

# HIV-AIDS RELATED MATERNAL MORTALITY IN BENIN CITY, NIGERIA

J.U. ONAKEWHOR, B.N. OLAGBUJI, A. B. ANDE, M.C. EZEANOCHIE, O.E. OLOKOR  
and F. E. OKONOFUA

Materno-Foetal Unit, Department of Obstetrics and Gynaecology, University of Benin Teaching Hospital,  
Benin-City, Edo State, Nigeria

*Corresponding Author: Dr. Biodun N Olagbuji*

*Email: [nelsonabiiodun@yahoo.com](mailto:nelsonabiiodun@yahoo.com)*

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## SUMMARY

**Objective:** To determine the causes and characteristics of maternal deaths in HIV-infected women.

**Design:** A retrospective study of maternal deaths in a cohort of HIV-infected women.

**Setting:** A facility-based maternal death review using case records and mortality summaries.

**Methods:** Thirty seven maternal deaths which occurred in HIV-infected women were reviewed in a university teaching hospital in southern Nigeria over a 4-year period. Causes and circumstances surrounding each maternal death were identified.

**Result:** One in every four maternal deaths occur in women with HIV infection. Majority (64.9%) of the women presented in advanced stage (WHO stage III/IV) of HIV syndrome while 86.5% had missed opportunities for antiretroviral programme. Pregnancy-related sepsis was the commonest cause of maternal death. Other common causes were death from tuberculosis and pneumonia.

**Conclusion:** HIV-related maternal death is emerging as a leading cause of pregnancy related death in Nigeria. There is need to scale-up preconception care and ensure comprehensive and sustainable prevention of mother-to-child transmission service for all pregnant women throughout Nigeria to reduce the burden of HIV/AIDS infection and minimize avoidable deaths from opportunistic infections.

**Keywords:** Maternal Death; HIV Infection; AIDS; Antiretroviral therapy; Nigeria.

## INTRODUCTION

The HIV pandemic remains a major health challenge facing the world. Of the estimated 33.2 million people living with HIV worldwide, more than two-thirds (22.5 million) live in sub-Saharan Africa, where women of childbearing age are most severely affected.<sup>1</sup> The scourge of the virus has ravaged the region's population with untold negative impacts on demography,

economic and social spheres as well as severe adverse effects on women's health.<sup>2</sup> In Nigeria, in spite of all efforts to combat the disease, HIV/AIDS remains a major public health problem with an estimated 4.6% (2.95 million) of the population infected with the virus; one of the highest numbers in the world. The recent sero-sentinel survey put the HIV infection rate at 4.6% in 2008.<sup>3</sup> Available statistics indicate that Nigeria currently has one of the highest rates of maternal mortality in the developing world; with evidence suggesting that maternal mortality ratio in the country has reached an all-time high of 1,100 per 100,000 live-births.<sup>4</sup> The persistently high maternal mortality in Africa, Nigeria inclusive, may be associated with increasing numbers of HIV-associated deaths.<sup>5</sup>

HIV/AIDS is now among the major causes of death among women in the reproductive age.. A specific example is a case of South Africa where confidential enquiries into maternal deaths identified HIV/AIDS as leading cause of maternal death.<sup>6</sup> Common causes of HIV/AIDS related maternal death include opportunistic infections such as pneumonia, tuberculosis, and severe malaria infections[1,5,7-9]. Its associated increase in anaemia and puerperal/postabortal sepsis may impact on the direct causes of maternal mortality. The purpose of this study was to determine the characteristics, causes of maternal mortality and avoidable contributory factors among HIV infected women who were managed at the University of Benin Teaching Hospital in Nigeria. To the best of our knowledge from available electronic literature search, this audit represents the only published information on maternal deaths in a cohort of HIV-infected subjects in the West African sub-region.

## METHODS

This was a facility based maternal death review conducted at the obstetric unit of the University of Benin Teaching Hospital (UBTH), an urban tertiary health centre which serves as referral centre for a population

of nearly 3 million people in southern Nigeria. Records of all the 37 maternal deaths that occurred in HIV infected women from January 2005 through December 2009 were analysed.

Ethical approval for this study was obtained from our institution's Ethics Review Committee. For the purpose of this study, maternal deaths was limited to those occurring in pregnancy or within 42-day time period after termination of pregnancy, from any cause related to or aggravated by pregnancy or its management and does not include accidental or incidental causes.

Maternal deaths were classified as direct and indirect deaths. Direct obstetric death refers to death directly caused by obstetric complications (pregnancy, labour and puerperium) while indirect deaths resulted from a previously existing disease or disease that was aggravated by pregnancy<sup>4</sup>. Deaths associated with HIV/AIDS co-infection as the primary cause were classified as indirect obstetric death. The primary causes of death were assigned based on the documentation from the multidisciplinary weekly departmental audit of maternal mortality by the consultant and resident staff of the department. Deaths that occurred at home, in the community and prior to arrival at our centre were not included in this review.

The UBTH is one of the pilot centres for the program on Prevention of Mother to Child Transmission (PMTCT) of Nigeria's Federal Ministry of Health [FMOH] and serves as a nodal centre for expanding PMTCT services into secondary and primary health care facilities in the south-south region. Specific PMTCT interventions for HIV infected women include pre-conceptual counselling and care, and antiretroviral treatment and prophylaxis. Also included are antenatal management, intrapartum, postpartum care of women who are HIV-infected and women of unknown HIV status for exposed infants.<sup>3</sup> In our unit, HIV testing and counselling is routinely offered to all pregnant women at the first prenatal visit.

HIV infected pregnant women referred from peripheral centres were also counselled and re-screened to confirm their HIV status. Also, base line CD4 count and other routine haematological profiles are done prior to commencement of antiretroviral therapy or prophylaxis. Classification of the severity of HIV infection is based on WHO staging of HIV disease. In cases where CD4 counts are not available, clinical staging is used. In our centre, HAART (Zidovudine, Lamudine & Nevirapine) is routinely used as the first line antiretroviral agents for the prevention of maternal to child transmission (PMTCT) while women with HIV infec-

tion diagnosed in labour are offered single dose nevirapine and Lamivudine and Zidovudine for one week to cover the "nevirapine tail". For every case of maternal death, information on demographic characteristics, gestational age at time of death, obstetric complications, investigations and management, organ system dysfunction, intensive care unit admission, mode of delivery, foetal outcome, duration of hospital stay, cause of death and classified cause (direct and indirect) were retrieved from case records. Any discrepancies that occurred from cause of death were resolved through autopsy reports by the pathologists.

Every maternal death was presented at the weekly departmental mortality review where the cause and circumstances surrounding each death including recommendations to prevent such death are agreed upon. This information is later coded into the departmental maternal mortality summary database. Analysis of data was done using descriptive statistics. Categorical variables were expressed as frequency (percentage) and continuous variables as mean, median and range.

## RESULTS

During the study period January 2006 to December 2009, a total of 8,529 women delivered at the UBTH. Of this total number, 564(6.4%, 564/8,808) women were infected with HIV. There were 8,203 live births and 151 maternal deaths in the hospital during the 4 year period under review, giving an overall maternal mortality ratio (MMR) of 1,875/100,000 live births. About one-quarter, 37(24.5%) of the total maternal deaths were related to HIV/AIDS infection. The demographic and clinical characteristics of women who had HIV-related deaths are shown in Table 1.

The mean age was 30 years {(standard deviation [SD], 5.0), range 19-42}, median parity was 2.0 (range, 0-11) and mean gestational age was 27.5 weeks (standard deviation [SD], 1.1). Most deaths (72.9%) occurred in the 26-35 year age group. Seventy percent of the women were in the parity group 1-4. A majority (86.5%) of these women did not have antiretroviral therapy (ART) initiated prior to presentation in our centre while half (51.4%) died during the postpartum period. Two-thirds (64.6%) presented with stage III/IV HIV disease. The median duration (days) at which mortality occurred following delivery was 4(range, 0-27).

Table 2 shows the yearly trend in the MMR over the period under review. The MMR ranged between 1,568 to 2,894/100,000livebirths.The MMR was highest (2,894/100,000 live births) in 2006 and lowest (1,568/100,000 live births) in 2007 with an increasing trend from 2007 to 2009.

The MMR for the HIV infected women during the period ranged between 314-666/100,000 live births. The proportion of HIV-infected women was highest in 2006, dropped in 2007 with an increasing trend to 2009.

Other common causes were death from tuberculosis, pneumonia, cerebral pathology (encephalitis, meningitis and toxoplasmosis) and unknown cause among women with WHO stage IV disease. Of the 11 women who died of pregnancy related sepsis, 5(45.4%) delivered vaginally while 3(27.3 %) each for caesarean delivery and post- abortal sepsis.

**TABLE 1** Demographic of cases of HIV/AIDS-related maternal death at the University of Benin Teaching Hospital

	n = 37	%
<b>Age</b>		
≤20	1	2.7
21 – 25	4	10.8
26 – 30	18	48.6
31 – 35	9	24.3
>35	5	13.5
Range	19 – 42	–
Mean ± SD	30.0 ± 5.0	–
<b>Parity</b>		
0	7	18.9
1 – 4	26	70.3
≥5	4	10.8
Range	0 – 11	–
Median	2.0	–
<b>Booking Status</b>		
Unbooked at UBTH	32	86.5
<b>Diagnosis of AIDS at referral</b>	24	64.9
<b>Gestational age at presentation in UBTH (weeks)</b>		
<13	4	10.8
13 – 28	14	37.8
>28	19	51.4
<b>ART prior to presentation in UBTH</b>		
Yes	5	13.5%
No	32	86.5%
<b>Situation at Death</b>		
Prenatal	18	48.6
Postpartum	29	51.4
<b>Education</b>		
Primary	13	35.1
Secondary	24	64.9
Tertiary	0	0
<b>Mode of Delivery</b>		
Caesarean section	7	18.9
Vaginal delivery	12	32.4
NA	18	48.6

**TABLE 2** Trends in Maternal Mortality Ratio

	2006	2007	2008	2009	Total
Total deliveries	1882	2409	2315	2202	8808
Live birth (n)	1520	2231	2200	2101	8203
Maternal death (n)	44	35	36	36	151
MMR (100,000 live birth)	2636	1568	1636	1713	1841
No of HIV infected women [n (%)]	121 (7.5)	152 (6.3)	149 (6.4)	142 (6.5)	564
No of HIV-related maternal death	10	7	6	14	37
MMR for HIV-non infected pregnant women	599	314	272	666	451

**Table 3:** Causes of HIV-related Maternal Deaths

Category	n = 37	%
<b>Direct Cause</b>		
Pregnancy related sepsis	11	29.7
Hypertensive Disease in Pregnancy	2	5.4
Obstetric Haemorrhage	1	2.7
<b>Indirect Cause</b>		
Tuberculosis	6	16.2
Pneumonia	4	10.8
Cerebral pathology		
Toxoplasmosis	3	8.1
Encephalitis	3	8.1
Meningitis	2	5.4
Anaemia	2	5.4
Unknown (Only WHO stage IV disease)	3	8.1

Among the overall causes of maternal mortality (2006-2009), HIV-related maternal death predominated (24.5%, 37/151)[Table 3], followed by direct obstetric causes - pregnancy related sepsis, obstetric haemorrhage and hypertensive disease in decreasing order. Of the total 37 maternal deaths associated with HIV/AIDS, indirect maternal deaths occurred in 23 (62.2%) of the HIV infected women while 14(37.8%) had direct maternal deaths. The most common cause of maternal death was pregnancy related sepsis (29.7%)Table 3.

## DISCUSSION

This maternal death review highlights the significant contribution of HIV/AIDS to maternal mortality in Nigeria; the country with second highest proportion of HIV/AIDS infected persons worldwide. HIV/AIDS related death was a leading cause of pregnancy-associated death accounting for 24.5% of the overall maternal mortality in this audit.

In this study, one in every 4 maternal deaths at the UBTH is associated with HIV/AIDS. The extent of the contribution of HIV/AIDS to the maternal deaths in this review may partly explain the rising rate of MMR in the hospital.

This trend is consistent with the increasing prevalence rate of HIV-infected women in this study, which was consistently higher than our national sero-prevalence rate<sup>3</sup>. This increased attributable maternal death to HIV is similar to reports from other African countries.<sup>5,10</sup> Other relevant findings in this study are non attendance of prenatal care with resultant late HIV diagnosis in advance stage (WHO stage III/IV) in majority (64.9%) of the women and the limited access to initiating antiretroviral therapy (ART) before the disease reached a critical situation. These findings were consistent with that of a previous study from South Africa, which reported that women attending prenatal clinic and receiving antiretroviral therapy are less likely to suffer maternal death.<sup>11</sup>

The low level of education (primary and secondary) in all the HIV infected women may be a reason for non-attendance of antenatal clinic prior to referral to our centre in majority of the women.

The Nigerian government with support from international partners is rapidly expanding access to Voluntary Counselling and Testing and antiretroviral treatment of HIV programme. In spite of this, a large population of HIV infected women still do not have access to these services. This clearly shows that missed opportunities for early diagnosis and treatment exist as reported previously in another African country with similar high HIV pandemic.<sup>12</sup> Strengthening the links between antenatal care at primary health care level and antiretroviral therapy programmes is critical for improving access to antiretroviral therapy for eligible HIV-infected pregnant women.

The age and parity distribution in this study are similar to our demographic obstetric characteristics. Of the 19(51.4%) patients who had postpartum death, the median survival was 4 days (0-27 days). The short median survival in this study might be related to the advanced stage of the despite the initiation of ART at presentation in our center. Mattin F et al, reported that median-term postpartum prognosis is good in HIV-infected women with access to HAART.<sup>12</sup>

The overall MMR of 1875/100,000 live births reported in this study is unacceptably high. Similar high rate were reported by studies from northern part of the country.<sup>14,15</sup> This is alarming despite the various international efforts to address maternal mortality, one of the most obvious forms of social inequality between

developed and developing nations. It is surprising that this high level of MMR remains after the declaration of the Millennium Development Goals (MDGs) about 10 years ago.

Attaining the MDG 5, the 5<sup>th</sup> goal, the reduction of maternal mortality by 75% may elude Nigeria by the end of 2015. In contrast to findings in this study, lower MMRs of 454 & 518/100,000 deliveries were previously reported from two secondary health facilities located in the same town with our hospital.<sup>16,17</sup>

It is probable that referral of critically ill women from lower health care centres for highly specialized care accounted for the high MMR reported in this study. The inclusion of maternal deaths among women who did not receive prenatal care in our centre in addition to lack of data on deliveries from referral centres could also contribute to the high MMR. There was dramatic drop in yearly MMR in 2007 with slight increasing trend in 2008 and 2009, although above the overall MMR. The higher MMR in 2006 might be a result of lower total deliveries in that year. Similar trend was also noted in the proportion of HIV- infected antenatal attendees. The HIV-associated MMRs over the study period were similar to that obtained in year 2002-2004 in a study from KwaZulu-Natal, South Africa.<sup>5</sup>

HIV/AIDS may contribute to maternal death in several ways: HIV infected women may be more at risk of direct causes such as puerperal sepsis and complications of caesarean sections or indirect causes where the infection itself or opportunistic infection such as tuberculosis progress faster in pregnancy. Additionally, death related to HIV/AIDS may be incidental to pregnancy.<sup>18</sup> Pregnancy-related sepsis (N=11,29.7%) was the commonest cause of death in HIV infected women in this study followed by chest infection(tuberculosis & pneumonia), infectious cerebral pathology(meningitis, toxoplasmosis, encephalitis) and unknown cause (in women with WHO stage IV disease) in decreasing rank of prevalence(Table 3).

These findings are similar to previous studies on maternal death among HIV-infected women in a nation where HIV prevalence is high.<sup>5,11</sup> Evidence is accumulating that tuberculosis associated with HIV/AIDS, sepsis, and other opportunistic infections are the main infectious causes of maternal deaths.<sup>19</sup> The presentation of majority (64.9%) of the women studied with advanced HIV disease may be an obvious reason why pregnancy related sepsis was commonest underlying factor for death. Furthermore, most of the women who died of sepsis had intrapartum care provided by unskilled birth attendants while all the women (3) who died following abortion had unsafe illegal abortion.

Pulmonary tuberculosis (n=6, 16.2%) was the second commonest cause of HIV-related maternal death in this audit. Of the total nine women who had tuberculosis related death during the study period, 67% (6 women) were attributable to HIV infection. Both TB and HIV infection are deadly combination in pregnant women.<sup>20</sup>

A review of the literature shows that tuberculosis associated with HIV/AIDS is an emerging major non-obstetric cause of maternal deaths in sub-Saharan Africa.<sup>17</sup> At the university teaching hospital Lusaka, Zambia; pneumonia and meningitis were also major contributory factors to maternal deaths.<sup>21</sup>

Findings from this study indicate the need for proactive scale-up of preconception care, a rudimentary part of comprehensive maternal health care in our environment, especially among HIV-infected women intending to get pregnant. This is a likely way of counselling women with advanced HIV disease, especially multifarious women on the detrimental impact of HIV co-infection in pregnancy, as studies have documented both adverse maternal and perinatal outcome in HIV-infected women.<sup>22,23</sup> These maternal death audit, highlight the need to extend comprehensive PMTCT programme to primary health care centres and operational links between all levels of health care and antiretroviral therapy programmes including HIV testing and counselling, the gateway to comprehensive PMTCT program, as rare encounter with higher level of health care are likely among women in indigenous population.

Also, we recommend treatment community package of care model in our environment, incorporating effective prevention strategies of non-obstetric infectious diseases such as HIV/AIDS, TB, bacterial sepsis, pneumonia and meningitis targeting HIV-infected and at-risk individuals.<sup>24</sup> Integration of informal maternity care providers into the national antiretroviral programme and provision of safe abortion are essential for reducing avoidable maternal deaths.

The findings of this study highlight the critical need to deliver empirically validated interventions to underserved population and suggest expansion of PMTCT service for all pregnant women throughout Nigeria to allow easy access to counselling, testing and treatment to reduce the burden of HIV/AIDS infection and minimize avoidable deaths related to HIV/AIDS. Also in this review, HIV/AIDS, besides being a leading cause of indirect maternal deaths, is emerging as a leading cause of pregnancy-related death in Nigeria.

Apart from presentation in advance stage of HIV, non initiation of antiretroviral therapy early in pregnancy appears to be the main underlying factor responsible for deaths in this study. The association between stage

of maternal disease and mortality supports the relevance of preconception care for HIV-infected women including counselling on the possible deteriorating effect of pregnancy on maternal health particularly in women with advanced disease.

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