

Amniocentesis is a safe and effective prenatal diagnostic tool: a clinical study in Eastern India

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ABSTRACT

Background: Aim of current study was to estimate the benefits of amniocentesis for diagnosis of fetal chromosomal abnormalities as well as the risk of miscarriage in Indian women and thus provide local data for counselling the prospective parents contemplating amniocentesis.

Methods: This retrospective study reviewed the miscarriage rate of 243 pregnant women who underwent midtrimester amniocentesis for prenatal diagnosis of fetal chromosomal abnormalities. 20 ml of amniotic fluid was aspirated under ultrasound guidance.

Results: Only three women had miscarriage, two of them within a week of the procedure and the other one after two weeks. The miscarriage rate in this study was 1.23% which was not statistically significantly different from the miscarriage rate found in a large trial, faster trial, taken as reference.

Conclusions: Two factors, indications for amniocentesis as well as the procedure itself, contribute to the risk of miscarriage. The procedure-related risk is very low and the total risk of miscarriage is around one percent. Amniocentesis is a safe and effective prenatal diagnostic procedure.

Keywords: Prenatal diagnosis, Amniocentesis, Miscarriage

INTRODUCTION

Chromosomal abnormality in fetus can have minimal to devastating consequences including severe mental and physical disability as well as short lifespan. Despite awesome progress in medical science diagnosis of chromosomal abnormalities in fetus remains a challenging task. The most common chromosomal abnormalities in newborns are trisomies 21,18,13, monosomy X and other sex chromosome aneuploidies.¹ These aneuploidies can account for up to 95% of those born with chromosomal abnormalities.² Amniocentesis is a prenatal invasive diagnostic test that entails tapping of small amount of amniotic fluid from the gestational sac. This was first performed for diagnosis of genetic diseases

(sex determination) of the fetus and reported by Fuchs and Riis in 1956.³ In 1966 Steele and Breg reported in their seminal paper that the fetal cells can be obtained from the amniotic fluid and can be cultured to allow successful fetal karyotyping.⁴ Karyotyping following amniocentesis enables us to diagnose chromosomal problem antenatally at a time when mothers can take an informed decision.

There is abundant research work showing the effectiveness and risks of amniocentesis in western countries.⁵⁻¹⁰ However, we have not come across any notable study in literature on amniocentesis in eastern India.

The aim of our study is to estimate the benefits of amniocentesis and risks, especially the risk of miscarriage in amniocentesis in our populations and thus provide local data for counselling the prospective parents.

METHODS

The miscarriage rate of 243 pregnant women who underwent midtrimester amniocentesis at a private diagnostic clinic at Kolkata between August 2010 and December 2014 was reviewed in this retrospective study. Local ethics committee approval was obtained for this study.

All these women were referred to the clinic for prenatal diagnosis by amniocentesis with valid indications. Only the women with valid indications of amniocentesis, with singleton live pregnancy, with at least 15 completed weeks of gestation and no history of bleeding per vagina and maternal pyrexia were included in the study. Each patient gave informed consent after counselling. Each of them was advised to empty her bladder before the procedure to avoid inadvertent bladder injury. A thorough ultrasound examination was carried out to confirm live, singleton pregnancy, period of gestation, any obvious fetal anomaly, placental location and visual estimation of liquor volume. Maternal abdomen was cleansed with antiseptics before advancing a 22 G spinal needle under ultrasonic guidance. No local anaesthesia was used for the procedures. The operator held the ultrasound probe in one hand and needle in the other. One assistant was used only to aspirate the amniotic fluid.

All efforts were made to avoid placental puncture. However, it was unavoidable in few cases. Initial 1.0 ml amniotic fluid was discarded to avoid maternal contamination. Approximately 20 ml of amniotic fluid was drawn in two sterile disposable syringes. The women were discharged within 30 minutes of the procedure with advice to continue broad spectrum antibiotic for 3 days.

Relevant maternal information and ultrasound findings were logged at the clinic when they came for the procedure. In subsequent follow-up visit or by direct questionnaire, pregnancy outcome data were collected.

The miscarriage rate as found in one large study,³ FASTER trial, was taken as reference rate. The miscarriage rate of our study was compared with the reference rate by Chi-squared test. All procedures were done by one of the authors (KM) trained in fetal medicine.

The miscarriage is defined as the loss of pregnancy before 24 weeks of gestation.

RESULTS

In this study the miscarriage rate for 243 pregnant women who underwent mid-trimester amniocentesis was

reviewed. As all these women opted for amniocentesis after counselling, there was no control arm.

The relevant characteristics of the participating women are given in Table 1.

Table 1: Characteristics of the women in the study.

Characteristics	Mean ± SD (n=243)	Range
Age	33.12 ± 4.23 years	20-41 years
Gestational age	117.56 ± 5.24 days	106-128 days

It is important to note that majority of the mothers were referred as the risk estimated by first and second trimester screening tests was high considering the cut-off value at 1 in 250. A notable number of mothers were referred with previous history of Down's syndrome or other chromosomal abnormalities. There were also other indications, for example maternal request (Table 2, Figure 1).

In this study there was no incidence of 'dry tap' i.e. in all cases amniotic fluid was obtained in first attempt. Also, there was no incidence of 'bloody tap' in this study. There was no incidence of 'culture failure' either.

Table 2: Indications of amniocentesis.

Indications of amniocentesis	Frequency
High risk for Down's syndrome or any other common chromosomal abnormalities on screening	205
Previous child birth with Down's syndrome or any other chromosomal abnormalities	24
Others	
1. Maternal request	3
2. Mother/Father balanced translocation carrier (h/o recurrent miscarriage)	5
3. Both parents beta thalassaemia carrier	6
Total	243

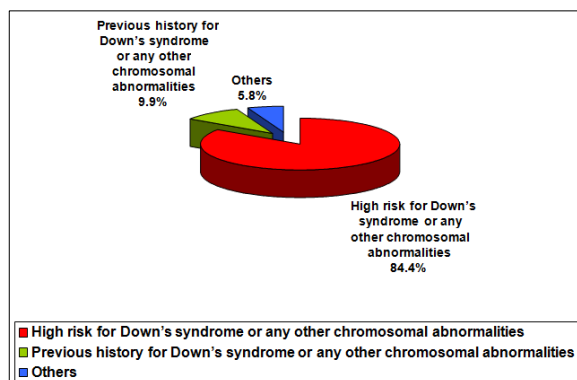


Figure 1: Indications of amniocentesis.

Of the 243 amniocentesis performed, only 13 fetuses had abnormal karyotype. Out of them nine were trisomy 21, three balanced translocations and one Turner's syndrome (Table 3, Figure 2).

Table 3: Fetal chromosomal status as obtained following amniocentesis.

Fetal karyotype	Frequency
Normal (46 XX or 46 XY)	230
Abnormal	
1. Trisomy 21	9
2. Balanced translocation carrier	3
3. Turner's syndrome	1
Total	243

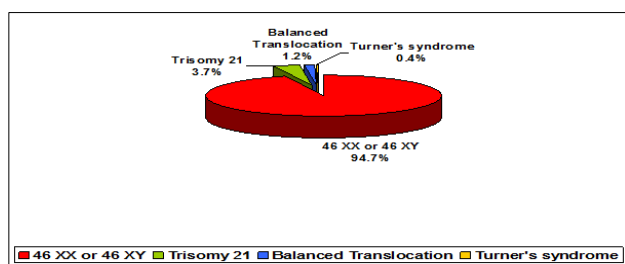


Figure 2: Fetal chromosomal status.

The focus of this study was to assess the miscarriage rate following mid-trimester amniocentesis in our local population. Of the 243 procedures performed only three patients had fetal loss before 24 completed weeks of gestation. Of these three miscarriages, two happened within a week of the procedure and the other one happened after two weeks. The miscarriage rate in this study was 1.23% which, compared with the miscarriage rate following amniocentesis as found in FASTER trial³ by Chi-squared test, was not statistically significantly different (Table 4, Figure 3).

Table 4: Miscarriage rate of amniocentesis.

Complication	Our study	Reference study (FASTER trial)	P value	Remarks
Miscarriage	1.23%	1.0%	>0.05	Not significant

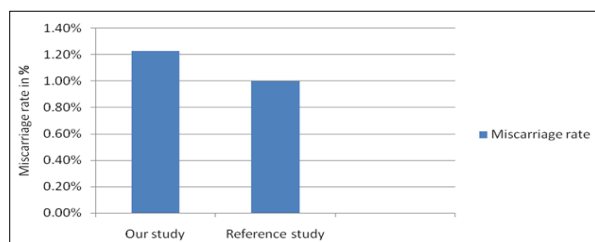


Figure 3: Comparison of miscarriage rate in our study with reference study.

DISCUSSION

On literature search we have not come across any notable study on amniocentesis in eastern India. These local data, we think, will be useful for counselling the prospective parents contemplating amniocentesis.

Miscarriage has been a major issue with amniocentesis for long time. In our study the principal goal has been to determine the miscarriage rate in amniocentesis. In this study the miscarriage rate was 1.23% which was not statistically and clinically significantly different from the miscarriage rate of 1% following amniocentesis as found in the FASTER trial.³ In FASTER trial, a large multicentric trial in USA, all the potential confounders (that may influence the miscarriage rate) were compared between those who underwent amniocentesis and those who did not undergo amniocentesis. The pregnancy loss rate in the amniocentesis group in this study is similar to 0.96% loss seen in the midtrimester amniocentesis group of the Canadian early and mid-trimester amniocentesis Trial study.¹¹ Hence we have taken the miscarriage rate of FASTER trial as reference for comparison.

To estimate the 'procedure-related' risk of miscarriage has been the focus of quite a few studies.^{3,10-15} Comparison of the outcome in pregnant women who had undergone amniocentesis with those who had not, will seem to provide the answer to this vexed issue. Such an approach, indeed, will overestimate the risk of amniocentesis procedure. Because the increased risk of miscarriage contributed by the indications of amniocentesis will be overlooked. For example, the screening tests such as increased fetal nuchal translucency and decreased maternal serum Pregnancy Associated Plasma Protein-A (PAPP-A) are associated with both increased risk of fetal aneuploidies as well as miscarriage and stillbirth.¹³

A randomized controlled study is the best possible way to measure the procedure-related risk of an invasive procedure such as amniocentesis. Only one such study on amniocentesis was carried by Tabor et al. in 1986.⁵ This study, a gold standard study in the field of fetal medicine, provides the best estimate of an excess pregnancy loss in low-risk women caused by amniocentesis.¹⁶ This study reported the amniocentesis procedure related risk of miscarriage in the study group was an additional 1% over the control group. Concerns were raised about the unexpectedly low background loss rate in the nonamniocentesis group in this study.³

It is an important fact to note that since the Tabor study there has been no randomized study on this issue and a number of recent publications have questioned this risk figure as 'historical' as it is a generally acknowledged fact that improvements in technology and operator experience are likely to improve the loss rate substantially.^{3,13} A systematic review and meta-analysis, that reported a miscarriage rate of 0.81% in the women who underwent amniocentesis, concluded that procedure-

related risk of miscarriage is much lower than currently quoted risk of additional 1%.¹²

Another publication lent support to the view the miscarriage risk, due to an invasive procedure (such as chorionic villus sampling or amniocentesis) per se, is very low.¹³

It is now ethically and realistically difficult to conduct any randomized trial as most of the women would opt for a diagnostic test like amniocentesis. In absence of such study it has been proposed that the procedure related risk can only be assessed after addressing the issue of adjustment of maternal demographic characteristics and components of first trimester screening test.¹⁴

This opinion is also shared by the Society of Obstetricians and Gynaecologists of Canada committee that many factors, such as maternal age, previous obstetric history, medical history, methodology of screening for aneuploidy, influence a person's background risk of pregnancy loss. The committee concluded that the risk of postprocedure loss is unique to the individual and is based on the multiple variables.¹⁵

As the background risk of pregnancy loss of an individual is unique, there is no single percentage that can be quoted as the procedure related loss. Though an individualised approach to appraise one's background risk of miscarriage will, therefore, provide more accurate estimate of procedure-related risk for Caucasian population,¹³ it needs to be validated for Asian women. Until then, our data will be useful to reassure pregnant women in our population that whatever individual risk of miscarriage or the risk of procedure related miscarriage may be, total risk of miscarriage will be around 1% and will help in allaying the remorse of someone who had a miscarriage following amniocentesis that most likely the miscarriage would have happened anyway regardless of amniocentesis.

Our study did not have any control arm as they all opted for amniocentesis. Besides, it has the limitation of being a retrospective study. However, with our data we have been able to establish a figure which gives an idea about the realistic risk and this assurance that the actual risk will turn out to be less if we can individualise a background risk of pregnancy loss.

In this study large majority of women have undergone amniocentesis as risks estimated by screening tests were considered high. It is encouraging to note that the women in this part of the world are now better aware of possible chromosomal abnormalities in the babies and their implications. Consequently not only many women are accepting the screening tests for identifying risks, very few people refuse invasive tests such as Chorion Villus sampling and amniocentesis after knowing the pros and cons.

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