ROLE OF SERUM CHOLESTEROL AND ALBUMIN LEVELS AS A RISK FACTOR FOR DEVELOPING SURGICAL SITE INFECTION

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Abstract

Background: Surgical site infection (SSI) causes significant morbidity and mortality in addition to lengthier hospital stays and higher healthcare expenses. The risk of SSIs can be significantly influenced by a number of patient-related factors (old age, nutritional status, pre-existing infection, and comorbid illness). The present study is thus designed to determine the role of serum cholesterol and serum albumin levels as a risk factor for developing surgical site infection following elective surgery. Materials and Methods: A prospective cohort study including 200 patients undergoing elective surgery was conducted at a tertiary healthcare center. The preoperative S. Albumin, S. Cholesterol, length of hospital stay, duration of surgery was considered for this study and its relation to surgical site infection was obtained. Data was analyzed using SPSS software ver. 21.0. Result: Out of the total 200 cases, SSI was observed in 54 cases (27%). Mean albumin levels were significantly lower in cases with SSI (p<0.01). However, mean cholesterol levels were comparable in cases with and without SSI (p>0.94). Mean hospital stay was significantly higher in cases who developed SSI (p<0.01). Conclusion: Observations made in the present study showed that pre-operative albumin level is a good prognostic indicator for predicting the development of surgical site infections after surgery. However, no significant association was observed with respect to cholesterol levels. 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.

INTRODUCTION

Surgical site infection (SSI) is defined as the infection related to an operative procedure that occurs at or near the surgical incision within 30 days of the procedure if no prosthetic is placed and up to 1 year if a prosthetic is implanted in the patient.¹ According to the US Centers for Disease Control (CDC) National Nosocomial Infections Surveillance system, SSI is the third most frequent nosocomial infection, accounting for 14%-16% of infections among hospitalized patients and 38% of infections in surgical patients.² The surgical site infection rates for laparotomy procedures are still higher i.e., up to 20% (range from 3.4% - 36.1% in different studies).³

In India, among tertiary care hospitals, incidence of SSI is 2.06% and 16.16% in MIS (minimal invasive surgery) and OS (open surgery) respectively.⁴ Another literature reported that the incidence of SSI is between 2% to 23% for all surgical procedures performed between year 1995 to 2010 in India.⁵ The CDC describes three types of surgical site infections - superficial, deep and organ or space SSI.⁶ The incidence of SSI varies according to the nature of the procedure (emergency/elective) and the degree of wound contamination. The Centers for Disease Control and Prevention (CDC) categorizes surgical wounds into four classes: clean, clean-contaminated, contaminated, and dirty-infected:⁷

- Clean: An uninfected operative wound in which no inflammation is encountered and the respiratory, alimentary, genital, or uninfected urinary tracts are not entered.
- Clean-Contaminated: Operative wounds in which the respiratory, alimentary, genital, or urinary tracts are entered under controlled conditions and without unusual contamination. Specifically, operations involving the biliary tract, appendix, vagina, and oropharynx, provided no evidence of...
infection or major break in technique is encountered.
• Contaminated: Open, fresh, accidental wounds. In addition, operations with major breaks in sterile technique or gross spillage from the gastrointestinal tract and incisions in which acute, non-purulent inflammation is encountered, including necrotic tissue without evidence of purulent drainage.
• Dirty-Infected: Old traumatic wounds with retained devitalized tissue and those that involve existing clinical infection or perforated viscera. Organisms causing postoperative infection were present in the operative field before the operation. SSI causes significant morbidity and mortality in addition to lengthen hospital stays and higher healthcare expenses.[8] As a result of time spent in hospitals, SSI can also have an impact on patient quality of life, efficiency and productivity. SSI are usually caused by exogenous and/or endogenous micro-organisms that enter the wound either during the surgery (primary infection) or after the surgery (secondary infection).

Primary infections, appearing within 5 to 7 days of surgery, are usually more serious.[9] Majority of SSIs involves only skin and subcutaneous tissue but sometimes can progress to deep and necrotizing infections. The usual presentation of infected surgical wound can be characterized by pain, tenderness, redness, raised localized temperature, swelling and pus discharge.[10,11]

The risk of SSIs can be significantly influenced by a number of patient-related factors (old age, nutritional status, pre-existing infection, and comorbid illness) and procedure-related factors (suture material, subpar surgical technique, prolonged surgery duration, pre-operative part preparation, and inadequate sterilization of surgical instruments).[2]

A few studies have reported a relationship between low serum albumin level and low cholesterol level in surgical site infection, length of hospital stay and death and is reported to be one of the major causes of morbidity and mortality among hospitalized patients.[12-15]

Hypolipidemia (hocholesterolemia - total cholesterol <150 mg/dl) is an independent predictor of clinical outcome in critically ill patients. Cholesterol plays an important role in gluconeogenesis and immune function. Lipoproteins, the transport form of cholesterol in blood, also serve as vehicles for fat-soluble vitamins, antioxidants, drugs, and toxins. One that seems especially important is related to the ability of lipids and lipoproteins to bind to and neutralize bacterial endotoxin (lipo polysaccharide [LPS]).[16] It has been noted that LPS in blood binds to LPS binding protein,[17] activating the cell surface CD14 receptor.[18] This stimulates the release of a cascade of pro-inflammatory cytokines, including tumor necrosis factor-α, IL-1, and IL-6.[19] If LPS binds to lipoproteins (e.g., cholesterol), then cytokine release is decreased.[20]

Malnutrition is a significant secondary factor that, in addition to the different primary causes of hypcholesterolemia, affects the majority of patients who present to a government facility in India. It has been established that nutritional deficiency is a key contributor to the development of postoperative problems. The prevalence of protein-energy malnutrition in surgical patients is high, ranging from 10% to 54%.

There is strong evidence that patients who exhibit signs of malnutrition are more likely to suffer complications and mortality than those who have enough nutritional reserves.[21] Serum albumin closely correlates with the severity of malnutrition and is a significant and reliable predictor of surgical risk; it is also a negative acute phase protein.[22] 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.[23] Malnutrition and inflammation suppress albumin synthesis.[24-26]

Our hypothesis was that the susceptibility to surgical site infections is correlated with preoperative levels of albumin and cholesterol. We conducted this study to determine the role of serum cholesterol and serum albumin levels as a risk factor for developing surgical site infection following elective surgery.

**MATERIALS AND METHODS**

A prospective cohort study was conducted at a tertiary healthcare center. Study was commenced after taking approval of Institutional Ethical Committee.

**Inclusion Criteria**
1. All the patients undergoing elective surgery in department of General Surgery in Dr. Susheela Tiwari Government Hospital, Haldwani.
2. Patients giving written informed consent to be part of the study.

**Exclusion Criteria**
1. Critically ill patients presenting in casualty requiring emergency OT.
2. Patients with immunocompromised state like HIV positive, on corticosteroids.
3. Patients with Diabetes Mellitus
4. Pregnant females
5. Patients who lost follow up.
6. Wound site previously infected.
7. Patients not giving consent to be part of the study.

**Methodology**

This study was carried out on 200 patients undergoing elective surgery in our hospital. Informed consents were obtained from all patients participating in the study. Confidentiality of the subjects was maintained before, during and after the study. The surgical procedures included in the study were inguinal hernia surgery, appendectomy and colorectal surgery, cholecystectomy, breast surgeries and other major elective procedures.
Prior to admission, proper screening along with detailed clinical evaluation of each patient was carried out in the form of the following: complete blood count, routine biochemistry (including LFT and Lipid profile), bleeding time, clotting time, urine examination, chest x-ray and ECG. For each surgery, a proforma was prepared that included the patient's serum albumin and cholesterol levels as well as their hospital stay and procedure duration. The patients were monitored till the date of discharge. Any surgical site infection seen was recognized. The preoperative S. Albumin, S. Cholesterol, length of hospital stay, duration of surgery was considered for this study and its relation to surgical site infection was obtained. Antimicrobial prophylaxis, treatment and type, culture and sensitivity of organism were not considered in this study.

Patients general vital charting (pulse rate, blood pressure, temperature), assessment of daily dressing was done daily. Wound condition was scored according to the Southampton Wound Grade system. All patients were educated about the symptoms and signs of surgical site infections like erythema, discharge, tenderness, seroma and hematoma, wound dehiscence etc. and instructed to report to us in case they developed any such symptoms and signs.

SSI was defined as per the CDC (Centre for Disease Control) criteria - superficial SSI: wound cellulitis /erythema /purulent discharge from the wound and deep SSI as any wound infection requiring surgical interventions, such as removal of sutures or clips, drainage of deep pus, packings etc.

Data Analysis
Data was analyzed using SPSS 21.0 (SPSS Inc., Chicago, IL, USA) using appropriate statistical tests.

RESULTS

Figure 1: Distribution of study groups as per presence of hypoalbuminemia

Figure 2: Distribution of study groups as per cholesterol levels

Figure 3: Mean albumin levels comparison among cases with and without surgical site infection

Figure 4: Mean cholesterol levels comparison among cases with and without surgical site infection

Figure 5: Mean hospital stay comparison among cases with and without surgical site infection
Prevalence of hypoalbuminemia was seen in 64.5% cases.

Prevalence of low total cholesterol levels were seen in 22.0% cases while in 15% cases total cholesterol levels were more than 200 mg%.

Table 3: Mean albumin levels comparison among cases with and without surgical site infection.

<table>
<thead>
<tr>
<th>Variables</th>
<th>SSI</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin levels (mg%)</td>
<td>No</td>
<td>146</td>
<td>3.28</td>
<td>0.46</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>54</td>
<td>3.03</td>
<td>0.53</td>
<td></td>
</tr>
</tbody>
</table>
Mean albumin levels were significantly lower in cases with surgical site infection (SSI) (3.03 vs 3.28 mg%; \( p \leq 0.01 \)) which is statistically significant.

<table>
<thead>
<tr>
<th>Variables</th>
<th>SSI</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>( p )-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol levels (mg%)</td>
<td>No</td>
<td>146</td>
<td>156.18</td>
<td>52.97</td>
<td>0.94</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>54</td>
<td>155.57</td>
<td>67.44</td>
<td></td>
</tr>
</tbody>
</table>

Mean cholesterol levels were comparable in cases with and without surgical site infection (SSI) (155.57 vs 156.18 mg%; \( p = 0.94 \)).

<table>
<thead>
<tr>
<th>Variables</th>
<th>SSI</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>( p )-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital stay (days)</td>
<td>No</td>
<td>146</td>
<td>7.99</td>
<td>2.25</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>54</td>
<td>18.11</td>
<td>3.50</td>
<td></td>
</tr>
</tbody>
</table>

Mean hospital stay was higher in cases who developed surgical site infection (SSI) (18.11 vs 7.99 days; \( p < 0.01 \)) which is statistically significant.

Table 6: Association of surgical site infections with hypoalbuminemia

<table>
<thead>
<tr>
<th>Hypoalbuminemia</th>
<th>SSI</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>59</td>
<td>71</td>
</tr>
<tr>
<td>Yes</td>
<td>87</td>
<td>129</td>
</tr>
</tbody>
</table>

\( p \)-value – 0.019 (RR – 1.23 (1.05 – 1.44))

Incidence of surgical site infections was 32.6% in cases with hypoalbuminemia as compared to 16.9% in cases with normal albumin levels (RR – 1.23; 95% CI - 1.05 – 1.44; \( p = 0.019 \)) which is statistically significant.

Table 7: Association of surgical site infections with total cholesterol levels

<table>
<thead>
<tr>
<th>Total cholesterol levels (mg%)</th>
<th>SSI</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>16</td>
<td>44</td>
</tr>
<tr>
<td>Yes</td>
<td>36.40%</td>
<td>100.00%</td>
</tr>
</tbody>
</table>

Irrespective of the cholesterol level, the incidence of surgical site infections was not significantly different (\( p = 0.134 \)).

Table 8: Association of surgical site infections with low albumin and total cholesterol levels

<table>
<thead>
<tr>
<th>Hypoalbuminemia + Low Cholesterol</th>
<th>SSI</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>126</td>
<td>167</td>
</tr>
<tr>
<td>Yes</td>
<td>75.40%</td>
<td>100.00%</td>
</tr>
</tbody>
</table>

Incidence of surgical site infections was 39.4% in cases with both low albumin and cholesterol levels as compared to 24.6% in cases with normal levels. The difference was not statistically significant (\( p = 0.08 \)).
On ROC curve analysis, we observed that only albumin levels were significant predictor of development of SSI in our study (AUC – 0.655; 0.578-0.816; p<0.01). The optimal cut-off of albumin level was <3.0 mg% with sensitivity and specificity of 81.8% and 40.1% and high negative predictive value of 91.8%.

### DISCUSSION

A frequent complication of surgery is an infection at the surgical site. Its morbidity includes everything from delayed healing to systemic sepsis. The economy and healthcare resources are significantly impacted. As a result of time spent in hospitals, SSI can also have an impact on patient quality of life, efficiency and productivity.[8]

The risk of SSIs can be significantly influenced by a number of patient-related factors (old age, nutritional status, pre-existing infection, and comorbid illness) and procedure-related factors (suture material, subpar surgical technique, prolonged surgery duration, pre-operative part preparation, and inadequate sterilization of surgical instruments).[2]

A few studies have reported a relationship between low serum albumin level and low cholesterol level in surgical site infection, length of hospital stay and death and is reported to be one of the major causes of morbidity and mortality among hospitalized patients.[12-15]

Present hospital based prospective observational study aimed to determine the role of serum cholesterol and serum albumin levels as a risk factor for developing surgical site infection following elective surgery. Study included 200 patients undergoing elective surgery in our hospital during study period. Mean age of the study cases undergoing elective surgeries in our hospital was 38.3 years with 8.5% being over the age of 60 years. Out of the total 200 cases, 57.5% were males and 42.5% were females. In present study, we observed Incidence of Surgical Site Infection (SSI) in 54 out of 200 cases (27%).

According to the US Centers for Disease Control (CDC) National Nosocomial Infections Surveillance system (NNIS), SSI is the third most frequent nosocomial infection, accounting for 14%-16% of infections among hospitalized patients and 38% of infections in surgical patients.[2] The surgical site infection rates for laparotomy procedures are still higher i.e., up to 20% (range from 3.4% - 36.1% in different studies).[3] In India, among tertiary care hospitals, incidence of SSI is 2.06% and 16.16% in MIS (minimal invasive surgery) and OS (open surgery) respectively.[4] Another literature reported that the incidence of SSI is between 2% to 23% for all surgical procedures performed between year 1995 to 2010 in India.[5]

The prevalence and risk factors for surgical site infection in surgical wounds have been assessed by a number of Indian authors. Out of 230 patients included, 53 were found to have an SSI, giving a total rate of SSI of 23%, as reported by Giri S et al.[27] In another similar study by Khadilkar R et al.[28] incidence of SSI was observed as 22%. Tevlin R et al.,[29] observed that prior to discharge 24.7% of total cases developed SSI; 8.6% superficial and 16.1% organ space SSI. Nwankwo E et al.[30] in their study observed that out of 2880 patients studied, 585 (20.3%) developed SSI.

As expected, we observed that prolonged hospital stays to be significantly associated with cases of SSI. Mean hospital stay was significantly higher in cases who developed SSI (18.11 vs 7.99 days; p<0.01). Similarly, Malik AZ et al.[31] found a significant difference in the average length of hospital stay between patients who developed SSI and those who did not (8.310.3 vs 3.32.9 days, p 0.01). Long-term hospitalization results in the colonization of microorganisms that may be resistant to common antibiotics, which in turn directly influences the patient’s vulnerability to infection by either diminishing host resistance or increasing the potential for bacterial colonization.

Malnutrition is a significant secondary factor that, in addition to the different primary causes of hypcholesterolemia, affects the majority of patients who present to a government facility in India. There is strong evidence that patients who exhibit signs of malnutrition are more likely to suffer complications and mortality than those who have enough nutritional reserves.[21] Serum albumin closely correlates with the severity of malnutrition and is a significant and reliable predictor of surgical risk; it is also a negative acute phase protein.[22]

In present study, mean albumin levels were significantly lower in cases with SSI (3.03 vs 3.28 mg%; p<0.01). Incidence of SSI was 32.6% in cases with hypoalbuminemia as compared to 16.9% in cases with normal albumin levels (RR – 1.23; 95%
CI - 1.05 – 1.44; p = 0.019). On ROC curve analysis, we observed that only albumin levels were significant predictor of development of SSI in our study (AUC – 0.655; 0.578-0.816; p<0.01). The optimal cut-off of albumin level was <3.0 mg% with sensitivity and specificity of 81.8% and 40.1% and high negative predictive value of 91.8%.

In a study, Delgado-Rodríguez M et al.[32] found that in both simple and multivariate analyses, serum albumin levels (lowest vs. highest quintile: adjusted odds ratio (OR), 1.9; 95% confidence interval, 1.2-2.9) and HDL-C levels (lowest vs. highest quintile: OR, 2.0; 95% confidence interval, 1.3-3.0) showed an inverse relationship and it was found to be statistically significant. Nowshad M et al.[33] studied whether there is an association between the preoperative levels of albumin with postoperative surgical site infection. Hypoalbuminemia was present in 87(33%) of the patients. Hypoalbuminemia was found to be associated with SSI with a relative risk of 1.98 and confidence interval of 1.07 to 3.61. Sodavadiya KB et al.[34] reported that frequency of patients developed SSI in hypoalbuminemia was 25 (44.6%) in number compare to n=18 (10.7%) in normal and to n= 03(12.5%) in hyperalbuminemia.

The Relative Risk between hypoalbuminemia and SSI is 4.17 with Confidence interval (2.46 to 7) (P = <0.001).

Cholesterol plays an important role in gluconeogenesis and immune function. Lipoproteins, transport form of cholesterol in blood, also serve as vehicles for fat-soluble vitamins, antioxidants, drugs, and toxins. One that seems especially important is related to the ability of lipids and lipoproteins to bind to and neutralize bacterial endotoxin (lipopolysaccharide [LPS]).[16] It has been noted that LPS in blood binds to LPS binding protein,[17] activating the cell surface CD14 receptor.[18] This stimulates the release of a cascade of pro-inflammatory cytokines, including tumor necrosis factor-α, IL-1, and IL-6.[19] If LPS binds to lipoproteins (e.g., cholesterol), then cytokine release is decreased.[20]

In present study, however, mean cholesterol levels were comparable in cases with and without SSI (155.57 vs 156.18 mg%; p=0.94). Incidence of SSI was 36.4% in cases with low cholesterol levels, which is slightly higher than cases with normal cholesterol levels (33.3%) and in cases with high levels (22.2%). However, the difference was not statistically significant (p=0.134).

Delgado-Rodríguez M et al.[32] study observed that among lipid fractions, HDL-C, and LDL-C levels showed independent, significant (P<0.01), and inverse relationships of a high level of cholesterol and serum albumin were found in 87 patients with only 3 (1%) developed SSI (p>0.05).

Contrary to the current findings, Sodavadiya KB et al.,[34] reported that there was a strong correlation between cholesterol levels and the occurrence of SSI, with the majority of SSI patients having hypcholesterolemia, and that this correlation was statistically significant (RR=3.98, CI= 2.28 to 6.95), p <0.001.

Thus, to summarize, observations made in the present study showed that pre-operative albumin level is a good prognostic indicator for predicting the development of surgical site infections after surgery. However, no significant association was observed with respect to cholesterol levels. Hence, serum albumin level should be done in all cases prior to surgery. By estimating albumin levels before surgery and adequately correcting lower levels, post-operative morbidity could be reduced in these patients.

CONCLUSION

Present study aimed to determine the role of serum cholesterol and serum albumin levels as a risk factor for developing surgical site infection following elective surgery. Study was conducted on 200 cases undergoing elective surgeries. Surgical site infections were observed one out of every three cases. Observations made in the present study showed that pre-operative albumin level is a good prognostic indicator for predicting the development of surgical site infections after surgery. However, no significant association was observed with respect to cholesterol levels.

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, post-operative morbidity could be reduced in these patients.

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