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Original Research Article

A forgotten risk factor for surgical site infection: Hypocholesterolemia

Manjunath B. D., Harindranath H. R., Abdul Razak*, Mohammed Arafath Ali

Department of General Surgery, Bangalore Medical College, Bangalore, Karnataka, India

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***Correspondence:**
Dr. Abdul Razak,
E-mail: arafathali0708@gmail.com

ABSTRACT

Background: Postoperative infection is one of the most common complications after any surgery. In the present study, surgical site infection (SSI) is described as; superficial (i.e., skin and subcutaneous tissues) and deep (i.e., fascia and muscles) infections occurring in the short term (i.e., 1-month) after surgery. The objective of this study was to detect various risk factors for SSI development.
Methods: In this study, we prospectively enrolled 217 patients undergoing spinal surgery over an 8 months period. In a prospective study from January 2017 to August 2017, 217 patients who were admitted and operated for elective hernia surgery in hospitals attached to Bangalore Medical College and Research Institute, patients with immunodeficiency disorders and obstructed hernias were excluded.
Results: Of 217 patients 35 (16.12%) patients developed SSI, multi-variant data analysis indicated that multiple factors correlated with an increased risk of SSI of which one of the important factor was hypocholesterolemia with 32.8% people developing SSI with p-value <0.01 along with Hypoalbuminemia and diabetes. Whereas other factors shuch as age had a minor role in increasing the incidence of SSI other factors such as smoking, alcoholism, gender, hypertension was found not to have much significant contribution in the development of SSI in the present study.
Conclusions: Hypocholesterolemia is one on the forgotten factors which is usually brushed aside whose consideration can lead to significant decrease in this preventable complication especially in a malnourished population presenting in a government setup.

Keywords: Hypocholestterolemia, Risk factors, Surgical site infection

INTRODUCTION

A Surgical site infection is an infection that occurs after surgery in the part of the body where the surgery took place, SSI can sometimes be superficial infections involving skin only or can include structures below skin, organs or implanted material.[1] SSI are the 2nd most common type of adverse events occurring in a hospitalized patient following surgery and are one of the most common surgical complication.[2] SSI are responsible for an increased economic burden to health care systems including additional postoperative hospital duration and costs.[3] Factors responsible include ASA score, Surgical wound class, blood transfusion, creation of ostomy, types of operation, use of drainage, sex and surgeons were important in predicting SSI after surgery.[4]

The role of cholesterol in the human body cannot be ignored as it is the precursor of five major classes of steroid hormones. Cholesterol affects gluconeogenesis and immune function; its transport forms, the lipoproteins, also serve as vehicles for fat-soluble vitamins, antioxidants, drugs, and toxins. These hormones are synthesized from cholesterol mostly in the adrenal gland and gonads in response to tissue-specific trophic hormones. These steroidogenic tissues are unique

in that they require cholesterol not only for membrane biogenesis, maintenance of membrane fluidity, and cell signalling but also as the starting material for the biosynthesis of steroid hormones and an integral part of cell membrane.[5]

Apart from various reasons of hypocholesterolemia, Malnutrition is an important secondary cause and is present in majority of patients presenting in a government setup in india.

Hence this study was taken to find association of the incidence of SSI in relation to Total cholesterol levels in 217 patients admitted for elective hernia repair in hospitals affiliated to BMC and RI.

METHODS

This is a prospective cohort study conducted in Victoria Hospital and Bowring and Lady Curzon Hospital affiliated to Bangalore Medical College and Research Institute and was approved by ethical committee. A study population of 217 patients, 63 patients from Bowring and Lady Curzon hospital and 154 patients from Victoria hospital admitted in Department of General Surgery for elective hernia repair (Inguinal/ Umbilical/ Paraumbilical/ Incisional) from January 2017 to August 2017.

Patients excluded from this study were

- Critically ill patients presenting in casualty like obstructed/strangulated hernias requiring emergency OT.
- Patients with immunocompromised states like HIV positive, on corticosteroids
- Pregnant females
- Patients who lost follow up.

Detailed information was given to the patients and informed consent was collected from them. The study design was approved by the Institutional Ethics Committee constituted as per ICMR guidelines.

Details of patients were recorded including history and clinical examination. Necessary pre-operative investigations were performed. Most likely variables having a possible relationship with post-operative complications related to this study were considered and evaluated at the time of admission and blood samples were obtained under fasting conditions.

Total cholesterol levels were classified into three categories (tertiles) according (<159, 160-239, and >240 mg/dl). The lower limit of the total cholesterol level was considered to be 160 mg/dl. Hypercholesterolemia (above 240 mg/dl) and borderline blood total cholesterol were generally accepted under the American Heart Association guidelines. Total serum Albumin were classified in 3 categories <3.5, 3.5-5.5, and >5.5 Patients were labelled as smokers with a 5-pack year history and who were presently smoking and those patients who were involved in alcohol consumption 3-4 times per week of approx. 250 ml and above for 5 years and above were labelled as alcoholics.

Antibiotic prophylaxis of Inj. Ceftriaxone 1g i.v. was given half an hour before the skin incision and repeated 6 and 12 hours.

Strict aseptic precautions were taken to minimize the chances of SSI including standard preparation of a patient before incision like spirit - povidone iodine - spirit sequence, irrigation with normal saline and povidone iodine solution before closing the wound, changing of gloves when handling a mesh, discharge on post-operative day 2.

All the surgeries done for hernia repair were open surgeries and no laparoscopic repairs were done.

Operative wounds were examined on the second, fifth and eighth postoperative days for signs of surgical site infection Incisional SSI both superficial and deep were defined according to CDC criteria and were recorded and SSI surveillance was extended to 30 days post-surgery.

RESULTS

Total of 217 patients who underwent open hernia repairs with mesh placement of which 170 (78%) were male patients and 47 (22%) were female patients.

Table 1: Gender distribution of study population.

Gender	Frequency (N)	Percentage
Male	170	78.3%
Female	47	21.7%

Majority of the patients in the present study population consisted of males 78.3%.

Table 2: Age distribution of the study participants.

Age (Years)	Frequency (N)	Percentage
0-20	3	1.4
21-40	102	47
41-60	78	35.9
61-80	33	15.2
81-100	1	0.5

Majority (47%) of the patients were belonging to the age group of 21-40 years. Mean age of study participants was 44.71±13.69 years.

73 patients had type 2 DM diagnosed pre-operatively and were on regular medications and were converted to insulin after admission, 1 patient of 18 years had type 1 DM. 83 patients were diagnosed hypertensives, 13

patients had both Hypertension with DM. The majority of the study population being middle aged were having concomitant comorbidities.

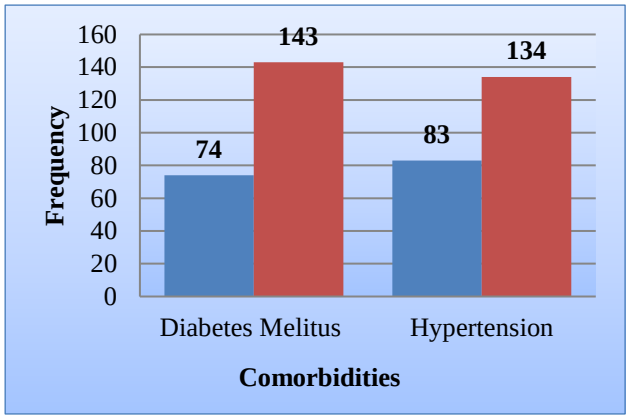

Figure 1: Comorbidities among the study participants.

People with 5-year history and regularly using on daily basis were labelled as smokers and alcoholics. Majority were non-smokers and non-alcoholics.

Table 3: Substance use by the study participants.

Substance use	Present N (%)	Absent N (%)
Tobacco	53 (24.4%)	164 (75.6%)
Alcohol	77 (35.5%)	140 (64.5%)

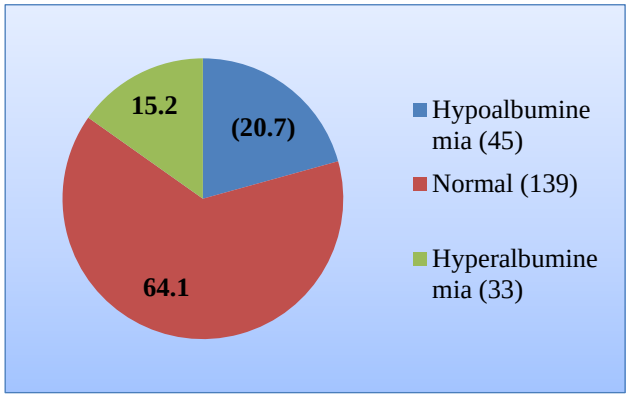

Figure 2: Distribution of serum albumin among study population.

Majority of patients were having a normal range of serum albumin (N = 139, 64.1%), of those having hypoalbuminemia (N = 45, 20.7%) were under nourished. Majority of the patients (N = 113, 52.1%) were having a normal level of serum total cholesterol and of those having a level of <160 mg/dl i.e.

Hypocholesterolaemia (N = 67, 30.9%) were under nourished. The overall incidence of postoperative SSI was 16.12% with n = 35 which include 2 patients with mesh infection with purulent discharge requiring secondary suturing after the control of infection, 7 patients had purulent discharge and 26 patients had erythema of wound.

Table 4: Distribution of study participants according to the total cholesterol levels.

Total Cholesterol	Frequency (N)	Percentage
Hyopcholesterolemia	67	30.9
Normal	113	52.1
Hypercholesterolemia	37	17.1

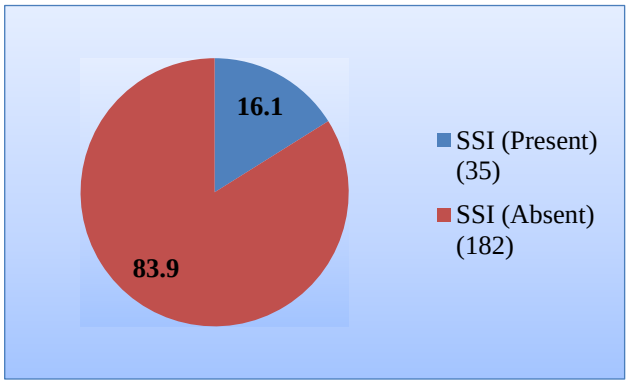

Figure 3: Incidence of SSI among the study population.

There is a significant association between cholesterol levels and the occurrence of SSI, with majority of the people with SSI had Hypocholesterolemia and it was found to be statistically significant (P = <0.001).

Table 5: Association between total cholesterol levels and occurrence of SSI.

Total Cholesterol Levels	SSI		Total	P value
	Present N (%)	Absent N (%)	217 (100%)	
Hypo cholesterolemia	22 (32.8)	45 (67.2%)	67	<0.001 Df = 2
Normal	9 (8.0)	114 (92.0%)	113	
Hyper cholesterolemia	4 (10.8)	33 (83.2%)	37	

*Chi-square test used

The factors associated with the development of superficial/deep SSI was hypocholesterolemia i.e. the lowest tertile (<160 mg/dl of total cholesterol) 34.92% n = 22 compared to 7.5% n = 9 in normal tertile i.e. between 160-240 mg/dl and 11.4% n = 4 in higher tertile i.e. >240 mg/dl.

We did not find any association between smokers/nonsmokers (15 and 16% respectively) and between alcoholics and non-alcoholics (16.8 and 15.7% respectively) in occurrence of SSI. 37% (n = 23) of diabetics were infected in the present study compared to only 14% (n = 10) of hypertensive and 7% (n = 1) of

patients who were both diabetics and hypertensive and 1.3% (n = 1) patients who were neither hypertensive nor diabetic. Result was statistically significant (p value <0.001) for patients with diabetes.

Table 6: Association between the various factors with the occurrence of SSI.

Factors		SSI		Total	P value
		Present N (%)	Absent N (%)	217 (100%)	
Gender*	Male	31 (18.2)	139 (81.8)	170	0.109 Df = 1
	Female	4 (8.5)	43 (91.5)	47	
Age**	0-20	0	3 (100)	3	0.248
	21-40	12 (11.8)	90 (88.2)	102	
	41-60	12 (15.4)	66 (84.6)	78	
	6-80	10 (30.3)	23 (69.7)	33	
	81-100	1 (100)	0	1	
Diabetes Mellitus*	Present	24 (32)	50 (67.6)	74	<0.001 Df = 1
	Absent	11 (7.7)	132 (92.3)	143	
Hypertension*	Present	11 (13.3)	72 (86.7)	83	0.365 Df = 1
	Absent	24 (17.9)	110 (82.1)	134	
Smoking*	Present	8 (15.1)	45 (4.9)	53	0.814 Df = 1
	Absent	27 (16.5)	137 (83.5)	164	
Alcohol Consumption*	Present	15 (19.5)	62 (80.5)	77	0.319 Df = 1
	Absent	20 (14.3)	120 (85.7)	140	
Albumin levels*	Hypoalbuminemia	14 (31.1)	31 (68.9)	45	0.005 Df = 2
	Normal	19 (13.7)	120 (86.3)	139	
	Hyperalbuminemia	2 (6.1)	31 (93.9)	33	

*Chi-square test; **Fischer's exact test

Patients with Hypoalbuminemia i.e. <3.5mg/dl had higher incidence of SSI (18.6% n=8) compared to normal S. albumin and above normal S. albumin levels (10.5% n=14 and 9.3% n=3) respectively and the result was statistically significant for the patients with hypoalbuminemia.

All patients who developed SSI were treated with i.v. antibiotics (1st empirically and then according to the results in culture and sensitivity reports) culture results showed staph aureus (52%) and Acinetobacter (15%)

DISCUSSION

Surgical site infection (SSI) is a major complication of surgery, associated with prolonged hospitalization, increased costs and increased morbidity and mortality. In recent years, randomized trials have identified a number of preventive measures that can substantially reduce the risk of SSI. These include appropriate perioperative antibiotic prophylaxis, maintenance of perioperative normothermia and control of hyperglycemia.[6,7] The wound healing process involves numerous functions, many of which depend on the presence of oxygen. Collagen production and development influence the strength of the wound which is directly correlated with the partial pressure of oxygen (PO_2) of the tissue. Synthesis of collagen, cross-linking and the resulting wound strength depend on the normal function of specific enzymes. The functions of these enzymes are directly related to the amount of oxygen present, e.g. hydroxylation of proline and lysine by hydroxylase enzymes.[8]

The stress response to surgery comprises of a number of hormonal changes initiated by neuronal activation of hypothalamic - pituitary - adrenal axis with overall metabolic effect of catabolism of stored body fules. Cortisol a stress hormone synthesized from cholesterol and secreted from adrenal cortex increases rapidly from a base line of 400 nmol/lit to >1500 nmol/lit in a span of 4-6 hours, feedback mechanism operating for pituitary - adrenal axis becomes ineffective after surgery, so concentrations of both hormones remain high.[9]

Although not many studies or research have been done pertaining to this topic nonetheless various literature quote the incidence of SSI ranging from 1-20% in various case series. In our study/series we found the overall incidence to be 16.12%.

In a study conducted by Morimoto M, et al. Serum total cholesterol concentrations <160 mg/dl were associated with an increased incidence of superficial and deep SSI.[10] Similarly, Delgado-Rodriquez et al in a prospective study to access the risk factors associated with nosocomial

infections found the both low levels (below 102 mg/dl) and high levels (above 290 mg/dl) of serum total cholesterol were associated with a high risk of SSI and RTI in comparison with the reference group (139-261 mg/dl) whose findings were consistent with the findings in present study.[11]

Several non-mutually exclusive explanations for the inverse association between total cholesterol and infections are possible. First, low total serum cholesterol may contribute to the development of infections. Circulating cholesterol-rich lipoproteins and triglyceride-rich lipoproteins have the capacity to bind and detoxify bacterial lipopolysaccharide (LPS). HDL has been shown to compete with LPS binding protein (LBP) for binding to LPS. The LPS-LBP complex attaches to the CD-14 receptor on cells, which, in turn, stimulates TNF production thus helping in combatting infection.[11]

Preoperative hypoalbuminemia is well known to be significantly associated with the development of and is an independent risk factor for the development of postoperative SSI. analysis of the relationship between serum albumin and the development of superficial and deep incisional SSIs showed that preoperative serum albumin <3.0 mg/dl increased the risk of SSI in this study.

Diabetes has a well know association with the incidence of postoperative infections hence strict control of blood glucose levels is a must before any elective surgery for favorable outcomes.

This study is a small attempt to create awareness to recognize the hypocholesterolemia as a risk factor for the development of SSI particularly in a government setup where patients who present are usually undernourished and should be taken under consideration.

CONCLUSION

Hypocholesterolemia is one on the forgotten factors which is usually brushed aside whose consideration can lead to significant decrease in this preventable complication especially in a malnourished population presenting in a government setup.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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