THE ROLE OF CARDIOTOCOGRAPHY IN ASSESSING THE CONDITION OF A FETUS IN PREECLAMPSIA

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The role of cardiotocography (CTG) in preeclampsia is still vaguely defined. The aim of this study was to investigate the possible role of CTG in assessing the condition of the fetus in preeclampsia with and without intrauterine growth retardation (IUGR) and to compare the CTG findings with Doppler parameters and perinatal outcome. The prospective study included 30 singleton pregnancies with preeclampsia completed by caesarean section. The study group was divided into subgroups based on the presence of IUGR in relation to the severity of preeclampsia. The control group consisted of 20 healthy women delivered by elective caesarean section. In 53.3% of preeclamptic cases, cardiotocographic findings differed from normal (p<0.001) and they were either warning or pathological. There were no significant differences in the presence of a pattern deviating from normal based on the severity of preeclampsia, and it was significantly more prevalent in preeclampsia with IUGR (p<0.01) than the one without it. The prevalence of CTG pattern types in the study group was significantly altered by presence of olygoamnion (p<0.05) as well as the parameters of the flow through the uterine arteries, umbilical artery and middle cerebral artery (p<0.05). Appar score significantly depends on the CTG findings and decreases with the unfavourable CTG pattern.

CTG and Doppler ultrasonography complement each other in order to improve perinatal outcome in preeclampsia. CTG is irreplaceable as a first measure of rapid assessment of the fetal condition in newly diagnosed cases of preeclampsia, aiming also to and in order to detect complications from umbilical cord during its follow-up. *Acta Medica Medianae* 2015;54(2):41-47.

Key words: cardiotocography, IUGR, preeclampsia, ultrasonography

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Introduction

Preeclampsia is a serious disorder, unique in human pregnancy characterized by generalized dysfunction of endothelial cells. The importance of preeclampsia is particularly high, it complicates on average 4% to 8% of pregnancies and has remained one of the two most common causes of maternal death both in developed (1-3) and developing countries (4). The syndrome of preeclampsia is associated with high risk of preterm delivery, IUGR, placental abruption and perinatal morbidity and mortality (5,6).

It is often associated with intrauterine growth retardation (IUGR), and IUGR in preeclampsia is

defined by the presence of placental insufficiency (7). Placental insufficiency in early IUGR is associated with histological signs of abnormal implantation (8). Uteroplacental insufficiency invol-ves factors that disrupt maternal-placentofetal exchange due to impaired uterine perfusion (as a consequence of the absence of changes in the spiral arteries) and due to deficient placental villi surface area for the exchange of oxygen and nutrients, as a result of changes in villi and their microcirculation. Insufficient conversion of the spiral arteries includes the presence of the smooth muscle cells, which leads to longer periods of vasoconstriction and major fluctuations in the delivering of oxygen in intervillous space. This reperfusion after ischemia leads to the oxidative stress and damages the tissue and the vasculature of the placenta.

Oxidative stress is a possible cause of apoptosis of endothelial cells, leading to capillary regression (9). This regression causes an increase in vascular resistance and changes in vascular parameters of the flow in the umbilical artery (10,11). Measurement of the flow in the umbilical artery is an indirect measurement of the resistance to the flow in placenta (12). In pregnancies complicated by hypertension and/or IUGR placental flow is often associated with the increased resistance. This can often result in absent or even reversed end-diastolic flow in the umbilical artery during the second or third trimester of the pregnancy (13,14). This justifies the evaluation of the uterine circulation by color Doppler ultrasound in order to predict IUGR (15) as well as measurement of the flow through umbilical artery as an important parameter in predicting perinatal outcome of IUGR fetus.

The role of cardiotocography (CTG) as a diagnostic method in preeclampsia is still vaguely defined. Major lack of CTG as a diagnostic method in chronic intrauterine fetal hypoxia is late occurence of changes (16). For the purpose of reduction of perinatal morbidity and mortality, the priority is given to other, more sensitive diagnostic methods such as Doppler ultrasonography, especially for the purpose of monitoring pregnancies complicated by preeclampsia and evaluation of the timing for the completion of pregnancy, i.e. planned delivery. However, highlighting the emergence of warning CTG phenomenon, before the onset of late pathological CTG records, could make a significant contribution in improving perinatal outcomes and position cardiotocography as a method that has its place in the diagnosis and monitoring of pregnancies with preeclampsia.

Aim

The aim of this study was to investigate the possible role of cardiotocography in assessing the condition of the fetus in pregnancies complicated by preeclampsia with and without IUGR, and to compare the CTG findings with Doppler parameters in uteroplacental, fetoplacental and fetal circulation, as well as perinatal outcome.

Patients and Methods

A prospective study was conducted at the Clinic of Obstetrics and Gynecology, Clinical Center in Niš. The study group consisted of 30 pregnant women whose pregnancies were complicated by preeclampsia, terminated by cesarean section: pregnancies were singletons, and there were no fetal anomalies and preexisting clinical disorders in pregnant women. The criteria for diagnosing preeclampsia were new-onset arterial hypertension, or diastolic pressure ≥90mmHg and systolic pressure ≥140 mmHg, measured on two separate occasions within 24 hours, with a gap of more than 6 hours, and proteinuria of \geq 300mg of protein in 24-hour urine samle which were developed after the 20th week of pregnancy in previously normotensive women (17). The study group was divided into two subgroups based on the presence of IUGR where the criterion for setting the diagnosis was birth weight of neonates below the tenth percentile for a given gestational age. Also, the division of the study group into two subgroups based on the severity of preeclampsia

was performed, where the criterion for the diagnosis of severe preeclampsia represented the presence of one of the following criteria: systolic blood pressure ≥160 mmHg or diastolic ≥110 mmHg, proteinuria $\geq 2g/24h$, elevated serum creatinine, persistent headache or cerebro-visual disorders, persistent epigastric pain, platelet count <100.000/mm3 and/or findings of microangiopathic hemolytic anemia (18). The control group consisted of 20 healthy pregnant women with singleton pregnancies, no fetal anomalies, delivered by elective Caesarean section due to other obstetric indications that cannot be linked to the etiopathogensis of tested disorders (previous Caesarean section, breech presentation, and ophthalmologic indication). The study was approved by the Ethical Committee of the Medical Faculty of Medicine of the University of Niš and with the informed consent of the involved participants.

Ultrasonogrphic Doppler measurements were conducted at the Clinic of Obstetrics and Gynecology, Clinical Center Niš on the ultrasonographic device Toshiba Nemio XG SSA - 580A with 3.5 MHz transabdominal transducer to the free floating convolutes of the umbilical cord with a pregnant woman on her semi-left side. The parameter values of uteroplacental, fetoplacental and fetal circulation were all measured within three days before delivery. Pulsatile index (PI), resistance index (RI) and systolic-diastolic index (S/D) were measured in all cases. The flows were measured through both uterine arteries, umbilical artery and middle cerebral artery. The flow in the uterine artery was qualified as (19):

- normal;

- pathological (if the average (left and right) S/D ratio was higher than 2.6 and the notch was present on both sides).

The flow in the umbilical artery was qualified as (20):

- normal;

- decreased (increased PI for more than 2SD compared to the average for a given gestational age based on reference standards, but still present end-diastolic flow);

- absent or reverse end-diastolic flow (ARED).

The flow through the middle cerebral artery is classified as:

- normal;

- present cerebral vasodilatation (when RI falls below 70) and

- present decompensated vasoconstriction (when RI returns to normal).

Ultrasound assessment of amniotic fluid volume used the AFI≤50mm values (amniotic fluid index) as a criterion for diagnosis of olygoamnion.

Cardiotocographic recording used conventional cardiotocographic equipment (Bistos BT-350, FC700 Gima and Hewlitt Packard 50A) with paper speed of 10mm/min and the cardiotocographic patterns of 30 minutes were visually analyzed on the day of caesarean birth. The analysis used the definitions and criteria of the National Institute of Child Health and Human Development (21), and the division of variable decelerations by severity is based on the grounds of Kubli et al (22). After analyzing the cardiotocographic pattern they were qualified as:

- Normal cardiotocographic pattern (reactive non-stress test or negative contraction stress test);

- Warning cardiotocographic pattern (nonreactive non-stress test with minimal variability or the presence of light variable decelerations during non-stress test or contraction stress test where the light variable decelerations include variable decelerations that last up to 30 seconds regardless of the depth of the fall in the fetal heart rate (FHR) or if FHR≥80 irrespective of the length of variable deceleration);

- Pathological cardiotocographic pattern (the presence of medium and severe variables or late decelerations where the medium variable decelerations include those which last 30-60s with FHR<70 or last more than 60s with $70 \le FHR < 80$, and the severe include variable decelerations that last longer than 60s with FHR<70).

The results were systematized, grouped and the database was created. Statistical analysis was performed by SPSS 15.0 program package. Continuous variables are presented as mean values, standard deviations and median, while the gualitative ones are presented by their frequency and percentage. Determination of the normality of distribution of continuous variables was performed by Shapiro Wilk test. If the distribution of continuous variables was normal, the comparison of arithmetic means values of two independent samples was performed by Student's t-test for independent samples, on Mann-Whitney U-test. The Kruskal-Wallis test was used for compa-ring non-normal continous variables for more than two groups. Comparison of absolute frequencies of categorical variables was performed by Chi-square test and his variants according to the size of the samles (Mantel-Haenszel's Chi-square test and Fisher's exact test).

Results

Table 1 shows the clinical characteristics of pregnancies complicated by preeclampsia compared to the control group. The parity of pregnant women was significantly higher in the control compared to the study group for p<0.01, which is not surprising, and is predominantly due to the manner of forming the control group, which primarily consists of women with a previous caesarean section as the main indication for repeated cesarean delivery and in order to avoid pathological conditions that could impair the quality of the control group. In preeclampsia, the average gestational age at the time of delivery was significantly lower than in the control group (p<0.001).

Among the laboratory-biochemical parameters, average values of D-dimer levels were significantly higher in preeclampsia, but did not exceed the upper limit of normal pregnancy values. The average number of platelets in preeclampsia was lower, and the values of biochemical parameters which are the main indicators of severity of preeclampsia, were higher. In the study group, severe preeclampsia was reported in 73.3% of patients, while in 63.3% preeclampsia was associated with IUGR. The average birth weight of neonates with preeclampsia was smaller and perinatal outcome poorer (Table 1).

Normal cardiotocographic pattern was present in all patients of the control group and in 53.3% of cases of preeclampsia the CTG findings differed from normal (p<0.001) and they were eather warning or pathological. The presence of normal CTG pattern is more frequent in the patients with mild preeclampsia compared to those with a severe form of the disease, but without statistically significant difference. It is noted that the warning cardiotocographic pattern was significantly more prevalent in the patients with severe preeclampsia (p<0.05) and this finding was dominant in this group of patients (Table 2).

Normal cardiotocographic pattern is statistically more frequent in preeclampsia without IUGR (p<0.01). In only about ¹/₄ of pregnancies where preeclampsia was associated with IUGR normal CTG pattern was present. In this subgroup also the finding of warning CTG pattern was a dominant finding (Table 3).

It was found that the prevalence of CTG pattern types in the study group was significantly altered by the presence of olygoamnion (Table 4). The pathological CTG pattern was reported only in the study group patients with present olygoamnion (p<0.05). In cases with olygoamnion, CTG finding in 72.7% deviates from the normal (warning or pathological).

Also, it was found that there was statistically significant correlation of pathological CTG pattern and pathological flow through the uterine arteries (p<0.05) in the study group (Table 5). It is obvious that in all cases of pathological CTG pattern it was about the presence of pathological flow in the uterine artery. If reduced and absent flow through the umbilical artery is viewed as pathological and when the warning and pathological CTG pattern is viewed as deviating from normal, there is a statistically significant correlation between CTG findings and flow through the umbilical artery (p<0.05). When warning and pathological CTG pattern are viewed as deviating from normal, there is a statistically significant correlation between CTG finding and flow through the middle cerebral artery (p<0.05), i.e. the pathological flow through the middle cerebral artery is associated with the warning or pathological CTG pattern.

Apgar score significantly depends on the type of CTG findings and decreases with the more unfavourable CTG patterns (Kruskal-Wallis test – p<0.01). It is the highest in normal, somewhat lower in warning, and much lower in pathological CTG patterns (Table 6). There was also a correla-

Table 1. The clinical characteristics of	of pregnancies complicated by	y preeclampsia compared to the control group	c
	n pregnancies complicated by	y preceduripsia compared to the control group	,

	Proocla	mncia ª	n=30	Control	aroup ^a	n=20
				Control group ^a 29.50± 4.54		
Age (years)						28.50
Parity	$1.40\pm$	0.62	1.00	$1.85\pm$	0.37 **	2.00
Gestational age (weeks)	36.63±	2.61	37.50	39.25±	0.97***	39.00
Sistolic blood pressure ^c	$166.00\pm$	17.88***	160.00	$106.50\pm$	11.93	110.00
Diastolic blood pressure ^c	107.07±	10.28***	105.00	65.75±	5.91	70.00
D-dimer ^c (ng/ml)	660.07±	658.15^{*}	505.00	447.00±	303.31	369.50
Platelet count ^d (x10 ⁹ /L)	201.03±	51.52	207.50	$253.10\pm$	71.87**	238.50
Aspartate transaminase ^c (U/L)	23.63±	8.57**	21.00	18.26±	6.24	17.45
Alanine transaminase ^c (U/L)	$18.51\pm$	7.75**	16.30	12.28±	5.03	9.65
Lactate dehydrogenase ^c (U/L)	467.97±	229.61***	416.30	308.07±	80.04	304.50
Uric acid ^c (µmol/L)	329.38±	82.03***	327.35	232.02±	39.58	225.15
Incidence of severe preeclampia	22	73.33%	***	0	0.00%	
Incidence of IUGR ^b	19	63.33%	***	0	0.00%	
Birth weight (grams)	2374.33±	849.02	2225.00	3425.00±	451.46***	3475.00
APGAR score 1 min	7.53±	1.57	8.00	8.80±	0.41***	9.00
APGAR score 5 min	8.10±	0.99	8.00	8.95±	0.22***	9.00

^a Data are presented as mean values \pm standard deviation, median, or as frequencies and percentages; ^b IUGR-Intrauterine growth retardation; ^c Highest value recorded; ^d Lowest value recorded; * – p<0.05; ** – p<0.01; *** – p<0.001

Table 2. Cardiotocographic findings in the subgroups of preeclampsia in relation to the severity of desease

Severe p	preeclampsia	n ^a n=22	Mild pr	eeclampsia ^a n	=8
8	36.36%		6	75.00%	
12	54.55%	*	1	12.50%	
2	9.09%		1	12.50%	
	Severe p 8 12 2	8 36.36% 12 54.55%	12 54.55% *	8 36.36% 6 12 54.55% * 1	8 36.36% 6 75.00% 12 54.55% * 1 12.50%

^a Data are presented as frequencies and percentages; * – p<0.05

Table 3. Cardiotocographic findings in the subgroups of preeclampsia with and without intrauterine growth retardation (IUGR)

Cardiotocographic pattern	Preeclamps	sia with IUGF	R ^a n=19	Preeclan	npsia witho	ut IUGR ^a n=11	
Normal	5	26.32%		9	81.82%	**	
Warning	11	57.89%		2	18.18%		
Pathological	3	15.79%		0	0.00%		
^a Data are presented as frequencies and percentages ** _ p <0.01							

Data are presented as frequencies and percentages ** - p<0.01

Table 4. Cardiotocographic findings in preeclampsia in relation to the presence of oligoamnion

Cardiotocographic pattern	With	Oligoamnion ^a	Without	Oligoamnion ^a				
Normal	3	27.27%	11	57.89%				
Warning	5	45.45%	8	42.11%				
Pathological	3	27.27%*	0	0.00%				
^a Data are presented as frequencies and percentages: $* = p<0.05$								

^a Data are presented as frequencies and percentages; * – p<0.05

Table 5. Cardiotocographic findings in preeclampsia in relation to the type of flow through the uterine arteries, umbilical and middle cerebral artery

Cardiotocographic pattern	Flow through the uterine arteries ^a								
		Normal	Pathological						
Normal	10	47.62%	4	44.44%					
Warning	11	52.38%	2	22.22%					
Pathological	0	0.00%	3	33.33%*					
Cardiotocographic pattern		Flow through the umbilical artery ^a							
		Normal	Decreased		ARED ^b				
Normal *	13	61.90%	1	16.67%	0	0.00%			
Warning	7	33.33%	4	66.67%	2	66.67%			
Pathological	1	4.76%	1	16.67%	1	33.33%			
Cardiotocographic pattern		Flow through the middle cerebral artery ^a							
		Normal	Corobroly	Decompensate					
		Normal	Cerebrar v	asodilatation	vasoco	Instriction			
Normal *	14	56.00%	0	0.00%	0	0.00%			
Warning	10	40.00%	3	60.00%	0	0.00%			
Pathological	1	4.00%	2	40.00%	0	0.00%			

^a Data are presented as frequencies and percentages; ^b ARED - Absent or reverse end-diastolic flow; * - p < 0.05

				Neonatal asphyxia						
X ±SD	Ме	n	No	Not present Mild n=21 n=4					Severe n=1	
3.14±1.10	8.00	14	12	57.14%	1	25.00%	1	25.00%	0	0.00%
7.54±1.05	8.00	13	9	42.86%	2	50.00%	2	50.00%	0	0.00%
1.67±2.52	5.00	3	0	0.00%	1	25.00%	1	25.00%	1	100.00%
7	.14±1.10 .54±1.05 .67±2.52	.14±1.10 8.00 .54±1.05 8.00 .67±2.52 5.00	.14±1.10 8.00 14 .54±1.05 8.00 13 .67±2.52 5.00 3	.14±1.10 8.00 14 12 .54±1.05 8.00 13 9 .67±2.52 5.00 3 0	.14±1.10 8.00 14 12 57.14% .54±1.05 8.00 13 9 42.86% .67±2.52 5.00 3 0 0.00%	.14±1.10 8.00 14 12 57.14% 1 .54±1.05 8.00 13 9 42.86% 2 .67±2.52 5.00 3 0 0.00% 1	$\begin{array}{c c c c c c c c c c c c c c c c c c c $	n=21 $n=4$.14±1.10 8.00 14 12 57.14% 1 25.00% 1 .54±1.05 8.00 13 9 42.86% 2 50.00% 2 .67±2.52 5.00 3 0 0.00% 1 25.00% 1	$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$

Table 6. Cardiotocographic pattern and perinatal outcome in preeclampsia

percentages;** – p<0.01

tion between CTG patterns and neonatal asphyxia, determined by the analysis of 3x4 contingency table which is an integral part of Table 6. It is evident that in the absence of neonatal asphyxia CTG pattern is usually normal. In the only case with severe neonatal asphyxia, CTG pattern was pathological.

Discussion

Our results demonstrated that the CTG pattern that deviates from the normal was more frequent in patients with preeclampsia than in the control group, and especially in preeclampsia associated with IUGR compared to the one without IUGR. According to clinical manifestations and severity of preeclampsia no statis-tically significant differece in CTG findings (severe preeclampsia compared to mild) was found. The appearance of a warning CTG findings, especially the occurence of variable decelerations was significantly greater in fetuses with preeclampsia and IUGR, as well as in our study, because these conditions are often associated with olygoamnion, and the decreased amount of amniotic fluid increases the risk of compression of the umbilical cord. In their statement, Kurjak and Matijević suggest that one third of fetuses with IUGR show positive oxytocin stress test (23). In chronic intrauterine fetal hypoxia, the pathological CTG pattern is only a late manifestation of placental insufficiency. In the initial stage of centralization of blood flow, CTG pattern may still be normal. However, in the advanced stage it comes to progressive changes, there is a significant reduction in the amount of amniotic fluid, oxytocin test become positive, followed by the appearance of pathological CTG finding even in peace (24). As the centralization of blood flow occurs only when the fetus is already suffering from hypoxia and acidosis, the pO2 and pH decline is present in fetal blood. The rate of perinatal mortality in this group of fetuses is high, and survived fetuses have a high incidence of neonatal complications such as neonatal asphyxia, meconium aspiration syndrome, hypoglycemia, polycythemia, necrotizing enterocolitis, and hemorrhage due to vasoconstriction and hypoxia in certain organs (25).

Therefore, for the purpose of reduction of perinatal morbidity and mortality, the advantage is given to a more sensitive diagnostic methods such as Doppler ultrasonography, especially for the purpose of monitoring pregnancies complicated by preeclampsia and planning a suitable moment to end a pregnancy. However, we believe that in pregnancies with preeclampsia CTG has its important place. In our study, cardiotocography is shown as a diagnostic method that correlates well with condition of the newborn, so the Apgar score of neonates significantly depends on the type of CTG pattern and decreases with the more unfaourable CTG patterns.

This supports the fact that the CTG could play a central role in the rapid assessment of the condition of the fetus in receiving preeclamptic women that are not controlled during pregnancy as the first measure that could reduce the time loss with other diagnostic methods to assess the condition of the fetus and thus improve perinatal outcome. A number of pregnant women whose pregnancy is not controlled is not small, especially in developing countries. Also, the role of the control in cases of previously diagnosed chronic uterine Doppler ultrasonography hypoxia using is important, when CTG monitoring can detect acute accidental events such as complications from umbilical cord, especially in the field of olygoamnion and when it can contribute to alter the decisions about the time of termination of pregnancy, i.e. to replace the planned delivery with an urgent one. The study of Rahman et al. suggested that cardiotocography as a simple and non-invasive method has its place especially as a screening in high-risk pregnant women in order to detect fetal distress already present, as well as to prevent delay in completion of pregnancy (26).

Our clinic does not have computerized cardiotocography, and we believe that neither do the perinatal departments of the most developing countries, but certainly that its implementation to wide use would reduce intra- and inter- observer variability in the interpretation of conventional CTG patterns and increase its diagnostic value (27,28).

Conclusion

Both cardiotocography and Doppler ultrasonography have their places in the monitoring of pregnancies complicated by preeclampsia. The two methods complement each other in order to improve perinatal outcomes. CTG is irreplaceable as a first measure of rapid assessment of the fetal condition in newly diagnosed cases of preeclampsia, aiming also to detect complications from umbilical cord during its monitoring, especially in olygoamnion.

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ULOGA KARDIOTOKOGRAFIJE U PROCENI STANJA FETUSA KOD PREEKLAMPSIJE

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Uloga kardiotokografije (CTG) kod preeklampsije još uvek je nejasno definisana. Cilj ovog rada bio je da ispita moguću ulogu CTG-u proceni stanja ploda kod trudnoća komplikovanih preeklampsijom sa i bez intrauterusnog zastoja u rastu (IUGR) i da komparira CTG nalaz sa Dopplerskim parametrima i sa perinatalnim ishodom. Prospektivna studija obuhvatila je 30 jednoplodnjih trudnoća sa preeklampsijom završenih carskim rezom. Ova ispitivana grupa podeljena je na podgrupe u odnosu na prisustvo IUGR i u odnosu na težinu preeklampsije. Kontrolnu grupu činilo je 20 zdravih trudnica porođenih elektivnim carskim rezom. Analizirane su kliničke karakteristike trudnica, dopplerski parametri, CTG zapisi i perinatalni ishod. Kod 53,3% slučajeva preeklampsije kardiotokografski nalaz je odstupao od normale (p<0,001), odnosno bio je upozoravajući ili patološki. Nije bilo značajne razlike u prisustvu zapisa koji odstupa od normalnog u odnosu na težinu preeklampsije, a značajno je bio prisutniji kod preeklampsije sa IUGR (p<0,01) u odnosu na onu bez niega. I kod teške preeklampsije i kod preeklampsije sa IUGR upozoravajući CTG zapis (p<0,05) je dominantan nalaz. Na zastupljenost tipova CTG zapisa u studijskoj grupi statistički značajno utiče prisustvo oligoamniona (p<0,05) kao i parametri protoka kroz uterine arterije, umbilikalne arterije i medijalnu cerebralnu arteriju (p<0,05). Apgar skor značajno zavisi od tipa CTG nalaza i smanjuje se sa nepovoljnijim CTG zapisima.

Kardiotokografija i Doppler ultrasonografija jedna drugu dopunjuju u cilju poboljšanja perinatalnog ishoda kod preeklampsije. Kardiotokografija je suverena kao prva mera brze procene stanja ploda kod novodijagnostikovanih slučajeva preeklampsije i u cilju otkrivanja komplikacija od strane pupčanika tokom njenog praćenja, posebno kod oligoamniona. *Acta Medica Medianae 2015;54(2):41-48.*

Ključne reči: kardiotokografija, IUGR, preeklampsija, ultrasonografija

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