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Predicting Perinatal Outcome through Changes in Doppler Studies after Antenatal Corticosteroids Administration in Preeclamptic Patients

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ABSTRACT

Background: New-onset gestational hypertension and proteinuria are symptoms of preeclampsia, a pregnancy complication. Both moms and their infants are affected by the illness.

Aim of the work: To assess the accuracy of Doppler indices during the third trimester in predicting fetal outcome after administration of corticosteroids in women with preeclampsia by performing antenatal Doppler indices and recording the fetal outcome after delivery.

Patients and methods: A prospective randomized controlled clinical trial with double blinding was done at El Galaa Maternity Teaching Hospital. Pregnant ladies between 32 to 36 weeks of gestation with preeclampsia who attend antenatal clinic and emergency room at El Galaa Maternity Teaching Hospital's Obstetrics and Gynecology Department.

Results: there was one case of stillbirth among Study cases. 40% of neonates of Study group were admitted to NICU versus only 2 neonates of control group, 34 % of Study cases' neonates showed RDS versus only one of control group. umbilical artery PI, RI, and S/D ratio showed significant decrease 48 hours after dexamethasone administration and then returned to baseline levels after 4 days of administration of dexamethasone.

Conclusion: Antenatal Doppler examination can identify foetuses at risk for NICU admission and morbidity after delivery, allowing for antenatal risk calculation and prognostication .

Based on the Doppler findings, in-utero transfer to tertiary care centres can be explored, providing for superior post-natal management and outcomes .

Neonatal outcomes are better for those born at or near term than for those born very preterm, indicating that gestational age is a significant factor of neonatal outcome.

Keywords: *Neonates; preeclampsia; Doppler evaluation; predicting; gestational age.*

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INTRODUCTION

New-onset gestational hypertension and proteinuria are symptoms of preeclampsia, a pregnancy complication. Both moms and their infants are affected by the illness. Only delivery can cure the illness once it is clinically manifest. In affluent countries, prenatal care surveillance for preeclampsia allows for early detection and delivery intervention. This management hasn't altered much in the last century, and it's proven to be quite helpful in lowering maternal mortality. Preeclampsia, which continues to be one of the primary reasons of pregnant women being sent to intensive care units in the developed world, has a high maternal morbidity rate. Furthermore, foetal mortality and morbidity are significant, due to both the disease's impact on the foetus and preterm. Preterm births are caused by the delivery of women to avoid the advancement of preeclampsia. This accounts for 15% of all preterm births. Maternal mortality is widespread in developing nations, where insufficient prenatal care limits preeclampsia surveillance, accounting for 50 000 fatalities per year. [1]

Pregnancy-Induced Hypertension (PIH) can diminish the placenta's blood-oxygen transfer area, disrupt the food supply balance between the mother and the placenta, and increase the risk of foetal hypoxia. In pregnant women with PIH, spastic small arteries are the primary cause of blood pressure increase and subsequent changes in cardiac and renal function. [2]

Screening for poor placentation and associated sequelae of pre-eclampsia, intrauterine growth restriction, and infant death is made easier by Doppler examination of the placental circulation. In order to better understand the pathophysiology of a wide range of abnormal pregnancies and their therapeutic therapy, foetal circulation must be assessed.[3] Power in three dimensions (3D) Doppler

ultrasound makes it easier to assess foetal cardiac blood flow and peripheral vascular trees, as well as foetal organ blood flow, placental vasculature and blood flow, and uterine cervix development. Quantitative and qualitative analyses of the vascularization and blood flow of foetal organs, the placenta, and the uterine cervix have become possible because to recent improvements in 3D power Doppler ultrasound and quantitative 3D power Doppler histogram analysis. This technique has the potential to aid in the examination of the foetal circulatory system and feto-placental function, and it has advantages over traditional two-dimensional power Doppler ultrasound assessments. Future study on foetal and placental blood flow may benefit from 3D power Doppler ultrasound, which can help with prenatal identification of foetal and placental vascular disorders. [4]

PATIENTS AND METHODS

El Galaa Maternity Teaching Hospital conducted a prospective double-blind randomised controlled clinical experiment.. Pregnant ladies between 32 to 36 weeks of gestation with preeclampsia who will attend antenatal clinic and emergency room at Obstetrics and El Galaa Maternity Teaching Hospital's Gynecology Department.A double blind randomized controlled trial performed, it will involve 100 Preeclamptic patients attending the antenatal clinic and intending to deliver at the emergency room. Doppler indices performed to the entire study sample with administration of corticosteroids to one group while the other was received placebo. Group 1 (the case group): This group consists of 50 patients receiving dexamethasone 6 mg intramuscularly 12 hours apart given in four doses between 32 weeks and 36 weeks. Group 2 (the control group): This group consists of 50 patient receiving a placebo given intramuscularly in four doses between 32 weeks and 36 weeks in the same manner. To insure that everyone has the chance of participation, randomization will be a computer-generated randomization mechanism was used Neither the patient nor the researcher will know whether they were given corticosteroids or a placebo. (This is a double-blinding approach.) The size, colour, and form of the placebo will be identical to the original.

Drug: The drug used in the study and placebo will be put in 100 numbered closed envelopes according to the table of random number and envelope will be allocated to each patient accordingly.

Inclusion criteria: Women who choose to have a lower segment caesarean section. patient presenting with mild preeclampsia, age ranging from (20-45), gestational age between 28 to 36 Weeks (by first trimesteric ultrasound or documented last menstrual cycle) and the patient's formal informed permission

Exclusion criteria: venous thrombosis (DVT and/or pulmonary embolism) OR arterial thrombosis (angina pectoris, myocardial infarction, stroke), epilepsy or seizure, any known cardiovascular, renal, or liver condition, autoimmune diseases, sickle cell disease, severe hemorrhagic disease, placenta previa abruptio placenta, grossly adherent placenta severe Preeclampsia, place

Eclampsia or HELLP syndrome, patients diagnosed with IUGR and maternal or fetal condition requiring immediate delivery

Both groups will be subjected to the following:

Ultrasound and Doppler studies will be performed to both of the study groups for comparison and control. Doppler performed for both groups of women before administration of dexamethasone and twice after its administration with first reading 48 hours after dexamethasone administration and second reading after another 48 hours (4 days after administration).

History taking: history of present pregnancy (abdominal enlargement, rupture of membranes, etc.), past history of pregnancy, exclude any medical disorder (metabolic disease, Thrombocytopenia, Hypertension, Diabetes mellitus, Cardiac disease, etc.) and menstrual history (to confirm LMP and this date is reliable).

General examination: Abdominal examination with particular emphasis on abdominal enlargement, obstetric ultrasound to document viability of pregnancy and to ensure the gestational age and fetal condition and CBC or hematocrit preoperative.

Ethics: Informed consent taken from all participates before recruitment in the study after explanation of the purpose and procedures of the study.

Statistical analysis: For metric data, descriptive statistics will be descriptive statistics shall be expressed as range, median, and inter quartile range, number, and proportions for discrete data; descriptive statistics will be expressed as range, median, and inter quartile range, number, and proportions for continuous data (for categorical data). The Statistical Package for Social Sciences (SPSS®) for Windows® version 16.0 was used to conduct the statistical analysis (SPSS Inc., Chicago, IL, USA).

RESULTS

Fetal weight	Control group	Study group	p-value $
First reading	2383.9 ± 734.1	1779 ± 679.4	0.002*
2nd reading	2453.7 ± 651.6	1762.88 ± 751.6	<0.001*
3rd reading	2633.2 ± 459.4	1848.6 ± 710.5	<0.001*
p-value#	0.3 (NS)	0.8 (NS)	

Table 1: Comparison of fetal weight among three readings in both groups:
$ P-value for unpaired t-test
# p-value for analysis of variance test
NS: not statistically significant difference
*Statistically significant difference

Fetal weight was significantly lower among preeclampsia cases compared to control group. There was no significant difference between serial estimations of fetal weight between both groups. Table 1

MCA		Control group	Study group	p-value $
S/D ratio	First reading	4.42 ± 1.3	6.55 ± 2.3	<0.001*
	2nd reading	3.7 ± 1.73	5.56 ± 1.8	<0.001*
	3rd reading	4.3 ± 2.18	5.73 ± 2.1	0.01*
	p-value#	0.2 (NS)	0.1 (NS)	
Pulsatility index	First reading	1.18 ± 0.4	1.66 ± 0.5	<0.001*
	2nd reading	1.07 ± 0.9	1.61 ± 0.7	0.01*
	3rd reading	1.2 ± 0.6	1.59 ± 0.8	0.03*
	p-value#	0.7 (NS)	0.9 (NS)	
Resistive index	First reading	0.68 ± 0.1	0.78 ± 0.2	0.02*
	2nd reading	0.71 ± 0.3	0.72 ± 0.09	0.8 (NS)
	3rd reading	0.69 ± 0.09	0.75 ± 0.1	0.02*
	p-value#	0.8 (NS)	0.2 (NS)	

Table 2: Comparison of MCA parameters three readings in both groups
$ p-value for unpaired t-test
# p-value for analysis of variance test
NS: not statistically significant difference
*Statistically significant difference
a, b denotes significance difference within serial readings among each group (post hoc analysis, Bonferroni test)

MCA Doppler parameters (PI, RI, S/D ratio) were significantly higher among study cases compared to control group with no significant difference between serial measurements before and after dexamethasone administration among study cases. Table 2

Umbilical artery		Control group	Study group	p-value $
S/D ratio	First reading	2.52 ± 0.9	3.91 ± 1.2 [a]	<0.001*
	2nd reading	2.6 ± 1.04	2.81 ± 1.08 [b]	0.4 (NS)
	3rd reading	2.4 ± 1.08	3.79 ± 1.9 [a]	0.001*
	p-value#	0.7 (NS)	0.007*	
Pulsatility index	First reading	1.42 ± 0.8	2.28 ± 1.1 [a]	<0.001*
	2nd reading	1.39 ± 0.9	1.51 ± 0.9 [b]	0.6 (NS)
	3rd reading	1.34 ± 1.02	2.09 ± 1.2 [a]	0.01*
	p-value#	0.9 (NS)	0.02*	
Resistive index	First reading	0.59 ± 0.1	0.69 ± 0.07 [a]	<0.001*
	2nd reading	0.54 ± 0.2	0.58 ± 0.1 [b]	0.3 (NS)
	3rd reading	0.58 ± 0.1	0.63 ± 0.2 [a]	0.04*
	p-value#	0.4 (NS)	0.01*	

Table 3: Comparison of umbilical artery Doppler parameters three readings in both groups
$ P-value for unpaired t-test
# p-value for analysis of variance test
NS: not statistically significant difference
*Statistically significant difference
a, b denotes significance difference within serial readings among each group (post hoc analysis, Bonferroni test)

Umbilical artery PI, RI, and S/D ratio showed significant decrease 48 hours after dexamethasone administration and then returned to baseline levels after 4 days of administration of dexamethasone. Table 3

Umbilical artery blood flow pattern		Control group		Study group		p-value $
First reading	AED	0	0%	20	40 %	0.001*
	RED	0	0%	27	54 %	
	Positive diastolic flow	50	100%	4	6 %	
Second reading	AED	0	0%	5	10%	0.001*
	RED	0	0%	25	50%	
	Positive diastolic flow	50	100%	20	40%	
Third reading	AED	0	0%	17	34 %	0.001*

	RED	0	0%	28	56 %
	Positive diastolic flow	50	100%	5	10%

Table 4: Comparison of blood flow pattern of umbilical artery among both groups
AED: absent end-diastolic, RED: reversed end-diastolic*statistically significant difference

		First reading	Second reading
Umbilical artery blood flow pattern	First reading	-	-
	2nd reading	<0.001*	-
	3rd reading	0.8 (NS)	0.01*

Table 5: Comparison of blood flow pattern of umbilical artery among study group
*Statistically significant difference
NS: not statistically significant difference

Ductus venosus PI and RI significantly decreased 48 hours after dexamethasone administration and then returned to baseline levels after 4 days of administration of dexamethasone. Table 6

Ductus venosus		Control group		Study group		p-value $
Pulsatility index	First reading	0.45 ± 0.1		0.69 ± 0.1 [a]		<0.001*
	2nd reading	0.41 ± 0.2		0.46 ± 0.1 [b]		0.2 (NS)
	3rd reading	0.47 ± 0.1		0.61 ± 0.2 [a]		0.001*
	p-value#	0.3 (NS)		<0.001*		
Resistive index	First reading	0.55 ± 0.09		0.71 ± 0.07 [a]		<0.001*
	2nd reading	0.54 ± 0.08		0.55 ± 0.1 [b]		0.3 (NS)
	3rd reading	0.56 ± 0.1		0.69 ± 0.1 [a]		0.04*
	p-value#	0.7 (NS)		<0.001*		
Negative a wave	First reading	0	0%	3	10%	0.7 (NS)
	2nd reading	0	0%	0	0%	
	3rd reading	0	0%	0	0%	
	p-value#	-		0.7 (NS)		

Table 6: Comparison of Ductus venosus Doppler parameters three readings in both groups
$ P-value for unpaired t-test
# p-value for analysis of variance test
NS: not statistically significant difference
*Statistically significant difference
a, b denotes significance difference within serial readings among each group (post hoc analysis, Bonferroni test)

The umbilical artery flow pattern, all of control group patients have positive diastolic flow pattern. Among study cases there was significant change of flow pattern 48 hours after dexamethasone administration and then returned to baseline levels after 4 days of administration of dexamethasone. Table 4, 5

		Control group		Study group		p-value
Neonatal outcome	Viable fetus	50	100%	48	96 %	0.9 (NS)
	Stillbirth	0	0%	2	4 %	
NICU admission		4	8 %	20	40%	0.01*
RDS		2	4 %	17	34%	0.01*

Table 7: Neonatal Outcome BETWEEN Both Groups Of The Study
*Statistically significant difference
NS: not statistically significant difference

There was one case of stillbirth among Study cases. 40% of neonates of Study group were admitted to NICU versus only 2 neonates of control group. 34 % of Study cases' neonates showed RDS versus only one of control group. Table 7

DISCUSSION

The effects of maternal dexamethasone on foetal and uteroplacental circulation in preeclamptic patients' pregnancies at risk of neonatal outcome were investigated in this study.

The umbilical artery (UA) and ductus venosus (DV) pulsatility index (PI) and flow velocity waveforms in

the research group's umbilical artery (UA) and ductus venosus (DV) both showed significant changes.

This is in line with the findings of [5], who discovered a significant temporary change in the velocity waveform and a reduction in the PI in the umbilical artery and ductus venosus after administering maternal prenatal betamethasone, a nearly identical drug.

Another study found that prenatal corticosteroid medication reduced the umbilical artery and ductus venosus PI within 24 hours [6].

The modifications could be saved for up to 48 hours.

According to a study of the literature, corticosteroid therapy improved umbilical artery blood flow waveforms in six of 17 trials [7].

Two days after dexamethasone administration, alterations in the umbilical artery waveform from reversed to absent and from absent to positive diastolic flow were identified in 32 of 50 individuals.

After 4 days, the undelivered foetuses' umbilical artery and ductus venosus velocity waveforms either reverted to their pre-treatment state or degraded further.

Following betamethasone treatment, the same side effects were reported [5].

According to a research by Robertson et al., babies with persistent absent end-diastolic flow were more likely to require assisted breathing in utero than neonates with transitory positive end-diastolic flow [8].

There was no link found between postnatal morbidity and pregnancies with persistent absent/reversed diastolic flow in the research [5].

One explanation is that the sample size was insufficient to find such a relationship.

The study included 33 women who were pregnant with a singleton and had severe foetal growth restriction and/or preeclampsia.

The rate of postnatal respiratory difficulties (RDS) was 34% in our research of preeclampsia-complicated pregnancies, compared to 4% in the control group.

The frequency of postnatal respiratory problems was 65 percent in a study of pregnancies afflicted by severe IUGR and/or preeclampsia with abnormal Doppler findings [5].

In a comparable study (IUGR foetuses born before 30 weeks of gestation with absent or reversed diastolic flow in the umbilical artery received 95 percent prenatal corticosteroids), 26 (65 percent) of 40 neonates had bronchopulmonary dysplasia (BPD) [9].

Van Stralen et al[10] questioned whether treating prematurely growth-restricted foetuses with prenatal corticosteroids was effective in a retrospective cohort study.

The benefits of corticosteroids in terms of respiratory outcomes are still debated.

In contrast to van Stralen et al[11] who found protective benefits for RDS, intraventricular haemorrhage, and death after betamethasone treatment in a group of SGA children delivered at 25 to 32 gestational weeks, Ley et al [11] found protective benefits for RDS, intraventricular haemorrhage, and death after betamethasone treatment in a group of SGA children delivered at 25 to 32 gestational weeks [10]. The inconsistent results could be explained by differences in treatment policies and definitions of foetal growth limitation between the studies. Wijnberger et al [12] In a group of 55 severely IUGR foetuses, researchers looked at the effect of glucocorticoids on Doppler velocity waveforms. In severely IUGR foetuses, there was no significant change in UA-PI during the 14-day observation period, but there was a substantial increase in the UA-PI/MCA-PI ratio and in DV-PI, as well as a significant drop in MCA-PI. These changes over time are equivalent to those reported in the entire population of IUGR foetuses evaluated longitudinally and may be explained by the progressive and gradual deterioration of the foetal state[13]. As a result of this investigation, it is possible to conclude that antenatal glucocorticoids have no effect on foetal Doppler waveform patterns of UA, MCA, or DV. Table 16 summarises studies on the impact of prenatal glucocorticoids on foetal Doppler velocity waveforms. The findings of Wijnberger et al (2004) study corroborate prior reports. Others Wallace and Baker,[16]; Edwards et al,[17] observed a brief restoration of end-diastolic flow in the UA in IUGR foetuses, which are at odds with Wijnberger et al,[14]; Senat and Ville,[15]. There were no significant changes in MCA flow after corticosteroid treatment. These findings are consistent with those of Simchen et al [18] and Thuring et al [19]. [5]. The prenatal brain is very sensitive to overperfusion and pressure changes, and cerebral blood circulation autoregulation successfully protects it, which could explain our findings [5]. It's worth noting that maternally given steroids have been linked to foetal body, limb, and respiratory movements being reduced.

Mulder et al.[19], Rotmensch et al.[20], diminished startle response to vibroacoustic stimuli Rotmensch et al.[21] and altered foetal heart rate variability on cardiotocography Mulder et al [20]. All of these studies were carried out in women who had normal UA FVWs. After maternal betamethasone dosing, Mulder et al [22] observed transitory reductions in foetal body and respiratory movements, as well as foetal heart rate fluctuation. These effects peaked two days following the start of treatment. Remarkably, Dawes and colleagues [23] Following the treatment of dexamethasone, there was an increase in foetal heart rate fluctuation. Fetal hypoxemia may be indicated by a decrease in foetal heart rate fluctuation and foetal movements [24]. The maternal uterine arteries in our investigation showed no significant effects of dexamethasone medication, which is consistent with prior studies that found no effects of corticosteroids on uterine arteries in pregnancies with imminent preterm birth [5].

CONCLUSION

Finally, maternal antenatal corticosteroid treatment caused a significant transient change in blood

velocity waveforms and a decrease in PI in the umbilical artery and ductus venosus, but had no effect on uteroplacental circulation, implying that corticosteroids have a direct effect on fetoplacental circulation.

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