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# Maternal oxygen inhalation affects the fetal hemodynamic in low-risk with uncomplicated late pregnancy

Xiu-Qin Wu<sup>1</sup>, Xiao-Feng Yang<sup>1</sup>, Lin Ye<sup>1</sup>, Xiao-bin Zhang<sup>1</sup>, Yong-Qiang Hong<sup>1</sup> and Wei-Hsiu Chiu<sup>2,3\*</sup>

## Abstract

**Background** Maternal oxygen inhalation during labor has not been shown to provide significant benefits to newborns. However, its impact on fetal hemodynamics in late pregnancy remains uncertain.

**Objective** This study aimed to investigate the association between maternal oxygen inhalation in the late trimester and changes in fetal hemodynamics. Specifically, we assessed the short-term effects of maternal oxygen administration on fetal Doppler parameters and evaluated whether this practice has potential benefits or risks for the fetus.

**Study design** These retrospective data were obtained from singleton pregnancies who underwent a after 32<sup>+0</sup> weeks prenatal ultrasound examination between January 2022 and December 2022. Participants were categorized into oxygen inhalation and non-oxygen inhalation groups. Oxygen inhalation was administered based on maternal request, primarily due to concerns about hypoxia from prolonged mask use during the COVID-19 pandemic, rather than clinical indication. Our study analysis was performed in August 2023. In oxygen inhalation group, pregnant women received oxygen inhalation with 3 L/min for 30 min by nasal cannula, and before went to department of ultrasound for sonographic assessment within 1 h. The CPR and PPI were predefined as primary outcomes prior to analysis. Each woman was recorded Doppler index and calculated placental pulsatility index (PPI) and cerebroplacental ratio (CPR). Moreover, fetal cardiac function was assessed within pulsed Doppler or M-mode.

**Main outcome** The primary outcome presented higher PPI, lower CPR, and lower birth weight for the exposure maternal oxygen inhalation group, compare to non-oxygen inhalation group.

**Results** A total of 104 singleton pregnancies were included in the final analysis (oxygen inhalation group: n = 48). No significant differences were observed in the resistance indices of the uterine arteries, umbilical arteries, middle cerebral arteries, descending aorta, ductus venosus, or umbilical vein. However, variations were noted in the oxygen inhalation group. Notably, indices with higher sensitivity for predicting adverse outcomes demonstrated significant differences between groups: PPI was higher in the oxygen inhalation group compared to the non-oxygen inhalation group ( $0.81 \pm 0.12$  vs.  $0.76 \pm 0.11$ ,  $p < .05$ ), while CPR was also lower in the oxygen inhalation group ( $1.98 \pm 0.56$  vs.  $2.28 \pm 0.70$ ,  $p < .05$ ). Additionally, birth weight was significantly lower in the oxygen inhalation group compared to the non-oxygen inhalation group ( $2983.78 \pm 468.18$  g vs.  $3178.41 \pm 477.59$  g,  $p < .05$ ).

**Conclusion** Our study found that brief maternal oxygen inhalation in the third trimester was associated with significant changes in fetal hemodynamics, specifically higher PPI and lower CPR. Both of these indices are sensitive markers

\*Correspondence:

Wei-Hsiu Chiu

qu4781@gmail.com

Full list of author information is available at the end of the article



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of unfavorable prenatal outcomes, indicating that maternal oxygen inhalation may adversely affect fetal health. These findings underscore the importance of carefully evaluating the use of oxygen inhalation in pregnant women, especially those in high-risk pregnancies. Additionally, monitoring Doppler indices before and after oxygen administration may help assess fetal well-being and guide clinical decision-making in these situations.

**Keywords** Prenatal ultrasonography, Maternal oxygenation inhalation, Placental pulsatility index (PPI), Cerebroplacental ratio (CPR), Hemodynamic

## Introduction

Maternal oxygen inhalation has historically been a widely used intervention to enhance fetal oxygenation, particularly during labor, in cases of suspected fetal deoxygenation or non-reassuring fetal status. In the past, routine oxygen supplementation was commonly administered to laboring women regardless of clinical indications. However, accumulating evidence suggests that this practice offers no clear benefit in the absence of maternal hypoxia [1]. As Abati et al. and others have highlighted, current guidelines recommend that oxygen administration should be reserved for cases where maternal hypoxia is confirmed or strongly suspected, rather than used indiscriminately [2, 3]. Despite these recommendations, maternal oxygen supplementation continues to be used in some clinical settings, particularly as a precautionary measure or in response to maternal concerns about fetal well-being in many Chinese hospitals, even in low-risk pregnancies. Given the ongoing debate and lack of conclusive evidence, further investigation into the effects of maternal oxygen inhalation on fetal and placental circulation remains essential.

In the clinical management of suspected nonreassuring foetal status, health care workers provide oxygen treatment, among other measures, to prevent foetal hypoxia for get nonreassuring foetal status out of the way [4]. Although the problem of an abnormal foetal heart rate can be alleviated with oxygen supplementation, the problem of foetal acid–base status cannot be resolved with oxygen supplementation [5]. Jouppila et al. analysed the influence of placental and umbilical venous blood flow in pregnant women who receive short-term oxygen inhalation. The results revealed that maternal oxygen inhalation elevates arterial oxygen partial pressure in pregnant individuals, however, the observed unchanged umbilical venous blood flow while significantly reduces intervillous blood flow. The observed vasoconstriction may be attributed to hyperoxia-induced alterations in placental perfusion, suggesting that modifications in fetal oxygenation could potentially trigger compensatory adjustments in umbilical circulation. This finding suggests that hyperoxygenation may lead to increased placental vascular resistance, potentially impairing transplacental oxygen and nutrient exchange [6].

Similarly, Khatib et al. reported that maternal hyperoxygenation was associated with a reduction in fetal pulmonary artery pulsatility indices in both intrauterine growth restriction (IUGR) and normally grown fetuses. This finding suggests alterations in pulmonary vascular resistance and subsequent redistribution of fetal circulation, potentially representing a compensatory physiological response to increased maternal oxygen levels. These results indicate that maternal hyperoxygenation may influence fetal hemodynamic adaptation and contribute to blood flow redistribution [7].

On the other hand, the advantages and potential risks of maternal oxygen inhalation have always been controversial. However, in their review, Fawole, B. and Hofmeyr concluded that there is insufficient evidence to support whether oxygen administration could help relieve foetal distress [1]. On the basis of the research of Abati et al., maternal oxygen administration could cause material exchange disequilibrium in the placenta [2].

The world was affected by the COVID-19 pandemic during the period from 2020 to 2022. In East Asian countries in particular, legal regulations mandated the continuous wearing of masks. For pregnant women were unaccustomed to prolonged mask use, this not only resulted in breathing discomfort but also raised concerns about potential impacts on the foetal oxygen supply. Consequently, some pregnant women proactively requested oxygen inhalation.

However, the use of oxygen supplementation, which affects fetuses during pregnancy, especially during low-risk uncomplicated pregnancies, is controversial. Only a few previous studies have investigated whether maternal oxygen inhalation affects foetal haemodynamics during prenatal examinations in late trimesters in women with low-risk and uncomplicated pregnancies. In this study, we aimed to determine whether late-trimester oxygen inhalation and foetal haemodynamic changes are relevant, the effects of short-term maternal oxygenation inhalation on foetal haemodynamic changes, and whether this practice could have any benefit or cause potential harm to fetuses.

## Methods

### Setting

Retrospective data were obtained from singleton pregnant women who underwent prenatal ultrasound examination after 32+0 weeks gestation between January 2022 and December 2022. Our study evaluated whether room air and oxygen inhalation between 32+0 and 40+6 weeks of gestation were associated with prenatal hemodynamic changes.

Oxygen inhalation was administered based on maternal request rather than clinical indications, primarily due to concerns about hypoxia associated with prolonged mask use during the COVID-19 pandemic. Oxygen therapy was subsequently provided following a standardized clinical protocol established within our institution. Pregnant women who requested oxygen inhalation received a consistent dosage of 3 L/min for a duration of 30 min via nasal cannula, in accordance with routine clinical practice [8–10]. In the oxygen inhalation group, pregnant women received oxygen inhalation and then underwent ultrasound for sonographic assessment within 1 h.

Regarding ethics approval and informed consent, our research was approved by the Medical Research Ethics Review Committee of Fujian Medical University Affiliated with Mindong Hospital Ningde (Issued: 2022083101 K). Our study was conducted in accordance with the ethical standards of the responsible committee on human experimentation and according to the latest version of the Helsinki Declaration, and all information from all patients or hospitals included in our research was anonymized. Informed consent was obtained from all participants included in this study. As part of standard hospital procedures, all patients provide written consent prior to undergoing medical examinations, granting permission for the use of their clinical data in research.

Except for foetuses conceived with assisted reproductive technology (ART), the gestational age (GA) of the foetuses was determined from the date of conception estimated by the foetal crown–rump length (CRL) at 11–14 weeks of gestation via ultrasound examination [11]. The exclusion criteria were a history of foetal chromosomal abnormalities, structural anomalies or other congenital heart defects (CHDs), early foetal growth restriction (FGR) [12], and maternal complications. In accordance with the ISUOG practice guidelines, the CRL, foetal biometry, Doppler indices of the middle cerebral artery (MCA), umbilical artery (UA), umbilical vein (UV), ductus venosus (DV) and uterine artery (Ut A), and foetal cardiac function were measured via ultrasound [13–17]. With built-in software, this ultrasound machine can handle most of the Doppler index data that are automatically calculated on tasks after the accurate Doppler waveform is traced.

A detailed foetal anatomical assessment with basic biometry was performed at each scan. According to the recommendation of the ISUOG practice guidelines, the estimated foetal body weight (FBW) was calculated via Hadlock's formula [13, 18]. This formula involves the summation of HC, AC, and femur length (FL) to give a number in millimeters. The regression equation of estimated FBW:

$$\text{Log}_{10} \text{ BW} = 1.326 - (0.00326 \times \text{AC} \times \text{FL}) + (0.0107 \times \text{HC}) + (0.0438 \times \text{AC}) + (0.158 \times \text{FL})$$

In all cases, fetal examinations were performed using a Voluson E10 ultrasound platform (General Electric Medical Systems, Milwaukee, WI, USA) with C2-9-D multi-frequency transabdominal transducers (XD Clear Wide Band Convex Probe). For fetal safety, all prenatal sonography procedures are performed in accordance with the guidance of the as low as reasonably achievable (ALARA) principle [19]. All the scans and fetal measurements were conducted by a single registered physician who had more than 10 years of experience in obstetric ultrasound scanning. To assess intraobserver repeatability, the reliability statistic was used to assess the agreement of intraobserver reliability among repeated fetal biometry measurements taken by the same examiner.

In the color Doppler evaluation of our study, the suitable size of the color box and adequate PRF and gain without noise and artifacts were optimized for color flow mapping and Doppler index acquisition. To avoid falsely finding that the Doppler velocities and waveforms were either absent or abnormal. The angle of insonation was kept as close 0 degrees as possible, or stability was maintained at less than 20 degrees. The Doppler spectrum was recorded in the absence of fetal breathing and limb movements. The Doppler exposure time was always kept as no longer than 5 min as possible [14]. All the Doppler index of the artery and venous in our study were calculated by software built-in ultrasound device.

### Fetal Doppler and cardiac function assessment

Doppler waveforms with indexes of the middle cerebral artery (MCA), umbilical artery (UA), uterine artery (UtA), umbilical vein (UV), ductus venosus (DV), and descending aorta (DAo) were obtained via transabdominal ultrasound [14, 15, 20, 21]. The cerebroplacental ratio (CPR) and the pulsatility index of the umbilical artery (PPI) were designated as primary outcome measures before conducting the analysis. The definitions and reference ranges for CPR and PPI were determined according to previously published normative data [22, 23]. The CPR was calculated as MCA PI/UA PI [24], while the PPI was derived from the formula:  $\text{PPI} = (\text{UA PI} + \text{mean UtA PI})/2$  [23]. Umbilical venous blood flow (UVBF) was estimated using UV diameter and mean velocity:  $\text{UVBF (mL/}$

min) = cross-sectional area of UV ( $\text{mm}^2$ )  $\times$  mean velocity ( $\text{mm/s}$ )  $\times$  60 [15].

Fetal echocardiography followed ISUOG guidelines, utilizing B-mode and color flow mapping [25]. Cardiac biometry, including length, width, circumference, and thoracic circumference, was measured in a four-chamber view at end-diastole, and the cardiothoracic circumference ratio (CTCR) = cardiac circumference/thoracic circumference was calculated. The global sphericity index (GSI) = end-diastolic length/end-diastolic width was also assessed [26].

Fetal cardiac function was evaluated using M-mode and pulsed Doppler. The shortening fraction (SF) = (EDD – ESD)/EDD was calculated separately for each ventricle, with end-diastolic diameter (EDD) and end-systolic diameter (ESD) measured via M-mode [16, 17, 27, 28]. Pulsed Doppler was used to assess E/A ratio and modified myocardial performance index (Mod-MPI). The E/A ratio was derived from early ventricular filling velocity (E) and atrial contraction velocity (A) in the four-chamber view [17]. Mod-MPI was determined by measuring isovolumetric time (a) and ejection time (b) for each ventricle: Mod-MPI = (a – b)/b [29].

### Statistical analysis

We performed statistical analysis using the Statistical Package for the Social Sciences (SPSS, Ver. 25.0 for Windows; Chicago, IL, USA). Mean with standard deviation (SD) or median of maternal basic and obstetrical characteristics, fetal biometry, prenatal Doppler flow index, and fetal echography were determined. Compared differences between two groups data using the Mann–Whitney U test, Chi-Squared Test of Independence, or Fisher's Exact Test. To account for multiple comparisons, we applied the Benjamini–Hochberg false discovery rate (FDR) correction to control for Type I errors. Statistical significance was determined by a probability value of  $p < 0.05$ .

## Results

### Information of maternal basic and obstetrical characteristics summary

Data of 104 fetuses were collected and analyzed during the study period (non-oxygen inhalation group: 56; oxygen inhalation group: 48). The median maternal age was 29.00 years old (range, 20–40 years old); the median maternal gravidity was 2 (range, 1–6) and the median maternal parity was 1 (range, 0–2). The median gestation age in ultrasound examination was  $35^{+2}$  weeks (range,  $32^{+0}$ – $40^{+0}$  weeks).

Table 1 presents the data of the maternal basic and obstetrical characteristics. In the non-oxygen inhalation group, the rates of C-section, preterm birth (PTB), and low birth weight (LBW) were 39.30%, 7.10% and 5.40%,

respectively. The distributions of parity, gestational age at birth, Apgar score, placental weight, preterm birth rate, and low birth weight rate were similar across oxygen inhalation groups and non-oxygen inhalation groups. Additionally, analysis of the estimated fetal weight (EFW) at the time of ultrasound demonstrated no statistically significant difference between the oxygen inhalation and non-oxygen groups ( $p = 0.120$ ), suggesting that baseline fetal growth was comparable across groups. Participants with oxygen inhalation cluster had lower birth weight ( $2983.78 \pm 468.18$  g vs.  $3178.41 \pm 477.59$  g,  $p < 0.05$ ) (Table 1 and Fig. 1).

### Associations of Doppler flow index with oxygen inhalation

Maternal oxygen inhalation was associated with increased PPI and decreased CPR. Participants whose pregnancy women were in the oxygen inhalation bunches had an elevated value in PPI (0.81 vs. 0.76,  $p < 0.05$ ) compared with maternal without oxygen inhalation (Table 2 and Fig. 2). It is also worth noting that analyzed using the Pearson product-moment correlation, there was a significant association of PPI with birth weight ( $r = -0.494$ ,  $p = 0.001$ ). Compared to the non-oxygen inhalation group, oxygen inhalation group had a decrease value of CPR (1.98 vs. 2.28,  $p < 0.05$ ) (Table 2 and Fig. 3). The index of MCA, UA, Dao, Ut  $A_{\text{avg}}$ ,  $UVBF_{\text{adj}}$ , and DV flow were no significant discordance (Table 2). The data of the fetal echography was given in Table 3. The cardiac size and function without obvious difference in two groups.

The CPR and PPI were predefined as primary outcomes prior to analysis, and both remained statistically significant even after multiple comparison adjustment (CPR:  $p = 0.002$ , PPI:  $p = 0.003$ ). In contrast, the secondary outcomes, including prenatal doppler index,  $UVBF_{\text{adj}}$ , and fetal cardiac function did not reach statistical significance ( $p > 0.05$ ) and remained non-significant after applying the Benjamini–Hochberg false discovery rate (FDR) correction.

## Discussion

### Principal findings

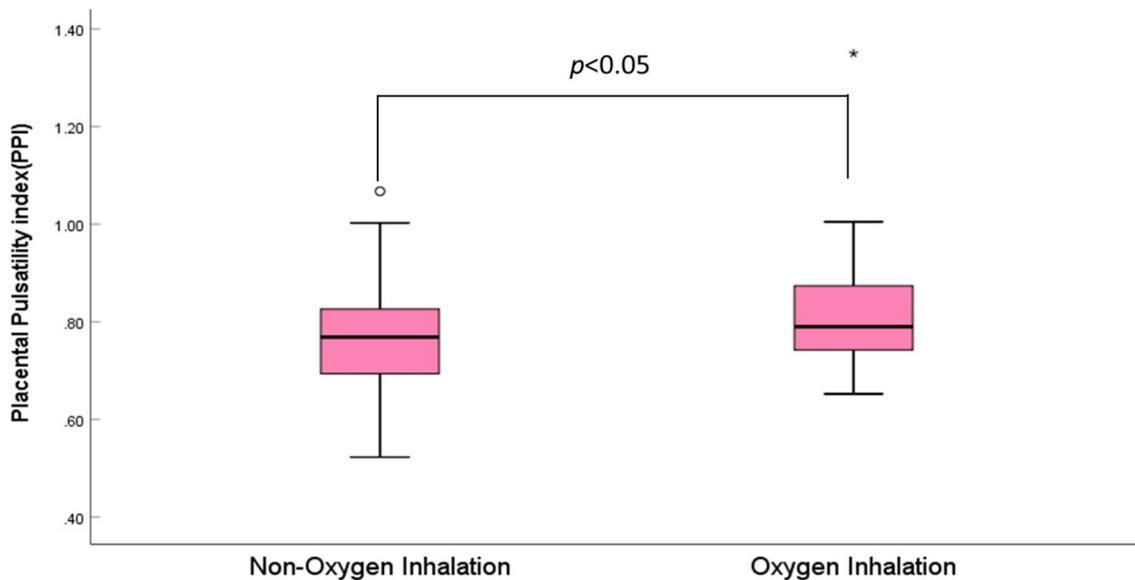
Although the various effect on maternal oxygen inhalation during labor has been numerous elucidated, the relationship of prenatal hemodynamic change versus maternal oxygen inhalation in low-risk, uncomplicated late pregnancy has not been widely studied. In our current study, maternal oxygen inhalation restricted the potential prenatal hemodynamic will be elaborated. In this Retrospective study, a high PPI, low CPR, and low birth weight were associated with maternal oxygen inhalation. We seriously deem maternal oxygen supplementation to be a highly correlated relationship with abnormal fetal Doppler flow index in low risk uncomplication

**Table 1** Maternal basic and obstetrical characteristics (N=104)

Variables	Non-oxygen inhalation group (n = 56)		Oxygen inhalation group (n = 48)		p-value
	Value	(Minimum–Maximum)	Value	(Minimum–Maximum)	
Maternal age (years)	28.68 ± 4.24	20.00–39.00	30.63 ± 3.56	24.00–40.00	0.012
Parity					
Nulliparous	21 (37.50%)	NA	15 (31.30%)	NA	0.436
Parous	35 (62.50%)	NA	33 (68.70%)	NA	0.348
GA at measurement (weeks)	35.01 ± 2.05	32.00–40.00	35.80 ± 1.80	32.00–39.71	0.027
GA at delivery (weeks)	39.12 ± 1.52	34.43–41.57	38.74 ± 1.32	35.14–41.29	0.144
PTB	4 (7.10%)	NA	3 (6.30%)	NA	0.714
Birth weight (g)	3178.41 ± 477.59	2050.00–4200.00	2983.78 ± 468.18	1920.00–3900.00	0.047
LBW at delivery	3 (5.40%)	NA	4 (8.30%)	NA	1.000
C-section	22 (39.30%)	NA	29 (60.40%)	NA	0.058
1-min Apgar score	10.00 ± 0.00	10.00–10.00	9.93 ± 0.33	8.00–10.00	0.169
5-min Apgar score	10.00 ± 0.00	10.00–10.00	10.00 ± 0.00	10.00–10.00	1.000
Placental weight (g)	520.15 ± 52.88	410.00–680.00	512.88 ± 49.61	423.00–741.00	0.357

Value data are given as mean ± SD, median, or n (%)

GA: gestational age; PTB: preterm birth; LBW: low birth weight;



**Fig. 1** The value of placental pulsatility index (PPI) after non-oxygen inhalation and oxygen inhalation

pregnancy, especially we found that the placental resistance and brain-sparing sign in the fetus with maternal oxygen supplementation significantly change in our current result.

**Results in the context of what is known**

Placental pulsatility index (PPI) is a sensitive index for evaluated placental resistance [23]. Our results show that the placental pulsatility index (PPI) in the both groups were  $0.76 \pm 0.11$  and  $0.81 \pm 0.12$ , respectively. PPI was

significantly higher in maternal oxygen inhalation group, compare with non- oxygen inhalation group ( $p < 0.05$ ).

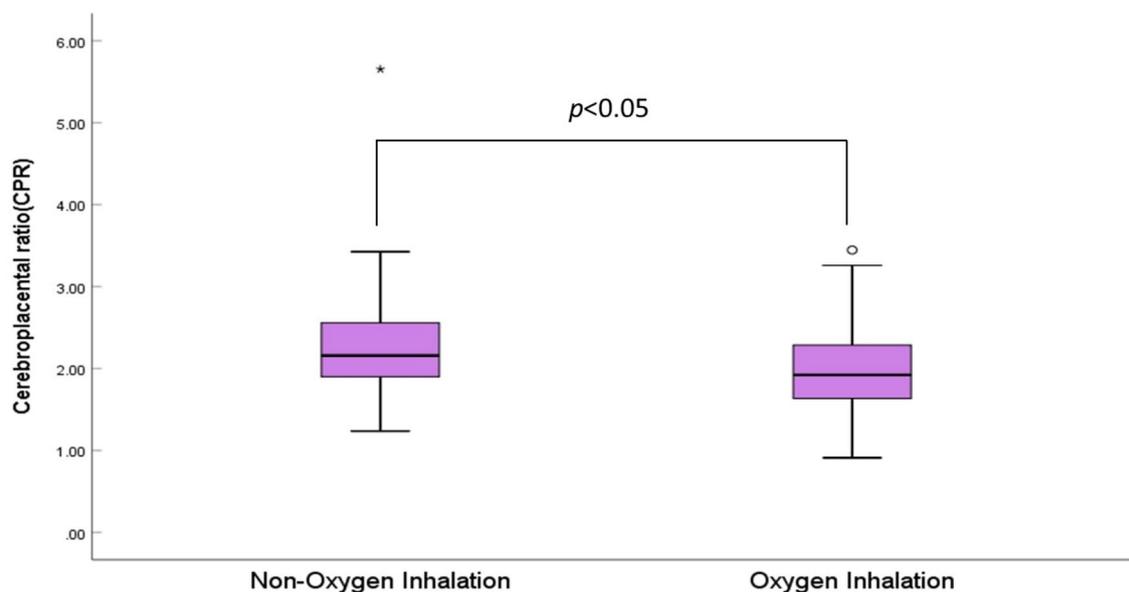
The observed increase in PPI following oxygen inhalation (Fig. 2) suggests elevated placental resistance, highlighting potential alterations in transplacental blood flow. Given that placental perfusion is critical for optimal nutrient and oxygen transfer to the fetus, these findings underscore the importance of PPI as a sensitive marker of placental impedance. Building on this, even minor variations in PPI may hold clinical significance when assessed

**Table 2** Prenatal Doppler flow index (N=104)

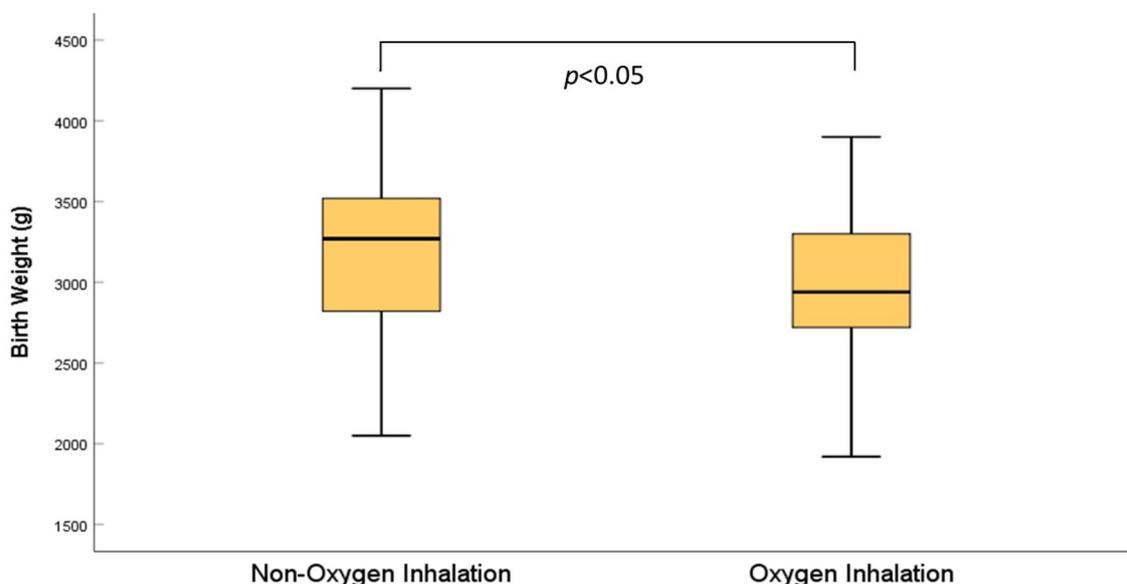
Variables	Non-oxygen inhalation group (n=56) Value	Oxygen inhalation group (n=48) Value	p-value
MCA			
PI	1.90±0.53	1.76±0.43	0.156
RI	0.83±0.16	0.80±0.08	0.191
UA			
PI	0.85±0.16	0.91±0.15	0.070
RI	0.57±0.07	0.60±0.06	0.074
Ut A <sub>avg</sub>			
PI	0.67±0.13	0.71±0.17	0.166
RI	0.45±0.06	0.47±0.07	0.188
DAo			
PI	1.87±0.39	1.86±0.39	0.960
RI	0.82±0.06	0.81±0.06	0.665
PPI	0.76±0.11	0.81±0.12	0.035
CPR	2.28±0.70	1.98±0.56	0.017
DV			
PIV	0.42±0.17	0.44±0.21	0.715
S/a	1.65±0.40	1.73±0.74	0.904
UV			
Circ (mm)	25.68±5.78	24.67±4.70	0.845
Area (mm <sup>2</sup> )	49.06±18.20	48.10±16.90	0.850
UVBF <sub>adj</sub> (ml/min/kg)	107.70±29.38	104.80±27.88	0.835

MCA: Middle cerebral artery, UA: Umbilical artery, Ut A<sub>avg</sub>: Mean of the left and right maternal uterine artery, DAo: Descending aorta, DV: Ductus venosus, UV: Umbilical vein, PI: Pulsatility index, RI: Resistance index, PPI: placental pulsatility index, CPR: cerebroplacental ratio, PIV: pulsatility index for veins (PIV), S/a: Peak velocity of systole to Peak velocity of atrial contraction ratio, and UVBF<sub>adj</sub>: Estimated fetal weight adjusted-umbilical vein blood flow

alongside other hemodynamic parameters. Gudmundsson et al. demonstrated that PPI exhibits superior sensitivity compared to conventional Doppler indices in predicting adverse pregnancy outcomes, reinforcing its potential to detect subtle placental vascular dysfunction and emphasizing the need for comprehensive fetal hemodynamic assessment [23]. Jouppila et al. reported that maternal oxygen inhalation significantly reduces intervillous blood flow, suggesting an increase in placental vascular resistance [6]. This observation is consistent with our findings, which demonstrate a higher placental pulsatility index (PPI) in the oxygen inhalation group, indicating potential alterations in placental perfusion that may affect fetal oxygen and nutrient transfer. The hyperoxia could cause the systemic vasoconstriction in the patients without hypoxic state [30], our study result showed that in the maternal uterine artery doppler flow index with higher resistance situation, both PI (0.67±0.13 vs. 0.71±0.17) and RI (0.45±0.06 vs. 0.47±0.07) were high in oxygen inhalation group, compare with control group. Similar, the high PPI might be stated by the maternal oxygen administration could cause that placental vasoconstriction [2]. Simchen et al. evaluated the uteroplacental and fetal Doppler change in maternal hyperoxia with and without normocapnia. They found a strong correlation between maternal hyperoxygenation and increased uteroplacental resistance with reduced uteroplacental flow [31]. In our previous study, the high PPI would be indicating the UVBF decreased [32]. The UVBF adjust by estimated fetal weight of our study, although there is no significant different between 2 group (p=0.835). But the estimated fetal weight adjusted-UVBF in non—oxygen



**Fig. 2** The value of cerebroplacental ratio (CPR) after non-oxygen inhalation and oxygen inhalation



**Fig. 3** The value of birth weight (g) after non-oxygen inhalation and oxygen inhalation

**Table 3** Fetal echography (N= 104)

Variables	Non-oxygen inhalation group (n= 56)	Oxygen inhalation group (n= 48)	p-value
	Value	Value	
CTCR	0.55 ± 0.27	0.54 ± 0.32	0.100
GSI	0.86 ± 0.14	0.84 ± 0.13	0.250
LV			
MV E/A ratio	0.70 ± 0.10	0.72 ± 0.09	0.252
MPI	0.44 ± 0.07	0.44 ± 0.06	0.865
SF (%)	42.46 ± 8.32	43.15 ± 7.55	0.609
RV			
TV E/A ratio	0.74 ± 0.10	0.77 ± 0.14	0.325
MPI	0.48 ± 0.13	0.45 ± 0.06	0.451
SF (%)	37.20 ± 8.10	35.23 ± 7.17	0.393

Value data are given as mean ± SD

CTCR: Cardiothoracic circumference ratio, GSI: Global Sphericity index, LV: Left ventricle, RV: Right ventricle, MV: Mitral valve, TV: Tricuspid valve, E/A ratio: early ventricular filling velocities divided by the ventricular filling velocities, MPI: Myocardial Performance Index, SF: Ventricular Shortening Fraction

inhalation group is slightly better than oxygen inhalation group (107.70 ± 29.38 ml/min/Kg vs. 104.80 ± 27.88 ml/min/Kg).

Moreover, the systemic vascular constriction would be occurred by in a hyperoxia condition [30]. The result of Valensise, Farsetti et al.'s study that found the umbilical vein size altered was related to increased maternal systemic vascular resistance [33]. Our study also revealed that smaller umbilical vein area (49.06 ± 18.20 mm<sup>2</sup> vs.

48.10 ± 16.90 mm<sup>2</sup>) and circumference (25.68 ± 5.78 mm vs. 24.67 ± 4.70 mm) was associated with the oxygen inhalation group. The smaller of umbilical vein size in our current study is consistent with Valensise, Farsetti et al.'s finding.

Simchen et al. assessed the Doppler flow diversification in maternal hyperoxia with and without normocapnia in the late third trimester. While the Doppler index changes without statistical significance, they found that decrease fetoplacental circulation, increased UA-PI and concomitant decrease in middle cerebral artery PI were observed in fetuses with maternal hyperoxia [31]. Similarity to our results, higher value of UA flow resistance and lower value of MCA flow resistance were found in the oxygen inhalation group without achieve statistical significance (Table 2). Nevertheless, we found a more sensitive index for detecting poor perinatal outcome, cerebroplacental ratio (CPR), is a prenatal measurement that assesses the blood flow to the fetal brain and placenta. The role of the cerebroplacental ratio lies in its ability to provide valuable information about the fetal circulatory system, specifically was a higher sensitivity to CPR than either Doppler index (UA, MCA) alone [34]. Acharya et al. established longitudinal sex-specific reference ranges for the CPR in low-risk pregnancies. These reference ranges may enhance fetal monitoring and risk stratification [22]. This ratio is often used in obstetrics to evaluate fetal well-being and to assess the risk of adverse outcomes. Abnormalities in placental perfusion would influence the fetal blood flow redistribution with decreased CPR

[35]. In our current study which declare that lower CPR in the fetuses in the maternal super-oxygenation group ( $1.98 \pm 0.56$  vs.  $2.28 \pm 0.70$ ,  $p < 0.05$ ) by our performed the statistical analysis (Fig. 3). Although the absolute difference may appear modest, its clinical significance becomes evident when considered in conjunction with other hemodynamic parameters. These collective changes can provide valuable insights into physiological adaptations and potential clinical implications. Khatib et al. demonstrated that maternal hyperoxygenation reduced fetal pulmonary artery pulsatility indices, suggesting changes in pulmonary vascular resistance and potential redistribution of fetal circulation. Our findings further support this hypothesis, as we observed a lower CPR in the oxygen inhalation group, indicating that maternal hyperoxygenation may impact fetal blood flow adaptation [7].

Table 1 showed that most labor outcomes did not seem to make a significant difference whether oxygen was given or not. The review analysis of Burd and Raghuraman, oxygen supplementation to maternal during intrapartum, ultimateness was not effect on Apgar scores irrespective of whether oxygen was provided [36]. Similar to our result, our study showed 1- and 5-minute Apgar scores, there were no significant differences in Apgar scores between groups.

On the other hand, Fig. 3. presented the newborn birth weight was lower in oxygen inhalation group compare with control group ( $2983.78 \pm 468.18$  g vs.  $3178.41 \pm 477.59$  g,  $p < 0.05$ ) in our study. Furthermore, a Mann–Whitney U test was performed to compare estimated fetal weight (EFW) at the time of ultrasound between the oxygen inhalation and non-oxygen groups, revealing no statistically significant difference ( $2264.53 \pm 578.61$  g vs.  $2417.18 \pm 529.53$  g,  $p = 0.120$ ) (Table 1). These findings indicate that fetuses in the oxygen inhalation group did not exhibit reduced growth prior to exposure, suggesting that the observed lower birth weight may be a consequence of maternal oxygen inhalation rather than pre-existing fetal growth restriction. The 2022 Todumrong, Natavadee, et al. research on use PPI in high risk pregnancy to predict FGR reported that lower birthweight was associated with a higher PPI [37]. The 2017 research analysis PPI useful in predict adverse outcome with suspected of intrauterine growth restriction of Gudmundsson et al., the results showed that lower birthweight was found in high PPI group [23]. Similar to our results, not only birth weight significantly differences but also in the correlation analysis separate two groups of our study, the correlation coefficient between birthweight and PPI was calculated using the Pearson product-moment correlation, the birthweight in significantly negative

relation to PPI in oxygen inhalation group ( $r = -0.494$ ,  $p = 0.001$ ).

Additionally, hyperoxia stimulates the generation of reactive oxygen species (ROS), which can induce oxidative damage to tissues, nucleic acids, and proteins, thereby causing cellular injury and inflammation. Within placental tissue, such oxidative stress may lead to cellular dysfunction and inflammatory responses, potentially impairing placental function [38]. Consequently, it is plausible that this damage could influence changes in the placental pulsatility index (PPI) and the cerebroplacental ratio (CPR), which in turn may affect fetal growth and development.

Our present study bespeaks that the higher resistance index in the UA, Ut A, DAo, DV, and lower resistance index in MCA occurred in the oxygen inhalation group. While without reached statistical significantly, prior to development of adverse prenatal outcomes, there has been mild alteration within statistical significantly in PPI and CPR level. This suggests that the microenvironmental change effects the adverse prenatal outcomes risk factor profile and not only the increased level of PPI and CPR might contribute to latency Doppler flow redistribution noted in fetuses of women with oxygen inhalation.

#### Clinical implications

In our finished of the current study, there was change in the more sensitive index for predicting unfavorable prenatal outcome, higher placental pulsatility index (PPI) and lower cerebroplacental ratio (CPR), correlated strongly with the maternal oxygen inhalation group compared with the non-oxygen inhalation group. In addition, according to the analysis data showed that the mean birth weight does decline after oxygen inhalation group. Together, through our results might could be assisted a careful evaluation of the decision-making process and feasibility evaluation in the treatment of oxygen inhalation in pregnancy women especially high-risk pregnancies. In parallel, a more sensitive Doppler index was applied to facilitate the assessment of changes in hemodynamic parameters both prior to and following treatment, specifically in clinical situations where such monitoring is deemed maternal oxygen inhalation necessary.

#### Research implications

Whether oxygen inhalation and fetal hemodynamic change are relevant to be explored. To demonstrate causality, our study attempts to quest the effect of short-term maternal oxygenation inhalation on fetal hemodynamic change in low-risk with uncomplicated late pregnancy. Future research could include analysis data in fetal anomalies, high risk pregnancy, or complications pregnancy.

### Strengths and limitations

The strength of our study is that we have focused on the prenatal hemodynamic change of low-risk with uncomplicated late pregnancy alone. The most previous literature only has given prenatal outcomes of maternal oxygenation inhalation during delivery. As our results of might could be assisted a careful evaluation of the decision-making process and feasibility evaluation in the treatment of oxygen inhalation in through pregnancy period.

This study has some limitations in our study. First, there were some existence latent biases due to retrospective without randomized design. Second, the current study was an analysis based on obstetric sonographic reports and clinical data within the limited sample size. Third, our study is limited to data from a local tertiary hospital, and the results cannot be extrapolated to other regional hospitals. Fourth, we included only normal fetuses, which do not include pregnancy complications, fetal anomalies, and genetic cases. Fifth, manpower limitations prevented the monitoring of longitudinal changes in fetal hemodynamic parameters, hindering a comprehensive understanding of temporal adaptations in fetal blood flow, with future studies benefiting from tracking these parameters over time to enhance clinical relevance and improve the accuracy of perinatal outcome assessments.

### Conclusion

In our study, we analyzed the association of maternal exposure oxygen supplementation with doppler index change during late pregnancy. The change in the more sensitive index for predicting unfavorable prenatal outcome, higher placental pulsatility index (PPI) and lower cerebroplacental ratio (CPR), correlated strongly with the maternal oxygen inhalation group compared with the non-oxygen inhalation group. To our knowledge, our current study is the first investigation to examine the impact of utero-placental and fetal hemodynamic changes usage PPI and CPR in uncomplicated low-risk late pregnancy with oxygen inhalation. Through our results might could be assisted a careful evaluation of the decision-making process and feasibility evaluation in the treatment of oxygen inhalation in pregnancy women especially high-risk pregnancies. Concurrently provided the gauging more sensitive Doppler index for observation before and after treatment in the necessary situation also.

### Acknowledgements

We acknowledge support from the Funding: Natural Science Foundation of Fujian (No. 2021J011449). Our work is supported by the Department of ultrasound and the Department of obstetrics and gynecology partnership Mindong Hospital Affiliated to Fujian Medical University, and funding from the Natural Science Foundation of Fujian funding scheme.

### Author contributions

WHC: conceptualization, methodology, formal analysis, investigation, resources, data curation, writing – original draft, project administration. XQW: methodology, formal analysis, investigation, resources, data curation, project administration. XFY: conceptualization, methodology, investigation, resources, data curation. LY: investigation, resources, data curation. XBZ: conceptualization, methodology, investigation, resources, data curation. YQH: conceptualization, methodology, formal analysis, investigation, resources, data curation, project administration.

### Funding

Natural Science Foundation of Fujian (No. 2021J011449).

### Data availability

Our data can be shared openly under certain condition of protect study participant privacy.

### Declarations

#### Ethics approval and consent to participate

This study received ethical approval from the Medical Research Ethics Review Committee of Mindong Hospital affiliated with Fujian Medical University (Approval Number: 2022083101K). Informed consent was obtained from all participants included in this study. As part of standard hospital procedures, all patients provide written consent prior to undergoing medical examinations, granting permission for the use of their clinical data in research.

#### Consent for publication

Written informed consent was obtained from the patient for the publication of any accompanying data. The patient was informed that personal information would be anonymized to protect confidentiality.

#### Competing interests

The authors declare no competing interests.

#### Author details

<sup>1</sup>Department of Ultrasound, Mindong Hospital Affiliated to Fujian Medical University, Fujian, China. <sup>2</sup>Department of Obstetrics and Gynecology, Chung Shan Hospital, No.11, Ln. 112, Sec. 4, Ren'ai Rd., Da'an Dist., Taipei City 10689, Taiwan. <sup>3</sup>Department of Obstetrics and Gynecology, Division of Prenatal Ultrasound, Gene Infertility Medical Center, Taipei, Taiwan.

Received: 7 February 2024 Accepted: 12 March 2025

Published online: 01 April 2025

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