The effect of umbilical cord loops around the fetal neck on the modified Doppler myocardial performance index (Mod- MPI) in a sample of Egyptian population.

Running Title: Effect of presence or absence of nuchal cord on Mod- MPI

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Abstract

Aim: To evaluate if there is a significant difference on the modified myocardial performance index (Mod-MPI) in cases of umbilical cord loops around the fetal neck (nuchal cord).

Methods: This was a cross-sectional study that included 60 healthy pregnancies between 28 to 35 weeks' gestation with a loop of cord around the neck (group A) and another 60 controls (group B). They were all undergoing ultrasound examination in a private clinic in Egypt from January 2021 till March 2022. Loops of cord around the neck were identified by grey scale and color Doppler. The Mod-MPI was used to assess fetal myocardial function using the Hernandez-Andrad et al. technique and the value was calculated according to Tei et al.

Results: There was no statistically significant difference between the age, BMI, nor the gestational age between both groups. However, there was a statistically significant difference regarding gravidity and parity between both groups with mean gravidity 2.13 +/- 1.41 and mean parity 0.87 +/- 1.10 for group A and mean gravidity 2.89 +/- 1.94 mean parity 1.44 +/- 1.42 (p=0.038 and 0.031) respectively. Finally, there was a statistically significant increase in the mean and standard deviation of the Mod MPI between Group A and B; 0.427 and 0.406 respectively. (p= 0.014)

Conclusion: We hope this study could provide valuable information for a comprehensive and objective evaluation of the effects nuchal cord on fetal wellbeing as well as guide intervention and provide new ways to reduce perinatal morbidity and mortality. We consider this a pilot and study and further studies with a larger sample size and follow up till delivery are required to be able to draw clearer and more solid conclusion.

Key words: Nuchal cord, Mod-MPI , fetal myocardial function.

Introduction

Umbilical cord around the fetal neck in not uncommon occurring in up to 25% of fetuses. Most cases have no consequences and are just incidental findings. Occasionally, it may form cord knots or tight cord around the neck. In such cases intrauterine growth retardation or oligohydramnious or diminished fetal kicks and rarely intrauterine fetal demise may occur. Such effects occur as a result hemodynamic affection when a tight cord is present (1), where variable degrees of compression of the umbilical vein ends in hypoxia and acidosis. (2) Presence of two or more cord loops around the neck during labor could alter the mode of the delivery as well as the early neonatal outcome. (3) Many fetuses delivered with a tightened cord present around the neck show petechiae on the face and retinal or conjunctival hemorrhage. In other cases, there is severe respiratory distress, hypotonia, and urgent need for resuscitation. (4) There are several risk factors for occurrence of nuchal cord; it was generally noticed with multiparity and increased maternal age, and male fetuses. Additionally, it was observed with increased fetal movements and polyhydamnious or increased liquor (3).

For over twenty years, the primary tool to assess fetal cardiac function was fetal echocardiography. It is a non-invasive modality assessing cardiac anatomy as well as hemodynamics. Two-dimensional imaging, M-mode, and pulsed wave Doppler are utilized used in fetuses as well as animal models to assess both systolic and diastolic functions all through gestation (5-8).

Tei and colleagues first described the myocardial performance index (MPI) aiming to assess and evaluate cardiac functions of adults having dilated cardiomyopathy. This non-invasive index is a Doppler-derived modality and has been reported as a useful index of global cardiac function. This MPI was calculated by adding the isovolumetric relaxation time (IRT) and isovolumetric contraction time (ICT) and dividing the sum by ejection time (ET) {(IRT + ICT)/ET} (9). Later this index (MPI) was used to assess the global myocardial function of the fetus by Tsutsumi and colleagues. (8) However, there was a noticeable variation in the reference values. This was mainly as a result of absence of clear identifiable landmarks in the obtained Doppler waves used to measure these specific time intervals. As a result, the modified myocardial performance index (Mod-MPI) was devised by Hernandez-Andrade and colleagues and used the Doppler echoes of the aortic valve (AV) and the mitral valve (MV) clicks. This lead to lesser variation in addition to better inter as well as intra-observer reproducibility when compared to the standard MPI. (10) Several conditions as intrauterine growth retardation (8,11–13), gestational or pregestational diabetes (14-18), twin to twin transfusion syndrome (TTTS) (19-22), congenital heart defects (23-26), and preeclampsia (27) demonstrated the value of the MPI and its recent modification to assess cardiac performance and function. Additionally, some authors recently estimated nomograms for the Mod MPI in second and third trimester (0.408 ± 0.08). They demonstrated that the Mod MPI was not changed by the mother's age, parity, or body mass index (BMI) (28)

Putting this into perspective we aimed in this study to assess the myocardial function by measuring the Mod- MPI in the presence of one loop of umbilical cord around the fetal neck and to compare it to fetuses with no nuchal cord.

Methods

This cross-sectional study was performed in a private clinic. The study group (A) included of 60 healthy pregnant women with a single fetus between 28 and 35 weeks of gestation with a loop of cord around the fetal neck. The control group (B) similarly included 60 healthy pregnant women between 28 and 35 weeks of gestation but did not have any loops around the neck at the time of measurements of the Mod MPI. The study started from January 2021 till March 2022. We excluded fetuses with anomalies, IUGR, SGA and mothers with any known medical disorders whether pregnancy related (eg preeclampsia) or not.

Following recruitment all patients provided a written consent after a thorough explanation of the study protocol. We recorded maternal demographic characteristics, medical and obstetric history.

The ultrasound examinations were carried out by one sonographer (S.E) who had enough experience in fetal US. All measurements were double checked, and an average was obtained. Pregnancy dating was accurately estimated by fetal crown– rump length at the 11th + 0 to 13th + 6 weeks' gestation if no accurate dates were obtained. All pregnant ladies had a detailed anomaly scan that included fetal echocardiograph. The scans were conducted trans-abdominally using 2 Machines, GE Voluson P8 and GE Voluson E8 (General Electric, Chicago, IL, USA).

Any loops of the umbilical cord around the neck were detected both by grey scale and color Doppler ultrasonography. These patients were assigned to group A. Patients with no loops around the neck were assigned as group B. we examined the loops of cord in the longitudinal view of the fetus (figure 1-2) and in the transverse view of the fetal neck. The latter was found to be more accurate than longitudinal view (figure 3-5)

We followed the Giacomello classification system for cord around neck (29-30):

- type A: a nuchal loop that encircles the neck in a freely sliding pattern, where the placental end crosses over the umbilical end; this pattern can undo itself
- type B: a nuchal loop that encircles the neck in a locked pattern, where the placental end crosses under the umbilical end; this pattern locks and cannot undo itself with potential for fetal morbidity or mortality.

It was difficult to differentiate between these two classifications in our study and not all patients were classified.

We the calculated the Mod MPI for all fetuses. We used the technique devised by Hernandez-Andrad et al. as shown in figure 6 (10). The measurements were done in the absence of any fetal movements nor respiratory movements and the mother voluntarily suspended her breathing. The velocity of the Doppler sweep was the highest velocity available (15 cm/s) for clear and accurate identification of the components of the Doppler tracing. Additionally, the E/A waveform was always displayed as positive flow. The angle of insonation was maintained below 30 degrees and the thermal and mechanical indices did not exceed 1. A cross-sectional cut of the fetal thorax was obtained in the four-chamber view and an apical projection (anterior or posterior) of the heart was obtained as shown in figure 7 and 8. The Doppler sample volume was put on the lateral wall of the ascending aorta, below the aortic valve and just above the mitral valve. The Doppler trace showed a clear echo corresponding to the opening and closure of the two valves at the beginning and at the end of the E/A (mitral valve) and AF (aortic valve) waveforms. The time periods were then estimated according to : the ICT was estimated from the closure of the MV, to the opening of the AV, the ET from the opening to the closure of the AV, and the IRT from the closure of the AV to the opening of the MV (figures 6-7-8). The result for the Mod-MPI was calculated as: (ICT + IRT)/ET (9)

Fig 1: (Longitudinal view) A Sagittal view of the fetus with loops of cord seen below the fetal chin using gray scale image.

Fig 2: (Longitudinal view) A parasagittal view of the fetus with loops of cord seen below the fetal chin using gray scale image.

Fig 3: (Transverse view) Cut-section in the fetal neck with loop of cord seen around the fetal neck using a gray scale image.

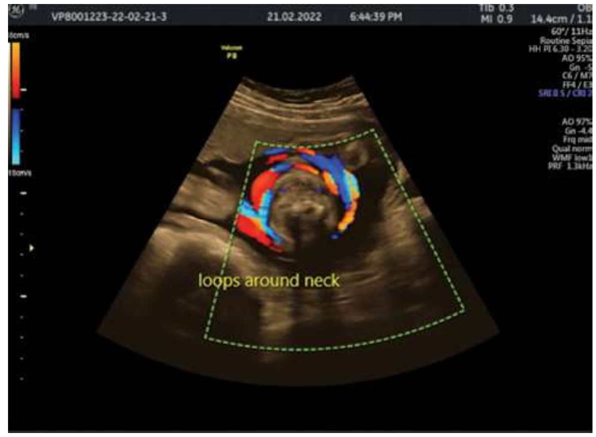

Fig. 4: (Transverse view) Cut-section in the fetal neck with loop of cord seen around the fetal neck using colour Doppler.

Fig. 5: (Transverse view) Cut-section in the fetal neck with loop of cord seen around the fetal neck using colour Doppler

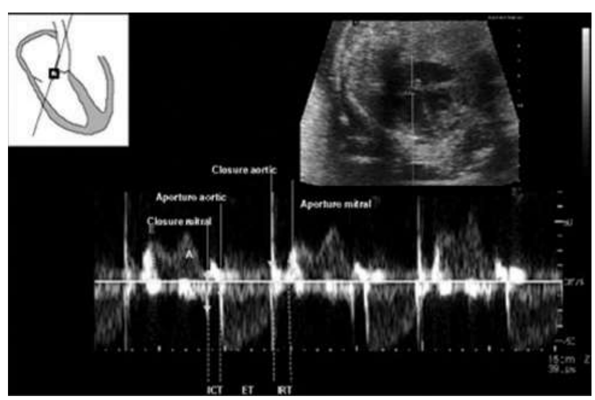

Fig 6: Doppler envelope of the modified myocardial performance index (Mod-MPI). The sample volume is located over the lateral wall of the aorta, close to the mitral valve. References for the time-period estimations are based on the echoes from the mitral and aortic valve movements. The E/A waveform is always displayed as positive flow. ET, ejection time; ICT, isovolumetric contraction time; IRT, isovolumetric relaxation time. (10)

Fig 7: An example of a case with a fetal heart apical view directed upward and obtained a modified myocardial performance index.

Fig 8: : An example of a case with a fetal heart apical view directed downwards and obtained a modified myocardial performance index.

Statistical analysis

Statistical analysis was performed using SPSS (Statistical package for the social sciences- IBM® SPSS® Statistics Version 20 for Windows, IBM Corp., Armonk, NY, USA). Data was represented as mean ± standard deviation. Data was explored for normality using Kolmogorov-Smirnov and Shapiro-Wilk tests. Data were non-normally distributed and Mann-Whitney U test was used to compare variables between the two groups. The results were considered statistically significant if the p value was less than 0.05.

Results

We approached 312 patients and collected the data of the first 60 who did not have a nuchal cord as controls (group B). Meanwhile any patient who had a loop of cord around the neck was allocated to group A. All other patients who did not have a nuchal cord after the control group was fulfilled were excluded. In our cohort the nuchal cord was identified in 19.1% of patients (60/312).

The mean age was the same across both groups being 29.9 years +/- 5.33 in group A and was 30.0 years +/- 5.72 in group B (p= 0.83). Similarly, the BMI and the gestational age at the time of the examination showed no statistically significant difference between both groups; group A mean BMI 26.8 +/- 2.85 and gestational age (GA) 31.4 +/- 1.93 while for group B mean BMI 27.5 +/- 3.47 and GA 31.1 +/- 2.16 (p=0.39 and 0.38) respectively. However, there was a statistically significant difference regarding gravidity and parity between both groups with mean gravidity 2.13 +/- 1.41 and mean parity 0.87 +/- 1.10 for group A and mean gravidity 2.89 +/- 1.94 mean parity 1.44 +/- 1.42 (p=0.038 and 0.031) respectively. Demographic data are represented in table 1.

Table 1: Demographic data of our study and control groups

	Group A	Group B	P value
Age (mean and SD)	29.9 +/- 5.33	30.0 +/- 5.72	0.83
BMI (mean and SD)	26.8 +/- 2.85	27.5 +/- 3.47	0.39
GA (mean and SD)	31.4 +/- 1.93	31.1 +/-2.16	0.38
Gravidity (mean and SD)	2.13 +/- 1.41	2.89 +/- 1.94	0.038
Parity (mean and SD)	0.87 +/- 1.10	1.44 +/- 1.42	0.031

As for the Mod MPI there was a statistically significant increase in the mean and standard deviation between Group A and B 0.406 and 0.427 respectively (p= 0.014) as shown in figure 9.

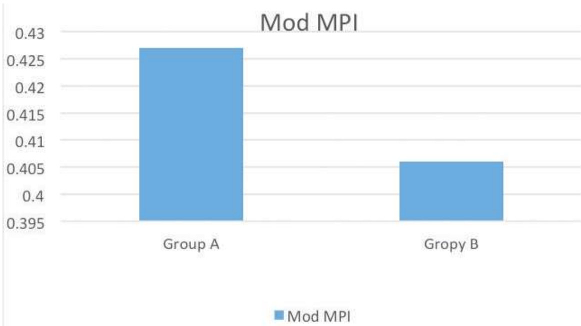

Figure 9: shows a significantly higher Mod MPI in Group A than Group B (P=0.014)

Discussion

While most nuchal cords have no or minimal adverse outcomes, some reports demonstrated poor outcomes which might be correlated with the number of cord loops around the fetal neck as well as the tightness of these loops. (4) In this study we aimed at utilizing the Mod MPI as a predictive tool for fetal hemodynamic changes which might be associated with significant undesirable consequences. We considered this a pilot study just to check if there would be a change in the Mod MPI when nuchal cords are present not knowing whether this will influence the neonatal outcome or not.

In our study we found that nuchal cords were common in women with lower parity rather than higher parities. This is contrary to what a recent study showed in 2021 were women of higher parity had more frequent loops of cord around the neck. (3) This team studied 250 patients and found that only 50 patients 20% were nullipara and the remaining 80% (200 patients) were multipara. We assume such a difference in to be related to sample size and GA at detection as they had a mean GA of 38.24 +/- 1.2 which is higher than our cohort's GA. However, we agree with their detection rate of nuchal cord, 18.8% vs 19.1% in our study. We also agreed with authors from other countries who have demonstrated similar incidence of nuchal cord 65 out of 350 or 18.6% (31) and 100 out of 506 or 19.8% (32). Other reports have shown an incidence of up to 25% (1).

We have found no correlation for the presence of a nuchal cord with the age of the patient, BMI or GA at the time of examination. This agrees with most other authors (3, 31,32) who also found no relation with these demographic parameters.

To date, there are only a few studies describing cardiac parameters of fetuses with loops of cord around neck. A former study suggested that the incidence of IUFD caused by nuchal cord is higher than without a nuchal cord. (33) Therefore, prompt, and correct assessment of the fetal hemodynamics and cardiac functions cannot be ignored in those fetuses. In 2012 Zuo and colleague utilized "velocity vector imaging" (VVI) to detect myocardial strain in such fetuses. They studied 35 patients and concluded that (VVI) might respond to changes in cardiac function in such fetuses. (1) However, (VVI) is a very demanding 2-dimensional image, that needs clear image acquisition to clearly identify endocardial borders, in addition to a small fetal heart volume and shadowing from the ribs and spines. (34,35)

In 2020, Seif et al., made a gestational age-based reference for the Mod MPI in the Egyptian population working on 1021 fetuses. (28) We agreed with their reference ranges whether in patients with or without nuchal cords. Other authors, however, reported a wider variation of reference ranges which might be attributed to different sample sizes and a wider range of gestational ages. (34)

In our study we have detected that the Mod MPI significantly increased in fetuses with a nuchal cord. Additionally, it was previously reported that it increased under different pathological conditions, as when there is an increase in the afterload due to increased placental resistance. (36) Our results also agree with Api et al., who detected an increase in the Mod MPI in fetuses of preeclamptic mothers. (37)

By this we can assume that Mod MPI increase might be a marker for cardiac strain in such fetuses. Whether this will affect the outcome or not is not known yet and this is a main limitation of the study as we did not follow up these fetuses. Other limitations include small sample size and imperfect classification of the nuchal cord in all the patients. However, we consider our strength to be proper assessment of this index by an experienced sonographer.

We hope this study could provide valuable information for a comprehensive and objective evaluation of the effects of nuchal cord on fetuses, as well as guide interventions and provide new ways to reduce perinatal morbidity and mortality. We consider this a pilot and study and further studies with a larger sample size and more follow up are required to be able to draw clearer and more solid conclusion.

Conflicts of interest: The authors have nothing to declare.

References

1. Dong Z, Chao W and Yue W. Deformation of the left and right ventricular longitudinal myocardium in fetuses with umbilical cord around neck. Chin Med J. 2012; 125: 1608-1613.
2. Baergen R. Cord abnormalities, structural lesions, and cord "accidents". Semin Diagn Pathol. 2007;24: 23-32.
3. Ibrahim G, Safwat M, Abdelmonem S, and Gadalla S. The Association between Nuchal Cord Detection and Perinatal Outcomes in Term Infants: A Prospective Study. Med. J. Cairo Univ. 2021; 89: 267-272.
4. Peesay M. Cord around the neck syndrome. BMC Pregnancy and Childbirth. 2012 ;12: Oral presentation.
5. Gui H, Linask K, Khowsathit P, Huhta C. Doppler echocardiography of normal and abnormal embryonic mouse heart. Pediatr Res. 1996; 40: 633–642.
6. Van Splunder IP, Wladimiroff W. Cardiac functional changes in the human fetus in the late first and early second trimesters. Ultrasound Obstet Gynecol. 1996; 7: 411–415.
7. Tsyvian P, Malkin K, Wladimiroff W. Assessment of mitral A-wave transit time to cardiac outflow tract and isovolumic relaxation time of left ventricle in the appropriate and small for gestational age human fetus. Ultrasound Med Biol. 1997; 23: 187–190.
8. Tsutsumi T, Ishii M, Eto G, Hota M, Kato H. Serial evaluation for myocardial performance in fetuses and neonates using a new Doppler Index. Pediatr Int. 1999; 41:722–727.
9. Tei C, Ling L, Hodge D, Bailey K, Ok J, Rodenheffer R, Tajik A, Seward J. New index of combined systolic and diastolic myocardial performance: a simple and reproducible measure of cardiac function – a study in normal and dilated

cardiomyopathy. J Cardiol. 1995; 26: 357–366.

10. Hernandez E, Lopez J, Figueroa H, Sanin J, Carreras E, Cabero L, Gratacos E. A modified ′ myocardial performance (Tei) index based on the use of valve clicks improves reproducibility of fetal left cardiac function assessment. Ultrasound Obstet Gynecol. 2005; 26: 227–232.

11. Benavides A, Scheier M, Cruz R, Crispi F, Figueras F, Gratacos E, Hernandez E . Changes in central and peripheral circulation in intrauterine growth-restricted fetuses at different stages of umbilical artery flow deterioration: new fetal cardiac and brain parameters. Gynecol Obstet Invest. 2011; 71: 274–280.

12. Comas M, Crispi F, Martinez R, Martinez J, Figueras F, Gratacos E. Usefulness of myocardial tissue Doppler vs conventional echocardiography in the evaluation of cardiac dysfunction in early-onset intrauterine growth restriction. Am J Obstet Gynecol. 2010; 203: 45.e1–45.e7

13. Crispi F, Hernandez E, Pelsers M, Plasencia W, Benavides J, Eixarch E, Noble F, Ahmed A, Glatz J, Nicolides K, Gratacos E. Cardiac dysfunction and cell damage across clinical stages of severity in growth-restricted fetuses. Am J Obstet Gynecol. 2008; 121: 254 e1–254.e8.

14. Garcia J, Jan M, Gonzalez M, Martinez N, Espada M, Gonzalez A. Fetal myocardial morphological and functional changes associated with well controlled gestational diabetes. Eur J Obstet Gynecol Reprod Biol. 2011; 154: 24–26.

15. Wong M, Wong W, Cheung Y. Fetal myocardial performance in pregnancies complicated by gestational impaired glucose tolerance. Ultrasound Obstet Gynecol. 2007; 29: 395–400.

16. Russell N, Foley M, Kinsley B, Firth R, Coffey M, McAuliffe F. Effect of pregestational diabetes mellitus on fetal cardiac function and structure. Am J Obstet Gynecol. 2008; 199: 312 e1–312. e7.

17. Campbell K, Thung S, Buhimschi C, Copel J, Bahtiyar O. The Tei index to assess myocardial performance in fetuses of diabetic mothers. Ultrasound Obstet Gynecol 2011; 38: oral presentation.

18. Sanhal C, Daglar H, Kara O, Uygur D, Yucel A. Assessment of fetal myocardial performance index in women with pregestational and gestational diabetes mellitus. J Obstet Gynaecol Res. 2017; 43: 65-72.

19. Mieghem T, Klaritsch P, Done ’E, Gucciardio L, Lewi P, Verhaeghe J, lewi L, Deprest J. Assessment of fetal cardiac function before and after therapy for twin-to- twin transfusion syndrome. Am J Obstet Gynecol. 2009; 200: 400 e1–400.e7.

20. Stirnemann J, Mougeot M, Proulx F, Nar B, Fouron J, Ville Y. Profiling fetal cardiac function in twin twin transfusion syndrome. Ultrasound Obstet Gynecol. 2010; 35: 19–27.

21. Raboisson M, Fouron J, Lamoureux J, Leduc L, Grignon A, Proulx F, Gamache S. Early inter- twin differences in myocardial performance during the twin- to-twin transfusion syndrome. Circulation. 2004; 110: 3043–8.

22. Habli M, Michelfelder E, Livingston J, Harmon J, Yen F, Polzin W, Crombleholme T. Acute effects of selective fetoscopic laser photocoagulation on recipient cardiac function in twin-twin transfusion syndrome. Am J Obstet Gynecol. 2008; 199: 412 e1–412.e6.

23. Youfang C, Guorong L, Boyi L, Zhenhua W. Cerebral vascular resistance and left ventricular myocardial performance in fetuses with Ebstein’s anomaly. Am J Perinatol. 2009; 26 253–8.

24. Szwast A, Tian Z, McCann M, Donaghue D, Rychik J. Right ventricular

performance in the fetus with hypoplastic left heart syndrome. Ann Thorac Surg. 2009; 87: 1214–1219.

25. Inamura N, Taketazu M, Smallhorn J, Hornberger L. Left ventricular myocardial performance in the fetus with severe tricuspid valve disease and tricuspid insufficiency. Am J Perinatol. 2005; 22: 91–97.

26. Inamura N, Kado Y, Nakajima T, Kayatani F. Left and right ventricular function in fetal tetralogy of fallot with absent pulmonary valve. Am J Perinatol. 2005; 22:199–204.

27. Api O, Balcin Emeksiz M, Api M, Ugurel V, Unal O. Modified myocardial performance index for evaluation of fetal cardiac function in pre-eclampsia. Ultrasound Obstet Gynecol. 2009; 33: 51–7.

28. Ali S, Okasha A , Elsirgany S, Elanwary S, Abdel-Rasheed M, Khalil A, Elsheikhah A. Normal reference ranges for fetal cardiac function: Assessed by modified Doppler myocardial performance index (Mod MPI) in the Egyptian population. Eur J Obstet Gynecol Reprod Biol. 2020; 251: 66–72.

29. Giacomello F. Ultrasound Determination of Nuchal Cord in Breech Presentation. Am J Obstet Gynecol. 1988; 159: 531-532.

30. Al-Kouatly H, Schuster S, Skupski D. Double Nuchal Umbilical Cord and Breech Presentation. The Value of Close Follow-Up. Gynecol Obstet Invest. 2003; 56: 121-123.

31. Singh G and Sidhu. Nuchal Cord: A retrospective analysis. Med J Armed Forces India, 2008; 64: 237-240.

32. Joshi K, Saxena R , Bhat M , Lomrod Y and Verma K. Incidence of cord around the neck and its effects on labour and neonatal outcome. Adv. Hum. Biol. 2017; 7: 15-18.

33. Hayes D, Warland J, Parast M, Bendon R, Hasegawa J, Banks J, Calpham L, Haeazell A.Umbilical cord charactaristics and their association with adverse pregnancy outcomes: A systematic review and meta-analysis. Journal Pone. 2020; 15: 1-36

34. Younoszai K, Saudek E, Emery P, Thomas D. Evaluation of myocardial mechanics in the fetus by velocity vector imaging. J Am Soc Echocardiogr. 2008; 21: 470-474.

35. Eidem W, Edwards M, Cetta F. Quantitative assessment of fetal ventricular function: establishing normal values of the myocardial performance index in the fetus. Echocardiography. 2001; 18: 9-13.

36. Ichizuka K, Matsuoka R, Hasegawa J, Shirato N, Jimbo M, Otsuki K, Sekizawa A, Farina A, Okai T. The Tei index for evaluation of fetal myocardial performance in sick fetuses. Early Hum Dev. 2005; 81: 273–279.

37. Api, O., Emeksiz, M.B., Api, M., Uğurel, V. and Unal, O. Modified myocardial performance index for evaluation of fetal cardiac function in pre-eclampsia. Ultrasound Obstet Gynecol. 2009; 33: 51-57.