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Incidence and Risk factors of Intraoperative Hyperglycemia in Non-diabetic Patients: A Prospective Observational Study

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ABSTRACT

Introduction: Intraoperative hyperglycemia is recognized as a significant concern, being associated with various complications such as surgical site infection, cardiovascular events, kidney injury, stroke, and even death. These complications can occur in both diabetic and non-diabetic patients. However, previous studies have not fully established the incidence and risk factors of intraoperative hyperglycemia in non-diabetic patients.

Objectives: The primary objective was to find the incidence of intraoperative hyperglycemia in non-diabetic patients. The independent risk factors for intraoperative hyperglycemia and the incidence of surgical site infection in patients with intraoperative hyperglycemia were the secondary outcome.

Methodology: A quantitative prospective observational study was performed after IRC approval. Six hundred five non-diabetic patients above 18 years who underwent intermediate- to high-risk surgery were included in the study. For 18 months capillary blood glucose levels were measured in all patients during surgery. Risk factors and postoperative surgical site infection was noted to identify relation and risk factors of intraoperative hyperglycemia.

Results: Seventy-eight (12.9%) patients developed hyperglycemia during surgery. The independent risk factors for intraoperative hyperglycemia were an ASA status ≥3, preoperative impaired fasting blood sugar (OR 20.27, 95%CI:10.19–37.63, p<0.001, intraoperative hypotension (OR 4.6, 95%CI: 2.36–8.97, p < 0.001), intraoperative blood transfusion (OR 4.45, 95%CI: 1.88–10.56, p < 0.001) and steroid use (OR 2.81, 95%CI: 1.38–5.73, p = 0.003). Surgical site infection was higher in patients with intraoperative hyperglycemia compared with patients without intraoperative hyperglycemia (5 [6.8%] vs. 9 [1.7%], respectively, p = 0.010).

Conclusion: Intraoperative hyperglycemia was observed among non-diabetic patients undergoing intermediate- to high-risk surgeries. Patients with risk factors for intraoperative hyperglycemia should undergo close monitoring of their blood glucose levels.

INTRODUCTION

Intraoperative hyperglycemia is associated with multiple complications such as postoperative surgical site infection, myocardial infarction, kidney injury, stroke and death.[1,2] Surgery and anesthesia cause a neuroendocrine stress response with release of counterregulatory hormones. These neurohormonal changes result in metabolic abnormalities including insulin resistance, decreased peripheral glucose utilization, impaired insulin secretion, increased lipolysis, and protein catabolism, leading to hyperglycemia.[3] Based on the above fact the risk of intraoperative hyperglycemia has been shown in both patients with and without diabetes. A direct correlation exists between blood glucose levels and the occurrence of complications.[4]

Reported incidence rates of intraoperative hyperglycemia in non-diabetic patients have varied, with some studies indicating rates as low as around 6%,while others report higher incidences.[4-9]

Patients with hyperglycemia who were treated with insulin exhibited an equivalent risk of adverse events compared to those with normal blood glucose levels.[10]Hence, managing hyperglycemia with insulin is critical for reducing intraoperative complications.

In addition, Perioperative hyperglycemia was identified as an independent risk factor for SSI when evaluated at the end of surgery and 12 hours after surgery.[7]However, compared with diabetic patients, non-diabetic patients were less likely to receive treatment with insulin for the same blood glucose level because the incidence of intraoperative hyperglycemia is underestimated and blood glucose level is not routinely obtained in non- diabetic patients. This study aimed to demonstrate the incidence of intraoperative hyperglycemia, find out the independent risk factors for intraoperative hyperglycemia in non-diabetic patients and to find out the incidence of surgical site infection in patients with intraoperative hyperglycemia.

METHODOLOGY

This was the prospective observational study conducted in the operation theater of the tertiary care hospital in the eastern part of Nepal. We choose consecutive sampling method to include study participants. After ethical approval was obtained from the institutional ethical board and after written informed consent, adult patients over 18 years of age who would be receiving general anesthesia for an intermediate- to high-risk surgery were enrolled in the study. Exclusion criteria were diabetic patients and patients with the history of high or abnormal blood sugar level. All the patients underwent standard general anesthesia procedures. All cases were monitored with standard basic monitor including automatic non-invasive blood pressure monitoring, electrocardiography and pulse oximetry. Depending upon the procedure and attending anesthesiologist the decision to perform invasive blood pressure and central venous pressure monitoring was made. Preoperative HbA1C values or fasting blood sugar (FBS) levels was reviewed to rule out preexisting undiagnosed diabetes mellitus (FBS ≥ 126 mg/dL or HbA1C ≥ 6.5%). Capillary blood glucose level information was collected after induction of anesthesia and at the end of surgery. The frequency of obtaining capillary blood glucose levels can be adjusted based on the preference of the attending anesthesiologist. Capillary blood samples were collected from the patient's fingertip. The glucose concentration was determined in fresh capillary blood by reflectance photometry using an Accu-Chek Inform II system (Roche, United States). The highest blood glucose level was recorded for the analysis. Hyperglycemia was defined as a blood glucose level of more than 180 mg/dL. Data including age, sex, body mass index, co-morbidities, preoperative FBS, American Society of Anesthesiologists (ASA) physical status, and HbA1C levels, intraoperative fluid, blood loss, vital signs, body temperature, steroid use(dexamethasone, hydrocortisone or methylprednisolone), and blood transfusion was recorded. Hypothermia was defined as a body temperature of less than 36 °C at least one time during surgery. Intraoperative hypotension was defined as having a mean arterial pressure of less than 65 mmHg at least one time during surgery. Impaired FBS was defined as glucose level

of 100–125 mg/dL. The patients were followed-up for 30 days following surgery to identify the incidence of surgical site infection (SSI). The primary outcome was the incidence of intraoperative hyperglycemia in non-diabetic patients. The independent risk factors for intraoperative hyperglycemia in diabetic patients and the incidence of surgical site infection in patients with intraoperative hyperglycemia were the secondary outcome.

All the required demographics and in hospital information were recorded in the Performa. Data were entered in Microsoft excel and statistically analyzed by using statistical package for the social sciences (SPSS) software version 20.0(SPSS Ltd, Chicago, IL, USA). Categorical data were presented as percentage and frequency while continuous data were presented as mean and standard deviation. Chi Square test was used for statistical analysis. A two-sided P value <0.05 was considered statistically significant

RESULTS

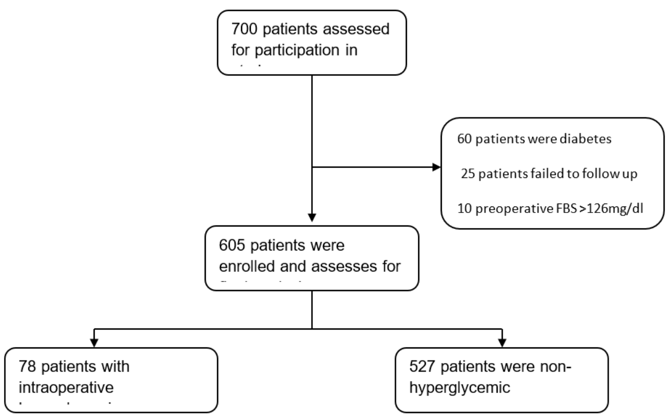

Fig 1: Flow chart of patient's selection

A total of 700 patients who were planned to underwent general anesthesia for an intermediate- to high-risk surgery were assessed, out of which, 95 patients were not included in the study due to various reason as mentioned in Figure1.In this study 605 patients were enrolled and included for final analysis for the development of intraoperative hyperglycemia and were followed up for 30 days in outpatient department to find out whether surgical site infection has occurred or not.

Demographic data and characteristics of the patients are shown in Table 1. Out of the 605 patients 355 were female while 250 were male patients. Patients age of eighteen years and above were included in the study. The youngest of those were thirty-nine while the oldest was sixty-nine years old. The mean age was 54.9 years with a standard deviation of 7.9. The average BMI of the patients was 24.01±2.23 kg/m^2. Most of the patients (69.3%) were of ASA physical status II , 24.6 % of patients had an ASA physical status ≥ III and remaining 5.78% were of ASA status I .

Table 1: Demographic of patients

Variables	Values
Age (years), mean±SD	54.9±7.9
Male sex, n (%)	250 (41.3)
Female sex, n (%)	355 (58.7)
BMI (kg/m^2), mean±SD	24.01±2.23
ASA status II, n (%)	421 (69.6)
ASA status III, n (%)	149 (24.6)
ASA status I, n (%)	35 (5.78)
Comorbidities, n (%)	
Hypertension	159 (26.3)
Coronary artery disease	18 (3)
Chronic kidney disease	3 (0.5)
Cerebrovascular accident	22 (3.6)
Cirrhosis	1 (0.2)
Malignancy	22 (3.6)
Chronic obstructive pulmonary disease	39 (6.4)
Emergency surgery	51 (8.4)

ASA (American Society of Anesthesiologists), BMI (Body mass index), FBS (Fasting blood sugar), ,(SD) Standard deviation

In this study the incidence of hyperglycemia was found in 78 patients(12.9%). The patients were divided into two groups, hyperglycemic group (n=78 cases) and non-hyperglycemic group (n=527 cases) Table 2. . Physical status of ASA ≥III had significant higher intraoperative hyperglycemia (p <0.001) compared to physical status ASA grade I and III. Patients with preoperative impaired FBS (OR 20.2, 95%CI: 10.19–37.63, p < 0.001), intraoperative hypotension (OR 4.6, 95%CI: 2.36–8.97, p < 0.001), intraoperative blood transfusion (OR 4.45, 95%CI: 1.88–10.56, p < 0.001), crystalloid usage >2 liters (OR 2.51,95%CI: 1.54 – 4.1, p<0.001) and steroid use (OR 2.81, 95%CI: 1.38–5.73, p = 0.003) were the independent risk factor for intraoperative hyperglycemiaTable2.

The surgical site infection at 30 days after surgery was higher in patients with intraoperative hyperglycemia than in patients without intraoperative hyperglycemia [6.4% vs. 1.7%, OR 3.94 (95% CI: 1.28–12.08), p = 0.010] figure 2.

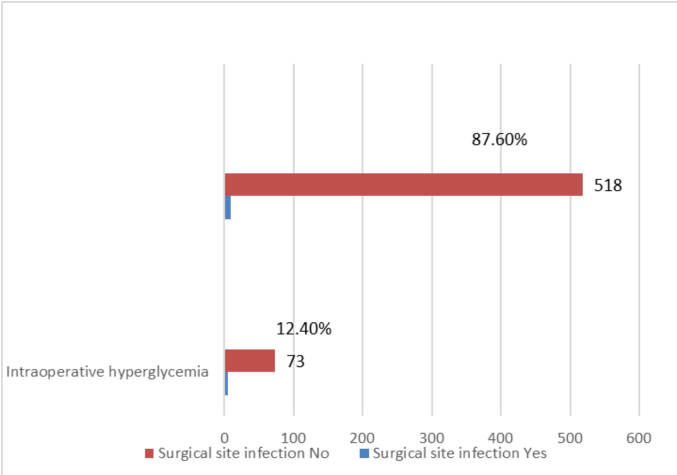

Fig 2: Surgical site infection and intraoperative hyperglycemia

Table 2: Analysis of comorbidities and intraoperative hyperglycemia

Comorbidities (n, %)	Hyperglycemic group (n=78)	Non-hyperglycemia group (n=527)	OR (95% CI)	p value
Chronic-obstructive pulmonary disease	8 (10.25)	31 (5.88)	1.83(0.81-4.14)	0.142
Malignancy	8 (10.25)	14 (2.65)	4.19(1.7-10.34)	0.001
Cirrhosis	1 (1.2)	0 (0)		
Cerebrovascular accident	9 (11.53)	13 (2.46)	5.16(2.13-12.51)	<0.001
Chronic kidney disease	1 (1.2)	2 (0.37)	3.41 (0.31-38.05)	0.29
Coronary artery disease	10 (12.82)	8 (1.51)	9.54 (3.64-25)	<0.001
Hypertension	45 (57.69)	114 (21.63)	4.94 (3.01-8.1)	<0.001
Pre-operative impaired blood sugar	64(82.05)	97 (18.40)	20.27 (10.19-37.63)	<0.001

Table 3 : Analysis of intraoperative events and hyperglycemia

Intraoperative events,n (%)	Hyperglycemic group (n=78)	Non-hyperglycemia group (n=527)	OR (95% CI)	p value
Intraoperative dextrose given	12 (15.38)	75 (3.95)	1.1 (0.57-2.12)	0.786
Crystalloid >2 liters	48 (61.53)	205 (38.89)	2.51 (1.54-4.1)	<0.001
Blood transfusion	9 (11.53)	15 (2.84)	4.45 (1.88-10.56)	<0.001
Duration of anesthesia >3 hours	6 (7.69)	20 (3.79)	2.11 (0.82-5.44)	0.113
Intraoperative hypotension	16 (20.51)	28 (5.31)	4.6 (2.36-8.97)	<0.001
Hypothermia	4 (5.12)	14 (2.65)	1.98 (0.65-6.18)	0.23
Steroid use	12 (15.38)	32 (6.07)	2.81(1.38-5.73)	0.003
Emergency surgery	16 (20.51)	35 (6.64)	3.63 (1.9-6.93)	<0.001
Surgical site infection	5 (3.9)	9 (1.70)	3.94 (1.28-12.08)	0.010

Table 4: Types of Surgery

Type of surgery	Hyperglycemia (N=78)	Non-hyperglycemia (N=527)	p-value
Abdominal Surgery	47(60.26%)	313(59.39%)	0.885
Urologocal Surgery	4(5.13%)	20(3.8%)	0.573
Neurosurgery	4(5.13%)	38(7.21%)	0.499
ENT Surgery	9(11.54%)	86(16.32%)	0.279
Obstetric and Gynecological Surgery	12(15.38%)	60(11.39%)	0.309
Orthopedic Surgery	2(2.56%)	10(1.9%)	0.694

DISCUSSION

In this study, the incidence of intraoperative hyperglycemia was found in non-diabetic patients undergoing intermediate to high-risk surgery under general anesthesia. Patient with physical status ASA ≥ 3, pre operative impaired fasting blood sugar and in patient where there was intraoperative use of steroid, blood transfusion, and crystalloid fluid more than 2 liters have shown higher proportion of intraoperative hyperglycemia. The risk of surgical site infection increased with the occurrence of intraoperative hyperglycemia.

We found that the incidence of intraoperative hyperglycemia was 12.9% in non-nondiabetic patients undergoing surgery.In the previous study conducted by S Varunya et al and P Chananya et al, incidence of intraoperative hyperglycemia was 14.7% and 16% which result was similar to our study.[9,6] In contrary previous studies conductedby G.Navendu et al, F Claudio et al andM. Gachabayo et al showed incidence of hyperglycemia ranging from 30 % to 50% which is higher than the current study.[11-13] There is less incidence of hyperglycemia in this study compared to the previous studies which might be due to less invasive surgical techniques in current practice.The variability in the results has also been found on the study conducted by Han et al. who reported an incidence of 35.5% of intraoperative hyperglycemia during liver resection, whereas incidence of 20% was reported by Bhattacharjee et al. in patient undergoing neurosurgery for traumatic brain injury.[7-8]More frequent monitoring of intraoperative blood sugar in non-diabetic patient is necessary as there is report of higher odds of adverse events occurring in hyperglycemic non-diabetic patients than those with hyperglycemic diabetes patients.[4]Previous studies conducted by De Vries et al. and Mansur et al. propose that keeping the blood glucose level less than 150mg/dl during the intraoperative period could reduce the intraoperative adverse effect and surgical site infection. While the risk of hypoglycemia was higher, no severe adverse events related to hypoglycemia were reported.[14] Kotagal et al. demonstrated that among non-diabetesmellitus patients, there was a dose-response relationship between the level of blood glucose and composite adverse (OR, 1.3 for blood glucose 125–180 mg/dL, 95% CI, 1.1–1.5; OR, 1.6 for blood glucose 180 mg/dL, 95% CI, 1.3–2.1).On the contrary, diabetic patients with hyperglycemia did not exhibit an elevated risk of adverse events, even among those with a blood glucose level of 180 or more (OR, 0.8; 95% CI, 0.6–1.0). Based on these findings, increased monitoring and treatment of intraoperative blood glucose in non-diabetic patients are warranted.[4]

In this study we found intraoperative hyperglycemia was significantly higher in patients who had preoperative impaired fasting blood sugar which was similar to the result of the study conducted by V Sermkasemsinet et al.[9] Biker et al. in his analysis revealed that patients with impaired fasting blood sugar who underwent major surgery had had 2.1 fold increased risk of perioperative cardiovascular compared with those with normal fasting blood sugar.[16] Similarly , E Z Fisman et al. and Davies et al. found patients had more major adverse events (i.e., death, myocardial infarction, or stroke) who underwent carotid artery stenting in comparison to those without FBS impairment.[17] The increased incidence of intraoperative cardiovascular events might be due to increased intraoperative hyperglycemia as suggested from our study finding. Future investigations should explore the necessity of delaying elective surgery until preoperative blood glucose levels are adequately managed.

This study showed a significant association between the steroid use and intraoperative hyperglycemia which was similar to the study conducted by, V Sermkasemsinet et al, Murphy GS et al.and Herbst RA et al.[9,19-20] In the previous studied it was found that though dexamethasone was associated with hyperglycemia but there was no increased incidence of postoperative surgical site infection.[21-22]

Our study showed the risk factor for intraoperative hyperglycemia was physical stats ASA ≥ III, intraoperative hypotension, blood transfusion, crystalloid fluid more than 2 liters and emergency surgery all were associated with increased blood glucose level intraoperatively. Similar finding was reported in the study conducted by V Sermkasemsinet et al and T. Vasanti et al. where blood administration, surgery duration, amount of intravenous fluids was significantly associated with increased blood sugar perioperatively.[9,23]

Nondiabetic hyperglycemia commonly arises following a traumatic or stressful event experienced by the body. Stress hyperglycemia is usually defined as hyperglycemia resolving spontaneously after dissipation of acute illness. The term generally refers to patients without known diabetes, although patients with diabetes might also develop stress hyperglycemia. However, the development of stress hyperglycemia is caused by a highly complex interplay of counter-regulatory hormones such as catecholamines, growth hormone, cortisol, and cytokines.[24] M. Souvik et al. also reported stress induced-hyperglycemic response in non-diabetic population undergoing major non-cardiac.[25]

In this study surgical site infection was higher in the hyperglycemic group of patients compared to non-hyperglycemic group. Our study findings were comparable to the study conducted by S Varunya et al. who concluded that the surgical site infection at 30 days after surgery was higher in patients with intraoperative hyperglycemia than in patients without intraoperative hyperglycemia [4 (6.1%) vs. 6 (1.6%), OR 4.03 (95% CI 1.10–14.70), p = 0.035].[9]This was supported by the finding of the study by G.C. Bellusse et al. concluded that perioperative hyperglycemia was identified as an independent risk factor for SSI and regarding the severity of hyperglycemia, there was a dose response effect; that is, as the exposure increased, so did the risk of SSI.[2]Based on the findings of this study, it is recommended that blood glucose levels be closely monitored in non-diabetic patients undergoing intermediate- to high-risk surgeries, particularly in cases where patients exhibit risk factors. Some of these factors are modifiable, indicating that intraoperative hyperglycemia can be prevented in many instances.

CONCLUSION

A significant incidence of intraoperative hyperglycemia was observed among non-diabetic patients undergoing intermediate- to high-risk surgeries. Since there is a significant association between the risk factor and intraoperative hyperglycemia, patients with risk factors should undergo close monitoring of their blood glucose levels.

LIMITATION OF THE STUDY

This is a single center-based study with moderate sample size and involvement of multiple centers with more patients would have improved the statistical power of the study. The other limitation of this study was the hemodynamic changes were not measured simultaneously with blood glucose level as surgical stress responses. The interval of capillary blood glucose (CBG) measurement among the study populations was not constant; it can vary depending on the duration of surgery.

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CONFLICTS OF INTEREST None

FINANCIAL DISCLOSURE None

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