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Original Article

Foeto-maternal outcome of HIV-positive pregnant women on Highly Active Antiretroviral Therapy

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ABSTRACT

Background: A human immunodeficiency virus (HIV) infection in pregnant women is an important medical challenge. There exist varied reports on the foeto-maternal outcome amongst HIV positive women in Africa. **Aim:** The study was to compare the foeto-maternal outcome among HIV-positive pregnant women who are on HAART with those that are HIV-negative. **Methods:** A comparative, case-control study of booked HIV-positive and HIV-negative women attending ante-natal clinic (ANC) in Abuja. One hundred and five serial eligible HIV-positive women who booked for ante-natal care between October 8, 2012 and April 29, 2013 were recruited and matched with the control. They were followed up to six weeks post-partum. Live babies were tested for HIV using DNA polymerase chain reaction (PCR) at six weeks post-partum. The data was analysed using statistical package for social science (SPSS) version 16. Chi-square at $\leq$ 0.05 at confidence level of 95% and Student t-test were used to determine significant association. **Results:** There were 112 HIV positive pregnant women among 1683 pregnant women during the study period giving a prevalence of 6.7%. The rate of preterm delivery was significantly higher among the HIV positive women (33% Vs 18%, *P*= 0.005). There was no case of vertical transmission. **Conclusion:** Maternal HIV infection was significantly associated with preterm delivery. There was no recorded vertical transmission. Strengthening the use of HAART may maintain zero vertical transmission among other precautionary measures.

Key words: HIV, HAART, pregnancy outcome, maternal and child health, vertical transmission, booked patient

INTRODUCTION

HIV/AIDS pandemic is one of the serious health crises in Nigeria[1-3] and indeed the world. A disproportionate burden has been placed on women and children who in many settings continue to experience high rates of new HIV infections and of HIV related illness

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and deaths.[4] In 2009, 33.3 million individuals were living with HIV of whom 15.7 million were women and 2.1 million were children under 15 years.[4,5] Globally, nearly all HIV infection in children are acquired from their mothers.[5] Most children less than 15 years living with HIV acquired the infection through mother-to-child transmission (MTCT).[4] This can occur during pregnancy, labour and delivery or during breast-feeding.[4] In the absence of intervention the risk of such transmission is 30-45%.[1, 5] The high burden of MTCT in sub-Saharan Africa compared to the rest of the world is due to the higher rate of heterosexual transmission, higher prevalence of HIV in women of reproductive age, high total fertility rate, characteristically prolonged breast feeding culture as well as poor access to prevention of mother-to-child transmission (PMTCT) interventions.[1,6,7]

Pregnancy outcome is affected by high maternal viral load, viral characteristics, advanced disease, immune deficiency, infection acquired during pregnancy or breast feeding, vaginal delivery with rupture of membrane for more than 4 hours/prolonged labour, prematurity, first of multiple deliveries, mixed feeding and presence or absence of PMTCT interventions.[5] The impact of HIV on pregnancy has been well documented. The overall evidence seems to be in support of HIV having a negative impact on pregnancy outcomes.[5] A Few studies mainly in developed countries interestingly, failed to demonstrate negative impact of HIV on pregnancy outcomes.[8] Differences in study population might explain this variation. It is possible that the adverse impact of HIV on pregnancy may not be demonstrable in situations where the study population comprises mainly asymptomatic HIV infected pregnant women. Some researchers have suggested that the higher maternal and perinatal morbidity and mortality associated with HIV infection might have been due to preexisting advance stage of HIV infection before conception.[9-11] Maternal and perinatal morbidity and mortality as well as HIV/AIDs burden are disproportionately higher in sub Saharan Africa compared to developed countries.[1] It has been suggested that the impact of HIV on pregnancy will likely erode the little efforts at reducing the high maternal and perinatal morbidity and mortality in the sub region.[4] Intermittent re-evaluation and assessing the feto-maternal outcome among HIV infected pregnant women may provide evidence on the impact of HIV on these health indices in the sub region. The information may be useful in planning appropriate modifications in interventions aimed at reducing the negative impact of HIV in the sub-region.

The aim of the study was to compare the feto-maternal outcome between HIV infected and non-infected pregnant women and determine the effectiveness of HAART in preventing vertical HIV transmission during pregnancy and puerperium.

METHODOLOGY

This was a longitudinal, comparative, case control study of booked HIV positive and HIV negative women attending ante-natal clinic (ANC) in the University of Abuja Teaching Hospital, Abuja, Nigeria. The hospital is a 350-bed hospital in Nigeria's capital city, Abuja. There are over 10,000 HIV positive persons including pregnant women accessing services at the special treatment clinic of the Hospital that is funded by the President's Emergency Plan for Aids Relief (PEPFAR) through the Institute of Human Virology Nigeria (IHVN) at no cost to the patients. One hundred and five consecutive eligible HIV positive women that booked for ante-natal care between October 8, 2012 and April 29, 2013 were recruited after obtaining their consent. Informed consent was obtained from each participant. The controls were 105 HIV negative pregnant women that were matched for age, parity and gestational age at booking. Inclusion criteria were all consecutive pregnant women who gave consent for the study. Those who withheld consent as well as those with co-existing medical disorders such as diabetic mellitus, chronic hypertension / renal disease and heamoglobinopathies were excluded.

Samples were collected and analysed at different stages. Blood samples were obtained from participants at the enrolment visit for Packed Cell Volume (PCV), blood group, Fasting Blood Sugar (FBS), liver function test and Electrolyte Urea and Creatinine (E/U/Cr). Absolute counts of CD4 cells were measured using the FACS Count system (Becton Dickinson). Viral load estimation was effected at 36weeks of gestation. Urine sample was also obtained for chemical analysis. Blood

samples for PCV, blood group, FBS, LFT, and E/U/Cr were analysed at the laboratory attached to special treatment clinic of university of Abuja Teaching Hospital. Those samples for viral load and DNA PCR were transported to IHVN central laboratory at the designated Hospital within Abuja for analysis. They were followed up through ante natal period, delivery and six weeks there after. Live babies were tested for HIV using DNA polymerase chain reaction (PCR) at six weeks postpartum.

The ethical approval for the study was sort and obtained from the Hospital Research and Ethical Committee. Ethical standards were adhered to in the collection, handling and processing of samples throughout the conduct of the study.

Statistical analysis

The data was analysed using statistical package for social science (SPSS) version 16. Chi square at significant level of less or equal 0.05 and confidence level of 95% was used to determine the significance for categorical variables and t-test was used for continuous variable.

RESULT

There were a total of 1683 pregnant women who booked for ante natal care during the recruitment phase among which 112 were HIV positive (74 newly diagnosed and 38 known HIV positive) giving a prevalent rate of 6.7%. Seven HIV positive women were excluded. Among those excluded was a patient who had sickle cell anaemia and 6 others that could not be absorbed due to completed sample size.

The two groups were similar in their demographic distribution (table 1). The mean age and standard deviation (SD) of the HIV positive women was 30.08 ($\pm$3.96) compared with 30.09 ($\pm$4.06) among the control. There was no statistical significance between the educational levels in the two group (*P*=0.468).When the past obstetric performance between the two groups was analysed, it was noted that the parity distribution between the two groups were similar, with the mean parity of 1.25 (SD=1.24) and 1.38 (SD=1.38) for HIV positive and HIV negative groups respectively. Table 2 shows previous obstetric performance of the participants. Thirty four nulliparous women in each group of the study were excluded in the evaluation of history of preterm birth and caesarean section since they had not had any pregnancy to the age of viability. In the same vein, the 18 primigravidae in HIV positive group and 25 in the HIV negative groups were excluded in the evaluation of past history of miscarriage because they had never been pregnant other than the index pregnancy. The history of preterm delivery, caesarean section and, miscarriage were relatively higher among women with HIV infection in pregnancy. The relationship was however not significant. The antenatal complications were low in both groups. There was no significant difference in the mode of delivery between the two groups. Table 4 reflects the outcome of pregnancy. Low birth weight fetuses were significantly more common among HIV positive women. There was no detectable vertical transmission.

DISCUSSION

There were 112 HIV positive women among the 1683 women that booked for antenatal care during the study period, given a prevalence rate of 6.7%. This figure is relatively lower than 8.3% earlier reported from the same institution.[9] The difference may be due to the global trend in the reduction in the prevalence of HIV infection. There was no statistically significant difference regarding the demographic distribution of the women in the 2 groups. There were relatively more educated and gainfully employed women among the HIV negative women but this was not statistically significant in this study. It is probable that education and gainful employment may reduce risky behaviors of contracting HIV but this remains a subject of further research. In this study the minority ethnic groups were in the majority. The minority ethnic group in each arm of the study was more than the sum of the three major ethnic groups in Nigeria in each arm, perhaps because of the location of the study site – a suburb of the capital city of Abuja, where there is a large presence of the indigenous community and the minority ethnic groups. Sixty per cent of the HIV positive and 53% of the HIV negative participants were also from the minority tribal group. The finding that HIV pregnant women were of higher parity compared with their negative pairs is in keeping with previous reports.[12,13] This was however, not statistically significant. Other

researchers have demonstrated increase risk of miscarriage among HIV pregnant women probably, contributing to their higher parity.[12,13] The contribution of maternal HIV infection to infant and childhood death is well documented.[14] This was however not corroborated in this study as the deaths reported in this series could not be attributed to HIV related complications with certainty even though post mortem examinations were not carried out on the dead babies.

Table 1: Socio - demographic characteristics of participants

	HIV POSITIVE		**HIV NEGATIVE**		***P*-value**
Age distribution	**No**	**(%)**	**No**	**(%)**	**1.000**
21-25years	15	14.3	15	14.3	
26-30years	39	37.1	39	37.1	
31-35years	44	41.9	44	41.9	
>35years	7	6.7	7	6.7	
Total	**105**	**100.0**	**105**	**100.0**	
Educational status					**0.468**
None	4	3.8	1	1.0	
Primary	15	14.3	12	11.4	
Secondary	45	42.9	45	42.9	
Tertiary	41	39.0	47	44.8	
Total	**105**	**100.0**	**105**	**100.0**	
Gravidity					**0.366**
1	18	17.1	25	23.8	
2-4	85	81.0	70	66.7	
≥5	2	1.9	5	4.5	
Total	**105**	**100.0**	**105**	**100.0**	
Parity					**0.981**
0	34	32.4	34	32.4	
1-2	56	53.3	56	53.3	
3-4	13	12.4	13	12.4	
>4	2	1.9	2	1.9	
Total	105	100.0	105	100.0	

Table 2: Previous reproductive performances of the patients

	HIV POSITIVE		**HIV NEGATIVE**		**P value**
History of Miscarriage	**No**	**%**	**No**	**%**	**0.103**
Yes	39	44.8	26	32.5	
No	48	55.2	54	67.5	
Total	87	100.0	80	100.0	
History of Preterm Delivery					**0.320**
Yes	19	26.8	14	19.7	
No	52	73.2	57	80.3	
Total	71	100.0	71	100.0	
History of previous C/S					**0.238**
Yes	20	28.2	14	19.7	
No	51	71.8	57	80.3	
Total	71	100.0	71	100.0	

C/S = caesarean section

Table 3:Pregnancy complications and mode of delivery

	HIV POSITIVE		**HIV NEGATIVE**		***P*-value**
COMPLICATIONS					
PROM[a]	5	4.8	2	1.9	0.249
Hospital Admission	3	2.9	0	0	0.081
Preeclampsia	2	1.9	0	0	0.155
GDM[b]	1	1	2	1.9	0.561
Oligohydramnious	4	3.8	1	1	0.174
GA[c] at delivery					**0.005[x]**
28-33weeks +6days	5	4.8	0	0	
34-36 weeks+6days	28	26.7	18	17.1	
≥37weeks	72	68.6	87	82.9	
Total	**105**	**100.0**	**105**	**100.0**	
Mode of delivery					**0.136**
VD[*]	89	84.8	96	91.4	
Spontaneous	88	83.8	92	87.6	
vacuum extraction	1	1.0	3	2.9	
AVBD[**]	0	0	1	1.0	
Subtotal VD	*89*	*84.8*	*96*	*91.4*	
CS[***]	16	15.2	9	6	
Elective	10	9.5	5	4.8	
Emergency	6	5.7	4	3.8	
Subtotal CS	*16*	*15.2*	*9*	*8.6*	
Total	105	100	105	100	
Puerperal complications					**0.134**
Yes	3	2.8	0	0	
No	102	97.2	105	100	
Total	105	100	105	100	

[a]PROM =Premature rupture of membrane, [b]GDM = Gestational diabetic mellitus, [c]GA = Gestational age, * VD = Vaginal delivery, ** AVBD =Assisted vaginal breech delivery, *** CS = Caesarean section, 0.005[x] = significant *P*- value

Table 4: Pregnancy outcome of participants

	HIV POSITIVE		**HIV NEGATIVE**		***P*-value**
Outcome of labour	No	%	No	%	0.565
Live birth	102	95.3	103	97.2	
FSB[a]	4	3.7	3	2.8	
MSB[b]	1	.9	0	0	
Total	107	100.0	106	100.0	
Birth weight					**0.002[x]**
1500-2099g	4	3.9	0	0	
2000-2499g	33	32.4	19	18.4	
≥2500g	65	63.7	84	81.6	
Total	102	100.0	103	100.0	
Infant at six weeks					**0.058**
Alive and well	99	97.1	103	100	
Alive but sick	1	1.0	0	0	
Dead	2	1.9	0	0	
Total	102	100	103	100	
DNA PCR at 6weeks					
Positive	0	0	NA[c]	NA	
Negative	102	100	NA	NA	
Total	**102**	**100**	**NA**	**NA**	

[a]FSB = Fresh still birth, [b]MSB = Macerated still birth, [c]NA = Not Applicable, 0.002[xxx] = significant p-value

The use of HAART is likely to improve the effect of HIV on survival of exposed babies. Unfortunately this study was not designed to evaluate the time of death in relation to use of HAART. There were more previous caesarean delivery among HIV positive participants when compared with their counterpart (20/71 vs 14/71). This association was however not significant. It is probable that the association is more casual than causal. Perhaps, those caesarean sections were for other obstetrics indications more so that evidenced had shown no added protection for women on HAART with viral load less than 1000 copies / ml. About thirty per cent of HIV positive women developed anaemia during antenatal period compared with 23.8% in the HIV negative counterparts. This was in agreement with findings from previous workers that had demonstrated increase in anaemia among HIV positive pregnant women.[15] This study demonstrated significant increase in the rate of preterm delivery among HIV positive women (P = 0.005) similar to observations by previous workers.[16,17] There was also a significant association between low birth weight and HIV positivity in pregnancy in this study (P = 0.002). Similar findings have been reported from studies conducted in Kano, Nigeria[16] and Botswana.[19] There was no congenital malformation at birth among the fetuses in this study despite the use of HAART by all HIV positive women. This may further strengthen the existing evidence for the safety of ARTs in pregnancy.[20,1] All (100%) of the living children of the HIV positive women tested negative for HIV using DNA PCR at six weeks of life. This is a major achievement in the fight against maternal to child transmission of HIV. Perhaps if these children were followed up to much longer time and their status remain zero vertical transmission, the conclusion would have been stronger. A study design to follow up women for up to at least a year when the baby could be safely weaned would form a subject of future research in this developing community where formula feeding can hardly be sustainable.

CONCLUSION

This study has demonstrated significant association between maternal HIV infection and preterm delivery and zero vertical transmission in mothers on HAART. There was no significant difference in maternal morbidity between the two groups. The shorter follow up period may have partly explained the zero vertical transmission but further research in that direction may be necessary. The continuing campaign for the primary prevention of HIV infection amongst women of reproductive age group should be sustained in order to reduce the burden of prematurity especially in developing societies like Nigeria. It may be rewarding to institute routine screening for the risk factors for prematurity in all HIV infected pregnant women. Where identifiable risk factors are isolated, effective treatment should be promptly instituted.

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