Early Outcome of Coronary Artery Bypass Graft Surgery in Patients with Preoperative Elevated Level of HbA1c with Diabetes Mellitus

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Abstract:

Introduction: Diabetes mellitus has been associated with an increased risk of adverse outcome after coronary artery bypass graft surgery. HbA1c is a reliable measure of long-term glucose control. It is unknown whether adequacy of diabetic control, measured by hemoglobin A1c, is a predictor of adverse outcomes after coronary artery bypass grafting. The predictive role of HbA1c on short term outcomes after coronary artery bypass graft surgery has not been evaluated. Diabetes mellitus has become a major health issue and contributes to morbidity and mortality from coronary artery disease. The purpose of this study is to determine the predictive role of preoperative elevated HbA1c on post-operative outcome in CABG patients.

Objectives: This study evaluates the early postoperative outcomes of CABG in terms of mortality and major post-operative morbidities like deep sternal wound infection, sepsis, stroke, renal failure, bleeding, arrhythmia, and mediastinitis in patients with preoperative elevated level of HbA1c.

Methods: This prospective study was done in National Institute of Cardiovascular Diseases (NICVD). Patients of coronary artery disease (CAD) with DM referred for CABG were enrolled for the study. Total 60 patients were allocated into two groups. Among them 30 patients with preoperative HbA1c of <7% and another 30 patients with preoperative HbA1c of > 7 % underwent CABG surgery from January, 2009 to December, 2010. The early postoperative outcomes were compared between two groups. Both groups were matched with no significant difference that could influence the postoperative outcome.

Results: In-hospital mortality was high in patients with preoperative elevated level of HbA1c. An elevated hemoglobin A1c level predicted in-hospital mortality after CABG surgery. Our study revealed that HbA1c greater than 7 % was associated with increase in mortality. For each unit increase hemoglobin A1c , there was a significantly increase risk of myocardial infarction and deep sternal wound infection. By using receiver operating characteristic value thresholds, renal failure, cerebrovascular accident and deep sternal wound infection occurred more commonly in patients with elevated hemoglobin A1c. Morbidity, infections and the composite outcomes occurred more commonly in patients with elevated HbA1c.

Conclusion: Elevated HbA1c is strongly associated with adverse events after coronary artery bypass graft surgery. Preoperative HbA1c measurement may allow for more accurate risk stratification in patients undergoing coronary artery bypass graft surgery.

Key Words: HbA1c, Diabetes Mellitus, CABG

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Introduction:

Diabetes mellitus is a clinical syndrome characterized by hyperglycemia due to absolute or relative deficiency of insulin.[2] Diabetes mellitus and its associated complications are a

major threat to public health globally. Worldwide prevalence of type 2 diabetes was 4.0% in 1995, and it is expected to rise to 5.4% by the year 2025, representing a 170% increase in the number of affected adults in developing countries. It is estimated that by the year 2025, there will be approximately 228 million adult diabetes in developing countries.[3] Hyperglycemia may be defined as elevated random plasma glucose level >11.1 mmol/L. Hyperglycemia is commonly present in the perioperative period in patients undergoing cardiac surgery in both diabetic and non diabetic patients, even during administration of insulin.[4]

Hyperglycemia contributes to excessive urine output from an osmotic diuresis, impair wound healing, increases the risk of infection and may impair blood pressure regulation.[5] A 20 mg/dl increase in blood glucose level was associated with more than 30% increase in adverse effects.[6] Intraoperative hyperglycemia increases the risk of postoperative outcome following open heart surgery more in diabetic patients than non-diabetic patients.[7] Hyperglycemia in the immediate post operative period remains an independent risk predictor of and may be a causal factor in deep sternal wound infection.[8] Diabetes mellitus has long been recognized as an independent risk factor for the development of coronary artery disease (CAD).[9] The prevalence of CAD in patients with type-2 diabetes ranges between 13% and 43%[9] and 20% to 30% of patients undergoing coronary artery bypass grafting surgery (CABG) have DM.[10] Type-2 diabetes is often asymptomatic in its early stages and remains undetected for several years before it is diagnosed. In undiagnosed diabetic population, asymptomatic hyperglycemia has been reported to predict increased risk of cardiovascular death and morbidity and mortality after cardiac surgery.[11]

Therefore, early detection, diagnosis, and treatment of type-2 DM are of utmost importance to prevent diabetic complications, and to improve short and long-term outcomes in patients undergoing CABG.[12]

The most widely used tests for the diagnosis of DM include fasting plasma glucose (FPG) and oral glucose tolerance test (OGTT). A multitude of reports have indicated that up to 50% patients with DM who were diagnosed by OGTT criteria would have been missed by FPG criteria.[13]

Despite being the diagnostic gold standard for DM, OGTT is costly, time consuming, and labor intensive and is impractical for diabetes screening. Therefore, an additional, simple, cost-effective, efficient, and patient-friendly method for detecting these diabetic subjects would be highly desirable. Another suggested measure for clinical screening of DM is hemoglobin A1c (HbA1c).[14] The HbA1c test, measures average blood glucose levels for a period of up to 3 months. HbA1c as a faster, easier test does not require fasting. An A1c level of approximately 5% indicates the absence of diabetes, and according to revised evidence-based guidelines, an A1c scores of 5.7% to 6.4% indicates prediabetes, and an A1c level of 6.5% or higher indicates the presence of diabetes.[15] HbA1c is not only used for therapeutic monitoring or as an alternative test for screening but also has been reported to be useful in predicting both early and late outcomes after CABG operations. A normal nondiabetic HbA1c is 3.5% to 5.5%, and each 1% increase in HbA1c corresponds to an increase in mean plasma glucose level of approximately 35 mg/dl, (2 mmol/L).[16]

HbA1c levels greater than or equal to 7% were associated with a significant increase in in-hospital mortality, renal failure, neurologic complications, and the composite index of infection compared with patients with and HbA1c of less than 7%.[1]

The prevalence of DM is expected to increase in developing countries. The patients undergoing CABG surgery constitute the high-risk group for DM. Mainly because of socioeconomic reasons, most of these patients are not aware of their disturbed glucose metabolism. These ignorance leads to adverse consequences with regard to prognosis in the short and long term after surgery. HbA1c measurements for patients who are undergoing CABG surgery may be useful and should be included in routine preoperative workup.[12]

Methods & materials:

This prospective, non-randomized clinical study was conducted in the department of cardiac surgery, NICVD, from January, 2009 to December, 2010. The study was carried out on patients with coronary artery disease who were scheduled for CABG with or without high preoperative HbA1c were included in the study. Patients with emergency CABG, redo CABG, history of myocardial infarction within 3 months, any surgical procedure for non-cardiac cause within 3 months, combined CABG and valve or other congenital heart diseases were excluded from the study.

After hospital admission all patients of coronary artery diseases with diabetes mellitus were assessed by

taking complete history and clinical examination, and then we measured HbA1c from biochemistry department of NICVD. Biochemistry department used konelab 60i analyzer to measure HbA1c. Normal value of HbA1c was 4.2 to 6.2% with this machine. According to serum level of HbA1c patients were divided into two groups. Patients with HbA1c <7% was considered as Group A and patients with HbA1c >7% was considered as Group B. Then evaluation of risk factors and co-morbid factors were done as per standard protocol. From history and preoperative investigations we collected data of age, sex, BMI, positive family history of CAD, angina status (CCS class), NYHA functional class, smoking habit. We also recorded some important co-morbid conditions including hypertension, arrhythmia, MI, COPD, dyslipidemia, renal dysfunction. From echocardiogram we recorded ejection fractions (EF %) , LV dysfunction in both groups. From CAG we recorded number of double vessel disease, triple vessel disease in both groups. We also did some necessary investigations including serum creatinine, blood urea, RBS, in study population. We collected intraoperative data of total operative time, number of grafts required in both groups. Postoperatively in the ICU we recorded total ventilation

time, how many patients developed atrial fibrillation, low cardiac output syndrome, post-operative MI, non-sternal wound infection, deep-sternal wound infection, CVD, renal failure, pulmonary complications. Postoperatively in the ICU we routinely did serum creatinine, blood urea, RBS, ABG, serum electrolytes in both groups, and all necessary data collected and recorded in data sheet from both groups for comparison and evaluation. During follow-up of the patients we examined sternal wound site and leg wound site for presence of any infection. We did echocardiography to determine ejection fractions (EF %). We also evaluate NYHA class and CCS class of all follow up patients. All data were analyzed by computer based SPSS (statistical program for social science) program.

Result:

The present study aimed at predicting the outcome of coronary artery bypass graft surgery (CABG) in patients with elevated hemoglobin A1c included a total of 60 patients of diabetes who underwent CABG. Based on the level of hemoglobin A1c, the patients were divided into two groups. The patients with hemoglobin A1c < 7% (Group-A) was considered as normal while patients with hemoglobin A1c $\geq$7% (Group-B) was considered as elevated. The findings of the study obtained from data analysis are documented below.

Age distribution:

Age distribution of the patients showed that 63.3% of patients in Group-A were between 50 – 60 years old as opposed to 33.3% of patients in Group-B. However, in Group-B all the patients were identically distributed among the three age categories. Although, the mean age was somewhat higher in Group-B compared to Group-A, but there was no significant difference between groups (p = 0.269).

Sex distribution:

There were 27(90%) male and 3(10%) female patients in Group-A and 25(83.3%) male and 5(16.7%) female s in Group-B.

Body Mass Index (BMI): Our study shows that 56.7% of patients in Group-A was of normal weight compared to 36.7% in Group-B. Overweight and obese patients were found higher in Group-B than that in group-A (63.3% vs. 43.3%). There was no significant difference between groups with respect to body mass index (p = 0.121).

NYHA class:

NYHA functional class demonstrates that NYHA class-II was 53.3% and class-III was 46.7% of patients in Group-A. In Group-B, 3.3% of patients belonged Class-I, 40.1% Class-II, 54.3% Class-III and another 3.3% Class-IV. The Chi-square (χ^2) analysis revealed that distribution of NYHA functional class between Group-A and Group-B was almost similar (p=0.439).
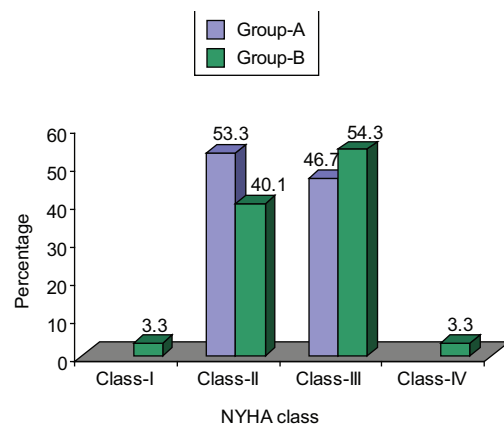

Fig.-1: *Comparison of NYHA class between groups*

CCS class:

Study result shows that CCS class – II was 70% in Group-A compared to 66.7% in Group-B. Class-III was observed in 26.7% of patients of the former group and in 30% of the later group. The groups were homogeneously distributed with respect to CCS class (p = 0.555).

Preoperative variables:

Smoking habit, hypertension, PVD, past myocardial infarction, dyslipidemia, left main disease and COPD were higher in Group-B than those in Group-A (73.3% vs. 56.7%; 90% vs. 73.3%; 23.3% vs. 13.3%; 56.7% vs. 43.3%; 40% vs. 33.3% and 36.7% vs. 13.3% respectively). However, patients with arrhythmia was two-times higher in Group-A compared to Group-B (13.3% vs. 6.7%). The blood urea, serum creatinine and RBS were almost similar in distribution between groups (30.9±6.2 vs. 30.5±5.8 mg/dl, p = 0.767; 0.9±0.2 vs. 1.0±0.2 mg/dl, p = 0.318 and 9.5±2.1 vs. 9.9±2.7mg/dl, p = 0.503 respectively) (Table I).

Intra-operative outcome:

In Group-A, 70% of the patients required 3 grafts and 16.7% needed 2 grafts, while in Group-B, 56% of the patients needed 3 grafts and in 36.7% needed 2 grafts.

However, no significant difference was observed between the groups in terms of number of grafts needed (p = 0.299). The total operative time was significantly higher in the Group-B than that in Group-A (p < 0.001) .

Postoperative outcome:

After CABG 20% patients in Group-B developed atrial fibrillation as opposed to 6.7% in Group-A (p = 0.127). Blood urea and serum creatinine were significantly raised in Group-B than those in Group-A (p < 0.001 and p = 0.037 respectively). Average ventilation time, length of ICU stay and hospital stay were higher in the Group-B than those in Group-A (p < 0.001 and p = 0.006 and p < 0.001 respectively). The incidences low cardiac output syndrome and renal failure were observed to be significantly higher in the former group than those in the latter group (p = 0.038 and p = 0.044 respectively).

Table-I

Comparison of preoperative variables between groups

Preoperative variables	Group		χ^2/t	df	p-value[#]
	Group-A (n = 30)	Group-B (n = 30)			
Smoking habit[#]					
Present	17(56.7)	22(73.3)	1.832	1	0.176
Absent	13(43.3)	8(26.7)			
HTN[#]					
Present	22(73.3)	27(90.0)	2.783	1	0.095
Absent	8(26.7)	3(10.0)			
PVD[#]					0.317
Present	4(13.3)	7(23.3)	1.002	1	
Absent	26(86.7	23(76.7)			
Past MI[#]					0.302
Present	13(43.3)	17(56.7)	1.067	1	
Absent	17(56.7)	13(43.3)			
Dyslipidemia[#]					
Present	11(36.7)	13(43.3)	0.278	1	0.598
Absent	19(63.3)	17(56.7)			
Left main disease[#]					
Present	10(33.3)	12(40.0)	0.287	1	0.592
Absent	20(66.7)	18(60.0)			
Arrhythmia*					
Present	4(13.3)	2(6.7)	0.741	1	0.335
Absent	26(86.7)	28(93.3)			
Blood urea[§]	30.9 ± 6.2	30.5 ± 5.8	0.298	58	0.767
Serum creatinine[§]	0.9 ± 0.2	1.0 ± 0.2	0.659	58	0.318
RBS[§]	9.5 ± 2.1	9.9 ± 2.7	0.674	58	0.503

Table-II

Comparison of postoperative outcome between groups

Postoperative outcome	Group		χ^2	df	p-value[#]
	Group-A (n = 30)	Group-B (n = 30)			
Atrial fibrillation*					
Present	2(6.7)	6(20.0)	3.158	1	0.127
Absent	28(93.3)	24(80.0)			
Blood urea§	34.7 ± 6.3	52.0 ± 20.7	4.349	58	< 0.001
Serum creatinine§	1.27 ± 0.73	1.79 ± 1.13	2.133	58	0.037
Low cardiac output syndrome*					
Present	2(6.7)	8(26.7)	4.356	1	0.038
Absent	28(93.3)	22(73.3)			
Local infection*					
Present	2(6.7)	4(13.3)	0.741	1	0.335
Absent	28(93.3)	26(86.7)			
Non-sternal infection*					
Present	2(6.7)	3(10.0)	0.218	1	0.500
Absent	28(93.3)	7(90.0)			
Deep sternal infection*					
Present	0(0.0)	1(3.3)	1.017	1	0.500
Absent	30(100.0)	29(96.7)			
Hospital stay§	10.1 ± 1.7	13.4 ± 3.3	4.891	58	<0.001
Early mortality*					
Present	1(3.3)	2(6.7)	0.351	1	0.500
Absent	29(96.7)	28(93.3)			
Renal failure*	1(3.3)	6(20.0)	4.231		0.044
Present					
Absent	29(96.7)	24(80.0)			
CVA*					
Present	1(3.3)	2(6.7)	0.351	1	0.500
Absent	29(96.7)	28(93.3)			
Ventilation time§ (min)	6.8 ± 0.7	14.2 ± 0.9	14.24	58	<0.001
Length of ICU stay§ (hours)	32.4 ± 4.7	40.3 ± 5.8	4.616	58	0.006
Pulmonary complications*	3(10.0)	5(16.7)	1.531	1	0.353
Present					
Absent	27(90.0)	25(83.3)			

\# Data were analyzed using χ^2 Test. * Fisher Exact Test was done to analyzed the Data.

Data were analyzed using Student's t-Test and were presented as mean ± SD.

NYHA functional class, 3 months after CABG:

Evaluation of patients by NYHA functional class, 3 months after CABG shows that 90% of the patients of Group-A and 80% of Group-B had NYHA functional
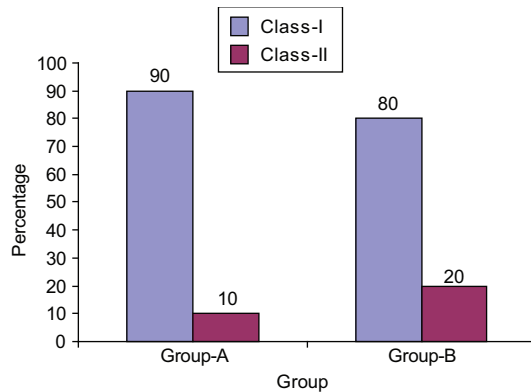

Fig.-2: *NYHA functional Class 3 months after CABG*

CCS class, 3 months after CABG:

Evaluation of patients by CCS class, 3 months after CABG revealed that that 93.3% of the patients in Group-A and 83.3% in Group-B fell in CCS Class-I.
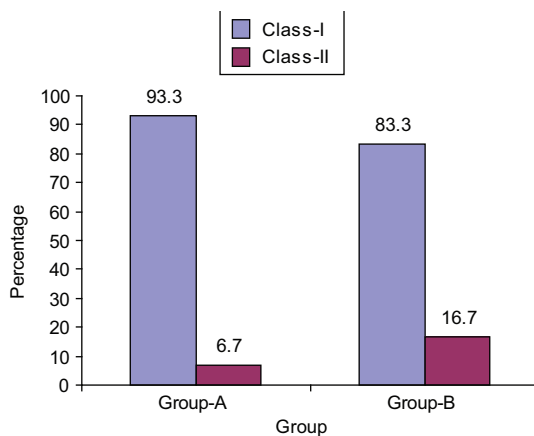

Fig.-3: *Distribution of CCS Class, 3 months after CABG*

Discussion:

The predictive role of hemoglobin A1c on short-term outcomes after coronary artery bypass graft surgery has not been evaluated in our country. It has been reported hemoglobin A1c is useful in predicting both early and late outcomes after CABG operations. Diabetes mellitus has become a major health issue and contributes to morbidity and mortality from coronary artery disease. Despite lifestyle changes and medications that have

been shown to decrease complications and death, many persons have poor glycemic control. This study evaluates the early post operative outcomes of CABG surgery in terms of mortality and major post-operative morbidities like deep sternal wound infection, sepsis, stroke, renal failure in patients with preoperative elevated level of HbA1c.

Data of different preoperative, peroperative and postoperative variables were collected by interview schedule, investigations, hospital records and were put in questionnaire and entered into computer.

The data obtained from the study were analyzed by computer based SPSS (statistical program for social science) programme and tested by Chi-square (χ^2) Test, Fisher Exact Test, and Student's t- Test.

Pre operative data shows Smoking habit, hypertension, PVD, past myocardial infarction, dyslipidemia, left main disease and COPD were higher in Group-B than those in Group-A (75.9% vs. 56.7%; 90% vs. 73.3%; 23.3% vs. 13.3%; 56.7% vs. 43.3%; 40% vs. 33.3% and 36.7% vs. 13.3% respectively).

The blood urea and serum creatinine were almost similar in distribution between groups (30.9±6.2 vs. 30.5±5.8 mg/dl, p = 0.767; 0.9±0.2 vs. 1.0±0.2 mg/dl, p = 0.318 S)

Pre operative data shows there was no significance of difference between two groups that can hamper result.

Per operative and post operative result data shows most of the patients required 3 grafts in both groups, total mean operative time was 261.3±32.4 minutes in group-A and 298.5±36.2 minutes in group-B. Operative time was significantly higher in group-B (p<0.001).

Blood urea and serum creatinine were significantly raised in Group-B (p<0.001, P=0.037). Average ventilation time, length of ICU stay and hospital stay were higher in the Group-B than those in Group-A.

Two patients developed low cardiac output syndrome in group-A and 8 patients in group-B (p=0.038) it was significant in group-B.

One patient developed renal failure in group-A and 6 patients in group-B it was significantly higher in group-B (p=0.044).

Our study demonstrates early outcome of CABG surgery in patients with preoperative elevated level of HbA1c with DM. Post-operative blood urea, serum creatinine and renal failure were significantly higher in patients with preoperative elevated HbA1c. Period of mechanical ventilation, ICU and hospital stay all were significantly

higher in patients with preoperative elevated HbA1c. There was significant difference between groups so, null hypothesis is rejected and alternative hypothesis is accepted.

From this study it can be concluded that preoperative elevated HbA1c is predictive of worse post operative outcome in patients with DM undergoing CABG surgery.

Conclusion:

This was a prospective observational study done in NICVD from January 2009 to December 2010. Sample size was 60, and sample was selected purposefully . among the 60 patients with coronary artery disease with DM 30 patients with preoperative HbA1c < 7% (group: A) underwent CABG surgery and the rest 30 patients with preoperative HbA1c > 7% (group:B) underwent CABG surgery. Data of different preopective ,peroperative and postoperative variables were collected by interview schedule and checklist. They were analyzed by spss programe and tested by Chi-square ((Ç2) test , Fisher Exact Test, and Student's t-test. Our study demonstrates early outcome of CABG surgery in patients with preoperative elevated level of HbA1c with DM . Pulmonary complications ,infective complications and arrhythmias were more common among patients with elevated HbA1c. Postoperative blood urea , serum creatinine and renal failure were significantly higher in patients with preoperative elevated HbA1c . Period of mechanical ventilation , ICU stay and hospital stay all were significantly higher in patients with preoperative elevated HbA1c .

From this study it can be concluded that preoperative elevated HbA1c is predictive of worse postoperative outcome in patients with DM undergoing CABG surgery.

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