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Association between mean platelet volume and the risk of type 2 diabetes mellitus among women with history of gestational diabetes mellitus

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Abstract

Aims The present study aimed to investigate the relationship between mean platelet volume (MPV) and the risk of type 2 diabetes mellitus (T2DM), among women with and without a history of gestational diabetes mellitus (GDM).

Methods Eight thousand one hundred eighty-one parous women of the '2007–2018 National Health and Nutrition Examination Survey (NHANES)' were classified into GDM and non-GDM groups based on self-reported GDM history. We investigated the independent association between the MPV and the risk of T2DM in these groups via multivariable regression analysis. A subgroup analysis was done for the GDM group.

Results After comprehensive adjustment for potential covariates, a significant positive correlation was observed between MPV and the risk of T2DM in women with a history of GDM (OR = 1.50, 95% CI 1.13–2.01, P = 0.006). There was a linear relationship between MPV and T2DM among women with a history of GDM, with each unit increase in MPV increasing the risk of T2DM by 50%. Subgroup analysis and interaction tests revealed a stronger significant effect on women with GDM history who had HbA1c ≥ 7%.

Conclusions MPV is strongly associated with the incidence of T2DM among U.S. parous women with prior GDM, indicating that MPV may be a potential biomarker of T2DM among women with a history of GDM.

Keywords Mean platelet volume, Gestational diabetes mellitus, Type 2 diabetes mellitus, NHANES

Introduction

Gestational diabetes mellitus (GDM) is defined as glucose intolerance of varying severity when it is diagnosed in the second or third trimester of pregnancy and not overt diabetes before pregnancy [1]. The incidence of GDM is approximately 6% in the U.S. [2]. GDM often involves underlying β-cell defects that arise due to the inadequacy of compensatory responses. This dysfunction is a risk factor for the later development of prediabetes and type 2 diabetes mellitus (T2DM) [3, 4]. Specifically, β-cell defects in women with GDM still exist or worsen postpartum although their hyperglycemia typically resolves following delivery [5]. Over time, the progressive

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worsening of β-cell function drives women who develop GDM progression from normal glucose tolerance to prediabetes and ultimately to T2DM [3, 5, 6]. Thus, the link between GDM and T2DM is rooted in the progressive loss of β-cell insulin secretion in the context of insulin resistance. Women with prior GDM have a 7- to tenfold greater risk of developing T2DM [7, 8]. According to a systematic review and meta-analysis published in 2020, approximately 26.2% of parous women were affected by T2DM after GDM [9]. As a result, women with a history of GDM should be given special clinical attention.

Assessment of risk factors is essential for the progression of T2DM in patients with a history of GDM. Glycated hemoglobin (HbA1c) is a valuable indicator of glucose control, and an HbA1c ≥ 7% indicates unsatisfactory control [10, 11]. Despite the increased availability of HbA1c, it is yet to be commonly employed to monitor diabetes mellitus in epidemiological or primary health care contexts.

The mean platelet volume (MPV), a measurement of the average size of platelets in the blood, reflects platelet function and activation [12]. Several findings have suggested that women with GDM may have higher MPV [13, 14]. Among 13,021 participants in the National Health and Nutrition Examination Survey (NHANES) 1999–2004, MPV was positively associated with the severity of diabetes mellitus and was most pronounced in subjects with MPV levels ≥ 9.31 fL [15]. A report from Japanese subjects revealed that the MPV of prediabetic individuals was greater than that of control individuals [16]. However, another study reported that diabetes mellitus was not independently associated with increased platelet size [17]. In addition, the relationship between the MPV and T2DM after GDM has not been reported.

Thus, this study aimed to evaluate the association between MPV and the risk of T2DM among women with a history of GDM on the basis of the NHANES.

Methods

Study population

The NAHNES is a research project of the National Center for Health Statistics (NCHS) that is designed to assess the health and nutritional status of adults and children in the United States. The NCHS Research Ethics Review Board approved the survey protocols, and each participant provided informed consent.

We selected data from the 2007–2018 cycle of the NHANES because only those cycles included reproductive health questionnaires concerning GDM issues. Overall, 20,902 women were enrolled in this survey over that period. The exclusion criteria were as follows: (1) missing GDM data ($n = 8139$) and T2DM data ($n = 311$); (2) pregnant women ($n = 312$) and nullipara ($n = 650$); (3) missing glycohemoglobin (HbA1c) data ($n = 411$) and MPV data ($n = 1084$); and (4) missing data on body mass index (BMI) ($n = 66$), education ($n = 10$), marital status ($n = 3$), poverty-income ratio (PIR) ($n = 817$), sedentary duration ($n = 29$), smoking status ($n = 6$), alcohol use ($n = 1139$), direct HDL-cholesterol, or total cholesterol ($n = 112$). Thus, 8181 subjects were ultimately included in this analysis (Fig. 1).

Dependent variable

The GDM diagnosis data were measured on the basis of each woman's self-reported answers to personal interviews: (1) item RHQ162, "During pregnancy, told you have diabetes?"; (2) item DIQ175S, "Whether GDM is your risk for diabetes or prediabetes?". Women who answered "yes" to either of these two questions were considered to have a history of GDM. According to the American Diabetes Association (ADA)' s diagnostic criteria, diabetes was obtained via a self-report questionnaire (DIQ010), which inquired, "Other than during pregnancy, have you ever been told by a doctor or health professional that you have diabetes or sugar diabetes?" Women who answered "yes" to either of these two questions were defined as having been diagnosed with diabetes; alternatively, individuals with an HbA1c level ≥ 6.5%, a fasting glucose level of ≥ 126 mg/dL, and a 2-h glucose level of ≥ 200 mg/dL were considered to have diabetes [18].

Independent variables

The mean platelet volume (MPV) was used as an exposure variable in our research. To ensure accuracy and uniformity of blood testing procedures, NHANES health technicians strictly followed the manufacturer's instructions. MPV was measured and reported as fL using the Beckman Coulter method of counting and sizing, automatic diluting, and mixing.

Covariates

The demographic variables included age, race, educational level, marital status and PIR; the laboratory data included HbA1c (%), direct HDL cholesterol (mg/dL), and total cholesterol (mg/dL); the questionnaire data included smoking status (smoking at least 100 cigarettes over the lifetime), alcohol consumption status (had at least 12 alcohol drink/1 year), and sedentary duration (minutes/day); and diabetes status was defined as the reporting of a diabetic diagnosis.

Statistical analysis

Categorical variables are reported as numbers (percentages), and the chi-square test was adopted to compare differences between the two groups. Continuous

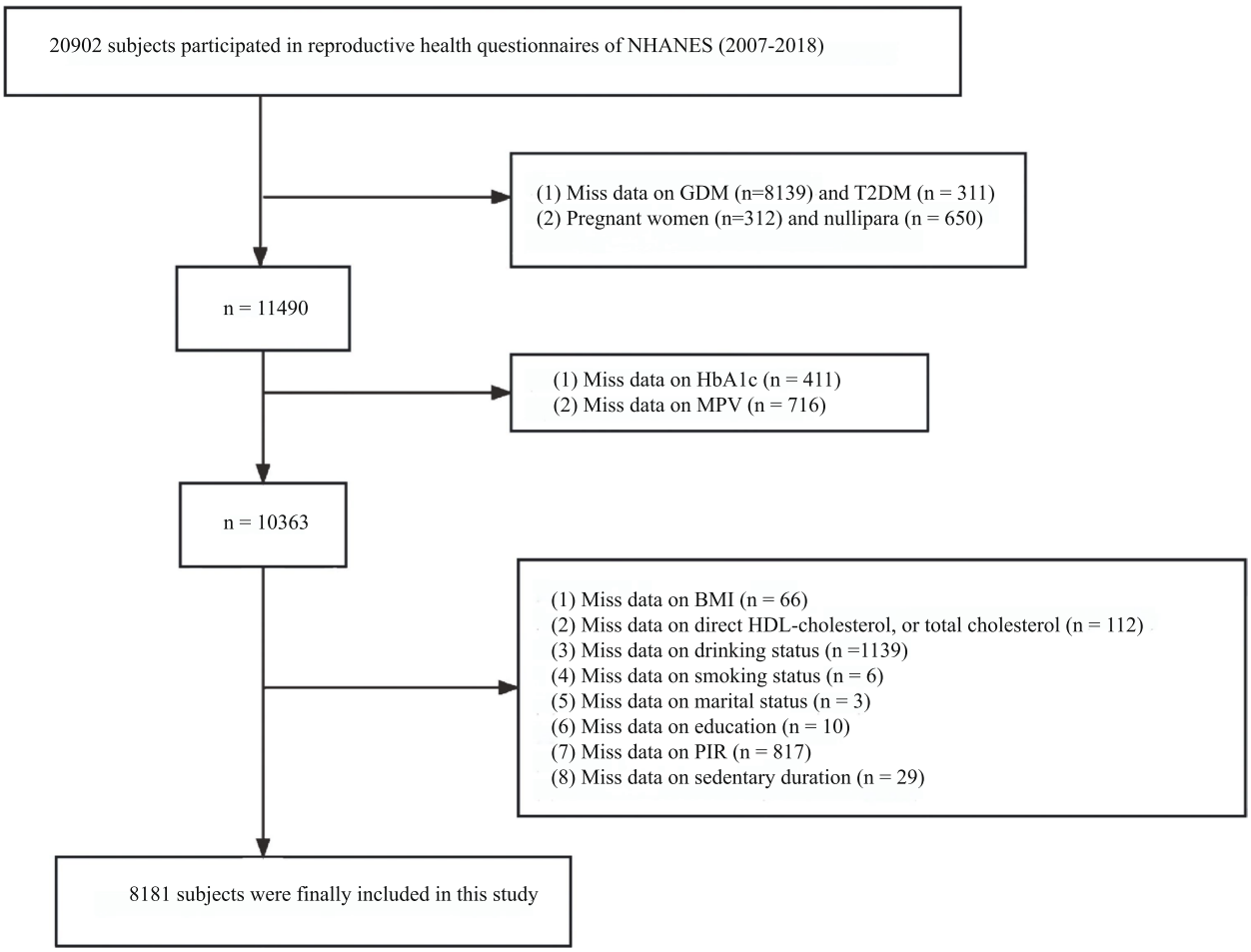

Fig. 1 Flow chart for the selection of participants in the cohort study. NHANES, National Health and Nutrition Examination Survey; HbA1c, glycohemoglobin; MPV, mean platelet volume; direct HDL-cholesterol, direct high-density lipoprotein cholesterol; PIR, poverty income ratio; BMI, body mass index

variables that did not satisfy the normal distribution criteria are presented as the medians and interquartile ranges [M (Q1, Q3)], and the Wilcoxon rank-sum test was used to compare differences between the two groups. The associations of variables with T2DM with and without history of GDM were first evaluated via univariate logistic regression analysis. Covariates were included as potential confounders if they were statistically significant in the univariate analysis. The relationships between MPV and T2DM in patients with and without history of GDM were investigated by using MPV data as a continuous variable and in quartiles. The associations were evaluated via odds ratios (ORs) and 95% confidence intervals (CIs). The following stratified multivariate logistic regression models were used to assess the effect of MPV on T2DM with and without history of GDM: Crude model: no adjustment; Model 1: adjusted for age, race, education, and marital status; Model 2: adjusted for the variables in Model 1 plus BMI, direct HDL-cholesterol, HbA1c, total cholesterol, alcohol consumption status, smoking status, and family income to poverty. In addition, we evaluated the linearity of the association between the MPV and T2DM with a history of GDM via a fully adjusted generalized additive model and smooth curve fitting. To investigate the relationship between the MPV and T2DM with a history of GDM in different subgroups, subgroup analysis was subsequently carried out. Stratification factors included age (< 50 years and ≥ 50 years), race (Mexican American, Hispanic, Non-Hispanic White, Non-Hispanic Black, and Others), BMI (< 25 kg/m^2, 25–30 kg/m^2, ≥ 30 kg/m^2), and HbA1c (< 7% and ≥ 7%), and interaction analysis was used to evaluate the heterogeneity of the associations between the subgroups.

In this study, R (http://www.R-project.org) and EmpowerStat software were used for data analysis, and $P < 0.05$ was considered statistically significant.

Results

Baseline characteristics

In total, 8181 parous women were included in the final analysis, of whom 1123 (13.73%) had T2DM (Table 1). The prevalence of T2DM in those with a history of GDM was significantly greater than that in the control group (27.37% vs. 12.58%, $P<0.001$), suggesting that GDM history may be a risk factor for the morbidity of T2DM. Compared with those without a history of GDM, women with a history of GDM tended to be slightly younger; were more prone to be Mexican American (21.52%), married/cohabiting (68.51%), and well educated (56.01%); and were more likely to have a higher BMI, HbA1c and MPV and lower direct HDL-cholesterol levels ($P<0.05$). However, there were no significant differences among the groups with respect to the family poverty income ratio, smoking status, alcohol use, sedentary duration, or total cholesterol.

Univariate analyses of T2DM patients with and without a history of GDM

Univariate analyses were performed between prior GDM pregnancies and non-GDM pregnancies according to the development of type 2 diabetes (Table 2). In summary, significant factors associated with higher odds of subsequent diagnosis of T2DM among women with GDM history included older age, being non-Hispanic white, having less education, and being widowed/divorced/separated; they also had higher BMI, MPV, and HbA1c, but lower direct HDL cholesterol (Table 2). In addition to the above variables, non-Hispanic black, other race, family poverty income ratio, smoking status, alcohol consumption, sedentary time, and total cholesterol were associated with a higher incidence of T2DM without a history of GDM.

Table 1 Basic characteristics and laboratory data for study population stratified by history of GDM

	Overall ***n*** **= 8181**	**No GDM** ***n*** **= 7549**	**Prior GDM** ***n*** **= 632**	***P***
Age (years)	52.00 (39.00, 66.00)	53.00 (40.00, 66.00)	44.00 (36.50, 54.00)	< 0.001
Race (%)				< 0.001
Mexican American	16.24	15.80	21.52	
Non-Hispanic White	11.37	11.33	11.87	
Non-Hispanic Black	43.89	44.42	37.66	
Other Hispanic	20.23	20.52	16.77	
Other Race	8.26	7.93	12.18	
Education (%)				0.016
Less than high school	26.56	26.72	24.68	
High school or equivalent	22.75	23.04	19.30	
College or above	50.69	50.25	56.01	
Marital status (%)				< 0.001
Married/cohabiting	58.49	57.65	68.51	
Widowed/divorced/separated	32.55	33.36	22.94	
Never married	8.96	8.99	8.54	
PIR	1.91 (1.03, 3.69)	1.91 (1.03, 3.69)	1.94 (1.04, 3.77)	0.905
BMI (kg/m^2)	28.76 (24.56, 33.85)	28.60 (24.50, 33.70)	30.58 (25.70, 36.30)	< 0.001
T2DM (%)	13.73	12.58	27.37	< 0.001
Smoked at least 100 cigarettes in life	38.66	38.71	38.13	0.776
Had at least 12 alcohol drink/1 year	59.26	59.09	61.23	0.293
Sedentary duration (minutes/day)	300.00 (180.00, 480.00)	300.00 (180.00, 480.00)	300.00 (180.00, 480.00)	0.540
HbA1c (%)	5.60 (5.30, 5.90)	5.50 (5.30, 5.90)	5.70 (5.30, 6.40)	< 0.001
MPV (fL)	8.10 (7.50–8.80)	8.10 (7.50, 8.80)	8.20 (7.60, 8.90)	0.048
Direct HDL-cholesterol (mg/dL)	54.00 (45.00, 66.00)	55.00 (46.00, 66.00)	51.00 (41.00, 60.00)	< 0.001
Total cholesterol (mg/dL)	195.00 (169.00, 222.00)	195.00 (169.00, 223.00)	193.00 (168.75, 218.00)	0.228

Median (interquartile range) for continuous variables, and *P* was calculated by the weighted linear regression. Percentage (%) for categorical variables, and *P* was calculated by weighted chi-square test

GDM Gestational diabetes mellitus, *PIR* Poverty income ratio, *BMI* Body mass index, *T2DM* Type 2 diabetes mellitus, *HbA1c* Glycohemoglobin, *MPV* Mean platelet volume, *Direct HDL-cholesterol* Direct high-density lipoprotein cholesterol

Table 2 Univariate logistic regression assessing risk factors for a subsequent diabetes diagnosis among U.S. women with and without GDM history

	without history of GDM *n* = 7549	*P*	with history of GDM *n* = 632	*P*
Age (years)	1.05 (1.05, 1.06)	< 0.001	1.08 (1.06, 1.10)	< 0.001
Race (%)				
Mexican American	Reference		Reference	
Non-Hispanic White	0.75 (0.58, 0.97)	0.030	2.14 (1.19, 3.85)	0.011
Non-Hispanic Black	0.59 (0.49, 0.72)	< 0.001	0.76 (0.46, 1.23)	0.257
Other Hispanic	1.15 (0.93, 1.41)	0.189	1.12 (0.64, 1.95)	0.702
Other Race	0.69 (0.51, 0.93)	0.015	0.62 (0.32, 1.23)	0.172
Education (%)				
Less than high school	Reference		Reference	
High school or equivalent	0.57 (0.48, 0.69)	< 0.001	1.05 (0.64, 1.73)	0.848
College or above	0.41 (0.35, 0.48)	< 0.001	0.57 (0.38, 0.87)	0.009
Marital status (%)				
Married/cohabiting	Reference		Reference	
Widowed/divorced/separated	1.94 (1.68, 2.24)	< 0.001	1.77(1.18, 2.65)	0.006
Never married	0.81 (0.61, 1.08)	0.159	1.45 (0.79, 2.69)	0.233
PIR	0.84 (0.80, 0.87)	< 0.001	0.91 (0.82, 1.02)	0.098
BMI (kg/m^2)	1.07 (1.06, 1.08)	< 0.001	1.06 (1.04, 1.08)	< 0.001
Smoked at least 100 cigarettes in life				
NO	Reference		Reference	
Yes	1.19 (1.03, 1.36)	0.015	1.01 (0.70, 1.43)	0.996
Had at least 12 alcohol drink/1 year				
NO	Reference		Reference	
Yes	0.50 (0.43, 0.57)	< 0.001	0.85 (0.59, 1.21)	0.367
Sedentary duration (minutes/day)	1.00 (1.00, 1.00)	0.002	1.00 (1.00, 1.00)	0.392
HbA1c (%)	8.21 (6.32, 10.67)	< 0.001	4.22 (2.76, 6.45)	< 0.001
MPV (fL)	1.17 (1.09, 1.25)	< 0.001	1.39 (1.16, 1.68)	0.001
Direct HDL-cholesterol (mg/dL)	0.98 (0.97, 0.98)	< 0.001	0.99 (0.97, 1.00)	0.025
Total cholesterol (mg/dL)	0.99 (0.99, 1.00)	< 0.001	0.95 (0.80, 1.13)	0.554

GDM Gestational diabetes mellitus, *PIR* Poverty income ratio, *BMI* Body mass index, *T2DM* Type 2 diabetes mellitus, *HbA1c* Glycohemoglobin, *MPV* Mean platelet volume, *Direct HDL-cholesterol* Direct high-density lipoprotein cholesterol

Association between MPV and T2DM

Table 3 shows a stratified analysis of the association between the MPV and T2DM based on GDM status. When we analyzed the MPV as a continuous variable, we found that the associations between T2DM with a history of GDM and the MPV were positive regardless of the type of adjusted covariate ($P < 0.05$). After converting MPV concentrations into categorical variables (quartiles) for sensitivity analysis, the risk of T2DM with a history of GDM showed a stepwise increase with the quartile of MPV (P for trend < 0.05) and was at the highest point in the highest MPV quartile group (Q4) (crude model: OR = 2.48, 95% CI: 1.42–4.33, $P = 0.001$; Model 1: OR = 2.91, 95% CI: 1.56–5.44, $P < 0.001$). In the unadjusted model and Model 1, we found that the MPV was associated with a risk of T2DM for women without a history of GDM ($P < 0.001$). However, we found no significant association between MPV and the risk of T2DM without a history of GDM after adjusting for all covariates in Model 2.

Results of linear regression of T2DM and MVP

To verify the reliability and stability of the multivariate regression analysis results, on the basis of the fully adjusted model (Model 2), we explored the possible linear relationship between MPV and T2DM with a history of GDM. The results indicated that the association between the MPV and T2DM was linear (Fig. 2). This finding agreed with the stepwise increased OR in the logistic regression analysis.

Subgroup analysis and interaction test

We found that the risk for T2DM in women with history of GDM was not consistently associated with

Table 3 Association between MPV and T2DM among women with or without GDM history

	With history of GDM (*n* = 632) OR (95% CI), *P*			Without history of GDM (*n* = 7549) OR (95% CI), *P*		
	Crude model	**Model 1**	**Model 2**	**Crude model**	**Model 1**	**Model 2**
MPV (continuous per one unit)	1.39 (1.16 1.68), < 0.001	1.58 (1.27, 1.98), < 0.001	1.50 (1.13, 2.01), 0.006	1.17 (1.09, 1.25), < 0.001	1.19 (1.11, 1.28), < 0.001	1.03 (0.94, 1.14), 0.476
MPV (quartiles)						
Q1 (4.70–7.50)	Reference	Reference	Reference	Reference	Reference	Reference
Q2 (7.50–8.10)	1.58 (0.88, 2.85), 0.129	1.41 (0.73, 2.73), 0.300	0.93 (0.41, 2.11), 0.861	1.04 (0.84, 1.29), 0.694	1.06 (0.85, 1.33), 0.591	0.97 (0.74, 1.28), 0.835
Q3 (8.10–8.80)	1.58 (0.90, 2.78), 0.112	1.70 (0.90, 3.19), 0.099	1.42(0.66, 3.07), 0.371	1.22 (0.99, 1.49), 0.075	1.18 (0.95, 1.46), 0.130	0.98 (0.75, 1.27), 0.854
Q4 (8.80–15.10)	2.48 (1.42, 4.33), 0.001	2.91 (1.56, 5.44), < 0.001	2.85 (0.85, 4.05), 0.1223	1.48 (1.21, 1.80), < 0.001	1.50 (1.21, 1.85), < 0.001	1.04 (0.79, 1.35), 0.795
P for trend	0.002	< 0.001	0.047	< 0.001	< 0.001	0.771

Model 1: adjusted for age, race, education, and marital status

Model 2: adjusted for: Model 1 + BMI + direct HDL-cholesterol + HbA1c + alcohol use + smoking status + triglyceride + PRI

Crude model: adjusted for none

GDM Gestational diabetes mellitus, *T2DM* type 2 diabetes mellitus, *MPV* mean platelet volume, *OR* Odds ratio, *CI* Confidence interval

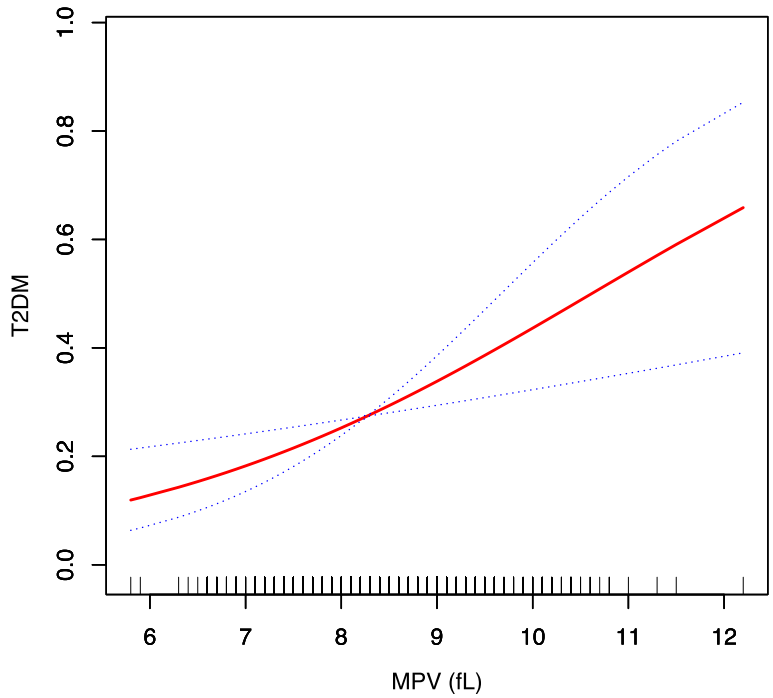

Fig. 2 Relationships between the MPV and T2DM in patients with a history of GDM according to smooth curve fitting

increased MPV in some subgroups (Fig. 3). A significant association of the MPV with T2DM secondary to GDM was observed in the subgroup stratified by age (all $p < 0.05$). For the subgroup stratified by race, BMI, and HbA1c, a connection with statistical significance was observed only among those participants who were Mexican American and non-Hispanic white and had a BMI ≥ 30 kg/m^2 and an HbA1c $\geq 7\%$. Furthermore, the interaction test revealed that an HbA1c level $\geq 7\%$ may influence the positive association between the MPV and T2DM with a history of GDM (p for interaction < 0.05).

Charateristics	N	T2DM with history of GDM	P value	P for interaction
Age (years)				**0.21**
<50	414	1.33 (1.01, 1.76)	0.044	
⩾50	218	1.75 (1.26, 2.43)	<0.001	
Race				**0.454**
Mexican American	136	1.74 (1.14, 2.65)	0.01	
Non–Hispanic White	75	1.84 (1.02, 3.33)	0.043	
Non–Hispanic Black	238	1.23 (0.89, 1.70)	0.217	
Other Hispanic	106	1.23 (0.80, 1.89)	0.348	
Other Race	77	1.05 (0.54, 2.02)	0.886	
BMI (kg/m2)				**0.465**
<25	130	1.38 (0.83, 2.28)	0.232	
⩾25, <30	163	1.07 (0.69, 1.65)	0.767	
⩾30	339	1.46 (1.14, 1.87)	0.003	
HbA1c (%)				**0.034**
<7	521	1.17 (0.90, 1.51)	0.232	
⩾7	111	2.48 (1.23, 5.01)	0.011	

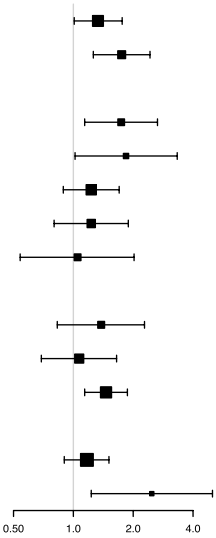

Fig. 3 Subgroup analyses of the effect of the MPV on T2DM patients with a history of GDM. HbA1c, glycohemoglobin; BMI, body mass index

Discussion

To the best of our knowledge, this report is the first study on the independent association between the MPV and the risk of progression from GDM to T2DM, as measured by quantitative MPV levels, and is one of the most extensive cross-sectional studies to explore this relationship. After adjusting for demographic data, lifestyle data, examination data, and laboratory data, we found that the MPV was not significantly associated with T2DM without a history of GDM, but T2DM patients with a history of GDM had significantly higher MPV levels than non-T2DM patients with a history of GDM. Additionally, subgroup analyses and interaction evaluations revealed significant moderating effects for HbA1c.

Many studies have examined risk factors or lifestyle behaviors among women in the U.S. with T2DM and a history of GDM [19–21]. As a potential indicator of gestational diabetes mellitus, the MPV can predict GDM in early pregnancy [22–24]. A meta-analysis revealed that the MPV was significantly increased in pregnant women with GDM during the third trimester, which is consistent with the highest degree of insulin resistance. However, this difference was not observed in the second trimester [13]. These findings suggest that the MPV might vary depending on the trimester of pregnancy. Early diagnosis of GDM can greatly improve the prognosis of mothers and children. However, few studies have demonstrated the relationship between the MPV and GDM after delivery.

Our results are consistent with those of previous studies. The American study included two population-based cohorts, a longitudinal community-based cohort ($n=3,248$) and a large population-based prospective study ($n=463,703$), which reported that the MPV was strongly associated with an increased risk of T2DM [25]. A study conducted in Japan indicated that the MPV was positively correlated with the early stage of T2DM according to findings in the prediabetes mellitus group and could be altered by improving hyperglycemia [26]. In addition, another prospective cohort study involving 14,009 participants reported that an MPV ≥ 9.80 fL was associated with a 92% increased incident risk of diabetes mellitus (95% CI 1.30–2.84) compared with those with an MPV < 7.50 fL in a middle-aged and older female Chinese population [27]. Nevertheless, our study was inconsistent with another study in which MPV levels were lower in T2DM than in control subjects (9.7 (1.7) vs. 10.3 (1.5), $P<0.001$) [28]; this study was conducted in all T2DM patients, and it is important to note that women who develop GDM have a chronic β-cell defect that ultimately drives the development of T2DM. Therefore, it is prudent to investigate T2DM with and without prior GDM separately using larger sample sizes for further potential correlation analyses. Our study segmented the history of GDM and no history of GDM for risk prediction to T2DM. Potential confounders (including demographic data, lifestyle data, examination data, and laboratory data) were accounted for to confirm the accuracy and stability of the results. Similarly, our study demonstrated that the corrected MPV was positively associated with T2DM among parous women with a history of GDM in the general American population but not with T2DM

among parous women without GDM. Therefore, our study results are more credible than those of previous studies.

In this study, all the included subjects were multiparous women. After excluding the interference of pregestational diabetes, women with a history of GDM had an increased risk of developing T2DM. Interestingly, among women with T2DM but no history of GDM, the correlation between the MPV and T2DM was found to be insignificant following adjustments for various potential confounding variables. These findings suggest that GDM significantly influences the development of T2DM and indicate a potential role for the MPV in this context. Several possible explanations for the positive association between MPV and diabetes mellitus are as follows. Women with GDM exhibit deterioration of β-cell function before they develop T2DM, but their glucose tolerance may remain within the normal range [3]. The apoptosis of pancreatic β-cells leads to progressive insulin deficiency. The ability of insulin to antagonize the effects of platelet agonists is mediated by activation of an inhibitory G protein by insulin receptor substrate (IRS)-1. Thus, insulin resistance reflects impaired insulin signaling and enhances platelet reactivity [29, 30]. Moreover, hyperglycemia can increase platelet reactivity via the osmotic effect of hyperglycemia and induce nonenzymatic glycation of surface proteins Ib and IIb/IIIa, which further decreases membrane fluidity [31, 32]. Diabetes is associated with inflammation and oxidative stress, which may result in increased platelet activation [33]. On the one hand, superoxide may increase platelet reactivity by enhancing intraplatelet release of calcium after activation, impairing endothelial function to reduce the production of NO [34–36]. On the other hand, inflammation can increase platelet reactivity by increasing the expression of proteins that activate platelets [37]. Women with a history of GDM are in a state of hyperglycemia, oxidative stress, and proinflammatory conditions at an earlier stage, and continued metabolic disturbances after pregnancy can lead to the development of T2DM. This imbalance may alter platelet function in the early stages of diabetes. In our study, the MPV interaction in T2DM patients with a history of GDM and HbA1c levels ≥ 7% was significantly greater than that in patients with HbA1c levels < 7%. Other researchers have also demonstrated a relationship between poor glycemic control and increased platelet activity in T2DM patients and have suggested that improved glycemic control reduces platelet activation [16, 38, 39].

The current study has several advantages. This is the first study to explore the relationship between the MPV and T2DM after GDM on the basis of the large sample size of the NHANES database to ensure authenticity and objectivity. Furthermore, we conducted multiple logistic regression analysis and subgroup analyses, which made the results of this study more accurate and reliable. However, there were also several limitations. First, the cross-sectional nature of the study did not allow us to ascertain temporality or causation. Second, we omitted the time of progression to T2DM from GDM because of the absence of data. While NHANES data are considered valuable for evaluating the prevalence of GDM in the general population [40–42], the identification of GDM women by self-reported GDM history and the possible impact of the GDM diagnostic criteria during the study period might have introduced some selection bias in this study. Third, the NHANES provides only a single measurement of MPV, which may not fully capture fluctuations in values. Finally, other potential confounding factors may not have been accounted for during the adjustment process.

Therefore, extensive prospective cohort studies are needed to collect evidence and determine potential mechanisms of action.

Conclusion

The measurement of MPV is both readily accessible and cost-effective within clinical practice. Our study revealed that MPV was positively associated with the risk of T2DM among women with a history of GDM in the American population. This finding implies that MPV may serve as a predictive marker for the progression from GDM to T2DM. However, it is crucial to investigate additional factors that may influence MPV and to monitor its temporal variations.

Abbreviations

T2DM	Type 2 diabetes mellitus
GDM	Gestational diabetes mellitus
MPV	Mean platelet volume
NHANES	National Health and Nutrition Examination Survey
ADA	American Diabetes Association
BMI	Body mass index
PIR	Poverty-income ratio
HbA1c	Glycohemoglobin, Direct HDL total cholesterol, Direct high-density lipoprotein cholesterol
OR	Odds ratio
CI	Confidence interval

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Authors' contributions

YW, RL and CW contributed to the study conception and design. Data collection and analysis were performed by YW YL and LH. The first draft of the manuscript was written by YW, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials
Publicly available datasets were analyzed in this study. These data can be found at https://www.cdc.gov/nchs/nhanes/index.htm.

Declarations

Ethics approval and consent to participate
This study involved human participants and was approved by the National Center for Health Statistics (NCHS) Research Ethics Review Board (approval ID: protocol #2005–06, protocol #2011–17, and protocol #2018–01; Centers for Disease Control and Prevention, NCHS Research Ethics Review Board approval, available from https://www.cdc.gov/nchs/nhanes/irba98.htm). The participants provided informed consent to participate in the study.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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