Research Square

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Nocturnal Oxygen Saturation in Late Pregnancy is Associated with Gestational Diabetes Mellitus in Women at High Risk for OSA

Guangjiao Wang
Peking University People's Hospital
Ran Hu
Peking University People's Hospital
Linyan Zhang[1]
Peking University People's Hospital
Guoli Liu
guoleeliu@163.com

Peking University People's Hospital

Research Article

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Abstract

Objective

This study aimed to investigate the association between mean nocturnal oxygen saturation ($MSpO_2$) in pregnant women at high risk of obstructive sleep apnea (OSA) and pregnancy complications. We focused on the $MSpO_2$during sleep monitoring in the first, second, and third trimesters, which is easy to measure and may have a warning role for pregnancy complications. Given that gestational diabetes mellitus (GDM) is typically diagnosed at 24–28 weeks, we interpreted the third-trimester findings as a concurrent association rather than a prospective prediction.

Methods

A retrospective analysis was conducted on 569 high-risk OSA pregnant women who underwent portable sleep monitoring. Participants were stratified by trimester (first, n = 90; second, n = 179; third, n = 300) and further categorized by $MSpO_2$ level (< 95% vs. ≥95%). Maternal and neonatal outcomes were compared, mainly including hypertensive disorders of pregnancy (HDP), GDM, postpartum hemorrhage, delivery gestational age, umbilical artery pH, placental weight, PLGF levels, and the rate of Apgar 1min ≤ 7. Logistic regression and receiver operating characteristic (ROC) analyses were performed to evaluate the discriminative ability of $MSpO_2$ for GDM. Multivariate logistic regression models were used to assess for effect modification by including an interaction term for obesity status and age.

Results

Lower $MSpO_2$($MSpO_2$<95%) in the third trimester was significantly associated with a higher incidence of GDM (P = 0.025). After adjusting for age, pre-pregnancy BMI, and PCOS history, $MSpO_2$ remained an independent protective factor against GDM (adjusted OR = 0.680, 95% CI: 0.533–0.869, P = 0.002). The model combining $MSpO_2$ with clinical risk factors yielded the highest AUC of 0.731, indicating its utility for concurrent risk stratification. No significant interaction effects were found for age or obesity. In the second trimester, low $MSpO_2$was associated with lower umbilical artery pH (P = 0.039) and higher placenta-to-newborn weight ratio (P = 0.037). However, no significant association was found between OSA and HDP. The association between oxygen saturation and GDM was consistent across subgroups defined by age and obesity status, with no significant interaction effects observed.

Conclusion

Lower nocturnal oxygen saturation in the third trimester is independently associated with an increased risk of GDM in high-risk OSA pregnancies. While temporality precludes prediction, $MSpO_2$ may serve as a useful biomarker for risk stratification, suggesting that the third trimester may represent a critical window during which oxygen metabolism abnormalities impact glucose metabolism. Prospective studies with pre-diagnostic SpO_2 monitoring are warranted.

1. Introduction

Hypoxic environments significantly increase the risk of pregnancy complications and adverse outcomes. Obstructive sleep apnea (OSA) is characterized by repetitive apneas and hypopneas during sleep, leading to oxygen desaturation, frequent arousals, sympathetic activation, and endothelial dysfunction. Studies have linked OSA to gestational hypertension, preeclampsia, gestational diabetes, and impaired fetal growth. Our previous research suggests that OSA is associated with hypertensive disorders of pregnancy (HDP), especially chronic hypertension. Pregnant women with both OSA and chronic hypertension may have a higher risk of developing preeclampsia. However, no significant association was found between OSA and gestational diabetes mellitus (GDM). OSA with oxidative stress is linked to pregnancy-related hypertension and diabetes. Traditionally, the frequency of respiratory events in sleep-disordered breathing (SDB) is assessed using metrics such as the apnea hypopnea index (AHI) or oxygen desaturation index (ODI). Various factors—including high-altitude environments, respiratory diseases, anemia, cardiovascular dysfunction, and subclinical conditions—can reduce oxygen saturation during pregnancy. Abnormal oxygen saturation is closely associated with adverse maternal outcomes and may influence pregnancy complications by affecting maternal hemodynamics and metabolic status. In this study, we aimed to evaluate the association of SpO_2in pregnant women at high risk of OSA who underwent sleep monitoring with pregnancy complications. We focused on average oxygen saturation during sleep in the first, second, and third trimesters, as it is easy to measure and may serve as a warning indicator. Importantly, while GDM is typically diagnosed at 24–28 weeks, our third-trimester SpO_2measurements were obtained after this diagnostic window. Therefore, we interpret these findings as a cross-sectional association and a potential risk stratification tool, rather than a prospective predictor. This distinction is critical for correctly understanding the clinical utility of late-pregnancy oxygen saturation.

2. Materials and Methods

Pregnant women at high risk of OSA who registered at the Department of Obstetrics of Peking University People's Hospital from January 2021 to July 2024 were selected as the observation group. Their clinical data were collected through medical record review for retrospective analysis. Inclusion criteria: High-risk OSA individuals who underwent regular prenatal checkups and delivered at Peking University People's Hospital, with complete clinical data, and underwent sleep monitoring during pregnancy. High-risk OSAS individuals were defined as those meeting at least one of the following criteria: 1. Snoring and/or apnea; 2. Chronic hypertension; 3. Pregestational diabetes mellitus (PGDM); 4. Obesity [pre-pregnancy body mass index (BMI) ≥ 28.0 kg/m^2]. Exclusion criteria: Multiple pregnancies or fetal malformations, severe mental illness, severe cardiopulmonary or hepatorenal diseases, previously diagnosed OSAS, regular CPAP treatment before or during pregnancy (defined as using a ventilator for at least 21 days per 30 days, with no less than 4 hours per night),

or other sleep disorders. A total of 569 pregnant women who met the inclusion and exclusion criteria were enrolled in the study. Based on the gestational period and sleep monitoring time, they were divided into the first-trimester group (90 cases), second-trimester group (179 cases), and third-trimester group (300 cases). Each group was further stratified according to the mean oxygen saturation (SpO_2) into two subgroups: SpO_2 ≥95% and SpO_2 <95%. This study was approved by the Ethics Committee of Peking University People's Hospital (Approval No.2023PHB210-001) and was granted an exemption from informed consent. Sleep Monitoring Method: A Type III portable sleep monitoring device (Nox-T3, manufactured by Nox Medical, Iceland) was used for home sleep monitoring. The mean SpO_2 was derived from the monitoring results.

Observed Indicators: General characteristics: Age, pre-pregnancy BMI, method of conception, neck circumference, history of PCOS, history of hypothyroidism, mean SpO_2, the lowest SpO_2, AHI, ODI. Maternal complications and outcomes: pregestational diabetes mellitus (PGDM), gestational diabetes mellitus (GDM), hypertensive disorders of pregnancy (HDP), and postpartum hemorrhage (PPH), placental growth factor (PLGF) of 15-20th gestational week. Neonatal outcomes: Gestational age at delivery, placental weight, placenta/newborn body weight ratio, and neonatal umbilical artery blood gas analysis (pH and 1-minute Apgar score < 7). Diagnostic Criteria: The diagnostic criteria were established with reference to the following Chinese clinical guidelines, as follows, Guideline for the Diagnosis and Treatment of Hypertensive Disorders in Pregnancy (2020), Guideline for the Management of Gestational Diabetes Mellitus: A Focus on Integrated Maternal and Neonatal Care (2024), Guideline for the Comprehensive Prevention and Management of Postpartum Hemorrhage (2023), Guideline for the Prevention and Management of Preterm Birth (2024).

All statistical analyses were performed using SPSS software (version 29.0). Continuous variables with a normal distribution are presented as mean ± standard deviation (mean ± SD), while those with a skewed distribution are expressed as median and interquartile range (IQR). Comparisons between two groups for normally distributed data with homogeneous variance were conducted using the independent samples t-test. For multiple groups, one-way analysis of variance (ANOVA) was applied. When data did not meet assumptions of normality or homogeneity of variance, the Mann-Whitney U test (for two groups) or the Kruskal-Wallis H test (for multiple groups) was used. Categorical variables were compared using the chi-square test. A two-sided p-value < 0.05 was considered statistically significant. Binary logistic regression was employed for multivariate analysis to assess the combined discriminative effect of multiple parameters, where P denotes the probability of a positive diagnosis. The discriminative performance was further evaluated using receiver operating characteristic (ROC) curve analysis. Given the timing of GDM diagnosis (24–28 weeks) and third-trimester SpO_2 measurement, we explicitly refer to the model's performance as concurrent risk stratification rather than prospective prediction.

3. Results

3.1 Comparison of general conditions of pregnant women (Table 1)

Table 1
Comparison of Baseline Characteristics and Sleep Parameters Among High-Risk Pregnant Women with OSA, Stratified by Trimester

Age (year)	**First trimester (n = 90)**	**Second trimester (n = 179)**	**Third trimester (n = 300)**	**Value**	***P***
	34.43(33.55,35.32)	**33.80(33.11,34.49)**	**33.38(32.90,33.86)**	**2.116**	**0.121**
Gestational age at delivery (week)	38.04(37.60,38.49)	37.17(36.58,37.76)	37.73(37.34,38.11)	2.695	0.07
Method of conception	26(34.21%)[a]	41(25.79%)	51(18.48%)[b]	9.238	0.010
Pre-pregancy BMI (kg/m2)	29.15(28.16,30.13)[a]	26.89(26.12,27.66)[b]	26.40(25.77,27.03)[b]	9.205	<0.001
BMI (kg/m2)	30.01(28.97,31.05)[a]	27.97(27.27,28.67)[b]	28.94(28.33,29.54)[b]	5.073	0.007
Neck circumference (cm)	37.21(36.66,37.76)[a]	36.21(35.68,36.74)[b]	35.93(35.61,36.26)[b]	6.046	0.003
History of PCOS	15(17.05%)	18(10.34%)	24(8.30%)	5.557	0.062
History of hypothyroidism	9(10.23%)	27(14.77%)	36(12.37%)	1.555	0.46
MSpO2 (%)	95.17(94.91,95.44)[a]	94.84(94.66,95.02)	94.61(94.46,94.75)[b]	7.515	<0.001
LSpO2 (%)	86.56(85.31,87.80)	87.04(86.21,87.87)	86.68(86.02,87.35)	0.292	0.747
AHI (times per hour)	4.20(2.08,9.53)	4.10(1.50,8.20)	4.60(1.70,8.20)	2.093	0.351
ODI (times per hour)	5.25(2.20,10.95)	4.30(1.50,8.80)	5.9(1.90,9.58)	3.059	0.217

Note:Data are presented as mean (95% confidence interval), median (interquartile range), or number (percentage), as appropriate. BMI: body mass index; PCOS: polycystic ovary syndrome; $MSpO_2$: mean oxygen saturation; $LSpO_2$: lowest oxygen saturation; AHI: apnea-hypopnea index; ODI: oxygen desaturation index.P values were derived from one-way ANOVA (for normally distributed continuous variables), Kruskal-Wallis H test (for non-normally distributed continuous variables: AHI, ODI), or Chi-squared test (for categorical variables: Method of conception, History of PCOS, History of hypothyroidism).Significant pairwise post-hoc comparisons (after adjustment for multiple testing) are indicated by different superscript letters (a, b) within a row. A group without a common superscript letter differs significantly from another group (e.g., for 'Method of conception', the first trimester group (a) differs significantly from the second and third trimester groups (b)).

The age range of 569 high-risk pregnant women with OSA was 20–46 years old. Maternal age showed a decreasing trend across trimesters, with mean ages of 34.43, 33.80, and 33.38 years, respectively; however, this difference was not statistically significant (P = 0.121). Similarly, no significant differences were

observed in gestational age at delivery (P = 0.07), history of hypothyroidism (P = 0.46), lowest SpO_2 ($LSpO_2$, P = 0.747), apnea-hypopnea index (AHI, P = 0.351), or oxygen desaturation index (ODI, P = 0.217).

Significant differences were identified across trimesters for several variables. The method of conception differed significantly (P = 0.010), with the highest rate observed in the first trimester (34.21%) compared with the third trimester (18.48%). Both pre-pregnancy BMI and current BMI exhibited significant differences (P < 0.001 and P = 0.007, respectively), with the first trimester group having the highest mean values (29.15 kg/m² and 30.01 kg/m²). Neck circumference was also significantly larger in the first trimester group (37.21 cm, P = 0.003). Furthermore, mean oxygen saturation ($MSpO_2$) was significantly higher in the first trimester (95.17%) compared to the second (94.84%) and third (94.61%) trimesters (P < 0.001). In summary, while basic demographic and several sleep-related parameters were comparable across gestational trimesters, the first trimester was associated with significantly higher pre-pregnancy BMI, current BMI, neck circumference, and oxygen saturation levels.

3.2 Association of maternal SpO_2 with adverse outcomes by trimester (Table 2)

Table 2
Association of Maternal Mean Oxygen Saturation ($MSpO_2$) with Pregnancy Complications and Outcomes and Neonatal Outcomes, Stratified by Gestational Trimester

	First trimester (n = 90)		**Second trimester (n = 179)**		**Third trimester (n = 300)**	
	MSpO2 (%) ≥ 95	**MSpO2 (%)<95**	**MSpO2 (%) ≥ 95**	**MSpO2 (%)<95**	**MSpO2 (%) ≥ 95**	**MSpO2 (%)<95**
Hypertensive disorders complicating pregnancy(HDP)	Value = 0.769 *P* = 0.381; HDP :Value = 2.956 *P* = 0.228; Preeclampsia and eclampsia:Value = 5.047 *P* = 0.276;		Value = 0.234 *P* = 0.628; HDP :Value = 0.338 *P* = 0.844; Preeclampsia and eclampsia:Value = 5.244 *P* = 0.390;		Value = 0.000 *P* = 0.992; HDP :Value = 0.488 *P* = 0.783; Preeclampsia and eclampsia:Value = 2.227 *P* = 0.817;	
Hyperglycemia in Pregnancy (HIP)	Value = 3.965 *P* = 0.138;		Value = 4.106 *P* = 0.128;		Value = 7.406 *P* = 0.025; GDM:Value = 7.398 *P* = 0.007; PGDM:Value = 0.350 *P* = 0.554;	
Postpartum hemorrhage(PPH)ml	400(320,450)	450(315,570)	400(280,600)	390(365,565)	400(300,500)	400(305,542.5)
	P = 0.325		*P* = 0.833		*P* = 0.391	
Fetal umbilical artery blood PH	7.32(7.28,7.35)	7.31(7.28,7.34)	7.31(7.26,7.37)	7.29(7.22,7.33)	7.31(7.27,7.34)	7.30(7.27,7.35)
	P = 0.368		*P* = 0.039		*P* = 0.673	
Apgar 1min ≤ 7	1(2.32%)	2(6.67%)	2(2.63%)	5(7.14%)	3(2.65%)	7(4.58%)
	P = 0.564		*P* = 0.260		*P* = 0.525	
Gestational age at delivery	38.29(37.57,39.14)	38.71(36.93,39.57)	38.71(37.57,39.14)	38.43(36.72,39.07)	38.57(37.29,39.26)	38.57(37.00,39.29
	P = 0.796		*P* = 0.141		*P* = 0.441	
Placental weight	560(500,660)	540(500,610)	550(500,595)	540(497.5,662.5)	510(480,600)	530(487.5,595)
	P = 0.556		*P* = 0.477		*P* = 0.955	
Placenta/newborn body weight ratio (%)	17.63(15.36,20.35)	17.05(15.67,18.46)	17.58(16.15,18.51)	18.70(16.42,22.37)	17.52(15.51,19.51)	16.54(15.24,18.75
	P = 0.648		*P* = 0.037		*P* = 0.15	
PLGF of 15-20th gestational week	123(87.50,235.00)	106.5(81.50,298.25)	140(86.50,222.50)	134(82.75,241.00)	146(75,290)	157(72.75,344.75
	P = 0.952		*P* = 0.962		*P* = 0.744	

Note: Data are presented as median (interquartile range) for continuous variables and n (%) for categorical variables. $MSpO_2$: mean oxygen saturation; HDP: hypertensive disorders of pregnancy; PIH: pregnancy-induced hypertension; DM: diabetes mellitus; GDM: gestational diabetes mellitus; GDM-A1: diet-controlled GDM; GDM-A2: medication-controlled GDM; PPH: postpartum hemorrhage.P values were derived from the Mann-Whitney U test for continuous variables (e.g., PPH, placental weight) and the Chi-squared or Fisher's exact test for categorical variables (e.g., HDP, GDM), as appropriate for comparisons between $MSpO_2$ ≥95% and < 95% groups within each trimester.The HDP was graded ordinally as: 0 (none), 1 (PIH), 2 (mild preeclampsia), 3 (severe preeclampsia), 4 (eclampsia), 5 (chronic hypertension), 6 (superimposed preeclampsia). The analysis for hyperglycemia classified patients as: 0 (none), 1 (GDM-A1), 2 (GDM-A2), 3 (pre-gestational DM). The significant P-value for GDM in the third trimester is derived from the comparison of all hyperglycemia categories (GDM and DM) versus none or only GDM versus none.

Stratification by both gestational trimester and maternal mean oxygen saturation ($MSpO_2$) level revealed several key associations with adverse outcomes. In the first trimester, no statistically significant differences were observed between the $MSpO_2$ ≥95% and < 95% groups for any of the measured outcomes, including hypertensive disorders of pregnancy (HDP) (P = 0.381), gestational diabetes mellitus (GDM) (P = 0.138), postpartum hemorrhage (P = 0.325), umbilical artery pH (P = 0.368), and the rate of Apgar 1min ≤ 7 (P = 0.564).

A different pattern emerged in the second trimester. While most outcomes were comparable, two significant differences were identified. The umbilical artery pH was significantly lower in the $MSpO_2$ <95% group (7.29) compared to the $MSpO_2$ ≥95% group (7.31) (P = 0.039). Furthermore, the placenta-to-newborn body weight ratio was significantly higher in the low SpO_2 group (18.70%) versus the normal group (17.58%) (P = 0.037).

The most pronounced effect was found in the third trimester regarding glycemic metabolism. The prevalence of GDM was significantly higher in the $MSpO_2$ <95% group compared to the $MSpO_2$ ≥95% group (P = 0.025). This association was further strengthened when comparing only GDM to no diabetes (P = 0.007). However, pre-gestational diabetes mellitus (DM) did not show a significant association with SpO_2 levels (P = 0.554). Other maternal and neonatal outcomes, including delivery gestational age, placental weight, and PLGF levels, showed no significant differences across all trimesters. As GDM is diagnosed before the third trimester, this association is interpreted as a concurrent metabolic correlate rather than a predictive marker.

3.3 Oxygen Saturation as an Independent Correlate and Enhancer of GDM Risk Stratification (Table 3)

Table 3
Univariate and multivariate logistic regression analyses of factors associated with gestational diabetes mellitus (GDM).

Variable	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P value	aOR (95% CI)	P value
Oxygen saturation (per 1-unit decrease)	0.636(0.503–0.805)	<0.001	0.680(0.533–0.869)	0.002
Maternal age (years)	1.050(0.983–1.121)	0.144	1.036(0.969–1.107)	0.305
Pre-pregnancy BMI (kg/m²)	1.115(1.055–1.178)	<0.001	1.101(1.041–1.165)	<0.001
PCOS history				
No	Ref		Ref	
Yes	2.905(1.009–8.366)	0.048	3.161(1.078,9.267)	0.036
Model Performance				
N	569		569	
AUC (95% CI)	0.658(0.587–0.729)		0.731(0.666–0.797)	
Hosmer-Lemeshow test	χ^2=8.816, p = 0.358		χ^2=11.325, p = 0.184	

Note:*aOR, adjusted odds ratio; AUC, area under the receiver operating characteristic curve; BMI, body mass index; CI, confidence interval; PCOS, polycystic ovary syndrome; Ref., reference group.The multivariate model adjusted for all variables listed in the table.Statistical significance was set at p < 0.05.*

We performed a series of logistic regression analyses to evaluate the association between oxygen saturation and the risk of gestational diabetes mellitus (GDM). First, a univariate logistic regression model was conducted with oxygen saturation as the sole predictor. This crude model revealed a significant association between lower oxygen saturation and an increased risk of GDM (OR: 0.643; 95% CI: 0.509–0.812; p < 0.001). Subsequently, a multivariate logistic regression model was constructed to adjust for potential confounding factors, including maternal age, pre-pregnancy BMI, and history of polycystic ovary syndrome (PCOS). Oxygen saturation remained significantly and independently associated with GDM (Adjusted OR: 0.680; 95% CI: 0.533–0.869; p = 0.002), after adjusting for these covariates. This confirms that the inverse relationship between oxygen saturation and GDM risk is independent of these established risk factors.

The discriminative performance of the different models was assessed using Receiver Operating Characteristic (ROC) curve analysis (Fig. 1). The area under the curve (AUC) for the model containing only oxygen saturation was 0.658. The model containing only the clinical risk factors (age, pre-pregnancy BMI, and PCOS history) showed better discriminative ability, with an AUC of 0.694. Most importantly, the combined model, which integrated oxygen saturation with the clinical factors, demonstrated the highest discriminative power, achieving an AUC of 0.731. Given that GDM is diagnosed before the third trimester, we interpret this combined model as a tool for concurrent risk stratification rather than prospective prediction.

3.4 No Effect Modification by Age or Obesity Status (Table 4)

Table 4
Analysis of interaction effects between oxygen saturation and high-risk factors on GDM.

Variable	Adjusted OR (95% CI)	P value
Model 1: Interaction with Advanced Age		
Oxygen saturation (per unit)	0.669 (0.507–0.885)	0.005
Advanced Age (Yes vs. No)	4370282.038 (0.000–6.733E + 27)	0.539
Oxygen saturation * Advanced Age	0.851 (0.508–1.427)	0.541
Model 2: Interaction with Obesity		
Oxygen saturation (per unit)	0.562 (0.410–0.771)	< 0.001
Obesity (Yes vs. No)	0.000 (0.000–1762.362)	0.101
Oxygen saturation * Obesity	1.513 (0.933–2.455)	0.093

Note:Model 1 and Model 2 are results from separate multivariate logistic regression analyses.The OR for oxygen saturation represents the effect per unit decrease.The immense OR and CI for Advanced Age and Obesity are due to quasi-complete separation in the data, suggesting a very strong (but imprecise) association that requires further investigation. The interaction terms, however, are stable and interpretable.GDM, gestational diabetes mellitus; OR, odds ratio; CI, confidence interval.

To investigate whether the protective effect of oxygen saturation on GDM risk was modified by other high-risk status, we tested for interaction effects by including interaction terms in the multivariate logistic regression models. After adjusting for covariates, no statistically significant interaction was observed between oxygen saturation and advanced maternal age (OR for interaction term: 0.851; 95% CI: 0.508–1.427; p = 0.541). Similarly, the interaction between oxygen saturation and obesity (based on pre-pregnancy BMI) was also not statistically significant (OR for interaction term: 1.513; 95% CI: 0.933–2.455; p = 0.093). These results indicate that the association between lower oxygen saturation and an increased risk of GDM is consistent across subgroups of women defined by age and obesity status, and the effect of oxygen saturation is not significantly enhanced in these high-risk populations.

4. Discussion

This study analyzed clinical data from 569 pregnant women at high risk for OSA to investigate the association between mean nocturnal oxygen saturation levels across different trimesters and the risk of gestational diabetes mellitus (GDM) and other adverse outcomes. The main findings were as follows: (1) Oxygen saturation levels in the third trimester were significantly associated with the risk of GDM, with a significantly higher incidence of GDM in the low oxygen saturation ($MSpO_2$ <95%) group; (2) Oxygen saturation was an independent correlate of GDM risk, and this association remained significant after adjusting for confounding factors such as age, pre-pregnancy BMI, and history of PCOS; (3) The discriminative performance for GDM was highest when oxygen saturation was combined with clinical risk factors (AUC = 0.731); (4) The association between oxygen saturation and GDM was consistent across subgroups defined by age and obesity status, with no significant interaction effects observed.

This study is the first to examine the relationship between oxygen saturation and GDM stratified by trimester, revealing a significant association only in the third trimester. This finding suggests that the third trimester may represent a critical window during which oxygen metabolism abnormalities impact glucose metabolism. However, it is crucial to interpret this finding in the context of GDM diagnosis timing. Since GDM is typically diagnosed at 24–28 weeks, our third-trimester SpO_2 measurements were obtained after diagnosis. Therefore, we do not propose that late-pregnancy SpO_2 can predict GDM; rather, the observed association reflects a concurrent pathophysiological state where hypoxemia and insulin resistance are closely intertwined. This distinction is clinically important: the third trimester may act as a “metabolic stress test” in which the deleterious effects of hypoxemia on glucose regulation become most apparent. While previous studies have primarily focused on the overall severity of OSA (e.g., AHI) in relation to GDM, our study, by focusing on the specific physiological parameter of oxygen saturation—which is easily monitored—further clarifies the direct role of hypoxemia in the pathogenesis of GDM. The increased metabolic load and exacerbated insulin resistance characteristic of late pregnancy may heighten the body’s sensitivity to hypoxemia, leading to a significant increase in GDM risk. Our interpretation of a cross-sectional association does not diminish the clinical value; instead, it highlights that women with low SpO_2in the third trimester may have more severe underlying metabolic dysregulation and may benefit from intensified glycemic management and postpartum follow-up.

Furthermore, multivariate regression analysis indicated that oxygen saturation was an independent protective factor against GDM (adjusted OR = 0.680). This finding holds considerable clinical significance, as it suggests that oxygen saturation may be a modifiable risk marker. Although traditional risk factors (e.g., age, obesity, PCOS history) demonstrated strong discriminative ability (AUC = 0.694), incorporating oxygen saturation further improved the model’s discriminative performance (AUC = 0.731), indicating that oxygen saturation provides additional value independent of traditional factors. Additionally, while no significant modifying effects of age or obesity status on the oxygen saturation-GDM relationship were detected, a trend towards an attenuated protective effect of oxygen saturation was observed in the obese subgroup (interaction OR > 1), and a trend towards an enhanced effect was noted in the advanced maternal age subgroup (interaction OR < 1). However, these interaction terms did not reach statistical significance, suggesting that the inverse association between oxygen saturation and GDM is generally consistent across pregnant women of different ages and BMI categories, and its effect size may not be significantly modified by these factors. Future studies with larger sample sizes are warranted to further investigate these trends.

It is noteworthy that, besides GDM, low oxygen saturation in the second trimester was also associated with decreased umbilical artery pH and an increased placental-to-neonatal weight ratio, suggesting that hypoxemia may affect the fetal metabolic environment through placental dysfunction. However, these

associations were not significant in the third trimester, which might be related to sample size limitations or population-specific characteristics, requiring further investigation.

Related research has also explored the role of blood oxygen saturation in diabetes. Among patients with type 1 diabetes (T1D), lower arterial oxygen saturation (SpO_2) is significantly associated with an increased risk of microvascular complications. A cross-sectional study of 659 T1D patients found that, compared to individuals with SpO_2 ≥96%, those with SpO_2 <96% had adjusted risks for albuminuria, retinopathy, and neuropathy that were 3.4, 2.8, and 5.8 times higher, respectively. Another Danish-Finnish multicenter study further confirmed that in T1D patients, lower SpO_2 was independently associated with decreased baroreflex sensitivity (BRS), an early marker of cardiovascular autonomic neuropathy, suggesting that hypoxemia may exacerbate microvascular damage through autonomic dysfunction. In populations with type 2 diabetes (T2D), among patients comorbid with OSA, nocturnal hypoxemia (particularly minimum SpO_2) is directly correlated with elevated blood glucose levels. The severe hypoxemia group (SpO_2 <90%) had significantly higher nocturnal blood glucose peaks, and multiple regression analysis confirmed that mean SpO_2 and minimum SpO_2 were independent predictors of nocturnal hyperglycemia.

The mechanisms underlying the impact of hypoxemia on glucose regulation are not fully understood. Integrating our findings, the observed independent inverse correlation between third-trimester oxygen saturation and GDM risk suggests that chronic intermittent hypoxemia may play a direct role in the pathogenesis of GDM. Potential mechanisms may involve multiple pathways, including the sympathetic nervous system, induction of inflammatory responses, and effects on insulin sensitivity. (1) Sympathetic excitation and hormonal regulation: Hypoxemia can trigger increased sympathetic nervous system activity, promoting the release of counter-regulatory hormones such as cortisol and catecholamines, which inhibit insulin secretion and stimulate hepatic glycogenolysis—processes highly consistent with the pathophysiology of GDM. (2) Inflammation and oxidative stress pathways: Intermittent hypoxemia can promote the release of inflammatory cytokines (e.g., TNF-α, IL-6) and increase oxidative stress, both known contributors to insulin resistance. Decreased oxygen saturation might enhance placental oxidative stress, further exacerbating glucose metabolism abnormalities. (3) Interference with insulin signaling pathways: Chronic hypoxemia can activate hypoxia-inducible factor (HIF-1α), which may subsequently inhibit tyrosine phosphorylation of insulin receptor substrate (IRS), leading to impaired pancreatic β-cell function and peripheral insulin resistance. The significant association between low oxygen saturation and GDM risk specifically in the third trimester observed in our study might be related to the amplification of the metabolic negative effects of hypoxemia against the backdrop of accelerated fetal growth and increased metabolic demands during late pregnancy.

Therefore, oxygen saturation emerges as a potential novel target for GDM risk stratification and intervention. Our findings have important implications for the clinical management of GDM. First, regarding screening strategies: Current GDM screening primarily relies on the oral glucose tolerance test (OGTT), typically performed at 24–28 weeks of gestation. Our study suggests that monitoring oxygen saturation (e.g., nocturnal pulse oximetry) in the third trimester could help identify high-risk individuals beyond traditional risk factors, particularly among women at high risk for OSA. Although this does not constitute early prediction, it can serve as a tool for concurrent risk reclassification. Women with low SpO_2 in the third trimester, even after GDM diagnosis, may represent a subgroup with more severe insulin resistance and may warrant stricter glycemic targets or more frequent fetal surveillance. Second, for women exhibiting decreased oxygen saturation in the third trimester, early interventions such as behavioral modifications (e.g., sleep position guidance, weight management) or, when necessary, respiratory support therapy (e.g., continuous positive airway pressure, CPAP) could be implemented aiming to improve oxygenation and potentially reduce the risk of GDM and its complications. Notably, the lack of significant interaction between oxygen saturation and advanced age or obesity in our study indicates that the impact of hypoxemia on GDM risk is prevalent across different high-risk populations, suggesting that intervention strategies might be applicable to a broader group. Furthermore, ROC analysis showed that the model combining oxygen saturation with clinical risk factors had the optimal discriminative efficacy (AUC = 0.731). Future research could explore developing a nomogram or risk score system incorporating oxygen saturation into a multifactorial risk assessment tool for GDM, facilitating individualized risk management.

This study has limitations. Its retrospective design precludes the establishment of causality, and the study population was limited to pregnant women at high risk for OSA, cautioning against overgeneralization of the findings. Most importantly, the cross-sectional timing of the third-trimester SpO_2 measurement—after GDM diagnosis—does not allow prospective prediction. Future prospective, multicenter studies dynamically monitoring oxygen parameters throughout pregnancy, particularly before 24 weeks, and incorporating more potential confounding factors (e.g., detailed diet, physical activity) are warranted to evaluate the true predictive value of early-to-mid pregnancy hypoxemia.

In conclusion, lower oxygen saturation in the third trimester is independently associated with GDM in high-risk pregnancies. While not a predictor due to temporal limitations, this association suggests that late pregnancy is a critical window in which hypoxemia and glucose dysregulation intersect. $MSpO_2$may serve as a useful biomarker for concurrent risk stratification and may help identify women who require intensified metabolic management. Prospective studies with pre-diagnostic SpO_2 monitoring are warranted to confirm its predictive potential.

Abbreviations

AHI: apnea-hypopnea index; AUC: area under the receiver operating characteristic curve; aOR: adjusted odds ratio; BMI: body mass index; CI: confidence interval; GDM: Gestational Diabetes Mellitus; HDP: hypertensive disorders of pregnancy; IQR: interquartile range; $LSpO_2$: lowest oxygen saturation; $MSpO_2$: mean oxygen saturation; ODI: oxygen desaturation index; OSA: obstructive sleep apnea; PCOS: polycystic ovary syndrome; PLGF: placental growth factor; PGDM: pre-gestational diabetes mellitus; PPH: postpartum hemorrhage; ROC: receiver operating characteristic; SDB: sleep-disordered breathing; SpO_2: oxygen saturation; T1D: type 1 diabetes; T2D: type 2 diabetes; Ref.: reference group.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Peking University People's Hospital (Approval No. 2023PHB210-001), and informed consent was exempted.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Guangjiao Wang performed the statistical analysis and drafted the manuscript. Ran Hu and Linyan Zhang were responsible for data collection. Guoli Liu served as the corresponding author and supervised this study.

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Declaration of Generative AI and AI-assisted Technologies in the Writing Process

The authors declare that no AI Tool was used in the manuscript writing. The authors take full responsibility for the integrity and accuracy of the content presented.

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Figures

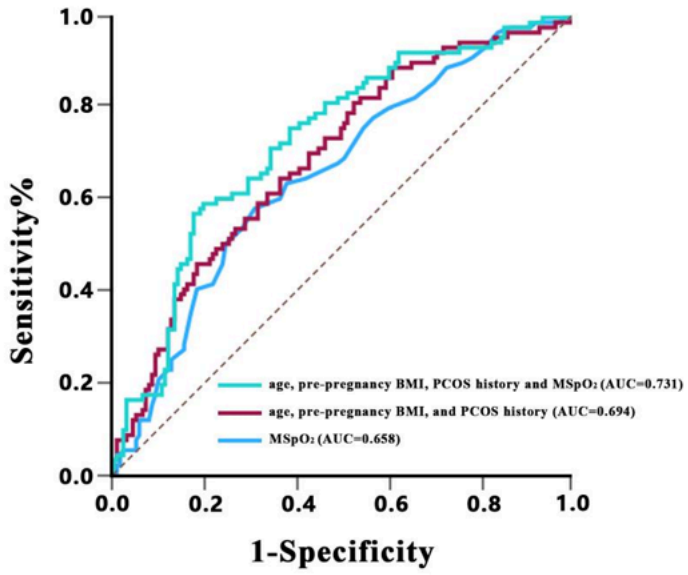


Figure 1

Receiver Operating Characteristic (ROC) curve analysis of different models