

Risk of Fetal Loss after Amniocentesis in Twins Comparing with Singleton Pregnancy

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Abstract

Introduction: Amniocentesis is one of the most widely used diagnostic interventions but despite its many advantages, it has side effects such as fetal loss. The importance of fetal loss after amniocentesis in twin pregnancies is very important and some researchers believe that in twin pregnancies, the risk of fetal loss after amniocentesis is higher than singleton. Therefore, the present study examined the rate of fetal loss after amniocentesis in twin pregnancies compared to singleton pregnancies.

Methods: This prospective descriptive-analytical study was performed on 712 mothers with singleton (628 cases) and twin (84 cases) pregnancies who referred to the obstetrics and gynecology clinic of Imam Khomeini Hospital in Ahvaz with Amniocentesis due to several reason during 2016-2020. A questionnaire containing information such as age, gestational age, number of pregnancies, childbirth and abortion, the cause of the diagnostic test, quarterly screening and NT ultrasound, and the result of amniocentesis were completed for patients. Patients were followed up during the first week, two weeks, and 60 days after amniocentesis, and finally data were analyzed by SPSS version24.

Results: The mean age of the patients was 31.96 ± 6.33 years and the mean gestational age at amniocentesis for all patients was 15.37 ± 0.7 . The mean NT in patients in the two groups did not differ significantly (1.60 ± 0.44 vs 1.54 ± 4.64 , $p=0.56$). the prevalence of preterm in twin mothers was 13.1% and, in the singleton was 1.75% ($p = 0.01$). The occurrence of fetal loss was 2.4% in the twin group and 2.07% in the singleton group which was not statistically significant ($p = 0.56$). in the twin group, one (50%) fetal loss occurred in the first week and another one (50%) occurred between 15 and 60 days. But in the singleton group, 7 cases (63.6%) in the first week, 1 case (9%) in 15 to 60 days, and 3 cases (27.3) after more than 60 days lost the fetus. Previous pregnancy records in twins showed that the mean Gravid ($p = 0.01$), Parity ($p = 0.01$) and Living child ($p = 0.02$) in preterm twins' patients were statistically significantly lower than in the term patients.

Conclusion: Our findings show that fetal loss following amniocentesis in twin pregnancies does not increase significantly compared to singleton pregnancies. However, our findings require repeated study in bigger sample size and as multi-centered as possible then It can be generalized to wider communities.

Keywords: Amniocentesis, Fetal Loss, Twins, Pregnancy

1. Introduction

Amniocentesis is the first invasive procedure used to diagnose and treat fetal diseases during pregnancy. (Connolly & Eddleman, 2016) It is currently the most common invasive genetic test in pregnant women. Amniocentesis is used as a basic invasive method for early detection of various pregnancy-related conditions, such as fetal karyotype, diagnosis of metabolic or enzymatic diseases, evaluation of severe hemolytic diseases, development of pulmonary maturation and diagnosis of fetal infections (Jummaat, Ahmad, & Ismail, 2019; Drukker, Sela, Ioscovich, Samueloff, & Grisaru-Granovsky, 2017). In addition, amniocentesis is used to inject various drugs into the amniotic cavity, to determine the composition of the amniotic fluid, and finally to drain Amniotic fluid (Theodora, Antsaklis, & Antsaklis, 2015). Despite the many benefits of amniocentesis, this procedure has side effects, including fetal loss. However, the actual risk of fetal loss with this method is not yet clear (Theodora, Antsaklis, Antsaklis, Blanas, Daskalakis, Sindos, Mesogitis, & Papantoniou, 2016). Therefore,

more research is needed to obtain clearer information. Amniocentesis is performed in pregnant women aged 35 years and older because the mother's chances of having a child with chromosomal abnormalities increase (Xiao, Yang, Zhang, Liao, Zhao, & Liao, 2016), as well as in mothers who have previously had a child with problems such as Down syndrome (Mukherjee & Chaudhury, 2015). Another important application of amniocentesis is in twin pregnancies. It has previously been shown that twin pregnancies have a higher risk of developing chromosomal abnormalities. In addition to genetic testing, amniocentesis is used in third-trimester screening tests to check for markers of fetal lung maturation in amniotic fluid (Boyer, Cameron, Munoz-Maldonado, Bronsteen, Comstock, Lee, & Goncalves, 2014; Ramirez-Montiel, Casillas-Barrera, Morales-Morales, Ortiz, Carrasco-Blancas, & Morales, 2017). The main concern is fetal complications. These complications include fetal loss, placental abruption, preterm delivery, and premature rupture of fetal membranes. Amniocentesis may also cause infection within the amniotic fluid, meaning that microorganisms can enter the amniotic cavity through the needle. The risk of fetal loss after amniocentesis has been assessed by several centers. The different results of these studies indicate the difference between the assessment methods and the studied populations (Theodora, Antsaklis, Antsaklis, Blanas, Daskalakis, Sindos, Mesogitis, & Papantoniou, 2016; Shirazi, Mohseni, & Ghajarzadeh, 2015). In general, the rate of fetal loss is based on three main studies in the 1970s that were not randomized. The Centers for Disease Control and Prevention (CDC) estimates that the rate of fetal loss after amniocentesis is 0.5%. Despite the fact that these studies were not random and that amniocentesis was not performed using ultrasound at the same time, this CDC estimate of post-amniocentesis abortion is still being used (Connolly & Eddleman, 2016). The importance of fetal loss after amniocentesis in twin pregnancies is very important to consultants, but few studies have examined the risk of fetal loss in amniocentesis in twin pregnancies, and some researchers believe that in twin pregnancies, the risk of fetal loss after amniocentesis is higher than singleton (Enzensberger, Pulvermacher, Degenhardt, Kawecki, Germer, Weichert, Krapp, Gembruch, & Axt-Fliedner, 2014; Wilson, Gagnon, Audibert, Campagnolo, Carroll, Brock, Chong, Johnson, MacDonald, Okun, & Pastuck, 2015). Due to the significant effect of amniocentesis on maternal and fetal health during pregnancy and the importance of public health in this regard, preventive strategies are recommended. Therefore, early detection of high-risk mothers for amniocentesis is critical from the perspective of therapeutic interventions (Lenis-Cordoba, Sánchez, Bello-Muñoz, Sagalá-Martinez, Campos, CarrerasMoratonas, & Cabero-Roura, 2013). Recent advances in amniocentesis have facilitated further analysis of singleton and twin pregnancies. Therefore, the present study examined the rate of fetal loss after amniocentesis in twin pregnancies compared to singleton pregnancies.

2. Material and Methods

After obtaining permission from the ethics committee of Ahvaz Jundishapur university of medical sciences, in a prospective descriptive-analytical study, This research was performed on 712 mothers with singleton (628 cases) and twins (84 cases) pregnancies who referred to the obstetrics and gynecology clinic of Imam Khomeini Hospital in Ahvaz with Amniocentesis due to several reason during 2016-2020. The information was based on the questionnaire, the results of amniocentesis and follow-up of patients on 7, 14 and 60 days after amniocentesis until term and their comparison. The sampling method in this study was a simple census of pregnant women who referred to the obstetrics and gynecology clinic of Imam Khomeini Hospital in Ahvaz during 1997-98. The study was performed on pregnant women who underwent amniocentesis at different times during preterm labor. Pregnant women were divided into singleton and twin groups. After receiving written consent to enter the study, the patients were given a questionnaire containing information such as: age, gestational age, number of pregnancies, childbirth and abortion, the reason for the diagnostic test, first trimester screening, NT ultrasound and amniocentesis results. Patients were monitored through pregnancy during the first week, two weeks, and 60 days after amniocentesis, and in case of abortion or preterm delivery, the age of fetal loss was compared with the information in the questionnaire and compared to the standard values of these parameters. Methods of performing amniocentesis: The surface of the mother's abdomen in the area of the uterus was disinfected and anesthetized. The specialist inserted a needle from the abdomen into the uterus and removed some amniotic fluid from the uterus with a syringe (1 cc per week of pregnancy). Then he gently removed the needle from his abdomen. All the time with the insertion of the needle, the needle path was controlled by ultrasound so as not to harm the fetus. After collecting the required information, data analysis was performed using SPSS statistical software (version 24). For quantitative variables, the mean and standard deviation were determined and for qualitative variables, absolute and relative abundance were determined. The chi-square, Fisher, and T-independent tests were used to compare different variables between the two groups, with a significance level of 0.05.

3. Results

Patients in the present study included 776 pregnant mothers with singleton (686) and twin (90) pregnancies who underwent amniocentesis. However, during the study, 6 twin pregnancy were excluded from the study due to medical abortion as well as 58 singleton pregnancy, and finally 712 pregnant patients with singleton pregnancies (628) and twins (84) entered the final analysis.

The mean age of the patients was 31.96 ± 6.33 years and no statistically significant difference was found between the ages of the two groups ($p = 0.79$). Also, the mean gestational age of patients during amniocentesis was 15.37 ± 0.7 weeks and no significant statistical difference was found between the two groups ($p = 0.69$). Previous pregnancy records in the studied patients showed that the mean of twin Gravid was statistically significantly higher than the singleton group ($p = 0.01$). But the mean of Parity ($p = 0.001$), Living child ($p = 0.03$), and Abortion ($p = 0.01$) were statistically significantly lower in twin patients than in singleton group. Also, the mean NT for all patients was 1.55 ± 0.15 and no statistically significant difference was found between the two groups ($p = 0.56$).

3.1 Results of Fetal Loss and Preterm Delivery in Both Groups

In the twin group, the incidence of preterm was 13.1% and in the singleton group it was 1.75%, which is statistically significant in the group of twins than singleton group ($p = 0.01$). The occurrence of fetal loss was 2.4% in the twin group and 2.07% in the singleton group, which did not have a statistically significant difference between the two groups ($p = 0.56$). Evaluation of fetal loss after amniocentesis also showed that of the two fetal loss cases in the twin group, one (50%) occurred in the first week and another one (50%) occurred between 15 and 60 days. But in the singleton group, 7 cases (63.6%) in the first week, 1 case (9%) in 15 to 60 days after the test, and 3 cases (27.3) after more than 60 days lost the fetus.

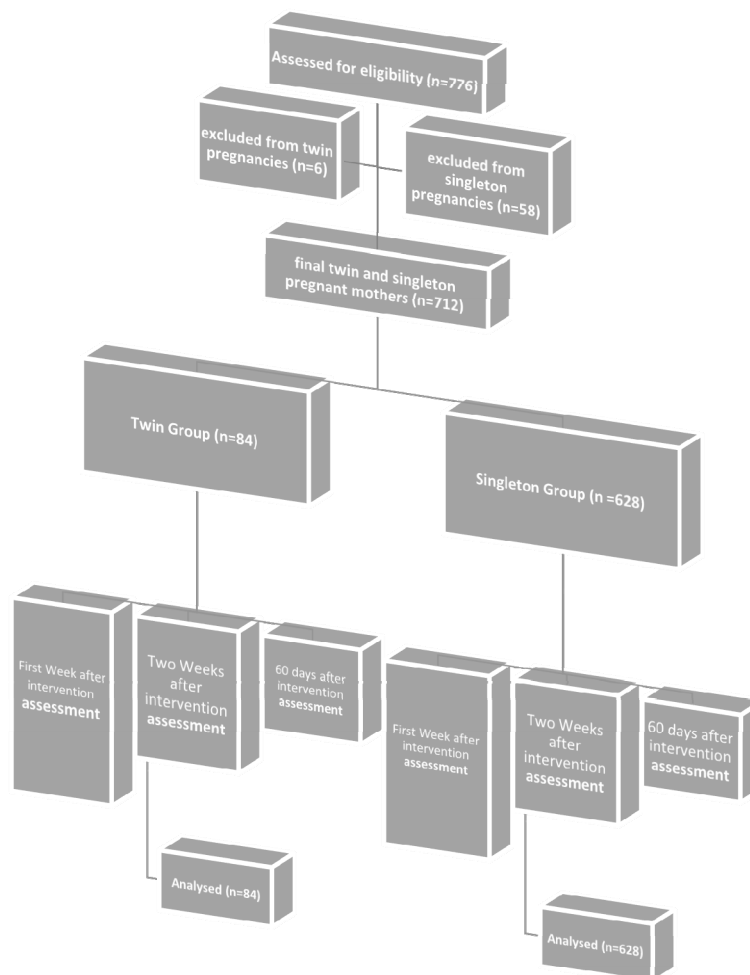


Figure 1. Schematic Material and Methods

Table 1. Patient's characterization in two groups of twin and singleton

Variables	Group		P value	
	Twin (n=84)	Singleton (n=628)		
Age (M±SD)	32.08±4.68	31.95±6.89	0.79	
Gestational age (M±SD)	15.4±0.77	15.37±0.69	0.69	
History of pregnancy	Gravid	1.68±1.30	1.23±0.70	0.01
	Parity	0.96±0.97	1.32±0.47	0.001
	Living child	0.94±0.90	1.05±0.22	0.03
	Abortion	0.85±0.37	1.38±0.97	0.01
NT	1.60±0.44	1.54±4.64	0.56	
Preterm N (%)	11 (13.1%)	11 (1.75%)	0.01	
Fetal Loss N (%)	2 (2.4%)	13 (2.07%)	0.65	
	Week 1	1 (50%)	7 (63.6%)	
	15 to 60 days	1 (50%)	1 (9%)	
	After 60 days	0	3 (27.3%)	

Time of fetal loss

3.2 Comparison of Twin Patients Based on Term and Non-Term

Of the 84 patients, 71 (84.5%) had term births, 11 (13.1%) had preterm births, one (1.2%) had fetal loss and 1 case was preterm, who also lost the fetus (1.2%). Also, one of the cases was a 16-week abortion due to the rupture of the membrane, and the other was a 24-week preterm. Also, a study of patients showed that most mothers (73.8%) underwent amniocentesis due to high-risk screening. Also, 2 cases (2.4%) underwent amniocentesis due to the result of abnormal ultrasound in one of the fetuses, which was reduced due to anomaly, and the fetus remained healthy and term. The mean age of pre-term patients was less than the term patients ($p = 0.04$) and the mean gestational age at amniocentesis did not show a statistically significant difference between the two groups ($p = 0.77$). Previous pregnancy records showed that the mean Gravid ($p = 0.01$), Parity ($p = 0.01$) and Living child ($p = 0.02$) in preterm patients were statistically significantly lower than in the term patients. but no significant statistical difference was observed for the Abortion ($p = 0.09$).

Table 2. Comparison of twin patients based on Term and non-Term

Variables	Group		P value	
	Term (n=84)	Pre-Trem (n=628)		
Age (M±SD)	32.52±4.53	29.69±4.92	0.04	
Gestational age (M±SD)	15.39±0.7	15.46±1.12	0.77	
History of pregnancy	Gravid	1.83±1.27	0.84±1.21	0.01
	Parity	1.07±0.98	0.38±0.76	0.01
	Living child	1.00 ± 0.89	0.38 ± 0.76	0.02
	Abortion	0.80 ± 0.44	1.00 ± 0.00	0.09
NT	1.62±0.45	1.50±0.42	0.37	

4. Discussion

The present study was conducted to compare the rate of amniocentesis fetal loss in twin and singleton pregnancies and, as previously presented, 2.4% in the twin group and 2.07% in the singleton group had fetal loss. There is no statistically significant difference between the two groups ($p = 0.65$). However, in the twin group, the prevalence of preterm was 13.1% and in the singleton group it was 1.75% and in the twin group, it was statistically significantly higher than in singleton group ($p = 0.01$). In general, the chances of preterm pregnancies in twins are much higher than in single twins, and the side effects are greater in twin pregnancies. In the following, due to the small sample size and single centrality of the present study, we will examine other studies conducted by other researchers to review their achievements, based on the reported results, to have a better understanding of the implications of the study hypothesis. In one study, Kalogiannidis et al., 2011 in Greece, compared the effects of amniocentesis on 6270 twin and singleton pregnancies. Maternal age was the main indicator of amniocentesis in both twins and singleton. The results showed that there was no difference in the rate of abortion (0.24% in singleton and 0% in twins). According to these results, the incidence of

amniocentesis side effects in twin pregnancies did not increase compared to singleton pregnancies (Kalogiannidis, Petousis, Prapa, Dagklis, Karkanaki, Prapas, & Prapas, 2011). In the present study, no statistically significant difference was observed about fetal loss between the two groups. Also, the sample size of the two studies was almost the same and indicates the similarity of the consequences of the intervention in both Asian and European societies. In another study, Lenis-Cordoba et al., 2013 in Spain, assessed the risk of fetal loss after second trimester amniocentesis in twin pregnancies. The findings showed that the rate of fetal loss 4 weeks after amniocentesis (2.7 vs. 2.6%) and the rate of fetal loss before 24 weeks of gestation (1.2 versus 1.1%) between the two groups is close to each other without statistically significant difference (Lenis-Cordoba, Sánchez, Bello-Muñoz, Sagalá-Martínez, Campos, CarrerasMoratonas, & Cabero-Roura, 2013). Although in their study the control group was designed and in the present study the singleton group was compared, the final result of both studies shows that amniocentesis will not increase the risk of fetal loss in patients. Other studies have reported a very low rate of fetal loss following amniocentesis in twin pregnancies. For example, Kan and colleagues in Hong Kong reported in 2012 that out of 105 twin pregnancies, 102 gave birth to live babies (Kan, Lee, Leung, Chan, Tang, & Chan, 2012). However, in some other studies, the results have been reported to be inconsistent with the present study, and contrary to our findings, amniocentesis has increased the rate of fetal loss in patients. In one study, Hanprasertpong et al., 2008 in Thailand, found that the rate of fetal loss 14 days after amniocentesis in pregnant women with twin pregnancies was 1.4% which showed Fetal loss in twin pregnancies after amniocentesis was higher than in single pregnancies (Hanprasertpong, Kor-anantakul, Prasartwanakit, Leetanaporn, Suntharasaj, & Suwanrath, 2008). In fact, contrary to the present study, fetal loss occurred in twin patients more than in single patients, but one of the reasons for this difference between the present study and their study could be the difference in the history of patients and the reasons for amniocentesis. Because in their study, all patients were intervened due to old age, while in the present study, patients for reasons including 62 people (73.8%) high-risk amniocentesis, 13 people (15.5%) due to parents with blood diseases, 7 people (8.3%) due to The history of children with genetic defects and 2 people (2.4%) also underwent amniocentesis due to abnormal ultrasound of one of the fetus. Inconsistent results are also seen in other studies. For example, Cahill et al. (2009) reported that people with twin pregnancies who underwent amniocentesis were more likely to lose their pregnancies than those who did not have amniocentesis (3.2% Compared to 1.4%) (Cahill, Macones, Stamilio, Dicke, Crane, & Odibo, 2009) and their findings on creativity are the results of our study which has been inconsistent with our results.

5. Conclusion

Our findings show that fetal loss following amniocentesis in twin pregnancies does not increase significantly compared to singleton pregnancies. However, our finding requires repeated study in bigger sample size and as multi-centered as possible then It can be generalized to wider communities.

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Conflict of interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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