AIDS briefs

Maternal death rate five times higher in women with HIV

CAROLE LEACH-LEMENS

Maternal mortality ratios in Johannesburg in HIV-infected women are more than six times higher than in HIV-negative women despite integration of antiretroviral treatment into prenatal services, reported Vivian Black and colleagues in a 5-year audit published in the August 2009 issue of *Obstetrics and Gynecology.*

If the United Nation's Fifth Millennium Development Goal (MDG) of reducing maternal mortality by 20% by 2015 is to be reached the causes of maternal mortality as well as of preventable contributing factors need to be clearly understood.

The global maternal mortality ratio of 400 per 100 000 live births as estimated by the World Health Organization does not reveal the considerable regional variations.

In 2005, South Africa, a middle-income country, had a ratio close to the global average but considerably higher than countries of similar gross domestic product per person, for example Portugal and Brazil, which had a ratio of 11 and 110 respectively.

Since 1998 HIV, an indirect cause of maternal mortality, has been the leading contributor to maternal mortality in South Africa, reversing previous declines seen in maternal mortality rates.

An audit of maternal deaths for the period 1996 - 1998 in Durban showed facility-based maternal mortality rates for women with HIV to be 323 per 100 000 compared with 148 per 100 000 for those not infected – over two times higher. Co-infection with tuberculosis had a considerable impact on outcomes.

The authors noted that HIV prevalence among women attending antenatal clinics has remained steady at between 28% and 33% over the past 4 years.

The authors reviewed maternal deaths at a tertiary level facility in Johannesburg for the 5-year period from 2003 to 2007. Variables of interest included: deaths due to HIV, the patterns of these deaths and changes over time. Antiretroviral therapy became available in 2004 and was integrated into an existing programme for prevention of mother-to-child transmission (PMTCT) in the prenatal clinic of the hospital at the facility. The authors assess its impact on maternal mortality.

HIV testing and counselling is offered at the first prenatal visit and CD4 cell counts are done for those who test positive. Eligibility for antiretroviral treatment is based upon a CD4 cell count <200 cells/mm^3 or WHO clinical stage 4. Women receive the standardised antiretroviral regimen of stavudine, lamivudine and nevirapine, along with co-trimoxazole prophylaxis. Single-dose nevirapine (for both mother and infant) was given for PMTCT during the period under review, prior to the updating of South African guidelines.

Patient case files, birth registers, death certificates and mortality summaries were reviewed. Maternal death was defined as death of a woman at the facility during pregnancy or within 42 days of childbirth. No information was available for women who died at home or at another facility. Cause of death was determined through multidisciplinary clinical case discussions. Annual maternal mortality ratios were calculated and disaggregated by HIV status.

For the period 2003 - 2007 a total of 108 (mean age 28.7 year) women died. It was the first pregnancy for 11%, a third of the proportion of all women in their first pregnancy delivering at the hospital.

HIV test results were available for 72% (76); almost 80% were HIV positive. The median CD4 cell count for 53 of HIV-infected women who had the test was 72 cells/mm^3 (interquartile range: 29 - 194 cells/mm^3).

Only two of the HIV-infected women had begun antiretroviral therapy. The authors note this clearly demonstrates that missed opportunities for starting treatment persist.

Most deaths were associated with advanced HIV disease, the most common causes being tuberculosis (36%) and pneumonia (20%). Median CD4 count in women whose death was due to an HIV-related illness was 50 cells/mm^3 compared with a median of 335 cells/mm^3 in HIV-infected women who died of non-related HIV causes.

The authors argue that most of the HIV-related deaths could have been avoided if antiretroviral therapy and co-trimoxazole prophylaxis had been started. In HIV-negative women or those of unknown status deaths were overwhelmingly due to obstetric causes, with hypertension accounting for over 50%.

While the number of deaths over the 5-year period ranged from 15 to 25, the number of live births remained constant at around 7 000 per year.

The authors note that while coverage of HIV testing increased each year (women in 2007 were 3.4 times more likely to have a known HIV status (95% CI 3.2 - 3.6) than those in 2003), HIV testing and follow-up after diagnosis remained the most significant programmatic weakness.

The authors suggest that systematic evaluation of the processes of HIV testing and care for pregnant women could be useful and might include: 'assessment of performance against predefined criteria and agreed targets, for example, routine provider-initiated HIV testing, provision of CD4 results at the second prenatal visit, a target time of three weeks from first visit to antiretroviral treatment initiation and active follow-up processes to ensure that women with advanced HIV disease are retained in care'. The authors highlight the use of mobile phone technologies as an effective means of follow-up in this setting.

While the numbers of women who began antiretrovirals increased over time, with coverage in 2007 estimated at 59.2%, the maternal mortality ratio for HIV-infected women was over 6 times higher than the ratio in HIV-negative women (776 versus 124 per 100 000), or 6.2 (95% confidence interval 3.6 - 11.4).

Of the total deaths, 44.3% (95%CI 30.8 - 54.8%) were due to HIV. The mortality rate among HIV-infected women who died of non HIV-related causes was 171/100 000, similar to that of HIV-negative women.

The authors note the importance of expansion of antiretrovirals to two primary health facilities close to the hospital led by nurses and midwives. Advantages include ensuring high-level coverage, bringing HIV care closer to the patient and potentially avoiding unnecessary referrals to tertiary care. They stress that integration of antiretroviral therapy into prenatal care will help secure the health of women as well as prevent transmission to newborns. Other factors the authors cite as barriers to uptake of PMTCT are: the framing of PMTCT itself as a paediatric issue, weak health systems, poor communication

between health workers and pregnant women as well as the fear of stigma.

Nearly three-quarters of all deaths occurred in the week after childbirth, and the authors stress the importance of strengthening postnatal health services.

Black V, *et al.* Effect of human immunodeficiency virus treatment on maternal mortality at a tertiary center in South Africa: A 5-year audit. *Obstet Gynecol* 2009; 114(2): 292-299.

Adapted from www.aidsmap.com with permission.

Workforce participation increases with time on treatment

CAROLE LEACH-LEMENS

The probabilities of being employed and being able to perform normal daily activities increased over a period of 3 years and beyond among adults on antiretroviral treatment in 3 South African settings, reported Sydney Rosen and colleagues in a study presented at the Fifth IAS Conference on Pathogenesis, Treatment and Prevention in Cape Town in July.

While improved survival and reduced mortality are proven outcomes of antiretroviral treatment programmes, long-term sustainability for resource-constrained countries is likely to be viewed more positively when treatment allows individuals to remain economically active.

Economic analysis and cost-effectiveness studies can provide ministers of finance in resource-constrained settings with important tools as they face difficult budgetary decisions relating to health and social concerns.

Monitoring the numbers of those returning to work or school following antiretroviral treatment is important in order to justify and support budgetary outlays and to project the potential positive impact of expanded treatment on a country's growth and development.

A 5-year prospective cohort study of the economic and social outcomes of antiretroviral treatment in South Africa was undertaken by Sydney Rosen and colleagues from the Center for International Health and Development, Boston University.

A random sample of 1 069 adult patients who were either waiting for treatment or who had been on treatment for less than 6 months was enrolled from 3 study sites in Gauteng and Mpumalanga.

Enrolment took place during 2005 and 2006. Interviews were conducted up to 4 times a year during routine clinic visits to assess ability to perform normal activities, general condition, employment, income sources and costs of obtaining treatment.

Analytic data (up to September 2008) included all interviews conducted between 1 month (30 days) before starting antiretroviral treatment and 3 years (1 080 days) after beginning treatment.

Women account for approximately 80% (845) of the cohort, with a mean age of 33.6 years and 37.4 years for men. Twenty-two per cent of women and 19% of men were employed in the formal sector; 21% of women and 22% of men were seeking work or unemployed. Just over 50% had permanent housing or lived in a flat.

The prevalence of pain, fatigue, nausea and skin problems decreased steadily over the entire 3 years on antiretroviral treatment. The probabilities of pain and fatigue fell from 74% to 29% and 75% to 11% respectively and the probabilities of nausea and skin problems fell from 31% to 4% and from 50% to 9% respectively.

The inability to perform normal daily tasks decreased steadily from 50% to 20% over a period of a year and from 20% to 8% after 3 years. No difference was seen by age or gender.

The probability of having a job increased over time on antiretroviral treatment from 29% in the month before starting treatment to 47% after 3 years. Significant differences were apparent after 1.5 years on antiretrovirals. There were no differences according to gender but the probability of being employed increased with age.

Important limitations noted by the authors include the high rate of loss from the treatment programme as well as significant loss to follow-up.

In addition, data collection (interviews) depended on the unpredictable situation of catching patients at the time of their clinic visits. The number of interviews per patient as well as intervals between interviews can vary considerably. The analysis did not include patients who died, discontinued treatment or who transferred to a different site.

The authors conclude: 'Improvement in economic outcomes appears to be substantial by the end of the first year on antiretrovirals and is sustained or increased over the second and third year'.

Rosen S, *et al.* Economic outcomes of antiretroviral treatment for individual patients: three-year follow up in South Africa. Fifth IAS Conference on HIV Pathogenesis, Treatment and Prevention, Cape Town, South Africa, abstract WEPED 194, July 2009.

Adapted from www.aidsmap.com with permission.

BRIDGET FARHAM

Single Suture

Blood test may predict IVF success

Patterns of gene expression in a woman's blood may provide a clue as to whether or not she may become pregnant using IVF. Cathy Allen of the Rotunda Hospital in Dublin, Ireland, and colleagues analysed the expression of thousands of genes in blood taken from 8 women before IVF embryo implantation. It appeared that expression levels of 200 genes seemed linked to whether implantation was successful.

Allen suggests that giving a blood test to women considering IVF could help them decide whether to go through with the procedure. Prior to implantation the eggs can be screened for the likelihood that they will implant properly, but this would be the first non-invasive test to help to predict whether a particular woman is a good candidate for IVF.

New Scientist, 4 July 2009: 15.