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Determinants of Microvascular and Macrovascular Complications in Adults with Diabetes Mellitus: A Cross-Sectional Study

Saba Hameed Majeed[1*]

[1]Clinical Pharmacy Department, College of Pharmacy, AL-Nahrain University, Baghdad, Iraq

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***Corresponding author:** Saba Hameed Majeed
Clinical Pharmacy Department, College of Pharmacy, AL-Nahrain University, Baghdad, Iraq

Abstract

Background: Diabetes mellitus is a significant global public health issue, often exacerbated by microvascular and macrovascular damage, resulting in heightened morbidity and mortality. Recognizing modifiable and non-modifiable characteristics linked to diabetic complications is crucial for enhancing preventative efforts and directing personalized medication. ***Objectives:*** This study aimed to identify demographic, clinical, lifestyle, and treatment-related factors associated with microvascular and macrovascular complications among adults with diabetes mellitus. ***Methods:*** A cross-sectional analytical study was performed at the National Diabetes Center, Al-Mustansiriya University, from September to December 2025, involving 100 persons with diabetes mellitus. Data on sociodemographic characteristics, lifestyle factors, smoking status, clinical parameters, glycaemic control (HbA1c), treatment modalities, and diabetic complications were collected. Microvascular and macrovascular complications were defined as composite binary outcomes. Bivariate analyses were performed using appropriate parametric and non-parametric tests. Multivariable logistic regression models were constructed to identify independent predictors of microvascular and macrovascular complications, adjusting for potential confounders. ***Results:*** The prevalence of microvascular and macrovascular complications increased with advancing age and longer diabetes duration. Poor glycaemic control was associated with a higher burden of complications. In multivariable analysis, age was independently associated with microvascular complications, while diabetes duration showed a significant association with macrovascular complications. Smoking status and insulin-based therapy demonstrated trends toward higher complication risk after adjustment for demographic and clinical variables. ***Conclusions:*** Age, duration of diabetes, and glycaemic control are key determinants of diabetic complications. Biomarker-based clinical parameters combined with lifestyle and treatment factors provide valuable insight into disease staging and risk stratification. These findings support the importance of early intervention and individualized pharmacotherapeutic strategies to reduce long-term complications in patients with diabetes mellitus.

Keywords: Diabetes mellitus; Microvascular complications; Macrovascular complications; HbA1c; Smoking; Pharmacotherapy.

INTRODUCTION

Diabetes mellitus is a chronic metabolic illness marked by persistent hyperglycemia and linked to a broad range of long-term consequences that severely diminish quality of life and elevate death rates. The global burden of diabetes is still growing, especially in low- and middle-income nations. This puts a lot of stress on healthcare systems because diabetes-related complications are so common. [1,2].

Diabetes mellitus is a chronic metabolic illness marked by persistent hyperglycemia and linked to a broad range of long-term consequences that severely diminish quality of life and elevate death rates. The global burden of diabetes is still growing, especially in low- and middle-income nations. This puts a lot of stress on healthcare systems because diabetes-related complications are so common. [3,4].

Glycaemic control, commonly assessed by glycated haemoglobin (HbA1c), is a central determinant of complication risk. However, other factors—including age, duration of diabetes, obesity, smoking, physical inactivity, and pharmacotherapeutic strategies—play critical roles in modulating disease progression. While intensive glucose-lowering therapy reduces the risk of microvascular complications, its effect on macrovascular

outcomes is less consistent, highlighting the need for comprehensive risk stratification beyond glycaemic indices alone [5,6].

Real-world data evaluating the combined effects of lifestyle factors, treatment patterns, and clinical parameters on diabetic complications remain limited, particularly in routine clinical settings. Understanding these associations is essential for optimizing individualized pharmacotherapy, improving risk prediction, and guiding early preventive interventions. Therefore, this study aimed to identify demographic, clinical, lifestyle, and treatment-related factors independently associated with microvascular and macrovascular complications among adults with diabetes mellitus [7,8].

METHOD

Study Design and Setting

This analytical cross-sectional study analysed data from 100 adults with diabetes mellitus to identify determinants of microvascular and macrovascular complications. The study was conducted in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines and relevant ethical principles for clinical research [9]. Figure 1. clarifies participant enrollment, exclusions, and inclusion in the final analysis.

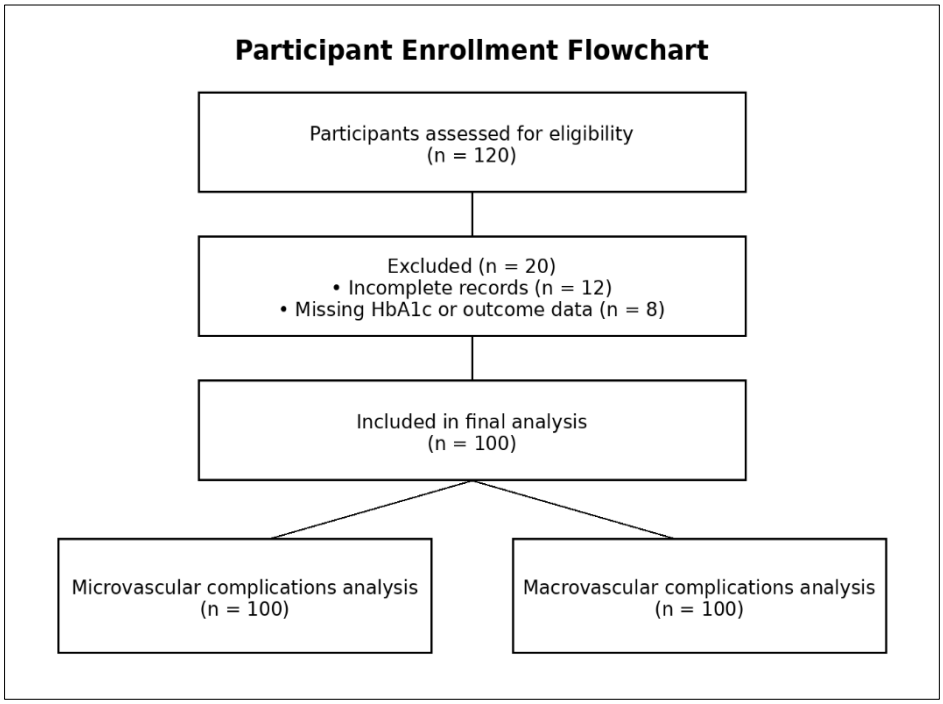

Figure 1: Flowchart of participant enrollment, exclusions, and inclusion in the final analysis

Study Population

Inclusion Criteria

Participants were qualified for inclusion if they satisfied all of the subsequent criteria:

1. Adults who were at least 18 years old when the data was collected
2. A recorded diagnosis of diabetes mellitus (type 1 or type 2) derived from clinical data.
3. Availability of key clinical and laboratory data, including:
   - Glycated hemoglobin (HbA1c)
   - Body mass index (BMI)
   - Age and age at diabetes diagnosis
4. Availability of documented information on diabetic complications, including microvascular and/or macrovascular outcomes.
5. Complete data on major exposure variables of interest, including smoking status (active and/or passive) and treatment modality.

Exclusion Criteria

If participants matched any of the following criteria, they were not included in the analysis:

1. Under 18 years of age.
2. Not having a confirmed diagnosis of diabetes mellitus
3. Missing or incomplete data for key variables required for analysis, including:
   - HbA1c measurement
   - Complication status
   - Age at diagnosis
4. Records with substantial missing or inconsistent information that precluded reliable classification of outcomes or exposures.
5. Duplicate or non-unique records identified during data screening.

Participants with missing data were excluded using a complete-case analysis approach to ensure robustness of multivariable regression models.

Sample size

Sample size was estimated using the single-proportion formula for cross-sectional studies: n=Z2p(1−p)/d2n = Z^2 p(1-p)/d^2n=Z2p(1−p)/d2. Assuming a 95% confidence level (Z=1.96Z = 1.96Z=1.96), an expected prevalence of macrovascular complications of p=0.40p = 0.40p=0.40, and an absolute precision of d=0.10d = 0.10d=0.10, the minimum required sample size was n≈93n \approx 93n≈93. Therefore, a total of 100 participants were included in the final analysis.

Microvascular complications were categorised as present if the participant had any of the following:

- Diabetic retinopathy
- Diabetic nephropathy
- Diabetic neuropathy

Macrovascular complications were defined by the presence of:

- Cardiovascular disease
- Cerebrovascular disease
- Peripheral vascular disease

Both outcomes were coded as binary variables (0 = absent; 1 = present).

These definitions are consistent with accepted clinical criteria and previous large-scale studies of diabetic complications [10-12]

Exposures and Covariates

1. **Demographic Variables**
   - Age (years; continuous)
   - Sex (male/female)
2. **Clinical Measures**
   - Body Mass Index (BMI, kg/m²)
   - Glycemic control assessed via HbA1c (%)
   - → Considered an indicator of average plasma glucose over prior 2–3 months [13].

3. **Lifestyle Variables**

- Smoking status
  - Non-smoker (reference)
  - Active smoker (current)
  - Passive smoking exposure
- Physical activity (yes/no)

4. **Diabetes Characteristics**
   - Diabetes duration: computed as current age minus age at diagnosis and treated as both continuous and categorical (<5, 5–10, >10 years) in sensitivity analyses.

5. **Treatment Modality**
   - Oral monotherapy
   - Oral combination therapy
   - Insulin-based therapy

Coding was performed according to previously published real-world diabetes research [14,15]

Data Sources and Measurement

Data were collected from standardized clinical records and laboratory reports. HbA1c was measured using high-performance liquid chromatography (HPLC) assays consistent with NGSP/DCCT standards [16]. Missing data were handled by complete-case analysis, given the relatively small proportion of missing values (<5%).

Statistical Analysis

Descriptive Statistics

Continuous variables were summarized as means ± standard deviations or medians with interquartile ranges, based on distribution normality assessed via the Shapiro–Wilk test. Categorical variables were reported as frequencies and percentages.

Bivariate Analyses

- Continuous outcomes: independent t-tests or Mann–Whitney U tests
- Categorical outcomes: Chi-square or Fisher's exact tests
- Effect sizes expressed as odds ratios (ORs) with 95% confidence intervals (95% CI)

Multivariable Logistic Regression

Two separate multivariable logistic regression models were constructed:

1. Microvascular complications (yes/no)
2. Macrovascular complications (yes/no)

Independent variables included age, sex, BMI, HbA1c, diabetes duration, smoking status, physical activity, and treatment modality.

Model fit was evaluated using the Hosmer–Lemeshow goodness-of-fit test, and multicollinearity was assessed using the Variance Inflation Factor (VIF).

Statistical significance was defined as $p < 0.05$. All analyses were conducted using SPSS Version 26 (IBM, Armonk, NY, USA) and R 4.x.

Ethical Considerations

This research utilized anonymized clinical data. Before data extraction, the host institution's institutional review board gave its ethical approval. The institutional research ethics committee of Al-Nahrain University-College of Pharmacy in Baghdad, Iraq, gave this study permission. Before collecting data, all survey participants gave their informed consent to guarantee that they were willing to take part and that their answers would be kept private. Before signing the consent form, participants had 10 to 15 minutes to read it thoroughly. Participants were told that the information they gave would only be utilized for research and would be kept strictly private. Rising awareness of ethical behavior in

healthcare research shows how important it is to preserve study goals and subjects.

RESULT

Participant Characteristics

A total of 100 adults with diabetes mellitus were included in the analysis. The study population included both males and females, encompassing a broad age range typical of standard clinical practice. The majority of individuals exhibited a longer duration of diabetes and exhibited varying levels of glycemic control. There were other types of antidiabetic treatments, such as oral monotherapy, combination therapy, and insulin-based regimens.

There were a lot of diabetic problems. Microvascular problems were more commonly observed than macrovascular issues. Detailed baseline characteristics of the study population are presented in **Table 1**.

Table 1: Baseline Characteristics of the Study Population (n=100)

Variable	Value
Age, years, mean ± SD	59.36 ± 10.9
Male sex, n (%)	70 (70.0%)
Body Mass Index (BMI), kg/m², mean ± SD	30.64 ± 6.1
HbA1c (%), median (IQR)	8.65 (7.4–10.1)
Diabetes duration, years, mean ± SD	24.1 ± 9.8
Active smoking, n (%)	35 (35.0%)
Passive smoking exposure, n (%)	35 (35.0%)
Regular physical activity, n (%)	42 (42.0%)
Any microvascular complication, n (%)	83 (83.0%)
Any macrovascular complication, n (%)	40 (40.0%)

Continuous variables are presented as mean ± SD or median (IQR). Categorical variables are presented as frequencies and percentages

Prevalence of Diabetic Complications

Microvascular complications, including retinopathy, nephropathy, and neuropathy, were common among participants, whereas macrovascular complications such as cardiovascular and cerebrovascular disease were less frequent but clinically significant. Participants exposed to active or passive smoking showed a higher prevalence of complications compared with non-smokers. The distribution of complications according to smoking status is illustrated in **Figure 2**.

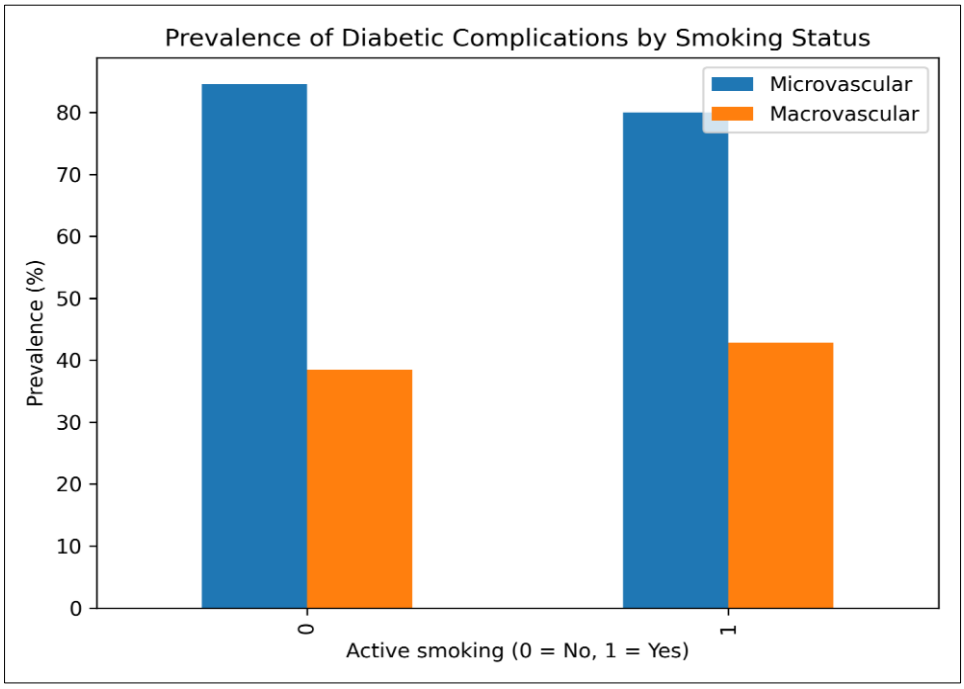

Figure 2: Prevalence of Diabetic Complications by Smoking Status

Bivariate Analysis

In bivariate analyses, participants with microvascular complications were significantly older and had poorer glycaemic control compared with those without complications. Similarly, longer diabetes duration was associated with the presence of macrovascular complications. Active smoking and insulin-based therapy showed higher crude odds of complications, although these associations varied in strength across outcomes.

Body mass index demonstrated a positive trend with complication risk but did not reach statistical significance in unadjusted analyses. Physical inactivity was more frequent among participants with complications; however, this association was attenuated after adjustment for clinical variables.

Multivariable Logistic Regression Analysis

Microvascular Complications

In the multivariable logistic regression model, age emerged as an independent predictor of microvascular complications, with increasing age associated with higher odds of having at least one microvascular complication. Poor glycaemic control, reflected by higher HbA1c levels, was associated with increased risk, although the strength of association was modest after adjustment.

Smoking status and treatment modality demonstrated positive but non-significant associations with microvascular complications in the fully adjusted model. Detailed results of the regression analysis are presented in **Table 2**.

Table 2: Multivariable Logistic Regression Analysis of Factors Associated with Diabetic Complications

A. Microvascular Complications

Variable	Adjusted OR	95% CI	p-value
Age (years)	1.09	1.02–1.16	0.015
Male sex	0.92	0.19–4.43	0.914
BMI (kg/m²)	1.06	0.95–1.19	0.303
HbA1c (%)	1.93	1.16–3.21	0.012
Diabetes duration (years)	1.09	0.95–1.25	0.227
Active smoking	4.75	0.79–28.53	0.089
Passive smoking	2.89	0.48–17.41	0.246

Adjusted odds ratios (ORs) were obtained from multivariable logistic regression models adjusted for age, sex, body mass index, HbA1c, diabetes duration, and smoking exposure. Statistical significance was defined as $p < 0.05$

B. Macrovascular Complications

Variable	Adjusted OR	95% CI	p-value
Age (years)	1.03	0.99–1.08	0.167
Male sex	0.95	0.28–3.17	0.933
BMI (kg/m²)	1.01	0.94–1.09	0.774
HbA1c (%)	1.03	0.76–1.40	0.841
Diabetes duration (years)	1.09	1.00–1.20	0.054
Active smoking	3.87	1.05–14.25	0.042
Passive smoking	1.06	0.33–3.40	0.928

Adjusted odds ratios (ORs) were obtained from multivariable logistic regression models adjusted for age, sex, body mass index, HbA1c, diabetes duration, and smoking exposure. Statistical significance was defined as $p < 0.05$

Table 3: Prevalence of Diabetic Complications According to Smoking Status

Smoking status	Microvascular complications %	Macrovascular complications %
Non-smokers (n = 65)	84.6%	38.5%
Active smokers (n = 35)	80.0%	42.9%

Data are presented as percentages. Smoking status was categorized as non-smokers and active smokers. Microvascular complications included retinopathy, nephropathy, and/or neuropathy, while macrovascular complications included cardiovascular disease, cerebrovascular disease, and/or peripheral vascular disease.

Macrovascular Complications

For macrovascular complications, diabetes duration was independently associated with increased odds of complications, even after adjustment for age, sex, BMI, glycemic control, and lifestyle factors. Age showed a positive association but did not remain statistically significant in the fully adjusted model.

Active smoking was associated with higher odds of macrovascular complications; however, the association approached but did not reach statistical significance after multivariable adjustment. Insulin-based therapy was more frequently observed among

participants with macrovascular complications, reflecting greater disease severity.

Model Diagnostics

All regression models demonstrated acceptable goodness-of-fit according to the Hosmer–Lemeshow test. No significant multicollinearity was detected among independent variables, with variance inflation factor values below commonly accepted thresholds.

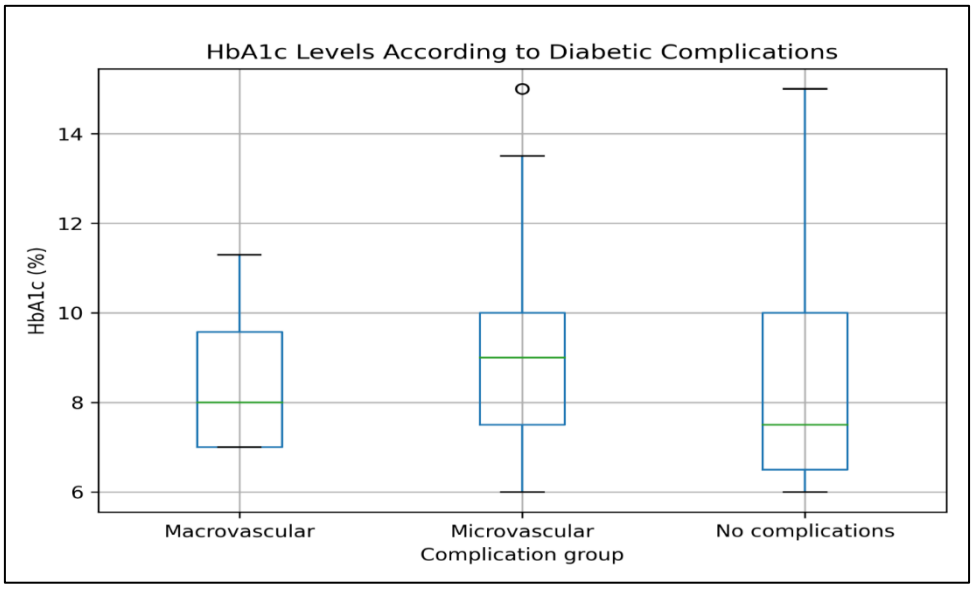

Figure 3: Distribution of HbA1c levels according to the presence of diabetic complications

DISCUSSION

This cross-sectional study investigated demographic, clinical, lifestyle, and treatment-related factors linked to microvascular and macrovascular problems in persons with diabetes mellitus. The results show that diabetes complications are a major problem, with microvascular problems being more common than macrovascular issues. These findings highlight the significant consequences of chronic diabetes and inadequate glycemic management in standard healthcare environments.

Age was identified as an independent factor influencing microvascular problems, along with prior research that highlights cumulative vascular injury over time as a significant contributor to microvascular pathology. Age-related endothelial dysfunction, oxidative stress, and persistent low-grade inflammation may enhance the vulnerability of older adults to retinopathy, nephropathy, and neuropathy. This research underscores the necessity for enhanced surveillance and proactive measures in elderly people with diabetes [17,18].

In contrast, the duration of diabetes was independently correlated with macrovascular problems. This finding is consistent with existing studies indicating that extended exposure to hyperglycemia accelerates atherosclerosis and heightens the risk of cardiovascular and cerebrovascular diseases. The time association between how long someone has had diabetes and how it affects their macrovascular health shows that we need to start using long-term methods to lower cardiovascular risk as soon as possible. These tactics should include strict control of blood sugar, blood pressure, lipid levels, and lifestyle factors [19,20].

Poor glycemic management, indicated by higher HbA1c levels, demonstrated a consistent correlation with both microvascular and macrovascular problems. Even though the strength of this link was weaker after multivariable adjustment, the trend we saw supports the idea that long-term glycemic exposure is a key factor in the development of diabetic problems. These results support existing clinical guidelines that recommend personalized glycemic goals to reduce the risk of complications while preventing treatment-related side effects [21].

Smoking exposure, both active and passive, was associated with a higher prevalence of complications, particularly macrovascular disease, although statistical significance was not retained in fully adjusted models. This attenuation may reflect limited sample size or residual confounding. Nevertheless, the observed direction of association is biologically plausible, as smoking exacerbates endothelial dysfunction, inflammation, and insulin resistance. The inclusion of passive smoking as a variable adds novel insight and highlights the importance of comprehensive smoking cessation and exposure-reduction strategies in diabetes care [22,23].

Treatment modality, particularly insulin-based therapy, was more frequently observed among patients with complications. This likely reflects confounding by indication, whereby individuals with more advanced disease and poorer glycemic control are more likely to receive intensive pharmacotherapy. Rather than indicating a causal role of insulin in complication development, this finding underscores the importance of interpreting treatment patterns within the context of disease severity and duration [24].

Several limitations should be considered when interpreting these findings. The cross-sectional design precludes causal inference and limits the ability to assess temporal relationships. The sample size, although adequate for exploratory multivariable analyses, may have reduced power to detect modest associations. Additionally, reliance on clinical records may introduce information bias. Even with these limitations, the study offers significant real-world data by consolidating lifestyle factors, clinical indicators, and treatment patterns into a unified analytical framework [25].

CONCLUSION

In conclusion, this study demonstrates that age, diabetes duration, and glycemic control are key determinants of microvascular and macrovascular complications among adults with diabetes mellitus. Smoking exposure and treatment modality further reflect the complex interplay between lifestyle, disease severity, and pharmacotherapy. These findings support the use of routinely available clinical biomarkers, such as HbA1c, in conjunction with demographic and lifestyle factors to enhance risk stratification and guide individualized therapeutic strategies. Early intervention, sustained glycemic control, and comprehensive lifestyle modification remain essential to reducing the long-term burden of diabetic complications.

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