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PREVALENCE OF UNDIAGNOSED DIABETES MELLITUS IN ACUTE CORONARY SYNDROME (ACS) PATIENTS

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Abstract:
The prevalence of undiagnosed diabetes mellitus (DM) among patients with acute coronary syndrome (ACS) is alarmingly high, impacting clinical outcomes and necessitating improved screening strategies. This study aim to quantify the prevalence of undiagnosed DM in ACS patients, comparing diagnostic criteria such as the Oral Glucose Tolerance Test (OGTT) and HbA1c levels. The findings highlight a substantial proportion of undiagnosed DM detected by several methods. Enhanced screening protocols integrating multiple diagnostic methods are crucial for optimizing management and improving cardiovascular outcomes in this high-risk population. After conducting research across various search engines, it has been determined that there is a notably high prevalence of undiagnosed diabetes mellitus among patients with acute coronary syndrome. This highlights the importance of implementing routine diabetes screening in this high-risk group. Detecting and managing diabetes early in ACS patients has the potential to enhance clinical outcomes and alleviate the burden of cardiovascular complications.

Key words: Undiagnosed diabetes mellitus, acute coronary syndrome, prevalence, cardiovascular risk.

Introduction:

Diabetes mellitus (DM) is linked to a heightened risk of cardiovascular morbidity and mortality, including coronary artery disease (CAD). Elevated glucose levels at admission in patients with acute coronary syndrome (ACS) serve as a significant independent predictor of hospital mortality, and this is especially critical for patients without a known history of DM. Acute Coronary Syndrome (ACS) encompasses a range of urgent cardiac conditions, including myocardial infarction and unstable angina, which are primarily driven by atherosclerotic plaque rupture and thrombosis. Diabetes Mellitus (DM), particularly Type 2 Diabetes, is a well-recognized risk factor for cardiovascular diseases, including ACS. However, the prevalence of undiagnosed diabetes in patients presenting with ACS remains a critical concern, as it can significantly influence management strategies and outcomes. Numerous studies have indicated a high prevalence of undiagnosed diabetes in patients

presenting with ACS. Research has shown that a substantial proportion of ACS patients have either newly diagnosed diabetes or impaired glucose tolerance when systematically screened during their hospitalization. Research has consistently demonstrated a high prevalence of undiagnosed diabetes among patients with acute coronary syndrome (ACS). Haffner et al. (1998) found that many myocardial infarction patients had previously undiagnosed diabetes identified through an oral glucose tolerance test (OGTT). Similarly, Bartnik et al.(1) reported that around one in three ACS patients had either newly diagnosed diabetes or impaired glucose regulation when assessed with OGTT. Norhammar et al.(2) also revealed that nearly 25% of patients tested shortly after an acute myocardial infarction were found to have undiagnosed diabetes using OGTT.

This review synthesizes the existing literature on the prevalence of undiagnosed diabetes mellitus in ACS patients, highlighting the implications for clinical practice and future research.

Prevalence of Undiagnosed Diabetes in ACS Patients:

The prevalence of undiagnosed diabetes among patients presenting with Acute Coronary Syndrome (ACS) is notably high, as evidenced by multiple studies.(2-5) This prevalence varies depending on the demographic and geographic population examined, the diagnostic criteria employed, and the methodologies utilized. For instance, the Euro Heart Survey on Diabetes and the Heart reported that approximately 22% of ACS patients had undiagnosed diabetes when screened using oral glucose tolerance tests (OGTT). Similarly, a study by Norhammar et al.(2) In the United States found that about 25% of ACS patients had undiagnosed diabetes, identified through HbA1c levels, reflecting contemporary diagnostic practices. Variations in diagnostic criteria significantly impact these findings, with studies using OGTT often reporting higher prevalence rates compared to those using fasting plasma glucose (FPG) or HbA1c alone. Bartnik et al.(1), for example, demonstrated that OGTT identified undiagnosed diabetes in 30% of ACS patients, a higher rate than when using FPG or HbA1c criteria. Additionally, the methodology of screening profoundly influences reported prevalence, with continuous glucose monitoring and comprehensive metabolic panels providing more accurate identification of glucose abnormalities than sporadic blood tests.

Roughly half of adults with diabetes worldwide remain undiagnosed, according to the International Diabetes Federation (IDF). In 2021, IDF estimated that out of the 537 million adults aged 20 to 79 living with diabetes globally, around half of them were unaware of their condition.(6, 7) In the United States, the Centers for Disease Control and Prevention (CDC) noted that approximately 23.8% of all adult diabetes cases were undiagnosed in 2020, equating to roughly 7.3 million adults unaware of their condition.(7, 8) Similar patterns are seen in Europe and other regions, where studies have found that between 22%-40% of diabetes cases go undiagnosed across various European countries.(8)

While there may be a scarcity of research specifically addressing the prevalence and epidemiology of undiagnosed diabetes mellitus in acute coronary syndrome (ACS) patients in Pakistan, relevant literature does exist. For instance, a study led by Sibghatullah Babar et al.(9) in Pakistan examined the prevalence of diabetes mellitus in cases of acute ischemic stroke. The study found that diabetes mellitus was present in 24% of cases (n=36). In another study conducted in Pakistan by Nasir Ahmed et al(10), it was reported that out of 250 patients diagnosed with acute coronary syndrome (ACS), 79 patients, accounting for 31.6% of the total, had diabetes. The prevalence of diabetes mellitus in this study was notable, with one out of every three patients diagnosed with acute coronary syndrome found to have diabetes. In a prospective cohort of patients with acute coronary syndrome, it was found that 57% of them exhibited abnormal glucose metabolism. Interestingly, around 66% of those who fulfilled the criteria for new diabetes were neither diagnosed nor treated for the condition by their managing physicians.(11)

Risk Factors: The relationship between undiagnosed diabetes and acute coronary syndrome (ACS) is complex, as undiagnosed diabetes can significantly contribute to the development and severity of ACS.

Undetected diabetes mellitus (DM) stands as a significant risk factor among patients experiencing

Acute Coronary Syndrome (ACS), profoundly affecting their prognosis and treatment. The intricate relationship between diabetes and ACS encompasses a variety of biological mechanisms, clinical presentations, and therapeutic strategies. This review aims to delve into existing literature regarding the risk factors associated with undiagnosed diabetes in ACS, elucidating its underlying pathophysiology, diagnostic hurdles, and therapeutic implications.

Pathophysiology of Undiagnosed Diabetes in ACS:

Undiagnosed diabetes contributes to the development of ACS through a multitude of pathways, including endothelial dysfunction, inflammation, hypercoagulability, and accelerated atherosclerosis. Elevated blood glucose levels exacerbate oxidative stress and impair endothelial function, heightening the risk of plaque destabilization and rupture, critical events in ACS.(12) Moreover, insulin resistance, characteristic of undiagnosed diabetes, fosters the release of pro-inflammatory cytokines, thereby promoting the progression of atherosclerotic plaques and facilitating thrombus formation.(13) Undiagnosed diabetes significantly contributes to the development of Acute Coronary Syndrome (ACS) through various interconnected pathways, including endothelial dysfunction, chronic inflammation, hypercoagulability, and accelerated atherosclerosis, collectively exacerbating cardiovascular risk and leading to adverse outcomes. Elevated blood glucose levels in undiagnosed diabetes cause oxidative stress, damaging endothelial cells, impairing vascular tone regulation, and promoting atherosclerosis; hyperglycemia-induced oxidative stress and resultant endothelial dysfunction are pivotal in plaque formation and destabilization, precipitating ACS. (12) Chronic inflammation, a hallmark of diabetes, involves elevated levels of pro-inflammatory cytokines like TNF-α, IL-6, and CRP, which exacerbate vascular inflammation, accelerate plaque growth, and increase instability, leading to plaque rupture and ACS.(13) Hypercoagulability in undiagnosed diabetes, characterized by increased platelet aggregation, elevated fibrinogen levels, and impaired fibrinolysis, enhances thrombus formation on ruptured plaques, raising the risk of occlusive thrombi that precipitate ACS.(14) The combined effects of endothelial dysfunction, chronic inflammation, and hypercoagulability accelerate atherosclerosis; hyperglycemia promotes the formation of advanced glycation end-products (AGEs), contributing to vascular stiffness and rapid plaque progression, further increasing the likelihood of plaque rupture and ACS.(15) These pathophysiological mechanisms highlight the multifactorial role of undiagnosed diabetes in ACS development, creating a high-risk environment for cardiovascular events.

Prevalence and Screening Challenges:

The prevalence of undiagnosed diabetes among ACS patients varies across studies but consistently remains high, ranging between 20% and 40%.(1) However, diagnosing diabetes during an ACS episode poses challenges due to stress-induced hyperglycemia, which may obscure underlying diabetes. Traditional diagnostic criteria, relying solely on fasting plasma glucose or HbA1c levels, may not accurately reflect glycemic status during acute illness, necessitating alternative screening methods such as oral glucose tolerance tests (OGTT).(16) Bartnik et al. (2004) conducted the Euro Heart Survey on diabetes and the heart, which revealed that approximately 20% of patients with coronary artery disease (CAD) had previously undiagnosed diabetes.(1) This large-scale study emphasized the need for comprehensive screening in ACS patients to identify occult diabetes early. Contrastingly, a study by McGuire et al. found a higher prevalence of undiagnosed diabetes in ACS patients, estimating it to be around 28%.(17) This study utilized a combination of fasting plasma glucose and HbA1c levels to diagnose diabetes, which might account for the higher detection rate compared to studies relying on a single diagnostic criterion. Further, Rao et al. reported an even higher prevalence, ranging from 30% to 40%, in their cohort of ACS patients.(18) They emphasized the importance of using oral glucose tolerance tests (OGTT) in addition to standard diagnostic measures, as stress-induced hyperglycemia during an acute event can obscure the underlying chronic hyperglycemia indicative of diabetes.

These studies collectively highlight the varying prevalence rates of undiagnosed diabetes in ACS patients, ranging from 20% to 40% depending on the diagnostic criteria and screening methods employed. This variability underscores the critical need for standardized diagnostic approaches and comprehensive screening strategies to ensure accurate identification and management of diabetes in ACS patients

Clinical Implications:

The presence of undiagnosed diabetes in ACS significantly worsens patient outcomes, leading to higher rates of recurrent ischemic events, heart failure, and mortality compared to normoglycemic individuals.(19) Furthermore, patients with undiagnosed diabetes often present with atypical ACS symptoms, such as silent myocardial infarction or non-specific complaints, delaying timely intervention and exacerbating myocardial damage.(12) The presence of undiagnosed diabetes in ACS patients significantly worsens outcomes due to several interconnected factors. Elevated blood glucose levels lead to increased oxidative stress, damaging endothelial cells and contributing to the destabilization and rupture of atherosclerotic plaques, which can precipitate ACS and recurrent ischemic events such as heart attacks. Additionally, chronic inflammation and insulin resistance in undiagnosed diabetes promote the release of pro-inflammatory cytokines, accelerating atherosclerosis and increasing the likelihood of plaque formation and subsequent cardiovascular events. The delayed diagnosis and lack of appropriate glycemic control mean that hyperglycemia's harmful effects on the cardiovascular system persist, worsening the prognosis and increasing the risk of complications like heart failure. Patients with undiagnosed diabetes often present with atypical ACS symptoms, such as silent myocardial infarctions or non-specific complaints, delaying recognition and timely treatment, leading to more extensive myocardial damage. Furthermore, undiagnosed diabetes frequently coexists with other cardiovascular risk factors, such as hypertension, dyslipidemia, and obesity, compounding the overall cardiovascular risk and making patients more susceptible to severe outcomes. Consequently, these patients face a higher incidence of recurrent ischemic events, increased rates of heart failure, and overall higher mortality rates compared to normoglycemic individuals, underscoring the importance of early detection and management of diabetes in patients with cardiovascular disease to improve outcomes and reduce complications.

Therapeutic Considerations:

Effective management of ACS in patients with undiagnosed diabetes requires tailored therapeutic strategies to mitigate adverse outcomes. Achieving optimal glycemic control is paramount, aiming to minimize hyperglycemia-induced myocardial injury and reduce the risk of recurrent ischemic events.(15) Pharmacotherapeutic interventions, including antiplatelet agents, statins, and renin-angiotensin-aldosterone system inhibitors, play a pivotal role in attenuating the progression of atherosclerosis and optimizing cardiovascular outcomes in this high-risk population.(20) Effective management of Acute Coronary Syndrome (ACS) in patients with undiagnosed diabetes necessitates tailored therapeutic strategies to mitigate adverse outcomes. This approach is essential due to the unique pathophysiological challenges and heightened cardiovascular risk posed by undiagnosed diabetes.

Firstly, achieving optimal glycemic control is paramount. Hyperglycemia is known to exacerbate myocardial injury during ACS and contribute to worse outcomes. Rydén et al.(15) in the European Society of Cardiology (ESC) guidelines highlight that maintaining blood glucose levels within a target range can reduce myocardial damage and improve survival rates. Intensive insulin therapy, aimed at maintaining glucose levels between 140-180 mg/dL, is recommended to manage hyperglycemia in the acute setting of ACS.

Secondly, pharmacotherapy plays a crucial role. Patients with undiagnosed diabetes and ACS benefit significantly from medications that address both cardiovascular risk and glucose metabolism. Antiplatelet agents, such as aspirin and P2Y12 inhibitors, are essential in preventing thrombotic events. Studies, such as those by Bhatt and Steg (21) demonstrate the effectiveness of

these agents in reducing recurrent ischemic events. Additionally, statins are indispensable in managing dyslipidemia and reducing atherosclerotic plaque progression. The PROVE-IT TIMI 22 trial specifically showed that intensive statin therapy provides greater benefits in ACS patients, including those with diabetes.(22)

Thirdly, addressing the renin-angiotensin-aldosterone system (RAAS) is vital. ACE inhibitors or angiotensin II receptor blockers (ARBs) are recommended for their cardio protective effects, particularly in patients with diabetes. These medications help reduce blood pressure, decrease myocardial workload, and improve overall cardiovascular outcomes. The HOPE study (Yusuf et al., 2000) confirmed that ACE inhibitors significantly reduce the risk of myocardial infarction, stroke, and cardiovascular death in high-risk patients, including those with diabetes. Moreover, lifestyle modifications and patient education are critical components of managing ACS in patients with undiagnosed diabetes. Emphasis on dietary changes, physical activity, and smoking cessation can substantially improve long-term outcomes. The Diabetes Prevention Program (DPP) study (23) demonstrated that lifestyle interventions are effective in delaying or preventing the onset of diabetes and its complications.

The effective management of ACS in patients with undiagnosed diabetes requires a multifaceted approach that includes rigorous glycemic control, comprehensive pharmacotherapy, and lifestyle modifications. By tailoring therapeutic strategies to address the specific needs of these patients, healthcare providers can significantly mitigate adverse outcomes and improve overall prognosis.

Table: Characteristics of various studies having undiagnosed DM.

Author	Study population	Patients	Prevalence of undiagnosed diabetes mellitus
W.K. Abdullatef et al.[24]	ACS	583	55%
Małgorzata Bartnik et al. [1]	ACS	1920	30%
Norhammar et al.[2]	ACS	164	25%
Muhammad Shamill Shamsul Ismail et al.	STEMI	85	22.4%
Muhammad A. Karamat et al.[25]	ACS	198	43%
McGuire et al.[17]	ACS	15,800	28%
Nasir Ahmed et al.[10]	ACS	250	31.6%
Agata Bronisz et al.[26]	AMI	200	36.0%
Lewczuk et al.[27]	ACS	69	56.6%)
Knudsen et al.[28]	STEMI	201	54%

Conclusion: The prevalence of undiagnosed diabetes mellitus is notably high among patients with acute coronary syndrome, underscoring the need for routine diabetes screening in this high-risk group. Early detection and management of diabetes in ACS patients could potentially improve clinical outcomes and reduce the burden of cardiovascular complications.

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