



The Indonesian Journal of General Medicine

The Analysis Study Of Type 2 Diabetes Mellitus As Risk Factor For Cardiovascular Disease: A Comprehensive Systematic Review

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Article History :

Received date : 2024/10/17
Revised date : 2024/11/25
Accepted date : 2024/12/18
Published date : 2025/02/08



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ABSTRACT

Background: Diabetes mellitus (DM) is prevalent worldwide and linked to rising cardiovascular morbidity and mortality, increasing healthcare burdens. DM complications include atherosclerosis, ischemic heart disease, and peripheral arterial disease, primarily driven by insulin resistance and hyperglycemia, leading to atherosclerosis progression. This systematic review aims to analyze current evidence on the risk factors influencing cardiovascular disease in diabetes mellitus type 2 patients based on literatures of the last 10 years. **Methods:** The study adhered to PRISMA 2020 standards, examining English literature from 2014 to 2024. It excluded editorials, reviews from the same journal, and submissions without a DOI. PubMed, SagePub, SpringerLink, and Google Scholar were utilized as literature sources. **Result:** Initially retrieving 360 articles from online databases (PubMed, SagePub, SpringerLink and Google Scholar) eight relevant papers were selected after three rounds of screening for full-text analysis. **Conclusion:** This study underline the importance of early intervention, dietary and lifestyle changes, and tailored medication in light of the substantial cardiovascular risks associated with Type 2 Diabetes (T2DM). Reducing risks requires a multimodal strategy that is customized to each patient's unique profile.

Keyword: type 2 diabetes mellitus, risk factors, and cardiovascular disease

INTRODUCTION

Diabetes mellitus (DM) is one of the most prevalent chronic diseases in almost every nation and is linked to an elevated risk of cardiovascular morbidity and mortality. Globally, the prevalence and incidence of cardiovascular illnesses and diabetes mellitus are rising. The death toll and health care costs are becoming more and more of a burden for both developed and developing nations.¹

DM causes several complications such as diabetic macroangiopathy, atherosclerosis, cerebral vascular dysfunction, ischemic heart disease, peripheral arterial disease, and other vascular illnesses. Insulin resistance and hyperglycemia are the two most major variables that contribute to the advancement of atherosclerosis in people who have diabetes. Insulin resistance in vascular cells plays an essential role in the advancement of atherosclerosis.^{2,3} Not only is it a primary cause of the start and progression of diabetes, but it is also a risk factor for other atherosclerotic disorders such as hypertension and dyslipidemia. Insulin resistance is a key contributor to the progression of

atherosclerosis. Patients who have insulin resistance frequently have several risk factors that, through a variety of processes, cause the advancement of atherosclerosis.⁴

There is a complicated relationship between insulin resistance, diabetes, and atherosclerosis, which is influenced by a number of different circumstances. The local inflammation in the arterial wall that is caused by dyslipidemia, more especially high levels of LDL cholesterol and high amounts of residual lipoprotein, is what causes the formation of atherosclerotic lesions. By expressing adhesion molecules and releasing cytokines and chemokines, vascular endothelial cells that have been damaged by oxidative stress or other stimuli are involved in the process.⁵

Diabetes mellitus accelerates the formation of atherosclerotic lesions due to various factors. High levels of tiny dense LDL cholesterol are atherogenic due to their reduced affinity to LDL receptors, increased tendency to transit into the subendothelial region, and poor anti-oxidant content. Monocytes from the

blood circulation attract these monocytes to the wound area, attaching themselves to the endothelium through binding molecules. When LDL cholesterol is high, it enters the subendothelial space and undergoes oxidation or modification. Macrophages are responsible for foam cell production and atherogenesis, as they can take up and deposit oxidized LDL cholesterol. When oxidized lipids are present, the endothelium secretes growth factors, transforming vascular smooth muscle cells into atherogenic proteins.⁶ This systematic review aims to analyze current evidence on the risk factors influencing cardiovascular disease in diabetes mellitus type 2 patients based on literatures of the last 10 years.

METHODS

Protocol

The author carefully followed the rules laid out in the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020. This was done to make sure the study met all its standards. The selection of this methodological approach was specifically aimed at ensuring the

precision and reliability of the conclusions drawn from the investigation.

Criteria for Eligibility

This systematic review investigate existing evidence on the risk factors influencing cardiovascular disease in diabetes mellitus type 2 patients based on literatures of the last 10 years. This study meticulously analyzed data on literatures to provide insights and enhance patient treatment strategies. The primary objective of this paper is to highlight the collective significance of the identified key points.

Inclusion criteria for this study entail: 1) Papers must be in English, and 2) Papers must have been published between 2014 and 2024. Exclusion criteria comprise: 1) Editorials; 2) Submissions without a DOI; 3) Previously published review articles; and 4) Duplicate entries in journals.

Search Strategy

The keywords used for this research are type 2 diabetes mellitus, risk factors, and cardiovascular

disease. The Boolean MeSH keywords inputted on databases for this research are: (*"diabetes mellitus, type 2"*[MeSH Terms] OR *"type 2 diabetes mellitus"*[All Fields]) AND (*"risk factors"*[MeSH Terms] OR (*"risk"*[All Fields] AND *"factors"*[All Fields]) OR *"risk factors"*[All Fields]) AND (*"cardiovascular diseases"*[MeSH Terms] OR (*"cardiovascular"*[All Fields] AND *"diseases"*[All Fields]) OR *"cardiovascular diseases"*[All Fields] OR (*"cardiovascular"*[All Fields] AND *"disease"*[All Fields]) OR *"cardiovascular disease"*[All Fields])) AND ((y_10[Filter]) AND (clinicaltrial[Filter]))

Data retrieval

The authors assessed the studies by reviewing their abstracts and titles to determine their eligibility, selecting relevant ones based on their adherence to the inclusion criteria, which aligned with the article's objectives. A consistent trend observed across multiple studies led to a conclusive result. The chosen submissions had to meet the eligibility criteria of being in English and a full-text.

This systematic review exclusively incorporated literature that met all predefined inclusion criteria and directly pertained to the investigated topic. Studies failing to meet these criteria were systematically excluded, and their findings were not considered. Subsequent analysis examined various details uncovered during the research process, including titles, authors, publication dates, locations, study methodologies, and parameters.

Quality Assessment and Data Synthesis

Each author independently evaluated the research presented in the title and abstract of the publication to determine which ones merited further exploration. The subsequent stage involved assessing all articles that met the predefined criteria for inclusion in the review. Decisions on including articles in the review were based on the findings uncovered during this evaluation process.

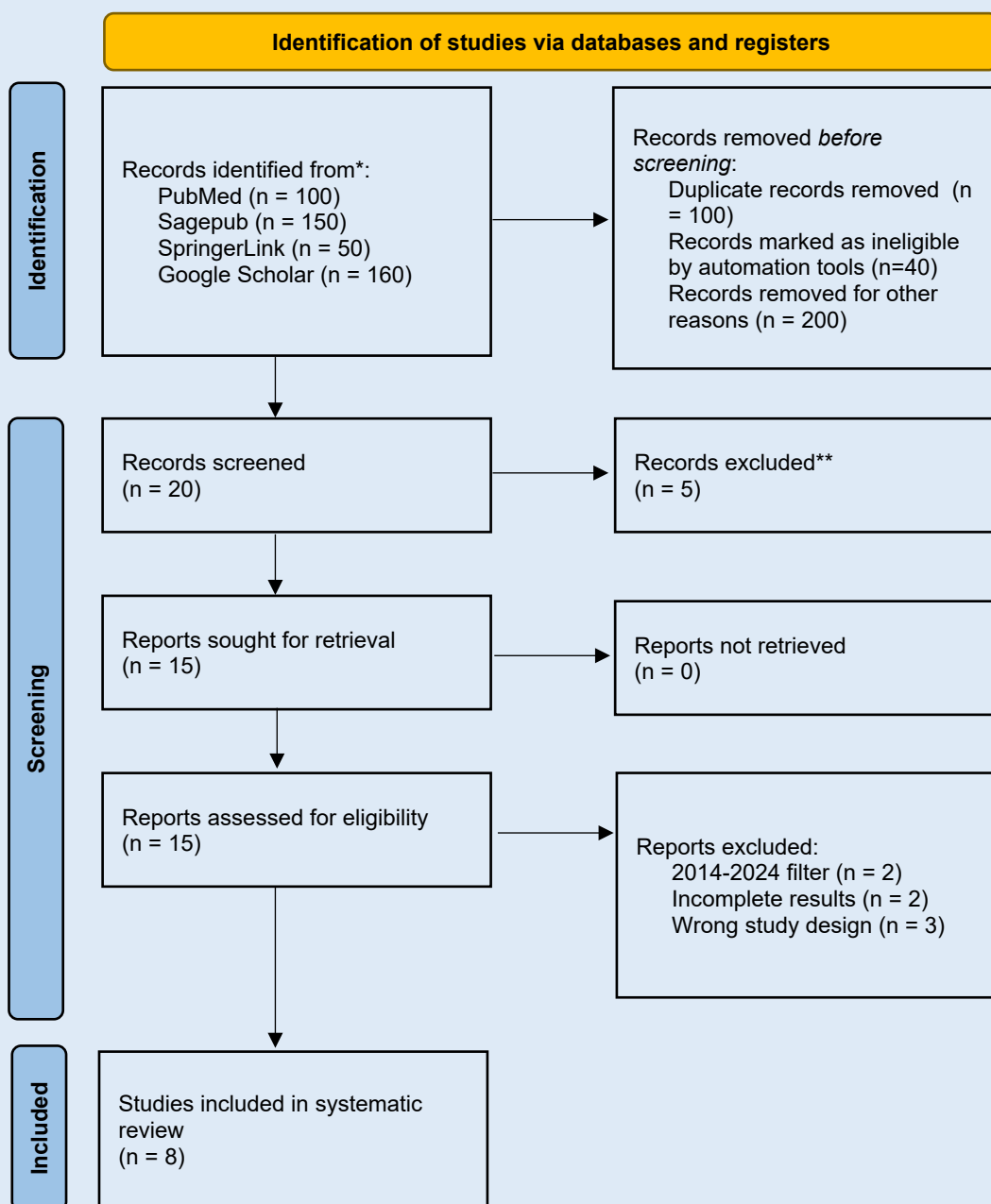


Figure 1. Article search flowchart

RESULT

The initial number of articles retrieved from online databases (PubMed, SagePub, SpringerLink, and Google Scholar) is 360 articles. After conducting three levels of screening, eight articles that directly relate to the current systematic review have been chosen for further assessment through full-text reading and analysis. Table 1 presents the selected literature included in this analysis.

Table 1. The literature included in this study

No.	Author	Origin	Method	Sample	Result
1.	Haque, et al. ⁷ (2020)	Bangladesh	Observational study	100 patients	The study found that 40.0% of patients with type 2 diabetes mellitus were in their 5th decade, with a mean age of 57.17±11.2 years. Most patients were obese, with 66.0% male and 75.5% female. Cardiovascular diseases were more common with longer diabetes duration, with 61.9% found in newly diagnosed patients. Microalbuminuria was found in 67.1% of patients with cardiovascular diseases and 42.9% without them, with a higher incidence in patients with cardiovascular diseases.
2.	Vitale, et al. ⁸ (2017)	Italy	RCT	2573 patients	The study found that people with higher intake of polyphenols had a more favorable cardiovascular risk factors profile than those with lower intake. The predominant classes of polyphenols were flavonoids and phenolic acids, with 47.5% and 47.4% respectively. The findings were similar when analyzing flavonoids or phenolic acids separately.

3.	Roubille, et al. ⁹ (2024)	France	RCT	959 patients	A study involving 959 patients with type 2 diabetes found that colchicine, taken daily, significantly reduced cardiovascular events in patients with a recent myocardial infarction. The study found that 8.7% of patients in the colchicine group experienced a primary endpoint event, while 13.1% experienced a placebo.
4.	Vitale, et al. ¹⁰ (2018)	Italy	Prospective study	2568 patients	A high rMED score indicates better diet quality and adherence to diabetes nutritional recommendations. However, only 17% and 30% of participants met fiber and saturated fat recommendations. High scores were associated with lower plasma lipids, blood pressure, glycated hemoglobin, and BMI. The Mediterranean diet's beneficial health effects are primarily due to its synergy among nutrients and foods.
5.	Magalhães, et al. ¹¹ (2019)	Portugal	RCT	80 patients	A significant interaction was found on carotid intimamedia thickness (cIMT) for both the MCT ($\beta = -4.25$, $p < 0.01$) and HIIT groups ($\beta = -3.61$, $p < 0.01$) after adjusting for sex, baseline moderate-to-vigorous physical activity, and mean arterial pressure changes using intention-to-treat analysis. HIIT showed positive changes in peripheral arterial stiffness indices, including carotid-

					radial arterial pulse wave velocity ($\beta = -0.10$, $p = 0.044$), carotid-distal posterior tibial artery pulse wave velocity ($\beta = -0.14$, $p < 0.01$), and distensibility coefficient ($\beta = -0.00$, $p < 0.01$). No effect on hemodynamic indicators was seen after the intervention.
6.	Walters, et al. ¹² (2021)	UK	RCT	83 patients	A study comparing 83 T2D patients and 36 healthy controls found that vitamin B1 levels were higher in T2D patients compared to controls. However, after a metabolic rehabilitation program, these vitamins increased but were not linked to improved cardiovascular function.
7.	Goldberg, et al. ¹³ (2022)	USA	RCT	3234 patients	The study found that metformin and lifestyle intervention did not significantly reduce major cardiovascular events in DPPOS over 21 years, despite long-term diabetes prevention. Risk factors such as group lifestyle intervention, extensive statin and antihypertensive use, and reduced metformin use may have diluted the interventions' effects.
8.	Matsumoto, et al. ¹⁴ (2022)	Japan	Cohort study	2535 patients	A study found that 132 elderly Japanese patients with type 2 diabetes (T2D) developed atherosclerosis (AF) over a 10.9-year median follow-up period. The adjusted risk factors for stroke, coronary artery disease, heart failure, and

					all-cause death were higher in elderly patients with AF compared to those without AF.
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Haque, et al.⁷ (2020) showed that Cardiovascular diseases were more common with longer diabetes duration, and microalbuminuria was found with a higher incidence in patients with cardiovascular diseases.

Vitale, et al.⁸ (2017) concluded that polyphenol intake is associated with a more favorable cardiovascular risk profile, and supports the consumption of foods and beverages rich in different polyphenol classes, particularly in people with diabetes.

Roubille, et al.⁹ (2024) found that patients with type 2 diabetes who took colchicine daily have significantly reduced cardiovascular events in patients with a recent myocardial infarction.

Vitale, et al.¹⁰ (2018) found that mediterranean diet is found beneficial in type 2 diabetes patients and prevents cardiovascular disease by targetting improvements in plasma lipids, blood pressure, glucose, and BMI.

Magalhães, et al.¹¹ (2019) found that after a one-year intervention, both the MCT and HIIT groups lowered cIMT in type 2 diabetic patients, but only the HIIT group improved peripheral artery stiffness and distensibility coefficient. Together, HIIT may alleviate type 2 diabetes' long-term vascular problems.

Walters, et al.¹² (2021) found that vitamin B1 levels found in T2D patients were higher, however it was not linked to improved cardiovascular function.

Goldberg, et al.¹³ (2022) found that metformin and lifestyle intervention did not significantly reduce major cardiovascular events in impaired glucose tolerance patients over 21 years, despite long-term diabetes prevention.

Matsumoto, et al.¹⁴ (2022) found that elderly patients with type 2 diabetes (T2D) developed atherosclerosis (AF) over a 10.9-year median follow-up period. The adjusted risk factors for stroke,

coronary artery disease, heart failure, and all-cause death were higher in elderly patients with AF compared to those without AF.

DISCUSSION

The systematic review underscores the multifaceted relationship between type 2 diabetes mellitus (T2DM) and cardiovascular disease (CVD). This discussion synthesizes findings from various studies, emphasizing the significant role of T2DM in increasing cardiovascular risk and exploring potential interventions for mitigating this risk.

Firstly, Haque et al. (2020) highlight the correlation between prolonged diabetes duration and increased CVD incidence, with a notable prevalence of microalbuminuria among patients with cardiovascular complications.⁷ This underscores the importance of early diabetes management and regular monitoring of renal function to mitigate cardiovascular risks. The high incidence of microalbuminuria in T2DM patients with CVD suggests that kidney damage may be an early indicator of cardiovascular issues in diabetic patients.¹⁵

Vitale et al. (2017) found that a higher intake of polyphenols is associated with a more favorable cardiovascular risk profile in T2DM patients. This finding supports dietary recommendations advocating for the consumption of polyphenol-rich foods and beverages, such as fruits, vegetables, and teas.⁸ The beneficial effects of polyphenols, particularly flavonoids and phenolic acids, on cardiovascular health, highlight the potential for dietary interventions to improve cardiovascular outcomes in diabetic patients.¹⁶

In a different approach, Roubille et al. (2024) demonstrated that colchicine significantly reduces cardiovascular events in T2DM patients who have experienced a recent myocardial infarction.⁹ This finding suggests that colchicine, an anti-inflammatory medication, could be a valuable addition to the therapeutic arsenal for reducing cardiovascular risks in diabetic patients, particularly those with a history of heart attacks. However, further research is needed to establish long-term safety and efficacy.¹⁷

The Mediterranean diet's benefits, as reported by Vitale et al.

(2018), further emphasize the role of nutrition in managing T2DM and preventing CVD. The study shows that adherence to a Mediterranean diet is linked to improvements in plasma lipids, blood pressure, glycated hemoglobin, and BMI.¹⁰ These findings advocate for lifestyle interventions focusing on dietary quality to reduce cardiovascular risks in diabetic patients. The synergy among various nutrients and foods in the Mediterranean diet appears to be particularly beneficial for cardiovascular health.^{18,19}

Exercise interventions also show promise in mitigating cardiovascular risks in T2DM patients. Magalhães et al. (2019) found that high-intensity interval training (HIIT) and moderate continuous training (MCT) both reduce carotid intima-media thickness (cIMT), a marker of atherosclerosis. Notably, HIIT also improved peripheral artery stiffness and distensibility.¹¹ These results suggest that incorporating HIIT into exercise regimens for T2DM patients could provide superior cardiovascular benefits compared to moderate exercise alone.^{20,21}

Contrastingly, Walters et al. (2021) reported that despite higher vitamin B1 levels in T2DM patients, these were not linked to improved cardiovascular function.¹² This finding highlights the complexity of nutrient interactions and the need for comprehensive strategies beyond vitamin supplementation to enhance cardiovascular health in diabetic patients. It also underscores the necessity for a holistic approach that includes diet, exercise, and possibly pharmacotherapy.^{22,23}

The long-term study by Goldberg et al. (2022) showed that neither metformin nor lifestyle interventions significantly reduced major cardiovascular events over 21 years, despite their efficacy in preventing diabetes.¹³ This suggests that while these interventions are effective for diabetes prevention, additional strategies are needed to specifically target cardiovascular risk reduction in T2DM patients. The interplay of multiple risk factors, including medication use and lifestyle changes, complicates the outcomes, indicating the need for multifactorial approaches.^{24,25}

Finally, Matsumoto et al. (2022) found that elderly T2DM patients have a higher incidence of atherosclerosis (AF) and related complications. This study highlights the increased vulnerability of elderly diabetic patients to cardiovascular diseases and the need for targeted interventions in this population.¹⁴ The elevated risks of stroke, coronary artery disease, heart failure, and all-cause mortality in elderly T2DM patients with AF call for comprehensive cardiovascular risk management strategies in older adults with diabetes.²⁶

CONCLUSION

In summary, the study underline the importance of early intervention, dietary and lifestyle changes, and tailored medication in light of the substantial cardiovascular risks associated with Type 2 Diabetes (T2DM). Reducing risks requires a multimodal strategy that is customized to each patient's unique profile.

DISCLOSURE STATEMENT

- Disclosure Statement : The authors have no conflicts of Interest to declare

- Funding Sources : None
- Acknowledgements : -
- Author Contribution : All authors discussed and contributed the final content for journal submission and publication

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