HIV in pregnancy: Severity of maternal disease a determinant of pregnancy outcomes

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Corresponding Author:
Dr. Onyeka I Uzoma,
Consultant, Obstetrics and gynaecology, Imo state University teaching hospital, Orlu, Nigeria, 1 Hospital road, Umuna, Box 8 - Nigeria

Submitting Author:
Dr. Onyeka I Uzoma,
Consultant, Obstetrics and gynaecology, Imo state University teaching hospital, Orlu, Nigeria, 1 Hospital road, Umuna, Box 8 - Nigeria

Other Authors:
Dr. Fredrick Anolue,
Consultant, Imo State University Teaching Hospital, Orlu. Department of Obstetrics and Gynaecology, No 1 Hospital Road, Orlu, 08 - Nigeria
Dr. Ephraim Dike,
Consultant, Imo State University Teaching Hospital, Orlu. Department of Obstetrics and Gynaecology, No 1 Hospital Road, Orlu, 08 - Nigeria
Dr. Chijioke Okeudo,
Consultant, Imo State University Teaching Hospital, Orlu, No 1 Hospital road Orlu, 08 - Nigeria

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HIV in pregnancy: Severity of maternal disease a determinant of pregnancy outcomes

Author(s): Uzoma Ol, Anolue F, Dike E, Okeudo C

Abstract

Background: The Human Immunodeficiency Virus is responsible for a global pandemic with a disproportionately higher prevalence in sub Saharan Africa. Infection with the virus in pregnancy is of particular importance given the added risk of mother to child transmission. Antiretroviral drugs are currently recommended for all pregnant HIV positive women.

Objective: To compare pregnancy outcomes for mother and baby based on the severity of maternal HIV disease.

Method: A prospective observational study of consecutive consenting pregnant women who tested HIV positive during pregnancy, labour and delivery at the Imo State University Teaching Hospital (IMSUTH), Orlu from 1st May, 2012 to 30th April 2013 was carried out. Sociodemographic information were obtained and entered into a questionnaire prepared for this study. Clinical staging, CD4 counts, information on pregnancy outcomes and infant HIV testing done at six weeks post partum were all obtained. The data was analysed using the statistical package for social sciences (SPSS) version 17.0 (SPSS Inc, Chicago, IL).

Results: The Prevalence of HIV in pregnancy at booking was 6.1%. Those with advanced disease accounted for 35.6% (37/104) while 64.4% (67/104) had early stage disease. The vertical transmission rate was 1.0%. There was one case of maternal mortality (0.9%), while the perinatal mortality rate was 5.8%.

Conclusion: Human immunodeficiency virus infection in pregnancy is a serious public health concern at the Imo State University Teaching Hospital, Orlu and its environs. Vertical transmission remains a challenge. Maternal mortality and vertical transmission are more likely to occur in those women with advanced disease.

Key words: HIV, pregnancy outcome, maternal HIV disease, outcome, preeclampsia, Orlu.

Introduction

Few, if any, maternal infection has attracted as much attention as HIV in pregnancy, as it is a public health issue of great importance. Infection may precede or occur during the index pregnancy. The prevalence of HIV in Nigeria is 4.1%. Maternal HIV disease may be early when the CD4 count is above 350 cells/ml or World Health Organization (WHO) stage 1 or 2 or advanced [when the CD4 count is less than 350 cells/ml or WHO stage 3 or 4]. A disproportionate burden has been placed on women and children, who in many settings experience high rates of new HIV infection and HIV related illnesses and death. Ninety percent of children acquire the infection through parent to child transmission. In the absence of any intervention, the risk of vertical transmission is 15-30% in non breastfeeding populations. In addition to vertical transmission, various pregnancy outcomes such as pre-eclampsia, perinatal mortality, birth weight, Apgar score at 5 minutes, maternal mortality, gestational diabetes mellitus, etc have been studied to assess the impact of this infection on them.

Few studies have compared these outcomes in early maternal HIV disease versus advanced maternal HIV disease. This study aims at comparing pregnancy outcomes in early and late maternal HIV disease at the Imo State University Teaching Hospital, Orlu, Nigeria.

Methods

This was a prospective observational study of consecutive consenting pregnant women who tested HIV positive during pregnancy labour and delivery at the Imo State University Teaching Hospital, Orlu between 1st May 2012 to 30th April 2013. The HIV Testing was done using serial testing with rapid test kits (using Determine test kit for screening), then a confirmatory test (using Unigold test kit), and when necessary a tiebreaker test (using Stat Pak test kit) as recommended by National Prevention of mother to child transmission guidelines. Data on age, parity, gestational age, marital status, educational level, clinical stage of the disease and CD4 count were obtained at booking. Similar information were obtained from booked and unbooked women who were determined to be HIV seropositive in labour and information on pregnancy outcomes were collated at
delivery. Infant HIV testing was done at 6 weeks post partum. Other data obtained included information on live births, stillbirths, Apgar score at 5 minutes, birth weight and HIV status of the infant. For the mother, the data obtained included maternal deaths, preterm delivery, pre-eclampsia/eclampsia, gestational diabetes mellitus and mode of delivery.

WHO clinical staging was used to help group these women into early and advanced disease. Clinical stages are categorized as 1 through 4, progressing from primary HIV infection to advanced HIV/AIDS. These stages are defined by specific clinical conditions or symptoms. Clinical Stage 1, asymptomatic or persistent generalized lymphadenopathy. Clinical Stage 2, moderate unexplained weight loss (< 10% of presumed or measured body weight), recurrent respiratory infections (sinusitis, tonsillitis, otitis media, and pharyngitis), herpes zoster, recurrent oral ulceration, papular pruritic eruptions, seborrheic dermatitis, fungal nail infections. Clinical Stage 3, unexplained severe weight loss (>10% of presumed or measured body weight), unexplained chronic diarrhoea for >1 month, unexplained persistent fever for >1 month (>37.6°C, intermittent or constant), persistent oral candidiasis (thrush), oral hairy leukoplakia, pulmonary tuberculosis (current), severe presumed bacterial infections (e.g., pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteremia), acute necrotizing ulcerative stomatitis, gingivitis, or periodontitis, unexplained anaemia, haemoglobin < 8 g/dL, neutropenia (neutrophils < 500 cells/µL), chronic thrombocytopenia (platelets < 50,000 cells/µL). Clinical Stage 4, HIV wasting syndrome, Pneumocystis pneumonia, recurrent severe bacterial pneumonia, chronic herpes simplex infection (oralabial, genital, or anorectal site for >1 month or visceral herpes at any site), oesophageal candidiasis (or candidiasis of trachea, bronchi, or lungs), extrapulmonary tuberculosis, Kaposi sarcoma, Cytomegalovirus infection (retinitis or infection of other organs), central nervous system toxoplasmosis, HIV encephalopathy, Cryptococcus, disseminated nontuberculosis mycobacteria infection, progressive multifocal leuкоencephalopathy, Candida of the trachea, bronchi, or lungs, chronic Cryptosporidiosis (with diarrhoea) chronic Isosporiasis, disseminated mycosis (e.g., histoplasmosis, coccidioidomycosis, penicilliosis), recurrent nontyphoidal Salmonella bacteremia, lymphoma (cerebral or B-cell non-Hodgkin), invasive cervical carcinoma, atypical disseminated leishmaniasis, symptomatic HIV-associated nephropathy, symptomatic HIV-associated cardiomyopathy, reactivation of American trypanosomiasis.1,4

The data were analysed using the SPSS software, version 17.0 (SPSS Inc, Chicago, IL). The study received the hospital’s ethical committee approval.

Results

A total of 1,189 women booked for antenatal care from 1st May 2012 to 30th April 2013 of this number, 72 tested positive for antibodies to HIV 1 and 2, giving a prevalence of 6.1% (72/1,189) at booking. However, a total of 104 pregnant seropositive women were used for the study; the additional 32 subjects who tested HIV positive were unbooked and tested positive in labour. Of the total number 64.4% (67/104) women had the early disease while 35.6% (37/104) had the advanced disease, of this number 69.2% (72/104) were booked while 30.8% (32/104) were unbooked.

The mean age of the study population was 29.0 years ± 5.1. The age range of 26-30 years contributed the highest proportion to the study with 34.6% (36/104) while those ≥ 20 years contributed the least 6.7% (7/104).

Table 1 shows the sociodemographic information of the respondents. Table 2 shows the parity distribution of the women. 15.4% (16/104) of the study population were primigravida, 75% (78/104) were multiparous, while 9.6% (10/104) were grandmultiparous. It was also noted that 65.4% (68/104) of the HIV infected women had a parity of < or = 2. In the multiparous group the early maternal HIV disease group vs. advanced maternal HIV disease group were 64.1% (50/78) vs. 35.9% (28/78). In the primigravida and grandmultiparous groups, this was 81.3% (13/16) vs. 18.7% (3/16) and 40% (4/10) vs. 60% (6/10) respectively.

The majority of the study population had attained secondary education 77.9% (81/104), while 11.5% (12/104) had primary education and 10.6% (11/104) had tertiary education.

There was one case of gestational diabetes mellitus in a patient with early disease (p = 0.455).

The mean gestational age at delivery was 39.1 weeks ± 2.15. There was no significant difference in mean gestational age between both groups, (p = 0.435).

Delivery by caesarean section accounted for 10.6% (11/104) compared to 89.4% (93/104) vaginal deliveries. The indications for caesarean section in this study were purely obstetric, 4 36.4% (4/11) were seen in the advanced maternal HIV disease group.
compared to 63.6% (7/11) in the other group while vaginal deliveries were 35.5% (33/93) and 64.5% (60/93) respectively, (p = 0.954).

Five cases of pre-eclampsia were seen, 4.8% (5/104) of the study population, 40% (2/5) of these were seen amongst the non severe disease group and 60% (3/5) in the advanced disease category (p = 0.242).

Live births were 94.2% (98/104), stillbirths were 5.8% (6/104) for the study population. In the non severe group stillbirths were 66.7% (4/6) compared to 33.3% (2/6) in those with advanced disease.

The mean birth weight was 3.2kg ± 0.53. There were a total of 8.7% (9/104) low birth weight babies; this value falls to 1.9% (2/102) when adjusted to accommodate only low birth weight at term. Equal numbers of term low birth weight babies were seen in both groups (i.e., 1 in each group), (p= 0.667).

The median (SD) CD4 cell count for the severe maternal disease group was 244 (97.79) and that for the early disease group was 477.76 (120.19), (p = 0.001).

The median (SD) Apgar score at 5 minutes was 10 (1.02) in the severe disease group and 10 (0.83) for the non severe disease group.

Postpartum haemorrhage was seen in a total of 4.8% (5/104) subjects, in the advanced maternal disease subset it occurred in 2.7% (1/37) compared to 5.9% (5/104) subjects, in the advanced maternal disease group (p = 0.456).

Vertical transmission occurred in 1 subject representing 1.0% (1/98) transmission rate (only live births were considered), (p = 0.170). This single transmission was seen in the advanced disease group (2.7%) compared to none (0%) in the other group.

Table 2 highlights the above pattern of mother to child transmission (MTCT).

There was 1 (2.7%) maternal mortality in the severe disease group and none (0%) in the early maternal disease group (p = 0.176).

Discussion

The prevalence of HIV in pregnancy at booking of 6.1% in this study was slightly higher than that quoted for the south eastern zone of Nigeria in a national study as well as a regional study done in this same zone.4-13 This may reflect the slight differences in prevalence between different states and localities within the zone as reflected in the 2010 National HIV Seroprevalence Sentinel Survey.4 The women who were within the 26-30 years age range had the highest prevalence in this study, which was similar to the findings in other studies.14,15 Various reasons have been put forward as to the increased infection rate in young women. These include untreated or undiagnosed asymptomatic sexually transmitted infections, multiple sexual partners and sexual intercourse with older men.14,15

Parity of 2 or less was shown in one study to be associated with increased risk of HIV infection, an association that was also seen in this study.16 In this study these women constituted 65% of the entire study population. It was however only among the women with parity > 4 that those with advanced disease formed a greater proportion. The advanced disease was less common in newly diagnosed primigravida and multiparous (parity of 1-4) women. A study in French Guiana had different findings with parity status > 4 and gravidity > 2 being associated with an increased risk of seropositivity.17

This study showed that only one case of gestational diabetes mellitus (GDM) occurred in the group with early disease compared with none in the advanced disease group (p= 0.4553). This was not statistically significant. Some studies have shown a link between HIV in pregnancy and GDM.18 Other studies do not.19 Here other variables should be considered such as family history of type II DM, age and lifestyle.18,19

Overall 4.8% of the women studied had pre-eclampsia. There were 2 cases in the group with advanced disease and 3 in the group with early disease (p = 0.242). One study done looked retrospectively at the incidence of preeclampsia in HIV infected pregnant women in three different time frames; 1984 to 1994, 1994 to 1998 and 1998 to 2003. The last period being the HAART period while the first was the no ARV period, the second was an intermediate period with moderate uptake of dual ARVs. The study showed a clear rise in prevalence in the HAART period.20 Another study which sampled a cohort of seronegative and seropositive women found no increase in the prevalence among the HIV infected group.21

Some studies have shown poor apgar scores (< 4) at 5 minutes being associated with advanced disease, this was not the case in this study as the median apgar scores were identical for both groups and none was below 5.18

There were differences in live births/stillbirths for both groups. The differences were not significant statistically. A study in Botswana showed that HIV infection was not associated with increased stillbirths.22

A different study linked advanced maternal disease with increased stillbirths particularly in symptomatic women. 23
The only case of maternal mortality was seen in a woman with advanced HIV disease. A study done in Kenya showed evidence of advanced disease being associated with increased maternal mortality.\(^2\)

The only case of mother to child transmission also occurred in the group with advanced disease. This represents a vertical transmission rate of 1.0% (live births only) for the entire study which agrees with numerous studies that place vertical transmission with prevention of mother to child transmission (PMTCT) measures at less than 2%. One study showed a decrease in the prevalence of MTCT during the HAART era.\(^7\)

It is imperative to note that WHO guidelines on the treatment/prevention criteria for adults and adolescents underwent revision in 2013.\(^8\) Current recommendations include commencement of triple ARVs at a CD4 count of 500 cells/mm\(^3\) or less, immediate commencement of treatment for CD4 of 350 cells/mm\(^3\) or less, in those with concomitant active Tuberculosis, those with Hepatitis B co-infection in the presence of severe liver disease and in pregnant or breastfeeding women with HIV. Also option B plus which advocates the initiation of treatment in HIV seropositive pregnant women and continuing lifelong therapy is also being recommended by WHO.\(^9\)

**Conclusion**

In conclusion this study has shown that vertical transmission and maternal death are more likely to occur in pregnant women with advanced maternal HIV disease.

**References**


25. WHO 2013 Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection.7: 92.
Illustrations

Illustration 1

Table 1: Sociodemographic Distribution of Respondents

<table>
<thead>
<tr>
<th>Age Distribution in years</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>15-20</td>
<td>7</td>
<td>6.73</td>
</tr>
<tr>
<td>21-25</td>
<td>18</td>
<td>17.31</td>
</tr>
<tr>
<td>26-30</td>
<td>36</td>
<td>34.62</td>
</tr>
<tr>
<td>31-35</td>
<td>34</td>
<td>32.69</td>
</tr>
<tr>
<td>36-40</td>
<td>9</td>
<td>8.65</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>104</td>
<td>100</td>
</tr>
</tbody>
</table>

Educational Status

- Primary Education: 12 (11.54%)
- Secondary Education: 81 (77.89%)
- Tertiary Education: 11 (10.57%)

**Total**: 104 (100%)

Marital Status

- Married: 103 (99.04%)
- Single: 1 (0.96%)

**Total**: 104 (100%)
Illustration 2

Table 2: Parity Distribution of respondents

<table>
<thead>
<tr>
<th>Parity</th>
<th>Early Maternal HIV Disease (%)</th>
<th>Severe Maternal HIV Disease (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>13 (19.40)</td>
<td>3 (8.11)</td>
</tr>
<tr>
<td>1-4</td>
<td>50 (74.63)</td>
<td>28 (75.68)</td>
</tr>
<tr>
<td>&gt; 4</td>
<td>6 (8.96)</td>
<td>6 (16.21)</td>
</tr>
<tr>
<td>Total</td>
<td>67</td>
<td>37</td>
</tr>
</tbody>
</table>
Table 3: Disease Severity and delivery route

<table>
<thead>
<tr>
<th>Disease severity</th>
<th>Mode of Delivery</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Vaginal Deliveries (%)</td>
<td>Caesarean Section (%)</td>
<td></td>
</tr>
<tr>
<td>Early Disease</td>
<td>60 (64.52)</td>
<td>7 (63.64)</td>
<td></td>
</tr>
<tr>
<td>Advanced Disease</td>
<td>33 (35.48)</td>
<td>4 (36.36)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>93</td>
<td>11</td>
<td></td>
</tr>
</tbody>
</table>
Table 4: Mode of Delivery

<table>
<thead>
<tr>
<th>Mode of Delivery</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caesarean Section Delivery</td>
<td>11</td>
<td>10.58</td>
</tr>
<tr>
<td>Vaginal Delivery</td>
<td>93</td>
<td>89.42</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>104</td>
<td>100</td>
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