4 DISCUSSION

4.1 HIV Prevalence in AMA Women

Data were collected over two six-month periods, February to July 2003 and February to July 2004. In 2003 the extent of the impact of HIV positivity on AMA counselling was beginning to be realised and this prompted the initiation of this study. Initially a retrospective analysis was undertaken to assess this impact using the Department of Human Genetics' files of AMA women counselled in 2003. Subsequently, a prospective analysis of HIV status of AMA women counselled was undertaken in 2004. Data from the retrospective study showed an HIV prevalence of 153/1000 (15%) in 2003, where the status of only 98 (58 %) of the 169 women was known or documented. In the prospective study of 2004, the HIV prevalence was 225/1000 (23%), where the status of 129 (71%) of 181 women was known. This is not a statistically significant increase in the prevalence of HIV ($p=0.235$). Of all 350 women seen in the two sample groups, the prevalence of HIV amongst women of known status was 194/1000 (19%).

Of the women aged 35 to 39 years, where HIV status was known, the prevalence of HIV was 200/1000 (32/160), while the prevalence among the women of 40 years and older, who were tested, was 179/1000 (12/67). There was therefore no statistically significant difference in HIV positive prevalence between the two age groups ($p=0.854$).

In studies conducted throughout South Africa, it has become evident that the HIV prevalence among women attending antenatal clinics is high. In a 2003 South African

survey (Doherty and Colvin, 2004) the prevalence of HIV was 198/1000 (19.8%) in the women aged 35-39 years and 172/1000 (17.2%) in women aged over 40 years. The data collected during this current study from the AMA clinics thus corresponds with the findings of Doherty and Colvin, suggesting that the AMA women seen for genetic counselling are representative of pregnant women of that age group in the country. If the HIV prevalence in South Africa continues to increase it could therefore be expected that the number of HIV positive women attending the AMA clinics will increase similarly unless an effective policy is developed and implemented to address this situation.

4.1.1 The Impact of HIV Status on Amniocentesis Uptake

Uptake of amniocentesis amongst all AMA women counselled was not statistically different between the two six-month periods investigated, with 58 (34%) of 169 AMA women in 2003, and 52 (29%) of 181 AMA women in 2004, having prenatal testing ($p=0.300$). The overall uptake of prenatal testing for chromosome analysis, over the two periods, was 31% (110/350). Analysis of the data revealed a significant association between HIV status and amniocentesis uptake. The HIV positive women were far less inclined to undergo prenatal testing, with only 6 (14%) of 43 HIV positive women having amniocentesis. By comparison 79 (43%) of 183 HIV negative women underwent amniocentesis. This is a statistically significant difference in amniocentesis uptake, $p<0.001$. HIV positive status therefore plays a major role in deterring AMA women from undergoing prenatal testing. It should also be noted that doctors are likely to be reticent about performing amniocentesis where a woman is known to be HIV positive and may advise an HIV positive AMA woman against amniocentesis, especially after a normal ultrasound examination.

4.1.2 Other Factors Influencing Amniocentesis Uptake

The uptake of amniocentesis in South African women of AMA is highly variable. One South African study showed an acceptance rate of 35% (Kromberg et al., 1989) and another showed an acceptance of testing as high as 76% (Viljoen et al., 1996). Neither of these studies addressed the impact of HIV on women's decision-making around amniocentesis, as these studies were carried out before HIV was recognised as being an issue.

There are numerous other factors that may influence the uptake of prenatal testing by women of AMA. A South African study (Kromberg et al., 1989) found that the reasons for non-uptake of prenatal testing included religious convictions, poor obstetric history, fear of miscarriage because of the procedure, and needle phobia.

A study in Australia indicated that women in public sector hospitals are less likely to have an amniocentesis than those in private hospitals (Halliday et al, 1995). This may suggest that women from less advantaged socio-economic and social backgrounds are less empowered to make decisions than those women in a higher socio-economic bracket. This could relate to our study group where 98% of the women were counselled in state hospitals.

In South Africa, where many women do not have a concept of Down syndrome (Christianson, 1996), there may be a lack of insight of the implications of raising a child with this disorder. Alternately, the community may be more accepting of children with disability and therefore less inclined to accept TOP. Counselling at our clinics usually

occurs without the attendance of the father and it could be suggested that women are perhaps fearful of making a decision without their partners. It is not known if women are more inclined to refuse amniocentesis where the partner is a new partner. It is frequently observed that counselled AMA women say they will discuss prenatal testing with their partners, and then do not return to the clinic.

Women in Australia who have had three or more previous births are less likely to undergo prenatal diagnosis (Halliday et al, 1995). This phenomenon was not examined in our study groups, but it would seem plausible that parity also plays a role in South Africa in the AMA women's decision not to undergo prenatal testing.

4.1.3 The AMA Women's Understanding of Risk

As noted in section 4.1.1, HIV positive women, at risk of MTCT during invasive testing, were significantly less likely to choose amniocentesis compared to the HIV negative women. It also became apparent during the study that the younger AMA women, who were at lower risk for chromosome abnormalities, were less likely to choose prenatal testing than the older AMA women. Combining the data from both six month groups, it is evident that there was a statistically significant difference in the uptake of testing between the two age groups, with a greater number of women aged 40 years and older, 43/107 (40%), choosing to have invasive testing for chromosome analysis, compared to the women aged between 35 and 39 years, where 67/243 (28%) chose to have testing ($p=0.024$). Although not an aim of this project, these findings suggest that the AMA women who were counselled about the risks associated with chromosome abnormalities as well as those counselled about the risk of MTCT appeared to have an appreciation of the concept of risk;

thus the older women who were at higher risk of having a chromosomally abnormal baby, were more inclined to opt for testing than the younger women of AMA, and the HIV positive women who were at risk of MTCT were less inclined to have amniocentesis than the HIV negative women.

There was no statistically significant difference in amniocentesis uptake between patients seen by counsellors as compared to those seen by the doctors in the department. A larger sample would have to be analysed to establish if this was indeed a factor.

Reviewing the results, it becomes apparent that further research is required to audit AMA counselling, the uptake and decline of amniocentesis by AMA women in South Africa, and the reasons behind this in the current scenario of the HIV pandemic.

4.1.4 HIV Positive Women, Amniocentesis and ART

The use of prophylactic treatment for HIV positive pregnant women at the time of amniocentesis was better established in 2004, but a consistent policy was still not available; the AMA women were therefore not afforded consistent care regarding ART cover during amniocentesis. Each hospital and each doctor made their own decisions regarding treatment for each individual AMA woman requesting invasive prenatal testing for chromosome abnormalities. ART cover ranged from a single dose of nevirapine prior to the procedure for some women, while others also received a month-long course post amniocentesis. Some women had to purchase their own ART. Women of unknown HIV status who underwent amniocentesis would not have been provided with any ART cover.

When the questionnaire was undertaken (2004), women of AMA requesting amniocentesis were no longer expected to purchase ART in the academic hospitals where the Genetic Counselling Clinics were held. There were, however, still difficulties accessing these drugs as no system was in place to assist these women in obtaining the medication at short notice. Each case had to be carefully followed up, with the requirement of a prescription from a doctor within the hospital to obtain the drugs. Two (13%) of the fifteen women participating in the questionnaire said that they would have considered amniocentesis if antiretroviral cover was readily provided. This lack of policy introduced more uncertainty for the HIV positive AMA women, and for the counsellors offering amniocentesis who could not be sure whether, or by what procedure, the ART could be accessed. It is also indicative of the lack of knowledge regarding the best possible prophylaxis for invasive testing in pregnancy, and symptomatic of the lack of clear direction in ART policy in the country at the time the study was undertaken.

Despite the many issues that surround the administration of ART in pregnancy (WHO, Geneva, 2004), including the unknown risk of MTCT at amniocentesis, HIV positive pregnant women should have access to ART. Only in this way will these women's right to make informed choices surrounding prenatal testing for chromosome abnormalities be guaranteed.

4.2 HIV Positive Women and TOP

The research instrument in the second part of this study was a questionnaire comprising of 14 questions. It was offered to HIV positive women who presented for AMA counselling during the period February to July 2004. Of the 29 HIV positive AMA women seen in the

six-month study period, 15 (52%) made themselves available and answered the questionnaire. Reasons for non-participation included: fear of disclosure, women leaving the clinic before the session was completed, and lack of availability of a translator. The number of women who participated was low, and the results therefore only suggest trends. Further study will be required to confirm these findings.

4.2.1 Termination of Pregnancy

For HIV positive women who are less than 20 weeks pregnant, the option of terminating the pregnancy based on the risk of transmission of the virus to the fetus is available (South Africa. Government Gazette, 1996: 4). Although with the availability of HAART the risk of MTCT is significantly reduced, this is only effective where patients on ART are fully compliant. At the time of the study, this reduction of MTCT risk was not a consideration because ART was not readily available. The option of TOP should ideally be discussed and offered to women during their post-test HIV counselling session, or as part of antenatal care once their HIV status is known. This is not always done, as was evident from the questionnaire, where only two (13%) of the 15 women remembered being told about the option of TOP based on the risk of vertical transmission of HIV to the baby. The reasons for this lack of knowledge are not clear; women who have just been informed that they are HIV positive may be overwhelmed by the result, and may not have assimilated all the information offered. HIV counsellors may not be fully informed of this option, or they may have personal and moral objections to termination of pregnancy and therefore refrain from discussing termination with the HIV positive women, although it is Antenatal Clinic policy to offer TOP to HIV positive pregnant women up to 20 weeks of pregnancy. Of the 15 HIV positive AMA women interviewed, five (33%) considered termination of pregnancy, based

on the vertical transmission risk of HIV to their fetus, after genetic counselling. One patient in the 2003 group, and one in the 2004 group, requested termination of pregnancy. Women who initially considered termination of pregnancy may have changed their minds for a number of reasons. It is speculated that the reasons are varied, but may include family or partner pressure to continue with the pregnancy, or pressure and fear of enmity from the nursing staff. It is important to confirm these trends through further research, and to elucidate the reasons for the women's lack of knowledge, so that in future, HIV positive women are better informed about the decisions they need to consider regarding their pregnancy.

Question nine asked what the woman's understanding was about the risk of HIV transmission to the fetus, with and without perinatal antiretroviral prophylaxis. Women's responses varied on this point; four (27%) of the 15 women interviewed believed that there was no risk of transmission when nevirapine was administered, and one woman thought that all babies born to HIV positive mothers would be infected. Of the ten (66%) women who were either too late to be offered TOP or who refused TOP, five (50%) did not understand the risk of MTCT of HIV correctly. Unless women are very clear on the risks of HIV transmission to the fetus, they are not able to make fully informed decisions surrounding TOP or prenatal testing for chromosome anomalies.

4.3 Future Management

The Primary Health Care Policy Guidelines as set out by the Department of Health (2000) aim to provide optimal and equitable health care in South Africa. They express the need for hospital staff to educate and counsel pregnant women about HIV and AMA. But as

discussed in section 1.2.2.1, the primary health care services do not appear to be screening appropriately for AMA or referring women for prenatal testing timeously. The Policy Guidelines also discuss the importance of training these staff in appropriate counselling and care of pregnant women requesting TOP. However, the unique requirements of HIV positive AMA women are not addressed. There is no mention of the difficulties facing these women regarding prenatal testing for chromosome abnormalities, nor do they discuss the importance of counselling HIV positive women about the option of TOP up to 20 weeks gestation for the risk of MTCT.

Traditionally, the role of the genetic counsellor is to discuss genetic risks, not a woman's HIV status and the implications of this to herself and the pregnancy. Given the omnipresence of HIV across all groups in South Africa, it is important to establish the HIV status of women prior to referral for genetic counselling and amniocentesis. Obtaining a positive HIV result is a traumatic event, requiring in-depth counselling, which should not be done concurrently with genetic risk counselling. Preferably, such HIV counselling, including the risk of MTCT of HIV and the option of termination of pregnancy, should occur prior to referral for genetic counselling.

Those not tested, or refusing testing, for HIV must be made aware of the risks of MTCT during amniocentesis. In this ideal situation, where all women referred for genetic counselling knew their HIV status, the genetic counsellor could:

1] Briefly discuss the implication of HIV to the pregnancy, and ensure that the patient is aware of the seriousness of HIV infection to herself and the fetus, and determine how she

is coping with this knowledge. Any new developments in ART policies, and the subsequent alteration of risks, should also be discussed.

2] Discuss the option of termination of pregnancy based on the high transmission risk, determining if this option had been offered to her during HIV counselling

3] Discuss the issues surrounding the risks of chromosomal abnormalities based on the woman's advanced age and offer amniocentesis

4] Inform the woman of the risks should she wish to have an amniocentesis.

Initially nevirapine was usually given prior to amniocentesis, although a standard policy was not in place during the study period at any of the hospitals where genetic counselling occurred. There is still uncertainty regarding the risk of drug resistance after a single dose administration, and the consequent effectiveness of perinatal nevirapine prophylaxis to reduce mother to child transmission of HIV (Eshlemann et al., 2001). Currently different policies for ART in pregnancy exist at the three academic hospitals where genetic counselling is offered:

- Coronation Hospital: All HIV positive pregnant women have CD4 counts performed. Women whose CD4 counts are below 200 are given combination ART, namely AZT and 3TC, and this therapy should then be administered lifelong. HIV positive pregnant women whose CD4 counts are above 200 are given a single dose of nevirapine at the time of delivery, as are the babies post-delivery (van der Merwe, personal communication, 2005). All HIV positive women of AMA requesting amniocentesis are given combination therapy (AZT and 3TC) from three days prior to amniocentesis. Women whose CD4 counts are below 200 are prescribed lifelong therapy. Women whose CD4 counts are above 200 are given the

therapy up to a month after the amniocentesis, and at the time of delivery are given a single dose of nevirapine (Adams, personal communication, 2005).

- Chris Hani Baragwanath and Johannesburg General Hospitals: the same policies are being followed at these hospitals; however HIV positive AMA women who have amniocentesis and are given combination therapy remain on this therapy, regardless of their CD4 counts, at least until the end of pregnancy. The medication is only discontinued if there are adverse side effects (Nicolaou, 2005; Jeebodh, 2005).

4.4 Limitations

Certain limitations became evident during the course of the study:

- The sample size for those completing the questionnaire was not large enough to achieve statistically significant responses, and the data therefore only suggests trends. The time constraints of the project limited the number of possible participants in the questionnaire.
- The proportion of HIV positive AMA women who participated in the questionnaire was low (15/29), and this is thought to be due to a number of factors: loss of the interpreter who was used during the counselling session where a woman was not English speaking, women not feeling comfortable discussing their HIV status, especially where it was recently diagnosed, and fear of disclosure of information to partners. This may have caused self-selection bias as women unwilling to think about their HIV positive status may not have participated in the study.

- The questionnaire was administered by a number of different counsellors and doctors of the Department of Human Genetics and therefore interpretation bias cannot be ruled out.
- In the 2003 sample, the HIV status of some women may have been known but not documented in the facesheets. By 2004, the counsellors and doctors of the Department of Human Genetics were aware of the study and therefore the importance of documenting the women's HIV status in their facesheets.

4.5 Recommendations

The following recommendations can be made from the findings of this study:

- HIV counselling and testing should be offered to all pregnant women of AMA prior to referral for Genetic Counselling. If HIV positive, these women should be given full HIV counselling on HIV risks to the mother and child, the risk of MTCT of HIV and the option of TOP (in women under 20 weeks gestation) based on these risks.
- HIV positive AMA women who do not request TOP should then be referred for genetic counselling. In the genetic counselling session a review of the women's understanding of the HIV MTCT risks, and the effectiveness of ART, should be done prior to counselling about the risk of having a chromosomally abnormal baby, the option of amniocentesis and the risk of vertical transmission of HIV during the procedure.
- HIV positive AMA women attending academic hospitals in Johannesburg and considering prenatal testing for chromosome analysis of their fetuses should have

prompt access to HIV combination therapy to reduce the risk of MTCT at the time of the invasive procedure. There should be a national standardisation of the approach to HIV positive AMA women requesting amniocentesis; this would require auditing as new drug therapies and government policies arise.

- Further studies to examine the rationale behind women's decisions about their pregnancies, their HIV status and their risk of having a baby with a chromosome abnormality are required before a full understanding of their decision-making process is achieved and therefore optimal genetic counselling implemented.
- Education of doctors, nursing staff and HIV and genetic counsellors at hospitals with respect to standardised and effective management of HIV positive AMA women during pregnancy and birth, including discussion of TOP.

4.6 Summary

The goals of genetic counselling include promotion of "health enhancing behaviours", improvement of risk perception and empowering patients to decide about their reproductive choices (Biesecker, 2001). All these goals are pertinent in the counselling of an HIV positive, pregnant woman of AMA.

It is essential that awareness of HIV is improved, and attitudes and social norms are changed (Lamptey, 2002). Reducing the transmission of HIV will slow the epidemic. For there to be a successful HIV prevention program, adequate medical care and treatment are essential. HIV counselling and testing are important for pregnant women to minimise vertical transmission. Future challenges include: reducing stigmatisation and

discrimination, increasing resources for prevention strategies, improved clinical care, better access to care, and improved infrastructure to deal with the epidemic (Lamptey, 2002).

4.6.1 Study Findings

The main findings of this study were the following:

- A significant proportion of AMA women counselled at the three main academic hospitals in Johannesburg are HIV positive
- HIV positive AMA women were less inclined to accept prenatal testing for chromosome abnormalities than the HIV negative AMA women
- A significantly higher number of the older AMA women requested amniocentesis compared to the younger AMA women.
- There is no standard approach for the management of HIV positive AMA women requesting amniocentesis with regard to the provision of prophylactic antiretroviral treatment at the time of prenatal testing.

Thus two of the five aims set out in section 1.4 were fully achieved: firstly, the documentation of the number of AMA women attending genetic counselling whose HIV status was known, and the percentage who were HIV positive, the secondly the comparison of amniocentesis uptake between HIV positive and HIV negative AMA women. The other three aims, which were to establish the women's perceptions regarding the impact of their HIV status on their future health and the health of their babies, the documentation of the HIV positive women's knowledge regarding termination of pregnancy for MTCT risk, and the impact on the women's decision making of ART requirement prior to amniocentesis, were partially achieved. Trends were established but need to be confirmed by further

studies. This was not possible in the time frame of the study. It can however be inferred from these data that the HIV positive AMA women were aware that HIV is a serious, terminal illness, that they were however mostly unaware of the option of TOP for the risk of MTCT, and those who considered TOP may have been dissuaded by fear of enmity from their families or from the nursing staff. Women appeared to appreciate the concept of risk as verified by the fact that the older AMA women, and the HIV negative AMA women, were more inclined to accept prenatal testing for chromosome analysis than the younger AMA women and the HIV positive AMA women.

Where HAART throughout pregnancy and delivery by caesarean section are available, the risk of mother to child transmission is reduced to 1.2% (Cooper et al., 2002). Where only a dose of nevirapine perinatally to mother and baby are available, the minimum risk of mother to child transmission of HIV is 13.1% during pregnancy and birth. If the infant or child is breast fed the risk of transmission is between 10 and 20%. If the mother dies the infant/child mortality rate increases three to four fold. The risk of a child having a chromosome abnormality ranges from 0.52% (35 year old mother) up to 12.5% (49 year old mother). These chromosomal risks cannot be looked at in isolation while disregarding the greater risks of HIV infection. This does not suggest that AMA counselling be negated, as the risks remain significant. And the double tragedy of an HIV positive child that also has Down syndrome exits. It is important that measures be put in place to deal with the increasing numbers of HIV positive pregnant women of advanced maternal age.

In conclusion, if the risks of vertical transmission of HIV from mother to child are reduced, and they become less significant than the risks associated with increasing maternal age,

then testing for chromosome abnormalities becomes a viable and relatively safe option for HIV positive AMA women.