

DIABETES AND CARDIOVASCULAR COMPLICATIONS**Aqsa Shahid¹, Alishbah Roobi^{*2}, Wania Nasir³, Hina Pervaiz⁴, Rida Sarwar⁵, Ayesha Waris⁶**^{1,*2,3,4,5,6}Department of Physiology, The University of Faisalabad, Faisalabad, Pakistan.¹aqsassahid6565@gmail.com, ²alishbahroobi.physio@tuf.edu.pk, ³wania.nasir.phy@tuf.edu.pk, ⁴2024-mphil-phsl-005@tuf.edu.pk, ⁵2024-mphil-phsl-001@tuf.edu.pk, ⁶2024-mphil-phsl-004@tuf.edu.pkDOI: <https://doi.org/10.5281/zenodo.23038448>**Keywords***Diabetes Mellitus, Cardiovascular Disease, Hyperglycaemia, Atherosclerosis, Endothelial dysfunction,***Article History***Received: 30 January 2026**Accepted: 15 March 2026**Published: 31 March 2026***Copyright @Author****Corresponding Author: *****Alishbah Roobi****Abstract**

The study concentrated on the relationship between diabetes mellitus and cardiovascular complications, including the underlying mechanisms, epidemiology, risk factors, and management of the condition. It was established that diabetes increased the risk of cardiovascular complications including coronary heart disease, stroke and heart failure, which contributed to increased morbidity and mortality rates globally. The analysis focused on the effects of prolonged periods of hyperglycaemia, which resulted in oxidative stress, endothelial dysfunction, inflammation and dyslipidaemia, which significantly increased the progression of atherosclerosis. The study also established that there was a higher likelihood of developing cardiovascular complications among individuals with diabetes as compared to those without the condition as revealed by the epidemiology of the condition. The major risk factors, including hypertension, obesity and insulin resistance were established as major contributors to the progression of the condition. The study also revealed the importance of an integrated management approach including lifestyle changes, pharmacological management and periodic assessment of the condition, which showed that effective management of the condition, including its complications was critical in improving health outcomes among patients.

INTRODUCTION

A chronic metabolic condition, diabetes mellitus is a condition that is denoted by high blood sugar levels has become huge concerns, with approximately 589 million individuals being projected to have the condition by 2024 (International Diabetes Federation, 2026). The incidence of diabetes is on the increase and adds to its prolific health consequences. In addition to its effect on glucose metabolism, diabetes is also critical in the onset of cardiovascular diseases (CVDs) causing maximum number of deaths amongst diabetics. Research indicates that diabetes patients are two to four times more susceptible to diseases such as coronary heart

disease, heart failure, stroke, and other cardiovascular complications than nondiabetics. (Siam et al., 2024).

The mechanisms that link diabetes to CVD are multifaceted and complex, involving both macrovascular and microvascular complications. Continuous hyperglycemia seen in diabetes is a cause for ROS production, which causes oxidative stress, thus leading to damage to endothelial cells, dysfunction of blood vessels, and inflammation (Zakir et al., 2023). Moreover, increased blood sugar levels result in the development of AGEs that interrelate with vascular receptors and increase oxidative stress and inflammation, thus promoting

atherosclerotic development (Nikolaeva and Johnstone, 2023).

The pathophysiology of cardiovascular complications in diabetes is compounded by other risk factors such as hypertension, insulin resistance, and dyslipidemia.

Hypertension, commonly noted among diabetic patients, leads to a significant likelihood of atherosclerosis because it is a complement to hyperglycemia that causes harm to the walls of blood vessels (Wong and Sattar, 2023).

Dyslipidemia, which involves higher levels of triglycerides and lower concentrations of HDL cholesterol, also exacerbates the risk of cardiovascular complications because it facilitates the build-up of plaques in the arteries (Feingold and Grunfeld, 2023). Moreover, insulin resistance, common in cases of type 2 diabetes, plays a critical part in the occurrence of adverse cardiovascular consequences because it interferes with normal glucose utilization and inflammatory reactions (Zamanian et al., 2024). For this reason, it becomes necessary to tackle the relationship between diabetes and cardiovascular risk factors to enhance patients' health. This will require an all-encompassing strategy that incorporates lifestyle changes, medication, and health screening to control blood glucose levels and

avoid cardiovascular problems among diabetic individuals (Zakir et al., 2023; Ma et al., 2022).

Pathophysiology of Cardiovascular Complications in Diabetes

The underlying pathophysiology of cardiovascular disease in patients with diabetes mellitus involves multiple mechanisms, including metabolic disturbances, vascular abnormalities, and inflammation, all of which donate to the rapid onset of cardiovascular problems (Jyotsna et al. 2023). Central to this process is chronic hyperglycemia, which promotes biochemical alterations that damage vascular cells and facilitate the development of atherosclerosis (Zakir et al. 2023). Persistent high blood glucose levels rise the making of Reactive Oxygen Species (ROS), leasing to a state of oxidative stress. ROS damages endothelial cells, which normally regulate vascular tone and maintain blood vessel integrity. In the diabetic state, the production of the ROS diminishes the bioavailability of nitric oxide (NO), which is a key molecule responsible for encouraging vasodilation (Nikolaeva, and Johnstone, 2023). Balta (2021) argue that, this impairment results in endothelial dysfunction, causing vasoconstriction, inflammation and the formation of thrombi, which are significant contributors to vascular disease.

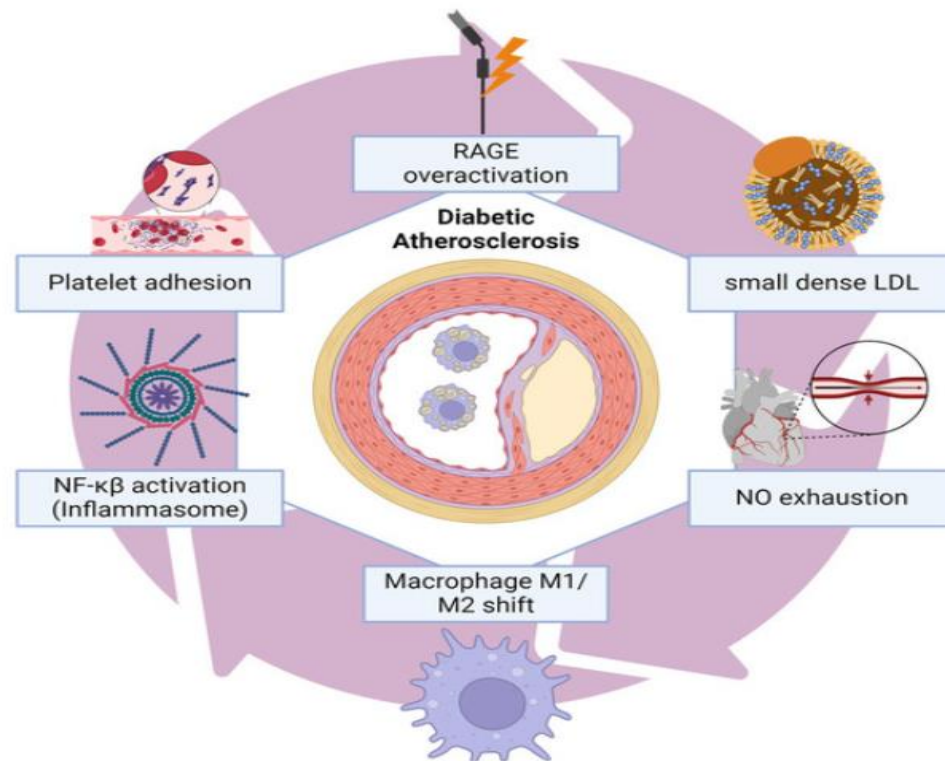


Figure 1: Pathways in diabetic atherosclerosis and coronary disease, highlighting key inflammatory and vascular mechanisms

Source: (Giraldo-Gonzalez et al. 2025)

At the beginning of the vascular pathology of diabetes, endothelial dysfunction is observed. The elevation of glucose levels leads to the activation of enzyme systems, including NADPH oxidase, which enhances the production of ROS, which, in its turn, triggers inflammatory pathways, including nuclear factor kappa B (NF κ B) (Zamanian et al. 2024). This promotes the production of adhesion molecules and inflammatory cytokines, which attracts these white blood cells towards the walls of the arteries. According to Poznyak et al. (2020), these immune cells produce a plaque by consuming oxidized lipoproteins to form foam cells in the inner lining of the arteries. Advanced Glycation End products (AGEs) are formed due to the non-enzymatic reaction of lipids and proteins at high glucose concentrations. According to Zgutka et al. (2023), AGEs activate their receptor, known as RAGE, which creates more oxidative stress and

damages the vessels. As mentioned by Ahmed et al. (2024), AGEs also contribute to hypertension and increased stiffness of the arteries.

Atherosclerosis is a key macrovascular complications, advances faster in diabetic people than in non-diabetic people. Rybníkářová, (2025) argue that, the oxidative alteration of the low-density lipoprotein (LDL) cholesterol is caused by hyperglycaemia and enhances the uptake of macrophages, which form foam cells and deposit plaque on arteries. With time, the plaques can become volatile and can rupture leading to thrombotic phenomena including myocardial infarction or stroke. Moreover, Feingold and Grunfeld (2023) discovered that, diabetes is linked to dyslipidaemia, i.e., high triglyceride and a low level of high-density lipoprotein (HDL) cholesterol, which worsens the progression of atherosclerotic plaques and predisposes to the development of vascular occlusions even more. The macrovascular complications caused by

diabetes include microvascular damage, leading to myocardial ischemia and diabetic cardiomyopathy, as well as impaired perfusion. Rupee et al. (2023) stated that, under this state, hyperglycaemia and insulin resistance change metabolic signaling within cardiomyocytes, resulting in mitochondrial dysfunction, fibrosis and defective calcium regulation, leading to decreased cardiac contraction and heart failure.

Impact of Hyperglycemia on Vascular Health

The chronic hyperglycemia, which is a typical feature of diabetes mellitus, has a well-reported and adverse effect on the vascular health. As per Clyne (2021) the vascular endothelium which controls blood vessel tone, vascular integrity and chronic high levels glucose levels can lead to dysfunctional inflammatory response over time. Hyperglycemia encourages the construction of reactive oxygen species (ROS) that, in its turn, decrease the bioavailability of nitric oxide (NO), which is a necessary molecule that promotes vasodilation and thrombosis prevention. Since the cause of endothelial dysfunction is the lack of NO, this becomes one of the factors leading to macrovascular and microvascular disorders commonly seen among patients with diabetes, in addition to oxidative stress (An et al. 2023). Yang et al. (2024) indicated that endothelial dysfunction may be identified at the early stages in patients with diabetes and may be used as an indicator of future cardiovascular conditions, including myocardial infarction and stroke. As per Pacinella, Ciaccio and Tuttolomondo (2022) such dysfunction is especially alarming because it is an indication of a defect in the functionality of blood vessels to act normally, and it increases the vascular disease development.

Epidemiological observations highlight the prevalence of hyperglycemia on the cardiovascular system. From global statistics, the total number of people who suffer from diabetes in the world was recorded in 2021 was more than 537 million as the numbers are only predicated increase more than 783 million individuals in 2045 (Setiawan, 2026). In addition to diabetes, according to Agrawal et al. (2026), the rising numbers of diabetes patients also mean increased

cardiovascular disease (CVD), where the risk is doubled for people with diabetes of CVD compared to non-diabetics. According to the findings of the meta-analysis, people with diabetes are 75% more likely than people without the disease to die from cardiovascular disease (Cai et al. 2020). As a major modifiable risk factor of cardiovascular morbidity and death, hyperglycemia must be addressed immediately, according to the concerning statistics.

On a cellular level, Advanced glycation end products (AGEs) are produced as a result of hyperglycemia and prevent vascular damage (Liu et al. 2023). The non-enzymatic glycation of proteins and lipids by a high glucose concentration results in AGEs, which stiffen blood arteries and reduce NO bioactivity (Twarda-Clapa et al. 2022). This leads to the activation of these AGEs with the help of specific receptors found in the endothelial cells, leading to oxidative stress and inflammation and causing damage to the vascular endothelium. In a similar manner, the accumulation of AGE in larger blood vessels worsens the atherosclerosis process, enhance lipid retention and the inflammatory cells recruitment on the artery walls, which results in the formation of plaques and the constriction of arteries (Castelli et al. 2023). These pathological processes predispose ischemic events, e.g. heart attack and strokes, by hindering the flow of blood and resulting in tissue damage. Hyperglycemia and vascular disease link can be further elucidated through evidence from clinical research. According to Stoberock et al. (2020), PAD and other cardiovascular conditions are highly common in poorly managed diabetics when compared with their non-diabetic counterparts. In a similar fashion, whereas conventional glucose management therapies may be utilized to alleviate microvascular issues, the same cannot be said for macrovascular diseases like cardiovascular deaths (GRADE Study Research Group, 2022). As per Olanrewaju et al. (2023) this has increased the interest in new therapeutic approaches, including SGLT2 inhibitors and GLP-1 receptor agonists, which can have other vascular benefits other than the regulation of blood glucose levels. Despite this,

according to Yang et al. (2024), studies have demonstrated that endothelial dysfunction persists despite improved glycemic control; this implies that there are other complicated mechanisms in which vascular complications related to hyperglycemia arise beyond just the management of oxidative stress and inflammation among others.

Impact of Insulin Resistance on Cardiovascular Health in Diabetes

Reduced cell sensitivity to insulin, the main hormone that regulates the process of glucose metabolism, is known as insulin resistance (Rahman et al. 2021). Roman & Stoian (2021) state that insulin resistance (IR) is a major contributing factor to cardiovascular disease, particularly in individuals with type 2 diabetes. Insulin resistance can cause compensatory hyperinsulinemia, inflammation, dyslipidemia, and endothelial dysfunction by interfering with glucose metabolism (Zhao et al., 2023). The above-mentioned physiological changes form a basis for the expansion of atherosclerosis, during which the fatty plaques accumulate in the arteries, causing their obstruction. Insulin plays a key role in health of the vascular system by mediating vasodilation and the integrity of blood vessels due to the production of nitric oxide (NO). In turn, insulin resistance results in reduced bioavailability of NO, resulting in impaired vascular dilation (Roy et al., 2023). As mentioned by Andreadi et al. (2022), in IR, apart from increasing blood sugar levels, it causes dysfunction in blood vessels, thus speeding up the development of myocardial infarction, stroke, and heart failure. It has been reported by Nakamura and Sadoshima (2020) that these alterations occur even before the appearance of diabetes, with studies indicating the involvement of IR in cardiac remodeling and fibrosis, thereby damaging heart function.

There are various epidemiological studies which suggest that insulin resistance directly contributes to CVD risk among diabetics (Kosmas et al. 2023). A study by Dastjerdi et al. (2025) found a strong correlation between the risk of cardiovascular problems and all-cause mortality

among type 1 diabetics and measures of insulin resistance, such as estimated glucose disposal rate (eGDR). It was shown that type 1 diabetics with poor eGDR and thus more prone to insulin resistance had greater rates of major cardiovascular events compared to those who had better insulin sensitivity (Zhang et al. 2024). It was emphasized by Gora, I.M., Ciechanowska, and Ladyzynski, (2021) that insulin resistance focuses on causing vascular dysfunctions irrespective of the presence of T2DM. Some recent studies have also highlighted that insulin resistance surrogates such as TyG index along with other IR biomarkers are associated with CVD incidence. Ren et al. (2020) found a link between a higher risk of ischemic heart disease, stroke, and heart failure and the TyG index, a more accurate indicator of insulin resistance. In addition, a study that was conducted longitudinally on elderly patients in China showed that sarcopenia, which is the muscle wasting disorder associated with aging, had an additive effect in terms of risk for developing cardiovascular diseases among patients with insulin resistance (Xu et al. 2024).

The consequences for patient care are significant, pointing out the importance of intervening early in order to treat insulin resistance in people with diabetes to avoid the onset of cardiovascular disease. Lifestyle modifications, such as losing weight, engaging in exercise, and changing diet, may prove beneficial in improving insulin resistance and reducing the threat of cardiovascular issues (Samuel et al. 2024). Furthermore, According to Brown et al. (2021), novel drugs such SGLT-2 inhibitors and GLP-1 receptor agonists may have an impact on cardiovascular and glycemic management. These drugs do not only reduce high levels of glucose but address other issues associated with metabolic disorders due to insulin resistance, such as lipid levels and high blood pressure (Freeman, and Pennings, 2018). It is crucial for clinicians to focus on preventive treatments to increase the body's insulin sensitivity because there is evidence linking insulin resistance to cardiovascular disease. This will minimize the risk of cardiovascular problems, which continue to be

the leading cause of mortality among diabetics, and prevent further development of insulin resistance, hence postponing the onset of type 2 diabetes (Jyotsna et al. 2023).

Epidemiology and Risk Factors Linking Diabetes with Cardiovascular Disease

Diabetes mellitus has been described as one of the most pressing health issues facing the entire world and that its connection with cardiovascular disease (CVD) does not favor to the magnitude of the burden it imposes on the health systems across the world. According to recent study, 589

million individuals in the 20–79 age range have diabetes, accounting for 11.1% of the overall population in this age range (Opata, and Opata, 2026). Epidemiological studies have revealed that diabetic individuals experience a significantly higher rate of cardiovascular disease compared to their non-diabetic counterparts (Siam et al. 2024; Wong, and Sattar, 2023). Siam et al. (2024) established that patients suffering from diabetes are 1.5 to 6 several times have more chances to encounter CVD, and they are also more likely to die because of CVD.

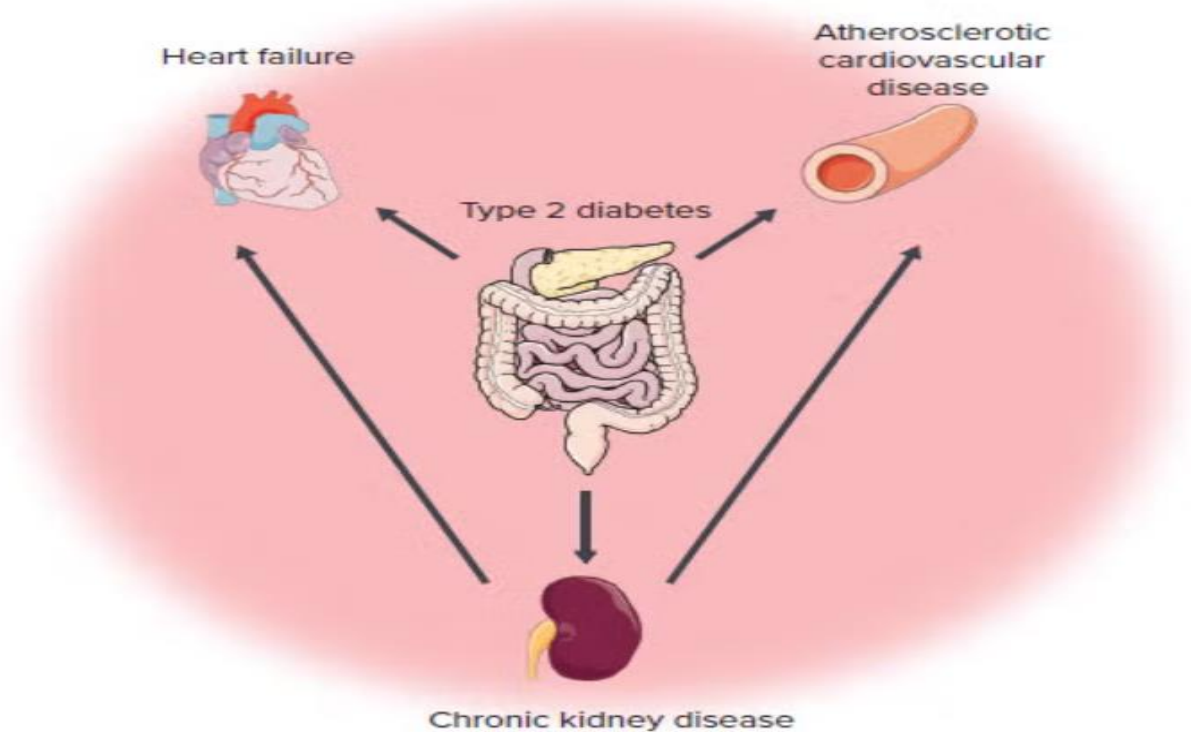


Figure 2: Interplay between Diabetes, Atherosclerotic Cardiovascular Disease, Heart Failure and Chronic Kidney Disease

Source: (Berger et al. 2025)

Furthermore, hyperglycemia, which is defined as excessive amounts of glucose in the blood, is a significant risk factor for the development of heart problems in diabetics (Mostafa, 2025). According to Libby (2021), this damage increases the possibility of atherosclerosis, or plaque buildup in the blood arteries, which raises the risk of myocardial infarction, stroke, and other cardiovascular problems. Insulin resistance, a

feature of type 2 diabetes, raises the risk of cardiovascular disease through dyslipidemia, which is characterized by greater triglycerides and lower HDL cholesterol, two independent risk factors for coronary artery disease (Młynarska et al. 2024). Sharma et al. (2020) discovered that another risk factor for cardiovascular disease in diabetics is hypertension, which shares characteristics with diabetes, such as endothelial dysfunction and increased resistance.

The combination of hypertension and hyperglycaemia results in an accelerated rate of development of cardiovascular complications, thereby increasing morbidity and mortality rates in diabetic patients (Yen et al. 2022). In addition, obesity and overweight, are main aspects for type 2 diabetes, also pose an added risk due to their ability to induce chronic inflammation, metabolic disorders, and lipid disorders, thereby making obesity an important modifiable risk factor for cardiovascular disease prevention (Dal Canto et al. 2019). In developing countries, the growing rates of diabetes have also been accompanied by a palpable rise in cardiovascular deaths, which is enhanced by the lack of access to early diagnosis, prevention and control of cardiovascular risk factors like high blood pressure and dyslipidaemia (Wurie, and Cappuccio, 2012). Conversely, Li et al. (2021) stated that the high-income nations have been partially successful in lowering the prevalence of age-based CVD mortality caused by the presence of better healthcare systems, early-stage interventions, and access to highly-technological medical therapies. Nevertheless, the overall disability-adjusted life years (DALYs) due to cardiovascular diseases are still on the rise with an ageing population, and the growth of diabetes rates (Pavlović et al. 2022). As per Thomas (2025) close to 29% of leading causes of heart disease were said to involve people who possess diabetes in England, which has increased during the past ten years.

Prevention and Management Strategies for Cardiovascular Complications in Diabetic Patients

For managing and preventing cardiovascular issues in diabetes, a multi-faceted, evidence-based approach is needed, which includes lifestyle, pharmacological, and regular risk assessment interventions. However, one of the most critical interventions for diabetes management is lifestyle modification, especially for cardiovascular risk factors that are modifiable, such as diet, exercise, and smoking cessation (Samuel et al. 2024). A heart-healthy diet is a critical intervention for diabetes management, as it helps control blood

glucose, blood pressure, and lipid profiles. According to Lv, Aihemaiti, and Guo (2024), the DASH diet consisting of a diet high in fruit, vegetables, whole grains, low fat milk products, protein and fat but excluding foods like saturated fat, sugar, and desserts has been proven effective in preventing cardiovascular disease in diabetic patients. Studies have shown that this diet is effective in lowering cholesterol levels, systolic and diastolic blood pressure levels, and 10-year cardiovascular risk by 13% (Akhlaghi, 2020; Onwuzo et al., 2023). According to Dobrosielski (2021), exercise in the form of 150 minutes of moderate exercise a week increases insulin sensitivity, reduces blood pressure levels, and glucose metabolism and hence cardiovascular disease risks.

Medication therapy is equally important in reducing cardiovascular risk among diabetic patients, with clinical recommendations showing strong approval for pharmacotherapy as part of the treatment of cardiovascular risks in diabetic individuals (American Diabetes Association, 2021). The use of statins that reduce low-density lipoprotein cholesterol levels is recommended for diabetic patients aged 40 to 75 years regardless of their lipid levels, since it reduces cardiovascular events among patients with these characteristics (Gheorghe et al. 2020). High-potency statins are combined with medications like ezetimibe and PCSK9 inhibitors to achieve the required LDL-C levels, with LDL-C target levels being below 70 mg/dL, or even lower, below 55 mg/dL in cases where there is existing cardiovascular disease (Masana et al. 2022). Management of hypertension with the help of ACE inhibitors, ARBs, and other antihypertensive agents is also important because in diabetes patients, elevated blood pressure might cause additional damage to their blood vessels.

Medication adherence is critical for managing cardiovascular risks in diabetes patients since it has a significant impact on health outcomes (Jyotsna et al. 2023). This was observed Mazhar et al. (2022) cardiovascular risk was reduced by 45–55% in those who took antihypertensive and lipid-lowering drugs at least 80% of the time (<50 percent). More so, there was a 19 percent

reduction in cardiovascular risk with a 10% increase in adherence especially in those with moderate albuminuria, an indicator of diabetic kidney disease (Lithovius et al. 2024). These results highlight the importance of adopting regular medication taking as a preventative measure of cardiovascular events. Interventions should be put in place to enhance compliance, and they have shown to be effective through patient education, automated once-month refill requests, and medication synchronization programs. Holistic, joint strategies involving education, frequent follow-up, and cooperation with clinics through pharmacy can enhance adherence and enhance the effectiveness of cardioprotective drugs in practice (Uchmanowicz et al. 2025). Medication adherence is achieved through adopting the stable medication use method, allowing enable caregivers to ensure the patient conforms to prescribed therapies, and thus alleviate cardiovascular risk. As per George, M., Maurina, and Schutte, (2025) such practice not only streamlines the process of cardiovascular complications but also helps in long term health and wellbeing of diabetic patients. Since medication adherence is one of the main determinants of success in diabetes control, its promotion should be a well-orchestrated task in clinical practice to ensure a higher quality of health results and avoidance of the advancement of vascular complications.

Social support, lack and stress are psychosocial factors that contribute largely to cardiovascular risk in diabetic persons. As per Asadi, (2025) poor self-care habits include intermittent glucose self-monitoring, inadequate dieting habits and physical inactivity and are associated with the occurrence of chronic stress and depressive characteristics and have been linked to an increased cardiovascular risk. Studies have established that diabetic patients who experience greater stress and depression are more prone to poor glycemic control, high blood pressure, and inflammation among other risk factors of cardiovascular events (Chakraborty et al. 2023; Randväli et al. 2024). As demonstrated in recent systematic reviews, stress management programs and cognitive-behavioral therapy (CBT) can have

a significant impact in reducing stress rates, bettering glycemic management, decreasing blood pressure and increasing physical activity among diabetic patients (Dong, Wang, and Yang 2023). On the other hand, the cardiovascular health has been reported to be improved by having better social support systems that help in creating a more adherent pattern of the treatment as well as encouraging healthier life habits (Pizga et al. 2022). Such findings suggest that attention should be paid to the well-being of the mental aspect and physical health of individuals with diabetes. Psychosocial strategies can be incorporated into the treatment of diabetic patients, thus providing a holistic strategy for the improvement of the patient's psychological state and cardiac condition. Due to the fact that emotions have a direct impact on self-care practices and risk factors, the issues of stress and depression must be addressed in order to reduce the cardiac risks of patients with diabetes (Cilli et al. 2022). This holistic practice affirms the promotion of healthier living and maximizes care outputs, which eventually lead to the enhancement of quality of life and long-term health conditions of people with diabetes.

Conclusion

Indeed, the research has demonstrated an elaborate connection between the condition and cardiovascular problems, with hyperglycemia being one of the critical factors that cause vascular deterioration, which then results in cardiovascular diseases such as coronary artery disease, stroke, and congestive heart failure. Chronic hyperglycemia is particularly important in the process, as it causes the generation of reactive oxygen species (ROS), which in turn leads to oxidative stress and inflammation of the affected vessels. Endothelial cell injury, impaired vasculature, and atherosclerotic plaques become the result of the changes, making people with diabetes more susceptible to the mentioned cardiovascular problems. In fact, because of their hyperglycemia, persons with diabetes mellitus are two to four times more likely to have cardiovascular problems than others. Aside from producing oxidative stress, the disease has been

linked to the generation of advanced glycosylation end products, which leads to more severe vascular lesions and contributes to the development of atherosclerosis.

Moreover, the research delved into the effects of insulin resistance, dyslipidemia, and hypertension as primary risk factors, which increase the cardiovascular load in individuals suffering from diabetes mellitus. The findings from the epidemiological studies further highlighted the necessity for developing appropriate treatment methods that can control the metabolic disturbances as well as the cardiovascular risks linked to the disease. The necessity of taking a holistic approach to diabetes management, which includes changes in food habits and physical exercise, as well as prescribing medications such as statins and antihypertensive meds, was emphasized. Such an approach is crucial to ensure proper health outcomes, prevent cardiovascular complications, and decrease the cardiovascular burden caused by diabetes.

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