

Impact of Maternal Corticosteroids on Foetal and Uteroplacental Blood Flow Dynamics in Preterm Pregnancies with Growth Restricted Foetus: A Prospective Observational Study

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ABSTRACT

Introduction: Foetal Growth Restriction (FGR) is a critical condition where a foetus fails to achieve its genetically determined growth potential for gestational age. Studies using doppler ultrasonography have shown beneficial modifications in blood flow indices following corticosteroid administration, though there are some concerns regarding potential adverse effects.

Aim: To evaluate the effects of maternal corticosteroids on foetal and uteroplacental blood flow dynamics in preterm pregnancies complicated by FGR.

Materials and Methods: A prospective observational hospital-based study was conducted at a Tertiary Care Centre in Puducherry, India over a period of 18 months from October 2022 to March 2024, involving pregnant women between 28 to 36 weeks of gestation diagnosed with FGR with normal doppler as per delphi consensus criteria. A total of 84 patients were enrolled in the study. Pretreatment doppler indices were recorded for Umbilical Artery (UA), Middle Cerebral Artery (MCA), and maternal Uterine Artery (UtA) at '0' hour and 24-48 and 72-

96 hours following corticosteroid administration, and neonatal outcome in terms of Appearance, Pulse, Grimace, Activity, and Respiration (APGAR) score and Neonatal Intensive Care Unit (NICU) admission were observed. Statistical analysis was done to determine the significance of the observations.

Results: Maternal corticosteroid administration significantly increased the UA Pulsatility Index (PI) at 24-48 hours (mean difference=0.107, $p<0.0001$) with return towards baseline at 72-96 hours (mean difference=0.020, $p=0.722$). MCA PI showed significant reductions at 24-48 hours (mean difference = -0.139, $p<0.0001$) and 72-96 hours (mean difference = -0.181, $p<0.0001$) compared to baseline. The UtA PI remained stable throughout the observation period. 51% neonates had APGAR score <7 at five minutes and needed NICU admission.

Conclusion: Maternal corticosteroids appear to positively influence foetal and uteroplacental blood flow in pregnancies affected by FGR. These findings may have clinical implications, enhancing strategies for the management of preterm FGR and improving outcomes for affected neonates.

Keywords: Antenatal corticosteroid, Doppler ultrasonography, Uteroplacental and foetal blood flow

INTRODUCTION

The FGR is a significant condition in which a foetus does not reach genetically predetermined growth potential for its gestational age [1]. This condition is multifactorial, often resulting from maternal, placental, or foetal factors, and is linked to adverse perinatal outcomes, including increased risks of stillbirth, preterm birth, and neonatal morbidity [2]. Preterm pregnancies, defined as deliveries occurring before 37 weeks of gestation, further complicate the situation, as the combination of FGR and prematurity heightens the likelihood of serious complications for the infant [3]. Studies have demonstrated the role of maternal corticosteroids in preterm foetuses [4-7].

Commonly used corticosteroids are betamethasone and dexamethasone. These steroids primarily promote foetal lung maturity by enhancing surfactant production, thus reducing the risk of respiratory distress syndrome [5,6]. In addition, studies reported improved uteroplacental blood flow dynamics following steroid administration [7,8]. However, the effect of Antenatal Corticosteroids (ACS) on preterm FGR remains controversial. Some studies have reported altered doppler velocimetry [8,9], whereas others could not find any change in doppler haemodynamics after administering corticosteroids in antenatal mothers with preterm FGR [10,11].

Therefore, the present study aimed to observe the effects of ACS administration on doppler flow indices i.e., PI in the UA, MCA, and UtA before delivery and neonatal outcomes following delivery in cases of preterm FGR.

MATERIALS AND METHODS

The present prospective observational study was conducted at the Tertiary Care Centre in Puducherry, India over a period of 18 months from October 2022 to March 2024 after obtaining Institutional Human Ethics Committee (IHEC) approval (MGMCR/Res/01/2021/62/ IHEC115). The participants were recruited from the Antenatal Clinic of the Department of Obstetrics and Gynaecology.

Inclusion and Exclusion criteria: Women with uterine height less than the period of amenorrhoea were subjected for sonography for confirmation of FGR [12]. Both multi and primigravida in the age group 18 to 35 years between 28 to 36 weeks of gestation with singleton pregnancies with no sonographically detected foetal anomalies and confirmed FGR, as per Delphi consensus criteria [13] were enrolled in the study after obtaining informed consent. However, patients who started corticosteroid therapy before enrolment in the study and those unable to complete the study because of intrauterine foetal death or needed early termination due to underlying maternal or foetal cause were excluded from the study.

Sample size calculation: The sample size was calculated to be 84 preterm FGR cases, considering the percentage of UA doppler change to be 73% from a study by Choudhary N et al., and a dropout rate of 10% [8].

Study Procedure

Women satisfying the inclusion criteria were enrolled and written informed consent was obtained to undergo multiple doppler

examinations. Doppler ultrasonography was utilised as the primary diagnostic tool, employing a WIPRO GE LOGIC Q P5 ultrasound machine. The mid portion of the free-floating umbilical cord segment was used to record the Doppler waveforms from the UA. The foetal MCA doppler flow was measured in its proximal one third portion. The right and left uterine arteries blood flow velocity were measured just above the point where they cross the iliac artery. The assessments were performed at three time points: baseline ('0' hours), 24 to 48 hours, and 72 to 96 hours after administering corticosteroids (betamethasone or dexamethasone). Measurements included the UA, MCA and UtA PIs to evaluate blood flow dynamics. All Doppler examinations were conducted by the primary investigator under the guidance of Foetal Medicine Specialist personnel to ensure consistency. Neonatal outcomes such as birth weight, APGAR score and NICU admission were assessed following delivery of the baby.

STATISTICAL ANALYSIS

Data collection involved gathering demographic information and recording Doppler assessment results in a structured data collection proforma. Quantitative data such as age, UA PI, MCA PI, UtA PI were calculated as mean and standard deviation whereas parity, associated disorders, type of corticosteroid calculated as frequency and percentage. Data analysis was performed using IBM-Statistical Package for Social Sciences (SPSS) version 21.0 (IBM-SPSS Science Inc., Chicago, IL). Descriptive statistics summarized participant characteristics and paired or independent sample t-tests were used for comparative analysis of doppler indices across time points. A p-value<0.05 was considered significant.

RESULTS

A total of 84 pregnant women diagnosed with preterm FGR participated in the study. The mean age of participants was 28.4 years (± 5.2), with 40 (47.6%) aged between 25 to 30 years. The mean gestational age at enrolment was 32.5 weeks (± 2.3), and 60 (71.42%) of the participants were primigravida. Additionally, 18 (21.42%) had hypertension, and 2 (2.38%) presented with overt diabetes, 11 (13.09%) had hypothyroidism indicating a diverse clinical profile. In the present study both betamethasone 44 (52.38%) and dexamethasone 40 (47.62%) were used.

Doppler ultrasonography assessments revealed significant changes in UA and MCA Pulsatility Indices (PIs) following corticosteroid administration. At baseline, the mean UA PI was 0.95 (± 0.25). After treatment, it increased significantly to 1.05 (± 0.20) at 24 to 48 hours with $p=0.020$ but returned to 0.93 (± 0.21) at 72 to 96 hours, indicating a transient effect of corticosteroids [Table/Fig-1].

Hours	Mean PI	Timepoint between	Mean Difference for PI	p value*
'0'	0.95 \pm 0.25	'0' and 24-48 hours	0.107	<0.0001
24-48 hours	1.05 \pm 0.2	'0' and 72-96 hours	0.020	0.722
72-96 hours	0.93 \pm 0.21	24-48 and 72-96 hours	0.127	<0.0001

[Table/Fig-1]: Umbilical Artery (UA) PI with mean difference.

*p value <0.05 significant

In contrast, the MCA PI decreased significantly from a baseline mean of 1.83 ± 0.29 to 1.69 ± 0.20 at 24 to 48 hours and 1.65 ± 0.22 at 72 to 96 hours ($p<0.0001$) [Table/Fig-2].

Hours	Mean PI	Timepoint between	Mean Difference of PI	p value
0' hour	1.83 \pm 0.29	0 and 24-48 hours	0.139	<0.0001*
24-48 hours	1.69 \pm 0.20	0 and 72-96 hours	0.181	<0.0001*
72-96 hours	1.65 \pm 0.22	24-48 and 72-96 hours	0.042	0.126

[Table/Fig-2]: MCA PI with mean difference.

*p value <0.05 significant

The analysis of maternal UtA flow showed stable results, with the mean UtA PI remaining constant at $0.84 \pm (0.14)$ at baseline, 24 to 48 hours, and at 72 to 96 hours. This indicates that corticosteroid administration did not significantly influence maternal blood flow to the placenta, highlighting the need for stable UtA function in managing FGR [Table/Fig-3].

Hours	Mean	Standard Deviation (SD)
0 hour	0.84	0.14
24-48 hours	0.84	0.14
72-96 hours	0.84	0.14

[Table/Fig-3]: Uterine Artery (UtA) PI

In the present study it was found that the mean birth weight of babies were 1.92 ± 0.37 kilograms. 43 (51.19%) neonates had APGAR score <7 at 5 minutes and needed NICU admission. [Table/Fig-4]

Parameters	Number of babies (n)	Percentage (%)
Birth weight (Kg) (mean \pm SD)	1.92 \pm 0.37	
APGAR score		
<7	43	51.19
>7	41	48.81
Total	84	100
NICU admission		
Yes	43	51.19
No	41	48.81
Total	84	100

[Table/Fig-4]: Neonatal outcomes.

DISCUSSION

The findings from the present study significantly enhance the understanding of how ACSs affect foetal and uteroplacental blood flow dynamics in pregnancies complicated by preterm FGR. The varied changes observed in the UA and MCA PIs following corticosteroid administration highlight the complex interactions between maternal treatment and foetal hemodynamic adaptations.

In a study reported by Barkehall-Thomas A et al., and Elwany E et al., mean age of the patient was $27.6(\pm 5.1)$ and $27.7(\pm 4.5)$ years, respectively [9,14]. In present study, the mean age of the patient was $28.4 (\pm 5.2)$ years. The shared reproductive mean age is comparable. The proportion of primigravida mother reported by Choudhary N and Thuring A et al., were 40% and 66.6%, respectively [8,11]. However, the present study reported 71.42% of primigravida. This higher proportion of primigravida women in studies shows that primigravida had higher risk profiles compared to multigravida women.

Most common high-risk factor associated with FGR as reported by Edward A et al., [15] and Thuring A et al., [11] was hypertension (50% and 55%, respectively). In present study, although the proportion was less, 21.4%, hypertension was most common medical disorder in the mothers with FGR. This higher incidence of hypertension in all studies indicated that Gestational Hypertension (GHTN) was a relatively common medical disorder associated with FGR cohort, warranting careful monitoring and management. Regarding the use of corticosteroids, Barkehall-Thomas A et al., [14], Thuring A et al., [11], Edward A et al., [15] and Nozaki AM et al., [16] administered betamethasone, while Elwany E et al., utilised dexamethasone for the entire study population [9]. In contrast, the current study employed both betamethasone and dexamethasone. This variation in corticosteroid administration underscores how choices may differ based on institutional protocols and the availability of the drugs.

Elwany E et al., Edward A et al., and Nozaki AM et al., compared the UA PI values between 0 and 24 hours, reporting values of

1.09±0.4, 1.05±0.39; 2.5, 1.6; and 2.84, 2.06, respectively [9,15,16]. Thuring A et al., compared the UA PI values between 0 and 48 hours and reported the value as 1.9,1.43 [11]. Choudhary N et al., compared the same between 0 and 24-48 hours with values of 1.73±0.73 and 1.54±0.76, respectively [8]. Irrespective of individual UA PI values, each study showed significant reduction UA PI at 24 hours or 48 hours. However, Nozaki AM et al., reported the return of UA PI to baseline in 48 hours [16]. In contrast, present study showed significant increase of UAPI at 24-48 hours post-corticosteroid administration and returned to baseline values by 72-96 hours. This may be due to difference in study population. In the studies referred to, FGRs were having abnormal doppler flow, whereas present study included FGR with normal Doppler flow.

An analysis of MCA PI values from the studies by Elwany E et al., [9], Choudhary N et al., [8] and Edward A et al., [15] between '0' and 24-48 hours revealed a significant reduction. In contrast, no changes were observed in the studies by Thuring A et al., and Nozaki AM et al., [11,16]. In the present study, MCA PI also decreased significantly from '0' hours to both 24-48 hours after corticosteroid administration, indicating a beneficial effect; however, the difference in reduction between the 24-48 hour and 72-96 hour intervals was not statistically significant.

On analysis of Ut A PI significant reduction was observed in the studies by Elwany E et al., and Edwards A et al., between '0' and 24 hours [9,15]. Choudhary N et al., and Thuring A et al., didn't observe any significant change [8,11]. Similar to Thuring A et al., [11] and Choudhary N et al., [8] present study shows no change in UtA suggesting that corticosteroid administration did not significantly affect the maternal blood flow to the placenta. This finding highlights that consistent UtA flow is critical for maintaining adequate placental function throughout pregnancy, particularly in FGR cases where placental insufficiency is a prevailing concern.

The birth weights reported by Barkehall-Thomas A et al., [14], Thuring A et al., [11], Edwards A et al., [15] and Nozaki AM et al., [16] were 1172 g, 660 g, 813 g, and 806.6 g, respectively, indicating confirmed FGR. In the present study, the mean birth weight was observed to be 1.92 kg. This variation is likely due to differences in the study populations. The percentages of neonates with an APGAR score of less than 7 at 5 minutes were 40.4%, 23%, and 12.5%, respectively in the studies by Elwany E et al., Thuring A et al., and Nozaki AM et al., [9,11,16]. In the present study, 51.1% of neonates had an APGAR score of less than 7 at 5 minutes post-birth and required NICU admission. Although the study population in the current research had normal Doppler flow, the reason for the higher proportion of low APGAR scores at five minutes compared to the other studies remains unclear. Further investigation is necessary to understand the underlying factors contributing to this discrepancy.

Limitation(s)

The limitations of the present study are it is single-centred study, both dexamethasone and betamethasone were used as per availability and inability to explain the high proportion of low APGAR score with NICU admission in spite of normal doppler before corticosteroid administration. Further research is suggested, as randomised multi-

centre trials comparing both betamethasone and dexamethasone for preterm FGR may be conducted.

CONCLUSION(S)

The present study highlights the substantial influence of maternal corticosteroids on foetal and uteroplacental blood flow dynamics in preterm pregnancies affected by FGR. Notable findings include a temporary increase in the UA PI and a persistent decrease in the MCA PI, suggesting enhanced placental perfusion and improved cerebral blood flow. These changes underscore the significance of optimising foetal blood flow through corticosteroid therapy resulting in favourable neonatal outcome. However, continued research will be crucial to enhance our understanding of the long-term effects of corticosteroids and to create tailored clinical interventions that prioritise both maternal and foetal health in this vulnerable group.

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