PERINATAL JOURNAL

Original Article

Perinatal Journal 2025; 33(2):23-29

https://doi.org/10.57239/prn.25.0332004

Effect of amniocentesis on feto-placental hemodynamics and fetal cardiac function: A comprehensive Doppler study

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Abstract

This study aimed to evaluate the effects of mid-trimester amniocentesis, with or without transplacental needle passage, on fetal and placental hemodynamics and fetal cardiac function using comprehensive Doppler parameters. This prospective cohort study, Doppler ultrasound examinations were performed immediately before and one hour after mid-tri- mester amniocentesis in 77 singleton pregnancies. Doppler parameters included uterine artery (UtA), umbilical artery (UA), middle cerebral artery (MCA), ductus venosus (DV), and left modified myocardial performance index (LMPI). Cases were further analyzed based on whether placental passage occurred during the procedure. No significant differences were observed in Doppler indices (UtA, UA, MCA, DV) or LMPI measurements following amniocentesis ($p>0.05$, for all parameters). Additionally, subgroup analysis revealed no significant impact of transplacental needle passage on fetal or pla- cental hemodynamics and cardiac function. Mid-trimester amniocentesis, performed with or without transplacental needle passage, does not adversely affect fetal or placen- tal hemodynamics, including fetal cardiac function. These findings support the safety and clinical reliability of the procedure.

Keywords: Amniocentesis, Doppler ultrasonography, fetal hemodynamics, myocardial performance index, fetal cardiac function

Introduction

Amniocentesis is the most widely used invasive prenatal diagnostic technique in which fetal cell samples are obta- ined from amniotic fluid to examine the genetic structure of the fetus .[1]. It is not complicated, but it is recommen- ded to perform this procedure in the mid-trimester after the 15th week of pregnancy to avoid complications .[2]. There are many risk factors for genetic disorders in the prenatal period, including parental characteristics, obs- tetric history, prenatal screening findings, and sonograph- hic findings. Prenatal diagnosis of genetic abnormalities in a fetus with a risk factor provides families with infor- mation about preparing for birth and postnatal outcomes. Although prenatal diagnostic tests provide families and clinicians with insight into the genetic structure of the fetus, it is important to provide evidence-based in- formation to families about the complications of these procedures .[3,4].

Fetal Doppler blood flow examination is a sonographic examination that provides important data on fetal he- modynamics and is frequently used in modern obstetrics in cases where the risk of fetal loss is high. [5]. Uterine ar- tery (UtA), umbilical artery (UA), middle cerebral artery (MCA), and ductus venosus (DV) Doppler examination is frequently preferred in obstetric practice. In the evalu- ation of fetal cardiac function, recent studies have shown that modified myocardial performance index (MPI) can provide data on fetal cardiac hemodynamics in diseases such as fetal growth restriction, preeclampsia, gestational diabetes, and intrahepatic cholestasis of pregnancy .[6–9].

Previous studies have examined the effects of amniocen- tesis on fetal heart rate (FHR) as an indirect indicator of fetal well-being. These investigations have demonstrated that FHR decreases following amniocentesis both in the early (immediate measurement) and late (measurement after 60 minutes) periods. Furthermore, it has been found that the decrease in FHR occurs significantly in both ch- romosomally abnormal and normal karyotype fetuses, and the decrease was significantly higher in fetuses with karyotype abnormalities than in fetuses with normal kar- yotypes. It was concluded that the FHR response to amni- ocentesis may be an

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indicator of fetal well-being, and that the association with abnormal karyotypes may be due to cardiac defects or developmental delay .[10–14].

A limited number of studies have examined the effect of amniocentesis procedure on fetal hemodynamics. The findings of these studies did not show any significant changes in fetal Doppler flow associated with the proce- dure. However, the Doppler examinations in these stu- dies mostly included maternal and placental functions, and fetal Doppler assessments limited to the UA and DV Doppler examinations .[15–18]. There is no study yet examining the effect of amniocentesis on fetal cardiac function. For this purpose, we aimed to evaluate the early placental and fetal effects of the amniocentesis procedure by inclu- ding UtA, UA, MCA, DV, and left modified myocardial performance index (LMPI) Doppler parameters. Addi- tionally, we sought to determine whether transplacental needle passage during amniocentesis influences these Doppler parameters.

Methods

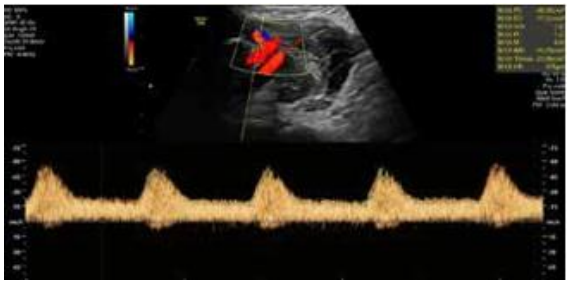
This prospective cohort study was conducted at Tepe- cik Training and Research Hospital, Izmir, Turkey, and Izmir City Hospital, Izmir, Turkey, between 2023 and 2024. The study protocol was approved by the Tepecik Training and Research Hospital Ethics Committee (Ap- proval number: 2023/06). All participants included in the study were informed about the study purpose, and their written informed consent was obtained.

Singleton pregnancies and those over 18 years of age who underwent amniocentesis due to increased risk of first- and second-trimester screening test (>1/270), pa- rental anxiety/request, sonographic soft marker findings, or advanced maternal age (>35 years) were included in the study. Exclusion criteria of the study were multiple pregnancies, fetal structural or genetic anomalies, paren- tal genetic abnormalities, suspected fetal infections, and early-onset fetal growth retardation.

Amniocentesis procedures were performed by mater- nal-fetal medicine specialists. All procedures were condu- cted after the 15th week of gestation under continuous ultrasound guidance to ensure safety and precision. A 22-gauge needle was inserted transabdominally into the amniotic cavity, carefully avoiding fetal structures. No anesthesia was used; however, local antiseptic was applied to the skin surface prior to needle insertion. Approxima- tely 15–20 mL of amniotic fluid was gently aspirated for diagnostic analysis from each patient.

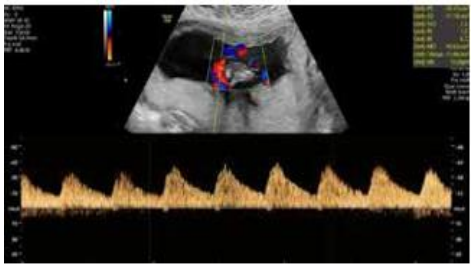
Ultrasonographic examination

Ultrasonographic examination was performed using a Voluson E8 specialist machine (GE Healthcare, Aust- ria) equipped with a 2–9 MHz 2D curvilinear transducer. Each participant underwent two detailed Doppler assess- ments: one hour before and one hour after the amniocen- tesis procedure, and all ultrasound measurements were conducted by a single experienced clinician (S.T.C.) to ensure consistency. In the ultrasonographic examination, the machine preset was set to 2nd-trimester obstetrics setting. Vascular flow was evaluated using pulsed-wave Doppler in the absence of fetal breathing and movement to avoid motion-related artifacts. Amniotic fluid index (AFI) was calculated by as the sum of the vertical dep- ths of four quadrants. UtA Doppler assessments were performed bilaterally in the sagittal plane. The right and left uterine arteries were visualized originating from the internal iliac artery and crossing the external iliac artery after angling the ultrasound probe towards the iliac fossae and lateral uterine walls. UtA measurements were obtai- ned using the smallest possible insonation angle (ideally close to 0°), with a peak systolic velocity exceeding 60 cm/ sec and a sample volume of 2.0 mm. Both pulsatility in- dex (PI) and resistance index (RI) values were recorded (Figure 1).

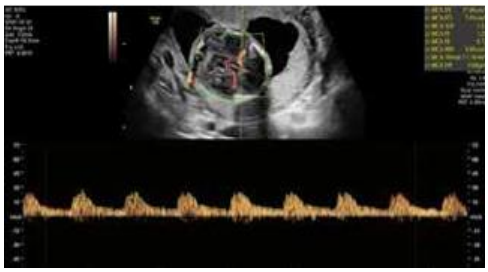


UA Doppler measurements were obtained from a free-floating loop of the umbilical cord, also ma- intaining an insonation angle as close to 0° as possible. PI and RI values were recorded (Figure 2). The MCA was visualized at the level of the circle of Willis using color Doppler imaging, following

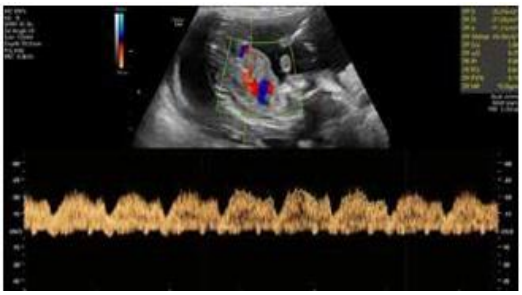
identification of the thala- mus and sphenoid bone wings in the axial plane of the fetal head.



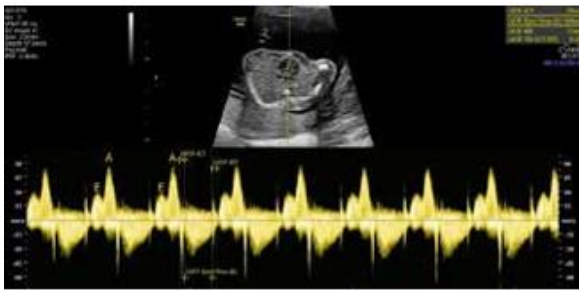
MCA Doppler measurements were obtained approximately 2 mm distal to its origin from the internal carotid artery, using the smallest possible insonation ang- le (ideally close to 0°). Angle correction was applied when necessary to ensure measurement accuracy. Both PI and RI values were recorded (Figure 3). The DV was exami- ned in either a mid-sagittal or cross-sectional abdominal view, depending on fetal position.



DV PI values were me- asured at the narrowest insonation angle achievable, with a 2 mm pulsed-wave Doppler gate placed at the isthmic portion near its origin from the umbilical vein (Figure 4). For assessment of fetal cardiac function using the LMPI, a 3–4 mm Doppler cursor was placed at the inner leaflet



of the mitral valve in an apical four-chamber view, and waveforms were captured using pulsed-wave Doppler. Isovolumetric contraction time (ICT) was defined as the interval from mitral valve closure to aortic valve opening, ejection time (ET) from aortic valve opening to closure, and isovolumetric relaxation time (IRT) from aortic val- ve closure to mitral valve opening. LMPI was calculated using the formula: (ICT+IRT)/ET (Figure 5).



Statistical analysis

Statistical analysis was performed using the SPSS software version 26.0 (IBM Corp, Armonk, NY, USA). Continu- ous variables were presented as mean ± standard deviation (SD) or median (minimum-maximum). Categorical vari- ables were reported as frequency and percentage. Pre- and post-amniocentesis Doppler measurements were compa- red using Paired samples t-tests for normally distributed data or Wilcoxon signed-rank tests for non-normally distributed data. Statistical significance was considered at a p-value of less than 0.05.

A power analysis was performed to determine the mi- nimum required sample size for detecting a significant difference in Doppler and LMPI parameters before and after amniocentesis. Assuming a medium effect size (Co- hen's d = 0.5), a significance level of $\alpha = 0.05$, and a power $(1–\beta)$ of 0.80, the required sample size was calculated to be at least 34 participants for paired comparisons.

Results

A total of 77 pregnant women who met the inclusion criteria during the study were included in the study. There were no complications such as miscarriage, fetal loss, and preterm premature rupture of membranes during pregnancy follow-up of the participants included in the study. The demographic and medi- cal characteristics of the participants were presented in Table 1. The mean maternal age of the partici- pants was 31.8±5.7 years, and the mean gravida was 2.4±1.4. The mean gestational age at measurement was 17.5±1.7 weeks, and the mean body mass index

(BMI) was 25.3±3.9 kg/m^2. In 28 (36.6%) cases, the placenta was located on the anterior uterine wall, and in 27 cases (35.0%), the needle passed transplacentally during the amniocentesis procedure.

Table 1. Demographic and medical characteristics of the participants

n=77	Mean±SD	Median (minimum-maximum)	n, %
Maternal age (year)	31.8±5.7	32 (18-46)	-
Gravida	2.4±1.4	2 (1-9)	-
Parity	1.1±0.9	1 (0-3)	-
Nulliparous	-	-	19 (24.6%)
Multiparous	-	-	58 (75.4%)
BMI at during test (kg/m^2)	25.3±3.9	25 (17.9-37.9)	-
Gestational age at measurement (week)	17.5±1.7	17.1 (15.4-22.1)	-
Placental location			
Anterior	-	-	28 (36.6%)
Posterior	-	-	47 (61%)
Fundus	-	-	2 (2.4%)
Passing the placenta			
Yes	-	-	27 (35%)
No	-	-	50 (65%)

Doppler AFI, and LMPI measurements before and after amniocentesis are presented in Table 2. There was no significant difference in the AFI values be- fore and after the procedure (73±27 mm vs. 76±27 mm, p=0.485). In the Doppler examinations, no significant difference was found in UA, MCA, and DV measurements (p>0.05, for all). Additionally, assessment of fetal left cardiac function using the LMPI revealed no significant difference between pre- and post-procedure measurements (0.44±0.05 vs. 0.44±0.05; p=0.625).

Table 2. Doppler, AFI, and LMPI measurements before and after amniocentesis

	Before the procedure (n:77)	After the procedure (n:77)	P
Right UtA PI	1.27±0.43	1.31±0.53	0.637
Right UtA RI	0.65±0.11	0.66±0.14	0.780
Left UtA PI	1.33±0.60	1.40±0.54	0.459
Left UtA RI	0.66±0.12	0.68±0.12	0.297

Placental needle passage occurred in 27 cases, while no placental passage occurred in 50 cases. Doppler, AFI, and LMPI measurements before and after amniocentesis for subgroup patients without placental passing are presented in Table 3. There were no statistically significant differences in AFI, Doppler, or LMPI measurements before and after the procedure in these cases (p>0.05, for all). Similarly, the analysis of cases with placental needle passage is presented in Table 4. The results showed no significant differences in AFI, Doppler, or LMPI measurements pre- and post-amniocentesis in this subgroup as well (p>0.05, for all).

Table 3. Doppler, AFI, and LMPI measurements before and after amniocentesis for subgroup patients without placental passing

	Before the procedure (n:50)	After the procedure (n:50)	p
Right UtA PI	1.29±0.43	1.28±0.51	0.911
Right UtA RI	0.66±0.11	0.66±0.15	0.940

Left UtA PI	1.37±0.63	1.38±0.56	0.878
Left UtA RI	0.67±0.11	0.67±0.12	0.825
UA PI	1.34±0.29	1.32±0.22	0.657
UA RI	0.77±0.10	0.76±0.07	0.833
MCA PI	1.93±0.50	1.95±0.45	0.894
MCA RI	0.91±0.17	0.90±0.10	0.647
DV PI	0.73±0.21	0.70±0.25	0.527
AFI (mm)	68±19	72±20	0.298
LMPI	0.44±0.05	0.44±0.05	0.524

Discussion

In this study, we evaluated the short-term impact of mid-trimester amniocentesis on fetal and placental he- modynamics using Doppler ultrasound parameters, inc- luding UtA, UA, MCA, DV, and LMPI. Our results demonstrate that the amniocentesis procedure does not significantly alter fetal or placental hemodynamics and does not affect fetal cardiac function, as measured by LMPI. Additionally, placental needle passage during am- niocentesis did not adversely impact any of these para- meters.

Amniocentesis is a widely utilized invasive prenatal diag- nostic procedure performed to obtain amniotic fluid for fetal genetic analysis. Despite its proven clinical value, its potential impact on fetal and placental hemodynamics re- mains under investigation. Previous studies have focused primarily on the maternal and placental circulation and have similarly reported minimal or no effects on Dopple indices after amniocentesis. Martinez et al. .[19], Haugen et al. [20], and Gungor et al. [21] reported no significant changes in umbilical artery Doppler parameters post-amniocente- sis, which is consistent with our findings. Weinraub et al. also found transient changes that were clinically insignifi- cant [22]. DV was evaluated following amniocentesis in only one study, and no significant change was observed [18]. However, these previous studies did not comprehensively investigate other critical fetal vessels, such as the MCA. To address these gaps, we included detailed fetal Doppler parameters, specifically MCA and DV, as sensitive markers for evaluating fetal hypoxia and compromised circulation. Previous studies suggest that alterations in MCA Doppler parameters reflect fetal compensation mechanisms to hypoxic or stress conditions .[23]. Our observation of unc- hanged MCA indices strongly suggests that mid-trimester amniocentesis does not significantly affect fetal cerebral circulation or induce acute fetal hypoxic stress. Additional- ly, our findings of stable DV indices indicate that the am- niocentesis procedure does not result in acute changes to fetal venous hemodynamics or increased cardiac preload, further supporting its safety in terms of fetal circulatory effects.

The MPI or Tei index, introduced by Tei in 1995 .[24], is the ratio of the sum of the ICT and IRT to the ET. The MPI is particularly valuable as it offers insights into global myo- cardial function, reflecting both systolic and diastolic per- formance and is a potentially useful predictor of global cardiac function that is not affected by heart size, shape, orientation, geometry or velocity .[8,9]. Its application in the fetus has advantages over its application in adults, as it is possible to measure atrioventricular and semilunar valve flows simultaneously, eliminating the inaccuracies inhe- rent in measuring different heart rates [4]. MPI is conside- red a reliable and useful tool for the examination of fetal cardiac function through different pathophysiological conditions such as fetal growth restriction, preeclampsia, gestational diabetes, congenital heart malformations and twin-to-twin transfusion syndrome or hypoxia, metabolic acidosis and increased fetal cardiac afterload .[7–9]. To our knowledge, our study is the first to specifically evaluate the LMPI following amniocentesis. Our findings showing no significant LMPI alterations indicate that fetal myocar- dial function remains stable post-procedure, suggesting minimal or transient fetal stress or cardiac adaptation.

The subgroup analysis of cases involving placental pas- sage of the amniocentesis needle is important, as previ- ous studies have indicated increased complication risks when placental passage occurs .[25–27]. These earlier studies highlighted concerns related to complications such as fe- tal loss, preterm premature rupture of membranes, and intra-amniotic infections when the needle traverses the placenta. However, our findings suggest no significant dif- ference in Doppler or LMPI measurements between

those with placental passage and those without. This result furt- her emphasizes the procedure's safety when conducted under ultrasound guidance by experienced practitioners.

A notable strength of our study is its prospective cohort design combined with comprehensive Doppler assess- ments immediately before and after the procedure, mi- nimizing potential confounding factors and enhancing result reliability. This approach significantly reduces po- tential confounding factors, enhances the reliability of our findings, and allows for precise evaluation of immediate hemodynamic effects. Moreover, our inclusion of multiple Doppler parameters, such as the UtA, UA, MCA, DV, and LMPI, provides a robust and comprehensive evaluation of fetal and placental hemodynamics. Nonetheless, our study's limitations include the short-term follow-up, po- tentially limiting the detection of delayed hemodynamic changes. Future research with larger cohorts and exten- ded observation periods is warranted to confirm these findings and to explore potential long-term fetal hemody- namic impacts. Additionally, research exploring potential long-term clinical outcomes and the correlation between immediate Doppler findings and later pregnancy or neo- natal outcomes would further enhance clinical understanding and guide best practices in prenatal care.

Conclusion

In conclusion, our results provide reassuring evidence that mid-trimester amniocentesis, whether performed with or without transplacental needle passage, does not adver- sely affect fetal or placental hemodynamics, including fetal cardiac function. These findings are valuable for cli- nicians in counseling families, especially those concerned about fetal stress or cardiac implications of amniocentesis. Further research with larger populations and long-term follow-up could provide additional insights into the broa- der implications of invasive prenatal diagnostic procedu- res on fetal health outcomes.

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