



Original Article

Effect of Elevated Glycated Hemoglobin on Sternal Wound Infection in Diabetic and Non-Diabetic Patients of Urgent Coronary Artery Bypass Grafting

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Abstract

Background: Incidence of cardiovascular diseases is high, and it occurs earlier in diabetic patient. This study aimed to examine the impact of elevated glycated hemoglobin (HbA1c) on the development of sternal wound infection in diabetic and non-diabetic patients who undergo isolated urgent coronary surgery.

Methods: This prospective study included all patients undergoing urgent coronary surgery through standard median sternotomy at Department of Cardiothoracic Surgery in Benha University Hospital. Patients were divided into 2 groups: Group 1 (n=40): diabetic cases and Group 2 (n=35): non-diabetic cases.

Results: The univariate logistic regression analysis showed that only HbA1c was a significant predictor for AF. While HbA1c, FBG and EF were the only significant predictors for sternal wound infection. Also, only HbA1c and FBG were significant predictors for 30-day mortality.

Conclusion: Patients with a higher HbA1c percentage experienced a higher incidence of deep sternal incision infection and mortality subsequent to coronary artery bypass grafting, as indicated by the findings. This suggests that diabetic patients need for stringent glycemic control prior to any surgical interventions.

KEYWORDS

Elevated Glycated Hemoglobin; Sternal Wound; Infection; Diabetic Patients; Non-Diabetic Patients; Coronary Artery Bypass Grafting

Introduction

Diabetic patients are highly susceptible to cardiovascular diseases, which typically manifest at an earlier stage. In diabetic patients with cardiovascular diseases who maintain superb glycemic control, the mortality rates are significantly elevated when contrasted with those of the general population [1].

The susceptibility to infections is heightened by DM, and there are a variety of pathogenic mechanisms that may contribute to this impact, including the hyperglycemic environment, during

an infection, certain white blood cells become immobilized, which leads to a decrease in chemotaxis, phagocytic activity, and interleukin production. This, in turn, makes certain pathogens more dangerous [2]. The production of advanced glycation end products is a result of hyperglycemia, which has the potential to diminish the functionality of host cells by influencing intracellular and extracellular death, chemotaxis, adhesion, phagocytosis, complement activation, and humoral response [3, 4]. In patients with diabetes mellitus, the likelihood of developing a surgical site infection is significantly

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elevated, particularly those who undergo cardiac surgery [5].

Inadequate preoperative glycemic control may lead to the failed implementation of optimal perioperative insulin treatment to mitigate the risk of surgical site infection. Patients become more susceptible to infections as a result of the negative impact of inadequate glycemic control on immunity. Additionally, glycated hemoglobin is only excreted at the very end of the red blood cell's natural cycle; hyperglycemia causes its irreversible formation. As a result, it is practicable to evaluate the glycemic control of the previous three to four months [6, 7]. Patients who undergo coronary artery bypass grafting may be at risk for sternal wound infection due to elevated preoperative glycated hemoglobin [8, 9].

The purpose of this study was to evaluate the risk of sternal wound infection in diabetic and non-diabetic patients who underwent emergency coronary surgery, as well as the role that elevated glycated hemoglobin plays in this process.

Patients and Methods

This prospective study included all patients undergoing urgent coronary surgery through standard median sternotomy at Department of Cardiothoracic Surgery in Benha University Hospital from May 2020 to May 2022.

The patients provided written consent that was informed. The purpose of the study was explained to each patient, and they were assigned a secret code number. The study was conducted with the approval of the Research Ethics Committee, Benha University Hospital.

Inclusion criteria were all patients (non-diabetic and diabetic) need isolated urgent coronary artery bypass grafting (CABG). Urgent CABG is a procedure that is required during the same hospitalization to mitigate the risk of additional clinical deterioration. This encompasses symptoms such as acute myocardial infarction, congestive heart failure, sudden chest pain, unstable angina with intravenous nitroglycerin, or rest angina, as well as a worsening general condition [10].

Exclusion criteria were patients undergoing elective coronary surgery, undergoing coronary surgery associated with heart valve surgery, who needed bilateral internal mammary arteries harvesting, refused giving consent for follow up and uncooperative patients during the study.

Grouping: Patients were divided into 2 groups: Group I (n=40): diabetic cases and Group II (n=35): non-diabetic cases.

All studied cases were subjected to complete history taking including, including [Personal history including (age, sex, marital status, occupation and body mass index (BMI)), smoking history, alcohol consumption, drug use and allergies), family history of diabetes mellitus, cardiovascular disease, hypertension (HTN), or other relevant diseases, past medical history including (Diabetes mellitus, HTN, coronary artery disease, previous surgeries, history of infections and other medical conditions), risk factors including (HTN [11], diabetes mellitus (defined as a fasting blood glucose level >126 mg/dl, random blood glucose \geq 200 mg/dl, or using antidiabetic drugs [12], hyperlipidemia [13], Smoking status (defined as smoking more than 10 cigarettes per day for a period of at least one year without attempting to cease) and peripheral arterial disease were determined by the pathologic conditions that result in a stenosis of at least 50% in the non-coronary artery circulation.

The presence of peripheral arterial disease was indicative of vascular disease]. Complete examination: General examination including [Vital signs including (temperature, respiratory rate, blood pressure, heart rate (HR), height, weight, body surface area, general appearance, cardiac examination including (Jugular venous distension, heart sounds, peripheral pulses and signs of congestive heart failure).

Routine laboratory investigations [Complete blood count, cardiac enzymes were included: creatine kinase, brain natriuretic peptide, troponin I, liver function (aspartate aminotransferase and alanine transaminase), kidney function (creatinine and serum urea), fasting and random blood glucose levels, glycated

Table 1: Basic characteristics, risk factors and clinical data of the studied group. Data presents as mean \pm SD or frequency (%)

		Group I (N=40)	Group II (N=35)	P
Age\ years		55.8 \pm 11.4	58.1 \pm 5.98	0.169
BMI		23 \pm 3.22	28.4 \pm 2.15	<0.001*
No. of diseased vessels		2.55 \pm 0.76	2.14 \pm 0.85	0.02*
		N (%)	N (%)	P
Gender	Male	24 (60%)	20 (57.1%)	0.08
	Female	16 (40%)	15 (42.9%)	
Risk factors	HTN	18 (45%)	7 (20%)	<0.001*
	Smoking	14 (35%)	12 (34.3%)	0.651
	Dyslipidemia	15 (37.5%)	11 (31.4%)	0.343
	Stroke	5 (12.5%)	4 (11.4%)	0.606
Clinical data	SBP	122.4 \pm 23.7	118 \pm 20.97	0.401
	DBP	76.1 \pm 11.9	74.4 \pm 11.95	0.538
	HR	80.3 \pm 12.7	78.5 \pm 10.9	0.515
	NYHA	II	11 (31.4%)	0.004*
		III	18 (51.4%)	
		IV	6 (17.1%)	

BMI: body mass index, **HTN:** hypertension, **SBP:** systolic blood pressure, **DBP:** Diastolic blood pressure, **HR:** heart rate, **NYHA:** New York Heart Association Functional Classification

hemoglobin (HbA1c), electrolytes, coagulation profile (international normalized ratio, partial thromboplastin time), and lipid profile (high density lipoprotein level, triglycerides, low density lipoprotein level, cholesterol level)]. Imaging services, such as transthoracic echocardiography and chest x-rays.

Trans-thoracic echocardiography:

The biplane modified Simpson's method was employed to measure the left ventricular end-diastolic dimension, left ventricular end-systolic diameter, left atrial diameter, and left ventricular ejection fraction using echocardiography. The total score was employed to evaluate the risk of stroke, and each factor was assigned a point value. The highest possible score is nine. The modified Simpson's method was employed to determine the LV ejection fraction: 2 orthogonal views—apical 4CH and apical 2CH are acquired, and endocardial borders are manually traced at the ES and ED. The left ventricle was divided into a collection of discs that were oriented perpendicular to the long axis of the ventricle. The individual volumes of these discs were summed by automated software. From the ED frame, the EDV

was computed. The ESV was computed from the ES frame. $EF = [(EDV - ESV) / EDV] \times 100 \%$

Noninsulin diabetes drugs and oral hypoglycemic agents were discontinued 24 hours prior to surgery. To attain glycemic control, short-acting insulin was administered through infusion or subcutaneous injection. The surgeon used insulin infusion to keep the blood sugar level at or below 180 mg/dL during the procedure and the first day after the operation. In order to keep glucose levels below 180 mg/dL, patients with persistently elevated glucose levels (>180 mg/dL) in the intensive care unit (ICU) needed continual insulin infusion. To keep their blood glucose levels at or below 150 mg/dL, patients who stayed a long time in the intensive care unit were given continuous insulin infusions. Following surgery, insulin therapy was maintained for one month, regardless of preoperative diabetes management.

Patients received pre-medication with intramuscular morphine (0.1 mg/kg) and were anesthetized with local anesthesia, sedation, and midazolam (0.07 mg/kg). Hemodynamic monitoring included a five-lead ECG, radial artery

Table 2: pre-operative laboratory data and ECHO data among studied groups. Data presents as mean \pm SD or frequency

		Group I (N=40)	Group II (N=35)	P value
FBG (mg\dl)		151.9 \pm 12.85	112.4 \pm 10.31	<0.001*
HbA1c		8.44 \pm 2.63	4.15 \pm 2.11	<0.001*
Hb (mg\dl)		11.99 \pm 1.85	12.4 \pm 2.31	0.330
Platelet count		380 \pm 75.3	419.8 \pm 77.4	0.375
TLC		9730 \pm 1325.31	9556.8 \pm 1273.3	0.875
Serum creatinine		1.11 \pm 0.25	1.08 \pm 0.22	0.493
Serum Urea (mg\dl)		20.6 \pm 4.55	21.5 \pm 3.44	0.231
SGOT (mg\dl)		30 \pm 7.31	29.8 \pm 7.44	0.875
SGPT (mg\dl)		32.7 \pm 14.3	31.8 \pm 14.5	0.781
Left ventricular function	Normal	13 (32.5%)	11 (31.4%)	0.081
	Reduced	16 (40%)	15 (42.9%)	
	Severely reduced	11 (27.5%)	9 (25.7%)	
EF (%)		42.5 \pm 9.94	47.8 \pm 9.15	0.031

FBG: Fasting Blood Glucose, **HbA1c:** glycated haemoglobin, **Hb:** haemoglobin, **TLC:** Total Leukocyte Count, **SGOT:** Serum Glutamic-Oxalo-acetic Transaminase, **SGPT:** Serum Glutamic Pyruvic Transaminase, **EF:** ejection fraction

* statistically significant as P value <0.05

cannulation, and a pulmonary artery catheter placed via the right internal jugular vein.

Using three thermos-dilution readings, the following parameters were averaged: heart rate (HR), systolic and diastolic blood pressure (BP), mean BP, central venous pressure (CV), mean PA, and cardiac output (CO). The cardiovascular system's additional computations comprised the cardiac index (CI), stroke volume index, left and right ventricular stroke work indices, systemic vascular resistance index, and pulmonary vascular resistance index. The ST-segment analysis was used to identify myocardial ischemia.

Coronary artery bypass grafting procedure:

With the use of single lumen endotracheal tube, median sternotomy was done Followed by harvesting of the left IMA (LIMA) with great saphenous vein harvesting if needed, then pericardium was opened and enlarged in order to localize the desired coronary arteries. Aorto-atrial cannulation was done followed by starting of cardiopulmonary bypass and Coronary artery bypass grafting. The grafts' patency was assessed using the transit time technique. Time under general anesthesia, total time on bypass, time under cross-clamp, and the presence or absence of intraoperative complications were all part of the operational data set. The results are shown as the average plus or minus the standard error of the average.

Table 3: Intraoperative data, length of hospital stay & ICU stay of the studied groups. Data presents as mean \pm SD

		Group I (N=40)	Group II (N=35)	P
Intraoperative data	Cross clamp time (min.)	69.8 \pm 10.3	66.2 \pm 12.6	0.177
	Total bypass time (min.)	102.3 \pm 9.56	98.4 \pm 8.12	0.058
Hospital LOS (d.)		9.38 \pm 4.13	8.32 \pm 5.26	0.337
ICU LOS (d.)		3.33 \pm 1.56	2.14 \pm 1.72	0.002*

LOS: Length of Stay, **ICU:** Intensive Care Unit

* statistically significant as P value <0.05

Table 4: Postoperative outcome among studied groups. Data presents as frequency (%)

	Group I (N=40)	Group II (N=35)	P value
Mortality <30 days	3 (7.5%)	1 (2.5%)	0.423
Sternal wound infection	Superficial	1 (2.5%)	0.01*
	Mediastinitis	0 (0%)	0.04*
Atrial fibrillation	2 (5%)	3 (8.6%)	0.423
Renal failure	3 (7.5%)	1 (2.5%)	0.214

* statistically significant as P value <0.05

Postoperative data included mechanical ventilation time, ICU stay, and the incidence of sternal wound infections (superficial, deep, or mediastinitis). Additional assessments encompassed mortality within 30 days postoperatively, hospital stay duration, and complications such as arrhythmias or heart failure. Radiological examinations, including chest x-rays and CT scans as needed, and trans-thoracic echocardiography were performed to support clinical evaluations.

Follow up:

Follow-up of sternal wound infections, of any severity or type, was conducted at 3 and 6-month intervals or until complete healing of the wound. Six-month mortality was also monitored.

Statistical analysis

In order to verify, input, and analyze the data, SPSS version 23 was used. These statistical methods were used to examine the outcomes of the current study. The quantitative variables were expressed as the mean plus standard deviation (SD), whilst the qualitative variables were expressed as percentages and numerical values.

Table 5: Univariate logistic regression for prediction of the adverse outcomes

		OR	95% CI	P value
AF	BMI (kg/m²)	0.8897	0.6271 to 1.2622	0.512
	HbA1c (%)	1.2967	1.0052 to 1.6727	0.045*
	FBG (mg/dL)	1.0254	0.9976 to 1.0539	0.073
	EF (%)	0.9744	0.8935 to 1.0627	0.558
	No. of diseased vessels	0.9608	0.2895 to 3.1889	0.947
Renal failure	BMI (kg/m²)	0.9372	0.5778 to 1.5200	0.729
	HbA1c (%)	1.1697	0.8389 to 1.6310	0.355
	FBG (mg/dL)	1.0244	0.9856 to 1.0647	0.220
	EF (%)	0.9490	0.8400 to 1.0723	0.401
	No. of diseased vessels	0.3846	0.0660 to 2.2420	0.288
Sternal wound infection	BMI (kg/m²)	1.1769	0.8735 to 1.5857	0.248
	HbA1c (%)	1.6654	1.2603 to 2.2007	<0.001*
	FBG (mg/dL)	1.0546	1.0230 to 1.0871	0.001*
	EF (%)	0.9026	0.8323 to 0.9789	0.013*
	No. of diseased vessels	1.0185	0.3642 to 2.8486	0.972
30-day mortality	BMI (kg/m²)	1.0483	0.7153 to 1.5364	0.809
	HbA1c (%)	1.5429	1.0828 to 2.1984	0.016*
	FBG (mg/dL)	1.0351	1.0008 to 1.0705	0.044*
	EF (%)	0.9575	0.8689 to 1.0552	0.381
	No. of diseased vessels	0.8056	0.2125 to 3.0538	0.750

OR: odds ratio, **CI:** confidence interval, **AF:** atrial fibrillation, **BMI:** body mass index, **EF:** ejection fraction, **HbA1c:** glycosylated hemoglobin, **FBG:** fasting blood glucose

* statistically significant as P value <0.05

. We used the arithmetic mean (\bar{X}), an average that shows the central tendency of the observations, to summarize the data. The standard deviation (SD) is a way to measure how far the results are from the mean. To compare the means of two different groups, the student "t" test was utilized. The chi-square test (X^2) is utilized to search for a link between two table variables. All the previous statistical analyses used a 5% significance level (P-value). When the P value is greater than 0.05, statistical significance is not proven. When the p-value is smaller than 0.05, the results are deemed to have statistical significance. The results have greater significance as the P value decreases.

Results

Table 1 there is preoperative matching of both groups with no significant difference. Table 2 there is preoperative matching of both groups with no significant difference.

Table 3 shows insignificant difference among both groups regarding cross clamp time or total bypass time and length of hospital stay. While there was significant longer ICU stay among diabetic cases with mean of (3.33 days versus 2.14 days among non-diabetics).

Table 4 shows a significant increased prevalence of superficial and deep sternal wound infection among diabetic cases (20% & 17.5% respectively versus 1.3% & 0% among non-diabetic cases).

Table 5 The univariate logistic regression analysis showed that only HbA1c was a significant predictor for AF. While the univariate logistic regression analysis showed that HbA1c, FBG and EF were the only significant predictors for sternal wound infection. Also, the univariate logistic regression analysis showed that only HbA1c and FBG were significant predictors for 30-day mortality. None of BMI, HbA1c, FBG, EF and No. of diseased vessels was as significant predictor for renal failure.

Discussion

Elevated HbA1c levels have emerged as a significant concern in the context of surgical outcomes, particularly in patients undergoing CABG. HbA1c, which stands for the average blood glucose levels over the past two or three months, is an essential measure for evaluating long-term glycemic control. In diabetic patients, a range of postoperative complications, including a heightened risk of infections, are associated with poor glycemic control, as indicated by elevated HbA1c levels [14].

Our study did not reveal any statistically significant differences between the two groups involved in the investigation, including age and gender. The number of diseased vessels and the BMI of diabetic patients were, however, significantly higher.

In agreement with us, Kim et al. [15], patients were categorized into 2 groups based on their HbA1c level (<7.0% or ≥7.0%), the study did not identify any statistically significant differences in age, gender, or BMI between the two groups.

In the current study, in terms of risk factors (dyslipidemia, stroke, or smoking), there was no statistically significant difference between the 2 groups that were examined. However, the prevalence of HTN was significantly higher among diabetic patients.

In parallel with our findings, Ramadan et al. [16] The two groups (HbA1c level <7.0% or ≥7.0%) did not differ significantly in terms of smoking. Regardless, they denied our claim that observed differences in HTN between the two groups were insignificant.

In disagreement with us, Kim et al. [15] demonstrated that there was no statistically significant difference among both groups (HbA1c level <7.0% or ≥7.0%) as regard HTN and cerebrovascular accidents.

In the present study, there was no statistically significant difference among both studied groups as regard clinical data (SBP, DBP or HR), while

NYHA class IV was significantly higher among diabetic cases (50%) than no diabetic (17.1%).

In parallel with our findings, Ramadan et al. [16] showed that there was a significantly lower in the NYHA class in HbA1c <7% compared to HbA1c ≥7% patients.

The two groups' laboratory data, which encompassed Hb, platelet count, total leukocyte count (TLC), serum creatinine, urea, serum glutamic-oxalo-acetic transaminase (SGOT), and serum glutamic pyruvic transaminase, did not demonstrate any statistically significant difference in our study. The glycosylated hemoglobin and blood glucose levels of the diabetic group were significantly elevated.

In agreement with us, Kim et al. [15] showed that there was no statistically significant difference between the two groups (HbA1c level <7.0% or ≥7.0%) in terms of hemoglobin level. However, the group with a HbA1c level of ≥7.0% had a significantly higher serum glucose level ($P<.001$).

As regard to our results, EF (Simpson) was significantly lowered among cases of group I (diabetic cases). Both groups indicated in significant difference with respect to the total bypass time or the cross-clamp time.

In agreement with us, Nicolini et al. [17] revealed that EF was significantly higher in groups with increased HbA1c level than those with decreased HbA1c level ($P=0.001$).

In contrast our results, Narayan et al. [18] found that there was no difference regarding EF between both groups (HbA1c level <6.5% or ≥6.5%).

According to our findings, there was no significant difference among both groups regarding length of hospital stay. While there was significant longer ICU stay among diabetic cases with mean of (3.33 days versus 2.14 days among non-diabetics).

In parallel with us, Almogati and Ahmed [19] reported that, there was no significant difference in the total length of hospital stay in HbA1c <7% compared to HbA1c ≥7% patients ($P=0.367$).

Regarding to the present study, there was a statistically significant increased prevalence of superficial and deep sternal wound infection among diabetic cases (20% & 17.5% respectively versus 1.3% & 0% among non-diabetic cases).

In agreement with us, Kim et al. [15] reported that the group with a HbA1c level of ≥7.0% had significantly higher rates of deep sternal infection than the group with a HbA1c level of <7.0% ($P<.001$).

The univariate logistic regression analysis showed that only HbA1c was a significant predictor for AF. While the univariate logistic regression analysis showed that HbA1c, FBG and EF were the only significant predictors for sternal wound infection. Also, the univariate logistic regression analysis showed that only HbA1c and FBG were significant predictors for 30-day mortality.

In accordance with us, Zhao et al. [20] proved that high HbA1c levels before surgery increased the likelihood of DSWI, but it was not a very good predictor of DSWI after surgery. The dose-response analysis revealed a strong nonlinear correlation ($p=0.03$) between HbA1c and DSWI. When HbA1c levels are above 5.7%, DSWI is significantly more likely.

Limitations

The study has a few caveats, such as a small sample size and the fact that the diabetic group had to have a semi-urgent operation because they were sicker than the non-diabetic group and could not have been more stringent about their diabetes control before the procedure. We also did not find out whether insulin-dependent patients fared worse than those whose diabetes was controlled with dietary changes or oral hypoglycemic drugs. A known factor that can influence outcomes, the duration of diabetes mellitus, was not assessed in each group. It is possible that other comorbidities

were not sufficiently accounted for in the analysis, which could have affected the results.

Conclusion

The findings demonstrated that patients with higher HbA1c percentage were associated with increased incidence of deep sternal wound infection and death after CABG. This suggests that diabetic patients need for stringent glycemic control prior to any surgical interventions.

Therefore, further investigations with larger and stratified sample size is recommended, standardizing the measurement of HbA1c and ensuring that measurements are taken at consistent intervals relative to surgical procedures will improve the reliability of the findings and extending the follow-up period post-surgery will allow for the identification of late-onset infections and complications, future research could explore the impact of preoperative interventions aimed at optimizing glycemic control on the incidence of SWI and randomized controlled trials assessing the timing of surgery based on HbA1c levels.

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