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### A study of surgical site infections associated with perioperative hyperglycemia in patients undergoing major emergency surgical procedures

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#### Abstract

**Objectives:** To study the frequency of surgical site infection (SSI) associated with peri-operative hyperglycemia with respect to superficial, intermediate and deep infections, and to study the correlation of SSI between preoperative, intra-operative and postoperative hyperglycemia.

**Methods:** This is a prospective study carried out from November 2017 to May 2019 on patients undergoing major emergency surgical procedures at Victoria Hospital, Bangalore Medical College and Research Institute. After obtaining institutional ethics committee clearance and written informed consents, patients >18yrs of age undergoing major emergency surgical procedures fulfilling the inclusion/exclusion criteria will be enrolled in the study are subjected to serial hourly measurements of Capillary random blood sugars using hand held glucometer in the pre-operative, intra-operative and post-operative period. The total sample size was 232 patients calculated according to statistical formula.

**Results:** Our study is indicative of a significant association of surgical site infections with peri-operative hyperglycemia, with the highest correlation with postoperative hyperglycemia. Although >90% of postoperative hyperglycemia was associated with uncontrolled diabetes, it can be seen that ~20-30% of subjects with pre- and intra-operative hyperglycemia were actually non-diabetics and may suggest a contributory role of stress-induced hyperglycemia in development of SSIs.

**Interpretation and Conclusion:** Very few studies have shown the relation between preoperative, intra-operative and postoperative plasma sugars and SSIs. Hence strict control of sugars more so in the postoperative period will decrease the incidence of SSIs and hence the morbidity, cost and hospital stay associated with it.

**Keywords:** Hyperglycemia, Diabetes mellitus, surgical site infections

#### Introduction

Surgical site infections (SSI) <sup>[1]</sup> has always been one of the major complication of surgery and trauma and has been documented for 4000-5000years. Emergency Surgical procedures like laparotomies form mainstay of general surgery for the treatment of conditions such as hollow viscus perforation, appendicitis, mesenteric ischemia, stab injury, solid abdominal organ injury with severe bleeding and haemoperitoneum <sup>[2]</sup> Microorganisms are normally prevented from causing infection in tissues by intact epithelial surfaces, most notably the skin. These surfaces are broken down by surgery. Reduced resistance to infection has numerous causes like malnutrition, metabolic diseases states like hyperglycemia, uremia and hyper bilirubinemia, immunosuppression, colonization and translocation in the GIT, poor perfusion, foreign body material and poor surgical technique <sup>[3]</sup>. Raised blood sugars due to diabetes mellitus or surgical stress delays wound healing and may lead to surgical site infections. Hyperglycemia compromises host immune functions, it also reflects the catabolism and insulin resistance associated with surgical stress <sup>[4]</sup>. Poor peri-operative sugar control increases the risk of infection and worsens outcomes from sepsis for diabetic and non-diabetic patients. Moderate hyperglycemia (>200mg/dl) at any time on the first postoperative day raises the risk of surgical site infections four fold after cardiac and non-cardiac surgery <sup>[5]</sup>. Insulin infusion to keep the blood-glucose below 110mg/dl was associated with a 40% reduction in mortality among critically ill postoperative patients <sup>[6]</sup>. Diabetes mellitus has been significant risk factor for several types of surgical complications, as well as SSI. Primarily this article shows an association not causation, between postoperative hyperglycemia and SSI.

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Important is the failure to find the association in vascular surgery patients, who presumably have the maximum rates of diabetes and had higher rates of SSI than did general and colorectal surgery patients. This leads one to think whether factors such as HBA1C level, nutrition, tobacco use, obesity, operative time, and tissue perfusion/oxygenation may be more important factors in the equation. Efforts are also underway to culture post-operative infections to understand whether the current given prophylaxis is not enough for today's bacteria<sup>[7]</sup>.

### Materials and Methods

Source of data: Patients undergoing major emergency surgical procedures at Victoria hospital, Bangalore Medical College and Research institute from November 2017 to May 2019 were included in the prospective study and information collected using detailed questionnaire. All the patients >18 years undergoing emergency surgical procedure including the diabetics and non-diabetics and also all of them giving written informed consent. All patients not giving consent for the study were excluded. Also patients with immune-compromised conditions such as those taking corticosteroids or with HIV infection were excluded.

Study methodology: After obtaining institutional ethics committee clearance and taking written informed consent for emergency surgical procedures, patients fulfilling the inclusion/exclusion criteria were enrolled in the study were subjected to serial hourly measurements of Capillary random blood sugars using hand held glucometer in the pre-operative, intra-operative and post-operative period.

### Patients who developed signs and symptoms of SSI were classified into

1. Superficial incisional SSI-involves only skin and subcutaneous tissue.
2. Deep incisional SSI-involves deep tissues, such as facial and muscle layers; this also includes infection involving both superficial and deep incision sites and organ/space SSI draining through incision
3. Organ/space SSI-infection involves any part of the anatomy in organs and spaces other than the incision, which was opened or manipulated during operation Any pus obtained will be subjected to pus culture and sensitivity

### Assessment tools

1. A thorough physical/clinical evaluation was be carried out and recorded in the case record form
2. Routine investigations were conducted to assess other factors leading to surgical site infections
3. Hand held glucometer was used to assess capillary sugar levels
4. Ultrasonography to assess deep incisional and organ/space SSIs
5. Pus culture and sensitivity from the wounds.

### Results

A total of 232 subjects were included in the study. Mean age of subjects was  $46.36 \pm 12.303$  years. Majority of subjects were in the age group 31 to 40 years (30.2%), 25.9% were in the age group 51 to 60 years, 25.4% were in the age group 41 to 50 years. According to the sex distribution in the study 81.5% (189) were males and 18.5% (43) were females. Majority of subjects were diagnosed to have Gastric Perforation (50.4%), 22.8% (53) were diagnosed to have duodenal perforation. 41.4% were diabetics, 28% HTN, 3% CKD, 8.6%

CLD, 3% were on Steroids. 46.6% were alcoholics and 12.9% were smokers. In the study 46.1% had Hb <12 gm% and 53.9% had Hb >12 gm%.

Plasma sugars were monitored peri-operatively as described previously upto 5th POD. The mean preoperative plasma sugars were found to be 178.8mg/dl with the highest individual mean to be 181.88mg/dl (Mean sugar value at 1hr of presentation). The mean intra-operative plasma sugars was 181.31mg/dl with the highest recordings seen at 1hr after the start of surgery (187.37mg/dl- Mean at 1hr intra-op). The mean post-operative plasma sugars was 167.08mg/dl with the highest mean sugars being 177.58mg/dl (POD1) and the lowest being 156.68mg/dl (POD4). In the study 45.7% and 47% of the subjects had GRBS levels of >200mg/dl in the preoperative and intra-operative period respectively. 49.6% of the subjects had GRBS>200mg/dl in the postoperative period. The data is suggestive of higher plasma sugar levels during the pre-operative, intra-operative and immediate postoperative periods with a reducing trend through POD2 and POD3 followed by a slightly higher values through POD4 and POD5.

The mean preoperative total counts were found to be  $12396.98 \pm 5470.43$  cells/mm<sup>3</sup>. The highest mean post-operative total count was  $13205.56 \pm 5046.37$  on POD1 with a decreasing trend noted thereafter. Considering co-morbidities diabetes was present in 41.4% of the subjects. SSI was not found in 172(74.7%) of the 232 subjects. Deep SSI was found in 7 of the total i.e. 3.0% and superficial SSI was found in 53 of the total i.e. 22.8% of the subjects. Among the SSIs 12(20%) of them developed on day 2, 31.7% developed on day 3, 25 (41.7%) developed on day 4.

In the study at pre-operative period, 45.7% had GRBS >200 mg/dl, at Intra-operative period, 47% had GRBS >200 mg/dl and at post op period, 49.6% had GRBS >200 mg/dl. Among those with SSI, 78.3% had Pre-Operative GRBS >200 mg/dl and among those with Diabetes, 71.9% had GRBS >200 mg/dl. Among those with SSI, 80% had Intra Operative GRBS >200 mg/dl and among those with Diabetes, 79.2% had GRBS >200 mg/dl. Among those with SSI, 91.7% had Post-Operative GRBS >200 mg/dl and among those with Diabetes, 92.7% had GRBS >200 mg/dl. 71.4% with deep SSI and 79.2% with superficial SSI had Pre-Operative GRBS >200 mg/dl. 71.4% with deep SSI and 81.1% with superficial SSI had intra operative sugars >200mg/dl. 71.4% with deep SSI and 94.3% with superficial SSI post-operative GRBS >200 mg/dl. Among those who developed SSI 47(78.3%) of the subjects had preoperative sugars, 48 (82%) has intra-operative sugars and 55 (91.7%) had postoperative sugars >200 mg/dl. Among those who had diabetes mellitus 69(71.9%) had preoperative sugars > 200, 76 (79.2%) had intra-operative sugars>200 and 89 (92.7%) had postoperative sugars > 200 mg/dl. A total of 53 subjects developed superficial SSI of which 42(79.2%) had preoperative sugars >200, 43(81.4%) had intra-operative sugars > 200, 50 (94.3%) had postoperative sugars > 200 mg/dl. A total of 7 subjects developed deep SSI. 5 (71.4%) had preoperative sugars >200, 5 (71.4%) had intra-operative sugars > 200 and 5(71.4%) had postoperative sugars >200mg/dl. On Pus culture among those subjects with SSI, most common organism isolated was E coli (33.3%), K Pneumoniare (16.7%). Others included 6.7% proteus, 3.3% gram negative fermenters and 3% pseudomonas.

### Discussion

Peri-operative hyperglycemia is an important marker for adverse events in surgical patients, with and without history of diabetes. Surgery in diabetic patients is known to be associated with

longer hospital stay, increased morbidity and mortality, and postoperative infection. Adverse effects may be worsened in diabetic patients who have acute hyperglycemia compared with those with chronic and sustained hyperglycemia. However, patients with newly diagnosed hyperglycemia have been shown to have higher mortality and lower functional outcome than those with normo-glycemia or with a known history of diabetes.

Among those with SSIs 78.3% had a preoperative GRBS of >200mg/dl, and 71.4% of deep SSIs and 79.2% of superficial SSIs were found to be associated with preoperative GRBS>200mg/dl. 91.7% of all SSIs were associated with intra-operative sugar levels of >200mg/dl (81.1% of superficial SSIs and 71.4% of deep SSIs had GRBS >200mg/dl intra-operatively). The strongest association seems to have been with Postoperative hyperglycemia as 91.7% of all SSIs were found in subjects with postoperative GRBS >200mg/dl. 94.3% of all superficial SSIs and 71.4% of deep SSIs showed a similar correlation with postoperative hyperglycemia (>200mg/dl). All the associations were found to be statistically significant at p value <0.001. There was significant association (p value <0.001) noted between peri-operative hyperglycemia and pre-existing diabetes (Diabetes was found to be present in 71.9%, 79.2% and 92.7% of preoperative, intraoperative and postoperative GRBS>200mg/dl respectively).

**Table 1:** Diabetes and intra operative plasma sugars and SSI

		>200 mg/dl		<200mg/dl	
SSI	Present	48	80%	12	20.0%
	Absent	61	35.5%	111	64.5%
Diabetes	Present	76	79.2%	20	20.8
	Absent	33	24.3%	103	75.7%

**Table 2:** Diabetes and postoperative plasma sugars and SSI

		>200MG/DL		<200MG/DL	
SSI	Present	55	91.7%	5	8.3%
	Absent	60	34.9%	112	65.1%
Diabetes	Present	89	92.7%	7	7.3%
	Absent	26	19.1%	110	80.9%

Thus, our study is indicative of a significant association of surgical site infections with peri-operative hyperglycemia, with the highest correlation with postoperative hyperglycemia. Although >90% of postoperative hyperglycemia was associated with uncontrolled diabetes, it can be seen that ~20-30% of subjects with pre- and intra-operative hyperglycemia were actually non-diabetics and may suggest a contributory role of stress-induced hyperglycemia in development of SSIs. In a study done by Gachabayov M31, Senagore AJ, Abbas SK, Yelika SB, You K, Bergamaschi R. Of 690 patients included, 112 (16.2%) had preexisting DM. Overall SSI rates were significantly higher in DM patients as compared to non-DM patients (28.7 vs. 22.3%, p=0.042). Postoperative hyperglycemia was more frequently seen in non-DM patients (46 vs. 42.9%). The SSI bundle reduced SSI rates (17 vs. 29.3%, p<0.001), but the rate of hyperglycemia remained unchanged for DM or non-DM patients (pre-bundle 59%; post-bundle 62%, p=0.527). Organ/space SSI rates were higher in patients with pre- and postoperative hyperglycemia (12.6%) (p=0.017). In a study done by Ashar Ata32, MBBS, MPH; Julia Lee, BS; Sharon L. Bestle, RN; *et al.* postoperative glucose levels were available for 1561 patients (74.70%), of which 803 (51.4%) were obtained within 12 hours of surgery. The significant univariate predictors of SSI in general surgery patients were increasing age, emergency status, American Society of Anesthesiologists

physical status classes P3 to P5, operative time, more than 2 U of red blood cells transfused, preoperative glucose level higher than 180 mg/dL (to convert to millimoles per liter, multiply by 0.0555), diabetes mellitus, and postoperative hyperglycemia. On multivariate adjustment, increasing age, emergency status, American Society of Anesthesiologists classes P3 to P5, operative time, and diabetes remained significant predictors of SSI for general surgery patients. After adjustment for postoperative glucose level, all these variables ceased to be significant predictors of SSI; only incremental postoperative glucose level remained significant. Subanalysis revealed that a serum glucose level higher than 140 mg/dL was the only significant predictor of SSI (odds ratio, 3.2; 95% confidence interval [CI], 1.4-7.2) for colorectal surgery patients. Postoperative hyperglycemia may be the most important risk factor for SSI. Aggressive early postoperative glycemic control should reduce the incidence of SSI. In a study done by Park C33, Hsu C, Neelakanta G, Nourmand H, Braunfeld M, Wray C, Steadman RH, Hu KQ, Cheng RT, Xia VW. Of 680 patients, 76 (11.2%) experienced postoperative SSIs. Among all intra-operative glucose indices analyzed, severe hyperglycemia (>or= 200 mg/dL) was independently associated with postoperative SSI (odds ratio [OR] 2.25, 95% confidence interval [CI] 1.26-4.03, P=0.006). The limitation of the study was that HbA1c (Glycosylated haemoglobin) was not considered in the study and confounding factors like nutrition, hypoalbuminemia was not considered among study subjects.

## Conclusion

Capillary plasma sugars are a simple and effective way to monitor hyperglycemia for the purpose of administration of insulin, but very few studies have shown the relation between preoperative, intra-operative and postoperative plasma sugars and SSIs. Hence strict control of sugars more so in the postoperative period will decrease the incidence of SSIs and hence the morbidity, cost and hospital stay associated with it.

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