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Effects of Antenatal Dexamethasone Administration on Feto-Placental Doppler and its Correlation with Perinatal Outcome in Cases of Placental Insufficiency

Esraa Mohamed Hassan Hemida[1], Magdy AbdelMohsen Olama[1] and Hager Abd El-Gawad Magdy[1]

[1]Department of Obstetrics & Gynecology, Faculty of Medicine for Girls, Al-Azhar University, Cairo, Egypt.

***E-mail: dresraamhassan2017@gmail.com**

Abstract

One of the common reasons for abnormal growth in the otherwise normal foetus is uteroplacental insufficiency and dysfunction. The aim of this paper assesses dexamethasone effects on fetal Umbilical and middle cerebral arteries as measured by Doppler ultrasonography after 24 hours following antenatal dexamethasone administration in cases of Placental insufficiency and impact of fetoplacental circulation variations on perinatal result. This study was a prospective cohort study that was conducted on 60 cases with singleton pregnancy were recruited from the 28th to the 36th weeks of gestation for administration of antenatal corticosteroids and were divided into two groups: Group A: 30 pregnant women complicated with placental insufficiency and Group B: 30 pregnant women with normal placental blood flow served as controls, at Al-Zahraa University Hospital of Al-Azhar University from November 2020 till November 2021. There is study showed that, following dexamethasone administration, group A showed a highly significant reduction in Umbilical artery RI, S/D ratio, middle cerebral artery-RI as compared with their baseline levels (P-value<0.001) and a significant difference in middle cerebral artery-RI and middle cerebral artery-PI (P-value = 0.002). Dexamethasone can improve blood flow in the foetal umbilical and middle cerebral arteries after only 24 hours of treatment in pregnant women with placental insufficiency, as measured by Doppler indices.

Keywords: Antenatal, Dexamethasone, Feto-placental, Doppler, Perinatal Outcome and Placental insufficiency.

1. Introduction

One of the common reasons for abnormal growth in the otherwise normal foetus is uteroplacental insufficiency or dysfunction. [1]

Preterm labour is the primary reason for perinatal morbidity and mortality globally, and placental insufficiency is connected to a number of obstetric illnesses, including pre-eclampsia and intrauterine growth restriction. Poor placental function is most commonly referred to as "placental insufficiency" within the medical profession. The lack of a universally accepted definition of placental

insufficiency and associated pathognomonic aspects was highlighted in one study. [2]

A birth weight below the third percentile, a head circumference below the tenth percentile or a length below the tenth percentile are all related issues to pregnancy that serve as diagnostic criteria for foetal growth restriction. [3].

Preterm births are becoming more common in several countries around world and have become a global health concern. Each year, there are fifteen million (11.1 percent) preterm births of all births worldwide, with approximately one million dying and several sufferings from acute and chronic diseases linked to prematurity. [4]

Antenatal corticosteroids are widely accepted as most effective treatment for reducing neonatal morbidity and mortality in preterm infants born among twenty-four- and thirty-four-weeks gestation, improving neonatal results and preparing foetus for ex-utero life with decreases in neonatal death, respiratory distress syndrome (RDS), cerebral haemorrhage, and necrotizing enterocolitis, with no risk to maternal wellbeing. [4, 5]

Doppler velocimetry has been suggested as a possible adjunct to methods like non-stress testing or biophysical profile in diagnosis of foetal growth restriction. [6]

Goal of this research was to assess dexamethasone effects on fetal Umbilical and middle cerebral arteries as measured by Doppler ultrasonography after 24 hours following antenatal dexamethasone administration in cases of Placental insufficiency and impact of fetoplacental circulation variations on perinatal result.

2. Patients and Methods

This study was a prospective cohort study that was conducted on 60 cases with singleton pregnancy were recruited from the 28th to the 36th weeks of gestation for administration of antenatal corticosteroids and were divided into two groups: Group A: 30 pregnant women complicated with placental insufficiency and Group B: 30 pregnant women with normal placental blood flow served as controls, at Al-Zahraa University Hospital of Al-Azhar University from November 2020 till November 2021.

2.1 Inclusion criteria

Gestational age from the 28^{th} to the 36^{th} weeks**,** singleton pregnancy, viable fetus with no congenital malformation, asymmetrical IUGR suspected placental insufficiency clinically by presence of fundal height less than expected for the calculated gestational age by last menstrual period or first trimester ultrasound, poor or loss of fetal body movements, breathing movements, and tone(poor biophysical profiles), presence of proven placental insufficiency diagnosed by oligohydraminos on ultrasound examination but without signs of preterm premature rupture of fetal membranes (PPROM), and abnormal uterine artery Doppler and decreased fetal biometric measurements, history of medical diseases for example; hypertension, diabetes, or rheumatic heart diseases and decision of termination within 24-48 hours of corticosteroid administration.

2.2 Exclusion criteria

Pregnant ladies before twenty-eight weeks or after 36 weeks of gestation, multiple gestation, cases who received corticosteroids in their pregnancies prior to the study, contraindication of corticosteroids administration, pregnancies whose fetuses had suspected structural malformations, symmetrical IUGR, Cases unsuitable for conservative management (e.g., studied case in labour, foetal death, PPROM, vaginal bleeding as in placenta previa and abruption placentae), Palpable uterine contractions, abdominal pain, a temperature above 38.5 degrees Celsius, and a white blood cell count more than sixteen. Are all symptoms that point to chorioamnionitis.

2.3 All studied cases were subjected to the following:

Informed written consent was taken from each participant before being involved in the research.

2.4 Eligible subjects included in this study were subjected to the following:

2.4.1 Complete history was taken with special emphasis on:

Personal history, Menstrual history (last menstrual period (LMP) for confirming pregnancy age), Medical history (history of diabetes mellitus, hypertension, cardiac difficulties, bleeding tendency, blood disease, bronchial asthma and allergy), History of surgeries: (particularly previous uterine scar as cesarean scar), Past obstetric history (especially details of previous pregnancies (Date, result, onset and mode of delivery, gestational age at delivery and any associated problem) and History of drug intake.

2.4.2 Patient complaint, History of the current pregnancy and History of satisfaction of fetal kicks:

They were asked about a method to estimate fetal well-being.

2.5 Then clinical examinations were done including:

The kit uses a double-antibody sandwich General checkup focusing on: Body mass index (BMI) is determined by a person's stats: height, weight, and age. The hemodynamic state is evaluated by taking a patient's temperature, pulse, and blood pressure. An evaluation of the heart and lungs. The abdomen was checked for the following (fundal level, foetal lie and presentation, foetal heart rate (FHR) auscultation, prior laparotomy scar presence).

2.6 Investigations:

Routine laboratory investigation including Complete blood picture (CBC) including total leucocytic count (TLC), blood sugar, blood group and Rh typing and urine analysis, Urinary albumin, C-reactive protein (CRP).

2.7 Abdominal ultrasonographic examinations: The Equipment (Voluson p8):

Ultrasound equipment used was 3.5- 5-MHz transabdominal at the ultrasound unit of the Obstetrics and Gynecology department at Al-Azhar University Hospitals in Egypt. All females were evaluated for Gross anatomical defects, foetal viability, and foetal biometry [biparietal diameter - femur length - abdominal circumference] were evaluated using transabdominal ultrasound.

2.8 Doppler velocimetry for the umbilical artery:

Doppler examination of foetal Umbilical artery was done with patients were placed in a semi-recumbent position with a left lateral tilt, and selected area of the amniotic cavity with several loops of cord seen by colour Doppler. Then using a pulsed wave Doppler on a in a free-floating loop of the mid portion of the umbilical cord away from the placental and fetal cord insertion., the characteristic sound and shape of the umbilical artery was identified. When the screen showed at least 3 consecutive wave forms of similar height, the image was taken and Doppler umbilical artery Resistant index (RI) and pulsatility index (PI) was estimated. A minimum of 3 separate readings were averaged before the final values were obtained. Umbilical artery Doppler studies were avoided during fetal breathing because of the effect of fetal breathing movements on waveform variability. The normal wave of the umbilical artery is a saw-tooth appearance. Decreased diastole, absent diastole or reversed diastole were considered as abnormal waves. The measurement of RI and PI of the umbilical artery was considered normal or abnormal according to percentiles for gestational age [8].

2.9 Doppler velocimetry for Middle cerebral artery:

For Doppler examination of the Middle cerebral artery, a transverse view of the foetal brain was taken immediately caudal to the trans-thalamic plane used to acquire biometric data for biparietal diameter and head circumference. The transducer was then positioned near the base of the skull, near the lesser wing of the sphenoid bone [9].

2.10 Antenatal corticosteroid (ACS) administration:

Then, 2 doses of twelve mg of dexamethasone were injected intramuscularly, 12 hours apart, into each female in the standard course of corticosteroids to induce foetal lung maturity. Twenty-four hours after finishing the dexamethasone regimen, Doppler velocimetry was performed on the umbilical and middle cerebral arteries. Follow up and termination of pregnancy was done after 24 hours after completion of dexamethasone (EIPICO) course and performing Doppler research. Doppler index changes before and after dexamethasone treatment were the primary endpoints measured. Secondary outcomes were the 1- and 5-minute Apgar score, the number of live births and stillbirths, the gestational age at delivery, the birth weight of the infant, the need for intensive care for the newborn, the incidence of respiratory distress syndrome and the use of mechanical ventilation.

2.11 Statistical analysis:

SPSS version twenty-three was used to perform statistical analyses on data in this research. The Shapiro-Wilks test was performed to ensure that the data followed a normal distribution. Numbers were expressed using the mean, the standard deviation, the median, and the range. Categorical information was summarized using percentages. Two-tailed Student's t-tests and one-way analysis of variance (ANOVA) were utilized, when applicable, to determine whether or not there was statistically significant variation across groups. To analyze qualitative factors, we employed the chi-squared test.

3. Results

There was no statistically significant difference between both studied groups regarding mean age, mean gravidity and parity, while there was a highly significant difference regarding mean BMI (P-value <0.001) as shown in Table. 1. Table .2 showed that there was significant variation among both groups as regarding medical disorders with (P-value < 0.001) and the majority of cases suffering from preeclampsia (56.6%). Table .3 showed that the mean gestational age at the duration of the first scan was 33.98±1.3 weeks in Group A while it was (33.27±1.73 weeks) in Group B with no variation among studied groups (P-value = 0.124). The mean gestational age at delivery was (36.34±2.45weeks) in Group A while it was (37.92±1.51weeks) in Group B With a highly significant variation (P-value < 0.001). The present study showed that biparietal diameter and head circumference were lower in fetuses with placental insufficiency than in the control group (P-value =0.041 and P-value = 0.003) respectively as shown in Figure .1. Amniotic fluid index was lower in fetuses with placental insufficiency than in the control group (P-value <0.001) as shown in Figure .2. This paper showed that, following dexamethasone administration, group A showed a highly significant reduction in Umbilical artery RI, S/D ratio, and middle cerebral artery-RI as compared with their baseline levels (P-value<0.001) and a significant difference in middle cerebral artery-RI and middle cerebral artery-PI (P-value = 0.002). There was variation among 2 groups, as in cases of placental insufficiency, the majority of cases (73.3%) had neonates with birth weight (1500 gm--2499 gm) and about 26.7% had neonates with birth weight (1000 gm--1499 gm), and in the control

group all cases had delivered babies with birth weight (1500 gm--2499 gm). (P-value 0.002) as represented in Table. 5. As regarding neonatal outcome of the current delivery there was no variation detected in both groups**.** Also, nine cases give birth to infants admitted to neonatal ICU more than 2 weeks; eight of them suffered from placental insufficiency with statistically significant difference (P –value =0.026). Moreover, there were decreases in mean Apgar score after one min, five minutes and 10 minutes in babies of cases with placental insufficiency group compared to babies of control cases) (P-value < 0.001).

Table (1): Demographic data distribution between both group (A) and group (B).

		Placental insufficiency Group {A} N=30	**Control Group{B} N= 30**	**P-value**	**Significance**
Age (years)	Range	20–38	20-40	0.2	NS
	Mean ± SD	27.13±4.6	28.87±5.69		
Gravidity	Primi	17(56.7%)	18(60%)	0.803	NS
	2-3	6(20%)	7(23.3%)		
	4-5	7(23.3%)	5(16.7%)		
Mean ± SD		2 ±1.34	1.87±1.3	0.698	NS
Parity	Zero	18(60%)	18(60%)	0.470	NS
	1	8(26.7%)	5(16.7%)		
	2-3	4(13.3%)	7(23.3%)		
Mean ± SD		0.567 ±0.817	0.7±0.988	0.571	NS
BMI (kg/m^2)	Range	19-39	18.5-28	<0 001	HS
	Mean ± SD	29.86±4.23	22.47±3.25		

-*P -value < 0.05: statistically significant, -Group (A): pregnant women complicated with placental insufficiency, -Group (B): pregnant women with normal placental blood flow served as controls.

Table (2): Medical disorders of cases between both Group A and Group B.

	placental insufficiency Group {A} N=30	**Control Group{B} N=30**	**P-value**
Free	0(0%)	26(86.7%)	<0.001**
Preeclampsia	17(56.6%)	0(0%)	
Systemic lupus erythromatosis	5(16.7%)	0(0%)	
Scleroderma on Plaquenil	3(10%)	0(0%)	
Anemia	2(6.7%)	4(13.3%)	
DM on Insulin	2(6.7%)	0(0%)	
Chronic Hypertension	1(3.3%)	0(0%)	

-Group (A): pregnant women complicated with placental insufficiency.
-Group (B): pregnant women with normal placental blood flow served as controls.

Table (3): Comparison between group A and group B regarding gestational age at the time fetal scan.

		Placental insufficiency Group {A} N=30			Control Group{B} N=30			P-value
Gestational age at time of fetal scan and first Doppler (weeks).	Range	30.43	–	35.57	32.14	–	36	0.124
	Mean ± S. D	33.98	±	1.3	33.27	±	1.73	
Gestational age at delivery(weeks). Mean ± SD		36.34±2.45			37.92±1.51			<0.001

-Group (A): pregnant women complicated with placental insufficiency.
-Group (B): pregnant women with normal placental blood flow served as controls.

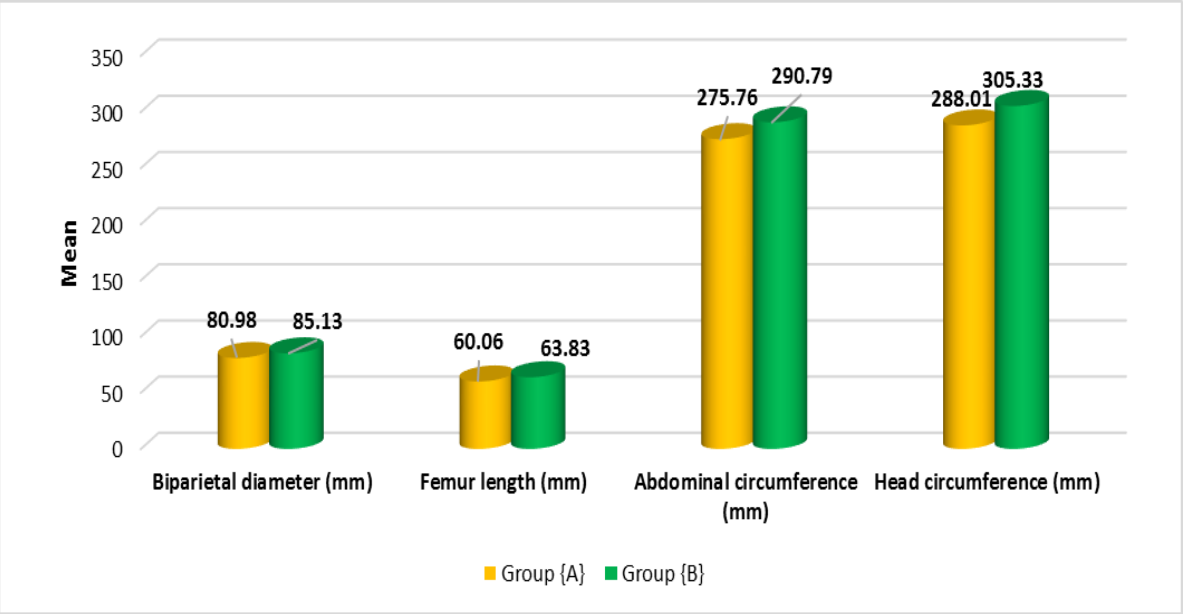

Figure (1): Fetal ultrasonographic biometry in both studied groups.

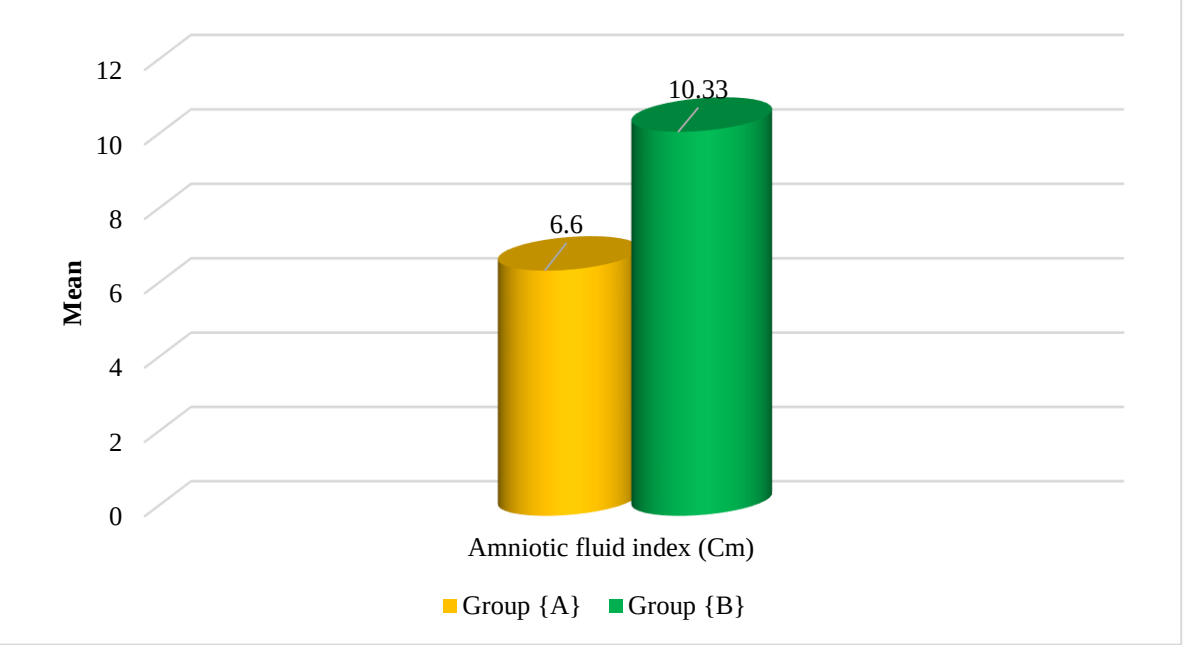

Figure (2): Amniotic fluid index (AFI) in both studied groups.

Table (4): Umbilical Doppler Indices changes of placental insufficiency group (Group A) before and after treatment with dexamethasone.

Variable	Mean ± SD Before treatment	Mean ± SD After treatment	P- value	Significance
Umbilical artery-RI	0.82 ±0.109	0.78 ± 0.12	0.001*	S
Umbilical artery-PI	1.46 ± 0.36	1.35 ±0.32	<0.001*	S
Umbilical artery S/D ratio	3.21 ± 0.49	3.03± 0.37	<0.001*	S
MCA-RI	0.82 ± 0.05	0.78±0.04	0.002*	S
MCA-PI	1.87 ± 0.19	1.79 ± 0.19	0.002*	S

P-value < 0.05: statistically significant (S), -RI, resistance index; PI, pulpability index; S/D, systolic/diastolic, MCA, Middle cerebral artery. NS: non-significant; S: Significant.

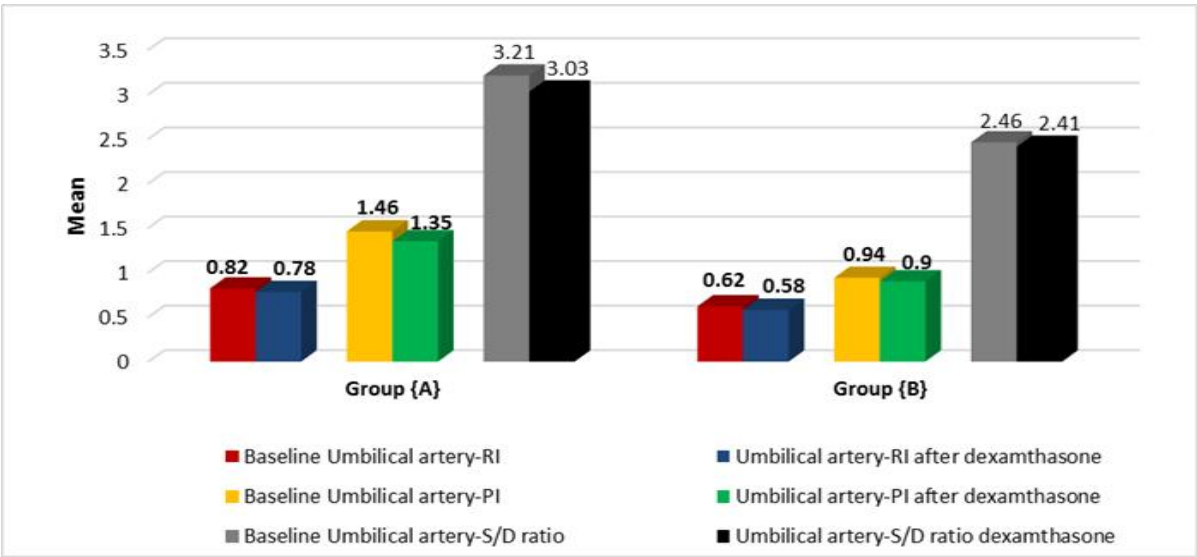

Figure (3): Umbilical Doppler Indices (RI, PI, and S/D ratio) changes of groups A, and B before and after treatment.

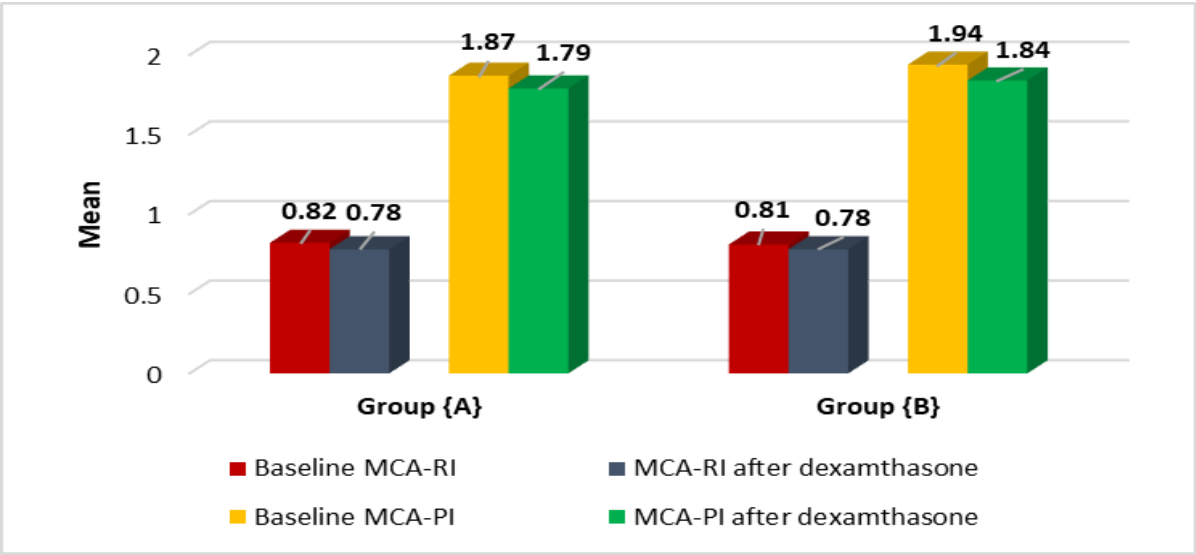

Figure (4): Middle Cerebral Doppler Indices (MCA-RI, and MCA-PI) changes of groups A, and B before and after treatment.

Table (5): Distribution of birth weight at delivery in studied groups.

Birth Weight (gm)	placental insufficiency Group {A} N=30	Control Group{B} N=30	P-value
1000-1499	8(26.7%)	0(0%)	0.002*
1500-2499	22(73.3%)	30(100%)	
Mean ± S. D	1908.5 ± 452.4	2215.4± 232.5	0.002*

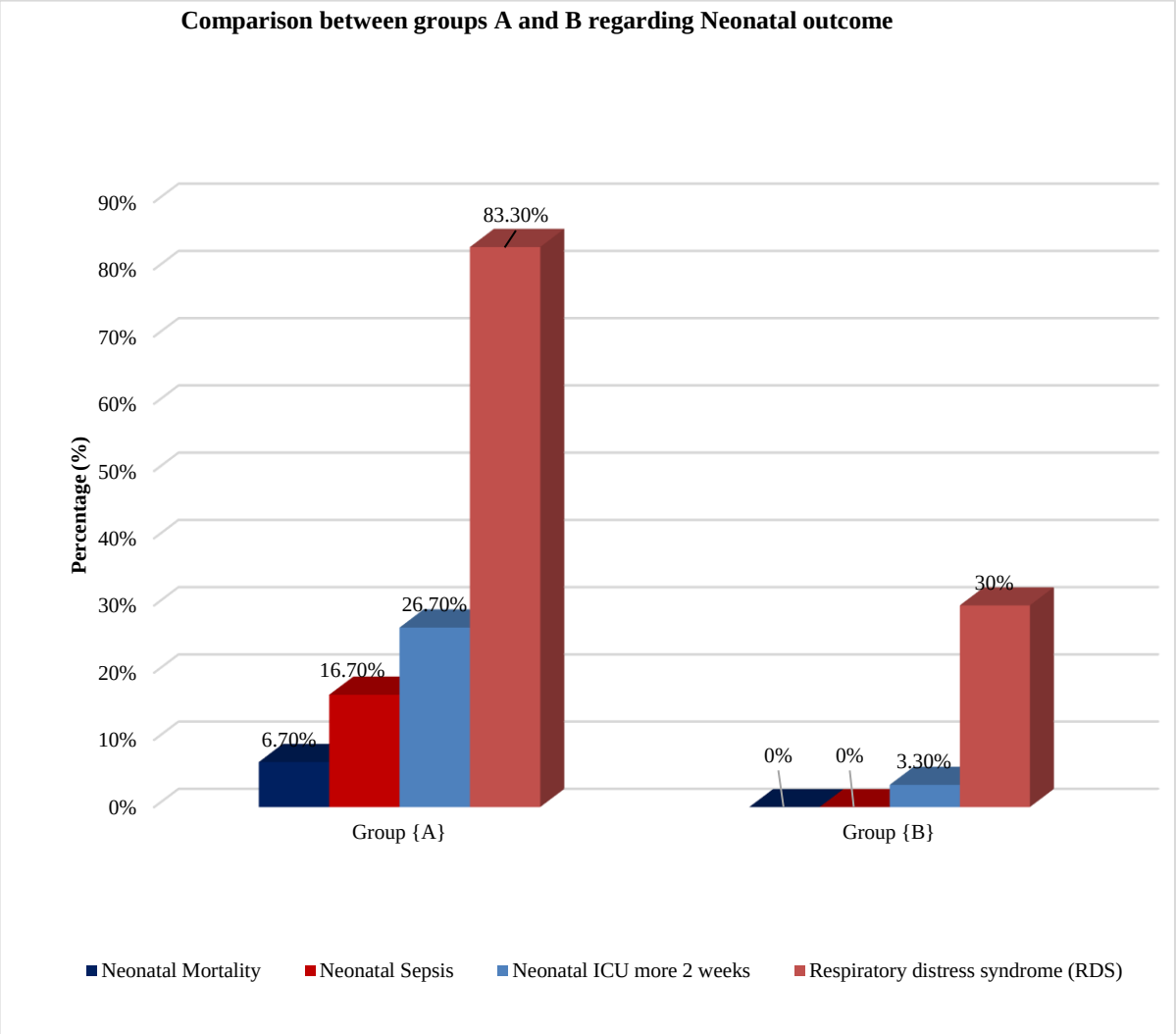

Figure (5): Umbilical Doppler Indices (RI, PI, and S/D ratio) changes of groups A, and B before and after treatment.

Table (6): Mean Apgar score after 1 min, 5 mins, 10 mins in studied groups.

	placental insufficiency Group {A} N=30	Control Group{B} N=30	P-value
Apgar score after 1 min	6.033±1.25	7.3±0.95	<0.001**
Apgar score after 5 mins	6.57±1.33	7.97±1.07	<0.001**
Apgar score after 10 mins	7.3±1.66	8.87±0.94	<0.001**

4. Discussion

There has been a lot of research on how antenatal corticosteroid therapy affects feto-placental vascular resistance, but the clinical results have been mixed. [11] Among these, the majority worried about the effects of steroid use during IGR-complicated pregnancies. [11].

There was no statistically significant difference between both studied groups regarding mean age, mean gravidity and parity, while there was a highly significant difference regarding mean BMI (P-value <0.001).

In line with our results, Logan et al., [12] found that the mean maternal age of the study females with preeclampsia and placental insufficiency was 26.1 years (SD=5.5) while the mean maternal age of the control group was 26.1 years ±5.3, respectively with no variation among both groups.

Also, Motedayen et al, [13] and Pretscher et al., [14] described that there was no statistical difference in maternal ages between placental dysfunction cases due to PE and the control group.

Nearer to our results, Elsnosy et al., [12] reported that mean years old of study group was 27.7 ± 4.5 and Anter et al., [5] reported that mean years old of study group was 24.58 ± 4.12. In another study by Belogolovkin et al., [15] they found Pregnancy-related hypertension was six percent more likely in females with great BMI (26.1-29 kg/m2) than in females with normal BMI (19.86-26 kg/m2). The underlying causes of placental insufficiency remain poorly understood, but most investigators agree that a common mechanism is abnormal uterine spiral artery remodeling, which is most likely caused by an imbalance in maternal angiogenic factors [16].

In addition, our results revealed that mean gestational age at delivery was lower in cases who were suffering placental insufficiency mean gestational age was (36.34±2.45weeks) while it was (37.92±1.51weeks) in control cases (P-value < 0.001). These results revealed that approximately half of the cases in the placental insufficiency group [14 (46.7%) delivered preterm compared to none in the control counterparts (P-value <0.001).

In agreement with Elsnosy et al., [11] study showed that gestational age at 1st scan was 30.9 ± 2.7 weeks while it was 31.3 ± 2.9 at delivery in cases prone to preterm labor. Regarding results of the Doppler measurements on comparing the Umbilical Doppler indices before dexamethasone administration, the mean umbilical artery resistance index (RI), S/D ratio was statistically significantly less in the control group matched to study group (A) (P-value < 0.001). Furthermore, no variation was detected among either studied group as regard to MCA-RI or MCA-PI (P-value=0.773 and P-value =0.292 respectively) (as shown in Table 18 and Figure 17-18). Lakhkar et al., [17] study shown that S/D ratio, PIand RI in the umbilical artery were all higher in IUGR than in a healthy pregnancy. Umbilical Doppler indices (S/D ratio, RI, PI) in the patients were significantly greater than in the controls, which is in line with the results of Fuchs et al. [18] In addition, our study showed that, following dexamethasone administration, group A (pregnant women complicated with placental insufficiency) showed a highly significant reduction in Umbilical artery RI, S/D ratio, middle cerebral artery-RI as compared with their baseline levels (P-value<0.001) and a significant difference in middle cerebral artery-RI and middle cerebral artery-PI (P-value = 0.002). Also, group B (pregnant women with normal placental blood flow served as controls) showed a decrease in both RI, PI, and S/D ratio, both MCA-RI and MCA-PI as compared with their baseline levels (P-value ≤ 0.001 for all except Umbilical artery-S/D ratio P- value = 0.001). El-Madany et al. [19], in related research on preeclamptic complications,

Patients who had placental insufficiency reported a significant difference among umbilical and MCA Doppler parameters (PI, RI, S/D ratio) between patients compared to the control group with a decrease forty-eight hours after the administration of dexamethasone, which then returned to baseline levels after four days of the administration of dexamethasone.

In agreement with this study, Haram et al., [20] described an association among dexamethasone treatments and reduced placental vascular resistance as reflected by waveforms got from UA. (P –value <0.001) Temporary changes in Doppler indices have been observed after maternal dexamethasone, but the mechanisms underlying these changes remain unclear. For example, El Snosy et al. [11] argue that changes in blood flow to the foetal brain are not likely to occur after dexamethasone treatment due to constriction of the ductus arteriosus. However, Koenen et al. [21] highlight the potential contribution of steroids via circulatory pathways that lead to foetal hypertension. In non-agreement with this study, Urban et al., [22] described that there was no variation detected in UA PI through administration of dexamethasone treatment. (P- Value =0.0001 and P-value =0.0137)

El-Madany et al., [19] reported that umbilical artery and ductus venous velocity waveforms of undelivered foetuses either reverted to their pre-treatment state or degraded further after four days.

As regard pregnancy outcomes, neonatal birth weight of cases with placental insufficiency. The mean weight at birth was 2474.4±452.4 gm in placental insufficiency group compared to 3074.79 ± 232.5 in control cases (P<0.001). The overall mortality was shown in 2 cases in placental insufficiency group (6.7%). Neonatal sepsis was detected in 5 babies of cases with placental insufficiency (16.7%).

In agreement to our finding, El-Madany et al. [19] reported that fetal weight was lower between preeclampsia cases placental insufficiency with compared to control group.

While in the study conducted by El-Haddad et al., [23] Out of total of sixty clinically diagnosed cases, thirty-six (sixty percent) of IUGR neonates had birth weights varying from 2.5 to three kgs, compared to seventeen (28.33percent) of neonates who did not find much advancement in birth weight despite hospital management.

5. Conclusion

Umbilical Doppler Indices improved after 24 hours of dexamethasone administration in pregnant women with placental insufficiency, suggesting that the corticosteroid's vasodilator effect improved blood flow in the foetal umbilical and middle cerebral arteries

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Conflicts of interest: No competing interests.

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