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# RETROSPECTIVE ANALYSIS OF THE OUTCOMES OF PATIENTS PRESENTING FOR GENETIC COUNSELLING WITH FETAL ABNORMALITIES

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**A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfillment of the requirements for the degree of Master of Science in Medicine in Genetic Counselling**

**Johannesburg, 2007**

# DECLARATION

I, Caryn Todd, declare that this research report is my own work. It is being submitted for the degree of Master of Science in Medicine in Genetic Counselling in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

day of , 2007.

# ABSTRACT

Fetal abnormalities are congenital abnormalities that are identified prenatally, which may be structural or functional in nature. Genetic counselling is a non-directive and non-judgmental process of information-giving, at the same time as providing psychosocial support. It is offered to women and their partners who have a fetal abnormality detected during pregnancy. When a fetal abnormality is detected, the patient can sometimes be offered a termination of pregnancy, and the decision of whether or not to continue the pregnancy is made by the patient.

The first aim of this research was to conduct an audit of the genetic counselling service provided by the Division of Human Genetics, NHLS and WITS, in order to assess the level of service being offered to patients with diagnosed fetal abnormalities. The second aim of the research was to determine what factors, if any, influenced the decision patients made regarding whether to continue or interrupt their pregnancy.

One hundred and seventy one files of women, who received genetic counselling for an identified fetal abnormality during pregnancy from the division between 2002 and 2006, were included in the retrospective clinical audit.

The patients seen for genetic counselling represent 1.1 % of the estimated number of women in Johannesburg who could have had abnormalities detected prenatally, based on the prevalence of congenital disorders in the area and an ultrasound prenatal detection rate of 56.2 %. Two thirds of patients who were offered TOP chose to terminate their pregnancy. The most clinically significant predictor of the decision to terminate an affected pregnancy was found to be an earlier gestation at offer of TOP, which suggests that earlier detection and diagnosis of abnormalities is beneficial to patients. Overall, 62 % of patients were not offered genetic counselling follow-up appointments after conclusion of their pregnancy. The genetic counselling service offered to patients thus needs to be improved, in particular, the follow-up service patients receive after TOP or delivery is not adequate.

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# NOMENCLATURE

Abn – Abnormality

AFP – Alpha feto-protein

AMA – Advanced maternal age

β-hCG – β-subunit of human chorionic gonadotropin

CI – Confidence intervals

CNS – Central nervous system

CVS – chorionic villus sampling

FISH – Fluorescent in-situ hybridisation

GC – Genetic counsellor

HIV – Human immunodeficiency virus

MRI – Magnetic resonance imaging

n – Number

NHLS – National Health Laboratory Service

NT – Nuchal translucency

NTDs – Neural tube defects

PAPP-A – Pregnancy associated plasma protein A

PCR – polymerase chain reaction

STORCH – Syphilis, Toxoplasmosis, Other, Rubella, Cytomegalovirus, Herpes

TOP – Termination of pregnancy

$uE_3$ – Unconjugated oestriol

U/S – Ultrasound

VSD – Ventricular septal defect

WITS – University of the Witwatersrand

Yr – Year

# CHAPTER 1 INTRODUCTION

## 1.1 Introduction

During the past three decades significant advancements have been made in the detection of fetal abnormalities. This has been made possible by fetal ultrasonography and medical genetic testing of fetal cells, obtained through invasive procedures (Chitty, Hunt, Moore et al., 1991; Grandjean, Larroque, Levi et al., 1999).

Women and their partners face emotionally difficult decisions including whether to interrupt or continue a pregnancy after the detection of fetal abnormalities (Drugan, Greb, Johnson et al., 1990). Genetic counselling should be offered to these women and their partners after the diagnosis of a fetal abnormality to provide information and psychosocial support to assist in possible decision making.

The aim of this project was firstly to audit the genetic counselling service provided by the Division of Human Genetics, National Health Laboratory Service (NHLS) and the University of the Witwatersrand (WITS) to women and their partners who have diagnosed fetal abnormalities. Secondly, we aimed to assess which factors may be associated with the decision patients make regarding terminating or continuing the pregnancy.

## 1.2 Types of fetal abnormalities

Congenital disorders (also termed birth defects) are abnormalities of structure or function, which are present at birth (Christianson, Howson and Modell, 2006). Fetal abnormalities are those congenital disorders that are detected prenatally.

They may also be either structural or functional in nature (Sanders, Blackman, Hogge et al., 2002).

Structural fetal abnormalities are those that affect the anatomy and morphology of the fetus, and often have an impact on function as a result. Structural abnormalities can affect single or multiple organs, limbs, or systems (Clayton-Smith and Donnai, 2002; Turnpenny and Ellard, 2005). Examples of structural fetal abnormalities include neural tube defects (NTDs), cardiac defects such as ventricular septal defect (VSD), renal agenesis, diaphragmatic hernia, omphalocoele, cleft lip and palate and skeletal abnormalities (Sanders et al., 2002). Structural fetal abnormalities can often be identified during diagnostic fetal ultrasound examination (Green and Statham, 1996).

Functional fetal abnormalities are disorders of the physiology or biochemistry of the fetus and are not usually associated with structural change. These abnormalities can sometimes be diagnosed prenatally by analysis of fetal cells obtained by invasive methods. Functional fetal abnormalities can include those conditions that may only have a clinical onset in later life. Examples of functional fetal abnormalities include cystic fibrosis (although this can be suggested by a finding of meconium ileus on ultrasound examination), Huntington disease and certain metabolic conditions (Turnpenny and Ellard, 2005).

## 1.3 Prevalence of fetal abnormalities

Congenital disorders, that can cause death and disability, affect approximately seven percent of babies born worldwide every year (Christianson et al., 2006). However, only a small percentage of congenital disorders can be detected prenatally. In South Africa, as in most of the world, many women do not have access to prenatal diagnosis and screening programs and therefore very few congenital disorders are detected before birth (Christianson et al., 2006).

No comprehensive data about the prevalence of detectable fetal abnormalities is available. The prevalence of congenital disorders can be used to estimate the prevalence of fetal abnormalities, but not all congenital disorders are expected to be detected prenatally. Grandjean et al. (1999) reported a prenatal detection rate of 56.2 % for congenital anomalies through ultrasound screening.

The number of live births recorded in the Johannesburg area in 2005 was 121 881 (StatsSA, 2006) and Christianson et al. (2006) reported a prevalence of 53.4 congenital disorders per 1 000 live births in South Africa. By calculation, the number of babies born with serious genetic congenital disorders born in the Johannesburg area in 2005 was approximately 6 508. Based on the report by Grandjean et al. (1999) 56 % (3 644 babies) of these could theoretically have been detected prenatally through ultrasound screening.

## 1.4 Detection of fetal abnormalities

Prenatal screening and diagnostic tests are available for the detection of fetal abnormalities. Screening tests allow groups of individuals at higher risk of having a baby with a specific congenital disorder to be identified. They can then be offered prenatal diagnostic testing, to confirm the diagnosis (Wald and Leck, 2000).

### 1.4.1 Screening tests for fetal abnormalities

A screening test involves the methodical application of a test or inquiry, to identify individuals at increased risk of a specific disorder or in this case pregnant women at risk of fetal abnormalities, who have not previously sought medical attention for that disorder. This allows those individuals at increased risk to benefit from further investigation or direct preventative action (Wald and Leck, 2000).

Screening tests may involve simple inquiries or special tests that separate higher risk patients from the general population. In a prenatal setting, inquiries may involve asking specific questions about maternal age, or asking general questions about the family history. Patients who could be identified through inquiry as being at a higher risk for fetal abnormalities include women older than 35 years (numerical chromosome abnormalities) and those with a positive family history of an inherited condition (Harper, 2004).

Tests available for screening include fetal ultrasound, maternal serum screening and molecular analysis to identify carriers of common autosomal recessive conditions.

Ultrasound is used in pregnancy as a screening tool, as well as a diagnostic tool for structural abnormalities. For screening purposes, ultrasound can be used to measure the nuchal translucency (NT) thickness between 11 and 13 weeks 6 days gestation. If NT is increased the risk for Down's syndrome, cardiac abnormalities, skeletal abnormalities and several other abnormalities is increased. Between 18 and 23 weeks ultrasound can be used to identify soft markers. Soft markers are signs identified on ultrasound that independently do not represent a problem, but which indicate an increased risk of a congenital disorder or chromosome abnormality (Green and Statham, 1996; Wald, Kennard, Donnenfeld et al., 2000; Papp and Fekete, 2003; Harper, 2004).

Maternal serum screening can be carried out in both the first and second trimester. It involves measuring the levels of various proteins in the blood of pregnant women and comparing them to reference levels. A positive maternal serum screen can indicate an increased fetal risk for Down syndrome, Trisomy 18, Trisomy 13 or open neural tube defects (Cunniff and the Committee on Genetics, 2004).

Other maternal serum screening tests that are routinely performed in South Africa include screening for Rhesus incompatibility and syphilis infection.

Women who are found to be seropositive for syphilis are treated with penicillin, which prevents congenital syphilis. Women who are Rhesus-negative are given anti-D injections to prevent maternal sensitization (Letsky, Leck and Bowman, 2000; Peckham and Newell, 2000).

When a patient is identified through screening as being at increased risk of having a baby with a congenital disorder, she may be offered prenatal diagnosis in order to obtain more information about the pregnancy (Harper, 2004).

### 1.4.2 Diagnostic tests for fetal abnormalities

Prenatal diagnostic tests provide a diagnosis, as opposed to modifying the risk that a congenital disorder is present, as screening tests do. Diagnostic tests should be offered to high-risk patients, identified through screening, where the financial and psychological costs of further testing are believed to be warranted (Green and Statham, 1996; Wald and Leck, 2000; Harper, 2004).

Prenatal diagnostic tests can be invasive or non-invasive. Non-invasive tests include ultrasound and magnetic resonance imaging (MRI). Invasive tests, such as chorionic villus sampling (CVS), amniocentesis, cordocentesis and fetoscopy can be used to obtain a sample of fetal tissue. Once a sample of fetal tissue and / or amniotic fluid has been collected a number of diagnostic tests can be performed. These include routine chromosome analysis, quantitative fluorescent PCR, molecular analysis, enzyme assays, and biochemical tests such as measuring alpha-feto protein and acetylcholinesterase levels, although these biochemical tests are not performed routinely in the state hospitals in Gauteng (Turnpenny and Ellard, 2005).

Some structural fetal abnormalities identified by ultrasound examination can be diagnostic of a specific disorder. In these cases ultrasound is a diagnostic tool (Green and Statham, 1996). In the past decade fetal MRI has become a useful

tool for the evaluation of fetal abnormalities, allowing detailed evaluation of the fetal anatomy, particularly the central nervous system (CNS), thorax, abdomen and placenta (Laifer-Narin, Budorick, Simpson et al., 2007). However, it is not widely available for fetal prenatal diagnosis in South Africa.

CVS is carried out during the first trimester, 11 – 13 weeks 6 days gestation, under ultrasound guidance either trans-cervically, or, more often, trans-abdominally. A sample of the chorionic villi is obtained, which can be analysed directly (when performing molecular genetic, FISH, or PCR analysis) or after cell culture (when performing routine chromosome analysis). The advantage of CVS is that it allows diagnosis in the first trimester, although it carries a miscarriage risk of 1 – 2 %, and is more technically difficult than amniocentesis (Green and Statham, 1996; Turnpenny and Ellard, 2005).

Amniocentesis, normally carried out between 16 and 20 weeks gestation, involves obtaining a sample of amniotic fluid from the uterus, trans-abdominally, under ultrasound guidance (Harper, 2004; Turnpenny and Ellard, 2005). The fetal cells obtained through amniocentesis have to be cultured before routine chromosome analysis can take place, and therefore results normally take 3 to 4 weeks. For molecular genetic analysis, PCR and FISH analysis the cells do not need to be cultured (Green and Statham, 1996). Amniotic fluid can also be used to perform enzyme assays and biochemical tests. The disadvantage of amniocentesis is that the results are available fairly late in pregnancy, although the miscarriage risk, of 0.5 - 1 %, is lower than that for CVS (Turnpenny and Ellard, 2005).

Cordocentesis is a procedure used to obtain a sample of fetal blood from the umbilical cord vessels, using ultrasound guidance. The blood can then be used to diagnose specific congenital disorders (Turnpenny and Ellard, 2005). Cordocentesis is carried out after 20 weeks, and is associated with a 2 to 3 % miscarriage risk (Cunniff and the Committee on Genetics, 2004).

Fetoscopy is a technique, not available in South Africa, used to obtain fetal blood or tissue samples, which may be needed for diagnostic analysis in rare disorders, such as epidermolysis bullosa. It is performed between 18 and 20 weeks gestation, using ultrasound guidance, and is associated with a 3 - 5 % miscarriage risk (Hurley and Rodeck, 2000; Turnpenny and Ellard, 2005).

## 1.5 Outcome of pregnancies that have fetal abnormalities diagnosed

When a fetal abnormality is detected during pregnancy the doctor (i.e. obstetrician or fetal medicine specialist) involved in the diagnosis of the fetal abnormality will decide whether to offer termination of pregnancy (TOP) depending on the gestation and the severity of the abnormality. The decision about whether to have TOP is made by the woman and her partner.

Part of the South African Choice on Termination of Pregnancy Act of 1996 states that termination of pregnancy can be carried out at any stage of pregnancy when two medical practitioners, or one medical practitioner and a registered midwife, believe that the continued pregnancy would result in a severe malformation of the fetus. Severe malformation is not defined in the act, and the decision to offer termination of pregnancy for fetal abnormalities is left to the discretion of the doctors involved.

The procedure used to carry out a TOP is dependent on the gestation of the pregnancy and the medical practitioner involved (Davies, Gledhill, McFayden et al., 2005). First trimester TOP is performed by administering drugs such as misoprostol, to induce miscarriage. Second trimester TOP is carried out in one of two ways. The first method, dilation and evacuation, involves the dilation of the cervix and the surgical removal of the fetus by means of forceps. The second method involves the dilation of the cervix, and then the use of prostaglandins or a prostaglandin-analog to induce labour. After 24 weeks gestation, the fetus may be viable, and a fetocide must therefore be performed. Fetocide involves

causing fetal demise prior to delivery by means of a potassium chloride injection into the fetal heart or umbilical cord. Following this, labour is induced and the fetus is delivered (Bourguignon, Briscoe and Nemzer, 1999).

## 1.6 Factors influencing a patient's decision to terminate a pregnancy after the detection of a fetal abnormality

The decision of whether to interrupt or continue a pregnancy in which fetal abnormalities have been identified is complex and has been shown to be dependent on many factors. The acceptance rate after an offer of TOP varies between studies, and may differ due to the circumstances of the patients included in the study and the type of abnormalities detected. Table 1-1 shows the rate of TOP from a number of studies.

**Table 1-1** Percentage of patients choosing termination of pregnancy after diagnosis of a fetal abnormality in 7 different research groups

| Fetal abnormalities detected in sample population | Uptake of TOP (%) | Reference |
|---|---|---|
| Ultrasound detected abnormalities, with normal karyotypes | 30.2 | (Pryde, Isada, Hallak et al., 1992) |
| Ultrasound detected abnormalities | 33.0 | (Rauch, Smulian, DePrince et al., 2005) |
| Ultrasound detected abnormalities | 50.5 | (Stoll, Tenconi, Clementi et al., 2001) |
| Perinatal lethal abnormalities | 66.9 | (Hassed, Miller, Pope et al., 1993) |
| Sex chromosome abnormalities, diagnosed by karyotyping | 68.0 | (Christian, Koehn, Pillay et al., 2000) |
| Chromosome abnormalities, diagnosed by karyotyping | 75.0 | (Drugan et al., 1990) |
| Abnormal invasive test result, including chromosome abnormalities and single gene disorders | 87.8 | (Zlotogora, 2002) |
| Ultrasound detected abnormalities, abnormal invasive test results | 76.3 | (Viljoen, Oosthuizen and van der Westhuizen, 1996) |

Factors that may influence the TOP decision that have been investigated include maternal and pregnancy factors. Maternal factors include maternal age,

reproductive history, religious and cultural beliefs, as well as individual attitudes towards termination of pregnancy. Pregnancy factors include the visualization of the abnormalities on ultrasound, the certainty of the diagnosis, the gestation of the pregnancy at diagnosis of the fetal abnormality, the severity of the abnormality, whether the abnormality is considered lethal or not, the number of organ systems affected, and the particular organ systems involved (Drugan et al., 1990; Green and Statham, 1996; Christian et al., 2000; Schechtman, Gray and Baty, 2002; Zlotogora, 2002; Rauch et al., 2005). It is often difficult to separate these factors and the influence they have on termination of pregnancy from one another, as many of them are closely linked (Green and Statham, 1996).

It has been shown that pregnancies with abnormalities that were either incompatible with life, or abnormalities that may have a severe impact on life, even with medical or surgical intervention, are more likely to be terminated (Schechtman et al., 2002; Zlotogora, 2002). Rauch et al. (2005) also found that couples were more likely to opt for TOP when abnormalities in multiple organ systems had been detected in their pregnancy.

Some studies have shown that abnormalities involving the central nervous system (CNS) are associated with the decision to terminate more frequently than abnormalities other systems (Schechtman et al., 2002; Rauch et al., 2005). The certainty of the diagnosis and prognosis has also been shown to influence the decision to interrupt or continue an affected pregnancy. Pryde et al. (1992) found that when a fetal abnormality had been diagnosed by ultrasound, and the prognosis was uncertain, parents tended to continue the pregnancy.

Christian et al. (2000) and Drugan et al. (1990) reported that couples with diagnosed chromosome abnormalities, who had visualized the fetal abnormalities on ultrasound were more likely to terminate than couples who had not. It is believed that this is because visualizing the abnormality, rather than a verbal explanation of diagnostic test results (e.g. karyotype or molecular results), makes it easier for parents to comprehend the abnormality.

Diagnosis early in gestation has been shown by some researchers to result in a decision to terminate, presumably because emotional bonding has not occurred to the same degree as at a later gestation (Zlotogora, 2002; Rauch et al., 2005). However, contrary to this studies by Drugan et al. (1990) and Pryde et al. (1992) found that the gestational age at diagnosis did not influence decision-making about TOP in patients with diagnosed fetal abnormalities.

Older couples have been shown to be more likely to interrupt an abnormal pregnancy than younger couples when serious anomalies are present, suggesting an influence of maternal age on decision-making (Schechtman et al., 2002). In contrast, Holmes-Siedle et al. (1986) reported that older couples were more likely to continue pregnancies with sex chromosome abnormalities, possibly because they had less chance of replacing the pregnancy with a subsequent normal pregnancy.

In South Africa 29 – 30 % of women attending antenatal clinics in Johannesburg are HIV positive (Mseleku, Smith and Guidozzi, 2005). It is possible that a woman's HIV status may have some impact on her decision regarding termination of pregnancy for a fetal abnormality, although there is no data available to support this hypothesis.

## 1.7 Genetic counselling

Genetic counselling is a process which aims to help people understand and adjust to the medical, psychological and familial implications of genetic conditions (Resta, Bowles Biesecker, Bennett et al., 2006).

Genetic counselling aims to assist people in understanding and adjusting to the medical, emotional, and familial repercussions of a genetic condition. It is a process that involves conversation and communication between the patient and

the genetic counsellor (Evans, 2006). It incorporates taking and interpreting family and medical histories to determine the risk of developing or passing on a genetic condition. Genetic counselling can provide information regarding the inheritance, testing, care, prevention and medical and community resources for a specific condition. Genetic counselling also aims to provide psychosocial support around decision-making, by acknowledging the patient's ability to make decisions and by discussing available options (Weil, 2000; Harper, 2004; Resta et al., 2006).

Genetic counselling is intended to be a non-judgmental, non-directive and supportive process. Non-directive counselling means that the genetic counsellor does not recommend or advise any particular choice to the patient, but instead provides information that allows the patient to make an informed decision (Harper, 2004).

### 1.7.1 Genetic counselling for fetal abnormalities

The role of the genetic counsellor when counselling parents who have a fetal abnormality detected in pregnancy is to provide information and psychosocial support, including support during decision-making. The counsellor provides the parents with comprehensive information regarding the detected fetal abnormality, the prognosis and risks for the fetus and what options are available regarding further testing, termination of pregnancy or care of the baby after birth. The provision of this information, at the parent's level of understanding, allows them to make an autonomous, informed decision regarding the pregnancy, that is in keeping with their ethical, social, and cultural beliefs (Weil, 2000; Harper, 2004).

The diagnosis of a fetal abnormality results in a variety of emotional reactions in the parent, including shock, grief, guilt, and worry (Sanders et al., 2002). The counsellor provides psychosocial support, by exploring the emotional and social consequences of a diagnosed fetal abnormality, in terms of its effects on the

couple, as individuals and as a partnership, their family and community. It may also include exploring the parent's feelings around the different options available to them, in order to assist with decision-making. This is often achieved through the use of anticipatory guidance, which involves exploring with the parents the implications of the possible outcomes. Reassuring parents that their reaction is normal in a genetic counselling session can help the parents to accept the way they are feeling (Weil, 2000).

Once the parents have made an informed decision regarding further testing (e.g. amniocentesis) or the outcome of the pregnancy (e.g. termination of pregnancy), it is the responsibility of the genetic counsellor to continue to support them and to help facilitate their choice. The counsellor assists the parents in obtaining further testing or termination of the pregnancy by referring the parents to the appropriate professionals. A follow-up appointment for the parents is made for an appropriate period after the initial session. This interval is dependent on the parent's needs, the gestational age of their pregnancy and on what action they have decided on. Follow-up appointments can be purely supportive in nature, or they may include result giving. Results could be either the invasive test results or the results of the examination of the fetus after termination, including post-mortem and X-ray results. If the parents have continued the pregnancy, the genetic counsellor can assist with planning the delivery and arranging for early intervention. The follow-up appointment after delivery will possibly involve an examination of the baby and referral of the baby for any necessary interventions, as well as the provision of psychosocial support (Weil, 2000).

### 1.7.2 Dealing with the emotional impact of terminating an affected pregnancy in genetic counselling

Parents who choose to terminate affected pregnancies often experience feelings of shock, denial and acute guilt (Dallaire, Lortie, Des Rochers et al., 1995; Fonda Allen and Mulhauser, 1995; Suslak, Scherer and Rodriguez, 1995).

Parents experience grief and mourning for the lost healthy fetus. They may feel that they have "abandoned the fetus" or "killed the baby" by interrupting the pregnancy, and feel guilty as a result of this belief. In order for them to reach a state of acceptance they will go through the typical grief responses, including anger, denial, guilt, depression, and bargaining (Dallaire et al., 1995; Fonda Allen and Mulhauser, 1995; Suslak et al., 1995; Weil, 2000). The role of the genetic counsellor in this situation involves a continuation of empathic, non-judgmental counselling and supporting the parents through the grieving process (Weil, 2000).

The genetic counsellor can also assess the parents' reaction to the TOP, and refer the parents to appropriate specialists when necessary. This may include referrals to psychologists and grief counsellors.

### 1.7.3 Dealing with the emotional impact of continuing an affected pregnancy in genetic counselling

When parents choose to continue an affected pregnancy they may experience grief regarding the loss of a normal, wanted child. This experience of grief and mourning may be much the same as the grief process experienced by parents who lose pregnancies or choose to terminate. The parents may feel uncertain as to what the future holds, leaving them feeling fearful, anxious and overwhelmed (Fonda Allen and Mulhauser, 1995). It is important that the genetic counsellor provides empathy, emotional support, normalization of the parents' feelings, and assists the parents to identify their individual and social support systems (Weil, 2000).

## 1.8 Genetic counselling clinics

The Division of Human Genetics, NHLS and WITS, runs Genetic Counselling Clinics at Chris Hani Baragwanath Hospital, Johannesburg Hospital, Coronation Hospital and Donald Gordon Medical Centre in Johannesburg, South Africa.

Pregnant patients, and if they wish, their partners, are referred for genetic counselling in two instances. Firstly, patients may be referred for genetic counselling if they are considered to be at increased risk of having a fetus with fetal abnormalities through a screening test or because of a history of fetal abnormalities. Secondly, patients may be referred if a fetal abnormality is detected by ultrasound examination or through invasive testing. Patients are usually referred for genetic counselling by clinicians and nurses and are seen by either genetic counsellors or clinical geneticists.

## 1.9 Purpose of this study

The study to be undertaken comprised two components: i) to audit the genetic counselling service provided to patients with fetal abnormalities by the Division of Human Genetics, NHLS and WITS, and, ii) to assess the factors that may be associated with a patient's decision to terminate a pregnancy after fetal abnormalities are detected.

Auditing the genetic counselling service provided to patients will provide knowledge about the patients that were seen and describe the service that they received. Knowledge about the service being offered to patients with fetal abnormalities will allow improvements in the service to be made, especially if short comings are identified.

The literature showed that some factors may be important predictors of parental decisions regarding termination of pregnancy for fetal abnormalities, although there is little consensus in the literature about which factors these are. Knowledge of the factors that may be associated with parental decisions regarding termination of pregnancy in our patient population would help the genetic counsellors in the unit to have greater understanding of their patients. This may give the counsellors more insight into their patients' experiences and provide more opportunities for the counsellors to address their patients' issues and to provide support to them.

## 1.10 Study objectives

The purpose of this study was, firstly to audit the service provided to patients with diagnosed fetal abnormalities in the Genetic Counselling Clinics. This was done by determining:

- How many patients were seen for genetic counselling for fetal abnormalities at the NHLS / WITS Genetic Counselling Clinics relative to the estimated number of congenital disorders that occurred in the Johannesburg area
- The demographics of the patients seen including age, ethnicity, employment status, and relationship status
- How many patients received follow-up appointments, including both patients choosing termination of pregnancy and those continuing the pregnancy, how many attended their follow-up appointments, and the time interval between the initial appointment and the follow-up appointment. The reason why no follow-up appointment was made, when this was the case, was also documented.

Secondly, factors that may be associated with the decision to terminate a pregnancy where a fetal abnormality has been identified were assessed by investigating:

- How many patients decided to terminate the pregnancy after the diagnosis of a fetal abnormality
- If patients decisions regarding termination of pregnancy were correlated with any of the following factors:

    - The circumstances of the patient (maternal age at diagnosis of the abnormalities, ethnicity, parity, relationship status, HIV status)
    - Gestation at diagnosis of the fetal abnormality
    - Gestation when TOP was offered
    - Whether the abnormality involved one or multiple organ systems
    - Whether there was CNS involvement or not
    - Whether diagnostic testing was performed
    - The result of the diagnostic testing

# CHAPTER 2 METHODS

This study was a retrospective clinical audit of the genetic counselling records at the Division of Human Genetics, NHLS and WITS, in Johannesburg, South Africa. The research project was approved unconditionally by the Human Research Ethics Committee (Medical) (Protocol number M060944) (Appendix A).

## 2.1 Study population

The study population included all pregnant women who received genetic counselling for an identified fetal abnormality during pregnancy, at a clinic run by the Division of Human Genetics, NHLS and WITS. A fetal abnormality in this study was defined as a congenital disorder that was detected prenatally and was either structural or functional in nature.

## 2.2 Study sample

Consecutive sampling was used to select the study sample. The sample included pregnant women who received genetic counselling for an identified fetal abnormality during pregnancy, at a clinic run by the Division of Human Genetics, NHLS and WITS, between January 2002 and December 2006. The clinics were run at Chris Hani Baragwanath Hospital, Coronation Hospital, Johannesburg Hospital or Donald Gordon Medical Centre. Most patients were seen by a genetic counsellor, although some were seen by clinical geneticists. Patients had been referred to the clinic, either when they had a family history of a genetic condition, when they were screen positive or when a fetal abnormality had been identified on ultrasound examination. Patients were only included in the study when a fetal abnormality had been identified on ultrasound or invasive testing. Patients who had a family history or who were screen positive were excluded

from the study when ultrasound examination or invasive testing did not reveal the presence of a fetal abnormality in the current pregnancy. Patients were also excluded from the study if they had had more than one pregnancy in which fetal abnormalities had been diagnosed.

## 2.3 Data collection

A genetic counselling file is made for every patient seen at the Genetic Counselling Clinics. These files include demographic information, a family history pedigree, notes made by the counsellor regarding the counselling session and a copy of a detailed report written to the referring doctor or the patient. The demographic information includes details about the patient and their partner including their names, dates of birth, employment details, contact details, hospital number or medical aid details, the referring doctors name, and the diagnosis (see Appendix B for an example of the information sheet). The family history is taken in the form of a three generation pedigree, and includes information about medical and social problems in the family. The counsellor makes notes about each session in the file, including information about what was discussed during the session, what options were discussed and offered, what decisions were made by the patient and psychosocial issues that arose.

After a patient has been seen for genetic counselling, their file is registered in the department and their name and the date of the session are written onto manual filing cards. These cards are specific for each diagnosis and include cards for fetal abnormalities, positive screening tests and other specific abnormalities. In addition, a Microsoft Access database of the patients seen for genetic counselling has been kept since 2002, which records the name of the patient, the date of the session and the diagnosis. Patients were identified from this database by searching for the relevant diagnosis, for example, fetal abnormalities. The Cytogenetic and Molecular Laboratories keep databases that record the results of all the prenatal tests performed. These databases record

the name of the patient, the result and the year the test was performed. These records were used to identify other patients who may have received genetic counselling for fetal abnormalities, but that were missed using the filing system and other databases. The relevant patient counselling files were obtained from the storage and filing facilities within the Division of Human Genetics, NHLS and WITS.

Each file was randomly allocated a subject code, which was typed into a master list with the patient's name. Only the researcher and her supervisors had access to the master list.

Information was then collected from the included files, and written onto the data collection sheet (Appendix C), along with the subject code that was recorded in the master list. To ensure anonymity, the data collection sheets did not contain patient names. Patients were identified by their subject code throughout the study.

Once information from each file had been entered onto a data collection sheet a database of the files which met the research criteria, as described in Section 2.1, was created using Microsoft Excel. Categorical information was coded in the database so that each variable had several options that were represented as numbers. The following information was entered into the database:

- Information about the patients with diagnosed fetal abnormalities seen for genetic counselling including:
    - Maternal date of birth
    - Maternal age at diagnosis of the fetal abnormality
    - Ethnicity - This was assumed from the patient's name and surname
    - Relationship status
    - Employment status
    - Parity
    - Number of fetuses in the pregnancy

    - The HIV status of the patient
- Information regarding the diagnosed fetal abnormalities including:
    - Gestational age at diagnosis
    - The fetal abnormalities identified
    - The number of organ systems affected. This was recorded as a value and then categorised into single or multiple abnormalities. Multiple organ systems affected included abnormalities that were separate entities in multiple organs, as well as abnormalities where an abnormality in one organ system caused abnormalities in other organ systems. For example, when hydrocephalus and NTDs occurred together it was recorded as abnormalities in multiple organ systems.
    - The organ system/s affected, which was further classified into whether there was CNS involvement, including intracranial abnormalities and neural tube defects, or whether there was no CNS involvement
    - The diagnostic procedures performed
    - The results of the diagnostic procedures
- Information regarding the outcome of the pregnancy was also collected, including:
    - Whether termination of pregnancy was offered to the patient
    - The gestational age at which termination of pregnancy was offered
    - The patient's decision regarding termination of pregnancy
- Information collected regarding the genetic counselling service provided to the patients with diagnosed fetal abnormalities included:
    - The initial reason for referral to genetic counselling
    - The dates of the genetic counselling sessions
    - The hospital where the patient was counselled
    - The number of genetic counselling sessions the patient had during the pregnancy
    - Whether a follow-up appointment was made and, if not, the reason for this

- Whether the patient attended the follow-up appointment
- The interval between the last appointment during the pregnancy and the follow-up appointment after the pregnancy

## 2.4 Data analysis

Microsoft Excel, Stata Statistical Software Version 8.0 and two statistical websites were used to perform the statistical analysis in this research. The statistical websites used were GraphPad (Motulsky, 2007) and Sisa (Uitenbroek, 1997). A statistician was consulted prior to the start of the project to ensure that the data were collected appropriately and for assistance with the analysis of the data.

### 2.4.1 Microsoft Excel functions

The count function in Microsoft Excel was used to determine the number of patients seen for genetic counselling regarding a fetal abnormality between 2002 and 2006. The count function was also used to determine the number of patients seen for genetic counselling in terms of their ethnic group, relationship status, employment status, parity, number of fetuses in the pregnancy, initial reason for referral for genetic counselling, and HIV status.

The count function was also used to describe the fetal abnormalities detected, in terms of the number of organ systems affected, the numbers of specific organ system/s affected, the number of patients who had abnormalities involving the CNS, the number of diagnostic procedures performed, and the number of diagnostic procedures with abnormal results. It was also used to describe the outcome of the pregnancy, in terms of how many patients were offered TOP and how many of those patients chose to terminate the pregnancy.

In addition, the count function was used to describe the genetic counselling service provided to patients, in terms of the number of genetic counselling sessions during the pregnancy, the number of patients who were given follow-up appointments for after TOP or delivery, and how many patients attended their follow-up appointment. The count function was also used to describe the reason why no follow-up appointment was made for after TOP or delivery.

The frequency function of Microsoft Excel was used to determine the trend in patient numbers over time.

The average maternal age, the average gestation at diagnosis of the fetal abnormality, the average gestation when TOP was offered, and the interval between the last appointment in the pregnancy and the follow-up appointment were calculated by using the average and difference functions of Microsoft Excel.

### 2.4.2 Proportion of patients with diagnosed fetal abnormalities who received genetic counselling from the Division of Human Genetics, NHLS and WITS

To determine the proportion of women with diagnosed fetal abnormalities seen for genetic counselling by the Division of Human Genetics, NHLS and WITS, it was necessary to look at the number of patients seen for genetic counselling for fetal abnormalities relative to the estimated number of congenital disorders in the Johannesburg area. This provides an over estimate of the number of fetal abnormalities detected, since not all congenital disorders are detected prenatally. In addition, the number of congenital disorders that would potentially be detectable prenatally was estimated.

### 2.4.3 Comparison of patients who chose to terminate an affected pregnancy and those who chose to continue

The Fischer's exact test (for categorical variables) and the two sample t-test with equal variance (for continuous variables) were used to determine whether there

were any significant differences between patients who chose to TOP and those who chose to continue their pregnancy, in terms of:

- Continuous variables -
  - Maternal age at diagnosis of the abnormality
  - Gestation at diagnosis of the abnormality
  - Gestation when TOP was offered
- Categorical variables -
  - Ethnicity
  - Relationship status
  - Parity
  - HIV status
  - Number of organ systems found to have abnormalities in the fetus
  - Whether there was CNS involvement or not
  - Whether diagnostic testing was performed
  - The result of diagnostic testing
  - The number of genetic counselling sessions the patient had during the pregnancy
  - Whether a follow-up appointment was made for after TOP or delivery
  - The interval between the last appointment in the pregnancy and the follow-up appointment.

Microsoft Excel was used to perform the two sample t-test, while two statistical websites, GraphPad and Sisa, were used to perform the Fischer's exact test. These tests analysed the variables as independent factors, assuming no relationship between them.

### 2.4.4 Determination of factors that may be associated with the decision to terminate or continue a pregnancy after the detection of a fetal abnormality

Logistic regression analysis, using Stata Version 8.0, was used to determine the variables that were the most likely to influence the decision patients make about whether to terminate or continue an affected pregnancy. The goal of logistic regression is to determine the best fitting, clinically realistic model that describes the relationship between a dependent variable (i.e. to terminate or continue an affected pregnancy) and a set of independent variables (categorical and / or continuous variables) (Bewick, Cheek and Ball, 2005).

Stepwise logistic regression is one method of entering the independent variables into the model, where the variables are entered sequentially and the statistical software (i.e. Stata Version 8.0) then excludes non-significant variables automatically when $p \geq 0.1$. The following variables were included in the stepwise logistic regression analysis, in a random order:

- Continuous variables -
    - Maternal age at diagnosis of the abnormality
    - Gestation at diagnosis of the abnormality
    - Gestation when termination of pregnancy was offered
- Categorical variables -
    - Ethnicity. This was simplified to a comparison between Black and White patients. Patients from other groups were excluded
    - Relationship status
    - Parity
    - Number of organ systems affected by the detected abnormalities
    - Whether there was CNS involvement or not

These variables were included in the stepwise logistic regression because they have been shown in the literature to have an influence on patients' decisions regarding TOP or continuation of a pregnancy after the detection of fetal

abnormalities. Certain variables that we suspected may also have an influence on the decision regarding the outcome of the pregnancy included the patient's HIV status, whether patients chose to have diagnostic testing, and the result of diagnostic testing. These variables were excluded from the logistic regression analysis since data were not available for all the patients in the sample group. Including these variables would have resulted in a considerable reduction in the sample number.

Based on the results of the stepwise logistic regression, where non-significant variables were automatically removed, manual logistic regression was then used to determine the best fitting model from the remaining variables, which included:

- Continuous variables –
    - Gestation at diagnosis of the abnormality
    - Gestation when termination of pregnancy was offered
- Categorical variables –
    - Ethnicity
    - Number of organ systems affected by the detected abnormalities.

The best model needed to be one that was acceptable with the clinically expected results. The model needed to fit with what made sense and could be explained through clinical experience, as reported in the literature. This was done by running a number of different models and assessing the results, eventually determining which model was most acceptable. For each independent variable in the model, an odds ratio with 95 % confidence interval was calculated.

# CHAPTER 3 RESULTS

## 3.1 Introduction

The first aim of this study was to describe the patients seen for genetic counselling after the diagnosis of a fetal abnormality at the Division of Human Genetics, NHLS and WITS, and to assess the service they received. The second aim was to determine which factors influenced patient choice regarding termination or continuation of the affected pregnancy. A retrospective clinical audit of the genetic counselling files was done to achieve these aims.

The results of this investigation are presented as follows:

- The trend in the number of patients with diagnosed fetal abnormalities seen for genetic counselling by the Division of Human Genetics, NHLS and WITS, from 2002 to 2006
- Description of the patients with diagnosed fetal abnormalities seen for genetic counselling
- Description of the fetal abnormalities diagnosed in those patients seen for genetic counselling
- Assessment of factors that may influence a woman's choice regarding termination of pregnancy for diagnosed fetal abnormalities
- The number of patients choosing termination of pregnancy for diagnosed fetal abnormalities after genetic counselling
- The genetic counselling service provided to patients with diagnosed fetal abnormalities at the Division of Human Genetics, NHLS and WITS

## 3.2 Number of patients seen for genetic counselling regarding a diagnosed fetal abnormality between 2002 and 2006

The number of patients seen for genetic counselling for a diagnosed fetal abnormality between January 2002 and December 2006 and fulfilling our research criteria was 171. Figure 3-1 shows the changing number of patients seen each year of the study period.

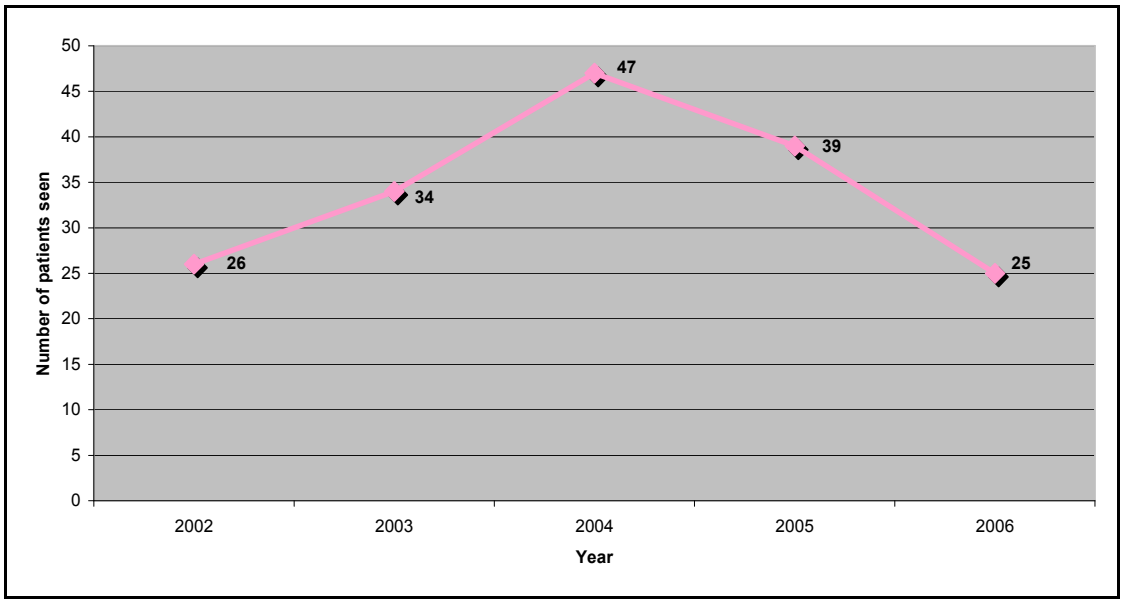


**Figure 3-1** Trend in the number of patients with diagnosed fetal abnormalities seen for genetic counselling at the Division of Human Genetics, NHLS and WITS, over the study period, January 2002 – December 2006.

The estimated number of babies born with congenital disorders (excluding conditions caused by teratogen exposure, e.g. Fetal Alcohol Spectrum Disorder) in the Johannesburg area in 2005 is 6 508. This is calculated by using the estimated prevalence of congenital disorders in South Africa of 53.4 per 1, 000 live births (Christianson et al., 2006) multiplied by the total number of live births in the Johannesburg area in 2005 (121 881) (StatsSA, 2006). Grandjean et al. (1999) estimated that 56.2 % of congenital anomalies are detectable prenatally through ultrasound screening. This suggests that approximately 3 657 of the 6 508 babies with congenital abnormalities born in 2005 could have been detected prenatally. As shown in Figure 3-1, 39 patients with diagnosed fetal

abnormalities were seen for genetic counselling in 2005. This represents 0.6 % (1 in 167) of the 6 508 individuals with congenital disorders and 1.1 % (1 in 91) of the individuals with congenital disorders that could have been detected prenatally by ultrasonography in the Johannesburg area in 2005.

## 3.3 Patient information

The average age of patients who received genetic counselling for a diagnosed fetal abnormality was 30 years and 7 months, with the youngest being 17 and the oldest 49 years old. The majority of patients were Black (123, 72 %), in a relationship but not married (105, 63 %), and approximately half were known to be employed (90, 53 %). The affected pregnancy was the first one for approximately 27 % of patients. The HIV status of the majority of patients was not known, but of those 46 patients whose status was known, 26 (57 %) were HIV positive. The description of the patients seen is reflected in Table 3-1.

**Table 3-1** Description of patients with a diagnosed fetal abnormality seen for genetic counselling by the Division of Human Genetics, NHLS and WITS.

| *Variable* | *Data* | | *Variable* | *Data* | |
|---|---|---|---|---|---|
| **Maternal age at diagnosis (yr)** | 30.60 ± 7.88 | | **Parity** | **n** | **%** |
| **Age range (yr) (n = 171)** | 17 – 49 | | 0 | **47** | (27.5) |
| | | | 1 | **52** | (30.4) |
| **Maternal ethnicity**[a] | **n** | **%** | 2 | **38** | (22.2) |
| Black | **123** | (72.3) | 3 | **22** | (12.9) |
| White | **26** | (15.3) | 4+ | **12** | (7.0) |
| Other | **21** | (12.4) | **Total** | **171** | (100.0) |
| **Total** | **170** | (100.0) | | | |
| | | | **Singleton / Twin** | **n** | **%** |
| **Employment status** | **n** | **%** | 1 | **163** | (95.3) |
| Employed, self-employed | **90** | (52.6) | 2 | **8** | (4.7) |
| Unemployed | **72** | (42.1) | **Total** | **171** | (100.0) |
| Student / Scholar | **9** | (5.3) | | | |
| **Total** | **171** | (100.0) | **HIV status** | **n** | **%** |
| | | | Unknown | **125** | (73.1) |
| **Relationship status**[a] | **n** | **%** | Positive | **26** | (15.2) |
| In a relationship | **105** | (63.3) | Negative | **20** | (11.7) |
| Married | **54** | (32.5) | **Total** | **171** | (100.0) |
| Single, widowed, divorced, or separated | **7** | (4.2) | | | |
| **Total** | **166** | (100.0) | | | |

a Some data were missing or unclear in the files, therefore the total does not add up to 171

## 3.4 Fetal abnormalities diagnosed in the study sample

The majority of patients seen for genetic counselling were initially referred because an abnormality had been detected on ultrasound. However, 14 % were initially referred for advanced maternal age and had fetal abnormalities detected by ultrasound examination or invasive testing after the initial genetic counselling referral (Figure 3-2).

Abnormalities in more than one organ system were detected on ultrasound in 102 patients (60 %), while 48 had a single organ system affected (28 %). No abnormality was seen on ultrasound in 21 patients (12 %). In these patients the fetal abnormality was diagnosed by invasive testing. There was intracranial CNS involvement in 60 (35 %) patients, with cardiovascular abnormalities and abnormalities of the neck and face comprising the next two largest proportions of systems with abnormalities (Figure 3-3). The two most common intracranial CNS abnormalities were hydrocephalus and Dandy-Walker malformations. In some of these patients the hydrocephalus was due to the Dandy-Walker malformation and in some patients the hydrocephalus was isolated or due to other causes. Cleft lip and / or palate was the most commonly detected abnormality affecting the neck and face, while VSD's were the most commonly detected cardiac abnormality. Approximately 44 % (75) of abnormalities were diagnosed after 24 weeks gestation.

All patients who received counselling had had ultrasound examination, and approximately two thirds had further diagnostic testing. Of those 44 pregnancies where a diagnosis was made through invasive testing, 25 also had abnormal findings on ultrasound examination (56.8 %). The most common abnormality diagnosed through invasive testing was Trisomy 21 (14, 32 %). Of the 14 pregnancies diagnosed with Trisomy 21, seven of these were considered to be at increased risk due to their advanced maternal age (AMA) and two of these also had abnormalities detected on ultrasound examination, two had positive maternal serum screening tests, two had been referred for family histories for other genetic

conditions and three had abnormalities detected on ultrasound. A summary of the referral indications, organ systems affected and testing is shown in Table 3-2.

**Table 3-2** Description of the fetal abnormalities diagnosed from January 2002 until December 2006, in patients who received genetic counselling from the Division of Human Genetics, NHLS and WITS.

| *Variable* | *Data* n | *Data* % |
|---|---|---|
| **Initial reason for referral for genetic counselling[a]** | | |
| Abnormality on U/S[f] | **140** | (81.9) |
| Advanced maternal age | **24** | (14.0) |
| Family History | **12** | (7.0) |
| Teratogen exposure | **5** | (2.9) |
| Positive screening test[b] | **4** | (2.3) |
| **No. of patients** | **171** | (108.1) |
| **Gestational age at diagnosis** | | |
| ≤ 12 weeks | **10** | (5.8) |
| 13-24 weeks | **86** | (50.3) |
| ≥ 24 weeks[g] | **75** | (43.9) |
| **Total** | **171** | (100.0) |
| **Organ systems in which abnormalities were detected on U/S[c, f]** | | |
| CNS (Intracranial) | **60** | (35.1) |
| Cardiovascular | **46** | (26.9) |
| Neck and face | **44** | (25.7) |
| Skeletal | **40** | (23.4) |
| Genitourinary | **35** | (20.5) |
| Amniotic fluid volume | **33** | (19.3) |
| Gastrointestinal | **31** | (18.1) |
| Pulmonary[d] | **26** | (15.2) |
| Fetal oedema | **19** | (11.1) |
| CNS (Neural tube) | **10** | (5.8) |
| Other | **9** | (5.3) |
| Growth retardation | **3** | (1.8) |
| **No. of patients** | **171** | (209.9) |

| *Variable* | *Data* n | *Data* % |
|---|---|---|
| **No. of organ systems with abnormalities detected on U/S[f]** | | |
| Multiple | **102** | (59.6) |
| Single | **48** | (28.1) |
| No abnormality on U/S | **21** | (12.3) |
| **Total** | **171** | (100.0) |
| **Diagnostic tests performed, excluding U/S[f]** | | |
| Amniocentesis | **50** | (51.5) |
| Cordocentesis | **30** | (30.9) |
| CVS | **14** | (14.4) |
| STORCH screen | **8** | (8.2) |
| **No. of patients who had diagnostic tests** | **97** | (105.0) |
| **Total tests performed[e]** | **102** | (100.0) |
| **Patient results for diagnostic tests, excluding U/S[f]** | | |
| Normal | **53** | (54.6) |
| Abnormal | **44** | (45.4) |
| **Total** | **97** | (100.0) |
| **Abnormal test results** | | |
| Trisomy 21 | **14** | (31.8) |
| Trisomy 18 | **10** | (22.7) |
| Single gene disorder | **6** | (13.6) |
| Trisomy 13 | **4** | (9.2) |
| Other chromosome abn | **3** | (6.8) |
| Turner syndrome | **3** | (6.8) |
| Triple X syndrome | **2** | (4.5) |
| Klinefelter syndrome | **1** | (2.3) |
| STORCH | **1** | (2.3) |
| **Total** | **44** | (100.0) |

a Some patients had more than one indication, but all had a diagnosed fetal abnormality
b Positive screening tests include AMA, positive maternal serum tests, increased nuchal translucency and soft markers on ultrasound
c More than one organ system can be affected in each pregnancy; therefore the total is greater than 100 %
d Pulmonary abnormalities are generally secondary to other abnormalities, e.g. skeletal or genitourinary abnormalities
e Some patients had more than one type of diagnostic test
f Ultrasound
g 24 weeks is considered the gestation of viability in South Africa

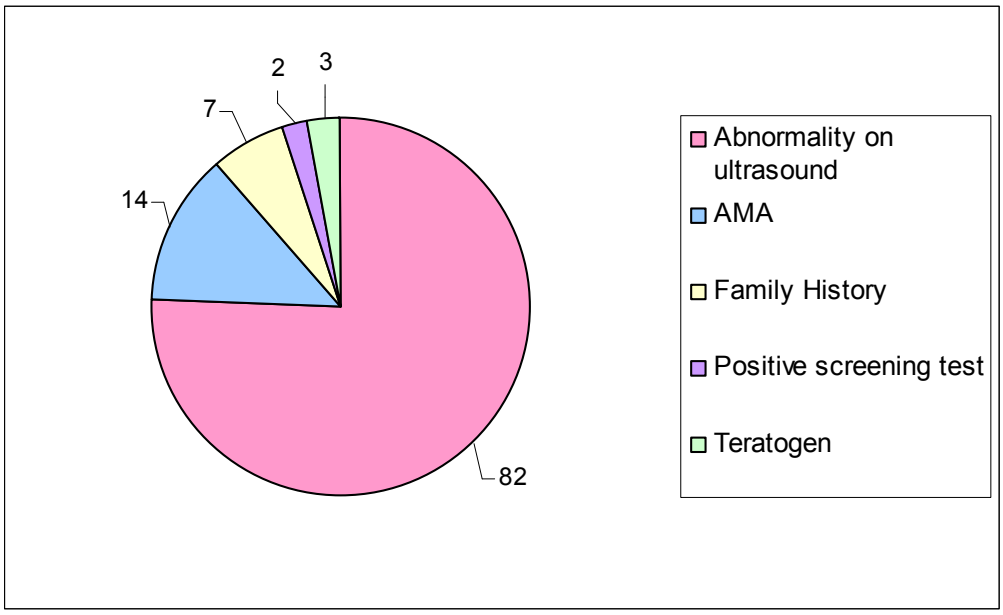


**Figure 3-2** Initial reason for referral to Genetic Counselling Clinics, run by the Division of Human Genetics, NHLS and WITS, in patients who had fetal abnormalities diagnosed in their pregnancy. Patients may have had more than one indication for referral.

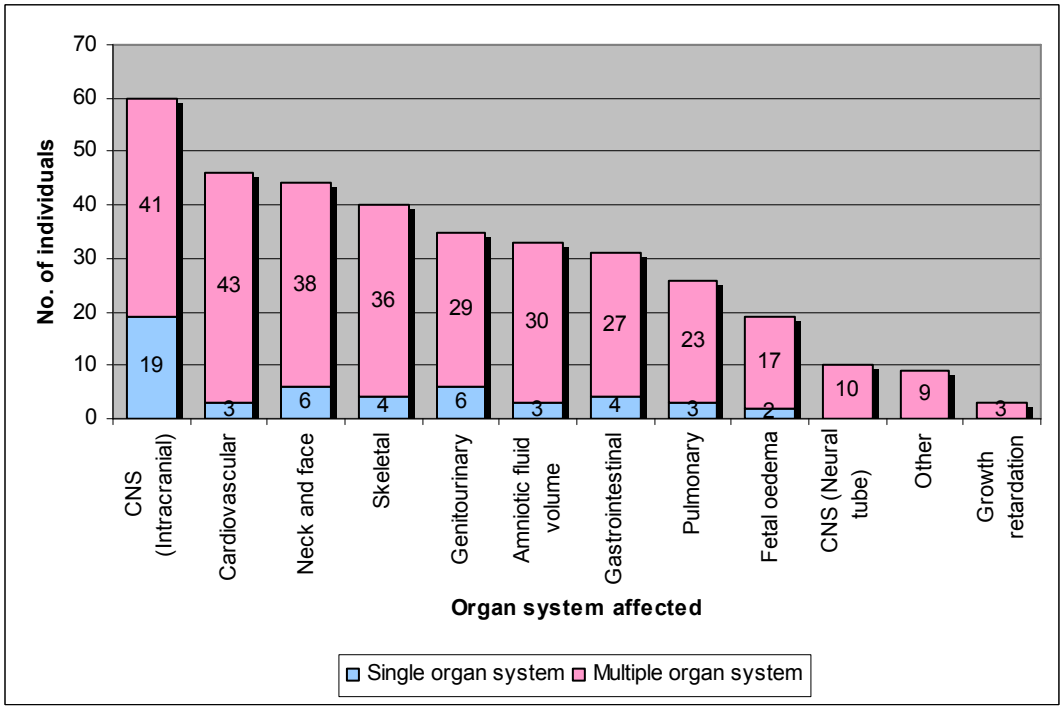


**Figure 3-3** Organ systems affected by fetal abnormalities that were detected on ultrasound, in patients who were seen for genetic counselling by the Division of Human Genetics, NHLS and WITS. The proportion of patients with single organ systems affected compared to the proportion of patients with multiple organ systems affected is shown.

## 3.5 Comparison of patients who chose termination of pregnancy to those who chose to continue their pregnancy after the diagnosis of a fetal abnormality

Univariate analysis was used to determine if any significant differences existed between those patients who chose to terminate their pregnancies with those who chose to continue their pregnancies, after the diagnosis of a fetal abnormality.

As shown in Table 3-3, Black patients were more likely to continue a pregnancy in which fetal abnormalities had been diagnosed than patients from other ethnic groups ($p = 0.031$). Although not significant, patients who chose to terminate their pregnancy after the diagnosis of a fetal abnormality were, on average 30.5 years old compared to those who chose to continue their pregnancy, who were on average 33.3 years old (Table 3-3).

**Table 3-3** Comparison of the patients who chose to terminate and those who chose to continue their pregnancy after the diagnosis of a fetal abnormality. All patients had genetic counselling provided by the Division of Human Genetics, NHLS and WITS and were offered TOP.

| Variable | TOP | | Continue | | p-value |
|---|---|---|---|---|---|
| **Mean maternal age (years) (n = 113)** | 30.534 ± 7.894 | | 33.300 ± 7.573 | | 0.074[a] |
| | **n** | **%** | **n** | **%** | |
| **Ethnicity (n = 107)** | | | | | |
| White | **18** | (26.9) | **4** | (10.0) | |
| Black | **45** | (67.2) | **29** | (72.5) | 0.031[b]* |
| Indian, Mixed ancestry, Other | **4** | (6.0) | **7** | (17.5) | |
| **Total** | **67** | (100.0) | **40** | (100.0) | |
| **Relationship status (n = 113)** | | | | | |
| Married, in a relationship | **68** | (93.2) | **37** | (92.5) | 1.000[b] |
| Single, divorced, widowed | **5** | (6.8) | **3** | (7.5) | |
| **Total** | **73** | (100) | **40** | (100.0) | |
| **Parity (n = 113)** | | | | | |
| 0 | **20** | (27.4) | **10** | (25.0) | |
| 1 | **25** | (34.2) | **9** | (22.5) | 0.292[b] |
| 2+ | **28** | (38.3) | **21** | (52.5) | |
| **Total** | **73** | (100.0) | **40** | (100.0) | |
| **HIV status (n = 45)** | | | | | |
| Positive | **9** | (60.0) | **16** | (53.3) | 0.757[b] |
| Negative | **6** | (40.0) | **14** | (46.7) | |
| **Total** | **15** | (100.0) | **30** | (100.0) | |

a 2-tailed p-value determined through two-sample t-test with equal variance
b 2-tailed p-value determined through Fischer's exact test
* Statistically significant at the 5 % level

Sixty nine percent (50) of the patients who chose to terminate affected pregnancies had abnormalities detected in multiple organ systems compared to 55 % (22) of patients who chose to continue their pregnancy (Table 3-4). There was no significant difference in the decision to TOP between patients who underwent diagnostic testing and had a normal result and those who had an abnormal result (Table 3-4). Pregnancies found to be affected by single gene disorders were terminated in the majority of pregnancies (five pregnancies versus one). The gestation when termination was offered was approaching significance as a factor influencing the decision to terminate an affected pregnancy. This suggests that for every week later in the pregnancy that TOP was offered, patients were less likely to terminate an affected pregnancy. The offer of TOP

was made at 26 weeks gestation on average when patients chose to continue the pregnancy. In contrast, TOP was offered on average at 23 weeks gestation when patients chose to terminate the pregnancy (Table 3-4).

**Table 3-4** Comparison of the diagnosed fetal abnormalities, including gestation at diagnosis and offer of termination, comparing patients who chose to terminate the affected pregnancy and those who chose to continue. All patients received genetic counselling from the Division of Human Genetics, NHLS and WITS, and were offered TOP.

| Variable | TOP | | Continue | | p-value |
|---|---|---|---|---|---|
| **Mean gestation at diagnosis (n = 113) (weeks)** | 22.603 ± 7.121 | | 24.550 ± 6.536 | | 0.155[a] |
| **Mean gestation at offer of TOP (n = 113) (weeks)** | 23.041 ± 6.957 | | 25.625 ± 6.740 | | 0.059[a] |
| | **n** | **%** | **n** | **%** | |
| **Gestation at offer of TOP (n = 113)** | | | | | |
| ≤ 12 weeks | 0 | (0.0) | 0 | (0.0) | |
| 13-24 weeks | 40 | (54.8) | 16 | (40.0) | 0.144[b] |
| ≥ 24 weeks[c] | 33 | (47.1) | 24 | (60.0) | |
| **Total** | **73** | (100.0) | **40** | (100.0) | |
| **Number of organ systems affected on ultrasound (n = 113)** | | | | | |
| No abnormality on U/S | **9** | (12.3) | **6** | (15.0) | |
| Single | **14** | (19.2) | **12** | (30.0) | 0.318[b] |
| Multiple | **50** | (68.5) | **22** | (55.0) | |
| **Total** | **73** | (100.0) | **40** | (100.0) | |
| **CNS vs. Non-CNS abnormality (n = 113)** | | | | | |
| CNS | **41** | (56.2) | **21** | (52.5) | |
| Non-CNS | **32** | (43.8) | **19** | (47.5) | 0.843[b] |
| **Total** | **73** | (100.0) | **40** | (100.0) | |
| **Whether diagnostic testing, apart from ultrasound, was performed (n = 113)** | | | | | |
| Yes | **49** | (67.1) | **24** | (60.0) | |
| No | **24** | (32.9) | **16** | (40.0) | 0.538[b] |
| **Total** | **73** | (100.0) | **40** | (100.0) | |
| **Diagnostic test result (n = 67)** | | | | | |
| Abnormal | **25** | (51.0) | **15** | (62.5) | |
| Normal | **24** | (49.0) | **9** | (37.5) | 0.455[b] |
| **Total** | **49** | (100.0) | **24** | (100.0) | |
| **Abnormal test result (n = 38)** | | | | | |
| Trisomy 21 | **9** | (36.0) | **4** | (26.7) | |
| Trisomy 13 / 18 | **8** | (32.0) | **6** | (40.0) | |
| Sex chromosome aneuploidies | **3** | (12.0) | **2** | (13.3) | 0.373[b] |
| Other chromosome abnormalities | **0** | (0.0) | **2** | (13.3) | |
| Single gene disorder | **5** | (20.0) | **1** | (6.7) | |
| **Total** | **25** | (100.0) | **16** | (100.0) | |

a 2-tailed p-value determined through two-sample t-test with equal variance
b 2-tailed p-value determined through Fischer's exact test
c 24 weeks is considered the gestation of viability in South Africa

## 3.6 Factors found to have an impact on a patient's choice regarding TOP for a detected fetal abnormality

From all the variables that were included in the stepwise logistic regression analysis, the following were found to be the ones that may be involved in a patient's decision to terminate or continue a pregnancy affected by a fetal abnormality (Table 3-5)):

- the ethnicity of the patient
- the number of organ systems affected
- the gestational age when the fetal abnormality was diagnosed, and
- the gestation when TOP was offered

CNS involvement, parity, relationship status and maternal age were eliminated from the model by the Stata Version 8.0 software, as $p \geq 0.1$.

**Table 3-5** Stepwise logistic regression results showing the factors that were considered influential in a patient's decision to terminate or continue a pregnancy affected with a fetal abnormality (n = 113). All patients in the sample group received genetic counselling from the Division of Human Genetics, NHLS and WITS. The odds ratios, significance levels, and 95 % confidence intervals are shown.

| Variable | Odds Ratio | 95 % Confidence Interval | | p-value |
|---|---|---|---|---|
| Single organ system affected | 1.74 | 0.319 | 9.529 | 0.521 |
| Multiple organ systems affected | 4.31 | 0.900 | 20.660 | 0.068 |
| White ethnic group | 4.81 | 0.980 | 23.652 | 0.053 |
| Black ethnic group | 0.33 | 0.083 | 1.318 | 0.117 |
| GA at TOP offer | 0.69 | 0.496 | 0.960 | 0.027* |
| GA at diagnosis of abnormality | 1.39 | 0.998 | 1.947 | 0.052 |

Further modeling of the variables determined by the stepwise logistic regression was performed to determine the most clinically significant variables in the regression model that were associated with a decision to terminate a pregnancy. The most important predictor was determined to be earlier offer of termination (23.041 ± 6.96 weeks of gestation vs. 25.625 ± 6.74 weeks of gestation; p =

0.027) (n = 113). This corresponds to an odds ratio for termination of pregnancy of 0.93 (95 % CI, 0.87, 0.99) for each week of advancing gestational age.

## 3.7 Patients' decisions about termination of pregnancy after the detection of fetal abnormalities

Termination of pregnancy was offered to approximately 69 % (117) of patients who had a fetal abnormality diagnosed. Fifty percent (58) of the patients were offered TOP after 24 weeks gestation, while 45 % (52) were between 13 and 24 weeks gestation, and only 4 % (5) were in less than 12 weeks gestation. Of those patients who were offered TOP, approximately 62 % (73) elected to terminate the pregnancy (Table 3-6 and Figure 3-4).

**Table 3-6** Pregnancy outcomes of patients with diagnosed fetal abnormalities who received genetic counselling from the Division of Human Genetics, NHLS and WITS.

| *Variable* | n | % |
|---|---|---|
| **TOP offer** | | |
| No. of patients offered TOP | **117** | (68.8) |
| No. of patients not offered TOP | **53** | (31.2) |
| **Total** | **170** | (100.0) |
| **Gestational age at offer of TOP** | | |
| ≤ 12 weeks | **5** | (4.4) |
| 13-24 weeks | **52** | (45.2) |
| ≥ 24 weeks[b] | **58** | (50.4) |
| **Total** | **115**[a] | (100.0) |
| **TOP choice** | | |
| No. of patients who had TOP | **73** | (62.4) |
| No. of patients who chose not to have TOP | **44** | (37.6) |
| **Total** | **117** | (100.0) |

a For two patients the gestation when TOP was offered was not known
b 24 weeks is considered the gestation of viability in South Africa

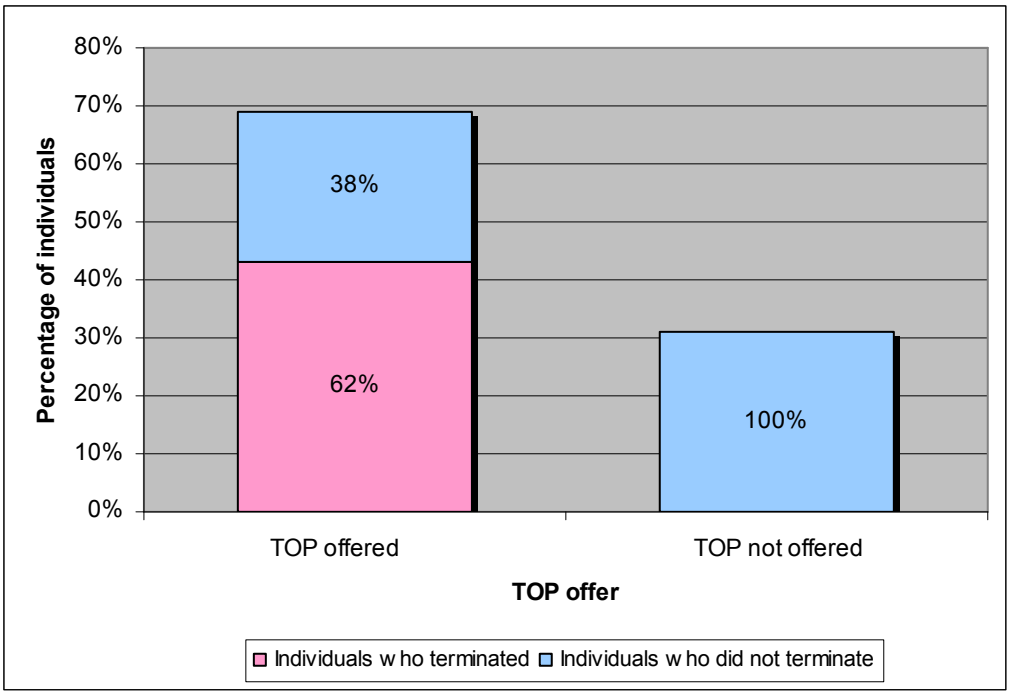


**Figure 3-4** Percentage of individuals, who received genetic counselling from the Division of Human Genetics, NHLS and WITS, and who were offered termination of pregnancy. The percentage of those who then chose to terminate the pregnancy is also shown.

## 3.8 Genetic counselling service provided to patients with diagnosed fetal abnormalities

The audit of the genetic counselling service offered to patients with diagnosed fetal abnormalities included determining the number of genetic counselling sessions the patient had during the pregnancy and whether they were followed-up after TOP or delivery (Table 3-7). If no follow-up appointment was made, the reason for this was determined from the records, if possible (Table 3-8).

The majority of patients who received genetic counselling for a fetal abnormality had one session during the pregnancy (99, 59 %). Patients who had more than one session tended to be those who chose to continue the pregnancy (Figure 3-5).

Data were available regarding the follow-up service offered to 167 of the 171 patients in the study. In 4 cases it was unknown whether the patient opted for TOP or not because they were not followed-up or notes were not made in the file. A follow-up appointment for after TOP or delivery was not made in 104 (62 %) cases. From Table 3-8, it can be seen that in 63 out of 104 (61 %) cases where no appointment was made, it was because no appointment was booked by the genetic counsellor involved (Figure 3-6). Therefore, in total, 63 out of 167 (38 %) patients who should have had a follow-up appointment did not, because it was not booked by the genetic counsellor. Significantly more patients were given follow-up appointments after TOP than after delivery after the continuation of the pregnancy.

When a follow-up appointment was booked, the patients attended the session approximately 78 % (29) of the time (Figure 3-7). Patients who chose to have TOP were seen for follow-up on average 57 days (approximately 8 weeks) after the last appointment in the pregnancy, while those patients who continued their pregnancies were seen on average 120 days (approximately 17 weeks) after the last appointment during the pregnancy. There was a significant difference ($p < 0.01$) in the interval between the last appointment in the pregnancy and the follow-up appointment between patients who chose to terminate affected pregnancies and patients who continued affected pregnancies.

**Table 3-7** Genetic counselling service provided by the Division of Human Genetics, NHLS and WITS, to patients with diagnosed fetal abnormalities, comparing patients who chose to terminate their pregnancy and those who continued their pregnancy. Patients who continued their pregnancy did so either by choice or because they were not offered termination of the pregnancy.

| *Variable* | *TOP* | | *Continue* | | *Combined* | | p-value |
|---|---|---|---|---|---|---|---|
| **No. of genetic counselling sessions during the pregnancy** | n | % | n | % | n | % | |
| 1 | 46 | (63.0) | **53** | (56.4) | **99** | (59.3) | |
| 2 | 17 | (23.3) | **29** | (30.8) | **46** | (27.5) | 0.587[a] |
| 3+ | 10 | (13.7) | **12** | (12.8) | **22** | (13.2) | |
| **Total** | 73 | **(100.0)** | **94** | **(100.0)** | **167** | **(100.0)** | |
| **Follow-up appointment after TOP or delivery** | | | | | | | |
| Follow-up appointment made | **37** | (50.7) | **26** | (27.7) | **63** | (37.7) | |
| Follow-up appointment not made | **36** | (49.3) | **68** | (72.3) | **104** | (62.3) | 0.004[a]** |
| **Total** | **73** | **(100.0)** | **94** | **(100.0)** | **167** | **(100.0)** | |
| **Follow-up appointment attendance** | | | | | | | |
| Patient attended | **29** | (78.4) | **20** | (76.9) | **49** | (77.8) | |
| Patient did not attend | **8** | (21.6) | **6** | (23.1) | **14** | (22.2) | 1.000[a] |
| **Total** | **37** | **(100.0)** | **26** | **(100.0)** | **63** | **(100.0)** | |
| **Interval between last appointment in pregnancy and follow-up appointment (days) (n = 55)** | 56.8 ± 25.97 | | 119.55 ± 118.23 | | 79.62 ± 79.19 | | 0.004[b]** |

a 2-tailed p-value determined through Fischer's exact test
b 2-tailed p-value determined through two-sample t-test with equal variance
** Statistically significant at the 1 % level

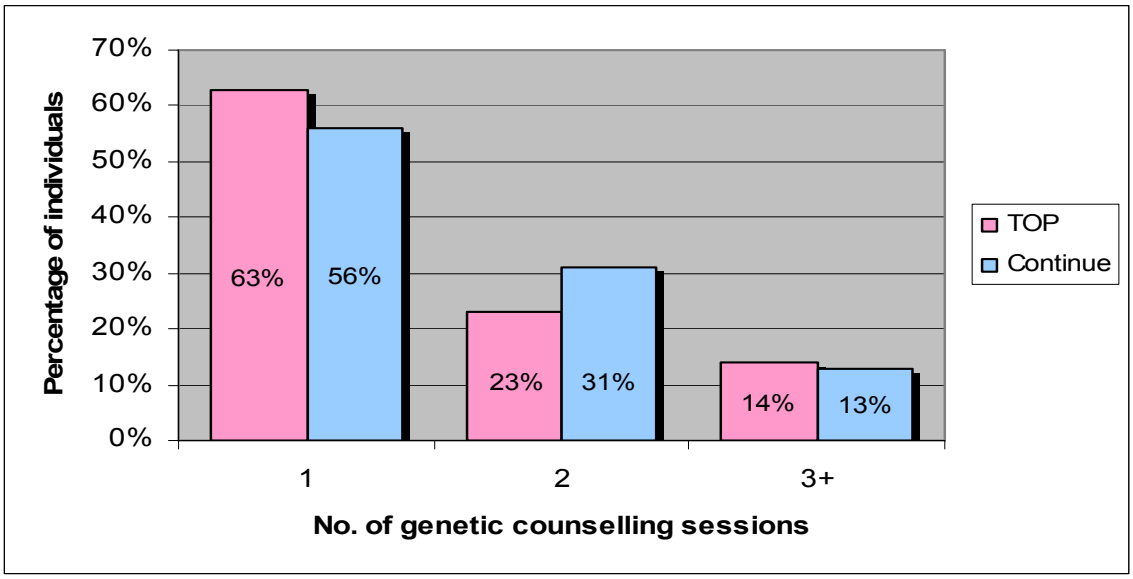


**Figure 3-5** Number of genetic counselling sessions provided by the Division of Human Genetics, NHLS and WITS, that patients had during the pregnancy in which a fetal abnormality had been diagnosed. The percentage of patients who had 1, 2 and 3 or more genetic counselling sessions is shown for those who chose TOP and for those who chose to continue their pregnancies, including all patients in the study.

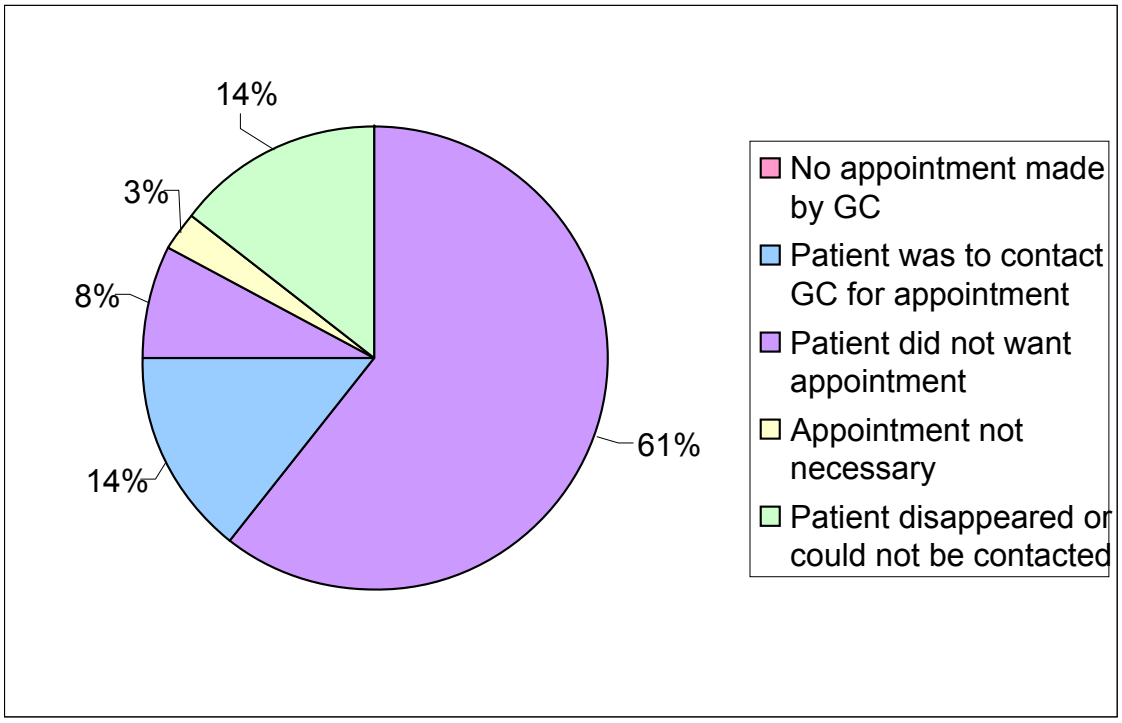


**Figure 3-6** Breakdown of the reasons why no follow-up appointment was made for after TOP or delivery for patients who received genetic counselling from the Division of Human Genetics, NHLS and WITS, after the diagnosis of a fetal abnormality.

**Table 3-8** Reason for no follow-up appointment being made for after TOP or delivery for patients who received genetic counselling from the Division of Human Genetics, NHLS and WITS, after the diagnosis of a fetal abnormality.

| Reason for no follow-up appointment | TOP | | Continue | | Combined | |
|---|---|---|---|---|---|---|
| | n | % | n | % | n | % |
| No appointment made by GC[a] | 23 | (63.9) | 40 | (58.8) | 63 | (60.6) |
| Patient was to contact GC for appointment | 4 | (11.1) | 11 | (16.2) | 15 | (14.4) |
| Patient did not want appointment | 5 | (13.9) | 3 | (4.4) | 8 | (7.7) |
| Appointment not necessary | 0 | (0.0) | 3 | (4.4) | 3 | (2.9) |
| Patient disappeared or could not be contacted | 4 | (11.1) | 11 | (16.2) | 15 | (14.4) |
| **Total** | **36** | **(100.00)** | **68** | **(100.00)** | **104** | **(100.00)** |

a GC – genetic counsellor

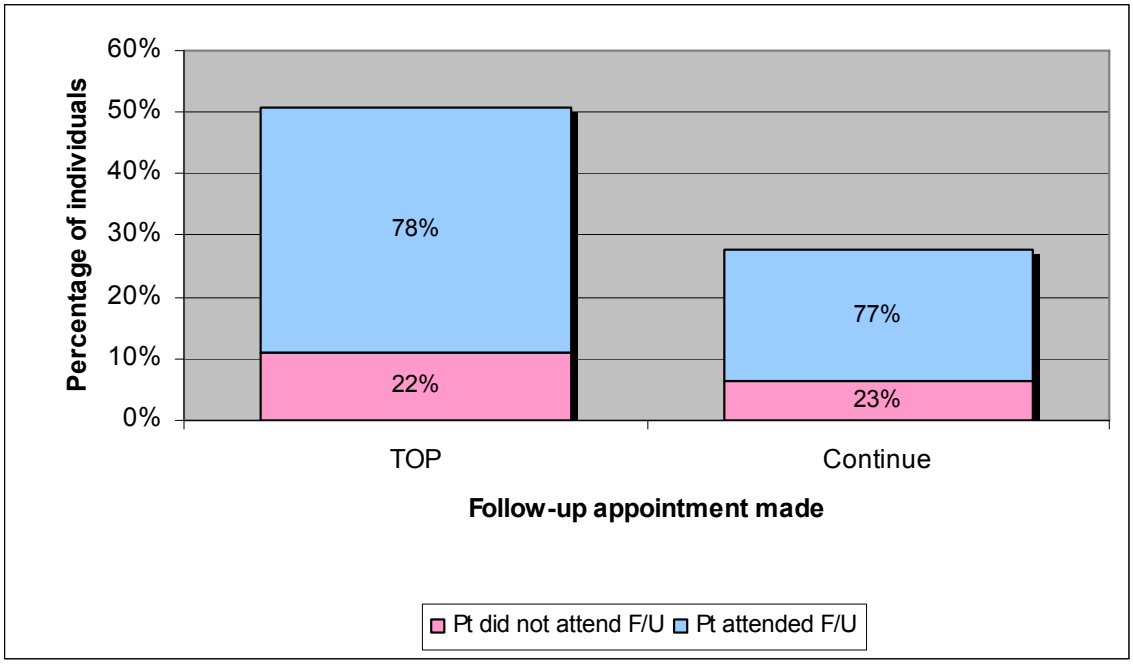


**Figure 3-7** Comparison of follow-up service offered by the Division of Human Genetics, NHLS and WITS, to patients who had TOP and those who continued their pregnancy after the detection of fetal abnormalities. The breakdown of what percentage attended their follow-up appointment is also shown.

# CHAPTER 4 DISCUSSION

## 4.1 Introduction

This research took the form of a retrospective audit of the genetic counselling files of patients who were seen for genetic counselling regarding diagnosed fetal abnormalities, in the Division of Human Genetics, NHLS and WITS, between 2002 and 2006.

This discussion will critically assess the results obtained during this research, following the format of the results. Limitations that were noted during the course of the research and recommendations for future research are included.

## 4.2 Patient numbers

### 4.2.1 Number of patients seen for genetic counselling regarding a diagnosed fetal abnormality between 2002 and 2006

A total of 171 patients were identified who had received genetic counselling for a diagnosed fetal abnormality by the Division of Human Genetics, NHLS and WITS between 2002 and 2006. This represents only 1.1 % of pregnancies expected to be affected by prenatally detectable congenital disorders, in the Johannesburg area (See Section 3.2). This may be explained by the fact that prenatal diagnosis and screening, as well as genetic counselling, are not accessible to all patients in Johannesburg, and therefore congenital disorders that would be detectable prenatally are not being detected. Another difficulty in the state health care system is that patients may not be appropriately referred from primary health care clinics to facilities where prenatal screening, diagnosis and genetic counselling are available (Christianson et al., 2006; Watcham, Schon and

Christianson, 2007). The genetic counselling service that is provided to couples who have had fetal abnormalities detected may have personal value for those who receive it, but the service has limited public healthcare value.

### 4.2.2 Trend in patient numbers over time

The number of patients seen for genetic counselling increased from 2002 until 2004, as the genetic counselling service grew and more clinics were developed. However, there has been a large decrease in the number of patients seen since 2004 (Figure 3-1), because one of the larger prenatal genetic counselling clinics stopped functioning in 2005.

## 4.3 Patient information

The majority of patients seen were Black (Table 3-1). The high proportion of Black patients in this study (123, 72 %) is comparable to the population statistics of Gauteng, where 74 % of the population is Black (StatsSA, 2001). Amongst the patients included in this study there was a high proportion of unemployment (72, 42 %). This high unemployment rate is in keeping with the fact that our Genetic Counselling Clinics function predominantly in tertiary state hospitals in the Johannesburg area, Gauteng. These hospitals mainly serve individuals who cannot afford private medical care and, therefore, a high proportion of unemployment would be expected in this sample group.

The HIV status of patients seen for genetic counselling for a diagnosed fetal abnormality was unknown for the majority of patients (125, 73 %) (Table 3-1). This could be due to a number of reasons: HIV testing may not have been performed, the genetic counsellors may not have requested the information or they may not have noted it in the file. Mseleku et al. (2005) reported that approximately 30 % of patients attending antenatal clinics at Johannesburg

Hospital were HIV positive. Approximately 57 % of patients (26) in our study, whose HIV status was known, were HIV positive. A possible explanation for this apparently increased prevalence is that genetic counsellors may be more likely to note when a patient is HIV positive, thus inflating the number of HIV positive patients relative to HIV negative patients.

## 4.4 Fetal abnormalities diagnosed in patients seen for genetic counselling

### 4.4.1 Initial reason for referral to genetic counselling

The majority of patients in this study were initially referred because an abnormality was detected on ultrasound examination (140, 82 %) (Table 3-2). The rest of the patients were initially referred because of an increased risk of fetal abnormality, which was determined through screening. Screening was done by asking about maternal age and family history, and ultrasound examination, including nuchal translucency measurement and the identification of soft markers. Our data is in keeping with a study by Hassed et al. (1993), done in the United States of America, who reported that abnormalities detected on ultrasound was the most common indication for referral for genetic counselling, with positive serum screening tests the second major reason. In our study, there were a low number of referrals to the genetic counselling service for positive serum screening tests, compared to Hassed et al. (1993), because serum screening tests are not available in the state hospital system in Gauteng, South Africa.

### 4.4.2 Gestation at diagnosis of the fetal abnormalities and offer of TOP

The mean gestation at diagnosis of fetal abnormalities was 23.3 ± 7.0 weeks with 44 % (75) of fetal abnormalities being diagnosed after 24 weeks gestation. Fifty

percent of patients (58) were only offered TOP after 24 weeks gestation (Table 3-2). This means that patients who wish to have TOP are often faced with having a fetocide due to the late gestation.

The gestation at diagnosis and at offer of TOP is in keeping with that found in international studies. A large study in 61 European obstetric units, found that only 44 % of fetal abnormalities were detected before 24 weeks, with diagnoses being made at 25.8 ± 7.5 weeks on average. They reported that the gestation at diagnosis was dependent on whether there were single or multiple abnormalities, and the type of abnormality detected (Grandjean et al., 1999).

There are a number of possible reasons for the offer of TOP being made so late in gestation in our clinics. Firstly, patients are being referred from primary health care clinics late in pregnancy, thus resulting in late assessment at a tertiary hospital where prenatal screening and diagnosis are more readily available (Christianson et al., 2006). In addition, many of the most frequently occurring abnormalities, such as hydrocephalus and skeletal abnormalities, are only evident at later gestations (Vaknin, Ben-Ami, Reish et al., 2006).

### 4.4.3 Organ systems affected by the fetal abnormalities

Intracranial CNS abnormalities (60, 35 %) were the most commonly detected abnormalities in our sample group, with cardiovascular abnormalities (46, 27 %) the second most common, followed by neck and face abnormalities (44, 26 %) (Table 3-2). A study conducted in an urban South African hospital looked at the frequency of involvement of specific organ systems in live born babies with congenital disorders (Delport, Christianson, van den Berg et al., 1995). The top three organ systems affected by abnormalities in this study were the CNS, including intracranial abnormalities and NTDs, the musculoskeletal system, and the cardiovascular system. Rauch et al. (2005) determined the frequency of involvement of specific organ systems when the abnormalities were detected

prenatally by fetal medicine specialists using ultrasound in the United States of America. They found that the cardiovascular system was the most commonly affected, followed by the neck and face, and the gastrointestinal system (Table 4-1).

**Table 4-1** Comparison of the three most frequently occurring abnormal organ systems in our study, another prenatal study and a group of babies born with congenital abnormalities

| **Our research group** | | **Rauch et al., 2005**[a] | | **Delport et al., 1995**[b] | |
|---|---|---|---|---|---|
| **Organ system** | **%** | **Organ system** | **%** | **Organ system** | **%** |
| Intracranial CNS | 35 | Cardiac | 39 | CNS (intracranial & NTD) | 19 |
| Cardiac | 27 | Neck and face | 32 | Musculoskeletal | 18 |
| Neck and face | 26 | Gastrointestinal | 30 | Cardiac | 15 |

a Prenatal study
b Postnatal study

Cardiac abnormalities were among the three most commonly detected abnormalities in all three studies shown in Table 4-1. The high number of prenatally detected cardiac abnormalities suggests a high level of expertise of the professionals performing the ultrasound examination in our study. This correlates with the fact that the majority of ultrasound examinations in this study were performed by fetal medicine specialists.

Delport et al. (1995) found CNS abnormalities to be the most commonly affected organ system in live born babies. Their study showed that 43 % of the reported CNS abnormalities were NTDs, while our study showed that only 14 % (10) of the CNS abnormalities were NTDs. This difference in the proportion of intracranial abnormalities versus NTDs may be explained by the fact that less intracranial abnormalities are detected postnatally since cranial ultrasound examinations are not routinely done, and such abnormalities may only be suspected when developmental delay becomes evident. In addition, the small sample number in this study may not accurately reflect the situation in the greater population. However, the proportion of NTDs, relative to abnormalities in other organ systems detected prenatally in our study (6 % of affected organ systems) was similar to Rauch et al. (2005) (11 % of affected organ systems).

Abnormalities of the neck and face were common in both this study and in the fetal abnormality study by Rauch et al. (2005). In Delport et al.'s study (1995), abnormalities of the neck and face were included within other organ systems, and therefore cannot be compared to our data.

Musculoskeletal abnormalities in our study only included skeletal abnormalities (40, 23 %), because muscle abnormalities are not detectable on ultrasound examination. This may account for the lower prevalence of musculoskeletal abnormalities in our study and that of Rauch et al. (2005), compared to the postnatal study done by Delport et al. (1995).

### 4.4.4 Diagnostic test results

Of the 97 patients who had invasive diagnostic testing or STORCH investigation, 45 % (44) had abnormal results (Table 3-2). Down syndrome was the most common chromosome abnormality detected by invasive testing (14, 32 %), with Trisomy 18 the second most common (10, 23 %) (Table 3-2). In a study of pregnant women attending the Antenatal Clinic at Groote Schuur Hospital, Viljoen, Oosthuizen and van der Westhuizen (1996) also reported that Down syndrome and Trisomy 18 were the most common chromosome abnormalities identified, each accounting for 32 % of the abnormalities.

One might have expected Down syndrome to have been diagnosed at a much higher frequency than Trisomy 18 because it is a more common chromosome abnormality. An explanation for the similar frequencies of Down syndrome and Trisomy 18 reported in these results may be that, when using second trimester ultrasound examination, Trisomy 18 has a prenatal detection rate of 64.9 % while Trisomy 21 has a prenatal detection rate of 26.7 % (Stoll et al., 2001). Since second trimester ultrasonography was the main screening tool used for the patients in this study, it is likely that many fetuses with Down syndrome are

missed, while those with Trisomy 18 are detected. This theory is supported by the fact that all the fetuses with Trisomy 18 diagnosed through invasive testing also had abnormalities detected on ultrasound, while only 5 out of the 13 fetuses (38.5 %) diagnosed with Down syndrome had abnormalities detected on ultrasound. Half (7) of the patients who had Down syndrome diagnosed through invasive testing were initially referred for AMA counselling, suggesting that AMA screening may be beneficial in the absence of other screening modalities. Only a small proportion of patients in this study presented early enough in the first trimester for nuchal translucency screening and maternal serum screening is not offered in the state hospitals. Second trimester ultrasound examination for fetal anomalies at 18 – 23 weeks gestation is often the only screening tool for Down syndrome available to non-AMA patients. As discussed, the detection rate of Down syndrome using ultrasound screening, without nuchal translucency screening, is low (26.7 %) in low-risk populations, resulting in many undetected cases (Stoll et al., 2001).

## 4.5 Comparison of those patients who chose termination of pregnancy to those who chose to continue their pregnancy after the detection of a fetal abnormality

Patients who chose termination and those who chose to continue their pregnancies after the detection of a fetal abnormality were compared in terms of their age, ethnicity, relationship status, parity, HIV status, gestation at diagnosis and offer of TOP, number of organ systems affected, CNS involvement, whether diagnostic testing was performed, and the result of diagnostic testing. The most relevant variables are discussed.

### 4.5.1 Ethnicity

Ethnicity was the only variable when analysed independently that was significantly different between patients who chose to terminate and those who chose to continue an affected pregnancy. Black patients chose TOP significantly less often than patients of other ethnic groups.

Black patients may be more likely to continue affected pregnancies for religious reasons, although this was not addressed in this study and may be an important factor for future research. A South African study comparing Muslim patients to patients of other religious groups found that religious belief was a significant factor in the decision about TOP (Viljoen et al., 1996).

Similarly, Black patients may be more inclined to leave the outcome of their pregnancy to fate. Kuppermann, Learman, Gates et al. (2006) reported that African-American women have higher levels of fatalism than women from other ethnic groups. They also showed that higher scores on a fatalism scale were associated with lower willingness to terminate an affected pregnancy (Learman, Drey, Gates et al., 2005).

We were unable to find any publications that looked at the reasons why Black South African women were less likely to terminate an affected pregnancy. This is a potential area for future research.

### 4.5.2 Maternal age, relationship status, and parity

Schechtman et al. (2002) found that older patients are more likely to terminate an affected pregnancy. However, in our study patients who terminated were on average younger, although this was only approaching statistical significance. Drugan et al. (1990), Pryde et al. (1992) and Rauch et al. (2005) showed no

impact of maternal age on the decision regarding TOP when abnormalities had been diagnosed.

Christian et al. (2000) showed that there is no significant impact of parental age or relationship status on the decision patients make regarding the outcome of a pregnancy with a diagnosed sex chromosome abnormality. The results of our study also show no influence of relationship status on the decision. Parity was also not found to be a significant factor in the decision to terminate an affected pregnancy in this study. This was also reported by Drugan et al. (1990), Pryde et al. (1992), and Rauch et al. (2005).

### 4.5.3 Gestation at diagnosis of the fetal abnormalities

The gestation at diagnosis of the fetal abnormality was not shown to be a significant indicator of the decision to TOP in this study. The same was reported by Pryde et al. (1992), but is in contrast to the conclusions of Rauch et al. (2005), who found that when fetal abnormalities are diagnosed earlier patients are more likely to opt for termination.

### 4.5.4 Gestation when TOP was offered

The offer of termination of the pregnancy was typically made late in the second trimester or in the third trimester, although it was on average later for patients who chose to continue their pregnancy than for those who chose to terminate. This suggests that when termination was offered later, patients were more likely to continue the pregnancy, although this was only approaching statistical significance and so should be interpreted with caution.

A possible reason for patients being less likely to terminate a pregnancy later in gestation is that the patient bonds more with the pregnancy as it progresses (Pryde et al., 1992; Drugan et al., 1990). In some religions TOP is absolutely

forbidden, for other religious groups late TOP is unacceptable (Zlotogora, 2002). This could also explain why patients are more likely to terminate affected pregnancies when the offer is made earlier. In addition, for some patients their moral and personal values and beliefs may make it unfavourable to choose termination at a later gestation. In addition, as the pregnancy progresses the procedure required to terminate the pregnancy may become more complex, and thus may impact on women's feelings and the decisions they make about TOP (Davies et al., 2005). Women may be less likely to terminate when the procedure required is more complicated and risky.

### 4.5.5 CNS involvement

Schechtman et al. (2002) report that when there is CNS involvement, patients are more likely to terminate an affected pregnancy. Our research showed that CNS involvement did not have a significant influence on the decision to terminate or continue an affected pregnancy. This may be because of the smaller size of the study population in this research project.

### 4.5.6 Diagnostic testing

When comparing patients who had diagnostic testing and those who did not, there was no significant difference in the decision regarding termination of pregnancy. There was also no significant difference between patients who had an abnormal diagnostic test result and those who had a normal diagnostic test result in terms of whether they chose TOP or continuation of the pregnancy. This suggests that the possibility of having a defined diagnosis compared to a collection of abnormalities on ultrasound examination does not impact the decision patients make about the outcome of the pregnancy. We could not find any literature that compared the decision about TOP made by patients who chose to have diagnostic testing and those who did not or the differences between patients with normal and abnormal results.

## 4.6 Factors found to have an impact on a patient's choice regarding TOP for a detected fetal abnormality

Variables that were identified through a stepwise logistic regression to have a significant or borderline significant impact on the decision to terminate or continue an affected pregnancy were manually modeled using logistic regression. Patients who were offered TOP at earlier gestations were found to be more likely to choose TOP than patients who were offered TOP later in their pregnancy. These results are in concordance with those of Rauch et al. (2005), who reported that earlier detection of fetal abnormalities was the most important factor associated with the decision to terminate an affected pregnancy.

Possible reasons for why patients may be more likely to opt for TOP at earlier gestations has been discussed under the univariate analysis (Section 4.5.4).

## 4.7 Decisions about termination of pregnancy

Termination of the affected pregnancy was offered to approximately 69 % (117) of the patients who had fetal abnormalities detected. Of those patients who were offered TOP, approximately 62 % (73) chose to terminate the pregnancy (Table 3-6). In a previous study, carried out in the Western Cape in South Africa, Viljoen et al. (1996) reported that 76 % of patients with a detected fetal abnormality opted for TOP. Conversely, Rauch et al. (2005) reported a 33 % TOP acceptance rate after the detection of a fetal abnormality in the second trimester, in a study done in the United States of America. It has been suggested that the characteristics of the fetal abnormalities detected and the population group of the patient have an influence on the decision patients make regarding TOP (Schechtman et al., 2002; Rauch et al., 2005). The difference in acceptance rates between the three studies mentioned here may therefore reflect differences in the study groups in terms of the characteristics of the fetal abnormalities detected, as well as different population groups.

## 4.8 Genetic counselling service offered to patients with diagnosed fetal abnormalities

Only 38 % (63) of patients with detected fetal abnormalities were seen for a follow-up genetic counselling appointment after termination or delivery (Table 3-7). The most common reasons for no follow-up appointment included no appointment being booked by the genetic counsellor (63, 61 %), the patient not contacting the genetic counsellor to make another appointment (15, 14 %) and the patient disappearing (15, 14 %) (Table 3-8). Information about whether the fetus was examined after a termination was not recorded in this study, but it would be a recommended variable for future research as it represents another form of follow-up.

Follow-up after the detection of a fetal abnormality is important for patients because it provides an opportunity for the results of any tests to be discussed and for the provision of psychosocial support. Patients who choose to continue their pregnancy need to be seen so the baby can be examined and appropriately managed and a diagnosis potentially made (Weil, 2000).

Patients who chose to terminate an affected pregnancy were more likely to have a follow-up appointment made than patients who continued the pregnancy to delivery. This may be because the genetic counsellor focuses on the emotional needs of patients who choose to terminate. It may also be because patients who choose termination are likely to deliver sooner than patients who choose to continue their pregnancy. It is often not possible for the genetic counsellor to predict the exact delivery date or to know the outcome of a continued pregnancy, which makes it difficult to know when to schedule the follow-up appointment. Patients who choose to continue an affected pregnancy are often told to phone the genetic counsellor after the birth of the baby or that they will be contacted

after the birth to organise an appointment, however, this invariably does not happen due to the difficulties discussed below.

In total, 38 % of patients did not have a follow-up appointment made because the genetic counsellor involved did not make the appointment. This may occur because the genetic counsellor plans to wait until after the expected delivery date to contact the patient to make an appointment, but then forgets to do so. It is possible that the counsellor does phone or make contact with the patient but forgets to make a note in the counselling file. A recommendation may be to make the booking at the final appointment during the pregnancy, for approximately 6 weeks after termination or the expected date of delivery. The appointment can be confirmed prior to the session, thus reducing the chance that the patient does not remember.

When follow-up appointments are made, the patients attended the appointment in 78 % (49) of cases (Table 3-7). This suggests that if the appointment is made, the patient is likely to come. This suggests that patients value the service that is being offered. This was true for both patients who chose to terminate and those who chose to continue their pregnancies.

When follow-up appointments are made they are, on average, 80 days after the last appointment during the pregnancy. When patients chose to terminate, the follow-up appointment occurred 57 days (~ 8 weeks) after the last appointment in the pregnancy (Table 3-7). The recommended interval, used by our department (Division of Human Genetics, NHLS and WITS), between the last appointment during the pregnancy and the follow-up appointment for patients who choose termination is 6 weeks, thus 8 weeks is probably acceptable. The interval for patients who chose to continue the pregnancy was, on average, 120 days (~ 17 weeks) (Table 3-7). It is difficult to judge the appropriateness of this interval, as the time between the last appointment in the pregnancy and the follow-up appointment after delivery depends on the gestation that the patient was seen at.

Some patients are seen early in the pregnancy, while others may be seen just before delivery.

## 4.9 Limitations of this research

From the beginning of this research project it was thought that notes in some of the counselling files may not be complete, and this could result in missing data. This was confirmed during the data collection phase of the research when information that was expected to be in the files was not found. However, we do not think that the missing information had a large impact on our results.

The sample population, although satisfactory for the scope of this research report, is not large enough to draw conclusions about the factors that may be associated with the decision to terminate a pregnancy affected by fetal abnormalities. The inclusion of more patient files would allow generalisations to be made.

## 4.10 Recommendations

### 4.10.1 Recommendations for future research

With respect to the specific variables that were recorded during the research, there are a number of additional variables that could have been recorded and analysed as they may be associated with the decision to terminate an affected pregnancy. These include the severity of the detected abnormalities, the religious beliefs of the patients and their education level. The inclusion of these variables in future work may provide more information regarding the decisions patients make regarding the outcome of affected pregnancies. In addition, when recording whether patients had diagnostic testing or not, it would be useful to record which patients were offered diagnostic testing. Patients who choose to

have diagnostic testing, specifically invasive testing, may be more likely to choose termination, than patients who decline diagnostic testing.

When assessing the genetic counselling service offered to patients with detected fetal abnormalities it would be beneficial to record when a fetus was examined after a TOP, as this would allow follow-up to be more thoroughly assessed.

### 4.10.2 Recommendations for improving the genetic counselling service offered

Follow-up appointments should be made during the last appointment in the pregnancy, regardless of whether the patient has chosen to continue or terminate the pregnancy. This will ensure that patients are adequately followed-up, and receive the necessary management and support.

Efforts should be made to develop and expand the genetic counselling service offered so that the larger community has access to it.

## 4.11 Conclusion

The genetic counselling service provided by the Division of Human Genetics, NHLS and WITS, to patients with diagnosed fetal abnormalities is limited in its availability to the larger community. The service may be valuable to the patients who have access to it, but it has limited public health care value.

The gestation when fetal abnormalities are diagnosed, and thus when TOP is offered, is consistent with the timing of the fetal anomaly scan. However, many fetal abnormalities could be detected earlier if ultrasound screening was initiated earlier in pregnancy. This research suggests that earlier gestation at offer of TOP is the most clinically important predictor of the decision to terminate an affected pregnancy. This supports the idea that the detection and diagnosis of fetal abnormalities as early in pregnancy as possible is beneficial for the patients

who are faced with the decision of whether to terminate or continue an affected pregnancy.

Two thirds of the patients who were offered termination of the affected pregnancy chose to undergo TOP. This reflects the importance of giving patients the choice to terminate a pregnancy when fetal abnormalities are detected.

The genetic counselling follow-up service that is offered by the Division of Human Genetics, NHLS and WITS, needs to be improved. Patients do not receive adequate follow-up, particularly those patients who choose to continue the pregnancy. This means that many babies with abnormalities that are known to the division are born and not assessed again. The fact that patients who do receive follow-up appointments generally attend the appointment indicates that the service is valued and wanted by the patients. Follow-up appointments should be booked at the last appointment during the pregnancy, and confirmed shortly before the appointment.

# APPENDIX A: ETHICS CLEARANCE CERTIFICATE

**UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG**

Division of the Deputy Registrar (Research)

**HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)**
R14/49 Todd

| | |
|---|---|
| **CLEARANCE CERTIFICATE** | **PROTOCOL NUMBER M060944** |
| **PROJECT** | Retrospective Analysis of the Outcomes of Patients Presenting for Genetic Counselling with Fetal.... |
| **INVESTIGATORS** | C Todd |
| **DEPARTMENT** | Dept of Human Genetics |
| **DATE CONSIDERED** | 06.09.29 |
| **DECISION OF THE COMMITTEE*** | APPROVED UNCONDITIONALLY |

**Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.**

**DATE**

**CHAIRPERSON** .....
(Professors PE Cleaton-Jones, A Dhai, M Vorster, C Feldman, A Woodiwiss)

*Guidelines for written 'informed consent' attached where applicable

cc: Supervisor : T Haw

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**DECLARATION OF INVESTIGATOR(S)**

To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10005, 10th Floor, Senate House, University.
I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

# APPENDIX B: GENETIC COUNSELLING INFORMATION SHEET

## NHLS - HUMAN GENETICS

**DIAGNOSIS:** **SURNAME:**

**APPOINTMENTS:**

Date: h At: By:

Date: h At: By:

Date: h At: By:

Date: h At: By:

Date: h At: By:

Hospital:

No: Fin Class:

Medical Aid:

Medical Aid No:

Member: ID No:

**REFERRED BY:**

Name:

Address:

Tel: Fax:

Name:

Address::

Tel: Fax:

**Index name (s):**

Date of Birth:

**Name (s) Ms:**

Maiden Name:

Date of Birth:

Occupation:

**Name(s): Mr:**

Date of Birth:

Occupation:

Street Address:

Code:

Postal Address:

Code:

**Telephone:** (H) Contact:

(W) Ms: Mr:

Fax: Ms: Mr:

Cell :Ms: Mr:

E-mail: Mr:

Ms:

Booking taken by: Phoned in by: Date: Faxed / Posted

Booking Confirmed: 1) 2) 3) 4) 5)

Previously counselled: Y / N Date: Where:

Previous genetic tests: Y / N Date: Where:

**BILLING**

Private patient: State patient:

| CGC number | Date | Billed | Initial | Review | Enter |
|---|---|---|---|---|---|
| | | | | | |

**OTHER TESTS**

# APPENDIX C: DATA COLLECTION SHEET

**SUBJECT CODE: _____.**

**Biomedical Information:**

1. Maternal date of birth:_____.

2. Maternal age at diagnosis of the fetal abnormality:_____.

3. Ethnicity:

| | | | |
|---|---|---|---|
| 1. White | ☐ | 2. Black | ☐ |
| 3. Indian | ☐ | 4. Mixed Ancestry | ☐ |
| 5. Other | ☐ | 6. Unknown | ☐ |

4. Relationship status:

| | | | |
|---|---|---|---|
| 1. Single | ☐ | 2. Divorced/Separated | ☐ |
| 3. Widowed | ☐ | 4. Married | ☐ |
| 5. In a relationship | ☐ | 6. Unknown | ☐ |

5. Employment status:

| | | | |
|---|---|---|---|
| 1. Employed | ☐ | 2. Unemployed | ☐ |
| 3. Self-employed | ☐ | 4. Unknown | ☐ |

Occupation:_____.

**Pregnancy History:**

6. Gravidity:

1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 ☐

7. Parity:

1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 ☐

8. Number of fetuses in the pregnancy:
1 ☐ 2 ☐ 3 ☐

9. Gestational age by sonar at the time of the diagnosis of the fetal abnormalities:
_____.

10. Total number of fetal abnormalities detected:
1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 ☐

11. Fetal abnormalities detected:
_____.

12. Number of soft markers identified on sonar:
1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 ☐

13. Soft markers detected:_____.

14. Fetal abnormalities detected in the following organ system(s):

| | | | |
|---|---|---|---|
| 1. Cardiovascular | ☐ | 2. Pulmonary | ☐ |
| 3. Neurological | ☐ | 4. Skeletal | ☐ |
| 5. Gastrointestinal | ☐ | 6. Genitourinary | ☐ |
| 7. Neck and face | ☐ | 8. Other | ☐ |

_____.

15. The abnormality was considered lethal:
1. Yes ☐ 2. No ☐

16. The prognosis of the fetal abnormality was certain:
1. Yes ☐ 2. No ☐

17. Diagnostic procedures performed:

| | | | |
|---|---|---|---|
| 1. Ultrasound scan | ☐ | 2. Amniocentesis | ☐ |
| 3. Cordocentesis | ☐ | 4. Chorionic villus sampling | ☐ |
| 5. STORCH screen | ☐ | | |

18. Result of diagnostic procedure:_____.

19. Was the patient referred to specialist doctors:
    1.Yes ☐ 2. No ☐

20. If yes, to what specialist doctors was the patient referred: _____.

21. Whether termination of pregnancy was offered:
    1.Yes ☐ 2. No ☐

22. What gestational age was termination of pregnancy offered:_____.

23. Was the pregnancy terminated:
    1.Yes ☐ 2. No ☐

24. Number of genetic counselling consultations during the pregnancy:
    1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐

25. Was a follow-up appointment made for after TOP or delivery:
    1.Yes ☐ 2. No ☐

26. Did the patient attend the follow-up appointment:
    1.Yes ☐ 2. No ☐ 3. Not applicable ☐

27. Interval between the last appointment in the pregnancy and the follow-up appointment after TOP and delivery:_____.

28. Reason for no follow-up appointment being made:
    1. No appointment made by GC ☐
    2. Patient was to contact GC for appointment ☐
    3. Patient did not want appointment ☐
    4. Was to be referred again if necessary ☐
    5. Appointment not necessary ☐
    6. Patient disappeared or could not be contacted ☐

29. Initial indication for genetic counselling:

1. Abnormality on ultrasound ☐
2. AMA ☐
3. Family History ☐
4. Positive screening test ☐
5. Teratogen ☐

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