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ORIGINAL ARTICLE

Correlation between HOMA-IR and Pregnancy Outcomes of GDM Patients Under Vitamin D Insufficiency or Deficiency

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SUMMARY

Background: **This study aimed to assess the effect of vitamin D insufficiency or deficiency in early pregnancy on the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) in women with gestational diabetes mellitus (GDM) and to determine the correlation between HOMA-IR and pregnancy outcomes.**
Methods: **General clinical data, HOMA-IR, β-Cell function index (HOMA-β), and pregnancy outcomes were retrospectively analyzed in 248 GDM patients with vitamin D insufficiency and 81 GDM patients with vitamin D deficiency from September 2019 through April 20, 2023. The correlation between vitamin D and HOMA-IR was analyzed using multiple linear regression.**
Results: **Vitamin D-deficient GDM patients had reduced insulin sensitivity (i.e. increased HOMA-IR). Using a median HOMA-IR of 2.78 as the threshold, the incidence of preterm birth events in the cohort above the threshold was 11.90% (20/168), which was statistically different from that of the cohort below the threshold ($p = 0.013$). Women with GDM who had a vitamin D deficiency and had a HOMA-IR greater than 2.78 had higher rates of preterm labor (23.40%, 11/47) and transport to the neonatal intensive care unit (NICU) (21.74%, 10/46) than patients with vitamin D insufficiency (both $p < 0.05$). Multiple linear regression analysis showed a negative correlation between 25(OH)D and HOMA-IR (β, 95% CI: -0.14 (-0.18 - -0.10), $p < 0.001$), and the adjusted model was significant (β, 95% CI: 3.82 (1.61 - 6.04), $p < 0.001$).**
Conclusions: **Vitamin D deficiency is associated with reduced insulin sensitivity in women with GDM. GDM women with higher HOMA-IR and vitamin D deficiency are at an increased risk of adverse pregnancy outcomes.**
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KEYWORDS

25(OH)D, insulin sensitivity, insulin resistance, HOMA-IR, gestational diabetes mellitus, pregnancy outcome

INTRODUCTION

Vitamin D (D2, D3) is a steroid derivative that exists in both D2 and D3 forms and is the only vitamin that can be synthesized in the body [1]. Vitamin D deficiency has now been found to be associated with a variety of diseases, such as tumorigenesis [2], immune system impairment [3], and increased cardiovascular disease [4]. In addition, vitamin D may promote female reproduc-

tive health [5]. Pregnant women have a 4- to 5-fold higher requirement for vitamin D due to changes in hormone levels and metabolic status, as well as fetal bone growth and additional calcium requirements [6]. Vitamin D deficiency in pregnant women is also a worldwide public health problem [7]. In clinical practice, human vitamin D levels are usually measured by measuring serum concentrations of 25(OH)D in the body.

Vitamin D receptors are expressed in many other tissues in addition to bone and small intestine, including tissues involved in the regulation of glucose metabolism such as pancreatic β-cells [8]. In addition, vitamin D affects insulin synthesis, secretion, and action in rodent models, which has stimulated interest in the study of vitamin D and diabetes [9]. The active form of vitamin D, 1,25-dihydroxyvitamin D (1,25(OH)2D3), effectively protects and enhances pancreatic β-cell function [10]. Vitamin D deficiency has been gradually recognized as one of the potential influencing factors of gestational diabetes mellitus (GDM) [11].

GDM is a disease caused by disorders of glucose metabolism during pregnancy, which can increase complications, including premature rupture of membranes, miscarriage, metabolic syndrome, and type 2 diabetes mellitus [12]. GDM leads to adverse neonatal outcomes such as macrosomia, congenital malformations, neonatal asphyxia, respiratory distress syndrome, neonatal hypoglycemia, and an increased risk of diabetes in adulthood [13]. Inadequate vitamin D intake increases the risk of developing GDM [14], and the exact cause of this risk is not fully understood. Currently, vitamin D deficiency is involved in the pathogenesis of GDM by the following possible mechanisms: vitamin D binds to the pancreatic β-cell vitamin D receptor through its active form, 1,25(OH)2D, which directly or indirectly regulates pancreatic β-cell secretion and function [15]; and vitamin D increases insulin sensitivity by stimulating the expression of insulin receptor and increasing insulin's response to glucose transport [16]; vitamin D inhibits oxidative stress damage to pancreatic β-cells induced by inflammatory factors [17]. Adequate vitamin D promotes insulin secretion and reduces insulin resistance (IR) [18]. Thus, vitamin D deficiency or insufficiency is associated with insulin sensitivity and β-cell function.

Clinically, the pathogenesis of GMD is mainly IR, followed by the presence of defective pancreatic β-cell function, as well as low-grade inflammation and immune dysfunction [19]. The HOMA homeostasis model is calculated using only fasting blood glucose (FBG) and fasting insulin [20]. Homeostasis Model Assessment of IR (HOMA-IR) is an index for evaluating IR, and HOMA-β evaluates the secretory function of pancreatic β-cells [21]. The threshold value of HOMA-IR varies in different regions and is influenced by race and testing methods. It is now generally accepted that a HOMA-IR of 2.5 or more defines IR. IR is associated with an increased risk of adverse pregnancy (premature birth) in women with GDM [22]. Current studies in populations with vitamin D deficiency associated with IR in pregnancy have less data and inconsistent results. In addition, there is also heterogeneity of IR in GMD women, and not all women with GDM have IR.

Based on the fact that vitamin D insufficiency or deficiency leads to reduced insulin sensitivity and impaired β-cell function, it is associated with the pathogenesis of GDM. There is a need to study IR and pregnancy outcomes in GDM women with vitamin D insufficiency or deficiency. Analysis of the correlation between the degree of IR and pregnancy outcomes in this study cohort could help identify women at higher risk for adverse pregnancy outcomes and enable clinically individualized treatment and monitoring strategies.

MATERIALS AND METHODS

Patients

This study was a multicenter retrospective observational study. From September 2019 through April 20, 2023, a total of 1,313 pregnant women were diagnosed with GDM in several hospitals, including Hainan Provincial People's Hospital, Haikou Hospital of The Maternity and Child Health, The Third People's Hospital of Haikou City, Hainan Modern Women and Children's Hospital, and Dongfang People's Hospital. This study was approved by the Ethics Committee of Hainan General Hospital. Patients who had blood 25(OH)D tested at 11 - 14 weeks were included, and these patients had not received vitamin D supplementation before the test. The study excluded women with thyroid disease, parathyroid disease, adrenal disease, liver failure, metabolic bone disease, and medications affecting vitamin D metabolism. Finally, 248 patients with vitamin D insufficiency as well as 81 patients with vitamin D deficiency were included.

Data on maternal characteristics included age, mode of gestation, number of delivery, education, weight and height before delivery, gestational age (weeks), gestational weight gain (GWG, kg), family history of diabetes, history of previous GDM, mode of delivery, and gender and weight of the newborn.

Pregnancy outcomes

Data on pregnancy and neonatal outcomes were obtained from medical records. Pregnancy outcomes consisted of maternal outcomes and neonatal outcomes. Maternal outcomes included: preterm labor (gestational age less than 37 weeks), induced labor (labor induced after 25 weeks due to stillbirth), preterm rupture of membranes, polyhydramnios/oligohydramnios, intrahepatic cholestasis, and postpartum hemorrhage. Neonatal outcomes included: macrosomia (fetal birth weight of 4,000 g, independent of gestational age) small for gestational age (< 10th percentile for gestational age), Apgar scores (1-minute and 5-minute), and referral to the neonatal intensive care unit (NICU) for various reasons.

Oral glucose tolerance test (OGTT)
Subjects were fasted for 10 - 16 hours prior to the test, and blood was drawn into a sterile tube by venipuncture in the morning. Anhydrous glucose (75 g) was dissolved in 300 mL of water and was consumed by the subjects within 2 - 3 minutes. Timing started from the first sip of glucose water, and blood was drawn for laboratory tests at 60 minutes and 120 minutes. The samples were centrifuged, and the upper layer of plasma was taken and then tested using a fully automated biochemistry instrument.

Vitamin D measurement
Blood was collected from patients at 11 - 14 weeks of gestation. Measurements were performed using liquid chromatography and mass spectrometry. The sum of serum 25(OH)D2 and 25(OH)D3 was used to reflect total serum 25(OH)D concentration. The inter- and intra-batch coefficients of variation for total serum 25(OH)D levels were 6.80% and 2.20%, respectively. The lower and upper limits of detection were 4.0 and 200 ng/mL, respectively. Vitamin D status was categorized as serum 25(OH)D levels < 20 - 30 ng/mL (50 - 75 nmol/L) for vitamin D insufficiency and < 20 ng/mL (50 nmol/L) for vitamin deficiency [23].

Evaluation of insulin sensitivity and β-cell function
Diagnosed with GDM, insulin sensitivity and β-cell function were further evaluated as recommended. Fasting insulin and FBG levels were measured using a fully-automated biochemistry.
HOMA-IR [24] was used to assess insulin sensitivity. HOMA-IR = (FBG (mmol/L) × fasting insulin (μIU/L)/ 22.5. If HOMA-IR is greater than 2.69, IR may be present.
The β-cell function index (HOMA-β) [24] was used to assess the ability of pancreatic β-cells to secrete insulin. HOMA-β = 20 × [fasting insulin (μIU/mL) ÷ (FBG (mmol/L) - 3.5)]. The higher the HOMA-β, the better the pancreatic β-cell function. If HOMA-β is below 50%, it may indicate poor pancreatic β-cell function or IR.

Statistical analysis
Statistical analyses were performed using SPSS 20.0 software. The Shapiro-Wilk test was used to determine the normality of the data. For continuous variable data in normal distribution shown as mean ± standard deviation, Student's *t*-test (two groups) was used for between-group comparisons; for continuous variable data in skewed distribution shown as median [1st quartile, 3rd quartile], Mann-Whitney U test (two groups) was used for comparisons between groups. Count data were expressed as frequencies and ratios and compared by chi-squared or Fisher's exact tests. Because vitamin D and HOMA-IR levels were skewed, they were transformed into natural logarithms for the analyses. With HOMA-IR as the dependent variable and vitamin D as the independent variable, multiple linear regression analyses were conducted with transformed natural logarithms. In Model 1, no variables were adjusted. In Model 2, demographically presented differential characteristics were used as adjustment variables. Images were plotted using GraphPad Prism 8. $p < 0.05$ was considered statistically significant.

RESULTS

General clinical data of patients
This study focused on GMD patients with vitamin D insufficiency or deficiency. A total of 1,313 GMD patients, out of which 642 were excluded due to no vitamin D data or normal vitamin D levels (n = 412), no complete demographic data (n = 150), missing HOMA data (n = 52), having as well as taking medications that may affect vitamin D metabolism (n = 16), and abortion before 20 weeks of gestation (n = 12). Ultimately, 248 patients with vitamin D insufficiency and 81 patients with vitamin D deficiency were included. Table 1 shows the characteristics of the study population. There were no significant differences between the groups regarding age, mode of gestation, pre-pregnancy BMI, gestational age, GWG, number of delivery, educational level, previous history of GDM, final mode of delivery, newborn's gender and weight, OGTT results, and HbAc1 level. Only a higher percentage of family history of diabetes mellitus was observed in vitamin D-deficient patients, 32.10% (26/81), which was significantly higher than that of vitamin D-insufficient patients (4.84%, 12/248).

Assessment of insulin sensitivity and β-cell function
At 11 - 14 weeks of gestation, the median vitamin D levels in vitamin D-insufficient and vitamin D-deficient women with GDM were 25.75 [23.3, 27.35] ng/mL and 17.4 [14.9, 18.7] ng/mL, respectively. Insulin sensitivity and β-cell function were next assessed in the two groups of patients as shown in Figure 1. The HOMA-IR levels were 2.72 [1.67, 3.86] and 3.10 [1.85, 4.88] in the two groups of patients, respectively, and there was a statistically significant difference in the HOMA-IR levels between the two groups ($p < 0.05$) (Figure 1A). No difference in HOMA-β was observed ($p > 0.05$) (Figure 1B).

Pregnancy outcomes
In GDM women with vitamin D insufficiency and vitamin deficiency, the median HOMA-IR was 2.78, and based on this median value as a critical value for grouping, the pregnancy outcomes of GDM women were observed, as shown in Table 2. The results showed that among these women, preterm labor events occurred in 27 cases, out of which 20 patients (74.07%, 20/27) occurred in the cohort above the cutoff value and were statistically different from the cohort below the cutoff value ($p = 0.013$). In these cohorts, 2 women were induced for intrauterine fetal death. In addition, a total of 33 deliveries were taken to the NICU immediately after de-

Table 1. General clinical characteristics of patients with vitamin D insufficiency and vitamin D deficiency.

Variables	Insufficiency (n = 248)	Deficiency (n = 81)	p-value
Age, (years)	32 [29, 35]	33 [29, 36]	0.303
Mode of pregnancy			
Spontaneous pregnancy	223 (89.92)	72 (88.89)	0.791
Assisted pregnancy	25 (10.08)	9 (11.11)	
Pre-pregnancy BMI (kg/m^2)	23.0 [20.7, 24.9]	22.8 [20.6, 26.1]	0.439
Gestational age (weeks)	38.26 ± 2.68	38.10 ± 2.47	0.516
Gestational weight gain (GWG), (kg)	11.5 [8.0, 14.0]	10.0 [7.8 - 14.0]	0.133
Number of delivery	1 [1, 2]	1 [1, 2]	0.952
Education, n (%)			0.868
0 - 5 years	74 (29.84)	26 (32.10)	
6 - 8 years	29 (11.69)	8 (9.88)	
≥ 9 years	145 (58.47)	47 (58.02)	
Family history of DM	12 (4.84)	26 (32.10)	0
History of gestational diabetes mellitus	31 (12.50)	8 (9.88)	0.523
Mode of delivery	n = 247	n = 80	
Spontaneous labor	149 (60.32)	41 (51.25)	0.153
Caesarean section	98 (39.68)	39 (48.75)	
Gender of newborns	n = 247	n = 80	
Male	148 (59.92)	38 (47.5)	0.051
Female	99 (40.08)	42 (52.5)	
Fetal weight	3,110 [2,852, 3,320]	3,060 [2,690, 3,390]	0.314
OGTT (mmol/L)			
FBG	4.90 [4.50, 5.40]	5.00 [4.80, 5.50]	0.117
60 minutes	10.60 [9.80, 11.90]	11.0 [10.10, 12.10]	0.162
120 minutes	9.30 [8.5, 10.4]	9.65 [8.52, 10.65]	0.466
HbAc1%	5.3 [5.1 - 5.7]	5.4 [5.1 - 5.7]	0.318

Data are expressed as n (%). FBG - fasting blood glucose. Continuous values were compared using Student's *t*-test or Mann-Whitney U test. Categorical values were analyzed using chi-squared or Fisher's exact test. p less than 0.05 was considered statistically significant.

livery, out of which 21 (63.64%, 21/33) occurred in the higher-than-threshold cohort; however, there was no significant difference from the lower-threshold cohort (p = 0.132). No other pregnancy outcomes were significantly different between the two groups. We hypothesize that in women with GDM, a HOMA-IR value exceeding the critical threshold is associated with an elevated risk of adverse pregnancy outcomes. Consequently, we categorized postpartum women with HOMA-IR values above this threshold into two distinct groups: those with vitamin D insufficiency (n = 121) and those with vitamin D deficiency (n = 47). Table 3 presents a comparative analysis of the pregnancy outcomes for these two cohorts. In the cohort with HOMA-IR above the critical value, 11 of 20 preterm deliveries occurred in the vitamin D-deficient cohort, accounting for 23.4% of the cohort, which was significantly higher than in the vitamin D-insufficient cohort (9, 7.44%, 9/121) (p = 0.004). Furthermore, 21 were sent to the NICU, and 10 occurred in the vitamin D-deficient cohort, which accounted for 21.74% and was significantly higher than in the vitamin D deficient cohort (11 cases, 9.09%, 11/121) (p = 0.029). No other pregnancy outcomes were significantly different between the two groups. These results suggest that in these women with GDM, a HOMA-IR above a critical value and vitamin D deficiency are associated factors influencing pregnancy outcomes in terms of preterm labor and admission to NICU immediately after birth.

Relationship between vitamin D levels and HOMA-IR

Multiple linear regression analysis determined the relationship between vitamin D and HOMA-IR levels in

Table 2. Comparison of pregnancy outcomes in patients with GDM based on HOMA-IR threshold.

Events	HOMA-IR ≥ 2.78 (n = 168)	HOMA-IR < 2.78 (n = 161)	p-value
Pregnant women			
Premature delivery	20 (11.90)	7 (4.35)	0.013
Induced labor	1 (0.60)	1 (0.62)	1
Preterm rupture of membranes	25 (14.88)	24 (14.91)	0.995
Polyhydramnios	7 (4.17)	3 (1.86)	0.337
Oligohydramnios	2 (1.19)	0 (0.00)	0.337
Intrahepatic cholestasis	2 (1.19)	2 (1.24)	1
Postpartum hemorrhage	2 (1.19)	0 (0.00)	0.499
Newborns	(n = 167)	(n = 160)	
Macrosomia	3 (1.80)	3 (1.88)	1
SGA	2 (1.20)	3 (1.88)	1
Apgar scores (1 min)	10 [10, 10]	10 [10, 10]	0.685
Apgar scores (5 min)	10 [10, 10]	10 [10, 10]	0.702
Admission to NICU	21 (12.57)	12 (7.50)	0.132

Data are expressed as n (%). Insufficiency - vitamin D insufficiency, deficiency - Vitamin D deficiency, SGA - small for gestational age. Chi-squared or Fisher's exact test was used, and p less than 0.05 was considered statistically significant.

Table 3. Pregnancy outcomes in GDM patients with vitamin D deficiency or insufficiency in cohorts with higher HOMA-IR thresholds.

Events	Insufficiency (n = 121)	Deficiency (n = 47)	p-value
Pregnant women			
Premature delivery	9 (7.44)	11 (23.4)	0.004
Induced labor	0 (0.00)	1 (2.13)	0.28
Preterm rupture of membranes	14 (11.57)	11 (23.40)	0.053
Polyhydramnios	1 (0.83)	1 (2.13)	0.482
Oligohydramnios	4 (3.31)	3 (6.38)	0.401
Intrahepatic cholestasis	1 (0.83)	1 (2.13)	0.482
Postpartum hemorrhage	1 (0.83)	1 (2.13)	0.475
Newborns	(n = 121)	(n = 46)	
Macrosomia	2 (1.65)	1 (2.17)	1
SGA	1 (0.83)	1 (2.17)	0.479
Apgar scores (1 minute)	10 [10, 10]	10 [10, 10]	0.531
Apgar scores (5 minutes)	10 [10, 10]	10 [10, 10]	0.563
Admission to NICU	11 (9.09)	10 (21.74)	0.029

Data are expressed as n (%). SGA - small for gestational age. Chi-squared or Fisher's exact test was used, and p less than 0.05 was considered statistically significant.

women with GDM, as shown in Table 4. Model 1 was a univariate analysis, showing that vitamin D level, age, and pre-pregnancy BMI were the correlates affecting HOMA-IR levels. Further, we adjusted age, GWG, BMI, and family history of diabetes to obtain Model 2, which was significant after adjustment (β, 95% CI: 3.82

Table 4. Multiple linear regression analysis revealing the relationship between vitamin D levels and HOMA-IR.

Variables	β (95% CI)	S.E	p-value	β (95% CI)	S.E	p-value
Intercept				3.82 (1.61 - 6.04)	1.13	< 0.001
Vitamin D	-0.16 (-0.20 - -0.11)	0.02	< 0.001	-0.14 (-0.18 - -0.10)	0.02	< 0.001
Age	-0.05 (-0.10 - -0.01)	0.03	0.04	-0.04 (-0.09 - 0.00)	0.02	0.068
GWG	0.03 (-0.01 - 0.06)	0.02	0.099	0.03 (0.01 - 0.07)	0.02	0.028
BMI	0.18 (0.13 - 0.23)	0.03	< 0.001	0.16 (0.11 - 0.20)	0.02	< 0.001
History						
0	0.00 (reference)			0.00 (reference)		
1	0.50 (-0.03 - 1.04)	0.27	0.068	0.19 (-0.29 - 0.68)	0.25	0.436

GWG - gestational weight gain, CI - confidence interval. Model 1 is a one-factor model; Model 2 is adjusted for age, GWG, pre-pregnancy BMI, and history of diabetes.

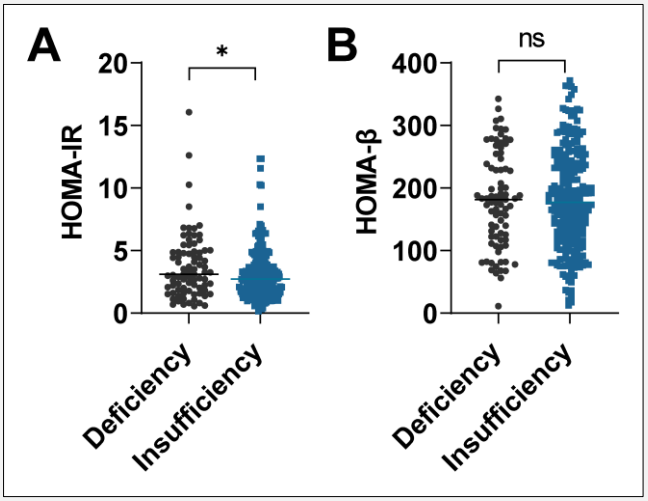

Figure 1. Comparison of insulin sensitivity and β-cell function in vitamin D-insufficient and vitamin D-deficient women with GDM.

A) HOMA-IR; B) HOMA-β. Comparisons between groups were made using the Mann-Whitney U test, * p < 0.05.

(1.61 - 6.04), p < 0.001), indicating that vitamin D was significantly associated with HOMA-IR after adjustment. In addition, in Model 2, vitamin D was negatively associated with HOMA-IR (β, 95% CI: -0.14 (-0.18 - -0.10), p < 0.001), and GWG and BMI were positively associated with HOMA-IR.

DISCUSSION

GDM has long been recognized as one of the major complications of pregnancy. Globally, about 1 billion people are currently suffering from vitamin D deficiency or insufficiency, and pregnant women and women of childbearing age are likely to be vitamin D deficient. Vitamin D, through its active form, directly or indirectly regulates the secretion and function of pancreatic beta cells, stimulates insulin receptors, and increases insulin sensitivity, which is related to the pathogenesis of

GDM. We found increased IR in vitamin D-deficient women with GDM. In the cohort with HOMA-IR higher than 2.78, vitamin D-deficient women with GDM had a higher rate of preterm labor and transport to the NICU than vitamin D-deficient patients in terms of pregnancy outcomes. In addition, in the multiple linear regression analysis with HOMA-IR as the dependent variable, vitamin D as the independent variable, and age, GWG, BMI, and family history of diabetes as the adjusting variables, the adjusted model was significant and confirmed the negative correlation between vitamin D and HOMA-IR.

Interest in vitamin D has increased over the past few decades as knowledge has improved about its wide-ranging effects in a number of physiological processes. Increasing concern has been raised about vitamin D deficiency worldwide because of its adverse effects on human health [25]. Consequently, vitamin D status is crucial to the health of pregnant women and the success of their pregnancies. Vitamin D deficiency during pregnancy is highly prevalent in different countries and races [26,27]. It appears that vitamin D supplementation does not consistently enhance insulin secretion and sensitivity in different populations, owing to differences in the duration of supplementation and the form of vitamin D supplementation [28]. Other studies with different perspectives have reported that the difference in the rate of vitamin D deficiency in early pregnancy is not statistically significant in GDM compared to normal pregnant women [29], and even a study found no significant association between vitamin D deficiency and IR in women with GDM [30]. In this study, univariate or multivariate linear analyses showed that vitamin D was a negatively correlated factor affecting HOMA-IR. It suggests that in this part of the GDM population with vitamin D insufficiency or deficiency, a reduction in vitamin D is associated with a reduction in insulin sensitivity. However, we did not observe a difference in HOMA-β in vitamin-deficient and vitamin D-deficient women with GDM. In addition, vitamin D deficiency inhibits the restoration of physiologic insulin secretion through proinflammatory properties and decreases calcium absorption from the duodenum and kidney to affect glucose, leading to increased blood glucose. However, we did not find a difference in glucose levels at 60 minutes and 120 minutes in the OGTT among vitamin D-deficient versus insufficient women with GDM. This suggests that the greater influence of vitamin D on insulin sensitivity is explained by its effect on insulin receptor expression and insulin response to glucose transport [16].

Regarding insulin sensitivity in women with GDM, we looked at the correlation between insulin sensitivity and pregnancy outcomes using the median HOMA-IR of this cohort as a threshold. Insulin sensitivity is significantly associated with the risk of adverse pregnancy outcomes [31]. In the present study, 24% of patients required insulin, with no difference in vitamin D-deficient and insufficient GDM women. In a previous study it was shown that insulin did not prevent adverse pregnancy outcomes and even women taking insulin had more cesarean section rates [32]. No variation was observed in the delivery method among women with GDM who were deficient or insufficient in vitamin D in this study. The HOMA-IR critical value of 2.5 [33], 2.69 [34], and even 2.0 [35] have been used as critical values for IR. In this study, we used the median value of HOMA-IR in the cohort (2.78) as the critical value to group the cohort into groups above and below the median value of HOMA-IR and to observe pregnancy outcomes. We only observed a difference in preterm labor rates between the two groups, with 11.90% in women with GDM with HOMA-IR $\geq$ 2.78 and 4.35% with HOMA-IR < 2.78. Next, we focused on the cohort with HOMA-IR $\geq$ 2.78 to further compare the pregnancy outcomes of vitamin D-insufficient versus vitamin D-deficient GDM women in the cohort. Vitamin D deficiency increased the rate of transport to NICU after delivery (21.71%). Finally, to observe the effect of vitamin D on HOMA-IR, we confirmed a negative correlation between vitamin D and HOMA-IR.

This study also has some limitations; it is a retrospective observational study, which may be subject to bias and confounding factors that may affect the accuracy and reliability of the findings. Our findings can only show that vitamin D deficiency is associated with increased HOMA-IR levels in GDM, but not directly prove that vitamin D is associated with the development of GDM. We only studied women with vitamin D deficiency and insufficiency in GDM, and the phenomenon that patients with vitamin D deficiency with higher HOMA-IR levels have higher rates of preterm labor and adverse neonatal outcomes only applies to cohorts with similar study populations. Finally, in future studies, it is necessary to design a prospective study to investigate the incidence of adverse pregnancies in GDM due to vitamin D deficiency, to search for a HOMA-IR threshold for the diagnosis of adverse pregnancy outcomes in a vitamin D-deficient cohort, as well as to analyze in detail the impact of these factors on various adverse pregnancy outcomes.

CONCLUSION

Vitamin D deficiency is associated with reduced insulin sensitivity in women with GDM. Adverse pregnancy outcome events are higher in GDM women with HOMA-IR above a median value of 2.78 and vitamin D deficiency.

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Data Availability Statement:
Data is available from the corresponding author on request.

Ethical Approval Statement:
All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. All subjects were approved by Hainan General Hospital (No. 2021HK 226).

Declaration of Interest:
The authors have no conflicts of interest to declare.

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