The Egyptian Journal of Hospital Medicine (October 2020) Vol. 81 (5), Page 2046-2053

Changes in Fetal and Uteroplacental Doppler Waveforms After Antenatal Dexamethasone Administration in Women at Risk of Spontaneous Preterm Birth

Mohamed Elsibai Anter[1], Ayman Abd Elkader Shabana[1], Sally Mohamed Ali Badr[2], Nehad Mahmoud Hoseny[1]

[1]Obstetrics and Gynecology Department, Faculty of Medicine, Menoufia University, Menoufia, Egypt

[2]Obstetrics and gynecology department, El-Bagour general Hospital, Menoufia, Egypt

***Corresponding author:** Mohamed E. Anter, **Mobile:** +20 1224462910, **Email:** Mohamedsibai681@yahoo.com

ABSTRACT

Background: Early detection of fetal risk is one of the main issues in today's obstetrics. Ultrasound diagnosis plays a significant role, as the introduction of the Doppler imaging method in the evaluation of blood flow has enabled non-invasive assessment of uteroplacental circulation.

Objective: To assess the impact of maternal dexamethasone on doppler waveforms velocity flow of the fetal umbilical and middle cerebral arteries and maternal uterine arteries in pregnant women at risk of preterm labor with normal fetal vascular resistance.

Patients and methods: This cross-sectional study was conducted at the Department of Obstetrics and Gynecology at Menoufia University hospital on 36 patients who were diagnosed as having threatened preterm birth. All the patients were enrolled in the study with routine follow up according to local protocols in the period between January 2019 and November 2019. Full history taking, full general, obstetric examination, and Ultrasound examination was performed.

Results: After dexamethasone administration, Umbilical A resistive and Pulsatility indexes were significantly decreased to (1.084 ± 0.118 and 0.66 ± 0.054) in comparison to before dexamethasone (1.121±0.124 and 0.70±0.058). Regarding the Uterine Doppler values, mean Pulsatility index before dexamethasone was 0.79±0.049 (right) and 0.78 ±0.038 (left) decreased significantly to 0.78±0.044 (right) and 0.77±0.036 (left) after dexamethasone. Similarly, the mean Resistive index before dexamethasone was 0.55±0.027 (right) and 0.54±0.026 (left) decreased significantly to 0.53±0.023 (for right and left) after dexamethasone.

Conclusions: dexamethasone administration for the pregnant mothers at risk of preterm labor enhance the flow of blood to the fetal umbilical, middle cerebral arteries and maternal uterine arteries 24 hrs. after its administration.

Keywords: Antenatal, Dexamethasone, Doppler waveforms, Fetal Health, Preterm Birth, Uteroplacental.

INTRODUCTION

Artificial corticosteroids have been successfully used for more than 20 years to promote the maturity of the fetal lung in situations where early birth is expected [(1)]. Maternal administration of artificial corticosteroids (betamethasone or dexamethasone), decreases newborn deaths, syndrome of respiratory distress, intraventricular hemorrhage, and necrotizing enterocolitis in preterm infants [(2)]. Serious side-effects on the neonate have not been described when prenatal treatment has been administered during the second half of pregnancy [(3)]. However, a transient decrease in fetal heart rate, fetal body movements, and Respiratory movements was confirmed after maternal betamethasone administration [(4)]. Biophysical activities monitoring is a powerful tool known for assessing fetal health. Studies presented initial evidence that antenatal steroids to improve the maturity of the fetal lung may lead to transient depression of biophysical activities of the fetus [(5)]. Indeed, conflicting results have been reported regarding the effects of betamethasone and dexamethasone on the fetal heart pattern [(2)]. Lately, Miller found that betamethasone and dexamethasone were accompanied by an increase in the long term and short-term variability and a decrease in the movements of the fetus on the first day after steroid administration followed by a decrease in heart rate variability of the fetus in the following day [(6)]. Conversely, another trial described a transient decrease in fluctuations of the fetal heart rate, fetal body, and respiratory movements after betamethasone, while still noting. On the first day after dexamethasone fetal heart rate fluctuations were increased [(7)]. These effects were more pronounced with betamethasone than dexamethasone [(8)].

Alteration of fetal heart rate characteristics was first recognized in 1995 [(9)]. It has been determined that, in more than a third of the examined fetuses, computerized fetal heart rate variation fell below the normal range, and this may indicate fetal hypoxemia [(10)]. Fetal health assessment with doppler waveform studies after maternal corticosteroid administration could therefore be considered important [(2)]. However, knowledge of the different fetal hemodynamic effects after exogenous corticosteroids is limited [(11)].

Another way to assess a fetus's condition is to measure the Doppler flow velocity of the umbilical artery and MCA of the fetus. This technique may be useful in specifying a fetus at risk and can be of clinical value in the differential diagnosis between changes caused by therapy in the biophysical behavior of the fetus and that of the fetal compromise [(12)]. Moreover antenatal administration of corticosteroids, given to accelerate the maturity of fetal lung and improve

Received:18 /7 /2020
Accepted:17 /9 /2020

perinatal outcome in pregnancies at risk of preterm birth, also increase secretion of corticotrophin-releasing hormone (CRH) which is a potent vasodilator of the fetal placental circulation and up-regulate the placental expression of it providing the possibility that corticosteroid therapy can change the blood flow of placental [7].

The present study aimed to assess the changes in fetal and uteroplacental Doppler waveforms after antenatal dexamethasone administration in women at risk of spontaneous preterm birth.

SUBJECTS AND METHODS

This cross-sectional study was conducted at the Obstetrics and Gynecology Department, Menoufia University Hospital from January 2019 to November 2019 after approval of the ethical committee of Menoufia Faculty of Medicine. The study included 36 women who were at risk of premature birth with uncomplicated singleton pregnancies between 24 and 34 weeks of pregnancy.

Ethical consideration: After obtaining approval from the local ethics committee of Menoufia University, women who agreed to participate gave their signed informed consent after the explanation of the trial benefits and hazards. All procedures were carried out following the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. **The trial was registered with the local ethics committee of the Faculty of Medicine, Menoufia University (Registration number: 11/2019OBSGN 27).**

Inclusion criteria:

The study included 36 women who were at risk of premature birth with uncomplicated singleton pregnancies between 24 and 34 weeks of pregnancy.

Exclusion criteria:

Patients with underlying medical illness, contraindication of corticosteroids administration, pregnancies with infants with major structural malformations, cases with Rh-negative mothers with a history of synthetization or positive Comb's test or other cases of documented fetal anemia, preeclamptic and diabetic mother were excluded.

Sample size: was calculated using PASS 11.0 and based on the expected mean difference for UA PI ratio of 0.04 between pre and post dexamethasone administration**. (13)** Assuming = 0.05 (standard value of 1.96), we calculated that we would need 36 pre-term patients to achieve a power of 80% (0.8).

At the time of Preliminary examination, all pregnant women had normal uteroplacental blood flow and at risk of preterm labor including prior preterm labor, preterm premature rupture of membrane, increase amniotic fluid, placenta previa, third trimester bleeding, and the previous history of uterine rupture or hysterotomy.

All cases were subjected to the following:

Complete history taking including personal history of mother: Name, age, residence, occupation, social, marital status and special habits of medical importance particularly smoking, alcohol intake or drug abuse, past history of medical problems, mode of delivery, gestational age by date and first trimetric ultrasonography and any medical problems or drug-taking during this pregnancy.

Past obstetric history including previous preterm labor, previous D &C, previous sections, previous uterine operations, complications in previous pregnancies, and during cesarean section.

Complete general examination: including vital signs, chest, cardiac, lower limbs, upper limbs, and breast examinations.

Abdominal examination:

Inspection: looking for fetal movement, scars of the previous Operation, any stria gravidarum or line anigra, and for evaluation of the uterus shape and observation of asymmetry. Palpation: assessment of fundal level. Auscultation: fetal heart auscultation.

Ultrasound examination using 2D grayscale and color Doppler (IBE Sonata plus ultrasound systems) via transabdominal approach the examination was done in supine slightly left lateral oblique position during the examination to avoid hypotension, fetal biometry was done including abdominal circumference (AC), femur length (FL), head circumference (HC), and biparietal diameter (BPD). Estimated fetal weight was calculated according to Hadlock formulas. Furthermore, amniotic fluid volume, placental grade, and Complete anomaly scan was done to exclude any structural abnormalities. Biophysical Profile Before Doppler assessment including Ultrasonography observations for fetal behavior for 30 minutes taking into consideration fetal tone, limb and breathing movements, and amniotic fluid index **[14].**

All pregnancies received steroid treatment in form of four consecutive doses of 6mg of intramuscular dexamethasone (Dexamethasone 8 ml, Sigma) 12 hours apart. The evaluation was done before and 24h after completion of the dexamethasone course by using a real-time ultrasound machine (IBE Sonata plus ultrasound systems) equipped with a convex linear 3–5MHz vector transducer with pulsed and color doppler options was used on the umbilical artery (UA), fetal (MCA) and maternal uterine arteries according to **Marchi *et al.* [15].**

Doppler's technique: In all Doppler measures, the angle of insonation should ideally be less than 30 ° near 0. The sweeping speed is 2.5 cm / s and the frequency of the pulse frequency range was from 3.5 to 5.5 kHz. Doppler spectrum recording during maternal voluntary apnea **(16)**. Doppler flow velocity waveforms (FVW) studies were done with pulsed-wave Doppler after real-time color flow localization of the umbilical artery, Middle cerebral artery, and uterine artery **(17).**

Umbilical Artery Doppler: The uterine contents are quickly scanned by the real-time ultrasound to select an area of the amniotic cavity with several loops of the umbilical cord, **(Figure 1a).** Ideally, these cord loops should not be close to the cord insertion.[18] Then using the Doppler pulsed-wave on a free loop of cord the distinctive sound and form of the umbilical artery waveform was demonstrated and the captured image was identified, (RI), (PI) were evaluated. An average of at least 3 separated readings will be calculated before getting the final values.

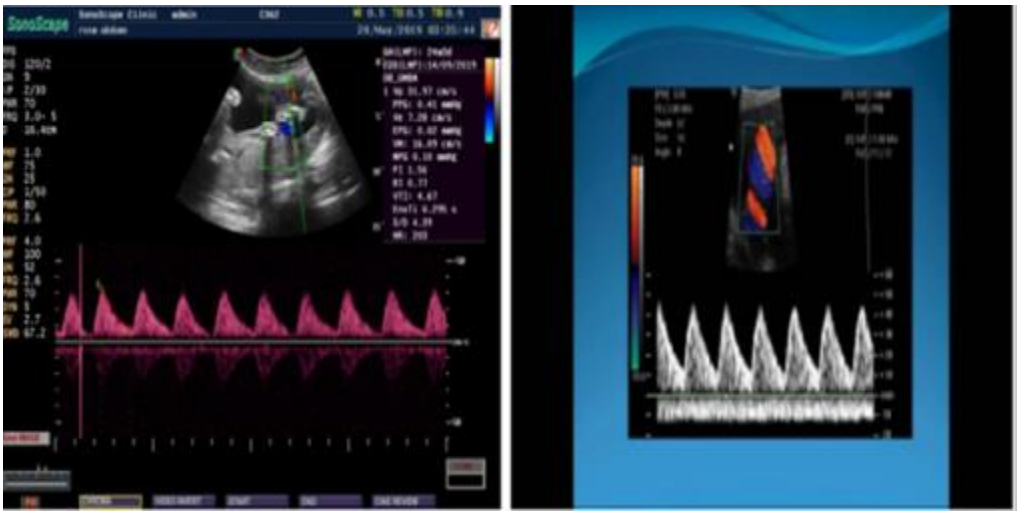

Fig. (1a): Doppler waveform of the umbilical artery. The uterine contents are quickly scanned by the real-time ultrasound to select an area of the amniotic cavity with several loops of the umbilical cord.

The Middle Cerebral Artery: The standard plane is visualized to measure the diameter of the biparietal bone. This plane involves the hypothalamus and the cave of septum pellucidum, **(Figure 1b)** **(19)**. The transducer was then moved towards the base of the skull at the level of the sphenoid bone (lower wing). Using imaging of color flow, the middle cerebral artery was seen as the main side branch of Willis circle, locating laterally in the borderline between the anterior and middle brain fossa.

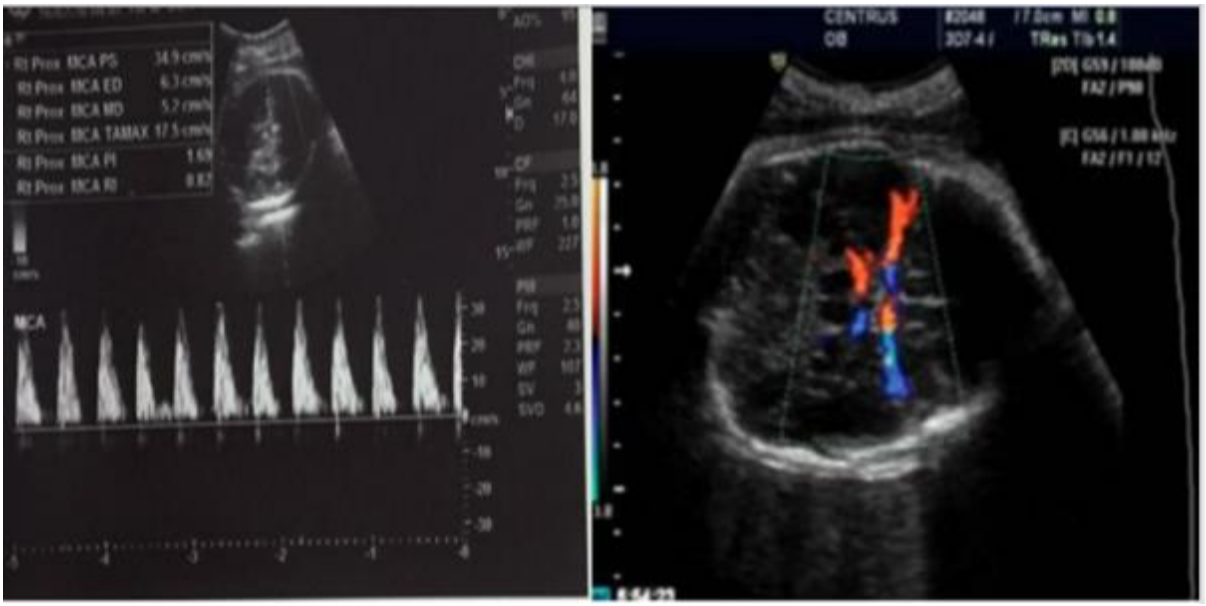

Fig. (1b): Doppler waveform of MCA. The standard plane is visualized to measure the diameter of the biparietal bone. This plane involves the hypothalamus and the cave of the septum pellucidum.

The pulsed Doppler sample gate was then positioned on the proximal third of the MCA, close to its origin in the internal carotid artery to get flow velocity waveforms [(20)], when the screen appeared with at least 3 sequential waveforms of the same height, the image was taken and MCA RI and PI were evaluated. At least 3 detached readings were calculated before the final values were received, caution must be taken for applying the minimum pressure on the mother's abdomen with the transducer, as the pressure on the fetal head is related to changes in intracranial arterial waveforms in normal gestations the diastolic component of the cerebral arteries is less than the umbilical arteries at any age of the pregnancy. So, the resistance of cerebral vascular remains higher than that of the placenta.

The Uterine Arteries: to localize the Uterine artery. The probe is placed longitudinally and angled medially in the lower lateral quadrant of the abdomen. Color flow mapping was useful to identify the left and right uterine arteries at the apparent cross over the external iliac artery. The sample gate was set at 2 mm, and measurements were taken 1cm distal to the site of crossing Doppler is used to obtain the waveforms, when at least three similar consecutive waveforms are obtained **(Figure 1c)** [(21)].

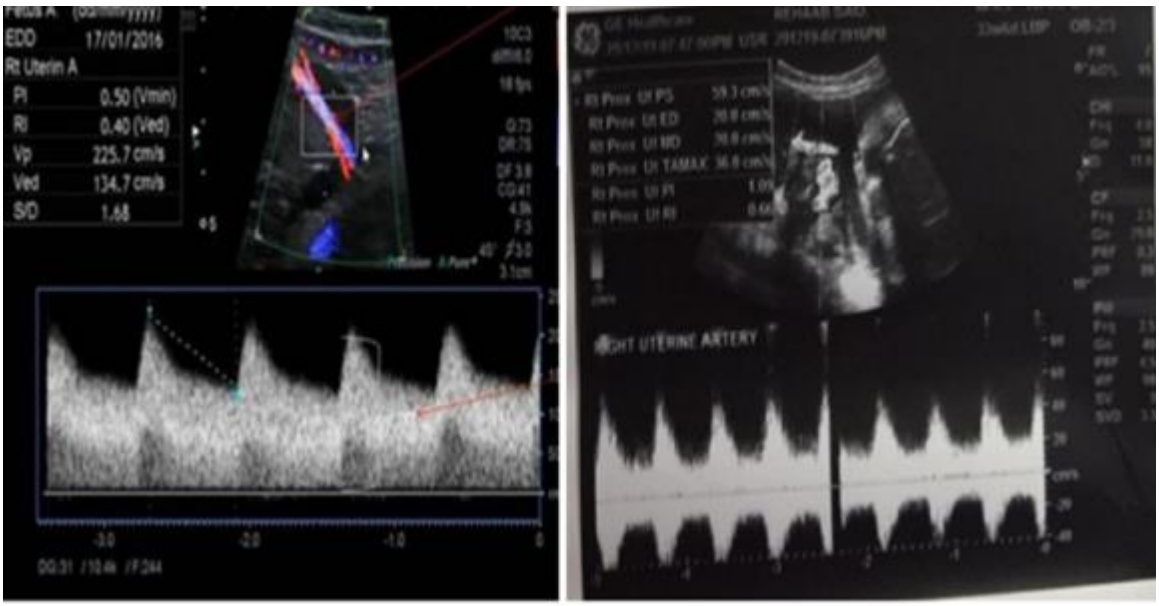

Fig. (1c): Doppler waveform of Uterine a. The sample gate was set at 2 mm, and measurements were taken 1cm distal to the site of crossing Doppler is used to obtain the waveforms, when at least three similar consecutive waveforms are obtained.

Statistical analyses

Results were scheduled and analyzed statistically using a PC and programs of MICROSOFT EXCEL 2016 and SPSS v. 21 (SPSS Inc., Chicago, IL, USA**.** Statistical analysis was done using Descriptive: e.g. percentage (%), mean, and standard deviation. Analytical: that involves Paired t-test. A value of P less than 0.05 was considered statistically significant.

RESULTS

In the present study, the mean age of the studied women was 24.58 ± 4.12 years, mean systolic and diastolic blood pressure was 115.0±16.73 and 76.67±10.82 respectively. While the mean gestational age was found to be 28.14 ± 2.97 weeks at examination and 31.58±2.79 at delivery. Regarding Ultrasound findings mean Femur length and Biparietal diameter was 5.26 ± 0.78 and 6.98 ± 0.76 respectively, mean head circumference 25.83±2.67mm, mean abdominal circumference was 23.36±2.24 mm, and mean fetal weight was 1256.44±440.42 gm**.** The current study showed that 18 neonates (50%) had Referral to PCU, 22 neonates (61.1%) had a 1-minute APGAR score <7 and 14 (38.9%) had 5 minutes APGAR score <7, more than half (58.3%) of neonates were females. Also, birth weight was in the range from 980-2618 gm with a mean of 1715.67 ± 432.88. Also, the current study shows that Gestational age was significantly increased at delivery (31.58 ± 2.79 wks.) than at examination (28.14 ± 2.97 wks.) with p-value <0.001 **(Table 1)**.

Table (1): Descriptive analysis of the studied cases regarding maternal and neonatal characteristics and Ultrasound findings (n=36)

Maternal characteristics	**Min. – Max.**	**Mean ± SD.**	**Median (IQR)**
Age (years)	18.0 – 34.0	24.58 ± 4.12	24.0 (21.50 – 28.0)
Parity	0.0 – 5.0	2.08 ± 1.27	2.0(1.0 – 3.0)
Blood pressure			
Systolic	90.0 – 140.0	115.0 ± 16.73	115.0(100.0–130.0)
Diastolic	60.0 – 95.0	76.67 ± 10.82	77.50(67.50 –87.50)
Gestational age			
At examination	24.0 – 33.0	28.14 ± 2.97	28.50(25.50 –30.0)
At delivery	26.0 – 36.0	31.58 ± 2.79	32.0(30.0 –34.0)
Ultrasound findings			
Femur length	4.06 – 6.89	5.26 ± 0.78	5.16(4.56–5.76)
Biparietal diameter	5.45 – 8.22	6.98 ± 0.76	7.20(6.27–7.54)
Head circumference	21.56 – 30.96	25.83 ± 2.67	26.10(23.22–27.39)
Abdominal circumference	18.79 – 26.89	23.36 ± 2.24	23.97(21.19–24.72)
Fetal weight in gm	645.0 – 2162.0	1256.44 ± 440.42	1223.5(795.5–1595.0)
Biophysical score	6.0 – 8.0	7.78 ± 0.64	8.0(8.0–8.0)
Neonatal characteristics	**Min. – Max.**	**Mean ± SD.**	**Median (IQR)**
Birth weight	980.0 – 2618.0	1715.67 ± 432.88	1698.5(1319.5-2080.5)
Gestational age	**Min. – Max.**	**Mean ± SD.**	**Median (IQR)**
At examination	24.0 – 33.0	28.14 ± 2.97	28.50(25.50 –30.0)
At delivery	26.0 – 36.0	31.58 ± 2.79	32.0(30.0 –34.0)
Referral to PCU	18 (50.0%)		
1-minute APGAR score <7	22 (61.1%)		
5 minutes APGAR score <7	14 (38.9%)		
Gender			
Male	15 (41.7%)		
Female	21 (58.350		

Our study evaluated that there was a significant decrease after dexamethasone taking in the UAPI value (from 1.121±0.124 to 1.084±0.118). Similarly, significant changes in the mean values of umbilical A RI in comparison to its value before dexamethasone administration (from 0.70± 0.058 to 0.66 ± 0.054). There was a significant decrease after taking dexamethasone in the MCA PI (from 2.04 ± 0.162 to 1.98 ± 0.171), with a significant change in MCA RI **(Table 2).**

Table (2): Umbilical A and fetal MCA before and after dexamethasone administration (n=36)**.**

		Before dexamethasone	**24 After dexamethasone**	**Paired t-test**	**P-value**
Umbilical A	PI Mean ± SD. Min. – Max. Median (IQR)	 1.121 ± 0.124 0.81 – 1.47 1.12(1.09 – 1.16)	 1.084 ± 0.118 0.78 – 1.43 1.09(1.03 – 1.13)	4.16	0.012*
	RI Mean ± SD. Min. – Max. Median (IQR)	 0.70± 0.058 0.55 – 0.82 0.69(0.66 – 0.73)	 0.66 ± 0.054 0.53 – 0.80 0.65(0.63 – 0.68)	3.72	0.035*
Fetal MCA	PI Mean ± SD. Min. – Max. Median (IQR)	 2.04 ± 0.162 1.52 – 2.21 2.09(1.90–2.18)	 1.98 ± 0.171 1.50 – 2.18 2.05(1.86–2.15)	3.95	0.027*
	RI Mean ± SD. Min. – Max. Median (IQR)	 0.81 ± 0.040 0.70 – 0.89 0.81(0.81–0.85)	 0.79± 0.033 0.70 – 0.88 0.80(0.80–0.85)	1.98	0.042*

Pulsatility index (PI), Resistive index (RI), * significant

Regarding the Uterine artery Doppler values, there were significant changes in the Pulsatility index and Resistive index before dexamethasone and 24 after dexamethasone. Mean Pulsatility index before dexamethasone was 0.79 ± 0.049 (right) and 0.78 ± 0.038 (left) decreased to 0.78 ± 0.044 (right) and 0.77 ± 0.036 (left) at 24 after dexamethasone. Also, mean Resistive index before dexamethasone was 0.55 ± 0.027 (right) and 0.54 ± 0.026 (left)

decreased to 0.53 ± 0.023 (for right and left) at 24 after dexamethasone, **(Table 3).**

Table (3): Uterine A before and after dexamethasone administration (n=36)**.**

Uterine A		Before dexamethasone	24 After dexamethasone	Paired t-test	P-value
Pulsatility index (PI)	Right Mean ± SD. Min. – Max. Median (IQR)	0.79 ± 0.049 0.71 – 0.91 0.78(0.76 – 0.80)	0.78 ± 0.044 0.69 – 0.89 0.77(0.76 – 0.79)	3.84	0.029*
	Left Mean ± SD. Min. – Max. Median (IQR)	0.78 ± 0.038 0.72 – 0.91 0.78(0.76 – 0.79)	0.77 ± 0.036 0.71 – 0.90 0.77(0.75 – 0.79)	3.292*	0.035*
Resistive index (RI)	Right Mean ± SD. Min. – Max. Median (IQR)	0.55 ± 0.027 0.50 – 0.60 0.55(0.52 – 0.57)	0.53± 0.023 0.50 – 0.59 0.54(0.52 – 0.55)	3.084*	0.037*
	Left Mean ± SD. Min. – Max. Median (IQR)	0.54 ± 0.026 0.50 – 0.59 0.54(0.52 – 0.55)	0.53 ± 0.023 0.50 – 0.58 0.53(0.51 – 0.55)	2.183*	0.040*

* Highly significant

DISCUSSION

Fetal (MCA PI/RI and UMA PI/RI) and maternal uterine arteries Doppler is a valuable diagnostic method in the evaluation of fetus's circulation. The current prospective observational study was designed to evaluate and compare fetal Doppler indices in the form of MCA PI/RI, UMA PI/RI, and maternal uterine arteries before and 24 hrs. after corticosteroid administration in a group of pregnant women at risk of preterm birth with gestational age between 24 to 34 weeks aiming to determine if corticosteroids administration has any effect on doppler indices or not. In the current study, umbilical artery Doppler indices showed a statistically significant decrease after 24 hours of taking dexamethasone. In agreement with our results, **Wallace and Baker**[(22)] study found a relationship between decreased placental vascular resistance and corticosteroid therapy as reflected by the waveforms obtained from the umbilical artery. The study of **Nozaki *et al.*** [(23)]**,** agreed with our study who found a decrease in the PI umbilical artery through 24 hours after parenteral corticosteroid treatment. Two studies on premature growth-restricted fetuses disagreed with our study showed that no impacts on PI in the umbilical artery**.** This may be because of the difference in the study population as they involved pregnant women with IUGR only, whereas our study involved all women who had a risk of early delivery. The distribution of blood vessels in blood flow in IUGR differs compared to normal growth fetuses [(8, 23)]**.**

The middle cerebral artery was examined also in our study before and 24hrs after taking dexamethasone. MCA Doppler indices decreased after therapy. The same results with those of **Chitrit *et al.*** [(2)]**,** which fetal MCA PI and RI had a significantly transient decrease after maternal dexamethasone administration**.** However, some studies differ with our outcomes but their study was on growth-restricted preterm fetuses where there was no impact found on PI in the fetal MCA [(8, 24)].

The two studies, by **Senat and Ville** [(8)] **and Tehrani *et al.*** [(24)]**,** reported that fetal circulation was studied for up to 14 days, pointing to the placenta insufficiency which may not have been severe enough to indicate premature birth. Furthermore, Senat and Ville in 2000 examined the impact of steroids on blood flow forms in IUGR fetuses, and no significant changes in PI and RI values were found in different vessels after the course of dexamethasone. However, the MCA PI showed a downtrend during the course and after stopping treatment. The change of its value can be explained by either the physiological deficiency of resistance in the brain of the fetus with the pregnancy predicted to be more pronounced in IUGR fetuses or the early mark of a redistribution of the flow of blood.

There was a statistically significant decrease in uterine artery Doppler Indices after 24 hrs. of taking dexamethasone in the current study. These results are consistent with the published data by **Chitrit *et al.*** [(2)], who noticed a significant transient decrease in the artery of uterine PI and RI after giving mothers dexamethasone in a healthy fetus. Also, **Wallace and Baker**[(22)]**,** found that there is an association between dexamethasone administration and a decrease in wave velocity of uterine artery flow in their study. However, **Thuring *et al.*** [(4)]**,** reported that there was no significant effect of corticosteroid treatment on Doppler indices in the uterine circulation in pregnancies with preterm premature birth**.** Although the moral mechanisms that illustrate a transient change in Doppler indices after giving maternal dexamethasone still unclear, there are some explanations such as **El Snosy *et al.*** [(13)] changes in blood flow to the fetal brain are unlikely to occur after dexamethasone treatment due to constriction of the ductus arteriosus. But also there is a central role of steroids through the circulatory mechanisms mostly fetal

hypertension may occur mentioned by **Koenen *et al.* [28].** Also, there is placenta secretion of the hormone-secreting corticosteroids that causes vasodilation [2]. There is an increase in blood pressure of the fetus which might explain the improved fetal perfusion. Also, a decrease in placenta resistance as a result of vasodilation by nitric oxide due to the increased secretion of the hormone secretion corticotropin is another indication. It was more likely to be useful in predicting the result of dexamethasone administration as Doppler data that combines the measurement of umbilical, cerebral, and uterine speed reflects that there is no evidence that these effects on the flow of blood are harmful to the fetus, but the most worrisome is data indicating a neurotoxic effect of dexamethasone [28].

Limitations of this study were Neonatal outcome was not assessed accurately because the PH of the umbilical artery was not measured after delivery due to reduced facilities in our hospital, so we only relied on the Apgar score. Also, a larger sample size was needed to be able to match Doppler results with gestational age. This study does not determine whether Dexamethasone is better than other steroids for the prevention of prematurity complications. Also, caution must be practiced especially with repeated courses.

CONCLUSION

Finally, we conclude that giving dexamethasone to pregnant women at risk of preterm labor enhances the flow of blood in the fetal umbilical and middle cerebral arteries and maternal uterine arteries after 24 hours of its administration.

Conflict of interest: No conflict of interest

Fund: No fund

Acknowledgment: Nil

Financial support and sponsorship: We have not received any funding from any corporate body or pharmaceutical company.

REFERENCES

1. **Cahill L, Hoggarth J, Lerch J *et al.* (2019):** Fetal brain sparing in a mouse model of chronic maternal hypoxia. Journal of Cerebral Blood Flow and Metabolism, 39(6):1172-84.
2. **Chitrit Y, Caubel P, Herrero R *et al.* (2000):** Effects of maternal dexamethasone administration on fetal Doppler flow velocity waveforms. BJOG: An International Journal of Obstetrics & Gynecology, 107(4):501-7.
3. **Royal College of Obstetricians and Gynecologists (2004):** About abortion care: what you need to know. London: RCOG.http://www.rcog.org.uk/womens-health/clinical-guidance/about-abortion-care-what-you-need-know
4. **Thuring A, Malcus P, Marsal K (2011):** Effect of maternal betamethasone on fetal and uteroplacental blood flow velocity waveforms. Ultrasound Obstet. Gynecol., 37(6):668–672.
5. **Yahia A, Hesham M (2018):** Corticosteroids Administration for Enhancement of Fetal Lung Maturity and its Effects on Doppler Indices. The Medical Journal of Cairo Universit., 86:35-41.
6. **Miller S, Chai M, Loose J *et al.* (2007):** The effects of maternal betamethasone administration on the intrauterine growth-restricted fetus. Endocrinology, 148(3):1288-95.
7. **Scheepens A, van de Waarenburg M, van den Hove D *et al.* (2003):** A single course of prenatal betamethasone in the rat alters postnatal brain cell proliferation but not apoptosis. The Journal of Physiology, 552(1):163-75.
8. **Senat M, Ville Y (2000):** Effect of steroids on arterial Doppler in intrauterine growth retardation fetuses. Fetal Diagnosis and Therapy, 15(1):36-40.
9. **Derks J, Mulder E, Visser G (1995):** The effects of maternal betamethasone administration on the fetus. BJOG: An International Journal of Obstetrics & Gynecology, 102(1), 40-46.
10. **Neilson J (2008):** Fetal scalp sampling in labor. BMJ., 336(7656): 1257–1258.
11. **Harman C, Ahmet A (2003):** Comprehensive assessment of fetal wellbeing: which Doppler tests should be performed? Current Opinion in Obstetrics and Gynecology, 15(2):147-157.
12. **Yagel S, Cohen S, Valsky D (2019):** Simplifying imaging of the abdominal fetal precordial venous system. Ultrasound in Obstetrics & Gynecology, 53(5):571-575.
13. **Elsnosy E, Shaaban O, Abbas A *et al.* (2017):** Effects of antenatal dexamethasone administration on fetal and uteroplacental Doppler waveforms in women at risk for spontaneous preterm birth. Middle East Fertility Society Journal, 22(1):13-7.
14. **Tehrani H, Khani B, Komrani Z (2014):** Comparison of the effect of betamethasone versus dexamethasone on the amniotic fluid index in the women at risk of preterm labor. Journal of research in medical sciences: the official journal of Isfahan University of Medical Sciences, 19(12):1124-29.
15. **Marchi L, Pasquini L, Elvan-Taspinar A *et al.* (2020):** Cardiovascular Hemodynamic Changes After Antenatal Corticosteroids in Growth Restricted and Appropriate for Gestational Age Fetuses. Ultraschall in der Medizin-European Journal of Ultrasound, 41(03): 292-299.
16. **Nardozza L, Júnior E, Rizzo G *et al.* (2018):** Fetal Growth Restriction: Current Evidence and Clinical Practice. https://www.springer.com/gp/book/9783030000509
17. **Wafa Y, Mohammed F, Deif O *et al.* (2019):** The Value of Middle Cerebral Artery and Umbilical Artery Doppler Indices in Assessment of Fetal Wellbeing and Prediction of Neonatal Outcome in Preeclampsia. The Egyptian Journal of Hospital Medicine, 74(7):1516-24.
18. **Adekanmi A, Roberts A, Akinmoladun J *et al.* (2019):** Uterine and umbilical artery doppler in women with pre-eclampsia and their pregnancy outcomes. Nigerian Postgraduate Medical Journal, 26(2):106-109.
19. **Murthy B (2019):** Imaging of Fetal Brain and Spine: An Atlas and Guide. Springer. https://www.amazon.com/Imaging-Fetal-Brain-Spine-Atlas/dp/9811358435

20. **Bhide A, Acharya G, Bilardo C *et al.* (2013):** ISUOG practice guidelines: use of Doppler ultrasonography in obstetrics. Ultrasound in Obstetrics & Gynecology: the official journal of the International Society of Ultrasound in Obstetrics and Gynecology, 41(2):233-8.
21. **Chaudhry R, Chaudhry K (2018):** Anatomy, Pelvis, Uterus, Arteries, Uterine. (updated 2018 In: Stat Pearls (internet) Treasure Island (FL): Stat Pearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK482267/.
22. **Wallace E, Baker L (1999):** Effect of antenatal betamethasone administration on placental vascular resistance. The Lancet, 353(9162):1404-1407.
23. **Nozaki A, Francisco R, Fonseca E *et al.* (2009):** Fetal hemodynamic changes following maternal betamethasone administration in pregnancies with fetal growth restriction and absent end-diastolic flow in the umbilical artery. Acta obstetricia et Gynecologica Scandinavica, 88(3):350-4.
24. **Wijnberger L, Bilardo C, Hecher K *et al.* (2004):** Effect of antenatal glucocorticoid therapy on arterial and venous blood flow velocity waveforms in severely growth-restricted fetuses. Ultrasound in Obstetrics and Gynecology, 23(6):584-549.
25. **Mousavi S, Taghavi S, Abbasalizadeh F *et al.* (2019):** Changes in fetal circulation after maternal corticosteroid administration: a systematic review. Int J Fertil Women's Med., 7(2):156-162.
26. **Robinson B, Emanuel R, Frim D *et al.* (1988):** Glucocorticoid stimulates expression of corticotropin-releasing hormone gene in human placenta. Proceedings of the National Academy of Sciences, 85(14):5244-5248.
27. **Korebrits C, Yu D, Ramirez M *et al.* (1988):** Antenatal glucocorticoid administration increases corticotrophin-releasing hormone in maternal plasma. Br J Obstet Gynaecol., 105: 556– 561.
28. **Koenen S, Mecenas C, Smith G *et al.* (2002):** Effects of maternal betamethasone administration on fetal and maternal blood pressure and heart rate in the baboon at 0.7 of gestation. Am J Obstet Gynecol., 186:812–817.
29. **Clifton V, Read M, Leitch I *et al.* (1994):** Corticotropin-releasing hormone-induced vasodilatation in the human fetal placental circulation. The Journal of Clinical Endocrinology & Metabolism, 79(2):666-669.