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Factors Affecting Vascular Complications in Patients with Diabetes Mellitus: A Literature Review

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LITERATURE REVIEW

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ABSTRACT

Vascular complications in patients with diabetes mellitus (DM) are a major cause of morbidity and mortality, presenting a considerable impact on quality of life and global health burden. Although diabetes management continues to improve, vascular complications remain a major challenge. It is important to understand the factors that influence these complications to support more effective prevention and management. To explore the factors influencing vascular complications in patients with DM. This study used a literature review method. Articles were searched through three major databases, namely CINAHL, PubMed, and Scopus, using keywords such as "vascular complications," "DM," and "factors affecting." Inclusion criteria included English-language articles published within the last ten years (2016–2025), in the form of original research relevant to vascular complications in patients with DM. Data were extracted manually using a table that included authors, objectives, design, samples, variables, and outcomes. Analysis was conducted using a qualitative descriptive approach to identify key themes. A total of 14 articles met the inclusion criteria. From the analysis, six main themes were obtained: biochemical factors and biomarkers, clinical factors, cardiometabolic risk factors, vascular structural and anatomical changes, molecular mechanisms, and prevalence of vascular complications. The results showed that high HbA1c levels, hypertension, diabetes duration of more than 10 years, and increased biomarkers such as Bisphenol A (BPA) significantly increased the risk of vascular complications. Vascular complications in patients with DM are multifactorial, involving complex interactions between biochemical, clinical, and molecular factors. A thorough understanding of these factors is essential to effectively prevent and manage vascular complications.

Key Messages:

- Vascular complications in DM are driven by multifactorial elements, including biochemical, clinical, and molecular factors that interact in complex ways.
- Understanding these influencing factors provides a foundation for developing targeted prevention strategies and personalized diabetes management.

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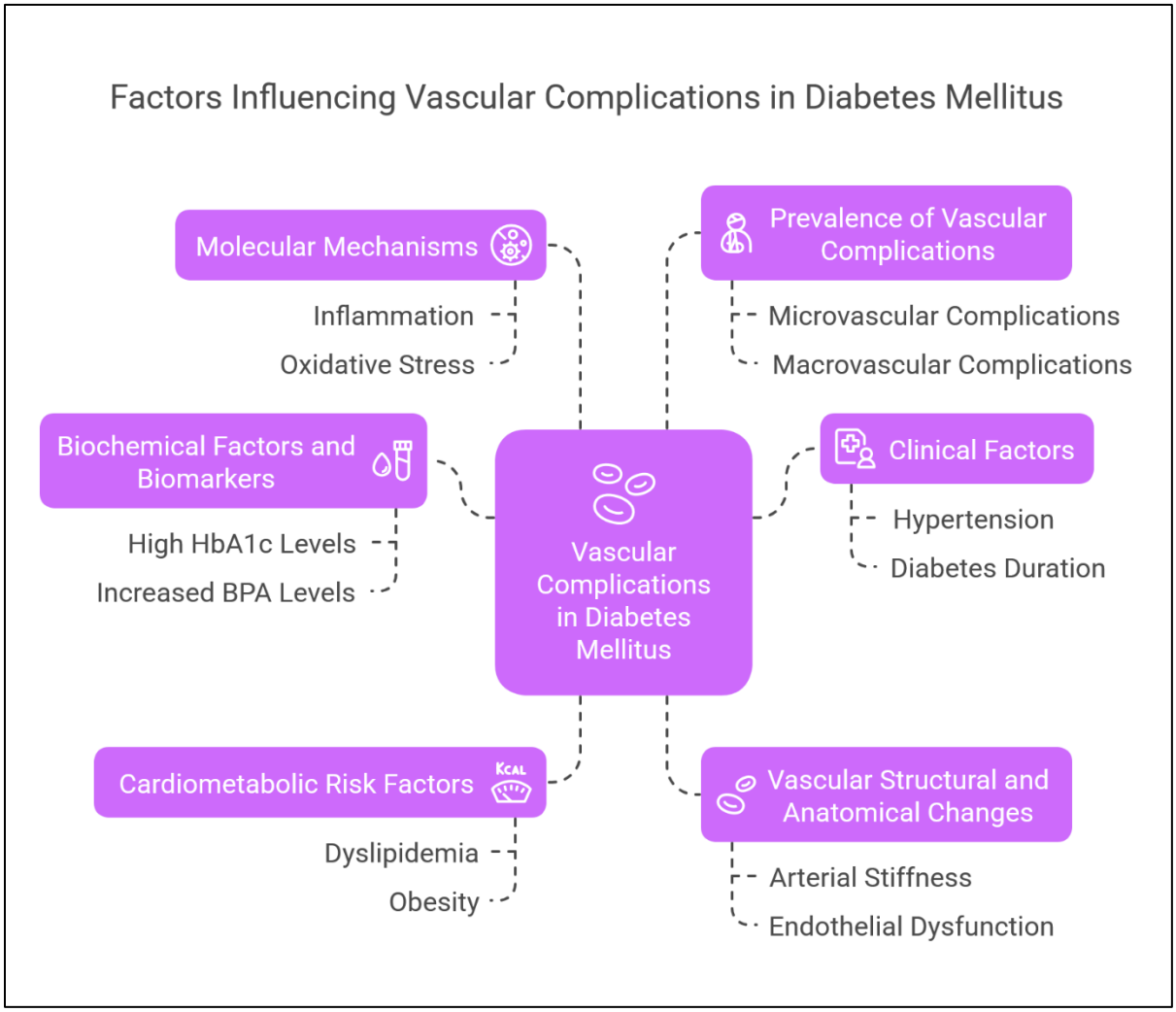

INTRODUCTION

Diabetes mellitus (DM) is one of the global health problems that continues to increase in prevalence from year to year, becoming a major challenge for health systems worldwide. According to data from the International Diabetes Federation (IDF) in 2023, an estimated 537 million adults (aged 20–79 years) worldwide are living with diabetes, and this figure is projected to increase to 643 million in 2030 and 783 million in 2045(1). At the national level, Indonesia is ranked seventh in the world with the largest number of diabetes sufferers, namely around 19.5 million adults, based on the same data.(2). This condition is exacerbated by the high number of undiagnosed cases, which reaches 52.8% of the total population of diabetes sufferers in Indonesia.(3).

DM has a broad impact on public health, economic burden, and patient quality of life. In terms of health, DM is a major cause of various chronic complications, such as cardiovascular disease, kidney failure, neuropathy, and retinopathy, which contribute to increasing rates of disability and death.(4). These complications often require intensive and long-term care, which places an additional burden on the health system. Economically, DM is a significant cause of increased health care costs, both for routine treatment and management of complications, burdening individuals, families, and governments.(5). DM patients also often face psychosocial challenges that affect their quality of life, including prolonged fatigue, limitations in daily activities, anxiety about possible complications, and the risk of depression due to emotional stress.(6).

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Vascular complications are one of the most serious consequences of DM (DM) and are the main cause of morbidity and mortality in patients. These complications are divided into two main categories, namely microvascular and macrovascular complications.(7). Microvascular complications involve damage to small blood vessels, which include diabetic retinopathy, diabetic nephropathy, and diabetic neuropathy. Diabetic retinopathy can cause visual impairment to blindness, diabetic nephropathy contributes to kidney failure requiring dialysis therapy, while diabetic neuropathy increases the risk of diabetic foot ulcers and amputations.(8). On the other hand, macrovascular complications involve large blood vessels and include cardiovascular diseases, such as coronary heart disease, stroke, and peripheral artery disease.(9).

DM can cause various specific vascular complications that have a significant impact on patient health. Diabetic nephropathy is one of the main microvascular complications characterized by damage to the renal glomerulus, which progressively reduces kidney function until it reaches end-stage renal failure.(7). This condition often requires patients to undergo dialysis therapy or kidney transplantation, which has a significant impact on quality of life. Diabetic retinopathy, another microvascular complication, occurs due to damage to the small blood vessels in the retina that causes fluid leakage, macular edema, and abnormal blood vessel formation.(8). If left untreated, this condition can lead to permanent blindness. In addition, macrovascular complications such as cardiovascular disease are one of the main causes of morbidity and mortality in diabetic patients. Chronic hyperglycemia and endothelial dysfunction accelerate atherosclerosis, thereby increasing the risk of coronary heart disease, myocardial infarction, and stroke.(10). Diabetic neuropathy causes pain, numbness, and diabetic foot ulcers, which in severe cases can lead to amputation.

Vascular complications in DM are influenced by various interacting risk factors, including biological, genetic, lifestyle factors, as well as inflammatory processes and oxidative stress. Biologically, chronic hyperglycemia is the main contributor to vascular damage in individuals with DM. One of the key mechanisms involves the formation of advanced glycation end products (AGEs), which bind to their receptors (RAGE) on vascular endothelial cells, triggering oxidative stress and inflammation that lead to endothelial dysfunction (11,12). Furthermore, comorbid conditions such as dyslipidemia and hypertension, which frequently coexist with DM, further contribute to vascular injury by promoting atherosclerosis and impairing vascular integrity (13,14). Genetic and epigenetic factors also play an important role, where certain gene polymorphisms and environmentally influenced epigenetic changes can increase an individual's susceptibility to vascular complications. Unhealthy lifestyles, such as smoking, a diet high in fat and sugar, and lack of physical activity, worsen vascular conditions.(10). Smoking increases oxidative stress and endothelial dysfunction, while poor diet and low physical activity accelerate insulin resistance and metabolic disorders. On the other hand, chronic inflammation and oxidative stress are key mechanisms in the pathogenesis of vascular complications, where hyperglycemia and dyslipidemia trigger the release of pro-inflammatory cytokines and reactive oxygen species (ROS) that damage the blood vessel wall.(15).

Although many studies have discussed vascular complications in DM, there is still a gap in understanding the relationship between specific factors and these vascular complications. While many primary studies have examined vascular complications in DM, there is a lack of scoping reviews that explore and map the range of contributing factors. This limits a broader understanding of the multifactorial nature of these complications (16,17). In addition, existing studies have not explored the factors that influence vascular complications in patients with DM. Then, there are still shortcomings in more comprehensive population-based studies and in data collection that covers a variety of diverse contexts. The study aims to explore the factors that influence vascular complications in patients with DM.

METHODS

Study Design

This study used a literature review design. The literature review approach was chosen because it provides a comprehensive overview of a broad and complex topic, and is useful for exploring existing literature without limiting it to a particular type of research. This approach is very suitable for use because it aims to explain the extent to which knowledge about vascular risk factors in DM has been understood

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and identify existing research gaps. This literature review goes through stages consisting of: (1) Identification of research questions; (2) Selection of relevant literature; (3) Data mapping; (4) Analysis of results; and (5) Preparation of a report that includes key findings, research gaps, and policy or practice implications. This process ensures that the literature evaluated includes a variety of types of studies and sources that are relevant to the research topic.

Search Strategy and Eligibility Criteria

The researchers conducted a literature search in three major databases, namely Scopus, PubMed, and CINAHL, which were selected based on their broad coverage of medical and health journals and their relevance to the topic of DM and vascular complications. Scopus was selected because it is a multidisciplinary database with a broad reach, covering global health literature. PubMed was selected because this database specifically provides scientific articles in the biomedical and health fields, including diabetes and vascular complications. CINAHL is a relevant database for nursing and public health studies. The keywords used in the search were "vascular complications," "DM," "risk factors," and MeSH terms such as "diabetes complications," "microvascular diseases," "macrovascular diseases." For the search, boolean operators such as AND, OR, and NOT will be used to combine keywords. The research question asked was: "What are the factors influencing vascular complications in patients with DM?" The search for articles was conducted using a combination of relevant keywords for each database, and the search will be reported using a PRISMA flowchart to illustrate the literature selection process (Figure 1).

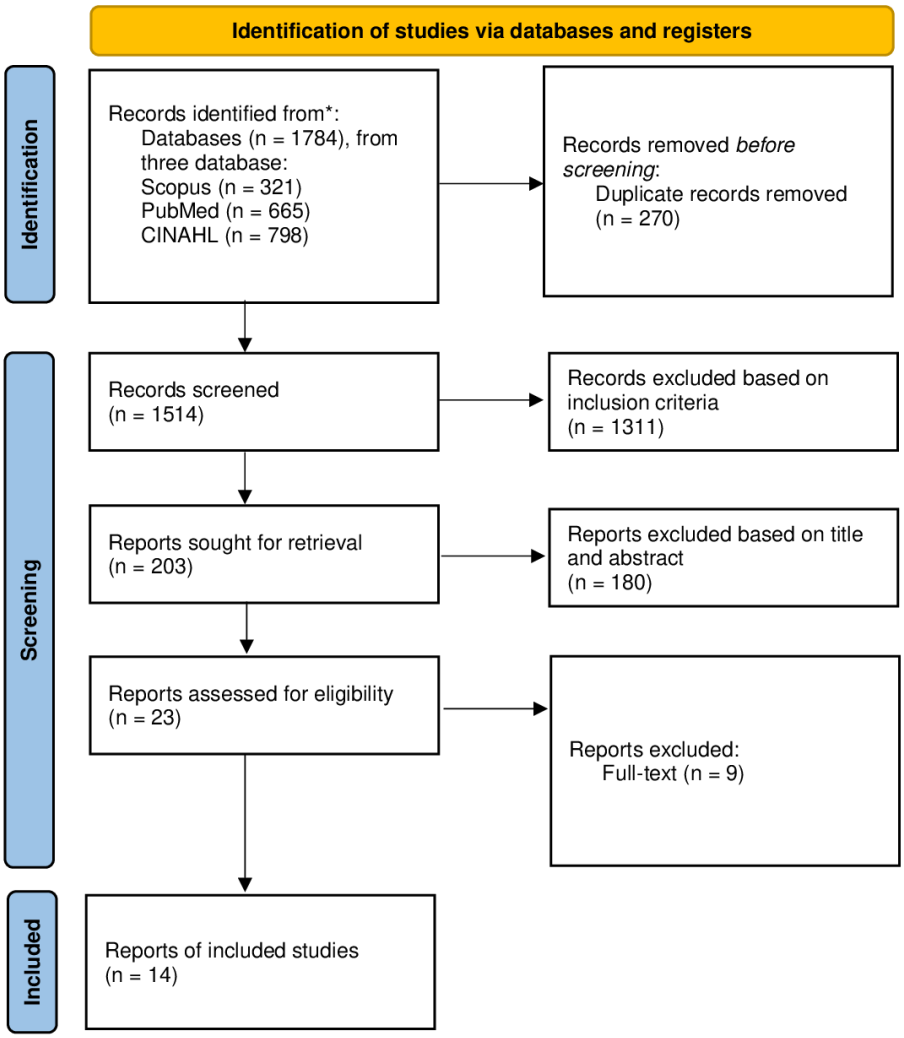

Figure 1. PRISMA Flow Diagram

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Inclusion and Exclusion Criteria

The inclusion criteria applied in this study used the PCC (Population, Concept, Context) concept. The population in question is patients with DM who experience vascular complications (both microvascular and macrovascular). The concepts considered are risk factors that influence vascular complications, such as hyperglycemia, dyslipidemia, hypertension, smoking, and other factors. The context of this review includes studies conducted in various countries or healthcare settings focusing on patients with DM. Inclusion criteria comprised studies published within the last ten years (2016–2025), written in English or Indonesian, and providing information on the relationship between risk factors and vascular complications in patients with DM. Exclusion criteria include studies that are not relevant to the topic of vascular complications or that do not focus on DM, and articles that are not available in full-text form. The selection of these inclusion criteria aims to ensure that the data analyzed is relevant and can provide a clear understanding of the risk factors for vascular complications in DM.

Data Extraction

Data extraction will be done manually using a table that includes columns such as authors, research objectives, study design, sample, country where the research was conducted, instruments used (e.g. questionnaires), and results obtained. This data extraction is carried out by two authors independently and each is an expert in their field. If there is a difference of opinion between the two authors regarding the extracted data, the solution applied is to invite a third authors who will assist in resolving the discrepancy. The third authors will have a role to cross-check and ensure the appropriateness of data extraction in order to produce more accurate and valid data.

Data analysis

The extracted data will be analyzed using a qualitative descriptive method with a thematic analysis approach. This thematic analysis is used to identify and describe the main themes that emerge in the literature related to factors that influence vascular complications in DM patients. The analysis process begins by re-reading the extracted articles to gain a deep understanding of the research context. Then, the authors will identify recurring themes in existing studies, such as biological factors, lifestyle, and environmental factors. Two authors will conduct this analysis independently, and if there is a difference of opinion regarding the grouping of themes, a third authors will be involved to provide additional opinions and resolve the differences. The results of this thematic analysis will describe a broader understanding of the risk factors that influence vascular complications in DM patients, as well as provide insight into gaps that need to be filled in further research.

RESULTS

The initial research results from three databases obtained 1784 reports. Then, the authors eliminated duplicate articles using the Mendeley application; there were 270 duplicate articles. After that, the authors eliminated reports based on inclusion criteria, 1311 articles that did not meet the established criteria. After that, the authors eliminated 180 articles that did not match based on title and abstract. Then, the authors read the full text article, the authors got 14 articles discussing factors that influence vascular complications in patients with DM (Table 1).

The results of this literature review provide a comprehensive overview of the various factors that influence vascular complications in patients with DM. Researchers identified six main themes that influence vascular complications in patients with DM, namely biochemical factors and biomarkers, clinical factors, cardiometabolic risk factors, structural and anatomical factors, molecular mechanisms, and the prevalence of vascular complications. Each theme reflects various aspects that contribute to the development of vascular complications, ranging from the role of specific biomarkers such as Bisphenol A (BPA) and Mean Platelet Volume (MPV), the influence of glycemic control, to complex molecular mechanisms such as m6A RNA modification.

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Table 1. Data Extraction

No	Authors	Objective	Country	Design	Sample	Variables and Instruments	Results
1	(18)	Examining the relationship between Bisphenol A (BPA) and vascular complications in T2DM.	India	Observational	120 participants (aged 35-65 years)	Variables: serum and urine BPA; Instruments:ELISA and Sirt1, Runx2, IL-1β gene expression.	Serum BPA was significantly higher in T2DM with CVD (1.63 ± 0.99 ng/ml; $p < 0.001$) than controls (0.67 ± 0.53 ng/ml).
2	(19)	Studying the relationship of CIMT with micro and macrovascular complications in diabetes.	India	Prospective Observational	100 T2DM patients	Variables: CIMT and vascular complications; Instruments:CIMT measurement by USG.	CIMT was significantly increased in retinopathy ($p=0.0001$) and PVD ($p=0.034$).
3	(20)	Assessing the prevalence of diabetes and vascular complications in Argentina	Argentina	Observational	12,832 adult patients	Variables: HbA1c, BMI, vascular complications; Instruments:Medical record data	Prevalence of macrovascular complications: myocardial infarction (11.5%), stroke (8.3%). HbA1c <7% in 70% of patients.
4	(21)	Determining the prevalence of vascular complications in T2 diabetes patients in rural India	India	Observational	390 T2DM patients	Variables: HbA1c, blood pressure; Instruments:Clinical and laboratory examination	Microvascular complications: neuropathy (44.9%), nephropathy (12.1%). High HbA1c significantly increased the risk of complications ($p < 0.05$).
5	(22)	Measuring the prevalence of vascular complications in T2 diabetes patients in Saudi Arabia	Saudi Arabia	Observational	748 T2DM patients	Variables: HbA1c, duration of diabetes; Instruments:Electronic medical record	Prevalence of neuropathy (5.6%), nephropathy (15%). Patients with high HbA1c were more susceptible to vascular complications (OR = 1.11, $p = 0.044$).
6	(23)	To examine the prevalence and risk factors for vascular complications in patients with type 2 diabetes.	China	Retrospective observational	3370 T2DM patients	Variables: Micro and macrovascular complications; Instruments:Electronic medical record	The prevalence of vascular complications was 73.2%; micro complications 57.5%, macro complications 51.4%. Risk factors include age, hypertension, duration of T2DM >10 years.
7	(24)	Reviewing the prevalence of vascular complications	Multi-country	Prospective observational	3525 T2DM patients	Variables: Micro and macrovascular complications; Instruments:Demogr	Micro prevalence 17.7%, macro 10.7%. Significant risk factors: age

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No	Authors	Objective	Country	Design	Sample	Variables and Instruments	Results
		in T2DM patients in the Middle East and Africa cohort				aphic data, HbA1c, duration of T2DM	(OR = 1.24), hypertension (OR = 2.84), dyslipidemia (OR = 1.96), smoking (OR = 1.37).
8	(25)	Studying the predictive factors of vascular complications in T2DM patients in Ethiopia	Ethiopia	Retrospective cohort	159 T2DM patients	Variables: FBS, cholesterol, proteinuria; Instruments:Longitudinal and survival analysis	The prevalence of vascular complications was 23.3%. Significant factors: cholesterol ≥ 200 mg/dl (HR = 1.54), serum creatinine (HR = 4.12), positive proteinuria (HR = 1.62).
9	(26)	Assessing the prevalence of diabetic cardiomyopathy (DbCM) in T2DM patients at San Diego Medical Center	US	Retrospective observational	15,182 T2DM patients	Variables: LV ejection fraction, left atrial enlargement; Instruments:Echocardiography	Prevalence of "pure" DbCM 2.9%, risk factors: moderate to severe hypertension (57%), CAD (35.9%), high HbA1c levels.
10	(27)	Evaluating the relationship of epicardial adipose tissue (EAT) with vascular complications in T2DM patients	Multi-country	Observational	1253 T2DM patients	Variables: EAT volume, CAC score; Instruments:Deep learning-based segmentation	EAT was positively correlated with CAD (p=0.0004), CKD (p=0.008), PAD (p=0.0005). Not significant for diabetic neuropathy or retinopathy.
11	(28)	Relating triglyceride-glucose (TyG) index to vascular complications in type 2 diabetes	China	Observational	4,721 hospitalized patients with T2DM	Variables: TyG, MAU, ABI; Instruments:Measurement of vascular parameters	TyG correlated with MAU (OR = 1.39, CI: 1.22-1.59) and ABI (OR = 1.42, CI: 1.14-1.76), especially at HbA1c > 8.6% (p < 0.001).
12	(29)	Comparing Mean Platelet Volume (MPV) in diabetes with and without vascular complications	India	Observational	90 patients	Variables: MPV, HbA1c; Instruments:Automated MPV assay	MPV was higher in diabetics with complications (9.19 ± 1.45 fL) than in diabetics without complications (8.50 ± 1.20 fL, p = 0.049).
13	(30)	Assessing micro- and macrovascular complications in the DISCOVER global study	Multi-country	Prospective cohort	11,357 patients with T2DM	Variables: HbA1c, micro and macro complications; Instruments:Medical records and longitudinal survey	The incidence of micro complications was 16% and macro complications was 6.6% within 3 years, the main risk factors were: high HbA1c (HR =

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No	Authors	Objective	Country	Design	Sample	Variables and Instruments	Results
14	(31)	Examining the role of m6A RNA modification in retinal pericyte dysfunction in diabetic vascular complications	China	Experimental studies	Diabetic mouse model and pericyte cell culture	Variables: m6A RNA modification, METTL3; Instruments:Gene expression, RNA-seq	1.08), smoking (HR = 1.17). METTL3 depletion prevents pericyte dysfunction and retinal vascular complications; METTL3 overexpression increases pericyte apoptosis ($p < 0.05$).

Note: Abbreviations

T2DM: Type 2 DM, CVD: Cardiovascular Disease, CIMT: Carotid Intima-Media Thickness, PVD: Peripheral Vascular Disease, CAD: Coronary Artery Disease, CKD: Chronic Kidney Disease, PAD: Peripheral Artery Disease, EAT: Epicardial Adipose Tissue, CAC: Coronary Artery Calcification, MAU: Microalbuminuria, ABI: Ankle-Brachial Index, MPV: Mean Platelet Volume, HR: Hazard Ratio, OR: Odds Ratio, CI: Confidence Interval

Theme 1: Biochemical Factors and Biomarkers

Biochemical factors, such as specific biomarkers, play an important role in vascular complications in patients with DM. One of the significant biomarkers is Bisphenol A (BPA), which is found in higher levels in type 2 diabetes patients with cardiovascular complications compared to the control group.(18). This increase suggests a link between BPA exposure and activation of inflammatory pathways and vascular calcification. In addition, higher Mean Platelet Volume (MPV) in diabetic patients with complications suggests platelet hyperactivity as one of the underlying mechanisms of vascular thrombosis.(19). Triglyceride-Glucose Index (TyG) is also a significant indicator, where TyG correlates with an increased risk of peripheral vascular stenosis and microalbuminuria, especially in patients with poor glycemic control (high HbA1c)(20).

Theme 2: Clinical Factors

Clinical factors, such as HbA1c levels and duration of diabetes, are major predictors of vascular complications. Elevated HbA1c has been shown to significantly increase the risk of micro- and macrovascular complications.(21). Conversely, a 1% decrease in HbA1c can reduce the risk of micro complications by 37% and macrovascular by 14%. Diabetes duration of more than 10 years also significantly increases the prevalence of vascular complications, reflecting the importance of early detection and management of diabetes to prevent long-term complications.(22).

Theme 3: Cardiometabolic Risk Factors

Cardiometabolic risk factors such as hypertension, dyslipidemia, and obesity contribute significantly to vascular complications in diabetic patients. Moderate to severe hypertension is a major risk factor for macrovascular complications such as coronary artery disease (CAD) and peripheral artery disease (PAD).(23). Dyslipidemia also worsens the risk by increasing atherosclerosis. In addition, obesity and high body mass index (BMI) have been found to be associated with increased vascular complications, although several studies have shown significant variability in their effects.(24).

Theme 4: Structural and Anatomical Factors

Vascular structural and anatomical changes also influence the risk of vascular complications in diabetes. Thickening of the arterial wall as measured by Carotid Intima-Media Thickness (CIMT) showed a significant association with retinopathy and PAD.(25). In addition, Epicardial Adipose Tissue (EAT) was found to be correlated with coronary artery disease (CAD), chronic kidney disease (CKD), and PAD. However, EAT was not significant for diabetic neuropathy and retinopathy, indicating different pathophysiological mechanisms between micro and macrovascular.(26).

Theme 5: Molecular Mechanisms

Vascular complications of diabetes also involve complex molecular mechanisms. Modification of m6A RNA through METTL3 overexpression was found to worsen retinal pericyte dysfunction and increase apoptosis, which ultimately worsened vascular complications.(29). Conversely, METTL3 depletion can

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prevent pericyte dysfunction and improve retinal microvasculature stability.(30). These findings highlight the potential for molecular-based interventions in the management of diabetic vascular complications.(31).

Theme 6: Prevalence of Vascular Complications

The prevalence of vascular complications in diabetic patients is very high and varies by region. Microvascular complications such as neuropathy (44.9%), nephropathy (15%), and retinopathy (23.3%) are common in diabetic patients with poor glycemic control (27). Risk factors such as high HbA1c, hypertension, and smoking increase the prevalence of these complications, indicating the importance of comprehensive risk factor management.(28).

DISCUSSION

Vascular complications in patients with DM are one of the main causes of morbidity and mortality that require serious attention. A thorough understanding of the factors that influence these complications is essential for early risk identification, development of preventive strategies, and improvement of clinical outcomes. The results of this literature review reveal the diversity of factors that contribute to vascular complications, including biological factors such as biomarkers Bisphenol A (BPA) and Mean Platelet Volume (MPV), clinical factors such as HbA1c levels and duration of diabetes, and molecular mechanisms such as m6A RNA modifications that affect microvascular function. A multidisciplinary approach in understanding the complex interactions between these factors can be the basis for optimizing diabetes management and preventing more serious vascular complications.(32).

Despite the comprehensive insights provided by this literature review, several limitations of the included studies must be acknowledged. Variations in study design, sample sizes, and populations across the reviewed articles may influence the generalizability and consistency of the findings (23). Some studies employed cross-sectional approaches, which limit causal interpretations, while others were conducted on specific populations, such as patients with long-standing diabetes or those from particular geographic regions, potentially reducing external validity (29). Additionally, the diversity in the biomarkers and outcome measures used across studies could contribute to heterogeneity in the results. These limitations highlight the need for future well-designed longitudinal and multicenter studies to validate the associations and mechanisms identified (31).

The findings of this review carry important clinical implications for the prevention and management of vascular complications in patients with diabetes mellitus. Identifying high-risk patients through early detection of biomarkers such as BPA, MPV, and TyG index could facilitate timely interventions (8). Integration of biomarker assessment with routine clinical monitoring, such as HbA1c and lipid profile evaluation, enables a more personalized and proactive approach to diabetes care. Moreover, recognizing the influence of molecular mechanisms like m6A RNA modification offers potential for novel therapeutic targets (33). These insights support the development of multidisciplinary strategies involving endocrinologists, cardiologists, and primary care providers to implement comprehensive vascular risk reduction plans, optimize metabolic control, and ultimately improve patient outcomes (8).

Biochemical factors and biomarkers play an important role in increasing the risk of vascular complications in patients with DM, as they can be early indicators of the pathological process. One of the significant biomarkers is Bisphenol A (BPA), which is found in higher levels in type 2 diabetes patients with cardiovascular complications compared to the control group.(8). BPA contributes to the activation of inflammatory pathways and vascular calcification, which may accelerate vascular endothelial damage.(34). In addition, Mean Platelet Volume (MPV) is an important indicator that describes platelet hyperactivity, where higher MPV values in diabetic patients with complications indicate the role of thrombosis in the pathogenesis of vascular complications.(35). Triglyceride-Glucose Index (TyG) has also emerged as a significant vascular risk marker, with a strong correlation to peripheral vascular stenosis (low ABI) and microalbuminuria (MAU), especially in patients with poor glycemic control.(36).

HbA1c is a biomarker widely used to evaluate glycemic control and has been shown to play a significant role in the development of vascular complications in patients with DM. Previous studies have shown that high HbA1c levels are correlated with an increased risk of microvascular complications, such

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as neuropathy and retinopathy, and macrovascular complications, including coronary artery disease (CAD) and stroke.(37). This is due to chronic hyperglycemia triggering the formation of Advanced Glycation End Products (AGEs), oxidative stress, and endothelial dysfunction, which ultimately compromises blood vessel integrity. In contrast, clinical evidence such as from the UKPDS study shows that a 1% decrease in HbA1c can reduce the risk of micro-complications by 37% and macrovascular by 14%. This effect is explained by a decrease in systemic inflammatory processes and improved vascular function due to better glycemic control.(38).

The duration of DM is a significant risk factor in increasing the prevalence of vascular complications, both micro and macrovascular. Studies have shown that patients with a duration of diabetes of more than 10 years have a significantly higher risk of vascular complications compared to patients with a shorter duration.(14). This is due to longer exposure to chronic hyperglycemia, which accelerates the formation of Advanced Glycation End Products (AGEs), increases oxidative stress, and worsens endothelial dysfunction. This condition triggers damage to small blood vessels, such as in neuropathy and retinopathy, and large blood vessels, such as in coronary artery disease (CAD) and peripheral artery disease (PAD)(39).

Hypertension is one of the major risk factors for macrovascular complications in patients with DM, especially CAD and PAD. Chronic high blood pressure causes increased hemodynamic stress and endothelial dysfunction, which accelerates the process of atherosclerosis and worsens tissue perfusion. Studies have shown that moderate to severe hypertension significantly increases the prevalence of diabetic cardiomyopathy (DbCM), a condition characterized by left ventricular hypertrophy, diastolic dysfunction, and myocardial fibrosis.(40). The combination of severe hypertension and chronic hyperglycemia exacerbates vascular damage through increased oxidative stress, inflammation, and activation of the renin-angiotensin-aldosterone pathway (RAAS), all of which contribute to decreased cardiac and vascular function.(41).

Dyslipidemia plays a crucial role in the pathogenesis of atherosclerosis and vascular complications in patients with DM. Increased levels of low-density lipoprotein (LDL) cholesterol and triglycerides, and decreased levels of high-density lipoprotein (HDL) cholesterol, accelerate the formation of atherosclerotic plaque through inflammatory mechanisms and lipid oxidation.(42). This process causes endothelial damage, narrowing of the vascular lumen, and high risk of coronary artery disease (CAD) and stroke. In addition, obesity or high body mass index (BMI) is also significantly associated with vascular complications.(43). Obesity triggers insulin resistance, oxidative stress, and systemic inflammation, all of which worsen vascular function and increase the risk of neuropathy, retinopathy, and peripheral artery disease (PAD).(44).

Molecular mechanisms play an important role in vascular complications in DM, especially through m6A RNA modification known to affect retinal pericyte function. Studies have shown that overexpression of METTL3, a key methyltransferase enzyme in m6A RNA modification, exacerbates pericyte dysfunction by increasing apoptosis, disrupting blood-retinal barrier function, and vascular permeability.(45,46). This process occurs through the regulation of target genes such as PKC-η, FAT4, and PDGFRA, which are involved in inflammatory signaling and vascular remodeling.(47,48). In contrast, METTL3 depletion was found to prevent pericyte dysfunction by improving the expression of these genes, thereby protecting the stability of the retinal microvasculature from damage caused by chronic hyperglycemia.(47,49).

CONCLUSION

This study analyzed 14 articles discussing factors that influence vascular complications in patients with DM. The analysis obtained six main themes: biochemical factors and biomarkers, clinical factors, cardiometabolic risk factors, structural and anatomical changes in the vasculature, molecular mechanisms, and prevalence of vascular complications. The results showed that vascular complications in diabetes are influenced by various factors, such as high HbA1c levels, hypertension, dyslipidemia, duration of diabetes more than 10 years, arterial wall thickening (CIMT), epicardial adipose tissue (EAT) volume, and molecular modifications such as m6A RNA. These findings strengthen the evidence that vascular complications in diabetes are multifactorial and involve complex interactions between biochemical, clinical, and molecular processes.

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The results of this literature review underscore the importance of patient education regarding glycemic control and management of risk factors such as hypertension and dyslipidemia. Nurses have an essential role in facilitating early detection of complications through monitoring of biomarkers such as HbA1c and MPV, as well as structural measurements like CIMT. In addition, nurses can provide ongoing support to patients to improve adherence to therapy and lifestyle modifications, including diet, exercise, and smoking cessation. Future research should investigate the potential of targeting m6A RNA modification pathways as a therapeutic strategy to prevent or mitigate retinal and vascular damage in diabetic patients. Additionally, studies exploring how m6A RNA interacts with other metabolic and inflammatory pathways may further elucidate its role in vascular complications associated with diabetes.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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