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The Outcome of Patients with Acute Coronary Syndrome Those Associated with Impaired Glucose Tolerance in AL-Nasiriya Governorate / Iraq

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Abstract: Prediabetes in the form of impaired glucose tolerance (IGT) is common among patients with acute coronary syndrome (ACS). IGT in patients admitted for ACS is associated with increased mortality. We aimed to determine the prevalence of prediabetes in the form of IGT among ACS patients who were known to be neither diabetic nor prediabetic and referred to early coronary angiography. The study included 284 participants. We divided into 2 groups: patients group and control group. The patients group were include 138 patients admitted in AL-Hussein teaching hospital with acute coronary syndrome in the form of ST-segment elevation myocardial infarction (STEMI) and non-ST-segment elevation myocardial infarction (NSTEMI). 98 patients with NSTEMI and 40 patients with STEMI. The control group were 146 participants in the form of medical staff and patients visiting the hospital with conditions other than the ischemic coronary artery disease. All participants were neither diabetic nor prediabetic. 2 hour post prandial blood sugar, blood sugar at 3 days and blood sugar after 6 weeks were done. 22% of the patients group and 6% of the control group were found to have IGT at 2 hour postprandial with highly statistically significant value (P value < 0.0001). 16.6% of the patients group and 7.5% of the control group were found to have IGT at 3 days after the admission with highly statistically significant value (P value < 0.001). 11% of the patients group and 2% of the control group were found to have IGT after 6 weeks of the presentation with also significant statistical value (P value < 0.005). IGT was found in 62% of the female and 38% of the male in patients group. 42% of NSTEMI and 28% of STEMI patients were ended with early percutaneous coronary angiography. There were 11 patient with IGT in the patients group died during the first week of presentation in comparison to 2 patients with normal sugar died during the same period with highly statistically significant value (P value < 0.0001). IGT is common in patients admitted with ACS. IGT is associated with higher mortality among those patients with previously unreported as diabetes mellitus and should be screened for.

Keywords: Acute Coronary Syndrome, Impaired Glucose Tolerance, Mortality, Coronary Angiography

1. Introduction

Impaired glucose tolerance and impaired fasting glucose form an intermediate stage in the natural history of diabetes mellitus [1]. Impaired fasting glucose (IFG) is defined as fasting plasma glucose values of 6.1-6.9 mmol/L and impaired glucose tolerance (IGT) is defined as 2 hour postprandial plasma glucose of 7.8-11.0 mmol/L [2]. Type 2 diabetes mellitus is a major health problem that is associated with significant mortality and morbidity [3]. Diabetes can be prevented or delayed through lifestyle interventions [4, 5]. Information that has been learned about the natural history and pathogenesis of diabetes indicates that this disease has a prolonged prediabetic phase [6]. The categories of impaired glucose tolerance (IGT) and impaired fasting glucose (IFG) have been officially termed prediabetes, because they are risk factors for future diabetes and for cardiovascular disease [7, 8]. Patients with impaired glucose tolerance (IGT) are at significant risk for diabetes [9, 10]. Both prediabetes and diabetes highly predispose to cardiovascular alterations [11]. Type 2 diabetes mellitus, a presently rapidly expanding disease [12], is a major risk factor for cardiovascular morbidity and mortality [13]. Established diabetes is associated with impaired prognosis after myocardial

infarction [11].

Newly detected abnormal glucose tolerance is one of the strongest prognostic factors following an myocardial infarction [14]. Strict insulin-based glucometabolic control improves survival in patients with diabetes and acute myocardial infarction [15]. Diabetes is also associated with worse outcomes of revascularization in the form of increased instent restenosis and increased major adverse cardiac events in percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) [16].

Very recently fasting blood glucose was found to be an independent risk factor for poor long term outcome and was associated with enhanced platelet reactivity and low response to clopidogrel in patients with acute coronary syndrome (ACS) and poor long term outcome of PCI [17]. Each 1% increase in glycated haemoglobin (HbA 1c) level was associated with a 14% increase in the incidence of fatal and nonfatal myocardial infarction [18]. A meta-analysis of several observational studies showed that the association of cardiovascular risk with post-challenge glucose concentration is stronger than that of fasting plasma glucose [19]. These data are supported by the Diabetes epidemiology: collaborative analysis of diagnostic criteria in Europe (DECODE), which showed that 2-hour glucose, but not fasting glucose, predicts cardiovascular disease mortality in individuals with glucose levels within normal range [17]. It still unknown which underlying metabolic abnormalities that cause the increased cardiovascular disease risk in people with elevated 2-hour glucose, the 2-hour glucose is closely related to peripheral insulin resistance and lack of beta cell compensation [20].

Prediabetes (impaired glucose tolerance) develops for the same reasons as type 2 diabetes [21]. There are various risk factors can increase the risk of developing prediabetes, these include: being overweight or obese, having a close family history of diabetes, little physical activity, previous history of gestational diabetes [22].

2. Aim of the Study

The aim of this study to determine the prevalence of impaired glucose tolerance in those patients with acute coronary syndrome who were known to be neither diabetic nor prediabetic and to know the outcome of those patients.

3. Method

3.1. Patients

The study was carried out on 284 participants. They were divided into 2 groups:

Group 1 (patients group): 138 patients presenting in coronary care unit in AL-Hussein teaching hospital from January 2017 – June 2017 with a new ischemic events in the form of acute coronary syndrome (ACS) which include STEMI (ST- segment elevation myocardial infarction) and NSTEMI (non-ST segment elevation myocardial infarction and unstable angina) were diagnosed according to the clinical, physical, ECG and laboratory findings.

There were 98 patients with NSTEMI and 40 patients with STEMI.

Group 2 (control group): 146 person who were medical staff or patients presenting to the outpatient clinic in AL-Hussein teaching hospital with condition other than the ischemic heart disease.

All the 284 participants were non diabetic (no previous diagnosis of diabetes nor prediabetics). Their ages range from 40-75 years. The participants were subjected to detailed medical history, clinical examination and ECG. Laboratory analyses including fasting blood sugar, 2 hour post prandial blood sugar, cardiac markers, renal function test and lipid profiles were withdrawn from the patients.

3.2. Materials

The patients with impaired glucose tolerance (IGT) at 2 hour post prandial sugar were followed by measurement of blood sugar after 3 days and then 6 weeks from presentation to document the true glucose intolerance from stress induced hyperglycemia. Glucose monitoring was stopped when the glucose level remain < 7.8 mmol/L [23].

The therapy for those patients with acute coronary syndrome after the usual treatment in coronary care unit were based on TIMI (Thrombolysis in Myocardial Infarction) score risk which is a simple prognostication scheme that categorize a patient's risk of death and ischemic events and provides a basis for therapeutic decision making [24].

TIMI Risk Score Calculation (1 point for each) include:

1. Age ≥ 65 year.
2. Aspirin use in the last 7 days (patient experience chest pain despite aspirin use in past 7 days).
3. At least 2 anginal episodes within the last 24 hours.
4. ST changes of at least 0.5 mm in contiguous leads.
5. Elevated serum cardiac biomarkers.
6. Known coronary artery disease (coronary stenosis ≥ 50%).
7. At least 3 risk factors for coronary artery disease, such as:
   a. Hypertension, blood pressure ≥ 140/90 or on antihypertensive medications.
   b. Current cigarette smoker.
   c. Low HDL cholesterol (< 40 mg/dL).
   d. Family history of premature coronary artery disease, include:
      A. Male first-degree relative or father younger than 55 year.
      B. Female first-degree relative or mother younger than 65 year.

Score interpretation:

1. Score of 0-1 = 407% risk
2. Score of 2 = 8.3% risk
3. Score of 3 = 13.2% risk
4. Score of 4 = 19.9% risk
5. Score of 5 = 26.2% risk
6. Score of 6-7 = at least 40.9 risk

Drug therapy was appropriate for those patients with low TIMI risk score. Early coronary angiography and revascularization were considered for those patients with medium to high TIMI risk score and those with low TIMI score risk who failed to settle with drug therapy.

The coronary angiography were done using standard techniques in AL-Nasiriya cardiac center.

4. Result

Table 1 show the characteristics of the study.

The mean age of all patients group in this study was 58± 11. It was noticed that 62% of the included patients were females while 38% were males. It was also noticed that the mean BMI among the patients (28± 4.2) was higher than the control group (23±4.6). Smoker were found to be 38.4% among the patients in contrary to 31.2% in the control group. Hypertensive patients were 62.5% among the patients group while 36.2% of the control group were found to be hypertensive.

Table 1. *The characteristics of the study.*

characteristics	Group 1 (patients)	Group 2 (control)
Age (years)	58±11	51±12
Gender	62% female 38% male	54% female 46% male
BMI	28±4.2	23±4.6
Smoking	38.40%	31.20%
Hypertension	62.50%	36.20%

Figure 1 shows the percentage of types of ACS in patients group

It was noticed that 60% of patients were admitted with non-ST-segment elevation myocardial infarction and unstable angina (NSTEMI) while 40% of the patients were found to have ST-segment elevation myocardial infarction (STEMI) as show in figure 1.

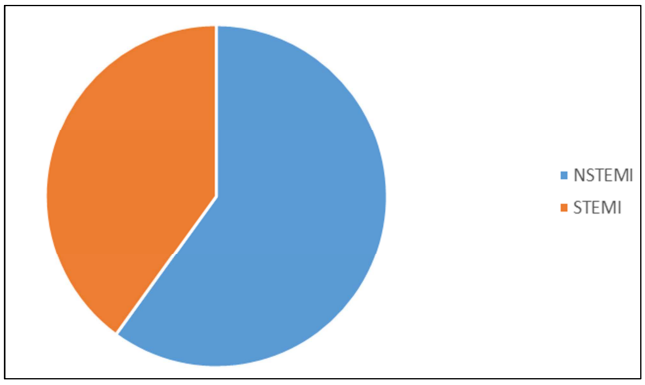

Figure 1. *Percentage of the types of ACS in patients group.*

22% of the patient's group were found to be have impaired glucose tolerance (IGT) at 2 hour post prandial while only 6% of the control group found to be have IGT at the same period and that was statistically significant (P value <0.0001), as shown in figure 2.

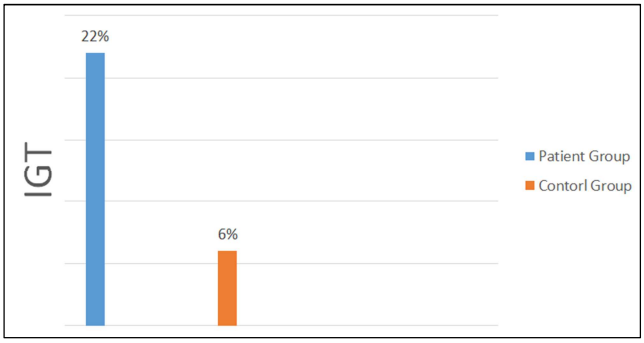

Figure 2. *The percentage of participants with impaired glucose tolerance (IGT) at 2 hour post prandial for patients and control group (P value < 0.0001).*

16.6% of the patient's group were found to be have impaired glucose tolerance (IGT) at day 3 while only 7.5% of the control group found to be have IGT at the same period and that was statistically significant (P value <0.001), as shown in figure 3.

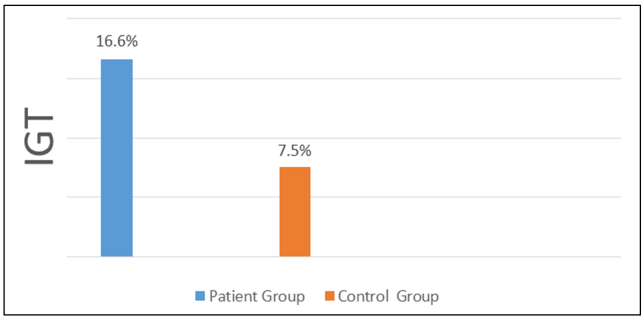

Figure 3. *The percentage of participants with impaired glucose tolerance (IGT) at day 3 for patients and control group. (P value<0.001).*

11% of the patients group were found to be have impaired glucose tolerance (IGT) after 6 weeks while only 2% of the control group found to be have IGT at the same period and that was statistically significant (P value <0.005), as shown in figure 4.

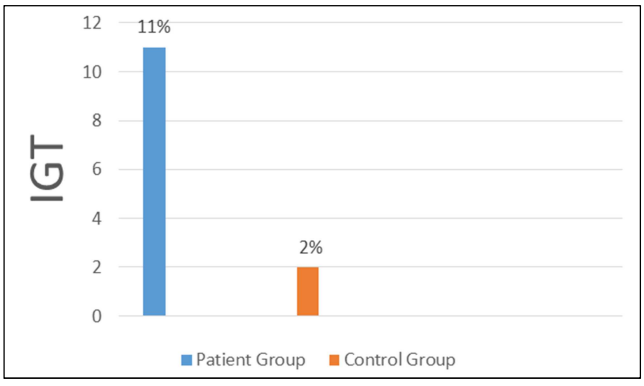

Figure 4. *The percentage of IGT after 6 weeks in patients and Control group (P value < 0.005).*

62% of the female in the patients group and 38% of the male in the same group were found to have impaired glucose tolerance (IGT) with statistically significant (P value < 0.05),

as shown in figure 5.

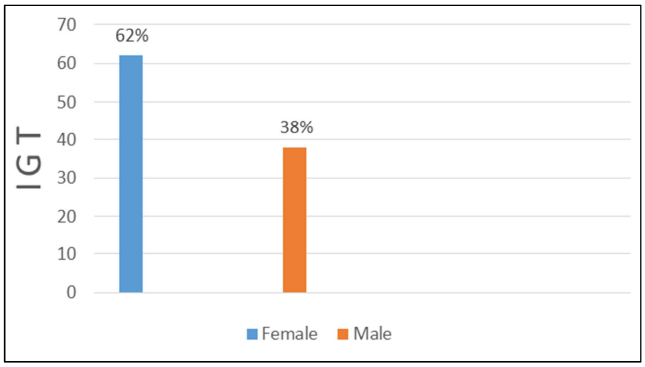

Figure 5. *Percentage of IGT regarding the gender of the patients group (P value < 0.05).*

Figure 6 show 42% of patients with NSTEMI (non ST-Segment elevation myocardial infarction and unstable angina) and 28% of patients with STEMI were ended with early percutaneous coronary angiography (PCI) in the cardiac center, as shown in the figure below:

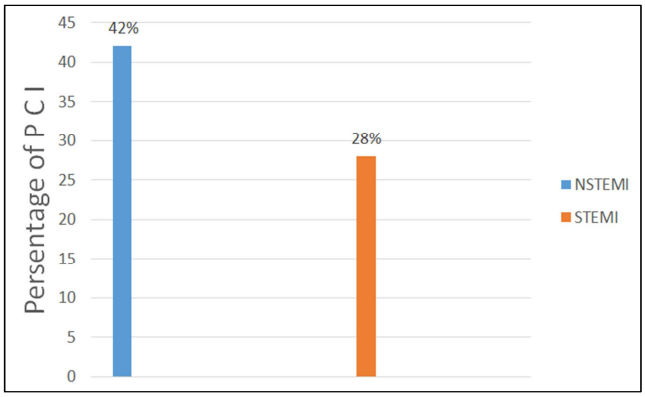

Figure 6. *Percentage of patients were ended with PCI in the cardiac center.*

11 patients with ACS those found to be have impaired glucose tolerance (IGT) were died during the first week of presentation in comparison with 2 patients with normal sugar state were died in that period of presentation with highly statistically significant value (P value < 0.0001) as shown in figure 7.

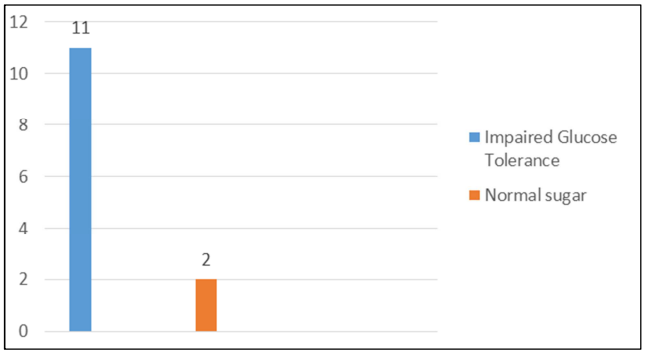

Figure 7. *The number of deaths of the ACS patients with it's correlation to IGT during the first week (P < 0.0001).*

5. Discussion

Impaired glucose tolerance (IGT) identify individuals at increased risk for developing diabetes [25]. It has been suggested that IGT and IFG are associated with varying rates of progression to diabetes and differences in cardiovascular disease risk [25].

In this study, we choose 284 participants who were known to be neither diabetic nor prediabetic and we divided into 2 groups: group 1 which include 138 patients were admitted in the AL-Hussein teaching hospital with ACS in the form of 98 patients with the diagnosis of NSTEMI (non-ST-segment elevation myocardial infarction and unstable angina) and 40 patients with the diagnosis of STEMI (ST-segment elevation myocardial infarction). Group 2, which was the control group and include 146 participants (medical staff and patients visiting the outpatient clinic in the AL-Hussein teaching hospital for medical advice for conditions rather than ischemic artery disease.

We found that 62% of the patients group were female while 38% of the same group were male. The burden of ACS is high in women. V. L. Roger, et al. [26] show women have higher rates of angina than do men. A female excess of angina prevalence was also demonstrated in a meta-analysis of data from 31 widely varied countries, including non-English speaking countries [27].

On cardiovascular computed tomography, women have been shown to have smaller coronary artery diameters than men do [28].

Recently, disorders of the coronary microvasculature and endothelial dysfunction have been implicated in the occurrence of coronary artery disease in women. Han et al. [29] studied women and men with early coronary artery disease and found that women have more disease of the microvasculature.

This study also revealed that the mean age was 58±11 year in the patients group while 51±12 year in the control group, BMI was 28±4.2 in the patients group and 23±3.6 in the control group with no clear differences between them. Smoking was documented in 38.4% in the patients group while in the control group was found to be 31.2%.

Hypertension was detected in 62.5% of the all patients group while 36.2% of the control group were found to be have hypertension. This finding correlate with other study, J. Spinar, et al. which found that the hypertension found in the majority of the patients with CAD were studied and found also that the hypertension doubles the risk of cardiovascular disease and accelerates significantly the development of atherosclerosis [30].

Figure 1 show that 60% of the patients group was NSTEMI (non-ST-segment elevation myocardial infarction and unstable angina) and 40% of the patients group was STEMI (ST-segment elevation myocardial infarction). Epidemiological data have shown that acute coronary syndrome (ACS) cases with STEMI appear to be declining and that NSTEMI occurs more frequently than STEMI [31, 32]. In the United States, it is estimated that > 780000 people

will experience an ACS each year, and approximately 70% of these will have NSTEMI [33].

Trends from the world's largest database of patients with ACS show that the percentage of patients with a diagnosis of NSEMI is rising dramatically [34]. This is likely to be due to the advent of more sensitive assays for myocardial injury, earlier pharmacotherapy, and reperfusion (and prevention) of STEMI [34, 35].

Figure 2 show that 22% of the patients group and 6% of the control group were found to be have impaired glucose tolerance (IGT) with statistically significant at 2 hour post prandial blood glucose and this correlate with a study, M. Bartnik, et al. which revealed about 25% of the acute coronary artery disease had IGT [36]. In China Heart Survey aimed at characterizing the glucometabolic state of patients with CAD with no history of diabetes revealed 32.6% of those patients had isolated IGT [37]. Jitender Mokta, et al. study showed a high prevalence of IGT (62%) in patients admitted with ACS in mountainous state on India [38].

Elevated plasma glucose levels on admission are very common in patients with acute myocardial infarction and can be the first indication of glucose intolerance [39]. It is important to mention that more than 50% of IGT and stress hyperglycemia at admission had IGT on repeat test at further time [40], this finding was consistent with our study as shown in figure 3 and figure 4, which revealed 16.6% of the patients group and 7.5% of the control group had IGT at 3 days with statistically significant (P value < 0.001) and 11% of the patients group and 2% of the control group had IGT after 6 weeks with also statistically significant (P value < 0.005).

The present results on the prevalence of IGT among the patients are in agreement with several recent reports. Meier et al., who found 24% of the patients had IGT after 4 weeks from the onset of ACS [41].

Figure 5 show that 62% of the female in the patients group and 38% of the male in the same group were found to have impaired glucose tolerance (IGT) with statistically significant (P value < 0.05). These results are in agreement with Annika Dotevall et al., who found that the majority of patients with ACS have abnormal glucose metabolism and that women are significantly more likely to have diabetes or IGT than men [42]. A heavier risk factors burden and a stronger effect of risk factors in diabetic and nondiabetic women than men might, at least partly, influence the effect on cardiovascular risk in women [43].

Figure 6 show 42% of patients with NSTEMI (non ST-Segment elevation myocardial infarction and unstable angina) and 28% of patients with STEMI were ended with early percutaneous coronary angiography (PCI) in the cardiac center. This result is differ from other study which revealed that the PCI was more common in STEMI patients compared with NSTEMI patients who had either coronary artery bypass grafting or medical management [44].

Figure 7 show that 11 patients with ACS those found to be have impaired glucose tolerance (IGT) were died during the first week of presentation in comparison with 2 patients with normal sugar state were died in that period of presentation with highly statistically significant value (P value<0.0001) which similar to a study, Prashanth Panduranga. et al. which demonstrate that IGT levels are associated with increased mortality in nondiabetic ACS patients [45].

The disparity in in-hospital mortality between ACS patients with IGT and normal sugar is not clearly elucidated. Various causes have been postulated to explain this disparity. Secondary to hyperdrenergic state following ACS, stress-related relative insulin deficiency develops leading to stress hyperglycemia [46]. Cardiovascular stress induces release of catecholamines, cortisol, and glucagon, leading to increases in glucose and free fatty acids that enhances hepatic gluconeogenesis, diminish peripheral glucose uptake, and decrease myocardial glucose utilization, all of which may have adverse effects on myocardial energy metabolism and function the presence of ischemia [46].

6. Conclusion

Prediabetic state, defined as IGT, was associated with an increased risk of cardiovascular disease in the form of acute coronary syndrome (ACS) and also associated with higher mortality in those patients comparing with ACS patients with normal sugar state.

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