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A study of HbA1c levels and outcome after cardiothoracic surgeries in the tertiary care hospitals

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Abstract
Introduction : Previous clinical studies have reported that clinical outcomes after myocardial revascularization are significantly worse in diabetic patients than in non-diabetic patients. Only few studies have reported the impact of baseline HbA1c levels on outcomes for diabetic patients after CABG. This retrospective hospital data based study therefore aimed to investigate whether preoperative HbA1c levels in diabetic patients are predictive of outcomes after off-pump CABG. **Methods:** Retrospective, Comparative & Analytical study. The data of inbound patients that required surgical operation was acquired from patients' record Randomization was done using computer tables in selecting data. All patients were stratified into two groups, depending on their preoperative HbA1c, Group 1 with HBA1C level < 7%, and group 2 with level >7%. Intraoperative and postoperative adverse events were recorded from hospital data. Complications like arrhythmias, cerebrovascular accidents, bleeding, renal dysfunction, perioperative myocardial ischaemia, etc. were documented. The two groups of patients were analysed concerning their demographic data, surgical risk, mortality, and morbidity. **Results:** Number of patients with severe LV dysfunction / Reduced EF were considerably & significantly high in group of Raised HbA1c along with the number of Hypertensive, Diabetics & Arrhythmias. The results of this study suggest that poor preoperative glycaemic control (HbA1C $\geq$7%) is a predictor of morbidity after CABG in terms of cardiac accidents, surgical site infections, need for dialysis, prolonged mechanical ventilation, prolonged hospital stay etc. **Conclusion:** In our opinion, preoperative HbA1c level is a strong predictor of morbidity after CABG. In elective situations, it has been proposed that these patients should be delayed for surgery until adequate glycaemic control is achieved. More prospective randomized long-term studies must be designed to study the adverse perioperative outcomes of diabetes in terms of preoperative HbA1c levels.
Keyword : Retrospective analysis , HbA1c % , CABG , Diabetes Mellitus.

Introduction

Diabetes mellitus (DM) 8.7% of the adult community in India, and its preponderance is rising[1]. Diabetes mellitus (DM) is an established risk factor for the development of coronary artery disease (CAD) and approximately 20% to 30% of the patients undergoing coronary artery bypass graft operation (CABG) have DM[2].Diabetes is also an independent risk factor for complications after cardiac surgery.Haemoglobin A1c (HbA1c) is a convenient and well-known biomarker in clinical practice. Poor glycaemic control, measured by glycosylated haemoglobin A1C (HbA1c), is associated with high incidence of micro and macro-angiopathy[1].

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Glucose in the blood binds to haemoglobin irreversibly to form a stable HbA1c complex. It illustrates the patient's prevailing sugar control over the past 120-150 days. Blood glucose levels regulate the glycosylation process of red blood cells. Given the lifespan of red blood cells, (90 to 120 days), continuous cell turnover and fluctuating glucose levels lead to a portion of HbA1c (normal range 4.0-5.9%) within the blood being glycosylated. Thus a measurement of the percentage of glycosylated haemoglobin complexes would be indicative of the patient's glucose levels over the previous 3 to 4 months. This is substantially more informative than a single blood glucose reading which is very labile and dependent on shortterm changes in diet and metabolic demands. As such, it has been deemed the gold standard for monitoring diabetic control[3]. HbA1c levels less than 7% are recommended by The American Diabetes Association a (ADA) and this is associated with reduced risk of complications related to diabetes mellitus[4]. Euro SCORE and American STS SCORE do include diabetes in the risk

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factors[5] but HbA1c level is not included as a risk indicator for cardiac surgery in any of the above mentioned preoperative risk scores. Previous clinical studies have reported that clinical outcomes after myocardial revascularization are significantly worse in diabetic patients than in non-diabetic patients.The morbitity and mortality levels of diabetic patients increased by 5-10 fold in post operation stage[6]. Only few studies have reported the impact of baseline HbA1c levels on outcomes for diabetic patients after CABG. This retrospective hospital data based study therefore aimed to investigate whether preoperative HbA1c levels in diabetic patients are predictive of outcomes after off-pump CABG .

Methodology

This Retrospective,Comparative & Analytical study involved Prior Consent from Hospital Authorities / Medical Superintendents of the Randomly selected Private Tertiary care hospitals in CG and Raipur to see the records of the patients from Medical Records Department (MRD) with the disclosure that we will use the data for study purpose only Identity(Names) were hidden & Medical record numbers were used to generate the data for analysis. The files containing information about the patients that CABG had been applied between previous 4 years were retrospectively analysed in a course of 6 months. The data of inbound patients that required surgical operation was acquired from patients' records. The study was conducted within ethical standards & doesn't involved any direct Intervention to any mentioned subjects nor any physical Examination was performed. Randomization was done using computer tables in selecting data. All Patients data had details of standard clinical examinations, routine biochemical and haematological investigations, including prior Echocardiography and Angiography. Diabetes mellitus was defined[4] as continuous plasma glucose level ≥200 mg/dl, fasting plasma glucose level ≥126 mg/dl, 2-h plasma glucose levels in the 75 g oral glucose tolerance test ≥200 mg/dl, HbA1c level ≥6.5%, or treatment with oral hypoglycaemic drugs or insulin injection.Those patients with coronary artery disease and coronary angiography and those who have been applied CABG in elective conditions as well as those patients whose haemoglobin (HbA1c) level was observed were accepted into study.The patients with the following were not included in the study; Myocardial infarction that was had three weeks before the operation, urgent operation, cardiogenic shock,

reoperation, left ventricular aneurysm reconstruction, CABG in beating heart, valve reconstruction or replacement, atrial fibrillation, renal failure and dialysis, those male patients with haemoglobin levels below 13 ml/dl, and women with 12 mg/dl and those patients with unacceptable thyroid test results.For the purpose of the present study, data of 100 of the randomly selected patients(candidates/study subjects) were retrospectively identified. The medical records for these patients were reviewed for the collection and classification. All patients were stratified into two groups, depending on their preoperative HbA1c, Group 1 with HBA1C level < 7%, and group 2 with level >7%.The hospital stay and the final outcome of the patient were noted.The performed anaesthesia, surgery and cardiopulmonary perfusion (CPP) methods were the same for all of the patients included in this study. It was observed that all patients were given general anaesthesia with intravenous induction with fentanyl, propofol, midazolam and vecuronium. All patients received intravenous antifibrinolytic agent(tranexamic acid) before skin incision. All surgeries were done with midline sternotomy incision. Anticoagulation was achieved with intravenous heparin. Intraoperative hyperglycaemia was observed to be managed with continuous insulin infusion to maintain target sugar level between 120 mg/dl to 180mg/dl. Postoperative glycaemic control was managed with either continuous infusion or subcutaneous boluses according to sliding scale. Intraoperative and postoperative adverse events were recorded from hospital data. Complications like arrhythmias, cerebrovascular accidents, bleeding, renal dysfunction, perioperative myocardial ischaemia, etc. were documented. The two groups of patients were analysed concerning their demographic data, surgical risk, mortality, and morbidity.Continuous data were expressed as mean ± standard deviation (SD) . The data were analysed by IBM SPSS Statistics 23. All quantitative data were coded and transformed into an excel master sheet for computer programming. A chi-square test was used to evaluate categorical variables for analysis.Overall, $p< 0.05$ was proposed to represent statistical significance after correction.

Results
Demographic and preoperative data of the patients are shown in Table 1. In terms of laboratory values; each patient's fasting blood glucose (FBG) displayed considerable difference between Group 1 and Group 2

Table 1 : Pre Operative Clinical Variables between the two groups

Clinical Variables affecting Outcome	HbA1c < 7.0% (n=50) Group 1	HbA1c >7 % (n=50) Group 2	P value
Age (Avg Mean)	59±2.31 years	65 ±3.53 years	0.2
Gender	M=36 (72%) F= 14 (28%)	M=32(64%) F=18(36%)	0.17
Hypertension / Raised BP	15 (30%)	34 (68%)	0.04 (Significant)
Diabetes	11(22%)	38 (76%)	0.001 (Significant)
CABG	31 (62%)	34(68%)	0.7
MVR	7 (14%)	9 (18%)	0.38
AVR	2 (4%)	5 (10%)	0.95

CABG ± MVR	0 (0%)	2(4%)	0.02 (Significant)
CABG ± AVR	5 (10%)	3 (6%)	0.14
DVR	5 (10%)	2 (4%)	0.27
LMCAS	19 (38%)	16 (32%)	0.6
EF (≤35)	1 (2%)	8 (16%)	0.026 (Significant)
Arrhythmias	6 (12%)	11 (22%)	0.04 (Significant)
CPB	17 (34%)	15 (30%)	0.47

(CABG - Coronary artery bypass grafting , MVR - Mitral valve replacement , AVR-Aortic Valve Replacement , DVR – Double valve replacement , LMCAS - left main coronary artery (LMCA) stenosis , EF - Ejection fraction , CPB- Cardiopulmonary bypass)

Number of patients with severe LV dysfunction / Reduced EF were considerably & significantly high in group two compared to group 1 (P value 0.03) along with the number of Hypertensive , Diabetics & Arrhythmias

Table 2:Per-operative outcomesbetween the two groups

Intra-operative Variables affecting Outcome	HbA1c < 7.0% (n=50) Group 1	HbA1c >7 % (n=50) Group 2	P value
Arrhythmias	16 (32%)	17 (34%)	0.1Not Significant (NS)
ST Segment elevations (New)	3 (6%)	2	0.61 (NS)
Requirements of Transfusion	11 (22%)	13	0.94(NS)
Inotropes requirements more than two	19 (38%)	21	0.38(NS)
IABP	2 (4%)	3	0.59(NS)
Deaths	1 (2%)	1	0.8(NS)

Table 3 : In-Hospital Variables affecting the outcome

In-Hospital Variables affecting Outcome	HbA1c < 7.0% (n=50) Group 1	HbA1c >7 % (n=50) Group 2	P value
Renal Failure requiring Dialysis	0	2	0.02 , Significant
Infection	0	2	0.02 , Significant
Prolonged Ventilation	1	8	0.01, Significant
Cerebrovascular accidents	0	0	Not Significant
Cardiac Accidents	0	2	0.01 Significant
Re-exploration	1	1	
Re- Intubation	0	1	0.03 , Significant
Requirement of Tracheostomy	1	1	Not Significant
Length of Hospital stay	6.5 days	8.1 days	0.38 Not Significant
Death	1	1	Not significant

Discussion

The results of this study suggest that poor preoperative glycaemic control (HbA1C ≥7%) is a predictor of morbidity after CABG in terms of cardiac accidents, surgical site infections, need for dialysis, prolonged mechanical ventilation, prolonged hospital stay etc.The majority of adult cardiac surgeries are CABGs, involving elderly patients with multiple comorbidities. Diabetes and hypertension are the known risk factors for coronary artery disease. More often , diabetes is diagnosed when the patient comes for CABG surgery. In the present study, we retrospectively evaluated data of 100 patients undergoing elective cardiac surgeries. Intraoperative and postoperative adverse events were recorded from hospital data. Complications like arrhythmias, cerebrovascular accidents, bleeding, renal dysfunction, perioperative myocardial ischaemia, etc. were documented. The two groups of patients were analysed concerning their demographic data, surgical risk, mortality, and morbidity. In a recent study consisting of 501 patients, it was reported that poor glycemic control (baseline HbA1c) prior to ischemic stroke is an independent risk factor for poor survival and a marker for increased stroke severity and unfavorablelong-term functional outcome[7]. In our study, 49 patients of 100 had diabetes. In patients with HBA1c >7 %, 76% of patients had diabetes and 24 % were undiagnosed diabetics, and they were not on any hypoglycaemic medication. Many studies, which compared diabetic and non-diabetic patients after coronary revascular-ization surgery have generated conflicting results[8,9]. Calafiore and colleagues, in their study proved that diabetes mellitus was an independent risk factor for early cardiac mortality and morbidity[9]. Rajakaruna et al, found comparable mortality outcomes in diabetic and non-diabetic patients[8]. Study done by Kubal et al reported that diabetic patients who were on insulin had increased postoperative complications than the patients who had mere history of diabetes[10]. The study done by Carson and colleagues compared outcomes in 41,663 diabetic patients with 1,05,123 non diabetic patients and found a near 30% increase in overall complications rate in diabetic patients compared non-diabetic patients[11]. Furnary and colleagues, reported that glycaemic control by continuous insulin infusion in perioperative period reduced mortality and infection rate among diabetic patients[12,13]. Preoperative HbA1c level still emerged as an independent predictor of mortality and wound infection after CABG in the

multivariate analysis, even after adjusting for mean glucose levels on the day of surgery and the first three postoperative days[14]. In our study Number of patients with severe LV dysfunction / Reduced EF were considerably & significantly high in group two compared to group 1 (P value 0.03) along with the number of Hypertensive , Diabetics & Arrhythmias in Pre Operative Clinical Variables between the two groups.Renal Failure requiring Dialysis , Surgical site Infection,Prolonged Ventilation period , Cardiac accidents and reintubation were SignificantIn-Hospital Variables affecting the outcome. Knapik et al[15] reported a retrospective review in 782 diabetic patients. For comparison of outcomes, patients were matched to achieve similar preoperative status with a use of a Greedy matching procedure. For matched patients elevated HbA1c levels >7% were significantly associated with increased incidence of perioperative myocardial infarct (MI) compared with the HbA1c.Alserius et al[16] conducted a prospective study correlating HbA1c concentrations with infection rate and mortality outcomes in 605 patients. Rates of superficial sternal wound infection were significantly increased in patients with HbA1c ≥6% (13.9% HbA1c ≥6% vs 5.2% when HbA1c.In this study, it was found that there was a significant relationship between HbA1c levels and the development of infection among the patients who had coronary artery bypass surgery.Some studies have pointed at diabetes as a risk factor for a poor outcome of operative mortality following CABG[10]. Similar to our findings, in some other studies, no significant relationship was found between diabetes and mortality[17,18].It is plausible from these data that HbA1c is also an independent predictor of postoperative adverse events that is not entirely due to intra and postoperative glucose control. More aggressive glucose management should be used in these patients in the perioperative period. Current guidelines according to the American Diabetes Association recommend HbA1c screening of diabetic patients as frequently as every three months in patients with elevated HbA1c levels (>7%) or in patients with medication adjustments to ensure an adequate treatment regimen[19] Current recommendations suggest that patients with diabetes aim to achieve HbA1c levels of at least less than 7%. We chose to order HbA1c for all patients to determine whether this approach would identify patients who had uncontrolled hyperglycaemia without a previous diagnosis of diabetes mellitus[20,21].

It is possible that a preoperative HbA1c level may provide more accurate prognostic information about outcomes after all major open cardiac surgeries compared with a diabetes status alone.

Conclusion

In our opinion, preoperative HbA1c level is a strong predictor of morbidity after CABG. In elective situations, it has been proposed that these patients should be delayed for surgery until adequate glycaemic control is achieved. More prospective randomized long-term studies must be designed to study the adverse perioperative outcomes of diabetes in terms of preoperative HbA1c levels.

Study limitations

The main limitations of this study include its retrospective design(data of past admitted patients) with a limited number of participants (n=100). We have not studied the longterm outcomes, and it may be that although we are not seeing any difference in short-term outcomes, they may become apparent in the long term. The strengths of our study include presence of an adequate control group consisting of non-diabetic patients.

Acknowledgement

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