

## Original Research Article

# Perioperative management of hyperglycemic patients undergoing surgery: an observational cross sectional study in a tertiary care hospital

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**Received:** 12 February 2024

**Revised:** 04 June 2024

**Accepted:** 04 July 2024

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## ABSTRACT

**Background:** Diabetes poses an additional risk during anesthesia, yet there is a lack of sufficient Indian data on perioperative antidiabetic drug use and its implications. This drove us to conduct the study.

**Methods:** Cross-sectional, observational study, conducted in a tertiary care hospital's general surgery and orthopaedics wards. Data collected from the first anaesthetist visit to 24 hours postoperative period included antidiabetic medications, anesthesia drugs, blood sugar levels, co-morbidities, concomitant medications, and intravenous (IV) fluids. Descriptive statistics and parametric tests were used for analysis.

**Results:** The study comprised 180 patients (62.8% males, median age 56 years), with diabetes duration predominantly between 1-5 years (28.3%). Preoperatively, metformin was the most prescribed oral hypoglycemic agent (72.2%), decreasing to 56.67% postoperatively. Intraoperatively, only 1.6% received insulin, while 98.4% received no drugs. Common postoperative antidiabetic agents included insulin BD (n=48). General surgery (73.3%) and orthopedics (26.7%) contributed 132 and 48 patients, respectively, with spinal anesthesia (68.3%) and bupivacaine (75.4%) being most prevalent. Blood glucose during surgery was effectively monitored. Hypertension (52.8%) was the most common co-morbidity, and Ringer lactate (60.8%) was the predominant IV fluid.

**Conclusions:** Adequate perioperative antidiabetic management was observed in hyperglycemic patients.

**Keywords:** Corticosteroids, Intravenous fluids, Blood sugar control, Anaesthesia, Diabetes

## INTRODUCTION

Diabetes mellitus (DM) is a global health concern affecting approximately 6.28% of the world's population, with an estimated 462 million individuals diagnosed with type 2 diabetes.<sup>1</sup> In India, a significant percentage of the population, particularly among urban and rural senior citizens, grapples with this metabolic disorder.<sup>2</sup> DM encompasses a spectrum of metabolic disorders diagnosed through criteria such as deranged glycosylated hemoglobin (HbA1c), fasting blood glucose, and postprandial blood glucose levels. The resultant hyperglycemia can manifest in acute symptoms like

hyperosmolar hyperglycemic state (HHS) or chronic complications such as retinopathy, neuropathy, nephropathy, and cardiovascular diseases.<sup>3</sup>

Patients with diabetes often face various stressors throughout their lives, including infection, trauma, surgery, and work-related stress.<sup>4</sup> Surgical interventions, in particular, require careful blood glucose management to prevent complications. This involves a complex interplay of pre-anesthetic medications, anesthetic drugs, skeletal muscle relaxants, and insulin administration. The potential drug-drug interactions between anti-diabetic medications, pre-anesthetic drugs, and anesthetics raises

concerns, especially considering the added risk of hypertension during anesthesia.

The management of diabetes during stressful situations like surgery lacks standardized treatment protocols or guidelines in India. Different theories exist regarding the continuation or discontinuation of anti-diabetic medications before surgery, and the literature provides no definitive answers. Consequently, there is a notable absence of Indian guidelines specifying which antidiabetic drugs or insulin preparations are preferred, their doses, duration of use, and the potential risks associated with their continuation or discontinuation perioperatively.

To address these gaps, this observational study was conducted in a tertiary care hospital. It aimed to evaluate the management of hyperglycemic patients undergoing surgery, focusing on antidiabetic drug use, co-medications, complications, and adverse effects.

## METHODS

The cross-sectional, observational study received approval from the institutional ethics committee (IEC) of Seth GS medical college and KEM hospital (EC/45/2019). Permission was obtained from the respective in-charges of orthopaedics and general surgery wards for conducting the study. Inclusion criteria encompassed individuals of either gender within the age range of 18 to 75 years undergoing surgery in the general surgery and orthopaedics ward. Patients with known diabetes or hyperglycemia who underwent non-cardiac elective or emergency surgery during the study period were eligible for inclusion. Exclusion criteria were applied to pregnant women, individuals with complicated diabetic conditions such as ketoacidosis or hyperosmolar coma, and those deemed ineligible by the principal investigator. Each participant provided written consent for their involvement.

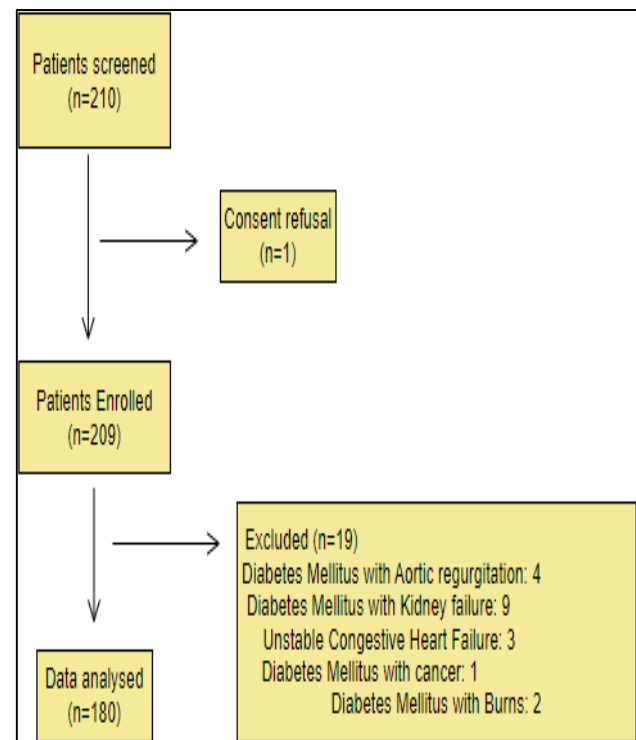
Demographic details, including initials, age, gender, in-patient department (IPD) number, date of admission, address, and contact information, were documented in the case record form. Patient files were meticulously examined to gather information on the history, duration, and treatment of diabetes. The time required to control blood sugar levels and any instances of surgery delay or postponement due to uncontrolled hyperglycemia were noted.

An analysis of patient notes on the day of surgery by anesthetists and surgeons provided valuable insights into anesthesia risk (ASA grades), type of surgery, pre-anesthetic medications administered, anesthesia type, intraoperative blood sugar levels, total fluids administered, duration of surgery, anesthesia used, and any adverse events during the perioperative period. Data collection spanned from the patient's initial visit by an anesthetist up to 24 hours postoperative, with a specific

focus on intraoperative and postoperative blood glucose levels. Upon the completion of the data collection period, all information from the case record forms was systematically entered into an MS excel Master-chart for analysis. Descriptive statistics, chi-square tests for categorical variables, parametric tests, and Pearson correlation were employed using IBM SPSS statistics software version 26. A significance level of  $p < 0.05$  was established to determine statistical significance.

## RESULTS

All participants in this study provided written consent, ensuring ethical compliance. The research trajectory is visually represented in Figure 1, providing a clear depiction of the study's progression. This study aimed to scrutinize the prescription practices concerning drugs for hyperglycemic patients, exploring any observed changes. The focus extended to identifying the most prevalent comorbid condition and the corresponding treatment drugs. Additionally, the study investigated the common intravenous fluids (IV) used in this perioperative setting. Furthermore, it assessed the impact of corticosteroids, beta-blockers, and thiazides on blood glucose control during the perioperative period. In total, 875 drugs were prescribed for the 180 patients, with 639 of them being antidiabetic medications.



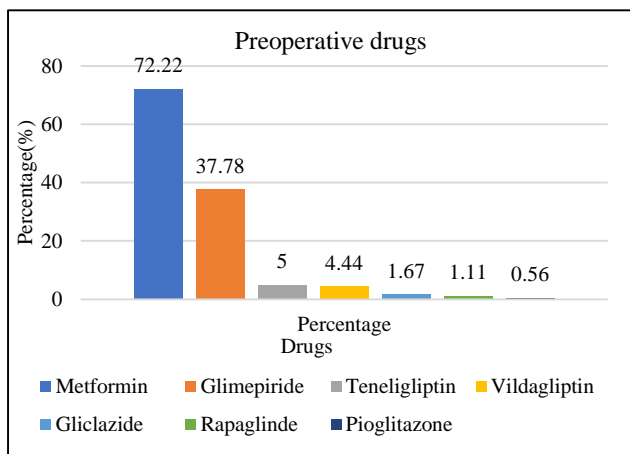
**Figure 1: Flow chart of patient recruitment.**

Table 1 elucidates the prescribing indicators, providing insights into the nuances of drug prescriptions. These indicators offer a comprehensive understanding of prescription patterns for hyperglycemic patients undergoing surgery.

**Table 1: Prescribing indicators.**

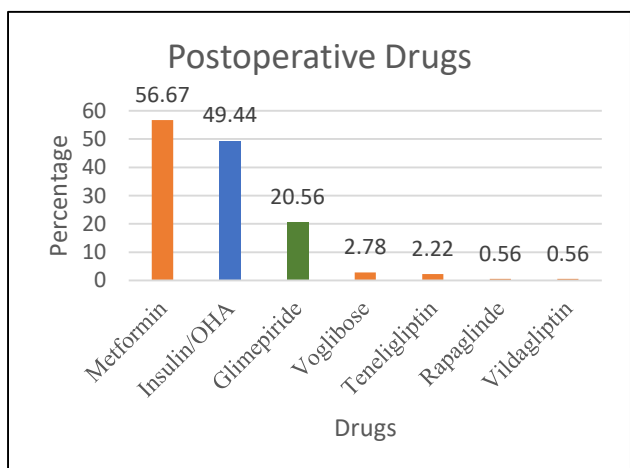
Prescribing indicators	N
Total number of prescriptions	180
Total number of drugs	875
Number of drugs per prescription	6.23±0.54
Total number of anti diabetic drugs	639
Number of anti-diabetic drugs per prescription	3.55±0.91
Total number of antidiabetics drugs as FDCs	93
Total number of adjuvants	236

Among the 180 patients enrolled in the study, 113 were male, constituting 62.8% of the participants, while 67 were female, representing 37.2% of the total. The analysis revealed that a significant majority of the study participants had a diabetes duration ranging from 1 to 5 years (Table 2).



**Figure 2: Pre-operative drugs prescribed.**

After surgery, the most frequently prescribed medications were metformin (56.67%), followed by a combination of insulin with oral hypoglycemic agents (49.44%), and glimepiride (20.56%), as illustrated in Figure 3.



**Figure 3: Postoperative drugs prescribed.**

The study comprised 180 patients undergoing surgical procedures, with 25% scheduled for elective surgery and 75% for emergency cases. General surgery accounted for 73.3% of patients, while orthopedics represented 26.7%. Notably, below knee amputation (36.11%) was prevalent in general surgery, while orthopedics commonly performed bipolar hemiarthroplasty (6.11%).

A significant portion of patients (133) belonged to ASA grade 2, and spinal anesthesia (68.3%) was the predominant mode of induction, followed by general anesthesia (23.3%). Bupivacaine was the preferred anesthetic in 136 cases, with fentanyl being the second most commonly prescribed in 73 cases. Anti-emetics were commonly used in 176 cases as adjuvants.

Blood sugar monitoring in hyperglycemic patients was tailored based on surgery duration, with a majority (110) falling within the 2-4 hours range. Surgery delay exceeding 10 days occurred in 24 cases, primarily due to uncontrolled blood sugar levels.

The most prevalent comorbid condition was hypertension (97 cases), followed by ischemic heart disease, stroke, hypothyroidism, epilepsy, chronic kidney disease, depression, cataract, right bundle branch block, and asthma. Amlodipine (30.56%) was the most prescribed antihypertensive, succeeded by telmisartan (16.11%), metoprolol (3.33%), atenolol (2.78%), and ramipril (1.67%).

Prescriptions involving thiazides, steroids, or beta-blockers numbered 26, with beta-blockers administered to 15 patients and steroids to 11. Ringer Lactate (60.8%) emerged as the preferred intravenous fluid.

Statistical analyses revealed no significant associations between postoperative blood sugar levels and age, gender, steroid or beta-blocker medication, and antidiabetic drug use. However, significant associations were identified with the type of surgery, intravenous fluids administered, and surgery duration. Additionally, a significant association was found between preoperative blood sugar levels and the type of antidiabetic drugs used.

Postoperative blood sugar levels were assessed in correlation with age, fluids given, and duration of diabetes. The analysis showed no statistical significance for correlation between age, fluids given, and duration of diabetes with postoperative blood glucose ( $r=0.062$ ,  $p>0.05$ ) by Pearson correlation analysis.

## DISCUSSION

The study revealed that the majority of patients undergoing surgical procedures were aged over 50, with a mean age of  $54.38 \pm 8.33$ . This observation aligns with the common occurrence of morbidity in the middle-age group, often associated with occupational stress and responsibilities, as well as unforeseen accidents.<sup>5</sup>

Consistent with findings from the Chen et al diabetes was more prevalent in the middle-age patients. Gender distribution indicated that more male patients with diabetes underwent surgery, consistent with data from the tertiary care hospital's 2020 annual report.<sup>6</sup> Nordstrom et al study in 2016 reported a prevalence of 14.6% for type 2 diabetes in men and 9.1% in women.<sup>7</sup>

The majority of patients in the study had chronic diabetes and were under treatment, emphasizing the importance of controlling hyperglycemia during surgery to enhance surgical outcomes. The study identified comorbid conditions, with hypertension (n=97) being the most prevalent. Vascular pathologies such as ischemic heart disease, chronic kidney disease, and stroke were commonly associated with diabetes, while unrelated conditions included cataract and asthma. Comparisons between diabetes with and without hypertension revealed higher rates of cardiovascular death, myocardial infarction, angina pectoris, amputation, and stroke in patients with both conditions, independent of other risk factors.<sup>8</sup>

Among the 180 patients, 112 had hypertension, and 98 were on antihypertensive therapy. Amlodipine emerged as the most frequently prescribed antihypertensive (30.56%), followed by telmisartan, metoprolol, and ramipril.<sup>9</sup> These findings highlight the prevalence of cardiovascular comorbidities in the studied population, emphasizing the importance of managing these conditions in the perioperative period.

The study involved a total of 180 patients, with 132 recruited from the general surgery ward and 48 from the orthopedics ward. The most common surgeries in general surgery were below-knee amputation and wound debridement, primarily addressing diabetic patients presenting with macrovascular complications and atherosclerosis, resulting in lower limb gangrene and non-healing ulcers. These findings were consistent with a study by Jackson et al which identified 247 diabetic patients undergoing similar procedures.<sup>10</sup>

In orthopedics, the predominant surgery was bipolar hemiarthroplasty, with a focus on emergency cases during the COVID pandemic when elective surgeries were restricted. Of the 180 patients, three exhibited stress hyperglycemia according to ADA guidelines, while the remainder had type 2 diabetes and were effectively managed with anti-diabetic medications. The study reflected the commonality of type 2 diabetes, mirroring the broader epidemiological trend.

The prescription analysis revealed that the total number of drugs across preoperative, operative, and postoperative periods was 875, averaging six drugs per prescription. The majority of prescriptions included antidiabetic medications (four per prescription), with a total of 93 fixed-dose combinations (FDCs) and 236 adjuvants. This aligns with findings from a study by Scheuer et al.<sup>11</sup>

Preoperatively, metformin was the most commonly prescribed antidiabetic, followed by glimepiride and insulin. The prevalent FDC consisted of metformin with glimepiride. The study indicated that 72.22% of patients received oral hypoglycemic agents as monotherapy, with metformin and glimepiride being the most common combination. However, 60.66% of patients prescribed 1-2 anti-diabetic medications exhibited uncontrolled blood sugar levels.

The study also addressed delays in surgery, with 47 cases reported. These delays, particularly during the COVID pandemic, were attributed to complications requiring general anesthesia and ventilator support, which were often unavailable. Intraoperatively, insulin was administered to three patients, and hourly glucose monitoring was conducted in all three.

Considering the duration of surgery, 110 (61.1%) of surgeries fell within the 2-4 hour range, with additional categories for shorter and longer durations. <2 hours 65 (36.1%) and >4 hours duration was 5 (2.8%) respectively for surgeries lasting over 4 hours, only 3 out of 5 were monitored hourly and managed with IV insulin infusion, highlighting the importance of tailored intraoperative management based on anticipated hemodynamic changes, fluid shifts, and operative times). In a retrospective study of 409 patients undergoing cardiac surgery, Ghandi et al reported that for each incremental change in intraoperative BG by 20 mg/dl above 100 mg/dl, there was a 30% increase in occurrence of adverse events including pulmonary and renal complications and death.<sup>12</sup>

In the postoperative period, metformin was the most frequently prescribed antidiabetic medication (56.67%), followed by glimepiride (20.56%) and teneligliptin (2.2%). Among patients, 31.6% received oral hypoglycemic agents as monotherapy, 49.44% received insulin with oral hypoglycemic agents (OHAs) in combination therapy, and 18.96% were on a combination of OHAs. Notably, 64.5% of patients prescribed 1-2 antidiabetic medications exhibited uncontrolled blood sugar levels.

The drugs prescribed in preoperative period was continued later in post operative period in 1/3<sup>rd</sup> of the patients, and others were started on insulin or in combinations. Postoperatively, there was a decrease in oral antidiabetic use, likely influenced by increased sugar consumption during the hypermetabolic stage and reduced calorie intake due to factors like fasting, stress, surgery, or medication-induced vomiting. Insulin usage increased, especially in major surgeries where general anesthesia was employed, leading to higher sugar intake. According to a study conducted (Setji et al) patients that have required IV insulin infusions can be transitioned to subcutaneous insulin once infusion rates if stable and sugars are controlled, particularly if a diet has been initiated.<sup>13</sup>

The study indicated that surgeries were commonly performed on patients classified as ASA grade 2, although 50 patients fell under grades 3 and 4, typically associated with higher risk and emergency surgeries. Spinal anesthesia was prevalent (n=123), particularly in limb surgeries, followed by general anesthesia in 48 patients, spinal + epidural, and regional block in seven patients each. Bupivacaine was the most commonly prescribed anesthetic agent, along with fentanyl, propofol, and lignocaine. To date, there is no proof that any anaesthetic agent is associated with better outcome in diabetic patients. There were no significant perioperative adverse events noted as seen in Cheisson study.<sup>14</sup>

Adjuvants commonly prescribed in the perioperative setting were antiemetics, aiming for smooth surgery conduct, symptomatic relief, or reducing anesthetic agent doses. Beta-blockers, primarily metoprolol followed by atenolol, were prescribed to 15 patients with comorbidities such as hypertension and ischemic heart disease. Beta-blockers were associated with potential deterioration of metabolic control in diabetes. According to a study conducted (Dindic et al) patients were divided into two groups, 1<sup>st</sup> group received beta blocker (Metoprolol/carvedilol) and second did not receive beta blocker with both being on insulin glargine. It was confirmed that the group of patients to which beta-blockers had been administered had statistically higher values of glycaemia and glycosylated haemoglobin. This indicates that the application of beta-blockers deteriorates glycoregulation, thus increasing the possibility of early manifestation of complications caused by diabetes.<sup>15</sup>

Corticosteroids, mainly hydrocortisone, were administered to 11 patients, primarily during intraoperative periods, and most commonly to those with asthma as a comorbidity. Glucocorticoids increase the risk of infection due to persistent hyperglycemia, which has a deleterious effect on patients' prognosis. Moreover, the control of transient hyperglycemia in similar situations during hospitalization has been associated with decreased mortality and complication rates.<sup>16</sup> Thus it is of importance to manage glucocorticoid-induced hyperglycemia due to its prevalence and impact on patient prognosis.

All 180 patients received intraoperative IV fluids, with Ringer lactate being the most common, followed by normal saline, and a combination of both. Ringer Lactate was preferred for controlled patients, while normal saline was chosen for uncontrolled patients to avoid the conversion of lactate into acetoacetic acid, potentially leading to ketoacidosis. In India only three types of IV fluid are available, only dextrose is not preferred as it increases the blood glucose levels in diabetics.<sup>17</sup>

Statistical analysis using the chi-square test indicated a non-significant association between postoperative blood sugar levels and age, gender, intake of steroid or beta-blocker medications, and antidiabetic drug use. However,

significant associations were found with the type of surgery, IV fluids administered, and the duration of surgery. Similarly, a significant association was observed between preoperative blood sugar levels and the type of antidiabetic drugs used.

The Pearson correlation analysis revealed no statistically significant correlation between age, fluids given, and the duration of diabetes with postoperative blood glucose levels ( $r=0.062$ ,  $p>0.05$ ). The absence of correlation between age and duration of diabetes might be attributed to the small sample size, which was impacted by the constraints imposed by the COVID-19 pandemic.

Several limitations of the study need to be acknowledged. The cross-sectional design allowed for only a single check of patient data, making it challenging to assess prior and subsequent sugar control and drug utilization. Additionally, the study faced difficulties in achieving an adequate sample size due to the limitations imposed by the COVID-19 pandemic. The representation of data was not consistent across surgical units, restricting the generalizability of the findings to a tertiary care setting.

## CONCLUSION

The study observed a satisfactory pattern of prescribed antidiabetic agents for hyperglycemic patients undergoing surgery. The perioperative stages showed hyperglycemia, which was managed cautiously to avoid the risk of hypoglycemia. The use of other anesthetic drugs was deemed appropriate, with a predominant preference for spinal anesthesia during surgeries. Patients with uncontrolled blood glucose levels received Normal saline. Perioperative blood glucose levels were monitored in adherence to guidelines. While there was minimal patient optimization before surgery, the adherence to perioperative management guidelines by the anesthetists demonstrated no deviations, and no adverse events were noted during the perioperative period.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee*

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**Cite this article as:** Sayed NA, Shetty Y, Salgaonkar S. Perioperative management of hyperglycemic patients undergoing surgery: an observational cross sectional study in a tertiary care hospital. *Int J Clin Trials* 2024;11(3):182-7.