The impact of HIV infection on maternal deaths in South Africa

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Aim. To assess the impact of HIV infection on maternal deaths in South Africa from 2008 to 2010.

Method. Data extracted from the National Committee on Confidential Enquiries into Maternal Deaths database of maternal deaths, numbers of births from the District Health Information System (DHIS), and the estimated prevalence of HIV infection in the general population from the antenatal HIV and syphilis surveys were analysed. Estimations of the institutional maternal mortality ratios (iMMRs) for HIV-positive women compared with HIV-negative women and women of unknown status were made for each province and category of underlying cause of disease.

Results. The estimated iMMR for HIV-positive women was 430/100 000 live births and that for HIV-negative women 75/100 000 live births. In all categories of causes of death, the iMMR was increased in HIV-positive women. The major categories of causes of maternal death in HIV-negative women were complications of hypertensive disorders of pregnancy (18.8/100 000 live births), obstetric haemorrhage (17.2/100 000 live births) and medical and surgical disorders (11.5/100 000 live births), while in HIV-positive women they were non-pregnancy-related infections (NPRIs) (267.3/100 000 live births), obstetric haemorrhage (38.4/100 000 live births) and pregnancy-related sepsis (miscarriages and sepsis following viable pregnancies – 34.1/100 000 live births). The major complications resulting in deaths were shock (38.0%), cardiac failure (31.9%) and respiratory failure.

Tuberculosis (26.9%), community-acquired pneumonia (26.7%) and pneumocystis pneumonia (13.3%), and cryptococcal meningitis (4.2%) and other meningitis (8.7%) were the main underlying causes of death in the NPRI group, of which 87.4% were HIV positive. Complications of highly active antiretroviral therapy (HAART) were recorded as the underlying cause of death in 73 women (8.1% of those on HAART).

Conclusion. HIV infection is the most important condition contributing to maternal death in South Africa. HIV-positive women are more likely to die of any underlying cause than HIV-negative women, with NPRI being the most common contributory condition.

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Sub-Saharan Africa is the epicentre of the HIV epidemic, and South Africa (SA) has the largest population living with HIV infection.[1] For the past 7 years the prevalence of HIV infection has been approximately 30% in women attending antenatal care in the public sector.[2] HIV infection has been recognised as having a major impact on maternal deaths in SA, but the maternal death classification system did not allow for detailed analysis of its impact.[3] The World Health Organization (WHO) has introduced a new classification system,[4,5] the introduction of which into the SA Confidential Enquiry into Maternal Deaths (CEMD) programme has made it possible to identify an underlying cause of death that is mutually exclusive from other causes, and also to record contributory conditions. HIV infection is regarded as a contributory condition in maternal deaths. The system enables the HIV status of all women to be recorded, and a detailed analysis of the impact of HIV infection to be made. This article reports on this analysis.

Methods

The National Department of Health implemented the CEMD programme during 1998 in SA. All institutional maternal deaths are entered into a maternal death notification form (MDNF), and each death is assessed by two assessors who complete a maternal death assessment form. The data from the MDNF are entered into a computerised database and sent to a national secretariat. The national secretariat also collects hard copies of the MDNF. The HIV status of every maternal death, the underlying cause of death, the contributory conditions and final complications resulting in death are recorded.

The WHO defines an underlying cause of death as 'the disease or injury which initiated the train of morbid events leading directly to death or the circumstances of the accident or violence which produced the fatal injury'.[6] This is the same as the primary cause of death, but because these terms are used differently in different settings and in order to avoid confusion and allow comparison it was agreed that it was preferable to stick to one agreed term. A contributory condition is defined as 'a significant condition that unfavourably influences the course of the morbid process and thus contributes to the fatal outcome, but which is not related to the disease or condition directly causing death'.[4] A contributing condition is therefore a condition present in the woman that may have contributed to, or been associated with, her

death (*played a part, aggravated to a degree*), but did not directly cause her death. It may be new or pre-existing, and there may be more than one. Contributing conditions are therefore not part of the classification of cause of death itself, but are nevertheless very important. In a case where an HIV-positive pregnant woman died due to tuberculosis, the underlying cause of death is therefore classified as tuberculosis and the contributory factor as HIV infection. In this way the impact of HIV infection can be assessed in all maternal deaths.

An assessment is also made on the quality of care. The data are analysed every 3 years and published in the Saving Mothers Reports (SMRs), which is disseminated to all healthcare workers.

The District Health Information System (DHIS) records all births in public health institutions in SA and a National HIV and Syphilis Antenatal Survey is conducted annually. Data from these sources are also used in the SMRs. The institutional maternal mortality ratio (iMMR) is calculated from the number of maternal deaths recorded by the National Committee on Confidential Enquiries into Maternal Deaths (NCCEMD), the denominator being the number of live births recorded by the DHIS.

Results

Over the 3-year period of the analysis (2008 - 2010), there were 4 867 maternal deaths in SA. NPRIs (mainly HIV/AIDS) were the most common conditions contributing to maternal death (1 969 deaths, 40.5%).

Close to 4 out of 5 women (79.3%) who died in pregnancy, childbirth or the puerperium were tested for HIV infection, and of those tested 70.4% were HIV positive. Table 1 shows details of the HIV status of all the women who died in the triennium under review. The proportional distribution of women tested is set out in the right-hand column.

Table 2 shows the age distribution of those who were tested in comparison with the general population in each age group. There was an excess of deaths in HIV-negative women aged <20 years and >35 years. The majority of deaths in HIV-positive women occurred between 25 and 39 years, slightly older than the peak age of pregnancy in the general population, which was 20 - 24 years.

Table 3 shows that most HIV-negative women were primigravidas, whereas most HIV-positive women were multiparous.

Among HIV-positive women, the majority of underlying causes of death were diagnosed antenatally, but most deaths occurred in the postpartum period. Table 4 shows the proportion of women tested for HIV infection per province for 2008 - 2010. KwaZulu-Natal had the highest proportion of HIV-positive maternal deaths, whereas the Western Cape had the lowest.

Table 5 shows the estimated iMMR per province for HIV-positive and HIV-negative women, and those whose HIV status was unknown. An inference was made that the proportions of women tested per province are the same as the proportions of the maternal

Table 1. HIV status, 2008 - 2010

HIV status	*n* (%)	% tested
HIV-negative	1 166 (24.0)	29.6
HIV-positive not requiring HAART	949 (19.5)	24.1
AIDS not receiving HAART	938 (19.3)	23.8
AIDS receiving HAART	882 (18.1)	22.4
Declined	39 (0.8)	
Unknown	992 (20.4)	

HAART = highly active antiretroviral therapy.

Table 2. Distribution (%) of maternal deaths with respect to age and HIV status, and compared with the general population

Age (years)	HIV-negative (*n*=1 166)	HIV-positive (*n*=2 769)	Unknown (*n*=1 031)	General population
<20	17.2	3.9	10.3	12.5
20 - 24	23.2	18.2	21.0	28.1
25 - 29	17.9	32.2	24.6	26.3
30 - 34	17.5	25.3	21.0	18.5
35 - 39	16.7	16.0	14.3	10.7
40 - 45	6.6	3.6	6.5	3.4
>45	0.7	0.4	1.1	0.5
Unknown	0.3	0.5	1.3	0.1

Table 3. Distribution (%) of maternal deaths with respect to parity and HIV status

Parity	HIV-negative (*n*=1 166)	HIV-positive (*n*=2 769)	Unknown (*n*=1 031)
0	41.3	26.2	29.7
1	21.9	29.2	21.0
2	17.1	22.6	16.1
3	8.1	10.3	8.3
4	5.7	5.2	6.5
5	2.3	1.6	1.8
≥6	2.1	0.7	3.2
Unknown	1.5	4.2	13.3

Table 4. HIV status of maternal deaths per province (%)

HIV status	EC	FS	GP	KZN	LIMP	MP	NW	NC	WC	Total
HIV-negative	27.9	26.0	19.7	18.0	28.2	20.1	16.1	35.4	42.1	23.5
HIV-positive	56.5	54.0	52.2	67.2	48.7	54.5	57.1	47.0	40.9	55.8
Unknown	15.6	20.0	28.2	14.8	23.1	25.4	26.8	17.7	17.1	20.8

EC = Eastern Cape; FS = Free State; GP = Gauteng Province; KZN = KwaZulu-Natal; LIMP = Limpopo; MP = Mpumalanga; NW = North West, NC = Northern Cape; WC = Western Cape.

Table 5. Approximate institutional maternal mortality ratio per province for HIV-infected women

	EC	FS	GP	KZN	LIMP	MP	NW	NC	WC	SA
Total live births, *N*	359 104	146 332	580 199	578 245	366 649	211 979	169 937	62 005	287 501	2 761 951
Women with unknown status,* *n*	56 142	29 266	163 511	85 533	84 520	53 939	45 519	10 964	49 058	573 414
Estimated women with known status	302 962	117 066	416 688	492 712	282 129	158 040	124 418	51 041	238 443	2 188 537
HIV prevalence†	28.1	30.1	29.8	39.5	21.4	34.7	30	17.2	16.9	29.4
HIV-positive women,‡ *n*	85 132	35 237	124 173	194 621	60 376	54 840	37 325	8 779	40 297	643 430
HIV-negative women,§ *n*	217 830	81 829	292 515	298 091	221 754	103 200	87 093	42 262	198 146	1 545 107
iMMR HIV-positive pregnant women/100 000	471.03	658.40	369.65	389.99	496.89	390.23	600.13	877.09	255.60	430.35
iMMR HIV-negative pregnant women/100 000	90.90	136.87	59.14	68.10	78.47	76.55	72.34	137.24	53.50	75.46
iMMR HIV-unknown pregnant women/100 000	197.71	293.85	151.67	195.25	168.01	185.40	230.67	264.49	87.65	179.80

Data include coincidental deaths.

EC = Eastern Cape; FS = Free State; GP = Gauteng Province; KZN = KwaZulu-Natal; LIMP = Limpopo; MP = Mpumalanga; NW = North West, NC = Northern Cape; WC = Western Cape; SA = South Africa; iMMR = institutional maternal mortality ratio.

* Number estimated by assuming the same proportion of women tested as tested in maternal deaths (Table 4 'Unknown', row 3). That proportion was used to calculate the number from the total births per province, and the remainder gives the estimated number of women with known status.

† Prevalence from national antenatal HIV and syphilis survey reports.

‡ Number estimated by subtracting 'Unknown' HIV status from total births and calculating the number from the antenatal HIV prevalence survey from the remainder.

§ Number estimated by subtracting the estimated number of HIV-infected women from the remainder.

deaths that were tested for each province. The Northern Cape had high iMMRs of 877.1/100 000 positive women. The overall SA iMMR was 430.35/100 000 HIV-positive women.

Table 6 shows the proportion of NPRI deaths per province, as well as the iMMR per province resulting from these deaths. There is a wide range in the iMMR among the 9 provinces, the Western Cape having the lowest and the Free State the highest. Table 7 shows the comparison of HIV status and categories of underlying causes of death.

Table 6. Distribution of non-pregnancy-related infection within the provinces

	n (%)	Institutional MMR
Eastern Cape	280 (14.2)	77.97
Free State	157 (8.0)	107.29
Gauteng	310 (15.7)	53.43
KwaZulu-Natal	544 (27.6)	94.08
Limpopo	219 (11.1)	59.73
Mpumalanga	157 (8.0)	74.06
North West	153 (7.8)	90.03
Northern Cape	58 (2.9)	93.54
Western Cape	91 (4.6)	31.65
Total	1 969 (100.0)	71.29

MMR = maternal mortality rate.

Table 7. Comparison of HIV status and causes of maternal death (using estimated institutional maternal mortality ratio per 100 000 live births)

Cause of death*	HIV-negative	HIV-positive	Unknown
Medical and surgical disorders	11.5	24.2	16.7
NPRIs	6.6	267.3	25.6
Ectopic pregnancy	0.3	3.0	9.1
Miscarriage	1.4	9.9	17.6
Hyperemesis gravidarum	0.2	0.2	0.0
Pregnancy-related sepsis	4.1	24.2	6.8
Obstetric haemorrhage	17.2	38.4	30.5
Hypertension	18.8	27.4	37.0
Anaesthetic complications	4.1	4.8	4.5
Embolism	3.2	4.0	3.0
Acute collapse, cause unknown	3.2	9.2	6.8
Unknown	3.7	15.7	10.1
Total	74.4	428.3	167.8

NPRI = non-pregnancy-related infection.

*Excludes coincidental deaths.

NPRIs had the highest iMMR (267.3/100 000 live births) and the iMMR for each condition, except for hyperemesis gravidarum, was higher in HIV-positive women. Among women who died from obstetric haemorrhage, the iMMRs were 17.2 and 38.4/100 000

live births in HIV-negative and HIV-positive women, respectively. Similarly, women who had puerperal sepsis and were HIV positive had a 6 times higher iMMR than their HIV-negative counterparts.

Table 8 sets out the sub-categories of causes of death for NPRIs. Only 5.2% of those who died due to NPRI were HIV negative; 87.4% were HIV positive and in 7.5% the status was unknown. Tuberculosis (26.9%), community-acquired pneumonia (26.7%) and pneumocystis pneumonia (PCP) (13.3%), and cryptococcal meningitis (4.2%) and other meningitis (8.7%) were the main underlying causes of death in the NPRI group.

Complications of antiretroviral therapy were recorded as the underlying cause of death in 73 women (Table 9). These complications are relatively rare, but the number of deaths more than doubled to 42 in 2010. The increase was probably associated with the use of nevirapine (NVP) in the highly active antiretroviral therapy (HAART) regimen. The majority of the complications were liver failure and Stevens-Johnson syndrome, both associated with NVP.

Table 10 gives the final causes of maternal death in relation to HIV status at the time of death. Respiratory failure was the most common final cause of death in HIV-positive pregnant women. Meningitis was the most common cause of cerebral complications, and pulmonary oedema occurred most frequently in the cardiac failure group.

Discussion

Data from the current SMR (2008 - 2010) show that HIV/AIDS is continuing to have a major impact on maternal deaths in SA. The previous SMR (2005 - 2007) also showed that HIV/AIDS was the commonest cause of maternal mortality, but the maternal death notification system at that time did not allow for detailed analysis of the impact of HIV. It is well known that the number and proportion of maternal deaths associated with HIV have been difficult to determine with any certainty. The new amendment to the 10th revision of the WHO *International Statistical Classification of Diseases and Related Health Problems* (ICD-10),[4] however, was introduced to the SA CEMD system in 2008 and allows for the underlying cause of death to be established with more precision. The underlying causes are now mutually exclusive and a contributory condition such as HIV status is recorded for all maternal deaths. Using this system, we were able to perform a more detailed analysis of HIV-related deaths than had been possible previously and found that HIV/AIDS was a contributory condition in approximately 40% of all maternal deaths in the latest triennium under review (2008 - 2010).

The data from the present report were analysed before scale-up of HAART for pregnant women in SA from a CD4 count of 200 cells/µl to 350 cells/µl. We anticipate that the scale-up will result in a decrease in HIV-related maternal mortality in the next 3 - 5 years, particularly given that antenatal HIV testing rates are over 90% in all provinces.

The introduction of the new WHO ICD-10 amendment also allowed us to establish that the estimated iMMR for HIV-positive women was 430/100 000 live births, and that for HIV-negative women 75/100 000 live births. Despite the challenges of identification and classification of the causes of death, these figures provide evidence of the severe impact of HIV on maternal mortality in SA, a country with a high burden of this viral pandemic. The SA CEMD process is very rigorous

Table 8. Sub-categories of non-pregnancy-related infections and HIV status for 2008 - 2010

	HIV-negative	HIV-positive not qualifying for HAART	AIDS not receiving HAART	AIDS receiving HAART	Decline	Unknown	Total	%
NPRIs	102	360	735	625	13	134	1 969	
PCP	2	38	123	87	1	10	261	13.3
Other pneumonia	48	122	177	121	5	53	526	26.7
TB	28	77	220	177	5	22	529	26.9
Endocarditis	0	0	0	1	0	1	2	0.1
UTI	0	1	0	0	0	0	1	0.1
Appendicitis	0	4	1	0	0	0	5	0.3
Malaria	1	3	0	0	0	2	6	0.3
Cryptococcal meningitis	1	10	41	26	0	4	82	4.2
Other meningitis	11	44	50	48	1	17	171	8.7
Kaposi's sarcoma	0	2	11	9	0	0	22	1.1
Toxoplasmosis	0	0	1	0	0	0	1	0.1
Hepatitis	5	2	0	9	0	1	17	0.9
Gastroenteritis	3	20	41	33	1	5	103	5.2
Wasting syndrome	0	12	38	26	0	4	80	4.1
ART complications	0	7	6	60	0	0	73	3.7
Other	3	18	26	28	0	15	90	13.3

NPRIs = non-pregnancy-related infections; HAART = highly active antiretroviral therapy; PCP = pneumocystis pneumonia; TB = tuberculosis; UTI = urinary tract infection.

Table 9. Rates of complications of antiretroviral therapy for 2008, 2009 and 2010

	2008	2009	2010
Maternal deaths due to complications of ARVs, *n*	14	17	42
Approximate HIV-infected pregnant women per year, *n*	279 798	279 650	277 216
Maternal deaths due to complications of ARVs/pregnant HIV-infected women/100 000 births	5.00	6.08	15.15
Maternal deaths on HAART, *n*	214	306	362
Deaths due to complications of ARVs (of all maternal deaths on HAART), %	6.5	5.6	11.6

ARVs = antiretrovirals; HAART = highly active antiretroviral therapy.

Table 10. HIV status categories for the final causes of maternal death (%)

	HIV-negative	HIV-positive not AIDS	AIDS not receiving HAART	AIDS receiving HAART	Declined	Unknown	Total
Circulatory system	38.0	33.5	20.6	22.8	28.9	44.2	32.2
Hypovolaemic shock	25.9	18.1	6.0	10.8	18.4	29.8	18.5
Septic shock	12.1	15.4	14.6	12.0	10.5	14.4	13.6
Respiratory failure	23.8	37.2	56.4	50.5	39.5	24.5	37.7
Cardiac failure	31.9	21.1	8.1	10.7	18.4	23.1	19.6
Pulmonary oedema	16.0	9.8	2.8	3.8	2.6	10.3	8.9
Cardiac arrest	15.8	11.3	5.3	7.0	15.8	12.8	10.8
Acute collapse due to embolism	5.4	2.9	1.1	1.7	0.0	1.8	2.7
Renal failure	9.0	7.7	6.8	7.2	2.6	8.0	7.8
Liver failure	5.8	4.5	3.4	7.6	5.3	4.3	5.1
Cerebral complications	19.2	16.5	16.5	15.8	7.9	21.1	17.8
Intracranial haemorrhage	6.9	2.8	1.1	1.0	2.6	7.0	3.9
Cerebral oedema resulting in coning	2.8	1.2	0.3	0.7	0.0	3.1	1.7
Meningitis	1.4	5.8	10.4	9.2	2.6	2.3	5.6
Cerebral emboli	0.4	0.2	0.4	0.3	0.0	0.2	0.3
Brain death following hypoxic event	3.5	2.3	0.9	0.8	0.0	3.7	2.3
Unspecified	4.3	4.2	3.4	3.8	2.6	4.8	4.1
Metabolic	5.2	7.6	9.0	11.4	2.6	6.2	7.7
Maternal keto-acidosis	1.0	1.0	0.3	1.1	2.6	1.0	0.9
Electrolyte imbalance	2.3	4.1	6.8	4.3	0.0	2.8	4.0
Thyroid crisis	0.3	0.0	0.1	0.0	0.0	0.0	0.1
Lactic acidosis	0.6	1.3	0.9	4.8	0.0	0.8	1.6
Other	1.0	1.3	0.9	1.1	0.0	1.6	1.2
Haematological	17.0	18.1	15.1	15.8	7.9	20.3	17.2
DIC	9.4	8.0	3.8	5.7	2.6	10.9	7.6
Severe anaemia	7.6	10.2	11.2	10.1	5.3	9.4	9.6
Immune system	0.4	32.4	66.1	59.2	13.2	4.0	30.6
Unknown	9.7	9.0	4.7	5.6	15.8	9.7	7.9
Other	4.7	4.5	1.9	3.2	10.5	4.2	3.8

HAART = highly active antiretroviral therapy; DIC = disseminated intravascular coagulation.

in that all maternal deaths are notifiable by law, and since 1998 the system has evolved to put into place mandatory review meetings on all maternal deaths in public sector hospitals. In addition, assessments of all maternal deaths are carried out by experienced obstetricians and midwives who take part in an annual continuing training programme, and there is a quality assurance system to check all the assessments. The thoroughness of this process reduces any misclassification in determining the underlying causes of death to a minimum, and we can state the negative impact that HIV has on maternal mortality with a fair amount of certainty.

Recently two significant reports provided estimates of maternal mortality trends using data collected through a variety of systems (data from vital registration, census and surveys) and mathematical

modelling.[7,8] Although the results of these two reports vary considerably, sub-Saharan African countries not surprisingly dominate the top 10 countries with the highest proportion of maternal deaths related to HIV. Sub-Saharan countries have the highest burden of HIV, and India was the only non-African country in the top 10 rankings. SA is ranked 6th (43%) among the top 10 countries with the highest proportion of HIV-associated maternal deaths in the United Nations inter-agency report,[8] and 5th (78%) in the Institute of Health Metrics and Evaluation report.[7,8] The figure of 43% in the inter-agency report is in keeping with our own figure of 40% for SA. Our neighbouring countries, Botswana, Swaziland, Lesotho, Zimbabwe and Namibia, ranked above SA in the inter-agency report with fractions of 78%, 75%, 59%, 53% and 50%, respectively. These figures illustrate the impact the HIV pandemic is having on maternal mortality in sub-Saharan Africa.

The high iMMR estimates in HIV-positive women in SA are clearly contributing to the high MMR of 310/100 000 live births reported for 2008 by Bradshaw and Dorrington.[9] This figure is accepted by the SA National Department of Health, was derived from vital registration data, census surveys, household surveys and mathematical modelling, and includes deaths outside maternity facilities.[9] It is likely that social determinants of health such as poverty, poor nutrition, lack of understanding on the part of the general population of health issues such as late booking for antenatal care, unbooked patients, and problems in accessing transport contribute to this high MMR. The iMMR of 75/100 000 live births for HIV-negative women in our report is much higher than that of similar low/middle-income countries such as Brazil and Argentina, and probably reflects the societal issues mentioned above. Brazil and Argentina do not have a high burden of HIV, but their distribution of underlying causes of death is similar to that in SA, with complications of hypertension and obstetric haemorrhage being the most common causes of maternal mortality.

The SA data show considerable variation in iMMRs between provinces. The Western Cape and Gauteng have the best figures, while the Northern Cape and Free State have the worst. These regional variations are probably due to the fact that the Western Cape and Gauteng have historically been the economic centres of SA and therefore have well-established healthcare systems, better human resources and better-functioning health facilities. Gauteng and to lesser degree the Western Cape do experience an influx of patients from neighbouring provinces seeking medical care, and their numbers should result in referral bias. However, the lower iMMRs indicate that these two provinces manage to provide appropriate healthcare to more complicated cases.

The most common underlying causes of death in HIV-positive women were tuberculosis, pneumonia, PCP and meningitis, and the iMMR for each of these conditions was higher than those for HIV-negative women. These figures suggest that measures against such co-morbid disease conditions must be strengthened so that they are detected early and treated timeously. Such measures should include education of all patients on the need to seek medical help if early signs of respiratory infection develop, and of health care workers to screen all patients, and in particular all HIV-positive women, for respiratory infections and tuberculosis. Tuberculosis and community-acquired pneumonia are the most common underlying causes of maternal death. In addition, tuberculosis cases may be concealed in the community-acquired pneumonia and meningitis groups. Screening must therefore include a symptom screen for tuberculosis.

One of the findings in this triennial report is of serious concern. We found an increasing trend in numbers of deaths from the side-effects of antiretroviral therapy over the 3-year period under review. The total number of deaths due to side-effects of HAART was 73 (14, 17 and 42 in 2008, 2009 and 2010, respectively; Table 9). In the previous report there were 2 deaths from lactic acidosis, while the current report found that most of the deaths (n=42) occurred in 2010 and were due to liver toxicity and Stevens-Johnson syndrome. The data indicate that these serious adverse events coincided with use of the NVP-based HAART regimen and the change in cut-off of CD4 counts from 200 to 350 cells/μl for pregnant women, resulting in large numbers of patients going onto a regimen containing NVP. We have also observed that reporting of drug adverse events in SA is poor, and there are anecdotal reports of increased skin rashes due to antiretroviral drugs by public sector dermatology clinics in the Durban area.

A very recent WHO technical report (June 2012) discusses the issues of the preferred non-nucleoside reverse transcriptase inhibitors (NNRTIs) in front-line antiretroviral regimens.[10] Briefly, efavirenz (EFA) is the preferred option, but concerns regarding its use in early pregnancy and for women who might become pregnant resulted in NVP being used in the HAART regimen in pregnancy. The clinical issues that have arisen from this decision include when to stop EFA and when to use NVP. Both drugs have side-effects, albeit at low rate; EVF has central nervous side-effects and suspected teratogenic effects, while NVP is associated with rashes, Stevens-Johnson syndrome and hepatotoxicity. The WHO technical report states that a review of the data on teratogenicity is reassuring, the teratogenicity rate being lower than that in the general population. Furthermore, case reports of hypersensitivity reactions when switching to NVP, the fact that pregnancy, race and gender are risk factors for side-effects of NVP, the declining costs and better efficacy of EFV, and the fact that this drug is now available as a part of a fixed-dose daily combination provides support for use of EFV as a simple first-line therapy even among pregnant women and those of reproductive age.[10] Our data on the NVP-based HAART regimen support the WHO guidance of using EFV as first-line therapy.

Recommendations based on the recent data under review (2008 - 2010) are as follows:

1. Promote 'know your status' and 'plan your pregnancies' in communities and in the health sector. Promoting 'know your status' should go beyond testing during the antenatal and immediate postpartum periods, and should also involve partners and all persons admitted to healthcare facilities.
2. Ensure that every health facility is able to screen for HIV infection and co-morbid conditions, to institute universal early initiation of the appropriate HAART regimen, and to recognise and treat respiratory infections and tuberculosis.
3. Consider incorporating the management of respiratory infections into the competencies of midwives and professional nurses.

Conclusion

HIV infection is the most important condition contributing to maternal deaths in SA. HIV-infected women are more likely to die of any underlying cause than HIV-negative women, with NPRIs being the most common. Respiratory infections are the most common underlying of cause of death. The new maternal death classification system facilitated understanding of the impact of HIV infection on maternal deaths and can be recommended to other countries. Improved maternal care with a special focus on HIV-positive pregnant women is a health priority in SA if any progress towards Millennium Development Goal 5 is to be made.

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