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# UNDIAGNOSED DIABETES MELLITUS IN ACUTE CORONARY SYNDROME (ACS) PATIENTS

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**Abstract:**
***Introduction:*** *One of the main risk factors leading to coronary artery disease (CAD) is diabetes mellitus. Type 2 diabetes prove to be an important cause of cardiovascular morbidity and mortality in patients admitted for suspected myocardial infarction. Diabetes mellitus is associated with worse prognosis in hospitalized patients with CAD.*
***Objective:*** *To determine the frequency of undiagnosed diabetes mellitus in patients with acute coronary syndrome in a tertiary care hospital in Faisalabad.*
***Materials and Methods***
***Study design:*** *Cross sectional study*
***Setting:*** *Department of Cardiology, Allied hospital, Faisalabad*
***Duration:*** *Six months (09-2018 to 03-2019)*
***Data collection procedure:*** *Total 140 patients meeting the inclusion and exclusion criteria were included in the study. Relevant data according to the predesigned questionnaire including age, gender, ACS category (STEMI, Non-STEMI or unstable angina) was recorded. For diagnosis of diabetes, 3 cc serum blood sample was taken for fasting blood sugar and HbA1c. Undiagnosed diabetes mellitus was recorded.*
***Results:*** *There were 110(78.6%) males and 30(21.4%) females in our study. The mean age of patients was 57.08±12.72 years. The mean height was 171.95±14.37 cm, mean weight was 80.70±11.23 kg and mean BMI was 26.89±3.64. There were 63(45%) patients with family history of diabetes. There were 60(42.9%) patients with Non-STEMI, 52(37.1%) with STEMI and 28(20%) with unstable angina. The mean HbA1c of the patients was 6.11±0.86. There were 10(7.1%) patients with undiagnosed Diabetes mellitus.*
***Conclusion:*** *The frequency of undiagnosed diabetes mellitus in patients with ACS was 7.1%.*
***Key words:*** *Undiagnosed Diabetes Mellitus, Acute Coronary Syndrome, type 2 diabetes, family history, STEMI,*

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## INTRODUCTION:

One of the main risk factors leading to coronary artery disease (CAD) is diabetes mellitus. In many previous studies, type 2 diabetes prove to be an important cause of cardiovascular morbidity and mortality accounting for 20% of the total number of patients admitted for suspected myocardial infarction [1]. Diabetes mellitus is associated with worse prognosis in hospitalized patients with CAD [2].Long-term follow-up reveals an increasing death rate, attributed to fatal re-infarctions and congestive heart failure [1].The risk of myocardial infarction in a diabetic patient is the same as non-diabetic patient with a previous myocardial infarction[3].

The incidence of diabetes is rising globally [4] and Pakistan is one of those countries which is contributing to the diabetes pandemic. According to WHO in 2014, 422 million adults have diabetes worldwide [5]. In 2015, National Diabetes Action Plan of Pakistan reported over 7 million people suffering from diabetes [6]. The term acute coronary syndrome (ACS) refers to any group of clinical symptoms consistent with acute myocardial ischemia and includes ST-segment elevation myocardial infarction (STEMI), non-STEMI and unstable angina.[7]

The most common cause of myocardial ischemia is initiation of atherosclerosis resulting into Atherosclerotic plague formation. The plagues may progress or stabilize but they have tendency to rupture resulting in thrombosis leading to ACS [7]. Diabetes is one of the main factors contributing to atherosclerosis [8]. So it is proposed that early detection and control of diabetes can curtail the incidence of ACS. In common practice, it is seen a number of patients with ACS are diagnosed with diabetes for the first time on their presentation.

There are previous studies which determine frequency of undiagnosed diabetes mellitus in patients with ACS [9, 10] and the results are variable. The most well known is the TRIUMPH trial in which a total of the 4193 patients who were tested for metabolic syndromes, 31.9% (1193 patients) had known diabetes mellitus at ACS presentation. In the remaining 3001 patients, 2854 were tested for diabetes mellitus through various tests of which a total of 10.1 % (287 patients) had underlying diabetes mellitus that was not previously diagnosed [11]. So we planned a study to look frequency of diabetes in our local population.

The rationale of my study is that as no local data is available regarding the frequency of undiagnosed diabetes in patients with ACS and diabetes is a major risk factor of ACS, I have designed this study to know the frequency of undiagnosed diabetes mellitus in patients presenting with ACS in Allied hospital, Faisalabad. Early diagnosis and management of diabetes in patients with STEMI or Non-STEMI or unstable angina can decrease morbidity and mortality and decrease length of hospital stay and cost of treatment.

## MATERIALS AND METHODS:

In this cross-sectional study, done at the Allied hospital, Faisalabad from September, 2018 to March, 2019, 140 samples were collected using non-probability consecutive sampling technique. Sample size of 140 patients estimated using expected prevalence undiagnosed diabetes mellitus 10.1% calculated with 95% confidence level and 5% margin of error. The objective of this study was To determine the frequency of undiagnosed diabetes mellitus in patients with acute coronary syndrome in a tertiary care hospital in Faisalabad. Anyone having any one of the following was labeled as having Acute Coronary Syndrome (ACS):

1. STEMI (ST-segment elevation): It was defined by ST segment elevation (> 1mm) on electrocardiography and a positive troponin blood test (qualitative) in the setting of symptoms : Angina i.e. chest pain or discomfort > 30 minutes; described as aching, pressure , tightness of burning, may radiate to the chest , arms, upper abdomen, neck or jaw.
2. NON-STEMI (non–ST-segment elevation): It was defined by positive troponin blood test with no ST elevation on electrocardiography in the setting of symptoms.
3. Unstable angina was diagnosed if the patient have a negative troponin blood test and any 1 of the following characteristics: new-onset angina (< 2 months) of at least class III according to the Canadian Cardiovascular Society, prolonged (> 20 minutes) angina at rest, recent (< 2 months) worsening of angina pectoris, or angina that occurred within 2 weeks of an acute myocardial infarction.

Any patient not previous known to have diabetes (type II) BSR > 200 mg/dl before their presentation of ACS diagnosed with Glycosylated hemoglobin (HbA1C) > 6.5 % at presentation was labeled as having Undiagnosed Diabetes Mellitus.

As per operational definition, patients of both genders of age 25 to 80 years old admitted with ACS in Bahria Hospital either through emergency or OPD were included in the study. Exclusion criteria for this study was:

1. Patients with secondary causes of diabetes. For example steroids/medication induced,

Hemochromatosis, Chronic pancreatitis, polycystic ovary syndrome (PCOS), Cushing's syndrome.
2. Patients with uncontrolled diabetes already on medications or diet control.
3. ACS does not include patients with secondary causes raised troponin, including renal failure (cr 1.3 mg/dl), pulmonary embolism, severe pulmonary hypertension, and sepsis (TLC > 11000/ mm2 and < 40000/mm2).

After approval of ethical review committee, a total of 140 patients meeting the inclusion and exclusion criteria were included in the study and an informed consent was taken as per Declaration of Helsinki. With detailed relevant history, relevant data according to the predesigned questionnaire including age, gender, ACS category (STEMI, Non-STEMI or unstable angina) was recorded. For diagnosis of diabetes, 3 cc serum blood sample was taken for fasting blood sugar and HbA1c. Undiagnosed diabetes mellitus was recorded (as per operational definition).

Data was analyzed in SPSS 20.0. We calculated frequency of undiagnosed diabetes mellitus in patients with ACS. Mean and Standard Deviation was calculated for numerical variables like age, HbA1C while qualitative variables like gender, presence of ACS according to its sub-types was presented as percentage and frequency. Effect modifiers like age, gender, weight, BMI and family history of diabetes mellitus, type of CAD was stratified and post-stratification chi-square test was applied. P-value $\leq$ 0.05 was considered significant.

## RESULTS:

There were 110(78.6%) males and 30(21.4%) females in our study. ***Figure-1***

The mean age of the patients was 57.08±12.72 years the minimum age was 25 years and maximum was 80 years. ***Table-1*** The mean height of the patients was 171.95±14.37 cm the minimum height was 76 cm and maximum was 195 cm. ***Table-2*** The mean weight of the patients was 80.70±11.23 kg the minimum weight was 58 kg and maximum was 125 kg. ***Table-3*** The mean BMI of the patients was 26.89±3.64 the minimum BMI was 19 and maximum was 43. ***Table-4*** There were 63(45%) patients with family history of diabetes and 77(55%) without family history of diabetes mellitus. ***Table-5*** There were 60(42.9%) patients with Non-STEMI, 52(37.1%) with STEMI and 28(20%) with unstable angina in our study. ***Table-6*** The mean HbA1c of the patients was 6.11±0.86 the minimum HbA1c was 5 and maximum was 13.9. ***Table-7***

There were 10(7.1%) patients with undiagnosed Diabetes mellitus and 130(92.9%) had no undiagnosed Diabetes mellitus. ***Figure-2***

There was no significant association between undiagnosed diabetes mellitus and age groups as the p-value was not significant. (p-value=0.53) ***Table-8*** There was no significant association between undiagnosed diabetes mellitus and gender as the p-value was not significant. (p-value=0.49) ***Table-8*** There was significant association between undiagnosed diabetes mellitus and BMI as the p-value was significant. (p-value=0.045) ***Table-10*** There was significant association between undiagnosed diabetes mellitus and Family History as the p-value was significant. (p-value=0.003) ***Table-11*** There was no significant association between undiagnosed diabetes mellitus and CAD as the p-value was not significant. (p-value=0.59) ***Table-12***

***Figure-1: Gender of the Patients***

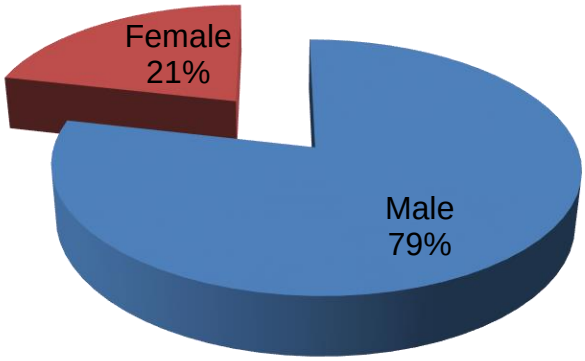

***Table-1: Age of the Patients***

| | |
|---|---|
| ***N*** | ***140*** |
| ***Mean*** | 57.08 |
| ***Standard Deviation*** | 12.72 |
| ***Min*** | 25.0 |
| ***Max*** | 80.0 |

***Table-2: Height of the Patients***

| | |
|---|---|
| ***N*** | ***140*** |
| ***Mean*** | 171.95 |
| ***Standard Deviation*** | 14.37 |
| ***Min*** | 76.0 |
| ***Max*** | 195.0 |

***Table-3: Weight of the patients***

| | |
|---|---|
| ***N*** | ***140*** |
| ***Mean*** | 80.70 |
| ***Standard Deviation*** | 11.23 |
| ***Min*** | 58.0 |
| ***Max*** | 125.0 |

***Table-4: BMI of the patients***

| | |
|---|---|
| ***n*** | ***140*** |
| ***Mean*** | 26.89 |
| ***Standard Deviation*** | 3.64 |
| ***Min*** | 19.0 |
| ***Max*** | 43.3 |

***Table-5: Family History of Diabetes mellitus***

| ***Family History*** | ***Frequency*** | ***Percent*** |
|---|---|---|
| Yes | 63 | 45% |
| No | 77 | 55% |
| ***Total*** | ***140*** | ***100*** |

***Table-6: Types of CAD***

| ***Types of CAD*** | ***Frequency*** | ***Percent*** |
|---|---|---|
| ***Non-STEMI*** | 60 | 42.9% |
| ***STEMI*** | 52 | 37.1% |
| ***Unstable Angina*** | 28 | 20.0% |
| ***Total*** | ***140*** | ***100*** |

***Table-7: HbA1c of the patients***

| | |
|---|---|
| ***N*** | ***140*** |
| ***Mean*** | 6.11 |
| ***Standard Deviation*** | 0.86 |
| ***Min*** | 5.0 |
| ***Max*** | 13.9 |

***Figure-2: Undiagnosed diabetes mellitus***

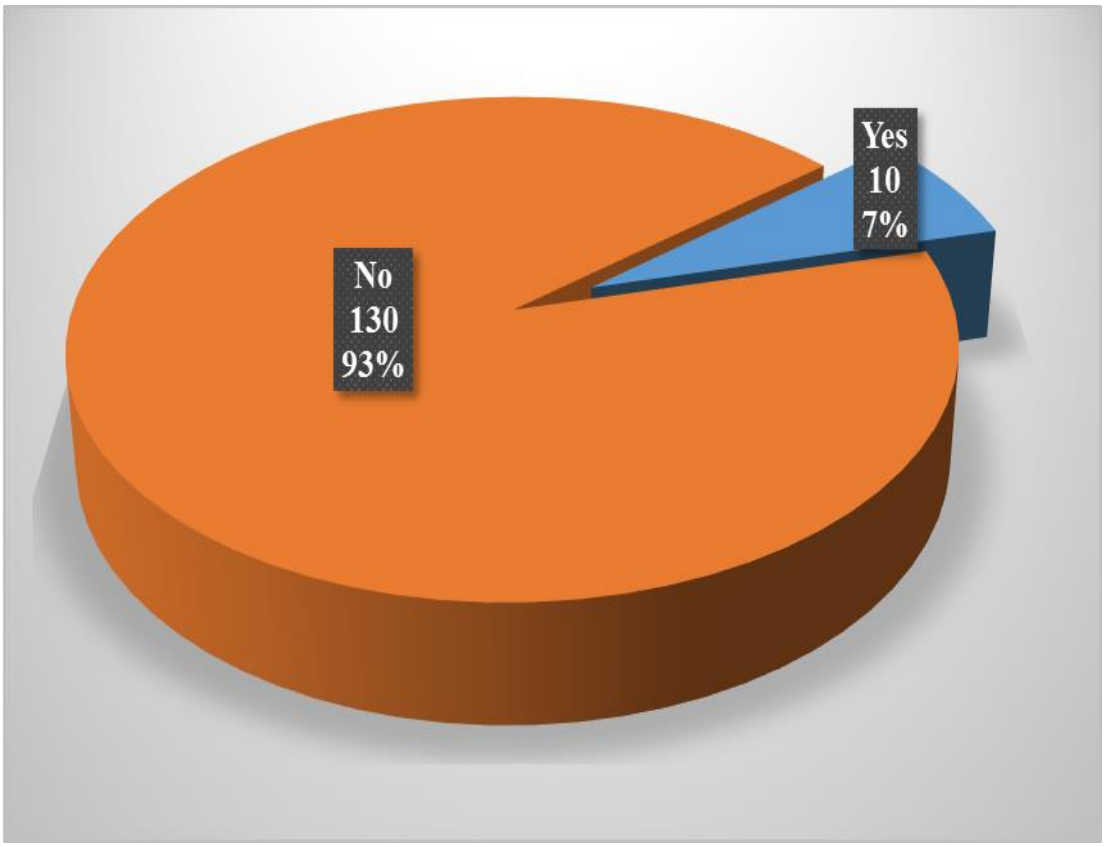


***Table-8: Undiagnosed diabetes mellitus stratified for Age groups***

| ***Undiagnosed diabetes mellitus*** | ***Age Groups*** | | | ***Total*** |
|---|---|---|---|---|
| | ***25-44*** | ***45-64*** | ***65-84*** | |
| ***Yes*** | 1(4.3%) | 7(9.5%) | 2(4.7%) | ***10(7.1%)*** |
| ***No*** | 22(95.7%) | 67(90.5%) | 41(95.3%) | ***130(92.9%)*** |
| ***Total*** | ***23(100.0%)*** | ***74(100.0%)*** | ***43(100.0%)*** | ***140(100.0%)*** |

***Chi-square= 1.27***
***p-value= 0.53***

***Table-9: Undiagnosed diabetes mellitus stratified for Gender***

| ***Undiagnosed diabetes mellitus*** | ***Gender*** | | ***Total*** |
|---|---|---|---|
| | ***Male*** | ***Female*** | |
| ***Yes*** | 7(6.4%) | 3(10.0%) | ***10(7.1%)*** |
| ***No*** | 103(93.6%) | 27(90.0%) | ***130(92.9%)*** |
| ***Total*** | ***110(100.0%)*** | ***30(100.0%)*** | ***140(100.0%)*** |

***Chi-square= 0.47***
***p-value= 0.49***

***Table-10:*** **Undiagnosed diabetes mellitus stratified for BMI**

| *Undiagnosed diabetes mellitus* | *BMI* | | | *Total* |
|---|---|---|---|---|
| | *19-27* | *28-36* | *37-45* | |
| ***Yes*** | 6(6.8%) | 3(6.0%) | 1(50.0%) | ***10(7.1%)*** |
| ***No*** | 82(93.2%) | 47(94.0%) | 1(50.0%) | ***130(92.9%)*** |
| ***Total*** | ***88(100.0%)*** | ***50(100.0%)*** | ***2(100.0%)*** | ***140(100.0%)*** |

***Chi-square= 5.65***
***p-value= 0.045***

***Table-11:*** **Undiagnosed diabetes mellitus stratified for Family History**

| *Undiagnosed diabetes mellitus* | *FH* | | *Total* |
|---|---|---|---|
| | *Yes* | *No* | |
| ***Yes*** | 9(14.3%) | 1(1.3%) | ***10(7.1%)*** |
| ***No*** | 54(85.7%) | 76(98.7%) | ***130(92.9%)*** |
| ***Total*** | ***63(100.0%)*** | ***77(100.0%)*** | ***140(100.0%)*** |

***Chi-square= 8.81***
***p-value= 0.003***

***Table-12: Undiagnosed diabetes mellitus stratified for Type of CAD***

| *Undiagnosed diabetes mellitus* | *CAD* | | | *Total* |
|---|---|---|---|---|
| | *Non-STEMI* | *STEMI* | *Unstable Angina* | |
| ***Yes*** | 4(6.7%) | 5(9.6%) | 1(3.6%) | ***10(7.1%)*** |
| ***No*** | 56(93.3%) | 47(90.4%) | 27(96.4%) | ***130(92.9%)*** |
| ***Total*** | ***60(100%)*** | ***52(100%)*** | ***28(100%)*** | ***140(100%)*** |

***Chi-square= 1.03***
***p-value= 0.59***

## DISCUSSION:

Diabetes is considered a highly 'vascular disease' with both micro vascular and macro vascular complications. Macro vascular complications start taking place long before the patient has overt diabetes.[12] Hyperglycemia is an independent risk factor for cardiovascular disease.[13]

HbA1c levels of more than 7% are associated with a significant increase in the risk of cardiac events and deaths. Interestingly, this correlation between higher HbA1c levels and increased cardiovascular morbidity occurs even before the diagnosis of clinical diabetes.[14] Heart disease in patients with Diabetes Mellitus is different from that in non-diabetics. Diabetics develop CAD earlier, and have more extensive atherosclerosis.[15] Several previous studies have shown that the prevalence of CAD is higher in patients with diabetes[117].[16]

Prior studies have shown that the presence of diabetes mellitus places patients with coronary disease at increased risk for recurrent cardiovascular events. In addition, the presence of metabolic syndrome without a diagnosis of diabetes mellitus is associated with a fivefold risk of progression to diabetes mellitus compared with those without metabolic syndrome.[17] While it has been shown that lifestyle changes, medical therapy and bariatric surgery can prevent progression to diabetes mellitus, it is not well understood if early detection and aggressive treatment of glucometabolic state improves cardiovascular outcomes. [18]

More recent studies in different diabetic populations have demonstrated either no benefit or increased adverse cardiovascular outcomes with intensive glycemic control.[19] According to Balakrishnan et al 2015 [10] the prevalence of

undetected diabetes mellitus in their high-risk population was substantially higher than that observed in the general population.[20]

Compared with unselected NHANES survey populations, their findings reported a 4.5-fold higher frequency of previously undetected diabetes mellitus which is 8.3% vs. 1.8% whereas the findings of our study are almost similar to the findings of this study as in our study the frequency of undiagnosed diabetes mellitus was 7.1%.[21]

Few studies have assessed the prevalence in patients without known diabetes mellitus undergoing elective percutaneous coronary intervention. Two small European studies utilized oral glucose tolerance testing and found previously undetected diabetes mellitus in nearly 20% using oral glucose tolerance testing this prevalence is much higher as compared to our study and we have used HbA1c for the diagnosis of diabetes rather than the oral glucose tolerance test. [22,23] One study that used A1c levels in patients without known diabetes mellitus undergoing elective percutaneous coronary intervention found one-third of patients had levels greater than or equal to 6% so these are also almost similar to our study as our study reported 7.1% prevalence of undiagnosed diabetes mellitus.[24]

At one-year follow-up, these patients had significantly higher rates of major adverse cardiac events, target vessel revascularization and cardiovascular mortality.[24] Ashraf et al 2016 [25] reported that in their study total of 693 ACS patients were enrolled among them 102 (14.7%) had undiagnosed (first time detected) diabetes. But these findings are higher than the findings of our study, as our study reported the frequency of undiagnosed diabetes as 7.1%.

According to Balakrishnan et al 40.5% of patients had an A1c of 6% or greater while in our study the mean A1c was 6.11±0.86 with minimum A1c 5.0 and maximum 13.9.[10] A study from Roger et al. reported 8.5% STEMI while in our study the STEMI among undiagnosed diabetes mellitus patients was 9.6% which is not very different and almost similar with the findings of Roger [26] on the other side Giraldez et al. showed Non-STEMI in patients with undiagnosed diabetes was 3.6% which is much lower as compared to our study.[27]

Detection of glucometabolic abnormalities with routine screening of A1c levels at the time of percutaneous coronary intervention may provide an opportunity for cardiovascular specialists to identify those who may benefit from targeted intervention to decrease the risk of progression to diabetes mellitus and its long-term sequelae. While A1c has been reported to be less sensitive for the diagnosis of diabetes mellitus than fasting blood glucose levels, the convenience of the non-fasting test allows for improved screening rates and therefore increased detection compared with standard methods. [28]

Currently, the ADA recommends screening for diabetes mellitus including the use of A1c in asymptomatic adults who have a BMI ≥ 25 kg/m2 or one or more additional risk factors for diabetes mellitus, including cardiovascular disease; if normal, repeat testing is recommended every 3 years. [29]

Despite this, a joint cardiovascular society recommendation that advocated for routine screening for diabetes mellitus in patients with cardiovascular disease was withdrawn, citing logistic difficulty with screening methods.[30] Although more research is needed, recognition of an abnormal glucometabolic state should lead to more aggressive lifestyle changes in combination with medical therapy targeted towards improvement of other cardiovascular risk factors.

## CONCLUSION:

The frequency of undiagnosed diabetes mellitus in patients with ACS in this study was 7.1%. A substantial proportion of patients with unrecognized diabetes mellitus, with ACS, support the need for a focus on routine screening. If identified early, treatment of diabetes has been shown to reduce micro and macrovascular complications.

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