

## The relationship between elevated HbA1c% and surgical site infection in patients undergoing CABG

Nezar Elnahal (MD)\*, , Mohamed MamdouhElsharawy(MD)\*, Mohamed Abdelshafy Mahmoud (M.S)\*, Mohamed Alanwar (MD)\*

*\*from cardiothoracic surgery department – Zagazig university*

**Corresponding author:**  
name Mohamed Alanwar  
Email  
[anwar7666@yahoo.com](mailto:anwar7666@yahoo.com)

### ABSTRACT

**Objective:** Controversy still exists whether adequacy of preoperative diabetes control measured by HbA1c% is a predictor of elevated incidence of surgical site infection (SSI) after CABG.

**Methods:** prospective study was done on 48 diabetic patients underwent CABG surgery. They were classified into 2 groups, Group (A): 24 patients with fair glycemic control (HbA1c is under or equal to 7%), Group (B): 24 patients with poor glycemic control (HbA1c above 7%). SSI either sternotomy or saphenous wound infection were studied in both groups.

**Results:** Superficial wound infection for group A was 12.5% and 25% for group B with significant statistical difference among the two groups. Deep Sternal Wound Infection (DSWI) was (4.1%) group A and group B with no statistical significance. As regard Saphenous wound infection was (8.3%) for group A and (25%) for group B with statistical difference, also group B has higher frequency of hospital re-admission and need inotropes more than group A.

**Conclusions:** Elevated HbA1c >7 in patients undergoing CABG associated with increased frequency of SWI and saphenous harvesting site infection but there was no significant increase in DSWI. Patients with elevated HbA1c >7 has more resistant peri-operative control of RBS. Finally we found that good peri-operative control of RBS associated with decreased rate of SSI after CABG. HbA1c is simple test that may offer the surgeon with better risk profile assessment and give additional prognostic data when discussing morbidity and mortality risks with patients and their relatives.

**Key words:** HbA1c%, glycosylated hemoglobin, outcome, coronary artery bypass grafting, surgical site infection.

### INTRODUCTION

**D**iabetes Mellitus (DM) is a well-known risk factor for coronary artery disease and its incidence is increasing significantly and the WHO estimates that by 2025, there are about 5.4% of the world population (approximately 300 million people) will be diabetic. The reported frequency of diabetes between patients undergoing coronary artery bypass surgery (CABG) has been valued to be 12- 38%<sup>[1]</sup>.

Patients with DM have had worse prognosis following CABG and have higher occurrence of mortality, sternal wound infections, renal failure, stroke, and increased need for inotropic support. Their time of admission is prolonged and hospital charges are enlarged. Diabetic CABG patients are more expected to need a repeat revascularization procedure, they have a higher possibility of readmission for cardiac-related problems by

24%, and a higher risk for re-admission in hospitals for any cause by 44% [2].

hyperglycemia has been shown to be an independent risk factor for infections either Intraoperative or postoperative. However, whether the preoperative chronic glycemic control is associated with the risk of infections remains an area of controversy. The glycosylated hemoglobin (HbA1c %) is a sensitive and reliable biomarker that provides a measure of glucose control status over the prior 2-3 months. The ADA (American Diabetes Association) suggests an HbA1c goal of less than 7% to reduce long-term complications of DM [3].

Superficial wound infection (SWI) involves only the skin or subcutaneous tissue [4]. Deep Sternal Wound Infection (DSWI) involves the muscle, bone, pericardium, and/or mediastinum. Additional conditions of DSWI may include purulent mediastinal drainage, positive cultures of mediastinal fluid or tissues, sternal instability or dehiscence, evidence of mediastinitis during surgery, abnormal sternotomy pain and fever  $> 38^{\circ}\text{C}$  [3].

DSWI have a significant impact on both patient prognosis and hospital budgets. It still had significant incidence that ranges between 0.5% and 6.8 % with in hospital death rate is between 7 and 35% [5].

As more number of diabetic patients being operated in our centre, we examined the effect and relation between preoperative HbA1c and SSI.

## PATIENTS AND METHODS

Our prospective study collected data from 48 diabetic patients (diabetes type 2) who were operated for CABG surgery at our institution over a period of 6 months. In all of those patients the efficacy of preoperative glycemic control was assessed by measuring the level of HbA1c. Patients were stratified into two groups, (group A) composed of 24 patients with HbA1c% below 7%. While the

second group (group B) of 24 patients with HbA1c% above 7%.

Inclusion criteria: Diabetic patients who did elective CABG surgery of all ages, both genders.

Exclusion

criteria: Emergency operations, redo-operations, immune-compromised patients such as patients on long term corticosteroid therapy, renal failure, hepatic cell failure , ...etc . Associated valvular lesions, patients without a mammary artery graft, complicated patients as (prolonged bypass time, prolonged ventilation in ICU and patients that re-explored for bleeding).

Control of blood glucose level of all patients was done conferring to The Society of Thoracic Surgeons (STS) guidelines (6) as the following:

Oral hypoglycemic agents and noninsulin diabetes drugs stopped 24 hour prior to surgery. Then , short-acting insulin either subcutaneous or an insulin infusion was initiated to attain glycemic control for hospital admitted patients awaiting surgery . In operating room and for at least 24 hour postoperative serum glucose levels are to be  $\leq 180$  mg/dL maintained by insulin infusion. When intravenous insulin infusions were discontinued, patients were turned into a subcutaneous insulin schedule . Patients who had persistent elevated serum glucose ( $>180$ mg/dL) were received insulin infusion to maintain serum glucose  $< 180$ mg/dL for the duration of their ICU stay and were monitored by random blood sugar every hour. All patients who required prolonged ICU stay because of ventilatory dependency requiring the need for inotropes, intra-aortic balloon pump, anti-arrhythmic or dialysis were received continuous insulin infusion to keep blood glucose  $\leq 150$  mg/dL. Insulin continued to all patients for one month after surgery regardless their preoperative management of DM .

Table (1): Protocol of intra and post-operative intravenous insulin infusion used in our study.

Blood Sugar	Regular Insulin IV Bolus	Infusion Rate
151-200	No bolus	2units/h
201-240	4 units	2 units/h
241-280	6 units	4 units/h
281-320	10 units	6 units/h

(Bojar, 2011).

For these patients, the following data were collected:

#### **Preoperative :**

Full medical history taking with special focus on Detailed history of Diabetes mellitus and its management as (onset of DM, type of treatment and presence of diabetes complications or not).

Full General and Local clinical examination of chest and heart were carried out . Routine hematologic investigations including fasting and postprandial blood sugar in addition to HbA1c% level were done . Radiological investigations were done and informed consents signed by the patients .

**Intra-operative :**Monitoring of random blood sugar (before CPB , at CPB ,before transfer to ICU) . Monitoring of CPB time , cross clamp time and operative time and inotropes support.

**Post-operative :**Monitoring of random blood sugar in ICU (every hour till insulin infusion transitioned to sub-cutaneous insulin). Ventilation time and ICU stay time. Careful Follow up of wound healing and looking for any symptoms or signs of SSI . Superficial wound infection manifestations at sternotomy wound or saphenous harvesting site include redness, swelling, discharge, skin dehiscence and

leukocytosis. Signs of DSWI include sternal instability / dehiscence, purulent discharge/ drainage from mediastinum with positive culture from wound or discharge , sternal osteomyelitis , chest x ray findings as sternal dehiscence .

#### **Follow up in ward and out-patient clinic:**

Follow up of all operated cases in ward and outpatient clinics for 30 days to assess postoperative outcome with special examination of sternotomy and vein harvesting site for previously mentioned manifestations of SSI . Random blood sugar to assess efficacy of outpatient glycemic control .

#### **Statistical Analysis**

Data were collected and entered to the IBM SPSS (Statistical Package for Social Science) version 20. Qualitative data were obtainable as number and percentages and compared using Chi-square test while quantitative data were presented as mean, standard deviations and ranges and compared between the two studied groups using Independent t-test. The confidence interval was set to 95% and p-value was considered non significant at the level of higher than 0.05 (NS), significant at the level of less than 0.05 (S) and highly significant at the level of less than 0.01 (HS).

## **Results**

This study was conducted with 48 diabetic patient undergoing CABG  
**pre-operative characteristics of the studied group:**

**Table (2): Baseline data of the studied group.**

	HbA1c>7	HbA1c<7	Test	p-value (Sig.)
Age (mean/years)	52 ±7	50.5±9.1	0.655	0.516(NS)
<b>Gender</b>				
Male	15 (62.5%)	16(66.7%)	0.091	0.76
Female	9 (37.5%)	8(33.3%)		(NS)

Out of the 48 patients, there were 24 patients has HbA1c>7. 15 male patients (62.5%) and 9 female patients (37.5%). Their mean age is 52.014± 7.08 years.while in other group there were 24 Cases 16 male

patients (66.7%) and 8 female patients (33.3%). Their mean age is 50.500 ± 9.10 years. There were no significant differences between age and sex of both groups.

**Table (3): Difference between both groups in body mass index(BMI) and ejection fraction(EF).**

	Group	Mean	Std. Deviation	T	P
<b>EF</b>	HbA1c>7	62.2083	7.41901	1.717	0.093 (NS)
	HbA1c<7	59.0000	5.36494		
<b>BMI</b>	HbA1c>7	33.4583	4.86316	1.880	0.066 (NS)
	HbA1c<7	31.1250	3.65124		

There was no significant difference between both groups in BMI and EF.

**Table (4): Difference between both groups in smoking, hypertension and previous MI.**

History	HbA1c>7		HbA1c<7		Test	p-value (Sig.)
	N	%	N	%		
<b>Smoking</b>	10	41.7%	12	50 %	0.33	0.56 NS
<b>Hypertension</b>	21	87.5%	15	62.5%	4.0	0.04 S
<b>Previous MI</b>	11	45.8%	12	50%	0.083	0.77 NS

There was a significant difference between both groups in presence of preoperative hypertension .It was found that group of HbA1c >7 were suffering from preoperative hypertension more than the other group. But there was no significant difference between both groups in incidence of smoking and presence of previous MI .

### Operative data of the studied patients

**Table(5): Difference between both groups in using inotropes and Intra aortic ballon pump(IABP)**

			Group		Total		
			HbA1c>7	HbA1c<7			
Inotropes	Used	Count	24	19	43	4.3	0.04*(S)
		%	100.0%	79.2%	89.6%		
IABP	No	Count	24	23	47	1.02	0.31(NS)
		%	100.0%	95.8%	97.9%		
	Yes	Count	0	1	1		
		%	0.0%	4.2%	2.1%		

Number of patients need inotropic support was higher in patients with HbA1c>7 than the other group ,but there was no significant difference between both groups in using IABP.

**Table(6): Intra-operative data of the studied patients**

	Group	Mean	P
CPB time	HbA1c>7	130±25	0.088(NS)
	HbA1c<7	118±19	
X clamp time	HbA1c>7	100±22	0.301(NS)
	HbA1c<7	93±22	
No of grafts	HbA1c>7	2.8±0.9	0.618(NS)
	HbA1c<7	2.7±0.7	

There was no significant difference between both groups in the following items Cardiopulmonary bypass (CPB) time, cross clamp time and number of grafts.

**Table(7): Post-operative Surgical Site Infection(SSl) in the studied groups**

		Group		P
		HbA1c<7	HbA1c>7	
SWI	No.of patients	3	9	0.046*(S)
	%	12.5%	37.5%	
DSWI	No.of patients	1	1	(NS)
	%	4.1 %	4.1%	
Saphenous	No.of patients	2	6	0.041*(S)
	%	8.3 %	25%	

SWI = superficial wound infection.      DSWI =deep sternal wound infection.

Group of patients that has HbA1c>7 was significant higher in SWI and saphenous wound infection while there was no significant difference between both groups in DSWI.

Re-admission for wound infection required for 5 patients (20.8%) in HbA1c>7 group, while no patient re-admitted in other group (p=0.018).

## DISCUSSION

In Egypt diabetes is a fast growing health problem with a significant impact on morbidity , mortality and health resources. currently the incidence of type 2 DM in

Egypt is around 15.6% of all adults aged 20 to 79years (8).

Patients with DM have had worse prognosis following CABG and have higher occurrence of mortality, sternal wound infections, renal

failure, stroke, and increased need for inotropic support. Their time of admission is prolonged and hospital charges are enlarged. Diabetic CABG patients are more expected to need a repeat revascularization procedure, they have a higher possibility of readmission for cardiac-related problems by 24%, and a higher risk for re-admission in hospitals for any cause by 44%

In 2011, the World Health Organization advocated the use of HbA1c in diagnosing diabetes. Elevated HbA1c predicts a high level of mortality and morbidity regardless of previous diabetic status. In specific, the mortality risk for CABG is increased fourfold at HbA1c levels  $>8.6\%$ . In elective conditions, it has been suggested that these patients should be postponed for surgery until acceptable glycemic control is realized<sup>[9]</sup>.

Sternal wound infection is still the major source of morbidity and death rate in the diabetic CABG patient and is more likely to happen when serum glucose surpasses 200 mg/dL in the postoperative period. One of the most significant improvements in prognosis among patient with DM has been the application of fitted perioperative glucose control. **Furnary and colleagues** described dramatic decreases in mortality and DSWI between diabetic patients (comparable to nondiabetic patients) controlled by a continuous insulin infusion started intraoperative and continued through the following 2 postoperative days. They referred these improvements to enhanced myocardial glycometabolic function linked with euglycemia attained by continuous insulin infusion to control glucose levels under 150 mg/dL in all diabetic patients in the operating room and in the ICU using a continuous insulin infusion<sup>[10]</sup>.

In this study the demographic criteria of the studied groups were comparable with mean age of  $(52.04 \pm 7.08)$  for patients with HbA1c $>7$  and  $(50.50 \pm 9.10)$  for patients with HbA1c $<7$  with no statistical significance between them. It was noticed

that There was no significant difference between both groups in BMI and EF while There was a significant difference between both groups in presence of preoperative hypertension. It was found that group of HbA1c  $>7$  were suffering from pre-operative hypertension more than the other group. But there was no significant difference between both groups in incidence of smoking and presence of previous MI. It was noticed also that Number of patients need inotropic support was higher in patients with HbA1c  $>7$  than the other group, but there was no significant difference between both groups in using IABP.

Group of patients that has HbA1c $>7$  was significant higher in SWI and saphenous wound infection while there was no significant difference between both groups in DSWI. It was found that patients with HbA1c above 7 has mean RBS  $210.62 \pm 48.23$  while patients with HbA1c below 7 has mean RBS  $140 \pm 23.40$ . This means that patients with HbA1c above 7 has poor control of RBS than patients with HbA1c below 7.

**Faritous and associates** showed a significant relationship between high levels of HbA1c  $>7$  and wound infection in study included 216 patients<sup>[11]</sup>. DSWI incidence as reported by **Alserius and his group** was higher in patients who had an HbA1c level of  $\geq 6\%$  but was not statistically significant. They demonstrated that elevated HbA1c% was associated with a significantly increased risk of SWI<sup>[12]</sup>.

**Fohl and co-worker** examined the relationship between HbA1c% and DSWI in 861 diabetic cardiac surgery patients whose postoperative blood glucose was maintained between 100-140 mg/dL. Preoperative HbA1c levels of  $> 8.5$  was found to be associated with an increased incidence of DSWI<sup>[13]</sup>. HbA1c% proved to be a powerful predictor of in-hospital mortality and morbidity postoperatively including Significant increase in DSWI in a study conducted by **Halkos and associates** on 3089 diabetic and non-diabetic patients. Moreover HbA1c  $\geq 8.6\%$  caused a



four-fold increase in mortality and increased postoperative complications such as renal failure , cerebrovascular accident and DSWI. Based on that results they proposed that elective patients should be delayed for surgery until adequate glycaemic control is achieved<sup>[14]</sup>.

**Knapik and co-investigators** conducted a retrospective review in 782 diabetic patients. For comparison of outcomes with tight post operative glycemic control, patients had elevated HbA1c levels >7% were significantly associated with increased incidence of perioperative myocardial infarct (MI) compared with the HbA1c <7% group and There were no significant differences in all other morbidity and early mortality<sup>[15]</sup>.

On contrast, other studies suggested that there is no strong relationship between elevated HbA1c% and SSI after CABG such as study carried out by **Hudson and associates** who examined 1.474 patients found no association between elevated HbA1c and infection after cardiac surgery. However they found that Thirty-day mortality and acute kidney injury were significantly higher in patients with HbA1c>6%<sup>[16]</sup> **Sevük and colleagues** indicated that elevated HbA1c levels in the preoperative period is not a risk factor for DSWI in patients undergoing CABG while good perioperative glycemic control decreases incidence of DSWI<sup>[3]</sup>. In Off-pump coronary artery bypass(OPCAB) patients with poorly controlled DM (HbA1c > 6.5) SSI was not related to elevated HbA1c levels as reported by **Matsuura and coworkers**<sup>[16]</sup> . **Engoren and associates** investigated the effect of HbA1c% on complications in 880 patients undergoing CABG who were managed with tight postoperative glycemic control. No relationship was found between HbA1c and sternal wound infections<sup>[18]</sup> .Same results were reported by **Göksedef and coworkers** but furthermore, they found 30-day mortality outcomes were similar for both well and poorly controlled HbA1c groups<sup>[19]</sup>

We implemented continuous insulin infusion to achieve glucose control on the day of surgery and in the intensive care unit. This may have accounted for the lack of a mortality difference between the two groups. Another explanation is that more number of patients are needed in both groups to reach a statistical significance in hospital and one year mortality. In contrast to our study, other studies evaluating the impact of diabetes on morbidity and mortality after CABG have resulted in different conclusions<sup>[20,21]</sup>

### CONCLUSIONS

Elevated HbA1c >7 in patients undergoing CABG increases incidence of SWI and saphenous harvesting site infection but there was no significant increase in DSWI. Patients with elevated HbA1c >7 has more resistant peri-operative control of RBS . finally we found that good peri-operative control of RBS associated with decreased rate of SSI after CABG. It is simple test that may provide the surgeon with a more accurate risk profile and provide additional prognostic information when discussing morbidity and mortality risks with patients and their families.

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