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The Role of Admission Hyperglycaemia as a Risk Factor for Surgical Site Infection in Orthopaedic Trauma Patients

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Abstract: Introduction: Acute hyperglycemia following traumatic injury is common. Studies have shown that 20- 30% of trauma patients present following injury with blood glucose values $\geq 200 \text{ mg/dL}$, and that a majority of patients demonstrate values \geq 150 mg/dL. The relationship between hyperglycemia and adverse outcomes, such as infectious complications, has been well described in the surgical literature. Post-traumatic hyperglycemia is less well-documented in orthopaedic trauma patients. Aim of the Study: The aim of this study was to evaluate the role of admission hyperglycaemia as a risk factor for surgical site infection in orthopaedic trauma patients. Methods: This was a retrospective observational study and was conducted in the Department of Orthopaedics Surgery of Brahmanbaria medical college Hospital, Brahmanbaria, Bangladesh during the period from October, 2020 to October, 2022. We included 130 patients who were admitted to orthopaedics surgery department. Result: Majority of our patients (41.54%) were aged 41-50 years and 65% patients were male compared to female (35%). The mean age was 45.69 ± 22.83 years. Majority (41.54%) of our patients had a preoperative American Society of Anesthesiologists (ASA) classification of II. Majority of patients 36.15% had type 1 open fracture. We found 45 patients with surgical site infection. Admission glucose more than 200 mg/dL was found higher (26.67%) in infected group. Among the hyperglycemic patients 36.36% were classified as ASA III & the surgical site infection for 30 days was found 54.55%. Conclusion: We found that orthopaedic trauma patients without a history of diabetes showed a significant independent correlation between an admission BG value of ≥200 mg/dL and 30-day surgical site infection (SSI). Because of this, admission glucose readings in orthopaedic trauma patients may be a key indicator of the risk of infection.

Keywords: Glucose, Hyperglycemia, Surgical Site Infection.

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INTRODUCTION

Acute hyperglycemia following traumatic injury is common. Studies have shown that 20– 30% of trauma patients present following injury with blood glucose values greater than 200 mg/dL, and that a majority of patients demonstrate values greater than 150 mg/dL [1]. The immediate physiologic response to traumatic injury is thought to result in certain autonomic and endocrine adaptations, such as increased catecholamine and glycogen levels, which may be deleterious to immune function [2–5]. Elevated blood glucose at admission and persistent hyperglycemia are risk factors for infectious complications, longer hospital and intensive care unit (ICU) length of stay, and increased risk of death [6]. Recent investigations have demonstrated that this significant relationship is independent from a history of diabetes mellitus [7, 8]. Specifically in trauma patients, acute stress hyperglycemia after injury is associated with a twofold increase risk of death compared with patients without hyperglycemia [9]. Biochemical changes related to the stress of injury, such as the production of cortisol and catecholamines, decreased gluconeogenesis, and hypothesized increased glycogenolysis, are to perioperative contribute post-traumatic and to hyperglycemia [10, 11]. Subsequent increased blood glucose levels adversely impact lysosomal oxidative

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function and alter the neutrophil and macrophage response to tissue trauma [3]. Therefore, hyperglycemia affects a biochemical and immunologic response to operative stress and injury. The normal physiologic response to injury results in the alteration of endogenous hormone production and metabolites, including increased serum cortisol production, insulin resistance, and subsequent hyperglycemia [12, 13]. Recent investigations suggest that a stress-induced hyperglycemic response following significant trauma is strongly correlated with clinical outcome, even after considering age and injury severity [14-16].

The relationship between hyperglycemia and adverse outcomes, such as infectious complications, has been well described in the surgical literature. Diabetic patients undergoing spinal fusion procedures have an elevated risk of surgical site infection (SSI), but this risk is not restricted to patients with a history of diabetes [17]. Post-traumatic hyperglycemia is less well-documented in orthopaedic trauma patients. According to the existing evidence from the critical care and general surgical literature, blood glucose (BG) values are effective markers for identifying patients at risk for infectious complications and clinical outcomes [18-20]. Previous research has suggested a relationship between stress hyperglycemia and surgery site infections (SSIs) in the orthopaedic community. However, these investigations were limited by the small number of infection outcomes they included-11 to 21 SSI cases each inquiry [21-23]. The fact that blood glucose measurements may be obtained by standard laboratory and point-of-care testing and are virtually always collected when a patient is admitted is ultimately what gives them therapeutic value [24].

Furthermore, additional evaluation of groups with a higher number of infection outcome events is required. The goal of this study was to look at the relationship between admission hyperglycemia and 30day SSI in orthopaedic trauma patients who had no history of diabetes. In nondiabetic orthopaedic trauma patients, we expected that admission hyperglycemia is strongly linked with 30-day SSI.

OBJECTIVE OF THE STUDY

The main objective of the study was to evaluate the role of admission hyperglycaemia as a risk factor for surgical site infection in orthopaedic trauma patients.

METHODOLOGY & MATERIALS

This was a retrospective observational study and was conducted in the Department of Orthopaedics Surgery of Brahmanbaria medical college Hospital, Brahmanbaria, Bangladesh during the period from October, 2020 to October, 2022. We included 130 patients who were admitted to orthopaedics surgery department. These are the following criteria to be eligible for the enrollment as our study participants: a) Patients aged upto 70 years old; b)Patients with operative management for an extremity, pelvic, or acetabular fracture; c) Patients with open reduction and internal fixation or intramedullary nailing; d) Orthopaedic trauma patients who were admitted to orthopedics surgery; e) Patients who were willing to participate were included in the study And a) Patients with a history of DM, b) Patients with Coagulopathy; c) Patients with previous surgical history; d) Patients received corticosteroids, or had been admitted to the ICU; e) Patients with any history acute illness (e.g., renal or pancreatic diseases, ischemic heart disease etc.) were excluded from our study.

Data Collection

All blood glucose values, including both fingerstick and serum levels, were prospectively recorded in the patient's electronic medical record. During the study period, there was no scheduled protocol for blood glucose evaluation in orthopaedic trauma patients who were not admitted to the ICU and had no history of diabetes. Orders for scheduled slidingscale insulin were not routinely administered. A majority of glucose values were gathered from basic metabolic panel profiles, which included serum blood glucose laboratory values, and were obtained at the discretion of the attending orthopaedic surgeon. Fingerstick glucose measurements were performed by trained nurses using the SureStep Pro Professional Blood Glucose Management System (OneTouch; Lifescan, Milpitas, California). We were unable to determine whether patients had had recent oral intake prior to the laboratory draw; therefore, all glucose values were considered random.

Definition of Hyperglycemia

Hyperglycemia was defined in two ways with use of methods described in the previous literature [6, 25, 26]. First, we defined it as two or more random glucose values of $\geq 200 \text{ mg/dL}$. Next, we used the hyperglycemic index to describe multiple glucose measurements taken at irregular sampling intervals over a period of time. The index represents the mean glucose level above 108 mg/dL and yields a better estimate of overall glucose control than a single value at admission or the highest value during the day [26]. The hyperglycemic index was calculated for each patient in our investigation. To calculate the hyperglycemic index, the area under the curve of all glucose values over the entire hospital stay is plotted. The hyperglycemic index is thus independent of the hospital length of stay. We considered a hyperglycemic index of ≥ 1.76 (equivalent to $\geq 140 \text{ mg/dL}$) as a potential marker of hyperglycemia [7, 8, 25]. In order to calculate the hyperglycemic index, patients were required to have at least two measured blood glucose values during the hospital stay. Blood glucose values obtained after the diagnosis of infection (including pneumonia, urinary tract infection,

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bacteremia, or surgical-site infection) were excluded from analysis to eliminate potential bias—i.e., the possibility that hyperglycemia was a result of the infection rather than a contributing risk factor.

Identification of Surgical-Site Infection

The primary outcome of thirty-day postoperative surgical-site infection was identified with the use of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnostic codes for postoperative infection (998.59) and wound dehiscence (998.32). All cases classified as infections were required to have undergone a reoperation for the infection. Superficial infections requiring only oral or topical antibiotics were not considered. The medical records of patients identified via ICD-9-CM codes were reviewed to confirm the presence of either positive intraoperative cultures, pathology specimens with microbiologic pathogens, or visible gross purulence at the operative site within thirty days after discharge from the index trauma admission.

Statistical Analysis

All data were recorded systematically in preformed data collection form and quantitative data was expressed as mean and standard deviation and qualitative data was expressed as frequency distribution and percentage. Statistical analysis was performed by using SPSS 21 (Statistical Package for Social Sciences) for windows version 10. Probability value <0.05 was considered as level of significance. The study was approved by Ethical Review Committee of Brahmanbaria medical college Hospital, Brahmanbaria, Bangladesh.

RESULT

Figure 1 shows majority of our patients (41.54%) were aged 41-50 years, followed by 31.54% were 51-60 years. Among all patients 14.61% & 12.31% patients were aged 61-70 & \leq 40 years old respectively.

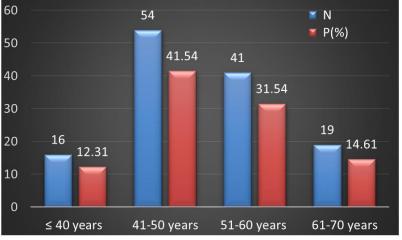


Figure 1: Age distribution of our study patients

Figure 2 shows the gender distribution of our study patients. Most of our patients (65%) were male compared to female (35%).

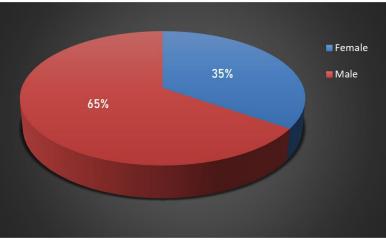


Figure 2: Gender distribution of our study patients

Table 1 shows the baseline characteristics of our patients. The mean age was 45.69 ± 22.83 years. Majority (41.54% & 31.54%) of our patients had a preoperative American Society of Anesthesiologists (ASA) classification of II & III (indicating mild & severe systemic disease). No patients were identified as

ASA class 5 (a moribund patient). Among all patients 36.15% had type 1, followed by 29.23% & 15.38% had type 2 & type 3A fractures respectively. Most of our patients (27.69%) had fracture in upper extremity region. Among all patients 73.85% patients had hypertension as a major comorbidity.

| Table 1. Dasenne characteristics of | our pu | |
|---------------------------------------|--------|----------------|
| Baseline | Ν | P (%) |
| Mean age (years) | 45.69 | 9 ± 22.83 |
| BMI (kg/m^2) | 28.67 | 7±4.24 |
| Systolic blood pressure (mm Hg) | 135.2 | 24 ± 20.78 |
| Diastolic blood pressure (mm Hg) | 83.94 | 1 ± 10.69 |
| ASA class | | |
| Ι | 21 | 16.15 |
| II | 54 | 41.54 |
| III | 41 | 31.54 |
| IV | 14 | 10.77 |
| V | 0 | 0.00 |
| Mean ISS | 8.9 ± | 2.6 |
| Open fractures | | |
| Type 1 | 47 | 36.15 |
| Type 2 | 38 | 29.23 |
| Type 3A | 20 | 15.38 |
| Type 3B | 14 | 10.77 |
| Type 3C | 11 | 8.46 |
| Fracture region | | |
| Upper extremity | 36 | 27.69 |
| Pelvis/hip | 34 | 26.15 |
| Femur | 22 | 16.92 |
| Tibia/ankle | 24 | 18.46 |
| Foot | 14 | 10.77 |
| Co-morbidities | | |
| HTN | 96 | 73.85 |
| Hypotension | 39 | 30.00 |
| Coronary artery disease | 45 | 34.62 |
| Chronic Obstructive Pulmonary Disease | 31 | 23.85 |
| Rheumatoid arthritis | 42 | 32.31 |
| | | |

Table 1: Baseline characteristics of our patients

ASA class=American Society of Anesthesiologists physical classification score; BMI= Body Mass Index; ISS=, Injury Severity Score

Table 2 shows that we found 45 patients with surgical site infection. Among those patients 66.67% were male & 33.33 were female. There were no significant differences of no. of comorbidities in both groups. Among infected patients 35.56% & 31.11% were classified ASA II & III respectively. There were no significant differences of injury severity score (ISS) in both groups. Among infected patients 31.11 %,

24.44% & 20% had type 1, type 2 & type 3 A fracture respectively. Followed by 15.56% & 8.89% had type 3B & 3C fracture respectively. Blood transfusion required more in not infected group. Admission glucose more than 200 mg/dL was found higher (26.67%) in infected group compared to not infected group (11.76%).

| Table 2: Association between Variables and Thirty-Day Surgical- | Site Infection | |
|---|----------------|--|
|---|----------------|--|

| Baseline | Surgical-Site Infection | | No Surgical-Site | | P-value |
|--------------------------|-------------------------|-------|----------------------|-------|---------|
| | (N = 45) | | Infection $(N = 85)$ | | |
| | Ν | P(%) | Ν | P(%) | |
| Mean age (years) | 47.69 ± 20.83 | | 42.69 ± 22.83 | | 0.167 |
| BMI (kg/m ²) | 28.67±4.24 | | 26.67±3.74 | | 0.128 |
| Gender | | | | | |
| Male | 30 | 66.67 | 55 | 64.71 | 0.024 |

Md. Saddam Hossain et al., East African Scholars J Med Sci; Vol-6, Iss-5 (May, 2023): 178-185

| Baseline | Surgical-Site Infection (N = 45) | | No Surgical-Site Infection (N = 85) | | P-value |
|-------------------------------------|-------------------------------------|-------|--|-------|---------|
| | N | P(%) | Ν | P(%) | |
| Female | 15 | 33.33 | 30 | 35.29 | 0.125 |
| Mean no. of comorbidities (SD) | 0.47 ± 0.01 | .58 | 0.52 ± 0.64 | | 0.324 |
| ASA class | | | | | |
| Ι | 9 | 20.00 | 12 | 14.12 | |
| Π | 16 | 35.56 | 38 | 44.71 | |
| III | 14 | 31.11 | 27 | 31.76 | |
| IV | 6 | 13.33 | 8 | 9.41 | |
| V | 0 | 0 | 0 | 0 | |
| Mean ISS | 8.9 ± 2.6 | | 8.9 ± 3.7 | | 0.041 |
| Open fractures | | | | | |
| Type 1 | 14 | 31.11 | 33 | 38.82 | < 0.01 |
| Type 2 | 11 | 24.44 | 27 | 31.76 | < 0.01 |
| Type 3A | 9 | 20.00 | 11 | 12.94 | < 0.01 |
| Type 3B | 7 | 15.56 | 7 | 8.24 | < 0.01 |
| Type 3C | 4 | 8.89 | 7 | 8.24 | < 0.01 |
| Blood transfusion | 29 | 64.44 | 65 | 76.47 | < 0.01 |
| Admission glucose ≥200 mg/dL | 12 | 26.67 | 10 | 11.76 | < 0.01 |
| Mean total hyperglycemic index (SD) | 1.5 ± 1.2 | | 0.96±1.7 | | 0.03 |
| Hyperglycemic index ≥1.76 | 35 | 77.78 | 71 | 83.53 | 0.013 |

Table 3 distributed our study patients by admission hyperglycemia. Among the patients admission hyperglycemia was found in 22 (16.92%). Among the hyperglycemic patients 36.36% were classified as ASA III, followed by 31.82 % & 22.73% were classified ASA II & I respectively. We didn't have any hyperglycemic patients identified as ASA V. Among open fractures, type 1 was found in 36.36 % patients & type 2 in 22.73% patients. Among hyperglycemic patients, 86.36% needed blood transfusion & 23.15% in non-hyperglycemic patients. The surgical site infection for 30 days was found 54.55% in hyperglycemic group & 30.56% in non-hyperglycemic group.

| Table 3: Distribut | ion of our study population by admission hyperglycemia |
|--------------------|--|
| | |

| Baseline | | n Hyperglycemia | No Admiss | P-value | |
|--------------------------------|-----------------|-----------------|------------------|----------------|-------|
| | (N = 22) | | (N = 108) | | |
| | Ν | P(%) | Ν | P(%) | |
| Mean age (years) | 46.64 ± 21 | .39 | 43.28 ± 20.7 | 73 | 0.320 |
| BMI (kg/m ²) | 29.67±4.84 | 4 | 25.87±4.14 | | 0.202 |
| Gender | | | | | |
| Male | 14 | 63.64 | 71 | 65.74 | 0.261 |
| Female | 8 | 36.36 | 37 | 34.26 | 0.163 |
| Mean no. of comorbidities (SD) | 0.49 ± 0.62 | | 0.50 ± 0.49 | | 0.212 |
| ASA class | | | | | |
| Ι | 5 | 22.73 | 17 | 15.74 | |
| II | 7 | 31.82 | 34 | 31.48 | |
| III | 8 | 36.36 | 49 | 45.37 | |
| IV | 2 | 9.09 | 8 | 7.41 | |
| V | 0 | 0 | 0 | 0 | |
| Mean ISS | 8.9 ± 1.6 | | 8.9 ± 3.1 | | |
| Open fractures | | | | | |
| Type 1 | 8 | 36.36 | 20 | 18.52 | 0.129 |
| Type 2 | 5 | 22.73 | 39 | 36.11 | 0.148 |
| Type 3A | 4 | 18.18 | 31 | 28.70 | 0.236 |
| Type 3B | 3 | 13.64 | 11 | 10.19 | 0.158 |
| Type 3C | 2 | 9.09 | 7 | 6.48 | 0.214 |
| Blood transfusion | 19 | 86.36 | 25 | 23.15 | 0.252 |
| 30-day site infection | 12 | 54.55 | 33 | 30.56 | 0.013 |

DISCUSSION

Acute hyperglycemia following traumatic injury has received significant attention in the critical care literature throughout the last decade. The relative ease with which such laboratory values are obtained and the applicability to immediate bedside practice have contributed greatly to the management of critically ill patients. Few topics have garnered such substantial influence in the surgical critical care community. However, the implications of acute hyperglycemia in nondiabetic, noncritically ill surgical patients have yet to be adequately investigated [26]. At present, there is a paucity of literature on hyperglycemia in nondiabetic patients following orthopaedic surgery [28]. We therefore evaluated the association of admission hyperglycemia with thirty-day surgical-site infection in a population of orthopaedic trauma patients without a history of diabetes.

Stress-induced hyperglycemia generally refers to an elevation in BG during periods of illness. While there is no consensus definition, previous literature has noted that without evidence of previous diabetes, stressinduced hyperglycemia may include truly nondiabetic patients in addition to patients with occult or previously undiagnosed diabetes [2, 3, 20]. Observational studies have shown that more than one-third of patients admitted to the hospital exhibit laboratory signs of hyperglycemia, defined as more than one fasting blood glucose level of ≥ 126 mg/dL or more than one random blood glucose level of $\geq 200 \text{ mg/dL}$, with 10% of the population developing newly discovered stress-induced hyperglycemia. In addition, the general trauma and critical care literature is replete with investigations on the relationship of hyperglycemia and morbidity and mortality following critical illness with some authors suggesting that ongoing persistent hyperglycemia and subsequent glucose control are predictive of outcome [14-16, 25, 28]. However, this has not been easily translated into results that may be applied in an environment outside of an ICU.

Previous investigations have demonstrated an association between hyperglycemia and infection in trauma [1, 16, 19]. However, the specific association between hyperglycemia and SSI in orthopaedic trauma patients has been limited to small sample sizes on infectious outcomes [20-22]. Our results reflect the significant association of admission hyperglycemia in a large data set of SSI outcome events which exceeds that of previous studies [20-22]. Admission hyperglycemia may represent an important marker for infection risk in orthopaedic trauma patients without diabetes. Identification of high-risk patients represents an important step in resource burden imposed by SSI. Our findings are consistent with those of a prior investigation on hyperglycemia in the orthopaedic trauma population [26]. This eliminated possible confounding such as severe injury and critical illness, which has been shown to be associated with stress

hyperglycemia. Furthermore, hyperglycemia was only evaluated in patients without a prior diagnosis of diabetes mellitus. Although uncontrolled diabetes is a known risk factor for postoperative infection, the relationship between acute hyperglycemia and infection in patients without a prior diagnosis of diabetes is not as well described. One recent prospective analysis demonstrated that elevated preoperative plasma hemoglobin A1C levels were associated with increased risk of infection in surgical patients regardless of the diabetic status. Several other authors have noted that hyperglycemia in patients without a history or diagnosis of diabetes may be due to undiagnosed diabetes or as a result of stress-induced hyperglycemia [29-32]. The association between admission hyperglycemia and increased infectious outcomes demonstrated in this study is consistent with the prior literature [7, 20]. Fracture region, open fracture, and male gender have all been demonstrated to be independently associated with development of SSI. However, hyperglycemia has not been a consideration in several investigations that have analyzed individual risk factors for deep infection. Our data indicate that although not only does hyperglycemia at admission have clinical relevance to deep SSI in this patient population, it also constitutes one of the strongest independent associations with infection [33, 34].

Although only 22/130 (16.92%) patients in our study presented with BG values > 200 mg/dL, this is consistent with other studies. A prospective study of nondiabetic adults presenting to a trauma center by Kopelman et al., revealed 13/ 1039 (1.3%) patient presented with BG values >200 mg/ dL, whereas 277/4671 (5.9%) patients in a study by Kerby et al., presented with BG values > 200 mg/dL [9, 32]. Estimates for the prevalence of undiagnosed diabetes in patients who present with BG values $\geq 200 \text{ mg/dL}$ vary from 17.5% to 54%, as determined by hemoglobin A1C values [9, 26, 35]. As previously undiagnosed diabetes has been associated with the development of SSI, it is within reason to suspect that the increased risk of SSI in patients who present with BG values $\geq 200 \text{ mg/dL may}$ be attributed to those without a formal diagnosis of diabetes [36]. This investigation is not intended to determine whether or not this claim is true; rather, it should be followed up with more research.

Limitations of the Study

Our study was a single centre study. Our small sample size was our major limitation. We didn't have any standard protocol for routine blood glucose monitoring in patients without a history of diabetes. After evaluating once those patients we did not follow them up for a long term and have not known other possible interference that may happen in the long term with these patients.

CONCLUSION AND RECOMMENDATIONS

In our study, we found that orthopaedic trauma patients without a history of diabetes showed a significant independent correlation between an admission BG value of $\geq 200 \text{ mg/dL}$ and 30-day surgical site infection (SSI).

Because of this, admission glucose readings in orthopaedic trauma patients may be a key indicator of the risk of infection. In the posttraumatic and postoperative period, hyperglycemia is a cause for concern and may assist identify a group of patients with musculoskeletal injuries who are significantly more likely to experience infection problems. This study demonstrates that managing blood glucose levels & understanding the link between hyperglycemia and infectious problems may have a significant impact on how orthopaedic patients are treated after surgery. So, further study with a prospective and longitudinal study design including larger sample size needs to be done to delineate the relationship between hyperglycemia and surgical-site infections following orthopaedic surgery.

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