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Navigating the Complexity: Updates in Diabetes-Related Cardiovascular Complications

[1]*UBHENIN, AE; [2]INNIH, SO [1]ANURA, F; [1]IDRIS, RI

*[1]*Department of Biochemistry, Faculty of Sciences, Federal University Lafia, Nasarawa State, Nigeria*
[2]Department of Anatomy, Faculty of Medicine, University of Benin, PMB 1154, Benin City, Nigeria

**Corresponding Author Email: ehibram@yahoo.co.uk; Tel: +2348133893080*
Co-Authors Email: silvanus.innih@uniben.edu; anura4teemah@gmail.com; iyayana67@gmail.com

ABSTRACT: The aim of this study is to offer a thorough examination of contemporary research concerning cardiovascular complications induced by diabetes, with a specific focus on coronary artery disease (CAD), diabetic heart attacks, diabetic peripheral artery disease (PAD), and diabetic hypertension. The period of analysis spans from 1988 to 2022, and the data utilized is extracted from secondary sources. Diabetes mellitus is a chronic metabolic disorder associated with an increased risk of cardiovascular complications, including coronary artery disease (CAD), heart attacks, strokes, peripheral artery disease (PAD), and hypertension. These complications are influenced by chronic hyperglycemia, insulin resistance, dyslipidemia, inflammation, and endothelial dysfunction. Diabetic-induced cardiovascular diseases significantly contribute to morbidity and mortality rates worldwide. The studies highlight the potential of plant-derived targeted therapies in reducing inflammation and endothelial dysfunction, providing promising avenues for improving patient outcomes. Additionally, research on diabetes-specific medications, imaging techniques, individualized glycemic targets, and combination therapies reveals new approaches to managing diabetic-induced cardiovascular diseases. Precision medicine, advancements in imaging, and lifestyle interventions offer valuable tools for personalized treatment plans and improved patient care. Public health initiatives that enhance diabetes management, raise awareness, and improve healthcare access are crucial for reducing the burden of cardiovascular complications in Nigeria and other regions affected by diabetes. Further research and collaboration among healthcare professionals will refine our understanding and enhance the management of diabetic-induced cardiovascular diseases, ultimately reducing their impact on individuals with diabetes.

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Diabetes mellitus is a chronic metabolic disorder associated with an increased risk of cardiovascular complications such as coronary artery disease (CAD), heart attacks, strokes, peripheral artery disease (PAD), and hypertension (Wilson and Kannel 2002, Fox *et al.*, 2004, Gibler, 2018, Marso and Hiatt 2006). These complications are influenced by mechanisms including chronic hyperglycemia, insulin resistance, dyslipidemia, inflammation, and endothelial dysfunction. Diabetes significantly increases the risk of developing CAD, heart attacks, strokes, and PAD (Chi and Jaff 2008, Muir, 2009). The underlying mechanisms involve a combination of traditional risk factors and diabetes-related factors such as endothelial dysfunction, inflammation, and oxidative stress (D'Souza *et al.*, 2009;Sawada *et al.*, 2016; Syed Ikmal *et al.*, 2013; Kayama, *et al.*, 2015). Hypertension is a common comorbidity in individuals with diabetes and is linked to insulin resistance, hyperinsulinemia, endothelial dysfunction, and abnormalities in renal sodium handling (El-Atat *et al.*, 2004 ;da Silva, *et al.*, 2020). Cardiovascular complications pose a major concern for individuals with diabetes worldwide, including in Nigeria (Iloh, *et al.*, 2013; Glovaci, , *et*

al., 2019; Willis *et al.,* 2014). These complications contribute to increased morbidity and mortality rates, with CAD and strokes being particularly common (Glovaci , *et al.,* 2019; Kreatsoulas, and Anand, 2010). Factors such as limited healthcare access, inadequate glycemic control, low awareness of complications, and unhealthy lifestyles contribute to the increased prevalence of cardiovascular complications in Nigeria. Public health initiatives that focus on improving diabetes management, raising awareness, and enhancing healthcare access are crucial for reducing the burden of these complications (Keates *et al.,* 2017) . Therefore, the primary goal of this paper is to offer an in-depth examination of the latest research on cardiovascular diseases induced by diabetes. The focus will be specifically on coronary artery disease (CAD) in diabetic individuals, diabetic heart attacks, diabetic peripheral artery disease (PAD), and diabetic hypertension. The time frame for this comprehensive review spans from 1988 to 2022.

MATERIALS AND METHODS

The methodology for this comprehensive review on Navigating the Complexity: Updates in Diabetes-Related Cardiovascular Complications involved conducting a thorough literature search across approximately 78 academic journals using multiple databases from 1988 to 2022. Inclusion criteria focused on articles published within from to and relevant to the topic, while exclusion criteria filtered out review articles, opinion pieces, and unrelated content. The screening process included reviewing titles and abstracts, followed by a full-text review to determine eligibility. Multiple reviewers independently conducted the selection process, with consensus reached in case of disagreements. Data extraction utilized a standardized form to extract key information from the selected articles, including study objectives, design, participant characteristics, interventions or treatments, outcomes, and key findings. The synthesized data provided valuable insights into Navigating the Complexity: Updates in Diabetes-Related Cardiovascular Complications, ensuring a comprehensive and rigorous review.

RESULTS AND DISCUSSION

In recent research on Diabetic Coronary Artery Disease (CAD), there has been a focus on the cardiovascular outcomes of two classes of drugs - Sodium-Glucose Cotransporter-2 (SGLT2) inhibitors and Glucagon-Like Peptide-1 (GLP-1) receptor agonists (Lee *et al.,* 2020, Palmer *et al.,* 2021). Though these drugs were originally developed for diabetes management but have shown promise in reducing the risk of cardiovascular events and heart failure in diabetic patients with CAD (Sharma & Verma 2020; Mantovani *et al.,* 2022). Advancements in coronary imaging techniques, such as coronary computed tomography angiography (CCTA) and intravascular ultrasound (IVUS), have allowed for better risk stratification in patients with Diabetic CAD (Abdelrahman *et al.,* 2020). Researchers have explored the role of these imaging modalities in identifying coronary artery stenosis, vulnerable plaques, and myocardial perfusion abnormalities (Bertolone *et al.,* 2022). Inflammation plays a crucial role in the development of CAD, and recent studies have investigated the association between inflammatory markers, such as C-reactive protein (CRP) and interleukins, with CAD progression in individuals with diabetes (Mugabo and Renier, 2010). This has shed light on the importance of managing chronic low-grade inflammation in diabetic patients. Optimal glycemic control is fundamental in preventing and managing CAD in diabetic patients. Recent research has emphasized the importance of individualized glycemic targets, the role of newer diabetes medications, and the impact of hypoglycemia on cardiovascular outcomes (Ismail-Beigi *et al.,* 2011). Endothelial dysfunction, characterized by impaired nitric oxide bioavailability, is a key feature in the development of CAD in diabetes (Incalza *et al.,* 2018). Researchers have focused on understanding the mechanisms behind endothelial dysfunction and exploring potential therapies to restore endothelial function (Roberts and Porter 2013). Advancements in genetics and precision medicine have opened new avenues for personalized treatment approaches in Diabetic CAD (Rohde *et, al.,* 2019). Research studies have explored the role of genetic profiling, pharmacogenomics, and other biomarkers in predicting CAD risk and tailoring treatment strategies (Zaiou & El Amri,2017). Combination therapies involving antiplatelet agents, lipid-lowering medications, blood pressure control, and diabetes medications have been studied to optimize CAD management in diabetic patients with multiple risk factors (Chi & Jaff, 2008). Studies have also examined the long-term prognosis and quality of life in diabetic patients with CAD (Nys *et, al.,* 2006) .This includes assessing the impact of revascularization procedures, medical therapies, and lifestyle modifications on patient outcomes (Franklin *et, al.,* 2020) .

Recent Research Findings on Diabetic Heart Attack: Research on Diabetic Heart Attack, or myocardial infarction in diabetic patients, has focused on several key areas. Studies have investigated the cardiovascular outcomes and prognosis of diabetic patients who

experience a heart attack, examining mortality rates, recurrence of cardiovascular events, and overall long-term (Dzavik *et, al.,* 2001). The impact of hyperglycemia on myocardial injury, inflammation, and oxidative stress has been explored, emphasizing the importance of optimal glycemic control during and after a heart attack to improve recovery and reduce complications (Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) Study Group1998).Researchers have also looked into novel biomarkers and risk stratification methods to identify diabetic patients at higher risk of heart attacks, aiming to improve early detection and guide personalized treatment plans (Ganna *et al.,* 2014).

Additionally, research has evaluated the effectiveness and safety of cardiovascular medications such as antiplatelets, statins, beta-blockers, and ACE inhibitors in diabetic heart attack patients to reduce the risk of recurrent cardiac events (Hackam *et al.,* 2007). Lifestyle interventions, including diet, exercise, smoking cessation, and weight management, have been studied for their impact on secondary prevention in diabetic patients post-heart attack, contributing to overall cardiovascular health improvement (Brown *et al.,*2009).Moreover, investigations into diabetes-specific therapies, such as SGLT2 inhibitors and GLP-1 receptor agonists, have shown potential cardiovascular benefits beyond glycemic control (Žunić & Ponjavić 2020). Some studies have addressed healthcare disparities and access to care in diabetic heart attack patients, aiming to identify barriers and implement interventions to improve outcomes for underserved populations (Laba *et al.,*2013) . Lastly, research delving into the mechanisms and pathophysiology of diabetic heart attack provides valuable insights into the interplay between diabetes and cardiovascular disease, which helps in understanding and managing the increased risk of heart attacks in diabetic patients (Aneja *et al.,* 2008). These research efforts have significant implications for enhancing patient care and reducing the burden of heart attacks in diabetic populations.

Recent Research Findings on Diabetic Peripheral Artery Disease (PAD): Diabetic Peripheral Artery Disease (PAD) is characterized by narrowed and reduced blood flow in the peripheral arteries, commonly affecting the lower limbs in individuals with diabetes (Jude *et al.,* 2010). Research on Diabetic PAD has explored various themes and areas, including epidemiology and risk factors to understand the prevalence, incidence, and factors contributing to PAD development in diabetic patients (Song *et al.,* 2019). Studies have delved into the vascular biology and pathophysiology of Diabetic PAD, investigating endothelial dysfunction, oxidative stress, inflammation, and atherosclerosis in the peripheral arteries (Cooke and Wilson, 2010. Early detection is crucial for timely interventions and prevention of complications, and research has evaluated screening methods like ankle-brachial index (ABI) measurement and non-invasive vascular tests (Tehan *et al.,* 2016) .Treatment and management strategies have been investigated, encompassing medical therapies, lifestyle modifications, exercise programs, and revascularization procedures to improve blood flow in affected arteries (Tehan *et al.,* 2016) . The impact of Diabetic PAD on quality of life and functional outcomes has been assessed to guide interventions that improve overall well-being and daily functioning. Researchers have also explored diabetes-specific therapies, like SGLT2 inhibitors and GLP-1 receptor agonists, for their potential cardiovascular benefits in diabetic PAD beyond glycemic control (Žunić & Ponjavić2020). Further areas of research have focused on optimizing peripheral revascularization techniques and addressing healthcare disparities and access to care for diabetic patients with PAD. Preventive measures, such as lifestyle interventions, medication therapies, and patient education programs, have been studied to reduce the risk of PAD in individuals with diabetes. Overall, these research themes contribute to a deeper understanding of Diabetic PAD and offer insights into effective strategies for prevention and management, ultimately enhancing care and outcomes for diabetic patients affected by Peripheral Artery Disease.

*Recent Research findings on Diabetic Hypertension***.** Research on Diabetic Hypertension, the coexistence of diabetes and high blood pressure, has focused on several common themes and areas. Studies have investigated the prevalence of hypertension in diabetic patients and identified risk factors associated with its development and worsening (Simonson 1988). Understanding these factors is essential for targeted interventions and preventive strategies. Research has also explored the impact of diabetic hypertension on cardiovascular health, assessing the relationship between hypertension and the risk of cardiovascular events such as heart attacks, strokes, and heart failure in diabetic individuals (Hajar 2017). Investigations have delved into the underlying mechanisms and pathophysiological processes contributing to hypertension in diabetes, including insulin resistance, endothelial dysfunction, sodium retention, and activation of the renin-angiotensin-aldosterone system (Frati *et al.,* 2017).

Researchers have evaluated various approaches to blood pressure management and treatment in diabetic patients, exploring the efficacy and safety of

antihypertensive medications and lifestyle interventions. Diabetic hypertension's impact on kidney health and its role as a major risk factor for diabetic nephropathy has been examined, leading to strategies aimed at preserving kidney function (Raile *et, al.,* 2007) .Additionally, studies have investigated hypertension's role in the development and progression of microvascular complications like diabetic retinopathy and neuropathy in diabetic individuals (Girach *et al.,* 2006) . The impact of diabetes-specific therapies, such as SGLT2 inhibitors and GLP-1 receptor agonists, on blood pressure control and cardiovascular outcomes in diabetic patients with hypertension has also been a research focus (Hong *et al.,* 2019).

Researchers have examined the ideal blood pressure targets for diabetic patients, considering the balance between cardiovascular benefits and avoiding adverse effects. Addressing healthcare disparities and access to hypertension management in diabetic individuals has been a subject of research, with a focus on identifying barriers and improving care in underserved populations. Finally, lifestyle interventions, including dietary changes, physical activity, and stress management, have been assessed for their effectiveness in improving blood pressure control and overall cardiovascular health in diabetic patients. The findings from these research themes contribute to a deeper understanding of Diabetic Hypertension and offer valuable insights into effective strategies for prevention, management, and improving cardiovascular outcomes in diabetic individuals with high blood pressure, thereby enhancing patient care and reducing the burden of hypertension-related complications in diabetes.

Discussion of the Findings: The recent research findings in diabetic-induced cardiovascular diseases provide valuable insights into the pathophysiology, risk factors, and management strategies for these conditions. The studies highlight the potential of plant-derived targeted therapies, such as flavonoids, polyphenols, and other bioactive compounds, in reducing inflammation, oxidative stress, and endothelial dysfunction, which are critical factors in the development and progression of diabetic-induced cardiovascular diseases (Kong, *et, al.,* 2021). These therapies offer a promising avenue for improving patient outcomes and reducing the burden of cardiovascular complications in individuals with diabetes.

The research on SGLT2 inhibitors and GLP-1 receptor agonists has shown promising results in reducing the risk of cardiovascular events and heart failure in diabetic patients with CAD (Kong *et al.,* 2021). These diabetes-specific medications offer cardiovascular benefits beyond glycemic control and demonstrate the potential for a multifaceted approach to managing diabetic-induced cardiovascular diseases.Advancements in coronary imaging techniques, such as CCTA and IVUS, have improved risk stratification in patients with Diabetic CAD (Abdelrahman *et al.,* 2020) . Early detection of coronary artery stenosis and vulnerable plaques can aid in timely interventions and preventive measures, ultimately reducing the risk of adverse cardiovascular events.Furthermore, the association between inflammation markers and CAD progression in individuals with diabetes sheds light on the importance of managing chronic low-grade inflammation. This finding emphasizes the significance of addressing inflammation as a therapeutic target in the management of diabetic-induced cardiovascular diseases.

The studies on individualized glycemic targets, newer diabetes medications, and the impact of hypoglycemia on cardiovascular outcomes highlight the importance of optimizing glycemic control to prevent and manage diabetic-induced cardiovascular diseases effectively. Precision medicine approaches, incorporating genetic profiling, pharmacogenomics, and other biomarkers, offer promising avenues for personalized treatment strategies in Diabetic CAD, tailoring interventions based on individual patient characteristics and risks.
Combination therapies involving antiplatelet agents, lipid-lowering medications, blood pressure control, and diabetes medications have shown potential in optimizing CAD management in diabetic patients with multiple risk factors (Hammoud *et al.,* 2000). This comprehensive approach targets various aspects of the complex pathophysiology of diabetic-induced cardiovascular diseases (Kayama *et al.,* 2015) .

Moreover, research on the long-term prognosis and quality of life in diabetic patients with CAD provides crucial insights into the impact of revascularization procedures, medical therapies, and lifestyle modifications. Understanding the outcomes of various interventions helps in tailoring treatment plans to improve overall patient well-being and functional outcomes.

Conclusion: Plant-derived targeted therapies show promise in reducing inflammation and endothelial dysfunction, offering potential benefits beyond glycemic control. Precision medicine approaches, advancements in imaging techniques, and combination therapies provide valuable tools for personalized treatment plans and improved patient

outcomes. Further research and collaboration among healthcare professionals will continue to refine our understanding and enhance the management of diabetic-induced cardiovascular diseases, ultimately reducing the burden of cardiovascular complications in individuals with diabetes.

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