lipoproteins—cholesterol's transport form in the blood—serve as carriers for fat-soluble vitamins, antioxidants, drugs, and toxins. Notably, lipids

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and lipoproteins possess the ability to bind to and neutralize bacterial endotoxin, known as lipopolysaccharide (LPS) [16]. In the bloodstream, LPS binds to LPS-binding protein [17], activating the cell surface receptor CD14 [18], which in turn triggers the release of pro-inflammatory cytokines, including tumor necrosis factor-α, IL-1, and IL-6 [19]. When LPS binds to lipoproteins like cholesterol, however, cytokine release is diminished, potentially reducing inflammatory responses [20].

Malnutrition is a significant secondary factor in hypocholesterolemia and affects a substantial number of patients in government healthcare facilities in India. Nutritional deficiency has been identified as a major contributor to postoperative complications, with the prevalence of protein-energy malnutrition among surgical patients ranging from 10% to 54%.

Evidence indicates that malnourished patients have a higher risk of complications and mortality compared to those with adequate nutritional reserves [21]. Serum albumin, which is strongly correlated with malnutrition severity, serves as a reliable predictor of surgical risk and is a negative acute phase protein [22]. During acute illness or stress, serum albumin levels decrease due to changes in hepatic metabolism and its redistribution into interstitial spaces [23]. Both malnutrition and inflammation are known to suppress albumin synthesis [24-26].

Based on these factors, we hypothesized that preoperative albumin and cholesterol levels might influence susceptibility to surgical site infections. This study was therefore conducted to evaluate hypocholesterolemia and hypoalbuminemia as potential risk factors for developing surgical site infections following elective surgery.

Material and Methods

After approval from the institutional ethical committee, this prospective study was carried out in the Department of General Surgery at SAIMS & PG Institute, Indore, Madhya Pradesh, India. A total of 100 patients, aged 18 years or older, who were undergoing elective surgery in the Surgery department were enrolled based on predefined inclusion criteria. Informed consent was obtained from each patient, and the study protocol was thoroughly explained to ensure understanding. Patient confidentiality was strictly maintained throughout the research process.

Inclusion Criteria

- All the patients undergoing elective surgery in Department of General Surgery at SAIMS & PG Institute, Indore, Madhya Pradesh, India.
- Patients giving written informed consent to be part of the study

Exclusion Criteria

- Critically ill patients presenting in casualty requiring emergency OT.
- Patients with immunocompromised state like HIV positive, on corticosteroids.
- Patients with Diabetes Mellitus
- Pregnant females
- Patients who lost follow up.
- Wound site previously infected.
- Patients not giving consent to be part of the study.

Methodology

Before admission, each patient underwent thorough screening and clinical evaluation, including a complete blood count, routine biochemistry (with liver function tests and lipid profile), bleeding time,

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clotting time, urine examination, chest x-ray, and ECG. The surgical procedures involved in the study included inguinal hernia surgery, appendectomy, colorectal surgery, cholecystectomy, breast surgeries, and other major elective operations. For each surgery, a proforma was created to record the patient's serum albumin and cholesterol levels, along with details about their hospital stay and surgery duration.

Patients were monitored until their discharge, and any surgical site infections (SSIs) that developed were documented. This study focused on the preoperative serum albumin, serum cholesterol, length of hospital stays, and surgery duration, examining their relationship to SSIs. Antimicrobial prophylaxis, treatment types, and culture and sensitivity of organisms were not part of this study.

General vital signs, such as pulse rate, blood pressure, and temperature, were charted daily, and wound conditions were assessed using the Southampton Wound Grade system. Patients were educated on the signs and symptoms of SSIs, including erythema, discharge, tenderness, seroma, hematoma, and wound dehiscence, and instructed to report any of these symptoms.

SSI was defined according to CDC criteria: superficial SSI includes wound cellulitis, erythema, or purulent discharge, while deep SSI involves any wound infection requiring surgical intervention, such as removal of sutures or clips, drainage of deep pus, or packing.

Statistical Analysis

The data for this study were recorded in Microsoft Excel 10.0 and analysed using IBM SPSS version 22.0. Continuous parametric variables were expressed as means and standard deviations, while non-parametric data were presented as medians and interquartile ranges. Categorical variables were reported as percentages, and the Chi-square test was utilized to compare these variables, with statistical significance set at $p < 0.05$. Additionally, ROC curve analysis was performed to evaluate the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of hypercholesterolemia and hypoalbuminemia as risk factors for developing surgical site infections following elective surgery

Results

A total of 100 patients were included in the study with majority 58 (58%) being males and 42 (42%) females. Majority (55%) of the patients were belonging to the age group of 21-40 years. Mean age of study participants was 38.72±10.56 years.

In the study, 52 patients were diagnosed with Type 2 Diabetes Mellitus (DM) prior to surgery and were on regular medications; however, they were switched to insulin after admission. One patient, aged 18, had Type 1 DM. Additionally, 40 patients were diagnosed with hypertension, and 7 patients had both hypertension and DM. The majority of the study population, being middle-aged, had concomitant comorbidities, highlighting the common prevalence of multiple health issues in this demographic.

In this study, individuals with a 5-year history of regular daily smoking or alcohol consumption were categorized as smokers and alcoholics, respectively. The majority of the study population, however, were non-smokers (75%) and non-alcoholics (65%).

Majority of patients were having hypoalbuminemia (65;65%) and remaining (35;35%) had a normal range of serum albumin. Prevalence of low total cholesterol levels were seen in 24 (24%) cases while in 14 (14%) cases total cholesterol levels were more than 200 mg%. Normal levels of cholesterol (100-200 mg%) was observed in 62 (62%) cases.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 07, 2024

Variables	Number of patients (N=100)	Frequency (%)
Hypoalbuminemia		
No	35	35%
Yes	65	65%
Total Cholesterol levels (mg%)		
<100	24	24%
100-200	62	62%
>200	14	14%

Table 1. Distribution of study groups as per presence of hypoalbuminemia and cholesterol levels

Out of the 100 patients in the study, 28 (28%) developed surgical site infections (SSIs), while the remaining 72 (72%) did not experience any infections. Mean albumin levels were significantly lower in cases with surgical site infection (SSI) (3.02 vs 3.27 mg%; p<0.01) which is statistically significant. Mean cholesterol levels were comparable in cases with and without surgical site infection (SSI) (156.17 vs 154.31 mg%; p-0.84). Mean hospital stay was higher in cases who developed surgical site infection (SSI) (18.21 vs 7.88 days; p<0.01) which is statistically significant.

Variables	SSI	N	Mean	SD	P value
Albumin levels (mg%)					
	No	72	3.27	0.44	<0.01 * Sig
	Yes	28	3.02	0.51	
Total Cholesterol levels (mg%)					
	No	72	156.17	51.87	0.84
	Yes	28	154.31	65.77	
Hospital Stay (days)					
	No	72	7.88	2.21	<0.01 *Sig
	Yes	28	18.21	3.28	

Table 2. Comparison among cases with and without surgical site infection depending upon mean albumin levels, mean cholesterol levels and mean hospital stay

The incidence of surgical site infections (SSIs) was notably higher in patients with hypoalbuminemia, recorded at 33.8% compared to 17.2% in those with normal albumin levels. This difference was statistically significant, with a relative risk (RR) of 1.20 and a 95% confidence interval (CI) of 1.04–1.46 (p = 0.011). In contrast, among patients with low cholesterol levels, the SSI incidence was 41.7%, slightly higher than the 22.6% in those with normal cholesterol and 28.6% in those with elevated cholesterol. However, this variation was not statistically significant (p = 0.112). Similarly, the incidence of SSIs was 47.1% in patients with both low albumin and cholesterol levels, compared to 24.1% in patients with normal levels of both markers. Though there was an observed increase, it did not reach statistical significance (p = 0.06). These results indicate hypoalbuminemia as a significant risk factor for SSIs, while low cholesterol, whether alone or combined with low albumin, does not show a statistically significant impact.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 07, 2024

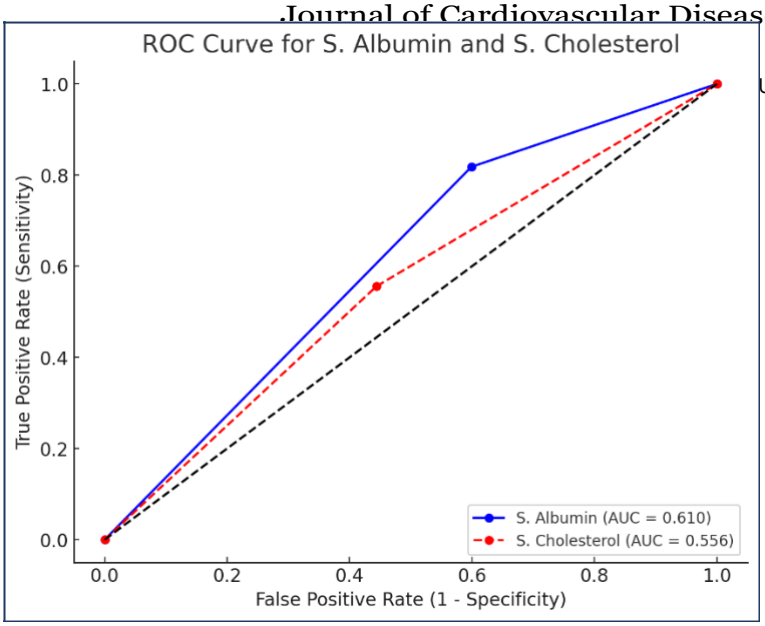
Variables	SSI			
	No	Yes	Total	P value
Hypoalbuminemia (mg%)				
No	29 (82.8%)	6 (17.2%)	35 (100%)	0.011 * Sig
Yes	43 (66.2%)	22 (33.8%)	65 (100%)	
Total	72 (72%)	28 (28%)	100 (100%)	
Total cholesterol levels (mg%)				
<100	14 (58.3%)	10 (41.7%)	24 (100%)	0.112 (Non-sig)
100-200	48 (77.4%)	14 (22.6%)	62 (100%)	
>200	10 (71.4%)	4 (28.6%)	14 (100%)	
Total	72 (72%)	28 (28%)	100 (100%)	
Hypoalbuminemia + Low Cholesterol				
No	63 (75.9%)	20 (24.1%)	83 (100%)	0.06 (Non-sig)
Yes	9 (52.9%)	8 (47.1%)	17 (17%)	
Total	72 (72%)	28 (28%)	100 (100%)	

Table 3. Association of surgical site infections with Hypoalbuminemia, Total cholesterol levels and low albumin and total cholesterol levels

The ROC curve analysis in this study showed that albumin levels were a significant predictor of surgical site infection (SSI) development, with an area under the curve (AUC) of 0.610 (95% CI: 0.568–0.810, $p < 0.01$). The optimal cut-off for albumin was determined to be less than 3.0 mg%, providing a sensitivity of 81.6% and specificity of 41.2%. This cut-off demonstrated a high negative predictive value of 91.6%, indicating that patients with albumin levels above this threshold had a lower likelihood of developing an SSI.

Area under the curve				
Test result variable (s)	Area	SE	P value	95% CI
S. Albumin	0.610	0.048	<0.01	0.568-0.810
S. Cholesterol	0.556	0.055	0.245	0.445-0.660
Parameters	Albumin cut off <3.0 mg%			
Sensitivity	81.6%			
Specificity	41.2%			
PPV	21.4%			
NPV	91.6%			

Table 4. ROC curve analysis for diagnostic accuracy of albumin and cholesterol levels for prediction of surgical site infections



Graph 1. ROC curve analysis for diagnostic accuracy of Serum albumin and Serum Cholesterol

DISCUSSION

Surgical site infections (SSIs) are a common complication following surgery, with consequences ranging from delayed healing to systemic sepsis. These infections place a significant strain on both the economy and healthcare resources. Additionally, the extended hospital stays associated with SSIs can negatively affect patients' quality of life, efficiency, and productivity [8].

The risk of SSIs is influenced by various patient-related factors, including age, nutritional status, pre-existing infections, and comorbid conditions, as well as procedure-related factors such as the choice of suture material, surgical technique, prolonged surgery duration, preoperative site preparation, and proper sterilization of instruments [2].

Several studies have found an association between low serum albumin and cholesterol levels with an increased risk of SSIs, prolonged hospital stays, and higher mortality rates, making these factors significant contributors to morbidity and mortality among hospitalized patients [12-15].

This prospective observational study aimed to investigate the role of serum cholesterol and albumin levels as potential risk factors for SSIs following elective surgeries. The study included 100 patients, with an average age of 38.7 ± 10.6 years, the majority (58%) of whom were between 21 and 40 years old. The gender distribution showed a male predominance, with 58 males (58%) and 42 females (42%).

In the present study, we observed an incidence of Surgical Site Infection (SSI) in 28 out of 100 cases (28%). According to the US Centers for Disease Control (CDC) National Nosocomial Infections Surveillance system (NNIS), SSI is the third most common nosocomial infection, accounting for 14%-16% of infections among hospitalized patients and 38% of infections in surgical patients [2]. The incidence of SSI in laparotomy procedures remains high, ranging from 3.4% to 36.1%, with an average of up to 20% in various studies [3]. In India, the incidence of SSI in tertiary care hospitals is reported to be 2.06% for minimally invasive surgery (MIS) and 16.16% for open surgery (OS) [4]. Other studies have reported SSI incidences ranging from 2% to 23% for all surgical procedures performed in India between 1995 and 2010 [5].

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 07, 2024

Several Indian studies have assessed the prevalence and risk factors for surgical site infections (SSIs) in surgical wounds. In a study by Giri S et al., 53 out of 230 patients developed an SSI, resulting in a total SSI rate of 23% [27]. Similarly, Khadilkar R et al. observed an SSI incidence of 22% [28]. Tevlin R et al. found that 24.7% of total cases developed an SSI before discharge, with 8.6% having superficial SSI and 16.1% experiencing organ space infections [29]. Nwankwo E et al. reported that out of 2880 patients studied, 585 (20.3%) developed an SSI [30]. In our study, prolonged hospital stays were significantly associated with the development of SSI. The mean hospital stay was notably longer for patients who developed an SSI (18.21 vs 7.88 days; $p < 0.01$). A similar finding was reported by Malik AZ et al., where the average length of hospital stay was significantly higher in patients with SSI compared to those without (8.310 vs 3.329 days, $p < 0.01$) [31].

Long-term hospitalization often leads to the colonization of microorganisms, some of which may be resistant to common antibiotics. This can increase the patient's vulnerability to infections by either reducing host resistance or enhancing the potential for bacterial colonization.

Malnutrition is another significant secondary factor, particularly in patients who present at government facilities in India. It is widely recognized that malnourished patients are at a higher risk of complications and mortality compared to those with adequate nutritional reserves [21]. Serum albumin levels are closely linked to the severity of malnutrition and serve as a significant and reliable predictor of surgical risk, as it is a negative acute-phase protein [22].

In the present study, we observed that mean albumin levels were significantly lower in cases with surgical site infections (SSI) (3.02 vs. 3.27 mg%; $p < 0.01$). The incidence of SSI was 33.8% in patients with hypoalbuminemia compared to 17.2% in those with normal albumin levels ($p < 0.05$). ROC curve analysis indicated that albumin levels were a significant predictor of SSI development ($p < 0.01$), with an optimal cut-off of <3.0 mg%, showing a sensitivity of 81.6%, specificity of 41.2%, and a high negative predictive value of 91.6%.

In line with our findings, a study by Delgado-Rodriguez M et al. found an inverse relationship between serum albumin levels and SSI, with a significant adjusted odds ratio (OR) of 1.9 for the lowest versus highest quintile of albumin levels [32]. Nowshad M et al. also found a significant association between preoperative hypoalbuminemia and postoperative SSI, with a relative risk of 1.98 (95% CI, 1.07 to 3.61)
[33]. Similarly, Sodavadiya KB et al. reported a higher frequency of SSI in hypoalbuminemic patients (44.6%) compared to those with normal (10.7%) or hyperalbuminemic levels (12.5%), with a relative risk of 4.17 (95% CI, 2.46 to 7; $p < 0.001$) [34].

Cholesterol plays a vital role in immune function and gluconeogenesis, and lipoproteins, the transport forms of cholesterol, help neutralize bacterial endotoxins like lipopolysaccharide (LPS). When LPS binds to lipoproteins, it can reduce the release of proinflammatory cytokines, such as tumor necrosis factor-α, IL-1, and IL-6. However, in the present study, we found no significant association between cholesterol levels and the incidence of surgical site infections (SSIs). The mean cholesterol levels were similar in both groups with and without SSI (156.17 vs. 154.31 mg%; $p = 0.84$). While 47.1% of patients with low cholesterol levels developed SSI, this was not statistically different from the incidence in patients with normal (22.6%) or high cholesterol levels (28.6%). Similarly, although there was an increase in SSI incidence among patients with both low albumin and cholesterol levels (47.1%) compared to those with normal levels (24.1%), this difference did not reach statistical significance ($p = 0.06$).

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 07, 2024

In contrast, previous studies have reported differing results. Delgado-Rodríguez M et al. found that HDL-C and LDL-C levels were inversely related to the incidence of nosocomial infections, though no significant association was found with total cholesterol levels [32]. Nowshad M et al. also observed no significant association between preoperative cholesterol levels and postoperative SSI [33]. However, contrary to our findings, Sodavadiya KB et al. reported a strong correlation between hypocholesterolemia and SSI, with a statistically significant relative risk (RR = 3.98, CI = 2.28 to 6.95; $p < 0.001$) [34].

In conclusion, our study suggests that preoperative albumin levels are a more reliable prognostic indicator for predicting the development of SSIs following surgery. In contrast, cholesterol levels, either alone or in combination with albumin, did not show a statistically significant impact on SSI incidence. Therefore, measuring and correcting low serum albumin levels before surgery could help reduce postoperative morbidity, while cholesterol levels may not require the same focus in SSI prevention.

CONCLUSION

In conclusion, our study highlights the significant role of preoperative serum albumin levels as a reliable predictor for the development of surgical site infections (SSIs) following elective surgeries. Patients with hypoalbuminemia were found to have a notably higher incidence of SSIs, and albumin levels below 3.0 mg% were identified as a key risk factor. On the other hand, while low cholesterol levels were observed in some patients with SSIs, no statistically significant relationship was found between preoperative cholesterol levels and the incidence of SSIs. Therefore, focusing on serum albumin as a risk factor for SSIs may offer a more effective approach to preoperative assessment and management.

We thus conclude that serum albumin level is a significant predictor for development of surgical site infections and should be done in all cases prior to surgery. By estimating albumin levels before surgery and adequately correcting lower levels, postoperative morbidity could be reduced in these patients.

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