

The effect of maternal HIV infection on maternal conditions and perinatal deaths in southwest Tshwane

R. C. PATTINSON, M. H. HULSBERGEN¹, L. VAN HOORICK¹

MRC Maternal and Infant Health Care Strategies Research Unit, Department of Obstetrics and Gynaecology, University of Pretoria, Pretoria, South Africa.

¹Registrar, Department of Obstetrics and Gynaecology, KULeuven, Belgium.

Correspondence at: Professor R.C. Pattinson, Department of Obstetrics and Gynaecology, Klinikala Building, University of Pretoria, PO Box 667, Pretoria, 0001.

E-mail: Robert.pattinson@up.ac.za

Abstract

Aim: To describe the effect of HIV infection on maternal and perinatal disease in south west Tshwane.

Setting: Southwest Tshwane has a low to low-middle income urban population and is served by Pretoria West and Laudium Midwife-Obstetric Units (MOUs) and Kalafong Hospital and fourteen primary care clinics which refer to those institutions. These are all public health institutions.

Methods: Only data from women from southwest Tshwane between 1 January 2006 and 30 September 2008 was used in the study. As part of routine audit, the maternal HIV status was recorded as well as major maternal antenatal and intrapartum complications. All perinatal deaths along with their HIV status were recorded in the Perinatal Problem Identification Programme (PIIP) and the primary obstetric cause and final neonatal cause of deaths. The causes of perinatal deaths from HIV infected, negative and unknown were analysed.

Results: There were 17184 births in southwest Tshwane in the time period analysed, of which mothers (86.1%) were counselled and (81.9%) were tested, and of these 21.5% HIV infected.

The incidence of hypertension in the HIV infected women was 3.2% significantly lower than the 5.0% in the HIV negative group (OR 0.63, 95% CI 0.50, 0.79). There was a trend to more HIV infected women had a PPH (OR 1.21, 95% CI 0.99, 1.47). The overall caesarean section rate was 28.3% with significantly more HIV infected women having both elective and emergency caesarean sections (OR 1.21, 95% CI 1.10, 1.31).

The perinatal mortality rate was 33.8/1000 births (> 500 g) in the HIV infected group and 26.1/1000 births in the HIV negative group (OR 1.30, 95% CI 1.03, 1.65) mainly due to the increased neonatal death rate. The low birth weight (LBW) rate for HIV infected women was 19.8% compared with 14.3% with HIV negative women ($p < 0.0000$); OR 1.47, 95% CI 1.32, 1.64). There significantly more perinatal deaths due to spontaneous preterm birth, infection and intrapartum asphyxia in the HIV infected mothers.

Conclusion: In southwest Tshwane a HIV infected mother has a decreased risk of hypertension, a trend towards increased postpartum haemorrhage and a thirty percent increased risk of having a perinatal death compared to an HIV negative mother, this is due mainly to spontaneous preterm birth, infections and intrapartum asphyxia.

Key words: HIV in pregnancy, perinatal mortality, intrapartum asphyxia, hypertension in pregnancy, spontaneous preterm birth.

Introduction

Maternal HIV infection is the most common underlying cause of maternal and infant deaths in South Africa. AIDS is the single most common cause of

maternal death, reported as being responsible for 43.7% of all facility based deaths (Moodley *et al.*, 2010) Eighty percent of the children who died and their or their mothers' HIV status was known were either infected or HIV exposed (Saving Children, 2005).

The effect on maternal conditions and perinatal deaths in South Africa is less clear. A review of the worldwide literature has demonstrated a clear association between HIV infection and stillbirth, the latter being almost four times more likely in an HIV infected pregnant woman than in one who is not (Brocklehurst and French, 1998). An association has also been found with low birth weight babies (Brad-dick *et al.*, 1990; Bulterys *et al.*, 1994; Taha *et al.*, 1995).

To help determine this relationship in our region, a study was carried out in southwest Tshwane. The aim was to examine the relationship between maternal HIV infection maternal conditions and perinatal death, and to determine the primary obstetric causes responsible for these perinatal deaths. During the period the relatively few women were on Highly Active Antiretroviral Therapy (HAART) and the standard Prevention of Mother to Child Transmission (PMTCT) for HIV protocol consisted of Nevirapine during labour only.

Methods

The people that attend the southwest Tshwane sub-district public medical services are mainly indigent, urban South Africans with black African being the most common race by far. The socio-economic status of this group is fairly homogeneous for the population served by the public health institutions. Patients using private health institutions were not included in this study. Southwest Tshwane sub-district is served by Pretoria West and Laudium Midwife-Obstetric Units (MOUs) and Kalafong Hospital. Fourteen primary care clinics refer to those institutions. Only data from women from these institutions in southwest Tshwane between 1 January 2006 and 30 September 2008 was used in the study.

As part of routine audit, the maternal HIV status was recorded as HIV negative, infected, declined or unknown in all women who gave birth from the area. Data on the CD4 count is not routinely collected and was not available for this audit. At the time of the study HAART was not readily available for pregnant women, and was only initiated at a CD4 count of 200. Hypertension, pre-eclampsia and eclampsia, postpartum haemorrhage and route of delivery are recorded routinely per patient on the patients data form. Postpartum haemorrhage was defined as the need for treatment, either medical or surgical. All perinatal deaths were also recorded in the Perinatal Problem Identification Programme (PIIP) (Pattinson, 2003a; 2003b) and the primary obstetric cause and HIV status was allocated to each death. The causes of perinatal deaths from HIV infected, negative and unknown were analysed.

Table 1. — Maternal HIV testing in southwest Tshwane.

	Number	%	% tested
HIV +	3014	17.5	21.4
HIV -	11053	64.3	
Declined	740	4.3	
Not Tested	2377	13.8	
Total	17184	100	

Standard statistical techniques were used to analyse the data. The Chi Squared Test was used to compare the groups of categorical data and the Odds Ratio and 95% Confidence Interval derived from this. Student t test was used to compare continuous variables. The PPIP audit has been registered with the Faculty of Health Sciences of University of Pretoria's ethics committee. All forms of patient identification were removed after data cleaning had been completed. The hospital superintendent has inspected the security of the databases and was satisfied with the anonymity of the women.

Results

There were 17184 births in southwest Tshwane in during the 33 month study period, of which mothers (86.2%) were counselled and (81.9%) were tested. Table 1 illustrates the results of HIV testing in the pregnant women. The HIV positive rate was 21.4% in the women tested. 11.7% of the HIV positive women were taking highly active antiretroviral therapy (HAART).

Table 2 and 3 compares the maternal conditions in HIV infected women with those not infected. There were 353 women on HAART, 4 women (1.1%) had hypertension, 7 women (1.98%) had pre-eclampsia or eclampsia, and in total 11 women (3.1%) had hypertensive conditions. Twenty women on HAART (5.6%) had a PPH, and 117 women (33.1%) had caesarean sections. Because of the relatively small number of women on HAART we combined all the HIV infected women into one group. HIV infected women had significantly less hypertensive conditions than HIV negative women. The HIV infected women also were delivered more frequently by caesarean sections and had a trend to more postpartum haemorrhage.

The mean birth weight of the babies from the HIV infected women was 2808.7 ± 707 g, and for the HIV negative mothers was 2942.4 ± 675 g ($p < 0.0001$). The low birth weight (LBW) rate for HIV infected women was 19.8% compared with 14.3% with HIV negative women ($p < 0.0000$); OR1.47, 95% confidence intervals 1.32 and 1.64) and 14.6% for the unknown status group.

Table 2. — Comparison of maternal conditions.

	HIV + (%)		HIV – (%)		Unk. (%)		Total (%)	
Hypertension	33	(1.1)	204	(1.8)	43	(1.4)	280	(1.6)
Pre-eclampsia and eclampsia	63	(2.1)	344	(3.1)	78	(2.5)	485	(2.8)
All hypertensive conditions	96	(3.2)	548	(5.0)	121	(3.9)	765	(4.5)
Caesarean Section	946	(31.4)	3040	(27.5)	877	(28.1)	4863	(28.3)
Postpartum haemorrhage	148	(4.9)	453	(4.1)	138	(4.4)	739	(4.3)
Total pregnant women in each group	3014		11053		3117		17184	

Table 3. — Comparison of maternal conditions in HIV positive and HIV negative women.

	P	OR	95% CI
Hypertension	0.0057	0.59	0.40-0.86
Pre-eclampsia and eclampsia	0.0084	0.66	0.50-0.88
All hypertensive conditions	0.00005	0.63	0.50-0.79
Caesarean section	0.00003	1.21	1.10-1.31
Postpartum Haemorrhage	0.057	1.21	0.99-1.47

OR - Odds Ratio; 95% CI – 95% confidence intervals.

The mortality rates are shown in Table 4, the mortality rates per primary obstetric cause are shown in Table 5 and the final neonatal causes of death in Table 6. The perinatal mortality rate (PNMR) was significantly higher in the HIV infected women due mainly to the increased neonatal death rate. Spontaneous preterm birth, intrapartum asphyxia and infections as the primary obstetric cause of death occurred significantly more frequently in HIV infected women, as did neonatal deaths due to immaturity.

Discussion

In this audit comparing HIV infected pregnant women with HIV negative pregnant women, the HIV infected women had significantly less hypertension, were more likely to have a caesarean section and tended towards having more postpartum haemorrhages. The PNMR and neonatal death rate (NNDR) were higher in HIV infected women due mainly to increased perinatal deaths due to spontaneous preterm birth, intrapartum asphyxia and infections. Infants of HIV infected women had a significantly lower mean birth weight than HIV negative women, but this appears to be due to more premature deliveries rather than growth restricted babies.

This paper suffers from the usual weaknesses of a retrospective study and the 18.1% where the HIV status was unknown and in those who were HIV infected the CD4 counts were not available. The unknown status being similar in numbers to the HIV infected group could significantly alter the results if the HIV status was known in all cases. Data was recorded just after delivery in the individual patient

data sheets. All stillbirths are discussed after delivery and neonatal deaths are discussed with the paediatricians at a weekly neonatal morbidity and mortality meeting. The PPIP form is filled in at these meetings. Thus the data was collected at the time of the events, which might mitigate some of the weaknesses.

The finding that hypertensive conditions were less frequent in HIV infected women in our population was a surprise, but is biologically plausible with HIV depressing the immune system. The prevalence of hypertensive conditions in this study was almost half of that recorded by Frank *et al.* (2004) who studied a similar albeit smaller population. This might be due to the less severe cases not being recorded on the data sheets. However, Frank *et al.* (2004) did not find any association between HIV infection and hypertensive conditions which is difficult to explain. Hall (2007) in reviewing the association of pre-eclampsia and HIV infection could not find a consistent answer. The association between pre-eclampsia is complex and can only be fully understood when the variables such as the CD4 counts, viral load and antiretroviral therapy are accounted for, which to date have not been (Hall, 2007).

During the study period, HIV infection on its own was not regarded as an indication for caesarean section because of limited resources in the sub-district and caesarean section was supposed to be limited to obstetric indications. The significantly more caesarean sections being performed in HIV infected women probably reflect the result of a more liberal approach to obstetric indications to caesarean sections in this population. The trend towards more postpartum haemorrhage in HIV infected women is

Table 4. — Mortality rates (500 g+) for HIV status.

	HIV +	HIV –	Unknown	P*	Odds Ratio*	95% Confidence Intervals*
SBR	23.6	21.4	21.7	0.52	1.1	0.8-1.45
NNDR	10.7	4.7	6.17	0.0004	2.26	1.4-3.6
PNMR	33.8	26.1	27.8	0.02	1.3	1.03-1.65

* Comparison between HIV positive and HIV negative groups
SBR – Stillbirth Rate; NNDR – Neonatal Death Rate; PNMR – Perinatal Mortality Rate.

Table 5. — Perinatal mortality rate (PNMR) per primary obstetric cause (500g+).

Primary Obstetric Cause (PNMR/1000 births per disease category)	HIV + deaths (n = 102)	HIV – deaths (n = 288)	Unk. deaths (n = 87)	P*	OR	95% CI*
Unexplained Stillbirth	7.63	8.14	7.70	NS		
Spontaneous Preterm Birth	7.30	3.80	8.98	0.017	1.93	1.11-3.32
Intrapartum Asphyxia	2.32	0.54	0.64	0.02	4.2	1.3-14.3
Trauma	0.66	0.36	0.64	NS		
Hypertension	2.99	3.08	2.25	NS		
Antepartum Haemorrhage	2.32	2.53	3.53	NS		
Infections	3.32	0.45	1.28	0.0001	2.32	2.32-24.66
Fetal abnormality	1.00	1.36	0.64	NS		
Maternal Disease	1.00	0.72	0.64	NS		
IUGR	0.33	0.27	0.64	NS		
Other	4.98	4.80	0.96	NS		
Total PNMR	33.84	26.06	27.91	0.02	1.3	1.03-1.65
Total Births	3014	11053	3117			

Unk. = Unknown; OR - Odds Ratio; 95% CI – 95% confidence intervals.

Table 6. — Final causes of neonatal death.

Final Cause Neonatal Death	HIV + (n = 31)	HIV – (n = 51)	Unk. (n = 21)	P*	OR	95% CI*
Immaturity Related	6.19	2.51	4.96	0.0038	2.47	1.31-4.66
Hypoxia	0.69	0.28	0.66	NS		
Trauma	0.00	0.00	0.00	NS		
Infections	1.03	0.28	0.66	NS		
Congenital abnormalities	0.69	0.37	0.00	NS		
Unknown/other	2.06	1.30	0.66	NS		
Total	10.66	4.74	6.94	NS		

Unk. = Unknown; OR - Odds Ratio; 95% CI – 95% confidence intervals
* Comparison between HIV positive and HIV negative groups.

probably the result of the increased caesarean sections in the HIV infected women and the association of thrombocytopaenia with HIV infection.

A recent study performed by researchers in KwaZulu-Natal has found similar increases in perinatal mortality. They showed a 75% increased risk of an HIV infected woman having an adverse pregnancy outcome (antepartum death, spontaneous abortion or stillbirth) (Rollins *et al.*, 2006).

The PNMR was significantly higher due to an excess of, spontaneous preterm birth, intrauterine

infection and intrapartum asphyxia. The lack of significance of unexplained stillbirths in the HIV infected group was most likely due to the lack of HIV testing in women who delivered unexplained stillbirths. Most of these women delivered macerated stillbirths and the clinicians were reluctant to request women to have HIV tests at that time. This is supported by the high prevalence of unexplained stillbirths in the unknown HIV status group. The relatively low rate of unknown HIV status in women with neonatal deaths is due to clinicians being more

active in counselling women for HIV testing where infant feeding choices become urgent and relevant.

The finding of more preterm births in HIV infected women has been well recorded and it appears that these babies are mostly appropriately grown premature infants than growth-restricted infants. Three other studies in South Africa have failed to show an association between growth restriction and the HIV positive status (Coetzee and Isaacs, 2006; Alberts *et al.*, 2007; Widmer *et al.*, 2007). Preterm labour can be explained by the probable greater prevalence of amniotic fluid infection in HIV infected women. This is also supported by the increased number of deaths due to congenital infections in HIV infected women.

The significant increase of intrapartum asphyxia in HIV infected babies was unexpected and unexplained. The routine delivery of HIV infected women by caesarean section in developed countries might have masked this observation. Fetal heart rate monitoring using ultrasound is the main method of fetal heart rate monitoring in the three units; internal monitoring and fetal scalp sampling are not performed because of our high prevalence of HIV infection and the relatively large numbers of women whose HIV status is still unknown. It is unlikely that there was reluctance for invasive measures as HIV infected women had about a twenty percent increased risk of having a caesarean section. A possible explanation is that these fetuses had severe congenital infections that were mistaken for intrapartum asphyxia. Alternatively, previous intra-amniotic infections might make the fetus more susceptible to hypoxia during labour due to the fetal immune response syndrome. The numbers of fetuses involved are small and this observation will need to be confirmed by other studies.

Conclusion

In southwest Tshwane a HIV positive mother has a thirty percent increased risk of having a perinatal death compared to an HIV negative mother. There was also a different pattern of primary obstetric causes of perinatal deaths in HIV infected pregnant women with spontaneous preterm birth, infection and intrapartum asphyxia occurring significantly

more frequently in HIV infected women. Surprisingly HIV infected mothers had a 37% reduction in hypertensive condition in pregnancy.

Acknowledgements

We would like to thank Mrs Cathy Bezuidenhout for entering and keeping the databases up to date and in helping extract the information.

References

- Alberts BC, Jeffery BS, Makin JD *et al.* Outcome of pregnancy in HIV infected women. 26th conference on priorities in perinatal care in Southern Africa. Hartenbos, March 2007.
- Braddick MR, Kreiss JK, Embree JB *et al.* Impact of maternal HIV infection on obstetrical and early neonatal outcome. *AIDS*. 1990;4:1001-5.
- Brocklehurst P, French R. The association between maternal HIV infection and perinatal outcome: a systematic review of the literature and meta-analysis. *BJOG*. 1998;105:836-48.
- Bulterys M, Chao A, Munyemana S *et al.* Maternal Human Immunodeficiency virus 1 infection and intrauterine growth: a prospective cohort study in Butare, Rwanda. *Pediatr Infect Dis J*. 1994;13:94-100.
- Coetzee EJ, Isaacs F. Does maternal HIV infection cause intrauterine growth restriction. A community based ultrasound study. Proceedings of 25th conference on priorities in perinatal care in Southern Africa. Champagne Sports Resort, March 2006.
- Frank KA, Buchmann EJ, Schackis RC. Does Human Immunodeficiency Virus Infection Protect Against Preeclampsia-Eclampsia? *Obstet Gynecol*. 2004;104:238-42.
- Hall DR. Is pre-eclampsia less common in patients with HIV/AIDS? *J Reprod Immunol*. 2007;76:75-7.
- Moodley J, Pattinson RC, Baxter C *et al.* Strengthening HIV services for pregnant women: An opportunity to reduce maternal mortality rates in Southern Africa/sub-Saharan Africa. *BJOG* 2010 (in press).
- Pattinson RC for the PPIP sentinel sites. Why babies die – a perinatal care survey of South Africa. *S Afr Med J*. 2003a;93(6):445-50.
- Pattinson RC. Challenges in saving babies – avoidable factors, missed opportunities and substandard care in perinatal deaths in South Africa. *S Afr Med J*. 2003b;93(6):450-5.
- Rollins NC, Hoosen MC, Bland RM *et al.* Pregnancy outcomes in HIV-infected and uninfected women in rural and urban South Africa. *J Acquir Immune Defic Syndr*. 2007;44:321-8.
- Taha TE, Dallabetta GA, Canner JK *et al.* The effect of human immunodeficiency virus infection on birth weight, and infant and child mortality in urban Malawi. *Int J Epidemiol*. 1995;24:1022-9.
- Saving Children 2005: A survey of child healthcare in South Africa. Government Printer, Pretoria, 2007.
- Widmer TA, Theron GB, Carolus E *et al.* Prevalence and risks of asymptomatic bacteriuria among HIV positive pregnant women. 26th conference on priorities in perinatal care in Southern Africa. Hartenbos, March 2007.