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Original Article

# Prevalence of Abnormal Glucose Regulation in Libyan Patients Presenting for Elective Coronary Angiography

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## Abstract

**Background:** Patients with coronary artery disease (CAD) frequently have multiple risk factors. Diabetes and impaired glucose tolerance (IGT) have been associated with cardiovascular events and cardiovascular disease mortality. **Aim of the study:** This study aims to determine the prevalence of abnormal glucose regulation (AGR) among Libyan patients, presenting for elective coronary angiography. **Methods:** All patients referred for a diagnostic coronary angiogram at the Catheterization Laboratory of National Heart Centre, Tajora, Tripoli, over a period of 1 year from April 2007 to March 2008, were included after consent. Patients with a history of diabetes were excluded from the study. Diagnostic coronary angiogram was performed for all included patients as well as a standard oral glucose tolerance test (OGTT) with 75 GM glucose. **Results:** Ninety-nine patients were included in our study, with a mean age of 54.6 ± 11.2 years. 49 (49.5%) of the enrolled patients showed either impaired or diabetic fasting or 2-h OGTT results. 22 (22.2%) patients were diabetic based on fasting blood glucose or 2-h OGGT result, and 21 (21.2%) have IGT. Of the 15 (15.2%) patients with impaired fasting glucose, 7 (46.7%) patient showed diabetic glucose tolerance, and 2 (13.3%) patients have IGT. Among patients with AGR, coronary angiogram showed significant CAD in 36 (73.5%), compared to 28 (56%) of patients with normal fasting and 2-h OGTT results. **Conclusion:** Abnormal glucose regulation was high among Libyan patients presented for elective angiography. OGTT should be part of the evaluation in this high-risk population.

**Keywords:** Abnormal glucose regulation, coronary angiography, coronary artery disease, diabetes mellitus, Libya, oral glucose tolerance test

## Introduction

Diabetes mellitus (DM) has been identified as an independent risk factor for atherosclerotic cardiovascular disease (CVD).[1-3] In the Framingham Study, the incidence of CVD is 2–3 fold higher in diabetic patients compared with nondiabetic subjects.[4] In patients with stable angina, the prevalence of glucose disturbances ranges from 43 to even 78%.[5] Abnormal glucose regulation is frequently observed in patients with acute myocardial infarction (MI). The prevalence of DM among Libyan patients hospitalized with acute MI was 48.2%.[6] However, a large proportion of adults meeting the diagnostic criteria for diabetes do, remain undiagnosed.

The glucose tolerance in patients with acute MI (GAMI) study showed that a substantial percentage of patients with acute MI have undiagnosed abnormal glucose regulation (AGR).[7]

Mortality after MI is 2–4-times higher among diabetic patients than in the nondiabetic.[8,9] Diabetic patients who have had MI have a higher mortality rate both in the early phase and during long-term follow-up.[10] In a study of 14,703 patients with MI, previously and newly diagnosed diabetes was associated with increased mortality at 1 year, by 43% and 50%, respectively.[11]

The increased CVD risk extends to glucose regulation abnormalities antecedent to diabetes diagnosis.[12,13] The impaired glucose tolerance (IGT) category has been more associated with cardiovascular morbidity and mortality than fasting plasma glucose.[14,15] It has been suggested that an oral glucose tolerance test (OGTT) should be part of the evaluation of overall cardiac risk in patients with coronary artery disease (CAD). Several studies from different populations reported an increased the prevalence of AGR among patients

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referred for coronary arteriography and with no previous history of diabetes.

The primary aim of this study is to determine the crude prevalence of AGR and other cardiovascular risk factors among Libyan patients, presenting for elective coronary angiography. A secondary aim was to identify the association of cardiovascular risk factors with positive coronary angiography.

## Methods

All patients referred for a diagnostic coronary angiogram at the Catheterization Laboratory of National Heart Centre, Tajora, Tripoli, over a period of 1 year from April 2007, and March 2008, were included after consent. Patients with a history of diabetes were excluded from the study. This study was carried out in accordance with the principles of the Helsinki Declaration. A formal approval was obtained from institutional authorities.

Demographic data collected included age, gender, previous history of ischemic heart disease, and cardiovascular risk factors, including the family of history of DM, history of smoking, systolic blood pressure (SBP)/diastolic blood pressure (DBP) ≥140/90 mmHg, or a history of hypertension. Body mass index (BMI) was calculated as the body weight (kg) divided by the square of the height ($m^2$) as well as waist circumference and waist:hip ratio (W:H ratio).

Urea, creatinine, and fasting lipid profile (total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL), and triglyceride levels were measured. Diagnostic coronary angiogram was performed for all included patients as well as a standard OGTT with 75 g glucose.

Patients were divided into four categories depending on the results of the OGTT according to WHO guidelines:[16]

NFG <110 mg/dl, impaired fasting glucose (IFG) >110 but <126, DFG >126.

NGT <140 mg/dl, IGT >140 but <200, diabetic glucose tolerance (DGT) >200:

- Normal; NFG <110 mg/dl, and NGT <140 mg/dl
- IFG: FBG >110 but <126 and NGT <140 mg/dl
- IGT: 2-h PG >140 but <200
- DM: FPG >126 and/or a 2–h ≥200.

We also used the American Diabetes Association (ADA) criteria to know the percentage of patients with abnormal glucose tolerance who do not meet the ADA diagnostic criteria of IFG.[17] Coronary angiography results were classified as negative or positive (>1 vessel) CAD.

Data were analyzed using the Statistical Package for Social Science (SPSS Inc., IBM, US), 19th version. Continuous variables are expressed as mean ± standard deviation (SD) and range. Categorical data are expressed as numbers and percentages. Student's *t*-test or Mann–Whitney test was used to compare continuous variables, and qualitative variables were analyzed with the Chi-square test. The odds ratio (OR) and its 95% confidence interval (CI) were presented to show the risks. Multivariate logistic regression analysis, using a enter method, was performed to examine relations between outcome and risk factors. Only variables with $P < 0.05$ at the univariate analysis were included into multivariable logistic regression model. $P < 0.05$ were considered to be statistically significant.

## Results

During the study period, 101 patients with no history of DM underwent OGTT. All patients recruited were presenting for elective day case diagnostic coronary angiogram. Two patients have been excluded from the final analysis (Non-Libyan); the study subjects included 99 Libyan patients.

### Demographic and baseline risk factor profiles for all patients

The mean (±SD) age was 54.6 ± 11.2 years (range 28–75), and 67.7% were male. The mean (BMI) ± SD was 28.8 ± 5.3 kg/$m^2$ (range 20.0–46.4). 26.3% had normal BMI; 37.4% were overweight, 33.3% were obese and 3% were morbidly obese, 44.4% were smokers. 50.5% were hypertensive. All patients had a history of ischemic heart disease, stable angina in 37.4%, unstable angina in 23.2%, and MI in 39.4%. 44.4% had a family history of DM, and 21.2% had a family history of ischemic heart disease [Table 1].

### Coronary angiography results

Significant CAD was identified in 64.6% of patients based on results of coronary angiography; one-vessel disease in 28 (28.3%), two-vessel disease in 15 (15.2%), and three-vessel disease in 21 (21.2%). In 35 (35.4%), there was no significant stenosis in the coronary arteries.

Positive coronary angiography was significantly associated with male gender ($P = 0.00$), smoking ($P = 0.00$), high waist hip ratio ($P = 0.01$), high triglyceride level ($P = 0.04$), and high SBP ($P = 0.01$) [Table 1].

Multiple logistic regression analysis showed that male gender (OR, 0.201; 95% CI, 0.05–0.811; $P = 0.024$), and smoking (OR, 0.219; 95% CI, 0.056–0.854; $P = 0.029$), were independent risk factors for positive coronary angiography.

### Oral glucose tolerance test results

Of the total cohort of patients, 15 (15.2%) patients had IFG, which was defined as FPG between 110 and 126 mg/dl, 14 (14.1%) were diabetics fasting glucose (FPG >126) and 70 (70.7%) had normal fasting glucose results (FBG <110). Out of seventy patients with NFG 19 patients (27.1%) had IGT and one patient (1.4%) had DGT. Based on the results of the OGTT and according to the WHO criteria, 41 (41.4%) demonstrated disturbances of glucose regulation, 24 (24.2%) had IGT and 17 (17.2%) had type 2 diabetes.

**Table 1: Patient demographics demonstrating the age, gender, and risk factor profiles. Comparisons are made between those with coronary artery disease and those with no coronary artery disease on catheterization**

| | All (*n*=99) | Normal coronary angiography (*n*=35) | Abnormal coronary angiography (*n*=64) | *P* | OR (95% CI)* |
|---|---|---|---|---|---|
| Age, mean±SD | 54.6±11.2 | 52.5±12.3 | 55.8±10.6 | 0.27 | 1.03 (0.99-1.07) |
| Male sex, *n* (%) | 67 (67.7) | 12 (34.3) | 55 (85.9) | 0.00 | 0.09 (0.03-0.23) |
| BMI, mean±SD | 28.8±5.3 | 29.5±5.9 | 28.4±4.9 | 0.56 | 0.96 (0.89-1.04) |
| Waist: hip ratio, mean±SD | 0.9±0.1 | 0.9±0.1 | 1.0±0.1 | 0.01 | 278.85 (1.53-50933.25) |
| Systolic BP, mean±SD | 128.3±17.8 | 123.8±17.2 | 132.9±17.4 | 0.012 | 0.97 (0.95-1) |
| Diastolic BP, mean±SD | 80.2±9.4 | 78.4±8.3 | 82.1±10.1 | 0.109 | 0.97 (0.92-1.01) |
| Total cholesterol, mean±SD | 147.2±40.9 | 156.1±42.9 | 142.3±39.2 | 0.13 | 0.99 (0.98-1) |
| LDL-C, mean±SD | 87.9±27.9 | 91.3±29.2 | 86.0±27.1 | 0.45 | 0.99 (0.98-1.01) |
| HDL-C, mean±SD | 36.6±10.8 | 38.5±9.4 | 35.5±11.4 | 0.14 | 0.97 (0.94-1.01) |
| TG, mean±SD | 127.4±58.5 | 116.3±64.6 | 133.5±54.5 | 0.04 | 1.01 (1-1.01) |
| FBS, mean±SD | 101.0±28.4 | 96.1±25.7 | 103.6±29.7 | 0.09 | 1.01 (0.99-1.03) |
| 2-h plasma glucose, mean±SD | 139.8±63.8 | 130.2±51.2 | 145.1±69.6 | 0.43 | 1 (1-1.01) |
| Current Smoker, *n* (%) | 44 (44.4) | 4 (11.4) | 40 (62.5) | 0.00 | 0.09 (0.03-0.25) |
| Family history of DM, *n* (%) | 44 (44.4) | 13 (37.1) | 31 (48.4) | 0.28 | 0.63 (0.27-1.46) |
| HPN, *n* (%) | 50 (50.5) | 22 (62.9) | 28 (43.8) | 0.08 | 2.12 (0.91-4.93) |

*Estimated by univariate analysis. BMI: body-mass index, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol, TG: Triglyceride, DM: Diabetes mellitus, HPN: Hypertension, OR: Odds ratio, CI: Confidence intervals, SD: Standard deviation, BP: Blood pressure

Abnormal glucose regulation was significantly associated with high BMI (*P* = 0.008), high SBP (*P* = 0.012) and positive family history of DM (*P* = 0.012) [Table 2]. Multiple logistic regression analysis showed that SBP (OR, 1.032; 95% CI, 1.004–1.06; *P* = 0.025), and family history of diabetes (OR, 0.372; 95% CI, 0.15–0.92; *P* = 0.033), were independent risk factors for IGR.

### Relationship between coronary artery disease and abnormal glucose regulation

Nearly 48.4% of those with positive coronary angiography had an abnormal 2-h glucose compared to 28.6% in those with normal coronary angiography results [Figure 1].

More patients with CAD and impaired glucose regulation were identified based on the glucose challenge; where 20.3% had overt DM diagnosed after a glucose challenge compared with 14.1% with DM based on an FPG [Figure 1].

The association between the presence of CAD and AGR was most significant among men than female gender with a *P* = 0.013 versus 0.694, respectively.

### Fasting glucose versus 2-h plasma glucose

On comparing the overlap of the FPG and the 2-h glucose, almost half (48.8%) of the patients with an abnormal 2-h glucose had normal fasting plasma glucose [Table 3]. Twenty-one individuals (21.2%) met both criteria, with an abnormal FPG and abnormal 2-h glucose [Table 3]. Even with the use of a low cutoff point of <100 mg/dl for defining the upper limit of normal FPG according to ADA criteria, 34.2% of the patients with an abnormal 2-h glucose had normal fasting plasma glucose [Table 3].

## Discussion

Our study showed higher rates of undiagnosed DM and impaired glucose regulation in Libyan patents presenting for coronary angiography than those seen in the general Libyan population. 49 (49.5%) of the total study population showed AGR. The percentage increased to 56.3% in those with a positive coronary angiogram. Even those with no significant CAD on catheterization 37.1% showed AGR. These proportions are higher than those reported in a Libyan population-based stepwise survey, which assessed the prevalence of cardiovascular risk factors among Libyans aged 25–64.[18]

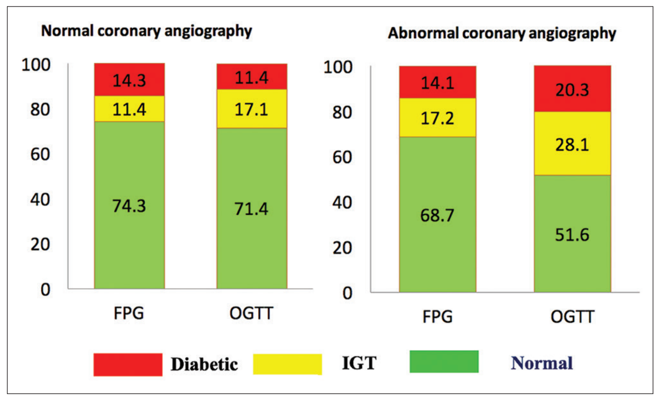


**Figure 1:** Relationship between coronary artery disease and abnormal glucose metabolism. CAD: Coronary artery disease, FPG: Fasting plasma glucose, OGTT: Oral glucose tolerance test.

The prevalence of type 2 diabetes and impaired glucose regulation in stepwise survey was 23.7%.[18]

### Relationship between coronary artery disease and abnormal glucose metabolism

Data from various studies showed that the prevalence of AGRs is considerably more common in patients with confirmed CAD than in the general population.[19,20] Patients with significant stenosis had higher fasting blood glucose (FPG), postload glucose, than individuals without or with nonsignificant stenosis.[21]

**Table 2: Subgroup characteristics according to glucometabolic category**

| | Normal glucose regulation ($n$=50) | Abnormal glucose regulation ($n$=49) | $P$ | OR (95% CI)* |
|---|---|---|---|---|
| Age, mean±SD | 53.2±12.3 | 56.0±10.0 | 0.244 | 1.02 (0.99-1.06) |
| Male sex, $n$ (%) | 34 (68) | 33 (67.3) | 0.945 | 1.03 (0.44-2.39) |
| BMI, mean±SD | 27.6±5.5 | 30.0±4.8 | 0.008 | 1.09 (1.01-1.19) |
| Systolic BP, mean±SD | 123.7±17.2 | 132.9±17.4 | 0.012 | 1.03 (1.01-1.06) |
| Diastolic BP, mean±SD | 78.4±8.3 | 82.1±10.1 | 0.109 | 1.05 (1.00-1.10) |
| Waist:hip ratio, mean±SD | 1.0±0.09 | 1.0±0.09 | 0.431 | 4.55 (0.05-407.88) |
| Total cholesterol , mean±SD | 146.7±38.1 | 147.6±43.9 | 0.911 | 1.00 (0.99-1.01) |
| LDL-C, mean±SD | 84.8±21.6 | 91.0±33.0 | 0.391 | 1.01 (0.99-1.02) |
| HDL-C, mean±SD | 37.1±11.1 | 36.0±10.5 | 0.687 | 0.99 (0.96-1.03) |
| TG, mean±SD | 115.2±42.0 | 139.9±69.8 | 0.112 | 1.01 (1-1.02) |
| FBS, mean±SD | 85.3±11.6 | 117.0±31.5 | 0.000 | 1.12 (1.07-1.17) |
| 2-h plasma glucose | 94.9±21.0 | 185.7±60.1 | 0.000 | 1.08 (1.05-1.11) |
| Family history of DM | 16 (32.0) | 28 (57.1) | 0.012 | 0.35 (0.16-0.80) |
| HPN, $n$ (%) | 21 (42.0) | 29 (60.4) | 0.068 | 0.47 (0.21-1.06) |
| Abnormal angiogram, $n$ (%) | 28 (56.0) | 36 (73.5) | 0.069 | 0.46 (0.20-1.07) |

*Estimated by univariate analysis. BMI: Body-mass index, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol, TG: Triglyceride, DM: Diabetes mellitus, HPN: Hypertension, OR: Odds ratio, CI: Confidence intervals, SD: Standard deviation, FBS: Fasting blood sugar, BP: Blood pressure

**Table 3: Distribution of 99 study subjects by fasting glucose and glucose tolerance categories according to world health organization (16) and American diabetes association (17) criteria**

| Fasting glucose category | Glucose tolerance category | | | Total, $n$ (%) |
|---|---|---|---|---|
| | NGT, $n$ (%) | IGT, $n$ (%) | DGT, $n$ (%) | |
| NFG | | | | |
| WHO | 50 (71.4) | 19 (27.1) | 1 (1.4) | 70 (100) |
| ADA | 46 (76.7) | 13 (21.7) | 1 (1.7) | 60 (100) |
| IFG | | | | |
| WHO | 6 (40.0) | 2 (13.3) | 7 (46.7) | 15 (100) |
| ADA | 10 (40.0) | 8 (32.0) | 7 (28.0) | 25 (100) |
| DFG | | | | |
| WHO | 2 (14.3) | 3 (21.4) | 9 (64.3) | 14 (100) |
| ADA | 2 (14.3) | 3 (21.4) | 9 (64.3) | 14 (100) |
| Total | | | | |
| WHO | 58 (58.6) | 24 (24.2) | 17 (17.2) | 99 (100) |
| ADA | 58 (58.6) | 24 (24.2) | 17 (17.2) | 99 (100) |

WHO: World health organization, ADA: American diabetes association, NFG: Normal fasting glucose, IFG: Impaired fasting glucose, DFG: Diabetic fasting glucose, NGT: Normal glucose tolerance, IGT: Impaired glucose tolerance, DGT: Diabetic glucose tolerance

In the present study, 48.4% of subjects with significant CAD had an abnormal 2-h glucose compared to 28.6% in those with no CAD ($P$ = 0.055). These are comparable to rates of undiagnosed DM and IGT in patients with CAD to those seen in the Euro Heart Survey on diabetes and the heart, where 32% had IGT and 14% had DM on OGTT.[22] Cardiovascular risk starts to increase long before overt DM occurs.[23]

## Fasting glucose versus 2-h plasma glucose

The association between AGR and the presence of significant CAD was stronger for the 2-h postglucose challenge than the FPG.[14] In patients with CAD, 20.3% had overt DM diagnosed after glucose challenge compared with 14.1% with DM based on an FPG.

For both those with positive and negative coronary angiogram, almost half (48.8%) of the patients with an abnormal 2-h glucose had normal fasting plasma glucose. In the Euro Heart Survey, two–thirds of patients with AGR on OGTT had normal FPG tests.[22] In another study, 59% of patients with newly diagnosed AGR had normal FBG and so would have remained undiagnosed without the performance of OGTTs.[19] The use of a FBG test alone may miss a significant number of patients with unrecognized glucose intolerance. The 2-h postglucose load in OGTT is a stronger predictor of the risk of future CVD events than FPG.[24,25] The cardiovascular events increased in a linear fashion without a threshold for 2-h postprandial plasma glucose.[26]

Early detection of AGR in patients with CAD identifies a population at increased risk of cardiovascular events. Addressing the postprandial plasma glucose excursions leads to significant cardiovascular risk reduction.[27] Long-term follow-up of patients with myocardial infarction showed that the presence of AGR, including IGT or diabetes, diagnosed by OGTT, increases the risk of cardiovascular events by around four times.[28] The European Association for the study of Diabetes recommends the use of an OGTT to investigate AGR in patients without known diabetes but with established CVD.[29]

Diabetic deaths account for 26.2% of all medical deaths in medical wards of the Tripoli Medical Centre and CVD account for 31.8% of all in-hospital deaths among Libyan patients.[30] Early detection and treatment of AGRs should favorably affect the prognosis for patients with CAD.

### Limitation of the study

First, the small sample size of this study with participants from a high-risk population. Second, the HbA1c values were not included in the study since the use of HbA1c levels for screening or predicting DM was not routine in our center during the study time. Third, patients with known history of diabetes were excluded, therefore, our study does not reflect the true prevalence of AGR in this high-risk population.

## Conclusion

Abnormal glucose regulation is highly prevalent in Libyan patients without previously known diabetes undergoing elective coronary angiography, found in 48.4% of the patients with significant CAD. As AGR is an important risk factor for cardiovascular morbidity and mortality, early diagnosis and treatment of AGR in patients with significant CAD will reduce the risks of progression of AGR and associated complications and therefore improve outcomes in this high-risk group. The use of an FPG test alone may miss a significant number of patients with unrecognized glucose intolerance. An OGTT should be part of standard risk-evaluation procedures in patients with CAD.

### Authors' contributions

Both authors have contributed to the inception of the study, data collection and analysis, and manuscript preparation and final approval.

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.

### Compliance with ethical principles

The study was carried out in accordance with the principles of the Helsinki Declaration. A formal approval was obtained from institutional authorities. OGTT is considered to be part of the optimal evaluation for patients with CAD. Verbal consent was obtained from all participants prior to the study.

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