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Original Research Article

Outcomes of amniocentesis at a tertiary maternal-fetal medicine unit in Malaysia: a five-year retrospective cohort study of cytogenetic yield and procedure-related complications

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ABSTRACT

Background: Amniocentesis is the most widely performed invasive prenatal diagnostic procedure worldwide. While its diagnostic accuracy is well established, procedure-related risks such as miscarriage and preterm prelabour rupture of membranes (PPROM) remain central to patient counselling. Although international safety and diagnostic outcome data are robust, regional evidence from Southeast Asia is limited. This study aimed to evaluate the cytogenetic yield and short-term complications of amniocentesis performed in a Malaysian tertiary maternal-fetal medicine (MFM) training centre over a five-year period.

Methods: A retrospective cohort study was conducted, including all women who underwent amniocentesis at hospital Tuanku Jaafar (HTJ), Seremban, between January 2018 and December 2022. Maternal demographics, ethnicity, indications, cytogenetic outcomes, and procedure-related complications within 14 days were extracted from hospital records. Descriptive statistics were used to summarise baseline characteristics and outcomes. Associations were analysed using Fisher's exact test, and binary logistic regression was performed to identify independent predictors of miscarriage and PPROM.

Results: A total of 650 amniocentesis were included. Most women were <35 years (34.8%) or 38-40 years (31.1%); the majority were Malay (73.8%). Advanced maternal age was the leading indication (54.6%). Cytogenetic analysis revealed normal results in 90.9% of cases. Abnormal findings included trisomy 21 (1.7%), trisomy 18 (3.4%), trisomy 13 (0.8%), and other aneuploidies (3.1%), yielding an overall abnormal karyotype rate of 8.9%. Procedure-related complications were rare, with miscarriage in 0.3% (n=2) and PPROM in 0.6% (n=4). An abnormal karyotype was significantly associated with miscarriage and PPROM in univariate analysis ($p<0.001$) and remained an independent predictor of PPROM on logistic regression (OR=2.74, 95% CI=1.5-5.1, $p=0.001$). No independent predictors of miscarriage were identified.

Conclusions: Amniocentesis in this tertiary MFM training centre was associated with a high diagnostic yield and very low short-term complication rates, consistent with international benchmarks. The clustering of complications among abnormal karyotypes suggests that biological vulnerability contributes to adverse outcomes independent of procedural factors. These findings reinforce the safety of amniocentesis in the hands of experienced practitioners and provide important regional data for patient counselling and training.

Keywords: Karyotyping, Preterm premature rupture of membrane, Miscarriage, Complication, Amniocentesis

INTRODUCTION

Amniocentesis is one of the most widely performed invasive prenatal diagnostic procedures and remains the gold standard for confirming fetal chromosomal abnormalities.[1,2] Since its introduction, refinements in ultrasound guidance, aseptic technique, and operator training have markedly reduced procedure-related risks.[3] Despite these advances, miscarriage, PPROM, and other adverse outcomes remain important considerations in both clinical practice and patient counselling.[4]

International experience demonstrates variability in diagnostic yield. A 30-year Taiwanese review reported abnormal karyotypes in 5-10% of cases, while a Turkish study documented yields between 5% and 15%.[5,6] Extensive national registry and multicenter cohort studies have also established that procedure-related pregnancy loss rates are lower than previously estimated, particularly when procedures are performed in high-volume tertiary centres.[7-9] A Thai study from Southeast Asia documented cytogenetic yields and complication rates comparable to international benchmarks, although outcomes differed between secondary and tertiary centres.[10] A United States study further compared outcomes of amniocentesis and chorionic villus sampling, reporting similar diagnostic utility with slightly different loss rates.[11]

Biological contributors are also important: adverse outcomes such as miscarriage and PPROM may reflect intrinsic fetal or placental pathology rather than the procedure itself.[12] Large cohorts from Egypt and China have confirmed the role of amniocentesis in detecting a wide spectrum of chromosomal abnormalities, including trisomies and structural rearrangements.[13,14] Updated meta-analyses reaffirm miscarriage risk estimates of approximately 0.1-0.3% for mid-trimester procedures.[15] These findings are consistent with earlier registry-based studies and systematic reviews.[16]

Randomized controlled trials and large cohort series demonstrated that early amniocentesis, performed before 15 weeks, is associated with higher risks of fetal loss and congenital anomalies.[17] Malaysian data from a five-year review confirmed low complication rates and emphasized the need for larger multicenter datasets to improve generalizability.[18] Similarly, a multicenter review of twin pregnancies reported fetal loss rates comparable to singleton pregnancies.[19] Procedural reviews continue to emphasize that complication rates are closely tied to operator expertise and institutional experience. Comparative studies of early versus mid-trimester procedures reinforce recommendations to restrict amniocentesis to 15 weeks or later.[20]

Recent advances in prenatal diagnostics, including molecular cytogenetics, have further increased diagnostic yield of invasive testing. Comprehensive reviews highlight the evolving role of invasive prenatal procedures within broader framework of genetic medicine.[21] Chromosomal microarray analysis has been shown to increase diagnostic yield beyond conventional karyotyping, detecting clinically relevant sub microscopic abnormalities.

HTJ, Seremban, is one of Malaysia's largest tertiary referral hospitals and a designated centre for MFM training. Given the limited local evidence, this study was conducted to evaluate outcomes of amniocentesis performed at HTJ between 2018 and 2022. The primary objectives were to determine cytogenetic yield and to assess the incidence of short-term complications, specifically miscarriage and PPROM, within 14 days of the procedure.

METHODS

We conducted a retrospective cohort study of all amniocentesis procedures performed at the MFM unit, HTJ, Seremban, between January 2018 and December 2022. The unit is a tertiary referral centre and national training site for the MFM subspecialty.

All women undergoing amniocentesis were eligible; cases with incomplete records or lacking 14-day follow-up were excluded. A total of 650 procedures were analysed. Maternal age, ethnicity, indication for amniocentesis, karyotype results, and complications were retrieved from the institutional registry and medical records.

Amniocentesis was performed by MFM specialists or fellows under USG guidance, with 15-20 mL of amniotic fluid being aspirated for cytogenetic analysis. The primary outcomes were miscarriage and PPROM within 14 days. Secondary outcome was cytogenetic yield (normal, trisomy 13/18/21, other aneuploidies, failed culture).

Data were analysed using SPSS v29.0. Descriptive statistics were presented as frequencies and percentages. Associations between predictors and outcomes were assessed with χ^2 tests (or Fisher's exact test as appropriate). Binary logistic regression was performed to evaluate independent predictors, and results were reported as odds ratios with 95% CI. A $p<0.05$ was considered statistically significant. Consent was waived due to the use of retrospective, anonymized data.

RESULTS

A total of 650 amniocentesis procedures were included in the study. Baseline characteristics are presented in Table 1. The majority of women were aged either <35 years (34.8%, n=226) or 38-40 years (31.1%, n=202), while 18.9% (n=123) were aged 35-37 years and 15.2% (n=99) were >40 years. The cohort was predominantly Malay (73.8%, n=480), followed by Chinese (10.5%, n=68), others (12.6%, n=82), and Indian (3.1%, n=20). The most frequent indication for amniocentesis was advanced maternal age (54.6%, n=355). Other indications included abnormal ultrasound findings (26.8%, n=174) and ultrasound soft markers (18.6%, n=121).

Karyotyping results are shown in Table 2. Of the 650 samples, 90.9% (n=591) were cytogenetically normal. Abnormal results included trisomy 21 in 1.7% (n=11), trisomy 18 in 3.4% (n=22), trisomy 13 in 0.8% (n=5), and other aneuploidies in 3.1% (n=20). One sample (0.2%) resulted in culture failure. The overall abnormal cytogenetic yield was 8.9% (58/650; 95% CI=7.0-11.4%).

Procedure-related complications within 14 days are summarized in Table 3. There were two miscarriages (0.31%; 95% CI=0.08-1.11%) and four cases of PPROM (0.62%; 95% CI=0.24-1.57%). Both outcomes were rare, and statistical power for subgroup analyses was limited.

Associations with miscarriage are detailed in Table 4. Miscarriages occurred only among women aged <35 years (2/226; 0.9%), with no cases in older groups (χ^2=3.76, p=0.288). Both miscarriages observed in Malay women (χ^2=0.71, p=0.871). All miscarriages occurred in abnormal ultrasound indication group (2/174; 1.1%), while no events occurred in the advanced maternal age or soft marker groups (χ^2=5.49, p=0.064). By karyotype, miscarriages were observed in trisomy 13 (1/5; 20.0%) and trisomy 18 (1/22; 4.5%), with no events among normal, trisomy 21, other aneuploidies, or failed samples (χ^2=78.0, p<0.001).

Associations with PPROM are presented in Table 5. PPROM occurred in women aged <35 years (3/226; 1.3%) and 38-40 years (1/202; 0.5%), with no events in the 35-37 or >40 age groups (χ^2=3.30, p=0.348). By ethnicity, cases were reported among Malays (3/480; 0.6%) and Others (1/82; 1.2%), but none in Chinese or Indian women (χ^2=1.04, p=0.793). According to the indication, PPROM occurred in advanced maternal age (2/355; 0.6%) and abnormal ultrasound findings (2/174; 1.1%), with no cases in soft marker indications (χ^2=1.58, p=0.455). By karyotype, PPROM clustered in trisomy 13 (1/5; 20.0%), trisomy 18 (2/22; 9.1%), and other aneuploidies (1/20; 5.0%), with no events among normal, trisomy 21, or failed samples (χ^2=66.6, p<0.001).

Multivariable logistic regression confirmed these patterns. The model for miscarriage did not converge to a stable solution due to the small number of events (n=2). For PPROM, model was statistically significant (χ^2=12.298, df=4, p=0.015; Nagelkerke R^2=0.26). An abnormal karyotype remained an independent predictor of PPROM (OR=2.74, 95% CI=1.5-5.1, p=0.001), whereas maternal age, ethnicity, and indication were not independently associated. Given rarity of complications, these adjusted estimates should be interpreted with caution.

Table 1: Baseline characteristics of women undergoing amniocentesis, (n=650).

Variables	N	Percentages (%)
Maternal age group (in years)		
<35	226	34.8
35-37	123	18.9
38-40	202	31.1
>40	99	15.2
Ethnicity		
Malay	480	73.8
Chinese	68	10.5
Indian	20	3.1
Others	82	12.6
Indication for amniocentesis		
Advanced maternal age	355	54.6
Ultrasound soft markers	121	18.6
Abnormal ultrasound findings	174	26.8

Table 2: Karyotyping results, (n=650).

Karyotype results	N	Percentages (%)
Normal	591	90.9
Trisomy 13	5	0.8
Trisomy 18	22	3.4
Trisomy 21	11	1.7
Other aneuploidies	20	3.1
Failed culture	1	0.2

Table 3: Procedure-related complications within 14 days, (n=650).

Complications	N	Percentages (%)
Miscarriage	2	0.3
PPROM	4	0.6

Table 4: Association between maternal/clinical factors and miscarriage within 14 days.

Variables	Miscarriage, N (%)	No miscarriage, N (%)	χ^2	P value
Age group (in years)				
<35	2 (0.9)	224 (99.1)	3.76	0.288
35-37	0	123 (100)		
38-40	0	202 (100)		
>40	0	99 (100)		
Ethnicity				
Malay	2 (0.4)	478 (99.6)	0.71	0.871
Chinese	0	68 (100)		
Indian	0	20 (100)		
Others	0	82 (100)		
Indication				
Advanced maternal age	0	355 (100)	5.49	0.064
Soft markers	0	121 (100)		
Abnormal USG	2 (1.1)	172 (98.9)		
Karyotype				
Normal	0	591 (100)	78.0	<0.001
Trisomy 13	1 (20.0)	4 (80.0)		
Trisomy 18	1 (4.5)	21 (95.5)		
Trisomy 21	0	11 (100)		
Other aneuploidies	0	20 (100)		
Failed	0	1 (100)		

Table 5: Association between maternal/clinical factors and PPROM within 14 days.

Variables	PPROM, N (%)	No PPROM, N (%)	χ^2	P value
Age group (in years)				
<35	3 (1.3)	223 (98.7)	3.30	0.348
35-37	0	123 (100)		
38-40	1 (0.5)	201 (99.5)		
>40	0	99 (100)		
Ethnicity				
Malay	3 (0.6)	477 (99.4)	1.04	0.793
Chinese	0	68 (100)		
Indian	0	20 (100)		
Others	1 (1.2)	81 (98.8)		
Indication				
Advanced maternal age	2 (0.6)	353 (99.4)	1.58	0.455
Soft markers	0	121 (100)		
Abnormal USG	2 (1.1)	172 (98.9)		
Karyotype				
Normal	0	591 (100)	66.6	<0.001
Trisomy 13	1 (20.0)	4 (80.0)		
Trisomy 18	2 (9.1)	20 (90.9)		
Trisomy 21	0	11 (100)		
Other aneuploidies	1 (5.0)	19 (95.0)		
Failed	0	1 (100)		

DISCUSSION

Five-year retrospective cohort study conducted at tertiary MFM training centre in Malaysia evaluated outcomes of amniocentesis, focusing on diagnostic yield and short-term complications. Study demonstrated an overall abnormal karyotype rate of 8.9% and complication rates of 0.31% for miscarriage and 0.62% for PPROM within 14 days of procedure. These findings reaffirm safety and diagnostic utility of amniocentesis in a high-volume tertiary setting and add valuable regional data to global literature.

Comparison with international data

The abnormal karyotype yield observed in this cohort aligns with reports from international series. A 30- year

Taiwanese experience documented abnormal yields of 5-10% depending on indication, while a Turkish study reported yields in a similar range.[5,6] Large registry and cohort studies from Europe also confirmed that procedure-related pregnancy loss rates were lower than historically estimated.[7-9] A Thai series further demonstrated diagnostic yields and complication rates comparable to international benchmarks, although outcomes varied depending on the level of care.[10] A United States study comparing amniocentesis with chorionic villus sampling similarly confirmed low procedure-related loss rates when performed in experienced centres.[11]

Our miscarriage rate of 0.3% is consistent with the most recent systematic reviews and registry studies, which place the procedure-related risk between 0.1 percent and 0.3 percent.[15,16] Earlier randomized controlled trials and comparative studies of early amniocentesis highlighted higher risks of the fetal loss and congenital anomalies before fifteen weeks, findings which consolidated the recommendation that procedures be restricted to the mid-trimester.[4,17,20]

Biological contributors to complications

Complications in this study clustered among pregnancies with abnormal karyotypes. Both miscarriages occurred in fetuses with trisomy 13 or trisomy 18, while PPROM was observed in trisomy 13, trisomy 18, and other aneuploidies. These findings suggest that part of the observed risk may be attributable to underlying fetal or placental pathology rather than the invasive procedure itself. Similar associations have been described in other cohorts, where biological vulnerability influenced outcomes more strongly than the procedure.[12]

Large-scale data from Egypt and China support this interpretation, demonstrating that aneuploidy and congenital anomalies are associated with increased baseline risk of adverse outcomes.[13,14] This distinction is important for patient counselling, as it separates inherent biological risks from the procedure related risk, thereby improving the accuracy of the informed consent discussions.

Regional context

Evidence from Southeast Asia remains relatively limited. Thailand's experience highlighted comparable outcomes but variability between secondary and tertiary centres.[10] In Malaysia, a five-year review also confirmed low complication rates, which is consistent with our findings.[18] Data from multicenter analyses, including studies in twin pregnancies, further demonstrate that invasive procedures remain safe even in more complex scenarios.[19]

Strengths and limitations

The strengths of this study include its relatively large sample size, standardized procedural approach, and conduct within a national MFM training center with high operator expertise. These factors enhance the validity of the observed complication rates. The retrospective design, however, limited the ability to control for confounders such as maternal parity, body mass index, or placental position. Additionally, the small number of adverse events (n=6) limited the statistical power for multivariable modelling of miscarriage. As this was a single-centre study, results may not be generalizable to lower-volume or resource-limited settings.

Implications and future directions

Clinically, this study reinforces that amniocentesis remains a safe and reliable diagnostic tool in high volume centers. The close association between abnormal karyotypes and adverse outcomes underscores the need for nuanced counselling, distinguishing biological from procedure-related risks.

Future research should prioritize multicenter collaborations in Malaysia and Southeast Asia, using prospective designs and standardized data collection. Comparative studies incorporating recent innovations, such as chromosomal microarray analysis, will also help define the added value of advanced technologies in improving diagnostic yield.[21]

CONCLUSION

This five-year retrospective cohort study, representing the most extensive Malaysian series of amniocentesis outcomes reported to date, provides robust evidence that the procedure, when performed in a tertiary maternal–fetal medicine training center, remains both safe and diagnostically valuable. The overall abnormal karyotype detection rate of 8.9% highlights the enduring clinical utility of amniocentesis in confirming chromosomal abnormalities, particularly in pregnancies complicated by advanced maternal age, abnormal ultrasound findings, or soft markers, in contexts where non-invasive prenatal testing is not universally accessible. The very low complication rates observed-0.3% for miscarriage and 0.6% for PPROM within 14 days-are consistent with the most favourable international benchmarks, underscoring the safety of the procedure when undertaken by experienced operators. Importantly, adverse outcomes clustered predominantly among pregnancies with abnormal karyotypes, suggesting that biological vulnerability rather than the invasive procedure itself accounts for much of the observed risk, a finding that refines the accuracy of patient counselling. By delivering the largest local dataset, this study advances knowledge and understanding in the field by filling a critical evidence gap in Southeast Asia, providing context-specific risk estimates to improve counselling and shared decision-making, reinforcing training standards for invasive prenatal diagnostics, and reaffirming the continuing role of amniocentesis as a reliable diagnostic tool alongside the expanding application of non-invasive technologies.

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REFERENCES

1. Ghi T, Sotiriadis A, Calda P, Da Silva Costa F, Raine-Fenning N, Alfirevic Z. ISUOG Practice Guidelines: invasive procedures for prenatal diagnosis. Ultrasound Obstet Gynecol. 2016;48(2):256-68.
2. American College of Obstetricians and Gynecologists: ACOG Practice Bulletin No. 162: Prenatal Diagnostic Testing for Genetic Disorders. Obstet Gynecol. 2016;127(5):108-22.
3. Seeds JW. Diagnostic mid-trimester amniocentesis: how safe? Am J Obstet Gynecol. 2004;191(2):607-15.
4. Tabor A, Philip J, Madsen M, Bang J, Obel EB, Nørgaard-Pedersen B. Randomised controlled trial of genetic amniocentesis in 4606 low-risk women. Lancet. 1986;1(8493):1287-93.
5. Chang YL, Chang SD, Chao AS, Wang CN, Cheng PJ. Thirty years of amniocentesis: a single-center experience in Taiwan. Taiwan J Obstet Gynecol. 2012;51(2):206-11.
6. Serin S, Deniz C, Arikan I. Retrospective analysis of the results of amniocentesis Procedure at a university clinic. Perinatal J. 2013;21(2):47-52.
7. Wulff CB, Gerds TA, Rode L, Ekelund CK, Petersen OB, Tabor A. Risk of fetal loss associated with invasive testing following combined first-trimester screening: a national cohort of 147,987 singleton pregnancies. Ultrasound Obstet Gynecol. 2016;47(1):38-44.
8. Akolekar R, Beta J, Picciarelli G, Ogilvie C, D'Antonio F. Procedure-related risk of miscarriage following amniocentesis and chorionic villus sampling: a systematic review and meta-analysis. Ultrasound Obstet Gynecol. 2015;45(1):16-26.
9. Tabor A, Vestergaard CH, Lidegaard Ø. Fetal loss rate after chorionic villus sampling and amniocentesis: an 11-year national registry study. Ultrasound Obstet Gynecol. 2009;34(1):19-24.
10. Pathompanitrat S, Choochuay P, Wannawat N. Second trimester genetic amniocentesis at a secondary center hospital in Southern Thailand. Thai J Obstet Gynecol. 2013;21(4):134-40.
11. Caughey AB, Hopkins LM, Norton ME. Chorionic villus sampling compared with amniocentesis and the difference in the rate of pregnancy loss. Obstet Gynecol. 2006;108(3pt1)612-6.
12. Ercan Ö, Köstü B, Arslan G, Bakacak M, Özer A, Arıkan D. Does amniocentesis increase the rates of fetal loss and poor pregnancy outcomes? Ann J Clin Anal Med. 2016;7(2):197-200.
13. El-Din SM, Ismail NA, Ramy AR. Fetal chromosome abnormalities and congenital malformations: an Egyptian study. Egypt J Hum Genet. 2007;8(2):131-45.
14. Zhang Y, Zhang S, Yin M, Xu J, Lei C, Wu J. Cytogenetic analysis of fetal chromosomal abnormalities by amniocentesis: review of 40,000 consecutive cases in a single Chinese center. Reprod Dev Med. 2017;1(2):84- 9.
15. Salomon LJ, Sotiriadis A, Wulff CB, Odibo A, Akolekar R. Risk of miscarriage following amniocentesis or chorionic villus sampling: systematic review and updated meta-analysis. Ultrasound Obstet Gynecol. 2019;54(4):442-51.
16. Firth HV, Boyd PA, Chamberlain P, MacKenzie IZ, Lindenbaum RH, Huson SM. Severe limb abnormalities after chorion villus sampling at 56-66 days' gestation. Lancet. 1991;337(8744):762-3.
17. Jummaat F, Ahmad S, Mohamed Ismail NA. Five-year review on amniocentesis and its maternal-fetal complications. Horm Mol Biol Clin Invest. 2019;40(2):1.
18. Navaratnam K, Khairudin D, Chilton R, Sharp A, Attilakos G, Stott D, et al. Fetal loss after chorionic villus sampling and amniocentesis in twin pregnancies: a multicenter retrospective cohort study. Prenat Diagn. 2022;42(12):1554-61.
19. Carlin AJ, Alfirevic Z. Techniques for chorionic villus sampling and amniocentesis: a survey of practice in specialist UK centres. Prenat Diagn. 2008;28:914-9.
20. Simpson JL. Invasive procedures for prenatal diagnosis: any future left? Best Pract Res Clin Obstet Gynaecol. 2012;26(5):625-38.
21. Wapner RJ, Martin CL, Levy B, Ballif BC, Eng CM, et al. Chromosomal microarray versus karyotyping for prenatal diagnosis. N Engl J Med. 2012;367(23):2175-84.

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