Is there any relation between neonatal nucleated red blood cells count and abnormal feto-maternal Doppler flow?

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Abstract: Background: Perinatal mortality is one of the most important medical subjects in Iraq nowadays. One of the leading causes of this mortality is the perinatal asphyxia. Prediction of perinatal asphyxia is still a matter of controversy, though, there is increasing evidence that hypoxic ischemic injury of neonate may occur during pregnancy rather than labor. Doppler echo study can conclude maternal as well as fetal circulation. Also there is a consideration to use nucleated red blood cells count as a marker of hypoxia. **Aim:** This study was set to assess the relation of impaired fetal Doppler studies, neonatal nucleated red cell counts and neonatal outcome, because detection of such risk factor; could help in prevention in so far as possible the perinatal mortality in the next pregnancies. **Patients and Methods:** This retrospective research included reserved data of 136 neonates who were born either by vaginal deliveries or caesarean sections under general anesthesia at Fatima Al-Zahraa Administrative hospital, Baghdad, Iraq; at the period from 1st of August 2015 to the 30th of October 2016. Doppler examination was done at the last week of pregnancy and nucleated red blood cells count was estimated for each neonate immediately after delivery. The neonates were divided into two groups; the 1st group (control group) was consisted of alive neonates with normal Doppler studies (Group I). The 2nd group was consisted of alive neonates having abnormal Doppler studies (Group II), which was divided into 3 subgroups, as the followings: Group II[a]: fetuses with abnormal Doppler studies of umbilical artery and/or fetal descending aorta with normal Doppler of maternal uterine artery. Group II[b]: fetuses with abnormal Doppler studies of umbilical artery and/or fetal descending aorta and abnormal studies of maternal uterine artery. Group II[c]: fetuses with absent or reversed diastolic flow in the umbilical artery and abnormal Doppler studies of maternal uterine artery. Intended data were: intrapartum fetal distress, respiratory distress syndrome, time length at neonatal care unit, nucleated red blood count >8/100 white blood cells. Other data were: gestational age at time of delivery, birth weight, amniotic fluid index, nucleated red blood count in relation to Apgar score at 5 minutes level as well as relation to severity of Doppler abnormalities in each of the 4 groups. Mother information included name, age, parity, blood group, medical history, surgical history, obstetric history, smoking and any medical treatment. Pregnant women who had suspicion of fetal compromise due to any of the following conditions was included at this study (inclusion criteria): preeclampsia, supposed IUGR, chronic hypertension, post maturity, oligohydromnios, history of early pregnancy loss or early neonatal death, antiphospholipid syndrome, abnormal fetal heart readings and chronic smoker. While the maternal exclusion criteria: maternal diabetes, multiple pregnancies, maternal cardiovascular diseases other than hypertension, fetuses with chromosomal or structural anomalies and chorioamnionitis. Modes of delivery at this study were vaginal deliveries or caesarean sections (only with general anesthesia). All data were represented in tables and figures. **Results:** this study showed that nucleated red cell counts are increased with the higher degree of feto-maternal Doppler abnormalities. **Conclusion:** Neonatal nucleated red blood cells count as one investigation of neonatal asphyxia has a strong relation with abnormal feto-maternal Doppler flow that might give a prompt clue for doctors and health-staff for direct detection of neonatal asphyxia incidence so as to help in rapid organization of "at high risk fetuses"; consequently, this may assist in declining the occurrence of adverse postnatal deadly products whether in the present or future pregnancies.

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1. Introduction:

Ultrasound technology offers methods for measuring both maternal and fetal circulation by Doppler echo. The ultrasound assessment in high risk pregnancies had reduced perinatal death rate with fewer increase of incidence of both induced labor and cesarean sections [(1)]. Reduction of the perinatal mortality takes the largest part of imperative medical aims nowadays [(2)] and since asphyxia is one of the utmost cause of perinatal mortality, so diagnosis of asphyxia is very important at the present time; which could be achieved by a number of methods including Doppler echo, Apgar score and nucleated red blood cells count, nevertheless, there is a rising evidence that neonatal hypoxic injury may be not related to labor but rather begins at pregnancy [(3)]. Nucleated red blood cells are immature red blood cells found in the fetal circulation at birth that may be increased by many acute or chronic morbid stimuli [(3,4,5)], so, increasing count of these cells can be used as a marker of hypoxia and possible chance of adverse outcome of affected newborn [(5)]. On the other hand, Apgar score is a quick and somewhat subjective method to assess the condition of newborn. The scores are conventionally can be determined at 5 minutes [(6,7)], however, this score as a lone does not proof birth asphyxia although it can highly signify if there is a problem needs an urgent explanation and managements. [(8)]

2. Methods:

This retrospective study was taken on at department of obstetrics and gynecology at Fatima Alzahraa administrative Hospital from the 1st of august 2015 till end of October 2016. Informed verbal consent was obtained from each women included in this study. From more than 300 pregnant mothers who were referred to the mentioned department for assessment of fetal wellbeing and to decide the type of delivery; only 136 cases were included in this study. Other women were excluded, either because they leave the hospital or it was unable to obtain acceptable Doppler, blood sample for them or having one of the following exclusion criteria: maternal diabetes, multiple pregnancies, maternal cardiovascular diseases other than hypertension, fetuses with chromosomal or structural anomalies and chorioamnionitis. Fetuses included in the study, were born by normal vaginal delivery or by caesarean section with general anesthesia using the safest anesthetic drugs to avoid any risk for both mother and her fetus. Every mother had ultrasonic examination to assess gestational age, amniotic fluid index, as well as complete Doppler studies of uterine arteries, umbilical artery, and fetal descending aorta within the last week of pregnancy, in addition, immediately after delivery; a blood sample was taken from the umbilical artery by needle aspiration then blood smear was prepared and stained by Lieshman stain to assess the nucleated red blood cell (NRBC) count, and neonatal NRBC >8/100WBC counts by light microscopy. Mother information included name, age, parity, blood group, medical history, surgical history, obstetric history, smoking and any medical treatment. Pregnant women who had suspicion of fetal compromise due to any of the following conditions was included at this study (inclusion criteria): preeclampsia, supposed IUGR, chronic hypertension, post maturity, oligohydromnios, history of early pregnancy loss or early neonatal death, antiphospholipid syndrome, abnormal fetal heart readings and chronic smoker. According to Doppler findings, fetuses were divided into two groups: The 1st group (Group I) was consisted of alive fetuses having normal Doppler studies of umbilical artery, fetal descending aorta as well as normal uterine artery and was regarded as the control group. The 2nd group was consisted of alive neonates having abnormal Doppler studies (Group II), which was divided into 3 subgroups, as the followings: Group II^a: fetuses with abnormal Doppler studies of umbilical artery and/or fetal descending aorta with normal Doppler of uterine artery. Group II^b: fetuses with abnormal Doppler study of umbilical artery and/or fetal descending aorta and abnormal study of uterine artery. Group II^c: fetuses with absent or reversed diastolic flow in the umbilical artery and abnormal study of uterine artery. The time of delivery was calculated depending on date of the last menstrual period and ultrasound findings. Maternal age was ranging from 17 to 49 years and parity was ranging from 0 to 11. Intended neonatal data were: Apgar score at 5 minutes, intrapartum fetal distress, respiratory distress syndrome, gestational age at delivery, fetal weight at delivery, amniotic fluid index (AFI) at last week of gestation, length of time of admission to the neonatal care unit (by days), neonatal NRBC counts and neonatal NRBC>8/100WBC counts, then data were represented in tables and figures.

3. Results:

Results according to the last Doppler studies were as followings: Group I (control group): 56 cases had normal Doppler study of uterine artery, umbilical artery and fetal descending aorta. Group II^a: 42 cases had abnormal studies of umbilical artery and/or fetal descending aorta, with normal uterine artery. Group II^b: 32 cases had abnormal studies of umbilical artery and/or fetal descending aorta with abnormal uterine artery. Group II^c: 6 cases had absent or reversed diastolic flow in umbilical artery with abnormal uterine artery blood flow. As shown in Figure1.

Regarding the neonatal outcome: 95 neonates had Apgar scores ≥7, and 41 neonates had Apgar scores of <7. As shown in table1 and Fig 2 & 3. It was noticed that perinatal data including; amniotic fluid index (AFI), fetal age and weight at birth were low in low Apgar score fetuses, while the NRBC >8/100WBC count was higher in the same group. As shown in table 2 and Fig.4 & 5.

When the perinatal data were evaluated in relation to the Doppler studies; The NRBC counts showed a step wise increase from group I to group II^{c}, while the birth weight was progressively lower among the four groups. Time of admission to neonatal care unites was the longest in group II^{b}. Amniotic fluid index, gestational age and Apgar scores were estimated also and shown in table 3 and Fig. 6,7,8 & 9.

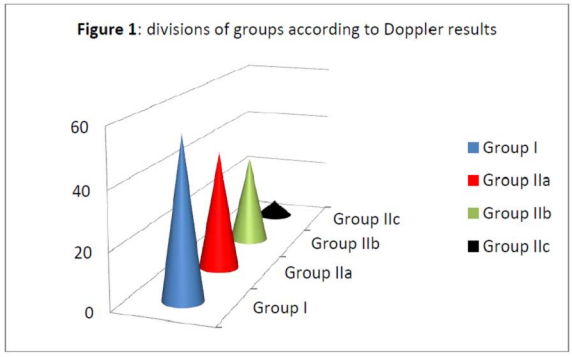
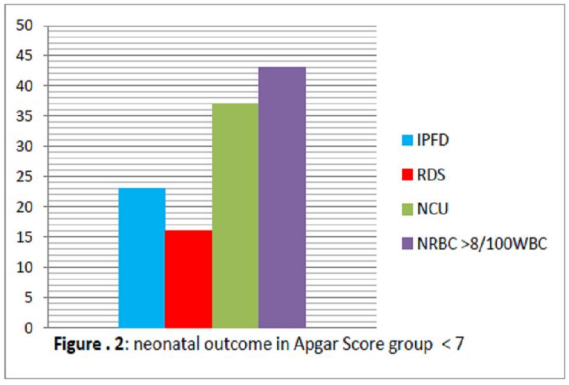


Table 1: Perinatal outcome in relation to the Apgar score at 5th Minute: (IPFD= intrapartum fetal distress, RDS= respiratory distress syndrome, NCU = neonatal care unit, NRBC >8/100 WBC = nucleated red blood count >8/100 white blood cells):

Perinatal outcome	Number of cases	APGAR Scores ≥ 7	APGAR Scores <7
IPFD	31	8	23
RDS	23	7	16
Admission to NCU	74	37	37
NRBC >8/100WBC	82	39	43



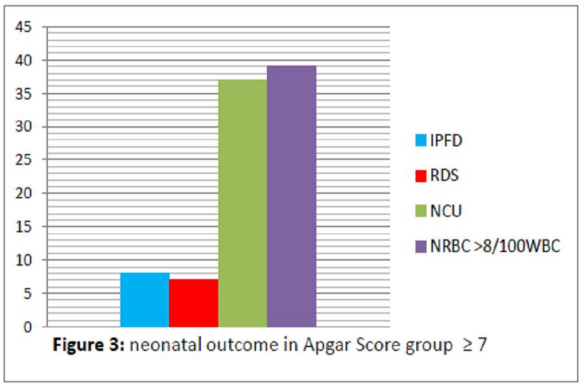
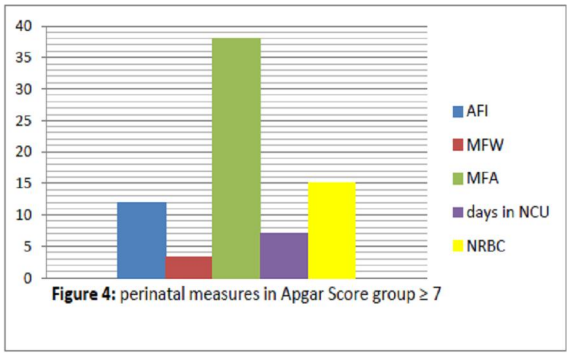
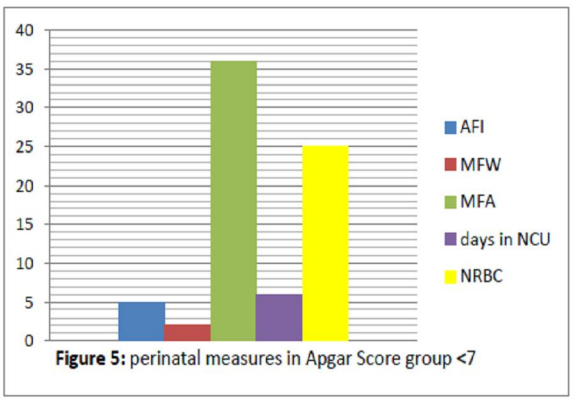


Table 2: Perinatal data in relation to Apgar scores: (AFI= amniotic fluid index, NCU = neonatal care unit, NRBC = nucleated red blood count):

Perinatal measures	APGAR scores≥7	APGAR scores<7
Mean AFI (cm)	12	5
Mean fetal weight (kg)	3.3	2.1
Mean gestational age (wk)	38	36
Time at NCU (days)	1	11
Mean NRBC counts	15	25





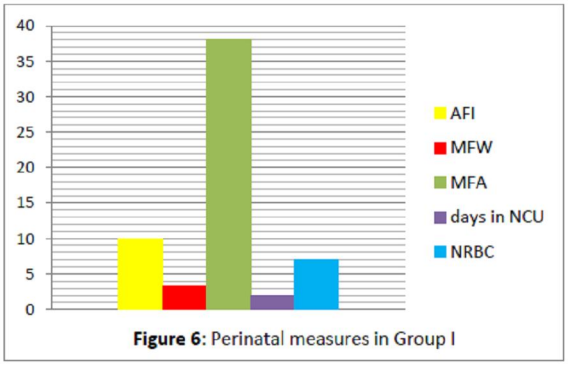


Figure 6: Perinatal measures in Group I

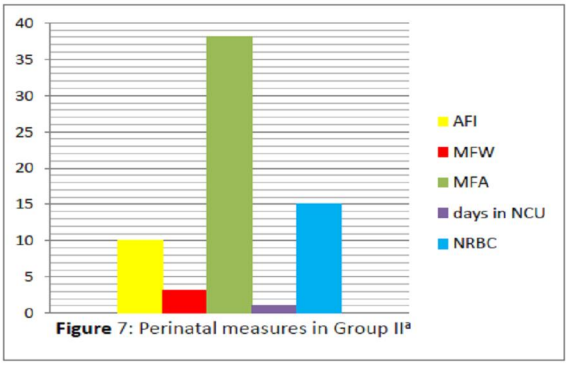


Figure 7: Perinatal measures in Group II[a]

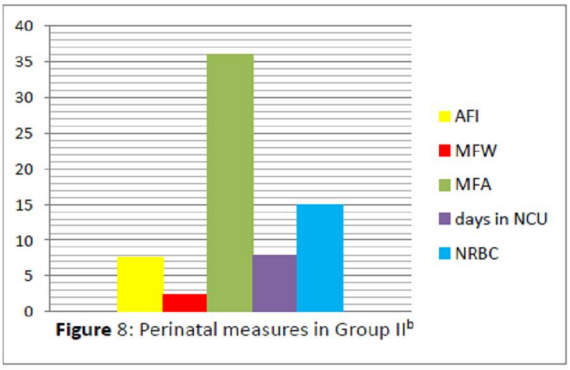


Figure 8: Perinatal measures in Group II[b]

4. Discussion:

This study was the 1st in Iraqi health society, and could be regarded as one of the other global similar studies, which may give verification to the previous worldwide studies since any Meta-Analysis can add a rigid base in documentation of medical facts [9]. In the ongoing study; the inclusion criteria were embracing all the problems that could truly affect the results of vascular feto-maternal Doppler studies as well as the results of nucleated red blood cell count, whereas the exclusion criteria were included all the medical cases which can give a false result of the neonatal asphyxia investigations. In the current study the Doppler study was used as an indicator for presence of risky vascular abnormalities because it is well documented that intrauterine fetal hypoxia induced by vascular abnormalities can affect Doppler result and causes subsequent perinatal morbidity represented by low Apgar score [10,11]. Also in placental dysfunction such as in pregnancy with hypertension, preeclampsia, intrauterine growth retardation, etc. the Doppler study of feto-maternal circulation is very important [10]. There is strong correlation between fetal hypoxemia and Doppler flow indices of uterine and fetal arterial with venous circulation, leading to growth restriction by reducing gas and nutrient transport [12,13]. Plus, Doppler velocimetry is non invasive technique which can be done with routine ultrasound examination without significant extra coast, in addition to its ability to determine the at- risk patients who need special care on the way to decrease the adverse pregnancy outcomes [14]. In the existing study; it was noticed that umbilical artery Doppler velocimetry was the most evaluated to reduce the perinatal mortality and morbidity. Increased flow resistance in the umbilical artery could denote abnormal placenta. Decrease utero – placental perfusion during uterine contraction can slow down gases exchange in the fetus who would be more liable to distress during labor [15,16]. In the ongoing results; group II (which included fetuses with abnormal Doppler studies) was divided to 3 further groups which were: group II[a]: included abnormal studies of umbilical artery and/or fetal descending aorta, with normal uterine artery, group II[b]: included abnormal studies umbilical artery and/or fetal descending aorta with abnormal uterine artery and group II[c]: included absent or reversed diastolic flow in umbilical artery with abnormal uterine artery blood flow as shown in Fig.1, in order to discriminate which group has the most effective vascular abnormal result. Apgar score at 5 minutes was used at this study because this score is well known to be used as a predictor for infant mortality and morbidity at the earlier life lime [17,18]. Also nucleated red blood cell in cord blood was used in the current study as one markers of perinatal asphyxia [19]. In table 1: The results showed that intrapartum fetal distress was associated with low Apgar score level, which was similar to previous documentation [20] resembling that of respiratory distress syndrome in relation to low Apgar score level [21]. Whereas number of cases admission to the neonatal care unit were equal in both Apgar score groups because within department of obstetrics and gynecology at Fatima Alzahraa administrative Hospital; it is a routine management to admit all the fetuses to the neonatal care unit, so as to avoid any sudden risky event that might lead to dangerous consequence on fetal well being, while the NNRBC >8/100 WBCs were more abundant at the group of low fetal Apgar score exactly like previous works [22]. Table 2 showed some perinatal data related to Apgar scoring one of these measurements were the mean AFI (in cm) which was decreased in the low

Apgar score group, going with previous facts [23]. Mean fetal weight (in kg) was also low in low Apgar score group, being the same with the previous information [24]. Mean gestational age (in wk) was smaller at the low Apgar score group, and the time of admission at neonatal care unit (days) was the longest at the low Apgar score group, because this is the most important period in determining the neonatal outcomes [25]. Mean NRBC counts was higher in low Apgar score group [26, 27]. In Table 3: The same perinatal data which had been studied in table 2 were also laid out there in the four groups that had been divided due to results of Doppler studies. Group I: All Doppler profiles were normal. Group II^{a}: included abnormal studies of umbilical artery and/or fetal descending aorta, with normal uterine artery, group II^{b}: included abnormal studies umbilical artery and/or fetal descending aorta with abnormal uterine artery and group II^{c}: included absent or reversed diastolic flow in umbilical artery with abnormal uterine artery blood flow, in order to distinguish which was the most effectual vascular abnormal result on those perinatal data. The mean AFI (in cm) was within normal level in the 1st and 2nd groups, which might give impression that level of amniotic fluid does not affect the end result of Doppler study of them, while it was decreased with 3rd and 4th groups which might give idea that level of amniotic fluid was affected by the bad result of Doppler study of these groups [23]. While the mean fetal weight (in kg) was progressively lower in the four groups which could give the initiative that the end results of Doppler study is strongly related to the fetal weight [15]. Mean gestational age (in wk) was progressively lower in the four groups which might provide the consideration that the end results of Doppler study have a strong relation with the fetal weight [28]. Whilst the time of admission at neonatal care unit (days) was the longest on the group II^{c}, which could offer the fact that this Doppler abnormality needs more time at neonatal care unit [16]. Mean NRBC count was increasing progressively in the four groups and had its peak at the 4th group (group II^{c}) suggesting that; this the most morbid Doppler results [28].

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