The Differences between Umbilical Artery Doppler Examination, Cardiotocography, Lactic Acid Levels of the Newborn and APGAR Score in Third Trimester Normal and High-Risk Pregnancy

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Background: *The high mortality rate of newborns due to asphyxia shows a lack of treatment and comprehensive prevention in newborns. There for an effective and efficient examination is needed in predicting the risk of fetal distress.*

Objective: *To evaluate the differences in fetal umbilical artery doppler, CTG, lactic acid levels of the newborn's umbilical cord and APGAR score of newborns in third trimester normal and high-risk pregnancy.*

Method: *This research is an observational analytic study with a case control design. The sample are third trimester women whom plan to be terminated according to inclusion criteria. According to the total sample count of 25 normal and 25 high-risk pregnancy groups. Data were analyzed using statistics.*

Results: *The majority of subjects are 20-35 years old in both groups, the highest gestational age are term in both groups, multigravida in both groups, the most common methods for giving birth in high-risk pregnancies are caesarean section, and vaginal birth in normal pregnancies. There were no differences in S/D Ratio, Pulsatile Index, Resistance Index, Lactic Acid and APGAR Score in high risk and normal pregnancy groups. There were no differences in CTG between both groups. There is no correlation of S/D Ratio, Pulsatil Index and Resistance Index with Lactic Acid in high risk and normal groups. There is no correlation of S/D Ratio, Pulsatil Index and Resistance Index with Apgar Score in high risk and normal groups.*

Conclusion: *There are no differences in umbilical artery doppler, CTG, lactic acid levels of the newborn umbilical cord and APGAR score in third trimester normal and high-risk pregnancy.*

Keywords: *Umbilical artery doppler, CTG, Lactic acid, High-risk pregnancy*

BACKGROUND

To this day, neonatal mortality rate is still very high, the World Health Organization quotes that 7,000 neonates worldwide die every day, 50% in the first week and 40% in the first 24 hours.[1] High-risk pregnancies has been associated with poor neonatal outcomes, proven by a study of Kacho et al which found umbilical pH and APGAR scores on 1st and 5th minute in high-risk mothers were significantly lower than in low-risk mothers.[2]

The systolic/diastolic ratio (S/D ratio) parameter of arterial umbilical Doppler examination can assess fetal umbilical cord blood flow which ables identifying fetal distress, especially in gestational age >30 weeks.[3,4] Frauenschuh et al[5,6] and Ying Gu[7] found that in umbilical artery Doppler examination of normal pregnancy, RI (resistance index), PI (pulsatile index), and S/D ratio decreases gradually as gestational age increases. In abnormal circumstances, RI, PI and S/D ratio of the umbilical artery will increase or undergo end diastolic flow or reversed end diastolic flow, which indicates fetal emergence.[5-7] This shows a decrease in blood flow accompanied by intrauterine hypoxia results in increased resistance to arterial flow umbilical which causes ischemic hypoxia in the fetus and anaerobic glycolysis and accumulation of lactic acid levels.[7]

Cardiotocography (CTG) may be carried out to assess fetal well-being including the presence of fetal distress by examining fetal heart rate and contractions.[8] Sandhu et al conducted CTG screening tests on high-risk pregnancy mothers, the study found as 150 samples with fetal distress, with 15% samples had normal CTG finding and 73% samples had abnormal CTG findings. Sensitivity, specificity and positive predictive value of CTG to predict APGAR score of <5 at birth were 66.7%, 93.3% and 53.3%.[9]

Lactic acid levels may represent fetal hypoxia through indirect examination of tissue hypoxia. Lactic acid levels in hypoxic state has become an important marker after it is known that metabolic acidosis causes elevated level of lactic acid. Lactasemia may cause increased intracranial pressure and necrosis in the brain.[10]

Effective and ergonomic examinations that can be used in daily practice are needed to predict the risk of fetal distress for more comprehensive prevention and intervention of the risks that may occur. This study will examine differences in umbilical arterial Doppler results, CTG findings, umbilical cord lactic acid levels and APGAR scores in high-risk and normal pregnant women, and assess the corelations between umbilical artery Doppler examinations with umbilical cord lactic acid levels and APGAR scores.

METHODS

This research is an observational analytic study with case control design. The study was conducted in the Department of Obstetrics and Gynecology in Haji Adam Malik General Hospital Medan and Sundari General Hospital in July to October 2019. The population of this study were in-labor 3rd semester pregnant women or with planned termination. Sample inclusion criteria were: 3rd trimester pregnant women to be terminated, all newborn neonates without congenital abnormalities and subjects willing to participate in the study. The exclusion criteria were: fetal death in the womb or fetal death in labor and subjects withdrew from the study. The number of samples in this study were decided to be 25 mothers in each group, which were normal pregnant women and high risk pregnant women groups.

The study subjects were examined and handled according to the Clinical Practice Guidelines of the Fetomaternal Division of H. Adam Malik Hospital Medan. Samples that met the inclusion criterias were examined with arterial umbilical Doppler and 20-minute CTG examination. Blood samples were taken on the umbilical cord immediately after the baby was born to assess lactic acid levels. APGAR score data were taken from medical records. The data is then tabulated and analyzed statistically.

RESULTS

In **Table 1**, we may see from the majority of the samples of both groups were 20-35 years old, namely of 19 high risk pregnant mothers (76%) and 24 normal pregnant mothers (96%). The majority of the gestational age were term pregnancy, namely of 22 high risk pregnant mothers (88%) and 24 normal pregnant mothers (96%). In both groups, majority are multigravid pregnancy, namely of 9 high risk pregnant mothers (36%) and 13 normal pregnant mothers (52%). The route of delivery in the high risk pregnancy group was by abdominal route (23 people, 92%) and in the normal pregnancy group the majority were by vaginal route (13 people 52%).

Table 1. Demographical characteristic of the subjects by age, gestational age, parity and delivery methods.

	High risk pregnancy		Normal pregnancy	
	n	%	n	%
Age (yrs)				
20-35	19	76	24	96
>35	6	24	1	4
Gestational age				
Preterm	3	12	1	4
Aterm	22	88	24	96
Parity				
Primi	8	32	6	24
Secundi	6	24	6	24
Multi	9	36	13	52
Grandemulti	2	8	0	0
Delivery				
Abdominal	23	92	12	48
Vaginal	2	8	13	52
Total	25	100	25	100

The high-risk pregnant mothers group consisted of 9 women (36%) with HIV, 5 with placenta previa totalis (20%), 4 with preeclampsia with severe symptoms (16%), 3 with age of >35 years (12%), 2 with grandemultigravida (8%), 1 with chronic PDA (4%), and 1 with eclampsia (4%).

Table 2. Distribution of S/D ratio, PI, RI, umbilical lactic acid and APGAR score in women with high risk pregnancy and normal pregnancy groups.

	High risk			Normal			p
	Mean	SD	95% CI	Mean	SD	95% CI	
S/D Ratio	2,72	0,36	2,58-2,88	2,87	0,56	2,64-3,10	0,291[a]
PI	0,95	0,12	0,91-1,00	0,96	0,12	0,91-1,00	0,981[a]
RI	0,62	0,05	0,61-0,65	0,64	0,07	0,61-0,67	0,535[a]
Lac tic acid	3,69	0,75	3,38-4,0	3,34	1,37	2,77-3,9	0,627[b]
APGAR	7,8	0,58	7,56-8,04	7,84	0,8	7,51-8,17	0,795[b]

a: T-independent, b: Mann-whitney

In fetal umbilical artery Doppler examination of high risk mother group obtained mean S/D ratio of 2.72 and a standard deviation (SD) of 0.36. The mean pulsatile index (PI) of high risk pregnant women is 0.95 and SD of 0.12. The mean resistance index (RI) of high risk pregnant women is 0.62 and SD 0.05. In the normal pregnancy group, the mean S/D ratio is 2.87 and SD 0.56. The mean PI of normal pregnant women was 0.96 and SD 0.12. The mean RI of normal pregnant women is 0.64 and SD 0.07. There were no significant differences between S/D ratio, PI and RI of both groups (p valure, respectively: 0.291, 0.981, and 0.535).

The obtained mean lactic acid levels in the high-risk pregnant group was 3.69 with SD of 0.75,

while in the normal normal pregnancy group was 3.34 with SD of 1.37. No significant difference of lactic acid levels (p 0.627) was found in the two groups. The obtained mean APGAR score in high risk pregnant women was 7.80 with SD of 0.58, whereas in normal pregnant women the mean was 7.84 with SD of 0.80. No significant difference of APGAR scores was found (p 0.795) in both groups.

Table 3. CTG finding comparison between high-risk pregnancy and normal pregnancy groups.

CTG	High risk		Normal		p
	n	%	n	%	
Category 1	25	100	25	100	1,000

In the CTG examination of high risk pregnant women and normal pregnancy, the overall findings was of category 1 with 25 people (100.0%) in each group, which did not show any different CTG findings (p= 1.00).

Table 4. Correlation of S/D ratio, PI and RI with umbilical lactic acid and APGAR Score in high-risk pregnancy and normal pregnancy groups.

	Lactic acid	
	R	p
S/D ratio	-0, 072	0,619
PI	-0, 177	0,222
RI	0,002	0,987
	APGAR Score	
	R	p
S/D ratio	0,017	0,908
PI	-0,271	0,057
RI	0,073	0,613

In **Table 4** shows that there were no correlation between S/D ratio (p= 0.619), PI (0.222) and RI (0.987) with lactic acid in both high risk pregnancy group and normal pregnancy group. There were no correlation between S/D ratio (p = 0.908), PI (0.057) and RI (0.613) with APGAR scores in both groups.

DISCUSSION

In this study, subjects of age group >35 years were found higher in high-risk pregnancy group compared to the normal pregnancy group. Pregnancy at risky age may increases both maternal and neonatal morbidity and mortality. A study by Ambrogio et al found that pregnant women aged >40 years have higher prevalence of respiratory distress syndrome, interventricular hemorrhage (IVH), neonatal death and intrauterine growth restriction. Pregnant women aged <17 years have higher risk of developing low birth weight and IVH,[11,12] preterm births, low APGAR scores and postnatal mortality.[13] (**Table 1**)

As shown in **Table 1**, mothers of high-risk pregnancy groups experienced preterm birth more than the normal pregnancy group. Perinatal and neonatal mortality and long-term morbidity are closely related to gestational age at delivery. High-risk pregnancies are more at risk of early termination of pregnancy, example in preeclampsia with severe symptoms in which continuing pregnancy may worsen the condition of the mother or baby, eclampsia, pulmonary hypertension, and heart disease. In a study by Halimi et al of 810 pregnant women, found that 48.7% of mothers experienced preterm birth with various risk factors including hypertension, obesity, and preeclampsia. Ogawa et al stated that pregnancies in older age (> 45 years) had a significant relationship with preterm birth.[14,15]

The majority of the high-risk pregnancy group is 9 multigravid mothers (36%), followed by 8 primigravida (PG) mothers (32%), 6 secundigravid mothers (24%), and 2 grandemultravida mothers (8%). Primigravida is a risk factor for high-risk pregnancy, especially in older age mothers. A study by Moses et al in older age PG women shows that 87 of 100 subjects had antenatal complications. Hypertension in pregnancy is found as much as 24% in older PG mothers. Laxmi et al stated that diabetes mellitus was 6% higher in primigravida of older age.[16,17] Complications of high parity, especially with old age and close pregnancies period are maternal anemia, postpartum hemorrhage, and fetal malpresentations.[18,19] (**Table 1**)

As shown in **Tabel 1**, the most common delivery route of the high-risk group was by abdominal (23 mothers, 92%). Study by Busaidi et al found several predictors of caesarean section: age (>25 years), history of previous caesarean section, high BMI, extreme infant birth weight (<2.5 kg, >4 kg), pre-pregnancy diabetes.[20] In this study, most indications for cesarean section are mothers with HIV (10 subjects), with 1 case with preeclampsia with severe symptoms, followed by total placenta previa of 5 cases, history of previous caesarean section of 5 cases, preeclampsia with severe symptoms and uncontrolled blood pressure of 1 case, eclampsia of 1 case and chronic PDA of 1 case.

As shown in **Tabel 2**, in the comparison of S/D ratio, PI dan RI of both groups, we obtained p values are 0.291, 0.981, 0.535 respectively, thus it was concluded that there were no significant differences between the S/D ratio, PI and RI of the two groups. The results of this study are supported by the findings of study by Kant et al, in the normal pregnant group, 34 mothers (97.1%) had umbilical arterial velocymmetry PI ratio ≤1.42, whereas in the high risk pregnant group, 6 mothers (17.1%) had umbilical arterial velocymmetry PI ratio above the gestational age-specific cut-off and 29

patients (82.9%) had umbilical arterial PI ratio below the gestational age-specific cut-off. The difference between the two study groups was not statistically significant.[21] However, according to Alfirevic et al, the use of umbilical artery Doppler ultrasound in high-risk pregnancy could reduce perinatal mortality.[22]

Lactate plasma level in umbilical artery and vein rises as gestational age increases, showing gradual development of intrauterine physiological lactaemia. Lactic acid dehydrogenase (LDH) is one of many markers of several disorders in neonates, one of which is asphyxia. In a study by Patavoukas et al, the median value of aLDH was higher (p= 0.001) in mothers with a history of chronic disease. There was no difference in aLDH in neonates from mothers with complications compared with normal pregnancies (> 612 μ/L, p= 0.95).[23] In accordance with the results of this study, there were no difference of fetal cord lactate value (p = 0.627) in both high-risk and normal pregnancy groups. No subjects in this study experiences fetal distress, and all of them had favorable outcomes assessed by APGAR scores. (**Tabel 2**)

This result contradicts the study by Mousa et al that found the mean±SD umbilical pH in the high-risk pregnancy group was lower than in the normal group, and a significant correlation was obtained between umbilical pH and low APGAR scores with the incidence of adverse neonatal outcomes such as NICU treatment and resuscitation procedures.[2] Naina Kumar et al said that hypoxia can occur due to impaired maternal oxygenation, placental perfusion or blood supply to the fetus. As a result of inadequate oxygenation, anaerobic metabolism occurs with the production of large amounts of organic acids, especially lactic acid. Lactic acid accumulation causes buffer system depletion resulting in metabolic acidosis with low fetal pH, fetal distress, and poor APGAR score at birth.[24] Fetal acidosis may increase the risk of cerebral paralysis, ischemic encephalopathy and neonatal death.[25-27]

In this study, there was no significant difference in APGAR scores found in high risk group and normal pregnancy group (p=0,795). (**Tabel 2**) APGAR score is influenced by gestational age, medication, resuscitation procedures, cardiorespiratory and neurological conditions. Many other modalities besides the APGAR score, namely poor CTG findings, umbilical arterial blood gas abnormalities, clinical brain function, neuroimaging, neonatal electro-encephalography, placental pathology, hematological studies, and multisystem organ dysfunction need to be considered for diagnosis of intrapartum hypoxia. Category I (normal) or category II CTG findings are associated with an APGAR score >7 at the 5th minute, normal umbilical arterial blood pH (± 1 SD), or both, are inconsistent with the incidence of acute hypoxia-ischemic.[28] In one study obtained mean APGAR scores in the first 1 and 5 minutes are significantly lower in high-risk mothers than in low-risk pregnancy. However there was no significant difference in the APGAR scores of the 10th and 15th minutes between the two groups.[2]

Preterm gestational age is known to be a strong risk factor for low APGAR scores.[29] However, this study found no difference in APGAR scores in high or normal risk pregnancies, where as 22 samples in the high risk group were at term gestational age and had good intrauterine fetal condition assessed before delivery.

In this study, all subjects obtained during the KTG examination with the results of category 1 (p = 1,000) indicating the absence of signs of fetal distress, this is supported by the normal APGAR score in each group. (**Tabel 3**). Fetal distress can be caused by insufficient placental circulation due to several diseases such as preeclampsia, but not all high-risk pregnancy conditions cause fetal distress, this is evidenced by the favorable CTG finding and APGAR scores in all subjects of this study.[30] A previous study showed there was no role of CTG monitoring in good perinatal outcomes, but only increases the number of caesarean sections. Other studies have shown that CTG monitoring has a good role in improving perinatal outcomes.[31]

A study by Sandhu et al conducting CTG in high-risk pregnant women acquired the sensitivity of CTG in predicting APGAR score <5 at birth was 66.7%, specificity was 93.3% and PPV was 53.3%. The study stated that CTG can be used to identify patients with neonatal outcomes and may improve treatment.[9] In the study of Gupta et al of 201 cases, 63.2% of cases had reactive CTG and 36.8% had non-reactive CTG. The most common indications for CTG monitoring were PIH (34.8%), previous caesarean section (15.4%), oligohydramnios (13.9%), postdate (12.4%), Rh negative and IUGR (6.5%) , GDM (5.5%) and anaemia (5.0%).[31] Sood et al concluded that intrapartum CTG monitoring can detect preexisting fetal distress and increase surgical interventions in high-risk pregnancies.[32] A study by Verma et al concluded that CTG can be used as a screening to detect and determine the right time to intervene fetuses with high risk.[33]

Analytical study showed that there were no correlation between S/D ratio (p= 0.619), PI (0.222) and RI (0.987) with umbilical lactic acid level in the high risk and normal pregnancy groups. There were no correlation between S/D ratio (p=0.908), PI (0.057) and RI (0.613) with APGAR scores in both groups. (**Tabel 4**)

In a normal pregnancy, the value of S/D ratio, RI and PI will decrease as the gestational age increases, to placental blood vessel development, luminal expansion, reduction of resistance and increase in umbilical arterial blood flow. When acute fetal distress occurs, the S/D ratio, RI and PI are significantly higher than the normal group. This suggests that in umbilical blood flow ultrasound examination of acute fetal

distress, increase blood vessel resistance and decrease blood flow may be found.[6] Increased umbilical artery resistance and decreased blood flow can result in increased local ischemic and hypoxia and anaerobic glycolysis, which ultimately leads to local accumulation of lactic acid.[34,35]

Study by Dai et al found umbilical arterial blood gas analysis, pH and PaO2 in high-risk pregnant women were significantly lower than in the normal group and negatively correlated with S/D ratio, PI and RI of umbilical artery Doppler ultrasound. PaCO2 and lactic acid were significantly higher in the high-risk pregnant group and positively correlated with S/D ratio, PI and RI. This suggests that umbilical artery Doppler ultrasound can assess local blood perfusion and the degree of hypoxia.[6] Study by Kant et al shown that Doppler ultrasound examination in high-risk pregnancies may improve fetal outcomes and prevent prenatal mortality.[21]

In a previous study comparing neonates who had APGAR scores <7 with APGAR scores> 7, higher umbilical vascular resistance was found in fetuses with APGAR scores <7. In contrast, another study found that abnormal umbilical artery Doppler ultrasound had no effect in determining further newborn care, birth weight, and gestational age.[36] The results of the former study showed that fetuses with abnormal umbilical artery Doppler ultrasound underwent earlier labor (<36 weeks of gestation, NICU treatment, and low APGAR score) compared to those with normal Doppler ultrasound results.[36-38]

CONCLUSION

In this study, the majority of the subjects were at the age of 20-35 years, multigravid and at term pregnancy in both high-risk and normal pregnancy groups. The majority of high-risk pregnancy mothers underwent abdominal delivery. The majority of normal pregnancy mothers underwent vaginal delivery. There were no significant differences between S/D ratio, Pulsatile Index (PI), Resistance Index (RI), umbilical lactic acid, APGAR scores and CTG findings of the high-risk and normal-pregnancy women. There was no correlation between S/D ratio, PI and RI with lactic acid in both groups. There was no correlation between S/D ratio, PI and RI with APGAR scores in both groups.

Further studies needs to be done with more specific research group case groups (preeclampsia, fetal distress, etc.), in order to find out whether umbilical artery Doppler examination and CTG have advantages in predicting fetal distress as proven with newborn umbilical cord lactic acid, thus it may made to be a mandatory examination of certain condition of mothers and fetuses.

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