

HIV infection: the course and outcome of pregnancy in the Gambia between 2005 and June 2011

Abstract

Background: The health of women and children affected by HIV in the countries hit by the epidemic including The Gambia remains one of the most critical areas of unmet need that the community faces today. In The Gambia, the era of single dose Nevirapine reduced MTCT 3 folds but events of pregnancy in relation to miscarriage, stillbirth, live birth, low birth weight, preterm delivery and neonatal and maternal death of PLHIV's was not described.

Aims/Objectives: To describe pregnancy outcomes among HIV infected and uninfected in the Gambia.

Materials and methods: Information of HIV positive pregnant mothers between January 2005 and June 2011 and a cross section of HIV negative mothers were retrospectively extracted from the records using a standardized data collecting tool. Data analysis was descriptive with Epi-info version 6.

Results, Summary/Conclusion: A total of 1111 and 743 pregnancies recorded for HIV infected and uninfected women respectively with similar median age of 28 years. The measured adverse outcome includes; Low Birth Weight; 128 (14.0%) Vs 58 (8.4%); P- 0.002; Preterm delivery 10 (1.1%) Vs 1 (0.1%); P <.001; Stillbirth rate was 26 (2.8%) Vs 5(0.7%) P-.0002). The majority of stillbirth (16) 61% were macerated. The rates of low Apgar scores (<7 in 5 minutes) was 341 (37.1%) Vs 198 (28.7%) P-0.002; Past history of miscarriage was 17 (0.91%) Vs 3 (0.16%) P-0.0001). The prevalence of adverse pregnancy outcome was more with type 1 virus 769 (69%). Majority (73% HIV 1; 60% HIV 2) had short term ARV drugs and less than 10% were on ART before pregnancy.

HIV factor have shown increased adverse pregnancy outcome in predominant non-HAART period. Therefore, the study result strongly supports interventions that could reduce or eliminate these adverse outcomes among reproductive age women living with HIV.

Keywords: pregnancy outcome, single dose nevirapine

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Introduction

In recent years, the HIV pandemic has become a major threat to public health issues of global significance.¹ The developing world contributes the majority of affected people. Two-thirds of infected adults and over ninety per cent of the world's HIV infected children are Africans.² The majority of those infected with HIV are female. Majority of them are in their reproductive age.^{3,4} One way of reducing and thereafter ensuring an HIV free generation is effective PMTCT programme. Therefore, measures to minimize mother to child transmission is a major focus of research. Evidence from research have shown that extended triple ARV prophylaxis in pregnancy and postpartum can reduce mother to child transmission to less than 2%. The significance of pregnancy in people living with HIV (PLHIV) is not limited to prevention of vertical transmission but maternal and fetal health and survival is essential in overall assessment of service delivery. Of all complications of pregnancy, HIV infection during pregnancy is currently the most topical and there are many published work in this field of medicine. Available literature have shown that during pregnancy, HIV infection poses greater challenges with regard to pregnancy complications, management of co-morbidities, extended family care (PMTCT-Plus) and mother to child transmission in the era of single agent antiretroviral prophylaxis.^{1,5} Some adverse outcomes

associated with HIV infection in pregnancy include spontaneous miscarriage, low birth weight, stillbirth, preterm delivery, low Apgar scores and vertical transmission is implicated in over 90% of infections in children.^{1,6-8}

In the literature, there are conflicting reports concerning the association between preterm birth or low birth weight and HAART.⁹⁻¹¹ but our study was during the single agent anti-retroviral prophylaxis for the prevention of mother to child transmission of HIV in the Gambia and the primary aim was to determine the frequency of occurrence of some obstetric complications among HIV positive mothers such as low birth weight, preterm delivery, stillbirth, Apgar scores and previous history of miscarriage. A cross section of HIV negative patients and their pregnancy outcome was also extracted and compared with HIV positive patients. Also in the cohort of HIV positive mothers the frequency and occurrence of these adverse outcomes was analysed in relation to strain of virus.

Methodology

Study design was a descriptive cross sectional study and the population was HIV positive and negative pregnant mothers between 2005 and June 2011 in the Gambia. Data Source was the medical records of all HIV positive women booked or referred and

delivered at all PMTCT sites in the country between 2005 and June 2011. Information was retrieved with a standardized data collecting tool. A call for antenatal hand held card was embarked and mothers encouraged to report where indicated. The same data collecting tool was used to extract information on matched for age and parity negative mothers using antenatal and labour ward registers.

Data collection

The PMTCT sites were identified. The total number of health facilities offering PMTCT services in the Gambia during the study period was 27. These hospitals and health centres were identified. The focal persons, regional directors and the officer in charge (OIC) of hospital management board were all contacted by telephone and email communications. The focal persons were identified and motivated to call the PMTCT mothers during the period under review (2005-2011 June) and inform them to bring their antenatal hand held cards. The data collecting tool has variables that could be properly filled using the antenatal cards. However, our substitute was the antenatal and labour ward registers. The data for negative mothers during the period under review was also collected. The methodology of matching for age and parity was implemented such as the name above or below the HIV positive events of labour and delivery was taken for similar age and parity. Data was entered into a computer database and consistent check was ensured to minimize data entering error. Power calculation was by Precision test which was used to calculate the comparable proportion of the two populations (HIV Positive and Negative). Calculated using the formula below: estimate ± margin of error due to sampling (e.g. 95% confidence interval for a proportion).

$$p - 1.96\sqrt{\frac{p \times (1-p)}{N}}, p + 1.96\sqrt{\frac{p \times (1-p)}{N}}$$

Table 1 The pregnancy outcome

	HIV POS n (%)	HIV NEG n (%)	P-Value
Low birth weight (<2.5kg)	128 (14.0)	58 (8.4)	0.002
Preterm delivery (<37 weeks)	10 (1.1)	1 (0.1)	0.001
Stillbirth	26 (2.8)	5 (0.7)	0.0002
MSB	16 (61%)		
FSB	10 (39%)		
Low Apgar score (<7 at 5mins)	341 (37.1)	198 (28.7)	0.002
Previous spontaneous miscarriage	17 (0.91)	3 (0.16)	0.0001

n= adjusted to actual data recorded

HIV status: 0=Negative; 1= Type 1; 2= Type 2; and 3= Dual infection (HIV 1 and 2)

Figure 1 Adverse pregnancy outcome in relation to strain of virus. The prevalence of adverse pregnancy outcome was more with type 1 virus 769 (69%).

HIV status: 0=Negative; 1= Type 1; 2= Type 2; and 3= Dual infection (HIV 1 and 2)

Figure 2 Frequency of adverse pregnancy outcome in various health centres in relation to HIV serostatus. Type 1 HIV virus is the main strain driving the epidemics in all PMTCT sites and has higher prevalence of adverse pregnancy outcome.

N= 1861

Proportion of Negative to Positive (743:1111)

The precision value was 2.2%. This was suggestive of good quality study with appropriate Power and comparable values. Data analysis was descriptive using Epi-info Version 6. Outcome measures; The frequency of occurrence of stillbirth, low birth weight, preterm delivery, Apgar score and previous history of miscarriage were measured among HIV positive mothers in the period under review. This was compared with HIV negative mothers. The prevalence of adverse pregnancy outcome in relationship to strain of virus was ascertained. The antiretroviral drug distribution among HIV cohort was also analysed.

Results

A total of 1111 pregnancies occurred among HIV infected women with the median age of 28 (15 to 50) years. A cross section of 743 pregnancies among HIV negative women with similar median age of 28 years was recruited.

Table 1 showed frequency of occurrence of low birth weight, low Apgar score, preterm delivery, stillbirth and past history of miscarriage in HIV Positive and Negative pregnancies. The findings revealed that maternal HIV infection was associated with significantly lower birth weight as (128 (14.0%) babies were born with birth weight below 2500g versus 58 (8.4%) for negative mothers; P-0.002; Preterm delivery 10(1.1%) versus 1 (0.1%) P <.001); Stillbirth rate was 26 (2.8%) versus 5(0.7%) P-.0002). The majority of stillbirth (16) 61% were macerated. The rates of low Apgar scores (<7 in 5 minutes) was higher in sero positive women (341 (37.1%) versus 198 (28.7%); P-0.002) (Figures 1) (Figure 2). Past history of miscarriage was significantly increased among HIV mothers 17 (0.91%) versus 3 (0.16%) P-0.0001) (Tables 2) (Table 3).

Table 2 Antiretroviral (ARV) drug distribution among the HIV positive cohort

(N=201)	S1 (N=769)	S2 (N=131)	S3
ART before 18(8.9%) Pregnancy	74 (9.6%)	7 (5.3%)	
Single dose NVP (4.5%)	562 (73.1%)	---	9
AZT at 34weeks (2.0%)		79(60.3%)	4

S1, HIV 1; S2, HIV 2; S3, HIV 1 and 2; NVP, Nevirapine; AZT, Zidovudine

Less than 10% of the HIV patients were on ART for their health before the onset of pregnancy irrespective of strain of virus. Most (73%) of HIV 1 patient had ARV prophylaxis with single dose NVP and 60% of HIV 2 had AZT for prophylaxis. Those with dual infection HIV 1 and 2 had low uptake of the ARV prophylaxis some had NVP a few AZT.

Table 3 Health centers and frequency of adverse pregnancy outcome in PLHIVs

Health center	FREQ	%
AFPRC	53	4.8
ASB	76	6.8
BAFROW	10	0.9
BANSANG	52	4.7
BASSE	79	7.1
BRIKAMA/HC	24	2.2
BANJULID/HC	18	1.6
BWIAM	26	2.3
ESSAU/HC	56	5
FATOTO	3	0.3
FAJIKUNDA/HC	72	6.5
GFPA	40	3.6
HOC	70	6.3
JFPH	110	9.9
25	2.3	
KEREWAN	18	1.6
KUNTAUR	28	2.5
RVTH (EFSTH)	79	7.1
SIBANOR	121	10.9
SEREKUNDA/HC	108	9.7
SOMA	26	2.3
SOS	14	1.3

Basse (7.1%) in the upper river region and JFPH (9.7%), Sibanor (10.9%) and Serrakunda (9.9%) in the western region have the highest cumulative rate of composite adverse pregnancy outcomes among people living with HIV (PLHIVs) in the Gambia.

Discussion

In our study the frequency of occurrence of low birth weight, low Apgar score, preterm delivery, stillbirth and past history of miscarriage in HIV positive pregnancy were more statistically significant than in HIV negative pregnancy. Many other studies conducted elsewhere during this period of relative little or single agent antiretroviral drug

in the prevention of mother to child transmission of HIV infection had similar results.¹²⁻¹⁸ Low birth weight has been suggested as a surrogate for prematurity in babies of HIV-infected mothers. In Nairobi, HIV-infected women were 3 folds more likely to deliver a low-birth-weight baby, especially in the presence of HIV-related symptoms.¹³ In Rwanda, birth weight was significantly lower in singleton babies of asymptomatic HIV positive women than in babies born to uninfected women.¹³

A large study in Nairobi showed an independent association between HIV infection and intrauterine and intrapartum death after excluding confounding factors such as presence of other sexually transmitted infection.¹³ In our study we observed that HIV infection is associated with increased stillbirth with trend towards macerated stillbirths (61%) which may exclude intrapartum event as the predominant cause. HIV-1 and HIV-2 infection in Africa have both been linked to a higher rate of spontaneous abortion.¹³ HIV seropositive women were 1.47 times more likely to have had a previous spontaneous abortion and this rose to 1.81 in women in Uganda who were seropositive for both HIV and syphilis.¹³ An American study showed a three-fold increase in early spontaneous abortion in a prospective follow-up study. More than half of these aborted fetuses had evidence of HIV infection, particularly with the thymus gland affected.^{17,18} In our study we observed that HIV positive mothers had increased miscarriage rate. Due to late booking for antenatal care it was relatively impossible for us to assess miscarriage rate in the index pregnancy. However, we assessed past obstetrics outcome for spontaneous abortion.

In our study there was little or no impact of ARV drugs on the occurrence of these adverse outcomes as it was given for short term in the majority of HIV patients (Table 2). Therefore, HIV may be the direct cause or a marker of a complex interaction of related medical and social conditions that affect pregnancy as suggested in UNAIDS/98 review.¹³ However, these complication rates varied in different settings and may reflect the level of endemicity of the epidemic and the nature of the HIV-related disease in different communities.¹⁴⁻¹⁸ Paradoxically, in developed countries, highly active antiretroviral therapy (HAART) begun before pregnancy or in early pregnancy has been associated with an increased risk of premature delivery and neonatal death.¹⁹ However, there are conflicting reports concerning the association between preterm birth or low birth weight and HAART.^{9-11,20}

A South African study presented data on pregnancy outcomes (spontaneous abortions, stillbirths, maternal and early neonatal deaths; birth weight; and HIV status) and estimated the relative risk factors in HIV-infected and uninfected women enrolled in a prospective mother-to-child transmission study investigating the risk of HIV transmission associated with exclusive breast feeding.²⁰ The study had inconclusive evidence regarding the association of preterm delivery and low birth weight to HAART. In our study, preterm delivery and low Apgar score were significantly higher in HIV positive than negative. Our finding was not influenced by ARV drugs as it was conducted before the Gambia started triple combination ARV drugs in the prevention of mother to child transmission of HIV. Our study showed that 73% and 60% of HIV 1 and 2 respectively had short term ARV prophylaxis just for the period of pregnancy to prevent mother to child transmission of HIV (Table 2). Overall, less than 10% were on ART for their health before pregnancy (Table 2). Of the 201 HIV positive patients with dual infection (HIV 1 and 2) only 6.5% had short term ARV prophylaxis. The strain of virus was also a factor in the prevalence

of adverse pregnancy outcome. In our study HIV 1 infection has the highest incidence of all adverse pregnancy outcomes.

The Gambia is divided into 6 socio-political regions. The population size is not evenly distributed. The western region comprises of 60% of the Population and most of them in their reproductive age.^{21–23} The 3 health centres in the western region have the highest cumulative rate of composite adverse pregnancy outcomes among people living with HIV (PLHIVs) in the Gambia (Table 3). The type 1 infection is yet the strain driving the epidemic.

Study limitation

In the data collection the challenges of seeing and extracting information from the available resources was frustrating. The registers were not found in some centres. The focal persons and officer in charge (OICs) in some centres do not have control of the record keeping of the registers and could not help when you needed them most. Recall bias and selection bias could not be completely avoided though not uncommon in retrospective studies although we made every effort to minimize the negative impact of these influence on the study.

Conclusion

HIV factor have shown increased adverse pregnancy outcome in predominant non-HAART period. Therefore, the study result strongly supports interventions that could reduce or eliminate these adverse outcomes among reproductive age women living with HIV.

Recommendations

It is pertinent for HIV response programs to recognize the indispensable association of evidence based practice and effective program implementation. Specialized care for HIV positive mothers in pregnancy should be implemented across the country, that midwives and RCH program managers should delete 4 visit antenatal care protocol in their memories in the management of HIV patients during pregnancy. PMTCT Health centres should have shared antenatal care with Obstetricians in close consultation by whichever means possible. There is need to conduct similar study during the era of triple ARV (HAART) and compare the outcomes. Sensitization of health workers and the PLHIV using the results of this study would influence practice and improve service delivery to our pregnant PLHIVs and their unborn children.

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Author's contributions

AM conceived the idea of the study and participated in its design. AM developed the data collecting tool and piloted it. GB and TD

supervised data collection at the various health centres. AM supervised data entry into a dedicated database. AM and NO took part in data cleaning and analysis. AM wrote the first draft of the manuscript. All authors read and approved the final manuscript.

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The UNAIDS The Gambia accepted the concept and subsequently sponsored this survey in 2013. The final copy has long been submitted to the country director's office. As a step down dissemination plan, this manuscript was developed for publication.

Conflicts of interests

The authors declare no conflicts of interest.

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