

CHAPTER 2

SUBJECTS AND METHODS

2.1 PATIENT ASCERTAINMENT

The study is a prospective, descriptive report of women of childbearing age from an urban black SA population, namely from Soweto, Johannesburg. The study was conducted at the Valvular Heart Clinic at the CHB Hospital which by nature of its situation serves such a population. Patients, who take warfarin regularly (mainly for a cardiac indication), attend this clinic at three monthly intervals, when they have a blood test to check INR levels and are examined by a cardiologist. They come to the satellite pharmacy at the clinic monthly to fetch their medication between their INR checks.

The study was conducted from June 2003 to November 2003, and most women eligible for the study should therefore have attended the clinic during this period (two cycles of three monthly visits). Women aged 18 - 45 years currently attending the Valvular Heart Clinic at the CHB Hospital, who have had at least one pregnancy on warfarin, were eligible for inclusion in the study. Ethics approval for the study was obtained from the Committee for Research on Human Subjects (Medical) of the University of the Witwatersrand (protocol number M020214).

Of the women approached to enter the study, 126 were interviewed. Two of these interviews were not included in the final analysis, because the subjects did not meet the inclusion criteria (see section 3.1). A total of 318 pregnancies were reported by the 124 women, 223 having been exposed to warfarin.

Unfortunately the exact number of women approached for the study was not recorded. However, it can be noted anecdotally that very few women who fulfilled the inclusion criteria refused to be interviewed. Those who declined to take part in the study were often tearful and stated that they were too traumatized by their experiences in pregnancy (on warfarin) to discuss details about these pregnancies.

2.2 INTERVIEW SCHEDULE

After obtaining written consent, study subjects were interviewed individually according to a set interview schedule (see Appendix A). The women were interviewed on the day they attended the clinic for their INR checks and doctor's appointment. To maintain privacy, they were interviewed in a quiet room or area away from other patients, but still within the clinic. Interviews were conducted by myself and a trained research assistant, Sister Thandi Zwane, from the Department of Human Genetics. Sister Zwane also acted as a translator, and she was present at every clinic where patients were recruited for the study. She conducted the interviews in languages other than English or Afrikaans where necessary. Demographic information gathered included the patient's date of birth/age, level of education, reason for requiring warfarin therapy, and date of commencing therapy. Where possible this information was verified with the patient's outpatient card.

The patient's usual current dose of warfarin, names and doses of concomitant medication, INR result of the current and previous visit, and the INR result six months prior to the current visit was verified by consulting the outpatient card and computerized data of blood results.

In order to ascertain the level of information being given to patients, directly relevant to their warfarin therapy, questions were asked about their current method of contraception, provision

of information regarding side effects of warfarin in pregnancy, and whether they had been referred for genetic counselling. Their knowledge of the side effects of warfarin in pregnancy was specifically questioned in an open-ended question.

To ascertain pregnancy outcomes in the study subjects, details were asked about each of their pregnancies, whether they were on anticoagulation in the pregnancy, the management during the pregnancies as regards timing of warfarin and heparin therapy, details of the outcome of each pregnancy, and details about any affected children.

Study subjects with children reported to be abnormal were offered an appointment at the Genetic Clinic at the CHB Hospital.

Where patients did not know about the effects of warfarin in pregnancy, they were not given specific information in this regard until the questionnaire had been completed. If they wanted more information, they were briefly counselled after conclusion of the interview about the risks to them and their fetus if exposed to warfarin in pregnancy. Specifically, they were told that warfarin crosses the placenta, and that some fetuses exposed to the drug in the first trimester could have abnormalities. The abnormalities that were emphasized were the underdevelopment of the nasal bone resulting in a very flat nasal bridge that could cause respiratory difficulty. The women were also told that some fetuses exposed to warfarin at any time during pregnancy were at risk of having brain abnormalities. Further, they were told that bleeding could occur in the warfarin-exposed fetus at any time during the pregnancy. They were told that this risk was particularly high if the fetus was exposed to warfarin around the time of delivery, which is why heparin therapy should be started before delivery. The women were also told that compared to other pregnant women, women on warfarin are at higher risk

for having a miscarriage or spontaneous intrauterine death, and that they were at increased risk of bleeding, especially during the delivery.

The women were also told that certain regimens in pregnancy (like changing warfarin to heparin from weeks six to twelve) could reduce the risks of having babies with nasal and bone abnormalities. The women were urged to contact their doctors at the Valvular Heart Clinic for more information regarding the safety of them falling pregnant. They were given specific instructions about what to do should they fall pregnant while taking warfarin. These details included presenting to the Antenatal Clinic at or before six weeks of pregnancy so that discussions about their anticoagulation could commence, and that they should attend the Obstetric Cardiac Clinic throughout their pregnancies for careful monitoring and care.

2.3 STATISTICAL ANALYSIS

Data were entered on a Microsoft Excel XP datasheet. Frequencies, means and percentages of the demographic data were calculated using this programme. These analyses were also conducted to determine the number of warfarin-exposed and non-exposed pregnancies, and the outcomes of these pregnancies were compared. The outcome differences between these groups were subject to chi-square analysis to determine if they were statistically significant. Chi-square analysis was performed with the assistance of Dr A B Lane of the National Health Laboratory Service, and by a statistician, Dr Ann Müller, of the Rand Afrikaans University. P-values of <0.05 were taken as significant.