Impact of Prediabetes on Acute Coronary Syndrome in Sohag University Hospital

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Abstract

Background: Diabetes mellitus is a known risk factor for cardiovascular disease. Diabetics with acute coronary syndrome (ACS) have a two- to four-fold higher chance of having unfavorable cardiovascular events than non-diabetics. It is becoming more and more obvious that poor glucose metabolism and the pre-diabetic condition are linked to unfavorable clinical results.

Objectives: The current study aimed to assess the effects of prediabetes on acute coronary syndrome outcomes at Sohag University Hospital.

Patients and methods; This was a prospective observational study carried out at Sohag University Hospital. Patients were divided into non-diabetic, prediabetic, and diabetic patients. All trial participants had thorough history-taking, clinical examinations, laboratory tests, and daily follow up (chest pain, ECG, blood pressure, fasting blood sugar, any sign of heart failure, or any complication occur).

Results: This study involved 100 patients with ACS, 20 (20%) patients were non-diabetics, 27 (27%) were prediabetics, and 53 (53%) were diabetics. During follow-up, there was a higher nonsignificant rate of death in prediabetic patients (7.41%) than in diabetics (5.66%) and nondiabetic (5%) ($p > 0.05$). Also, the prediabetic group showed a higher nonsignificant abnormal change in ECG (81.48%) than the diabetic (81.13%) and nondiabetic (80.00%) ($p > 0.05$).

Conclusion; In ACS, patients with normoglycemia had a better prognosis than those with prediabetes, but prediabetes and DM patients had comparable results.

Keywords: Prediabetes; Diabetes; Acute coronary syndrome; Outcome.

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Introduction

Diabetes mellitus (DM) is one of the non-communicable diseases (NCDs) that has become a major worldwide health issue. The global burden of diabetes mellitus (DM) has increased significantly in recent decades, affecting over 476 million people worldwide (**Lin et al., 2020**). DM is one of the most important risk factors for coronary artery disease, and 37% of patients with acute coronary syndrome (ACS) have DM (**Zhou et al., 2018**).

Acute coronary syndrome (ACS) is the sudden decrease of myocardial blood supply, including ST-segment elevation myocardial infarction, non-ST-segment elevation myocardial infarction, and unstable angina. Despite important scientific progress in its management, patients with ACS remain at a higher risk of complications such as heart failure, arrhythmia, sudden death, and stroke (**Bergmark et al., 2022; Bhatt et al., 2022**).

Cardiovascular disease is more than 10 times more likely to develop in those with DM (**Faxon et al., 2004**). Cardiovascular problems account for 77% of diabetes-related hospital admissions in the US. Accelerated atherosclerosis progression is a major aspect of diabetes that contributes to this (**Scognamiglio et al., 2006**).

To avoid problems and the progression to overt diabetes, prediabetes must be treated early and effectively since it is linked to a large elevation in cardiovascular morbidity and death (**Chobanian et al., 2003**).

Regardless of the existence of diabetes mellitus, higher fasting glucose levels were linked to poorer clinical outcomes in individuals with ACS (**Sinnaeve et al., 2009**). Higher fasting glucose was a predictor of poor prognosis in individuals without diabetes who presented with acute STEMI (**Bartnik et al., 2004**).

Patients hospitalized with ACS who are non-diabetic often have impaired glucose tolerance (**Norhammar et al., 2002**). Regarding the predictive influence of "prediabetes" on the clinical outcome of ACS, the data is debatable. In this research, we aim to determine the effect of diabetes and prediabetes on patients with ACS and their outcome in Sohag university hospital.

Patients and methods

Between June 2021 and December 2022, prospective observational research was performed at the Department of Internal Medicine, Sohag University Hospital including patients with ACS. All patients had given their informed consent. The Sohag University Faculty of Medicine's medical ethics committee has approved the study.

Inclusion criteria: All patients with ACS admitted in CCU in the period of study.

Exclusion criteria: patients under 18 years old and pregnancy.

All patients underwent thorough history taking (age, sex ,smoking, known diabetic, positive family history for premature CVDs, history of prior percutaneous coronary intervention (PCI) or coronary arteries bypass grafting (CABG), ACS, or hypertension). Clinical evaluations including body mass index (BMI), and laboratory tests (consisting of troponin, HbA1C, lipid profiles, creatinine, fasting blood glucose levels, and eGFR). Patients were classified into three groups based on their levels of HbA1c: non-diabetic (these were patients with ACS adimtted to CCU in the period of study), prediabetic, and diabetic

patients. Daily follow up chest pain, ECG, Echo, blood pressure, fasting blood sugar, any sign of heart failure, or any complication (pulmonary edema or hemodynamic unstability)occurred.

On the first day of admission, following an overnight fast, a fasting venous blood sample was obtained for measurement os serum level of total cholesterol, triglycerides, high- density lipoprotein, and fasting blood glucose. The Friedewald equation was used to determine low-density lipoprotein cholesterol **(Friedewald et al., 1972).** Laboratory investigations were carried out using fully automated spectrophotometer Beckman coulter AU480 (Becman coulter diagnostics, Washington, USA). Glycohemoglobin in blood was measured using Hitachi cobas e 411 (Roche diagnostics, Rotkreuz, Switzerland). Troponin I was measured used the third generation AIA-Pack assay for cTnI TOSOH Coroporation, Tokyo, Japan.

According to the ADA guidelines, prediabetes is characterized by impaired glucose tolerance and/or impaired fasting glucose. Fasting plasma glucose (FPG) levels of 100 to <126 mg/dl and HbA1c levels of 5.7% to< 6.5% were considered to be impaired fasting glucose.

Prediabetes is a word used to describe people whose blood sugar levels are higher than normal but below the threshold for diabetes **(ADA, 2010)**. FBG ranges from 6.1 to <7.0 mmol/L is called impaired fasting glucose (IFG) (normal value less than 5.6 mmol/L). Blood glucose levels in IGT vary from >7.8 to <11.1 mmol/L (normal value less than 7.8 mmol/L **(Mozaffarian et al., 2008)**.

Unstable angina, non-STEMI, and STEMI were all ACS. All patients had chest pain of an ischemic nature that persisted or other acute signs of myocardial ischemia that persisted for more than 10 minutes at rest or with light activity. STEMI is characterized by persistent ST-segment elevation (at least 2 mm in two contiguous precordial leads or at least 1 mm in two limb leads), new left bundle branch block, or new Q waves in two contiguous leads, as well as an increase in biochemical indicators of myocardial necrosis (creatine kinase-MB and/or troponin) that is at least twice the upper limit of normal. Non-ST-elevation A new/dynamic electrocardiogram change that is consistent with ischemia, such as ST- segment depression of at least 1 mm, a transient ST segment elevation or ST-segment elevation of less than 1 mm, or a T wave inversion of more than 2 mm, must be present in at least two adjacent leads to be considered an ACS. The development of biochemical markers that were at least twice the upper limit of normally identified non-STEMI (**ESC Guidelines, 2021**).

Statistical analysis:

STATA 14.2 was used to examine the data (Stata Statistical Software: Release 14.2 College Station, TX: StataCorp LP.). Mean, standard deviation, median, and range were the metrics used to express quantitative data. The student t-test, ANOVA, Kruskal Wallis, Mann-Whitney, and Chi-square tests were all utilized. If the P value was less than 0.05, it was deemed significant.

Results

This study involved 100 patients with ACS, their mean age was 57.62±9.65, 37% were females, 63% were males, 20 (20.00%) patients were non-diabetics, 27 (27.00%) prediabetics and 53 (53.00%) were diabetics. All diabetic patients were uncontrolled. 37% were hypertensive, 29%

were current smokers, the mean BMI was 30.85 Kg/M2 ±3.43 and 14% had previous PCI or CABG. There was substantial variation between all study groups as regards age, hypertension, smoking, and BMI ($p < 0.05$). Also, there was substantial variation between non-diabetic and diabetic as regards age, smoking, and previous PCI or CABG ($p< 0.05$). Additionally, there was substantial variation between diabetic and prediabetic as regards sex, hypertension, smoking, and BMI ($p< 0.05$) (**Table.1**).

Table 1. Comparison between patients regarding demographic and history data

Variables	Non-diabetics N=20	Prediabetes N=27	Diabetes N=53	P value	P1	P2	P3
Age (years)							
Mean ± SD	52.8±11.88	57.93±8.91	59.28±8.62	0.04 *	0.21	0.03	1.00
Median (range)	51.5 (30:73)	60 (42:75)	58 (41:75)				
Gender							
Females	6 (30.00%)	6 (22.22%)	25 (47.17%)	0.07 $	0.55	0.19	0.03
Males	14 (70.00%)	21 (77.78%)	28 (52.83%)				
Hypertensive							
No	16 (80.00%)	22 (81.48%)	25 (47.17%)	0.002 $	1.00	0.01	0.003
Yes	4 (20.00%)	5 (18.52%)	28 (52.83%)				
Smoker							
Non-smoker	10 (50.00%)	14 (51.85%)	38 (71.70%)	0.01 $	0.43	0.004	0.04
Current smoker	10 (50.00%)	11 (40.74%)	8 (15.09%)				
Ex-smoker	0	2 (7.41%)	7 (13.21%)				
BMI Kg/m2							
Mean ± SD	30.23±2.77	29.67±2.25	31.69±3.93	0.03 *	1.00	0.30	0.04
Median (range)	30 (25:35)	30 (25:33)	31.2 (24:46)				
Previous PCI or CABG							
No	20 (100%)	24 (88.89%)	42 (79.25%)	0.07 $	0.25	0.03	0.36
Yes	0	3 (11.11%)	11 (20.75%)				

BMI (body mass index); CABG (coronary artery bypass graft). P value compared the three groups, P1 compared non-diabetic and prediabetic, P2 compared non-diabetics and Diabetics, P3 compared prediabetics and diabetes
*ANOVA test was used with post hoc Bonferroni test for pairwise comparison. $ Chi Square test or fisher exact test was used for comparison of the three groups and for pairwise comparison

The presenting symptoms including chest pain dyspnea and pulmonary edema were more prominent in diabetic and prediabetic patients than in non-diabetics but without substantial variation between all study groups (p > 0.05) (**Table.2**).

Table 2. Comparison between patients regarding presentation

Presentation	Non-diabetics N=20	Prediabetes N=27	Diabetes N=53	P value	P1	P2	P3
Chest pain	19 (95.00%)	24 (88.89%)	45 (84.91%)	0.79 *	0.64	0.65	0.71
Chest pain & dyspnea	0	1 (3.70%)	1 (1.89%)				
Dyspnea	0	0	2 (3.77%)				
Pulmonary edema	1 (5.00%)	2 (7.41%)	5 (9.43%)				

P value compared the three groups, P1 compared non-diabetic and prediabetic, P2 compared non-diabetics and Diabetics , P3 compared prediabetics and diabetes. * Chi Square test was used for comparison of the three groups and for pairwise comparison

Regarding diagnosis, 62% had STEMI, 14% had NSTEMI, and 24% had unstable angina. The mean of systolic blood pressure (SBP) was 122.5 mmHg ±21.48, the mean of diastolic blood pressure (DBP) was 79.4 mmHg ±15.56, the mean of pulse was 85.27 beat/ min ±15.05, 16% had Fine basal crepitation, 9% had Scattered crepitation, 1% had Ejection systolic murmur and 3% had Lower limb edema. There was no substantial variation between all groups as regards diagnosis, SBP, DBP, pulse, chest examination, cardiac examination, and lower limb edema (p > 0.05) (**Table. 3**, **Fig.1** and **2**).

Table 3. Comparison between patients regarding clinical picture at presentaion

Variable	Non-diabetics N=20	Prediabetes N=27	Diabetes N=53	P value	P1	P2	P3
Diagnosis:				0.69 $	0.39	0.49	0.82
• STEMI	15 (75.00%)	15 (55.56%)	32 (60.38%)				
• Non-STEMI	2 (10.00%)	5 (18.52%)	7 (13.21%)				
• Unstable angina	3 (15.00%)	7 (25.93%)	14 (26.42%)				
Systolic blood pressure (mmHg):				0.28 *	1.00	1.00	0.35
Mean ± SD	123±22.27	117.04±18.15	125.1±22.59				
Median (range)	120 (70:180)	120 (70:160)	120 (80:200)				
Diastolic blood pressure (mmHg):				0.32 *	0.59	1.00	0.53
Mean ± SD	81.5±18.99	75.56±11.87	80.57±15.74				
Median (range)	80 (30:120)	80 (40:90)	80 (40:140)				
Pulse (beat/min):				0.59 *	1.00	1.00	1.00
Mean ± SD	82.2±16.09	86.44±14.46	85.83±15.09				
Median (range)	90 (40:110)	90 (50:110)	90 (40:120)				

Chest examination: • Clear • Fine basal crepitation • Scattered crepitation	17 (85.00%) 2 (10.00%) 1 (5.00%)	21 (77.78%) 4 (14.81%) 2 (7.41%)	37 (69.81%) 10 (18.87%) 6 (11.32%)	0.74 $	0.82	0.42	0.74
Cardiac examination: • Clear • Ejection systolic murmur	20 (100%) 0	27 (100%) 0	52 (98.11%) 1 (1.89%)	0.64 $	1.00	1.00	1.00
Lower limb edema: • No • Yes	20 (100%) 0	26 (96.30%) 1 (3.70%)	51 (96.23%) 2 (3.77%)	0.68 $	1.00	1.00	1.00

P value compared the three groups, P1 compared non-diabetic and prediabetic, P2 compared non-diabetics and Diabetics, P3 compared prediabetics and diabetes. *ANOVA test was used with post hoc Bonferroni test for pairwise comparison. $ Chi Square test or fisher exact test was used for comparison of the three groups and for pairwise comparison

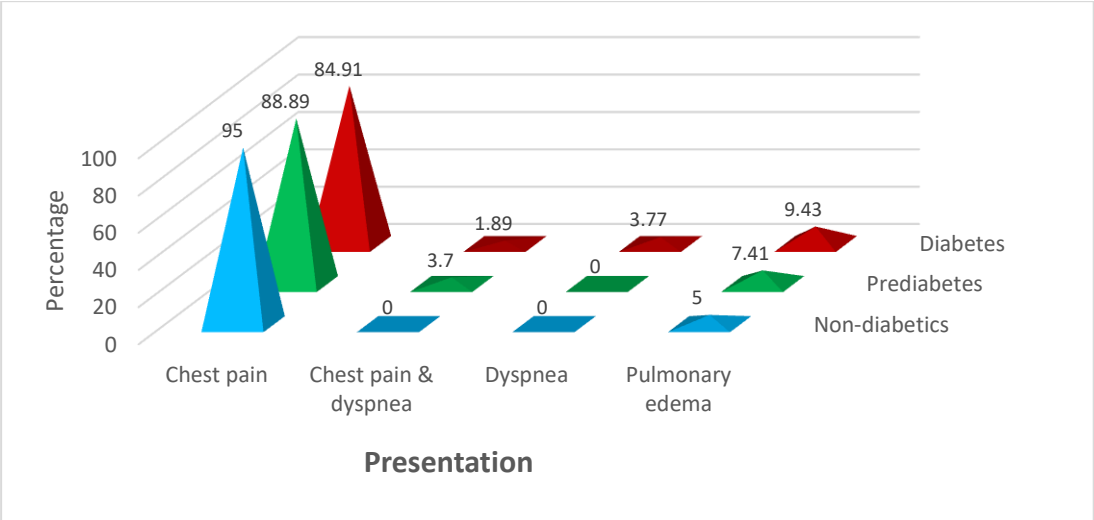

Fig.1. Relation between presence of diabetes and presentation

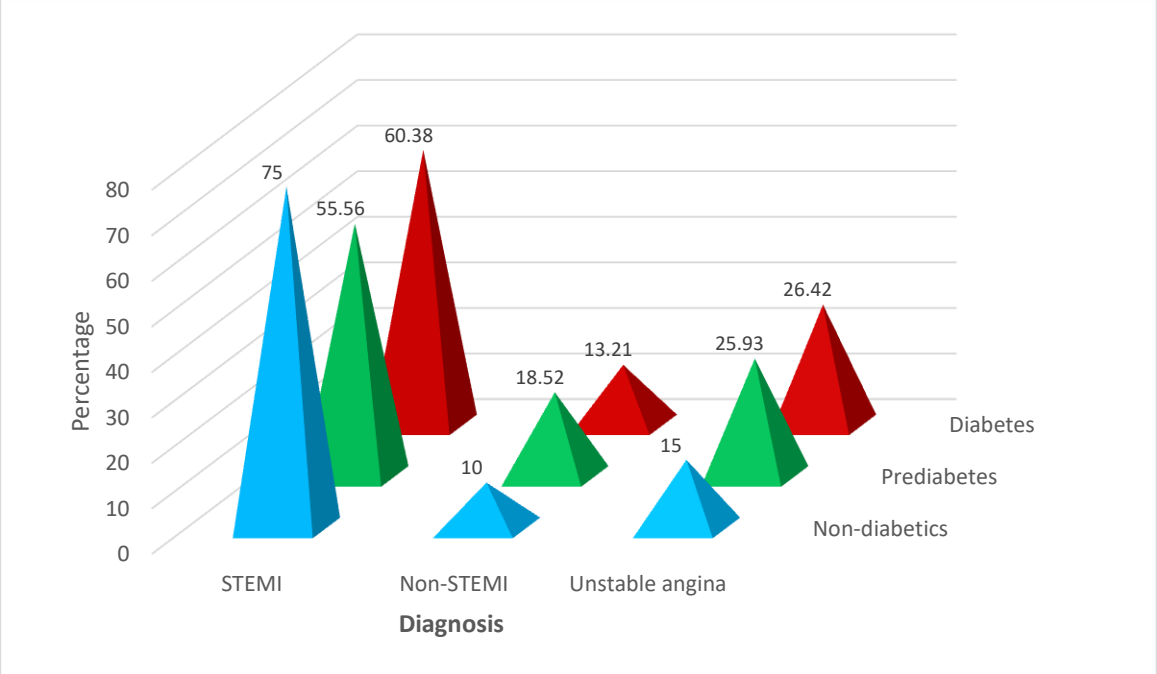

Fig .2. Relation between the presence of diabetes and diagnosis

There was substantial variation between all study groups as regards cholesterol, TG, HbA1c and fasting blood glucose (p< 0.05). Also, there was substantial variation between non-diabetic and diabetic as regards HbA1c and Fasting blood sugar (p< 0.05). Additionally, there was substantial variation between diabetic and prediabetic as regards cholesterol, HbA1c, and Fasting blood glucose (p< 0.05) (**Table.4**).

Table 4. Comparison between patients regarding baseline laboratory findings

Variables	Non-diabetics N=20	Prediabetes N=27	Diabetes N=53	P value	P1	P2	P3
Cholesterol (mg/dL) Mean ± SD Median (range)	191.45±57.91 200 (105:260)	168.78±41.62 165 (105:260)	201.06±58.14 200 (61:350)	0.045 #	0.24	0.56	0.01
Triglyceride (mg/dL) Mean ± SD Median (range)	136.2±112.10 107 (72:593)	106.74±35.08 100 (55:195)	140.85±112.17 109 (71:815)	0.25 #	0.31	0.73	0.10
Troponin I Negative Positive	3 (15.00%) 17 (85.00%)	7 (25.93%) 20 (74.07%)	14 (26.42%) 39 (73.58%)	0.57 #	0.48	0.37	1.00
HbA1C (%) Mean ± SD Median (range)	5.34±0.24 5.4 (4.7:5.6)	5.99±0.19 6 (5.7:6.4)	9.37±1.86 9 (6.5:13)	<0.0001 *	0.32	<0.0001	<0.0001
Fasting blood glucose (mg/dL)	105.15±7.70	143.37±24.79	230.77±69.05	0.0001 #	0.000	0.00	0.0001

Mean ± SD Median (range)	102.5 (95:125)	140 (109:190)	218 (120:400)		1	01	

P value compared the three groups, P1 compared non-diabetic and prediabetic, P2 compared non-diabetics and Diabetics, P3 compared prediabetics and diabetes . *ANOVA test was used with post hoc Bonferroni test for pairwise comparison # Kruskal Wallis test was for comparison of three groups and Mann-Whitney test was used to compare two groups

During follow-up, there was a higher nonsignificant rate of death in prediabetic patients (7.41%) than diabetics (5.66%) and nondiabetic (5%) (p > 0.05). Also, the prediabetic group showed a higher nonsignificant abnormal change in ECG (81.48%) than the diabetic (81.13%) and nondiabetic (80.00%) (p > 0.05) (**Table. 5,Fig.3**).

Table 5. Comparison between patients regarding follow-up

Variables	**Non-diabetics N=20**	**Prediabetes N=27**	**Diabetes N=53**	**P value**	**P1**	**P2**	**P3**
Chest pain							
• Improved	19 (95.00%)	25 (92.59%)	50 (94.34%)	0.93 *	1.00	1.00	1.00
• Arrested	1 (5.00%)	2 (7.41%)	3 (5.66%)				
Follow-up ECG							
• Normal	4 (20.00%)	5 (18.52%)	10 (18.87%)	0.63 *	0.29	0.70	0.58
• Abnormal:	16 (80.00%)	22 (81.48%)	43 (81.13%)				
• Raised ST segment	15 (75.00%)	15 (55.56%)	32 (60.38%)				
• Depressed ST segment	1 (5.00%)	6 (22.22%)	6 (11.32%)				
• Biphasic T wave	0	1 (3.70%)	1 (1.89%)				
• Inverted T wave	0	0	3 (5.56%)				
• Lt bundle branch block	0	0	1 (1.89%)				

P value compared the three groups, P1 compared non-diabetic and prediabetic, P2 compared non-diabetics and Diabetics, P3 compared prediabetics and diabetes. * Chi Square test or fisher exact test was used for comparison of the three groups and for pairwise comparison

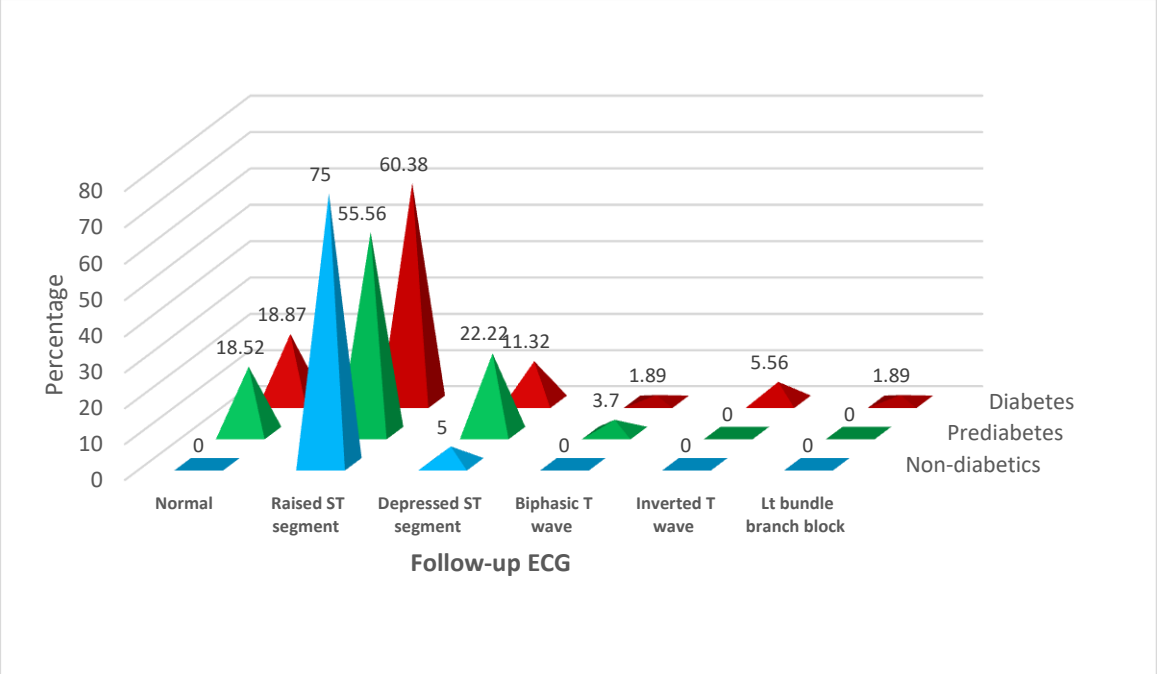

Fig .3. Relation between the presence of diabetes and follow-up ECG

Discussion

Worldwide, cardiovascular disease (CVD) continues to be the leading cause of mortality. Chronic and ACS are the most prevalent types. Although their causes are complex, behavioral risk factors including inactivity, poor eating habits, drinking, and weight gain-which also contribute to metabolic syndrome and diabetes-are among them. Elevated blood glucose values have a significant role in the development of atherosclerosis, plaque, and unfavorable outcomes in the general population **(Avogaro et al., 2019).**

In this study, we determined that among 100 patients with ACS, 53% of patients had diabetes and 27% had prediabetes.

Hyder and Mohammed (2016) found that Diabetics made up over two-thirds (62,4%) of ACS patients. Similarly, **AlNemer et al.(2012)** study on participants in the Saudi Project for Assessment of Acute Coronary Syndrome (SPACE) found that diabetics made up 57.9% of ACS patients.

Muhammed et al. (2019) found that ACS Groups A (normoglycemic group, N = 228), B (prediabetes group, N = 177), and C (diabetic group, N = 326) of patients were separated. 24% of the participants in the research were prediabetics. There were only 8 individuals among those with HbA1C levels in the prediabetic category who were also receiving medical care. 7% of patients in the diabetic group had just received their diagnosis, meaning that 26% of the study's participants were newly prediabetic or diabetic.

This emphasizes the widespread frequency of aberrant glucose profiles in patients hospitalized with ACS and the increased incidence of glucose abnormalities in Egypt.

These findings demonstrate that the majority of ACS patients have metabolic abnormalities, such as prediabetes and diabetes, which raise the likelihood of serious clinical events shortly. However, adopting an active lifestyle and/or

receiving pharmaceutical treatment will improve these individuals' prognosis. The risk of developing T2DM in patients with prediabetes has been shown to decrease with lifestyle interventions that encourage weight loss through a low-calorie diet and exercise, and it has been hypothesized that metformin pharmacotherapy can also halt the development of T2DM in prediabetic patients. Current recommendations urge that patients with established T2DM and prediabetes be treated with lifestyle change and/or medication to postpone organ damage, even if rigorous glycemic regimens have not been demonstrated to reduce mortality in patients with acute MI and T2DM. Determining metabolic abnormalities in ACS patients may thus have significant therapeutic ramifications that may be utilized to enhance long-term prognosis. Along with stringent hypertension and cholesterol treatment, the ADA advises people with CAD and T2DM to lose weight and reduce their risk of cardiovascular disease (**ADA, 2022**).

With the help of our research, we were able to show that there was no statistical variation between the groups when it came to the diagnosis of STEMI, non-STEMI, unstable angina, blood pressure, pulse, and cardiac examination ($p > 0.05$). **Elsliney et al. 2018** found that concerning ST-segment deviation (ST elevation or depression) and values of cardiac enzymes, there was no discernible variation between the three groups that were examined. **Norhammar et al. (2002)** observed a non-significant variation in ST-segment deviation across their research subgroups, indicating that ST-segment deviation did not significantly affect the patient outcomes as reported by ACS. **Winzap et al. (2019)** found that patients with diabetes also had a greater heart rate than non-diabetics, although there was no discernible change in blood pressure.

In this research, we discovered a considerable variation in HbA1C (%), fasting blood glucose (mg/dL), and cholesterol (mg/dL) between the analyzed groups ($P < 0.05$). Moreover, we found that there was considerable variation between prediabetics and diabetics as regards Cholesterol (mg/dL) ($p < 0.05$). While there was insignificant variation between studied groups as regards Troponin ($p > 0.05$). A study by **Winzap et al. (2019)** found that in comparison to non-diabetics, diabetic individuals had substantially lower levels of HDL-C, LDL-C, and total cholesterol, but higher levels of triglycerides (all $p < 0.001$). Additionally, diabetic individuals exhibited significantly greater CRP levels ($p < 0.001$)

In this study, ACS patients with prediabetes/diabetes had a significantly higher risk of adverse in-hospital outcomes when compared to people without diabetes. However, there was insignificant difference between the stages of diabetes and (clinical presentation and follow-up data). This was in accordance with **Giraldez et al., 2013** who found that patients with high-risk non-ST-segment elevation ACS often had undetected diabetes and prediabetes, and these patients seemed to have inferior short-term results.

Conclusion

Prediabetes with ACS patients had a worse prognosis than those with normoglycemia, but prediabetics and diabetics patients had comparable results. These findings support the notion that prediabetes increases the risk of CV events.

Study limitations: Given that T2DM is a chronic condition that results in chronic organ damage over time, our

study's sample size is rather small, particularly for patients with newly diagnosed prediabetes and DM, and the follow-up period is relatively brief. Given that this evaluation is susceptible to memory mistakes and inaccuracy, we were unable to identify the length of T2DM in each instance.

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