# Prevalence of Abnormal Glucose Regulation in Patients with Coronary Artery Disease.

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#### **ABSTRACT**

**Background:** To find out that oral glucose tolerance test (OGTT) is useful for characterization of the glucose metabolism. And To assess the correlation between abnormal glucose regulation and coronary artery disease (CAD) in Bangladeshi patients. **Methods:** This study was carried out in University Cardiac Centre, Bangabandhu Sheikh Mujib Medical University (BSMMU) from June 2004 to May 2005. Total 200 consecutive patients with CAD and 100 normal subjects were included in this study. Subjects with known diabetes were excluded from the study. Patients with CAD were chosen as case and normal subjects without ischemic heart disease were taken as control. Oral glucose tolerance test (OGTT) was done and results were compared between the groups. This research was done with the research grant from University Grant Commission. **Results:** Incidence of impaired glucose tolerance (IGT) and diabetes mellitus (DM) were significantly high (P = 0.0001 and P = 0.001) in patients with CAD. The incidence of impaired fasting glucose (IFG) was also higher (P = 0.453) in the CAD patients than normal group. In this study, patients with CAD without previous diagnosis of DM had a high prevalence of abnormal glucose tolerance test than normal subjects. **Conclusion:** In this study, patients with CAD without previous diagnosis of DM had a high prevalence of abnormal glucose tolerance test than normal subjects. The risk of developing CAD is continuously related to blood glucose level whether it is pre diabetic, IGT, IFG or frank DM.

Keywords: Oral glucose tolerance test, coronary artery disease, impaired glucose tolerance, impaired fasting glucose.

#### INTRODUCTION

Assessment of glucose tolerance may be needed in patients with coronary artery disease in search of appropriate diagnostic level to define impaired glucose tolerance as a risk factor from macro vascular disease. The traditional risk factors are not sufficient to explain all the epidemiological variables that occur with coronary artery disease.(CAD).<sup>[1-3]</sup> Some alternative proposals such as infective-inflammatory origins, low birth weight and insulin resistance have been examined as risk factor for CAD. As a matter of fact chronic infection and low birth weight may influence these effects on CAD by developing insulin resistance.<sup>[1-6]</sup>

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The importance of insulin resistance state has been highlighted by the American Diabetic Association (ADA) revised criteria by changing the plasma level of blood glucose in the diagnosis of diabetes where the set level for diagnostic criteria for diabetes has been brought down from 7.8 mmol/L to 7 mmol/L (Venous plasma).<sup>[7]</sup> Even more

aggressive screening by using fasting glucose level of ≥110 mg/dL (6.2 mmol/L) as a marker of insulin resistance has been suggested by others to identify not only the patients with hyperglycemia but also those with insulin resistant without significant hyperglycemia at risk of developing macrovascular complications. [8] We tried to assess the glucose intolerance pattern among the patients with known CAD. It seems that this part of the world is the right place to search and confirm glucose intolerance as a risk factor of CAD. Bangladesh as a country of huge population can give us a scenario about the relationship between glucose intolerance and CAD.

#### MATERIALS AND METHODS

This observational cross sectional study was carried out in department of Cardiology, BSMMU from June 2004 to May 2005. Patients and normal subjects with known diabetes were excluded from the study. Brief medical history about the risk factors for CAD like- hypertension, diabetes, smoking, dyslipidaemia, h/o angina, any clinical and ECG evidence of ischemic heart disease, peripheral artery disease, h/o of stroke, h/o coronary intervention etc. were taken from both groups. Patients with CAD

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were chosen as case and normal subjects without ischemic heart disease were taken as control. Total 200 consecutive patients with CAD as case and 100 normal subjects as control were included in this study. All of them consented to participate in the study. Oral glucose tolerance test (OGTT) was done in both groups and then compared. The test was done in the Laboratories of BSMMU. Interpretation of OGTT:<sup>[9]</sup> Normal glucose regulation: Fasting: <6 mmol/l and two hours after glucose:<7.8 mmol/l. Impaired fasting glucose (IFG): Fasting ≥6.1 mmol/l, but <7 mmol/l & two hours after glucose <7.8 mmol/l. In impaired glucose tolerance (IGT): Fasting <7 mmol/l and two hours after glucose ≥7.8 mmol/l, but <11.1 mmol/l. In Diabetes mellitus (DM): Fasting ≥7 mmol/l or, two hours after glucose ≥11.1 mmol/l.

#### **Statistical Analysis:**

Statistical analysis was conducted using SPSS 11.5 for windows software. Categorical data were expressed as frequencies and corresponding percentages. Parametric data were expressed in mean  $\pm$  SD. Parametric data were evaluated by independent sample "t" test and categorical data were evaluated by Chi-square test as needed. Level of significance for all analytical test were set at 0.05 and p value  $\leq$ 0.05 is considered significant.

#### **RESULTS**

Table 1: Demographic data of the study subjects

| Variables              | Case    |        | Control | P      |       |
|------------------------|---------|--------|---------|--------|-------|
|                        | (n=200) |        | (n=100) |        | value |
|                        | No.     | (%)    | No.     | (%)    |       |
| Age (years)            |         |        |         |        |       |
| Mean±SD                | 57.65   |        | 54.16   |        | 0.019 |
|                        | ±12.13  |        | ±11.93  |        | *     |
| Range                  | 30.0    | 85.0   |         |        |       |
| 33.086.0               |         |        |         |        |       |
| Sex                    |         |        |         |        |       |
| Male                   | 159     | (70.7) | 66      | (29.3) | 0.000 |
| (n=225)                |         |        |         |        | 1***  |
| Female                 | 41      | (54.7) | 34      | (45.3) | 0.488 |
| (n=75)                 |         |        |         |        | ns    |
| BMI (mg/k <sup>2</sup> |         |        |         |        |       |
| Mean±SD                | 23.93   |        | 23.83   |        | 0.783 |
|                        | ±2.99   |        | ±3.09   |        | ns    |
| Range                  | 16.0    | 33.7   |         |        |       |
| 16.033.7               |         |        |         |        |       |
| SBP (mmHg              |         |        |         |        |       |
| Mean±SD                | 137.65  |        | 135.45  |        | 0.235 |
|                        | ±14.08  |        | ±15.58  |        | ns    |
| Range                  | 110.0   | 160.0  |         |        |       |
| 110.0160.              |         |        |         |        |       |
| 0                      |         |        |         |        |       |
| DBP (mmH               | ý.      |        |         |        |       |
| Mean±SD                | 87.40   |        | 85.93   |        | 0.183 |
|                        | ±9.39   |        | ±9.31   |        | ns    |
| Range                  | 70.0    | 100.0  |         |        |       |
| 70.0110.0              |         | ar. 1  |         |        |       |

Comparison between mean $\pm$ SD values done by unpaired Student's 't' test, and comparison between categorical values done by Ztest ns = Not significant, \* = Significant at P<0.05, \*\*\* = Significant at P<0.001.

Table 1 shows the age distribution and BMI were almost identical between the case  $(57.65\pm12.13)$  and

the control (54.16±11.93) groups. Cases are mostly male patients. Both systolic and diastolic pressure were higher in case group.

Table 2. Medical History of Patient group (n=200)

| Medical History               | Case No. | (%)    |
|-------------------------------|----------|--------|
| ST elevated MI                | 12       | (6.0)  |
| Non ST elevated MI            | 4        | (2.0)  |
| Q wave MI                     | 113      | (56.5) |
| Unstable angina               | 22       | (11.0) |
| Stable angina with ECG change | 26       | (13.0) |
| Elective CAG                  | 23       | (11.5) |
| Medication                    | 90       | (45.0) |
| Peripheral artery disease     | 53       | (26.5) |
| Stroke                        | 18       | (9.0)  |
| Smoking                       | 94       | (47.0) |
| Hypertwntion                  | 124      | (62.0) |
| Dyslipidaemia                 | 54       | (27.0) |

The medical history among case group – more than half (56.5%) of the patients were presented with Q wave MI. Hypertension and smoking were the most common risk factors in case group.

Table 3: Risk factors of the study subjects

| Risk factors                   | Case |        | Control |        | P Value   |
|--------------------------------|------|--------|---------|--------|-----------|
|                                | No.  | (%)    | No.     | (%)    |           |
| Smoking (n=127)                | 94   | (74.0) | 33      | (26.0) | 0.0001*** |
| Hypertension (n=191)           | 124  | (64.9) | 67      | (35.1) | 0.0001*** |
| Dyslipidaemia<br>(n=77)        | 54   | (70.1) | 23      | (29.9) | 0.001**   |
| Diabetes<br>mellitus<br>(n=24) | 21   | (87.5) | 3       | (12.5) | 0.0001*** |

Comparison between categorical values done by Ztest. \*\* = Significant at P<0.01, \*\*\* = Significant at P<0.001.

Table 3 indicates that the presence of the modifiable risk factors - smoking, hypertension, dyslipidaemia, diabetes are significantly high in the case group than the control.

Table 4: Status of OGTT of the study subjects:

|            | į į  |        |         |        |                     |
|------------|------|--------|---------|--------|---------------------|
| OGTT       | Case |        | Control |        | P value             |
|            | No   | (%)    | No.     | (%)    |                     |
| IFG (n=7)  | 5    | (71.4) | 2       | (28.6) | 0.453 <sup>ns</sup> |
| IGT (n=78) | 68   | (87.2) | 10      | (12.8) | 0.0001***           |
| DM (n=21)  | 18   | (85.7) | 3       | (14.3) | 0.001**             |

Comparison between categorical values done by Ztest. ns = Not significant, \*\*= Significant at P<0.01, \*\*\* = Significant at P<0.001.

Table 4 indicates that the presence of impaired glucose tolerance (IGT) and diabetes mellitus (DM) are significantly high in case group. The incidence of impaired fasting glucose (IFG) is also higher in the case group than the control, but is not statistically significant.

Table 5 states that total number of IFG/IGT/DM is significantly high in the case group (85.8%) than the control (14.2%).

#### **DISCUSSION**

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In this study mean age was almost same in both groups and male was more in case (patient) group (>70%) in comparison to control (normal subject) group (<30%). So, there is male predominance for CAD. (P = 0.0001) [Table-1]. More than half (56.5%) of the patients were presented with Q wave MI among case group. Hypertension and smoking were the most common risk factors in this group. [Table-2]. The incidence of risk factors, like smoking, hypertension, dyslipidaemia, diabetes mellitus all are significantly high in patient group. (P = 0.0001, P = 0.0001, P = 0.001 & P = 0.0001respectively). [Table-3]. After OGTT- the presence of IGT and DM were significantly higher (P = 0.0001 and P = 0.001) in case group than control group. IFG was also higher in case group than control, but this was not significant. (P = 0.453) [Table-4]. The presence of higher blood glucose level in the form of impaired fasting glucose (IFG), impaired glucose tolerance (IGT), diabetes mellitus (DM) were significantly high in CAD patients in comparison to control group. (P = 0.0001) [Table-5]. Bartnik et al also found that abnormal glucose regulation is more common in patients with coronary artery disease. [10] They demonstrated that the assessment of glucometabolic state among these patients should influence their future management because it has great potential to improve the outcome.

|                       | Case |        | Control |        | P value   |
|-----------------------|------|--------|---------|--------|-----------|
|                       | No   | (%)    | No.     | (%)    |           |
| IFG/IGT/DM<br>(n=106) | 91   | (85.8) | 15      | (14.2) | 0.0001*** |

Comparison between categorical values done by Ztest. \*\*\* = Significant at P<0.001

Hu et al suggested OGTTs should be done routinely to assess the risk of CAD as abnormal glucose regulation is common in CAD.<sup>[11]</sup>

In another study there were more than 60% of the patients in cardiac rehabilitation had impaired glucose metabolism and among them 18% of the patients would be misclassified if the OGTT was omitted.[12] Mulder et al also suggested that OGTT would be the best test to assess the presence of previously undiagnosed diabetes or impaired glucose metabolism in hyperglycaemic patients with ACS. [13] While these suggestions are being made at the developed world, the link between insulin resistance to CAD seems to be much relevant in this part of the world. Studies showed that this part of the world has got highest incidence of CAD and these people in this region has got more insulin resistant trait than others. [14-17] Singapore National Heart Survey has focused that insulin resistance (IR) may be major contributory factor among the Asian Indians towards development of CAD. They found that the Asian Indian had more IR traits among three ethnic groups

in Singapore and this ethnic difference in prevalence of IR could explain the differential CAD rate in Asian Indian. [17] A study showed abnormal glucose tolerance is an important determinant for long-term prognosis after coronary angioplasty but not the diameter of small vessels. [18] Taubert et al suggested screening for diabetes should be performed routinely as preventive efforts for high risk patients scheduled for coronary angiography. [19]

Bartnik et al also demonstrated abnormal glucose regulation has prognostic implications in patients with CAD and suggested an OGTT is the appropriate test for the clinical assessment of CAD patients. A study with patients undergoing vascular surgery found that preoperative OGTT could detect increased risk of developing cardiovascular events and mortality during long-term follow up. In another study of high risk population with multiple risk factors for CAD, English et al found high prevalence of abnormal glucose regulation in the form of IGT and overt DM. Almost two-thirds of patients with significant CAD had abnormal glucose regulation.

### **CONCLUSION**

The risk of developing CAD is continuously related to blood glucose level whether it is pre diabetic, IGT, IFG or frank DM. As there is increased incidence of CAD in this poverty stricken population, therefore glucose tolerance test can be a routine investigation for the primary prevention of the disease. OGTT should therefore, be a routine screening procedure as it easily discloses the glucometabolic state.

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