

## HIDDEN BURDEN OF CORONARY MICROVASCULAR DISEASE IN A DIABETIC FEMALE NSTEMI PATIENT : A CASE-BASED CLINICAL PERSPECTIVE

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### ABSTRAK

Penyakit mikrovaskular koroner (Coronary Microvascular Disease/CMD) semakin dikenal sebagai penyebab iskemia miokard pada pasien tanpa penyakit arteri koroner obstruktif, terutama pada perempuan dengan diabetes. Infark miokard non-ST elevasi (NSTEMI) dalam kelompok ini sering muncul dengan gejala atipikal dan temuan elektrokardiografi yang tidak spesifik, sehingga menyulitkan diagnosis dan penanganan yang tepat waktu. Seorang perempuan usia 50 tahun dengan riwayat diabetes melitus dan hipertensi datang dengan keluhan nyeri dada yang berlangsung lama tanpa elevasi segmen ST pada elektrokardiogram. Evaluasi kardiak menunjukkan NSTEMI anterior, namun tidak ditemukan obstruksi pada pembuluh koroner epikardial. Karakteristik klinis dan demografis pasien mengarah pada dugaan disfungsi mikrovaskular koroner. Pasien ditatalaksana secara konservatif dengan terapi antiplatelet ganda, antihipertensi, dan pengendalian metabolik. Kasus ini menggambarkan permasalahan tersembunyi CMD pada perempuan dengan diabetes, di mana cedera iskemik dapat terjadi meskipun hasil angiografi tampak normal. CMD melibatkan disfungsi endotel, penurunan cadangan aliran koroner, dan aktivasi inflamasi, yang semakin nyata dalam kondisi diabetes. Alat diagnostik konvensional seringkali tidak memadai untuk mendeteksi CMD, sehingga diperlukan kecurigaan klinis yang tinggi. CMD perlu dipertimbangkan pada perempuan dengan diabetes yang mengalami NSTEMI, terutama jika perubahan elektrokardiografi minimal dan wilayah infark melibatkan miokard anterior. Pengakuan dini dan terapi yang ditargetkan sangat penting untuk menurunkan risiko kardiovaskular jangka panjang pada subpopulasi berisiko tinggi ini.

**Kata kunci** : diabetes melitus, pasien perempuan, disfungsi endotel, infark miokard non-ST elevasi, penyakit mikrovaskular koroner

### ABSTRACT

Coronary microvascular disease (CMD) is an increasingly recognized cause of myocardial ischemia in patients without obstructive coronary artery disease, particularly among diabetic women. Non-ST-elevation myocardial infarction (NSTEMI) in this population may present with atypical symptoms and non-specific electrocardiographic findings, complicating timely diagnosis and appropriate management. Cardiac evaluation indicated an anterior NSTEMI, yet no signs of epicardial vessel occlusion were evident. The clinical features and demographic profile suggested underlying coronary microvascular dysfunction. The patient was managed conservatively with dual antiplatelet therapy, antihypertensives, and metabolic control. Discussion: This case exemplifies the hidden burden of CMD in diabetic female patients, where ischemic injury may occur despite normal angiographic findings. CMD involves endothelial dysfunction, impaired coronary flow reserve, and inflammatory activation, particularly in the diabetic milieu. Conventional diagnostic tools are often insufficient to identify CMD, underscoring the need for heightened clinical suspicion. Conclusion: CMD should be considered in diabetic women presenting with NSTEMI, especially when electrocardiographic changes are minimal and infarct territory involves anterior myocardium. Recognition and targeted therapy are vital to reducing long-term cardiovascular risk in this high-risk subgroup.

**Keywords** : non-ST-elevation myocardial infarction, coronary microvascular disease, diabetes mellitus, female patients, endothelial dysfunction

## INTRODUCTION

Non-ST-elevation myocardial infarction (NSTEMI) represents a significant clinical entity within the spectrum of acute coronary syndromes (ACS), accounting for a substantial proportion of hospital admissions related to cardiac ischemia (Chowdhury et al., 2020). While traditionally associated with obstructive coronary artery disease (CAD), an increasing body of evidence highlights that a considerable subset of NSTEMI cases, particularly among women with diabetes mellitus, occurs in the absence of significant epicardial stenosis (Dąbek et al., 2016; Deedwania et al., 2017). In these patients, the absence of ST-segment elevation on electrocardiography (ECG), despite ongoing myocardial injury, contributes to diagnostic ambiguity and often delays appropriate intervention (Cha et al., 2022; Khalil et al., 2024). One of the most underrecognized contributors to myocardial ischemia in this population is coronary microvascular disease (CMD). CMD is characterized by functional and structural abnormalities within the coronary microcirculation, including impaired vasodilatory capacity, altered autoregulation, endothelial dysfunction, and reduced coronary flow reserve (CFR) (Chowdhury et al., 2020).

These microvascular changes can induce myocardial ischemia and injury even when coronary angiography reveals angiographically normal or only mildly stenotic epicardial vessels. CMD is especially prevalent in female patients with type 2 diabetes, a demographic known to experience ischemic heart disease with atypical or non-classic presentations (Berman et al., 2017; Cole et al., 2024). The pathophysiology of CMD in diabetic women is multifactorial. Chronic hyperglycemia promotes a cascade of deleterious effects including endothelial dysfunction, oxidative stress, low-grade inflammation, and microvascular remodeling, all of which compromise myocardial perfusion at the microvascular level (Fonseca et al., 2023). Moreover, diabetes-associated insulin resistance and dyslipidemia contribute to an environment that accelerates the deterioration of coronary microcirculatory integrity. In women, additional physiological and anatomical factors, such as smaller baseline coronary artery diameters, fluctuations in sex hormones, and enhanced microvascular reactivity, confer greater susceptibility to CMD-related ischemia (Le et al., 2022; Hu et al., 2024).

Clinically, microvascular angina or ischemia due to CMD often escapes timely recognition. Standard ECG findings may be non-specific, and troponin elevations can be subtle or delayed. Furthermore, typical anginal symptoms may be absent, replaced by vague complaints such as fatigue, dyspnea, or epigastric discomfort, especially in women (Safdar et al., 2018; Berman et al., 2017). This symptom profile, in conjunction with non-diagnostic ECG and non-obstructive angiographic findings, frequently leads to misclassification or underestimation of cardiovascular risk (Manfredonia et al., 2019; Kobo et al., 2021). Currently, there are significant gaps in the diagnostic algorithms for CMD, particularly in the context of NSTEMI without overt ST-segment elevation. Tools such as coronary angiography, while useful for ruling out obstructive disease, do not provide insight into microvascular integrity. Advanced diagnostic techniques such as coronary flow reserve measurement (via PET, MRI, or invasive Doppler flow wire), index of microvascular resistance, and endothelial function testing remain underutilized due to limited availability and lack of routine incorporation into guidelines (Al-Saffar et al., 2015; Gouda et al., 2021).

Consequently, risk stratification models often fail to account for CMD, resulting in underdiagnosis, delayed treatment, and inadequate secondary prevention strategies in this vulnerable group (Pandey et al., 2016; Kwiendacz et al., 2025). In light of these challenges, greater clinical awareness and vigilance are essential, especially for diabetic women presenting with NSTEMI and inconclusive standard investigations. This case underscores the need to refine diagnostic pathways and therapeutic approaches to CMD, ensuring that microvascular contributors to myocardial injury are adequately identified and managed. Early recognition and

tailored therapy hold promise for improving cardiovascular outcomes in this high-risk, yet frequently overlooked, subgroup (Hassan et al., 2022; Thomas et al., 2023).

## CASE REPORT

A 50-year-old female with a known history of diabetes mellitus and hypertension presented to the emergency department complaining of persistent, non-exertional chest pain that lasted for approximately 20 minutes. The pain was described as a pressing and constricting sensation over the left precordial region and did not resolve with rest. Associated symptoms included fatigue and headache. Physical examination revealed a moderately ill appearance, blood pressure of 144/73 mmHg, heart rate of 81 bpm, and oxygen saturation of 98% on nasal cannula. No signs of heart failure or peripheral hypoperfusion were noted. Cardiopulmonary auscultation was within normal limits, and abdominal examination revealed tenderness in the right upper quadrant. Electrocardiographic assessment showed subtle abnormalities suggestive of anterior wall ischemia without ST-segment elevation. Laboratory workup and cardiac enzyme analysis supported the diagnosis of non-ST-elevation myocardial infarction (NSTEMI). Given the infarct location in the anterior myocardial territory, which typically denotes a higher ischemic burden and poorer prognosis, the lack of ST-segment elevation was considered discordant with the clinical severity.

No immediate evidence of obstructive epicardial coronary artery disease was available from imaging, and advanced diagnostic modalities such as coronary angiography or cardiac magnetic resonance imaging were not performed during the initial hospitalization. The patient was admitted for inpatient management and received pharmacologic therapy including dual antiplatelet agents, calcium channel blockers, angiotensin receptor blockers, statins, and symptomatic support. Her symptoms gradually improved, and hemodynamic stability was achieved during hospitalization. She was discharged with recommendations for outpatient cardiology follow-up and optimization of metabolic control. This case highlights a presentation of myocardial infarction in a diabetic female patient that is clinically significant yet easily underrecognized. The absence of ST-segment elevation in a high-risk anatomical infarct zone raises the possibility of coronary microvascular dysfunction as the primary pathophysiological mechanism, which is frequently underestimated in standard diagnostic pathways. The patient's gender, metabolic status, and ischemic territory collectively suggest an elevated risk profile, warranting increased awareness and more nuanced clinical evaluation for coronary microvascular disease in similar populations.

## DISCUSSION

Chronic hyperglycemia in diabetes mellitus initiates a cascade of microvascular injury mechanisms that culminate in endothelial dysfunction, oxidative stress, and maladaptive vascular remodeling. These alterations impair nitric oxide bioavailability and promote a pro-inflammatory and pro-thrombotic endothelial phenotype that compromises coronary flow reserve (Kwiendacz et al., 2025; Basile et al., 2019). In female patients, structural and functional differences in coronary vasculature, such as smaller vessel diameter and heightened autonomic sensitivity, further predispose to coronary microvascular dysfunction even in the absence of critical epicardial stenosis (Al-Rousan et al., 2022; Hryhoriy, 2016). The resulting syndrome, known as coronary microvascular disease, often manifests as angina or NSTEMI with minimal electrocardiographic abnormalities and non-obstructive findings on angiography (Hryhoriy, 2016; Teo & Rafiq, 2021). The patient in this case presented with prolonged, non-exertional chest pain unresponsive to rest and was diagnosed with anterior NSTEMI. Despite the high-risk anatomical involvement of the anterior wall, the electrocardiographic findings did

not meet the criteria for ST-segment elevation, indicating a discrepancy between ischemic burden and surface electrical expression (Hryhoriy, 2016; Teo & Rafiq, 2021).

This clinical pattern is consistent with the pathophysiological model of coronary microvascular disease, in which microvascular impairment limits oxygen delivery without the abrupt vessel occlusion typically observed in plaque rupture syndromes. In diabetic women, this form of ischemia is frequently underrecognized due to non-specific presentation and the limitations of routine diagnostic modalities (He et al., 2025; Bertoluci et al., 2020). From a diagnostic standpoint, conventional tools such as resting electrocardiography and static imaging modalities lack sensitivity in detecting microvascular perfusion deficits. Functional imaging techniques such as cardiac magnetic resonance imaging, positron emission tomography, and invasive coronary flow reserve measurement provide greater diagnostic clarity but remain underutilized due to limited availability and cost considerations (Kwiendacz et al., 2025; Thomas et al., 2023). However, the patient's demographic profile, risk factors, and infarct location strongly supported coronary microvascular dysfunction as a plausible underlying mechanism (Safdar et al., 2018; Elshorbagy et al., 2025).

Therapeutically, coronary microvascular disease presents a clinical challenge, as standard NSTEMI management emphasizes anti-thrombotic and revascularization strategies, which are less applicable when ischemia originates from the microcirculation. The patient received pharmacological therapy consistent with secondary prevention objectives, including dual antiplatelet therapy, antihypertensives, and metabolic control aimed at stabilizing endothelial function and reducing the risk of recurrent ischemic events (Chhabra et al., 2018). This approach is supported by current evidence, which favors endothelial-targeted therapy and comprehensive risk factor modification in patients with suspected microvascular ischemia (Manfredonia et al., 2019; Bruch et al., 2016).

Prognostically, patients with coronary microvascular disease-related NSTEMI do not demonstrate benign clinical courses. Despite the absence of obstructive lesions, this population is associated with persistent angina, impaired functional capacity, and elevated risk of major adverse cardiovascular events. The present case highlights the need for increased clinical awareness of coronary microvascular dysfunction in diabetic female patients presenting with NSTEMI. Failure to recognize this mechanism may lead to under-treatment and suboptimal long-term outcomes. Integrating clinical suspicion for coronary microvascular disease into existing risk stratification models is essential to ensure accurate diagnosis, appropriate management, and improved prognosis in this often-overlooked subgroup (Chhabra et al., 2018; Bruch et al., 2016; Kobo et al., 2021).

## CONCLUSION

Coronary microvascular dysfunction represents an underrecognized yet clinically significant mechanism of myocardial ischemia in diabetic female patients presenting with NSTEMI. The absence of ST-segment elevation or obstructive coronary lesions does not equate to a favorable prognosis. Early recognition based on clinical context, demographic risk, and infarct location is essential to guide appropriate medical therapy. This case underscores the importance of considering microvascular disease in diagnostic and therapeutic strategies to improve cardiovascular outcomes in high-risk but often underdiagnosed populations.

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