

Indications for Invasive Prenatal Diagnostic Procedures at a Dedicated Fetal Medicine Centre: An 8 Year Audit 2003-2010

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SUMMARY

Objective: Analyze indications and type of prenatal diagnostic procedures performed.

Method: This retrospective audit was conducted at a dedicated fetal medicine center in Petaling Jaya. All invasive prenatal diagnosis procedures performed from 2003 up until 2010 (amniocentesis, chorionic villous sampling and fetal blood sampling) were analyzed.

Result: A total of 1560 invasive prenatal diagnostic procedures were performed during the 8 year period. Advanced maternal age is the leading indication for invasive prenatal diagnostic procedures followed by fetal abnormalities. The fetal loss rate was 0.2% for amniocentesis and 1.2% for CVS.

Conclusion: Advanced maternal age is the leading indication for invasive prenatal diagnostic procedures at this centre but is on a declining trend. The fetal loss rates are comparable to auditable standards set by professional bodies, in this case, the Royal College of Obstetricians & Gynecologists of London.

KEY WORDS:

Prenatal diagnosis; amniocentesis; chorionic villous sampling; fetal blood sampling

INTRODUCTION

Established invasive prenatal diagnostic procedures include amniocentesis, chorionic villous sampling (CVS) and fetal blood sampling (FBS). The tests harvest amniocytes, placental trophoblasts and fetal blood respectively. These tests are invasive in nature and not without complications. Amniocentesis and chorionic villous sampling are associated with an additional miscarriage risk of 1% above the background risk¹. The fetal loss rate after fetal blood sampling may range from 1.4% up to 25% depending on the indication with the highest loss rate in the non-immune hydrops group^{2,3}. Clinical governance would require it that auditable standards be put in place in centers performing these tests. This study was conducted to study trends in indications for invasive prenatal diagnostic procedures. A

secondary outcome assessed was miscarriage as the endpoint complication of procedures performed. Comparison was made against established auditable standards by the Royal College of Obstetricians & Gynecologists, United Kingdom¹.

MATERIALS AND METHODS

Fetal Medicine & Gynecology Center (FMGC) is a dedicated fetal medicine center in Petaling Jaya, Selangor. It serves as a referral centre in the private sector as well as receives walk-in cases. Invasive prenatal testing is performed for the following indications:

1. Advanced maternal age (AMA)
2. Fetal abnormalities on ultrasound scanning
3. Previous fetal abnormality
4. Abnormal triple test (hCG, unconjugated oestriol and α -fetoprotein)
5. Abnormal double test (α -fetoprotein and β -hCG)
6. α and β -thalassemia
7. Maternal anxiety (usually for history or family history of malformations or aneuploidies)

The first trimester screening (FTS) model involving serum free β -hCG, placental associated plasma protein-A (PAPP A) and nuchal translucency (NT) for trisomy 21 was introduced in 2008. Following this the center ceased to offer the triple test as the preferred biochemical screening test for trisomy 21 unless the women presented beyond the window period of 11⁺⁰ to 13⁺⁶ weeks of gestation. The center continues to receive referrals for the indications listed above.

This is a retrospective study involving all invasive prenatal diagnostic procedures performed during the 8-year period. Procedures performed include amniocentesis, CVS and FBS. All procedures were performed exclusively by the three resident consultants. Procedures were performed using aseptic technique under ultrasound guidance. Local anaesthesia is only given for CVS and FBS. Antibiotic cover is not routinely given. All women are advised to rest at home for 2 days following procedures and a 48-hour medical leave certificate is issued. Amniocentesis is performed with 22G 90mm spinal needle (Terumo ®). CVS is performed using the Robinson CVS pack consisting of an 18G X 150mm guide and a 21G X 200mm sampler (Cook ®). FBS is performed using a

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Table I: Pregnancy loss by procedure

Procedure 2001-2010	Total	Miscarriage	
Amniocentesis	1139	3	0.3%
Chorionic villous sampling	575	7	1.2%
Fetal blood sampling	69	0	0%

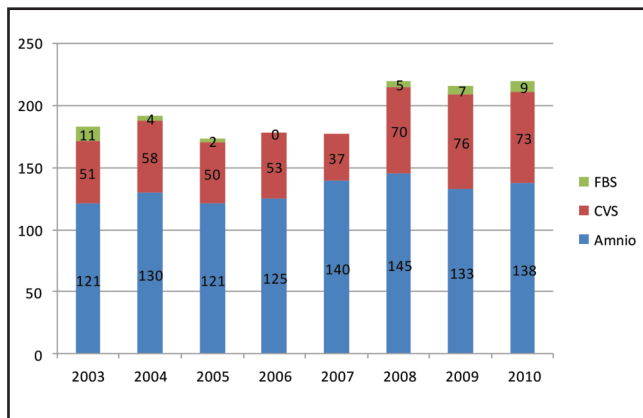


Fig. 1 : Procedures by year 2003-2010.

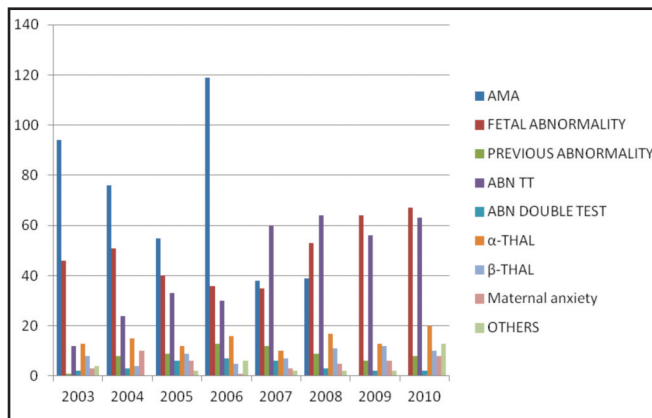


Fig. 2 : Bar chart for number of procedures performed by indications.

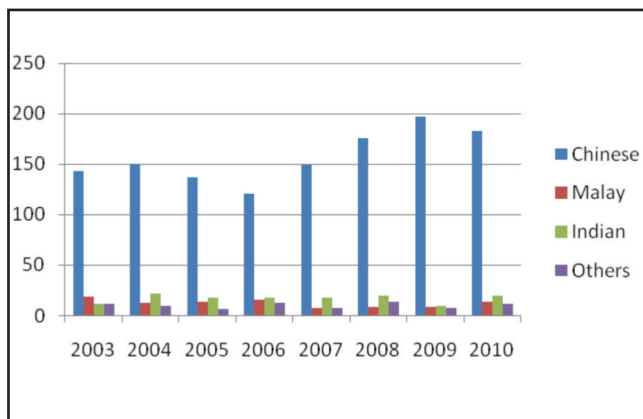


Fig. 3 : Ethnic make-up of women having invasive procedures.

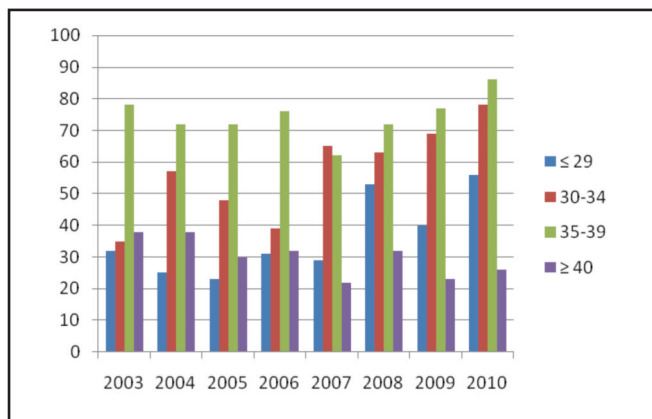


Fig. 4 : Number of procedures by age groups by year.

20G X 150mm cordocentesis needle (Laboratoire C.C.D.). Amniocentesis is only performed after 15 weeks gestation and CVS after 10 weeks gestation. Both transabdominal and transcervical CVS were performed until 2005. Only transabdominal CVS was performed from 2006.

Following the procedures, patients are advised to notify the center and respective consultant should any symptoms of complication arise. All results are directly communicated to patients via telephone by the respective consultants. This presents as a second opportunity for the centre to capture complications should they have occurred. Patients were subsequently followed up by their respective obstetricians.

All invasive procedures performed were recorded in a specific audit form that required the following data entered for every case: maternal age, parity, gestational age, indication for testing, type of prenatal procedure performed, tests requested, test result and miscarriages. Parity and gestational age analyses are not performed due lack in consistency of documentation.

This is an eight year audit involving procedures performed from the year 2003 up until 2010.

RESULTS

A total of 1560 procedures were performed during the 8-year period from 2003-2010. The following number of procedure were performed: 1053 amniocenteses, 468 chorionic villous samplings and 39 fetal blood samplings. Amniocentesis by far was the most common procedure performed (67.5%). CVS contributed 30% of procedures performed.

Figure 1 graphically represents the number of procedures performed.

The amnio:CVS ratio averaged 2.3 amniocentesis to a CVS. There is an apparent rise in CVS procedure from 2008 causing a reduction in the ratio the last 3 audit years.

Figure 2 represents the number of procedures performed by indications. AMA and fetal anomalies were the leading indications for invasive PNDs. AMA was the leading

indication up until 2006. After this there was a sharp decline in AMA related procedures. There were no procedures for AMA in 2009 and 2010.

Figure 3 represents the ethnic make-up of women having invasive prenatal procedures. Chinese women formed the majority of women undergoing invasive testing (80.7%). Other ethnic groups remained stable at 20%.

Figure 4 represents the number of women undergoing procedures by age groups. Women aged 35-39 were more likely to undergo invasive testing. Age-indication analysis was not possible.

Table I lists the number of miscarriages after the procedures. The miscarriage rates are 0.3% and 1.2% for amniocentesis and CVS respectively. There were no FBS related pregnancy losses.

DISCUSSION

This is the first local audit of center-specific invasive prenatal diagnostic procedures in a fetal medicine unit. The center averages 195 procedures per year. This is in excess of the minimum standard rate of 30 procedures per year per operator set by the expert committee of the Royal College of Obstetricians & Gynecologists of London (RCOG)¹. As no local standards have yet been set the RCOG standards have been adopted for comparison.

Amniocentesis is the most common procedure performed by far. CVS accounted for 22-30% of total procedures performed during the 8 year period. The main indication for CVS is for the diagnosis of thalassemia. 3-5% of the Malaysian population is thought to be carriers of one of the array of thalassemia genes⁴. Rarely is it employed for the purpose of karyotype or quantitative fluorescence polymerase chain reaction (QFPCR) for rapid testing for chromosomes 13, 18, 21, X and Y. CVS has the advantage of allowing for earlier diagnosis as it is recommended from 10 weeks onwards^{1,5}. The introduction of CVS coincides with the rise in CVS procedures from 2008. The introduction of FTS has shifted the intervention point to earlier in pregnancy. This may explain the reduction in amnio: CVS ratio after its introduction. Amniocentesis is not recommended prior to 15 weeks due to an increased risk of talipes^{6,7}. Fetal blood sampling is rarely performed due its inherently high pregnancy loss rate ranging from 1-24% depending on its indications³.

AMA was the leading indicator for prenatal diagnosis prior to 2008. The center saw a reduction in prenatal diagnosis for AMA after 2008. The introduction of the first trimester screening (FTS) has reduced unnecessary procedure rates for AMA⁸. FTS which incorporates testing of pregnancy-associated plasma protein A (PAPP-A) and free β -hCG gives a sensitivity of 95% for a false positive rate of 5%^{9,10}. By incorporating FTS the detection rate of trisomy 21 is doubled with a 10-fold reduction in need for invasive prenatal testing¹¹. By adopting this policy the center has managed to reduce invasive testing for AMA as illustrated in Figure 2. AMA, the main indication for invasive testing prior to 2008, eventually did not figure towards the last 3 audit-years. The

number of procedures performed for all other indications has remained constant over the study period.

The indications summarized from the activity of this center would be representative of the standard fetal medicine center. There is a possibility however that the trends observed are skewed as this is a private facility where laboratory costs are absorbed by patients. At the time of writing the laboratory costs of invasive prenatal testing are borne by patients in the public sector too. The exception being FBS. The cost for prenatal diagnosis is high. The true picture of prenatal diagnosis and subsequent uptake of invasive testing will remain elusive in the foreseeable future.

Tabor *et. al.* reported, from a large national registry, that the miscarriage rate for amniocentesis is 1% above the background risk¹². A randomized controlled trial (RCT) comparing pregnancy loss rates of amniocentesis and CVS reported equal pregnancy loss rates between the two procedures¹³. The miscarriage rate of 0.2% for amniocentesis at this center comparable to auditable standards published. There was a high case load to maintain the skills involved for the procedures. With a load of 163 cases per year the center would approximately perform 3 procedures per week. The center-specific CVS miscarriage rate of 1.2% is in keeping with auditable standards that suggest CVS loss rates are perhaps slightly more than that of amniocentesis¹. Unlike amniocentesis the CVS miscarriage rate has not reduced despite the high case load and constant practice. This is also observed in a large European survey¹⁴. This is probably an inherently unmodifiable risk of CVS. There were no fetal loss after FBS but the numbers are insufficient to arrive at a reasonable conclusion. It must be emphasized that the loss rates of this centre are crude estimates without a control comparison to qualify it from the background miscarriage risk.

There are no studies comparing transcervical and transabdominal approaches for CVS. In the center's experience all fetal losses after CVS were prior to 2006 when the transcervical route was used. There have been no losses since a shift to the transabdominal route from the 309 CVS performed since 2006.

Laboratory costs at this center are borne by patients. The costs for karyotype and PCR are substantial. Costs issues could influence the choices patients eventually make. The number of patients who decline testing was not recorded. The actual number of women where prenatal diagnosis is indicated could be underestimated. As with any other retrospective analysis of data there is the possibility of data collection and reporting bias.

All centers performing invasive prenatal testing should keep up to date with current trends in screening and testing as well as conduct continuous prospective audits into procedure-related complications.

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