



Outcome of Pregnancy among HIV Infected Women: A Retrospective Cohort Study in a Tertiary Care Hospital in Bangalore, India

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INTRODUCTION

Ever since 1986, when the first known case of HIV in India was diagnosed amongst female sex workers in Chennai, this virus has been affecting the people of India without sparing any age, sex or race. In 2009, according to National AIDS Control Organization (NACO), the average adult HIV prevalence in India was 0.31% and had the third largest number of people living with HIV/AIDS.¹ Of all HIV infections in India, 39% are among women.¹

ABSTRACT

Background- HIV positive women have been reported to have a higher incidence of adverse pregnancy outcomes.

Objectives- To determine the incidence of maternal and perinatal morbidity and mortality among HIV infected and HIV non-infected pregnant women.

Methods- This retrospective, record-based, cohort study included 79 HIV infected and 79 HIV non-infected pregnant women, matched for 5 year age group and parity. Data was abstracted from medical records and analyzed using SPSS-18 software.

Findings- Mean haemoglobin and weight prior to delivery was lower in exposed cohort (10.82 vs. 11.50 g%, $p=0.011$; 59.50 vs. 65.02 kgs; $p=0.003$ respectively). Exposed cohort had greater incidence of antenatal infections (12.70% vs. 3.80%, $p=0.043$), postpartum infections (19.10% vs 5.10%; $p=0.007$) and caesarean section (92.30% vs. 26.60%, $p=0.000$). Low birth weight was 2.74 times more common in neonates of HIV positive women ($p=0.009$). Neonatal hospitalization was longer (range: 3-58 vs. 1-51 days, median: 6 vs. 4 days; $p=0.007$) and neonatal complications were 3.95 times more common in the exposed cohort ($p=0.007$). Caesarean section and neonatal complications were independent risk factors associated with outcome of pregnancy in HIV positive women.

Conclusion- A significant association exists between HIV infection and anaemia, antenatal and postpartum infections, lower maternal weight gain, caesarean section, low birth weight in neonate and duration of neonatal hospitalization.

Keywords: HIV, maternal morbidity, mortality, neonatal morbidity, pregnancy

A number of studies, many of which were conducted in developing nations, have concluded that several adverse pregnancy outcomes, including complications of both early and late pregnancy, are associated with maternal HIV infection.²⁻⁶ HIV-1 and HIV-2 infection in Africa have both been linked to a higher rate of spontaneous abortion and ectopic pregnancy.²

HIV positive women have been reported to more commonly develop infections of the genital tract like gonorrhoea, chlamydia, candida and trichomoniasis.^{2, 3, 4} A study found that 33 % of HIV-

positive pregnant women in South Africa had a concurrent positive syphilis serology, which was three times higher than the incidence in HIV uninfected women.³ Further, several systemic infections including bacterial pneumonia and UTIs are more common during the antenatal period in HIV positive pregnant women.⁵

Rates of preterm labour in HIV-positive women have been reported to be as high as double those noted in HIV negative women.⁶ Preterm rupture of membranes and abruptio placentae have been noted to occur more frequently in HIV positive pregnant women.⁷ Many researchers have observed that neonates born to HIV positive women were more likely to have low birth weight and higher incidence of a variety of neonatal complications including neonatal septicaemia than the newborns of HIV negative women.^{6,8}

According to sentinel surveillance data of Government of India, Karnataka is classified as a "high prevalence state".⁹ Since few such studies have been conducted in this part of India in a tertiary level health care scenario, this research was undertaken with the objective of determining the incidence of maternal and perinatal morbidity and mortality among HIV infected and HIV non-infected pregnant women in a tertiary hospital in Bangalore, a South Indian city.

METHODS

This was a retrospective record-based cohort study and was conducted in a tertiary care hospital in Bangalore city located in the South Indian state, Karnataka. The study was conducted over a period 2 months, July to September 2013.

Sample size estimation-We included 79 HIV infected and 79 HIV non-infected pregnant women. The basis for sample size selection is as follows: a study carried out in Maharashtra, India revealed that the prevalence of low birth weight was 36% in neonates born to HIV positive pregnant women and 10% among neonates of HIV negative pregnant women.¹⁰ In order to demonstrate statistical significance between these two groups, with a confidence level of 95% and with the power of the study being 95%, the required number of subjects to be tested in each group was 66. We added 20% to the sample size in order to compensate for incomplete records, if any. Hence, a total sample size of 79 was estimated.

Ethical clearance was obtained from the Institutional Ethical Review Board. Permission was obtained from the authorities of the college and hospital to access the records at the medical records

department. A semi-structured questionnaire was designed for the purpose of data collection.

An exposed cohort was defined as a pregnant woman who had been diagnosed with HIV/AIDS either before or during the present pregnancy either at the study hospital or outside, immaterial of other co-morbid conditions, and has delivered at the study hospital. A non-exposed cohort was defined as a pregnant woman who had been found to be HIV-negative during the present pregnancy either at the study hospital or outside, adequately matched for age (5-year interval groups) and exact parity and delivered at the study hospital. The primary end point was the outcome of pregnancy and associated events in mothers and newborns of both cohorts.

For the purpose of selection of subjects for the exposed and non-exposed cohorts, a preliminary review of records was first conducted, which showed that about 30 HIV positive women had delivered over the past 2 years. Hence, records of six years (from 2008 to 2013) were reviewed until 79 HIV positive women were recruited under the study group, exposed cohort. Further, choice of subjects for the non-exposed cohort group was done by matching for age (5-year interval age groups) and exact parity in order to eliminate the confounding effect of these two factors. Using the parturition register, HIV negative women, who met with the criteria for non-exposed cohort and had delivered within 3 months before or after the date of delivery of the exposed cohort, were stratified based on age and parity. From this list of potential subjects, the final HIV negative matching subject was randomly chosen with the help of random number table. In this manner, 79 HIV negative women were recruited as the non-exposed cohort. Next, the hospital numbers of respective neonates were retrieved from the birth register at Medical Records Department (MRD).

Data collection and entry: Access to records was obtained from MRD and data was abstracted using a semi-structured questionnaire. Data was first entered into Microsoft Excel and analysis was carried out using Statistical Package for the Social Sciences (SPSS) Version 18.0.

STATISTICS: Descriptive statistics such as mean and standard deviation were computed to summarize the quantitative data. Qualitative data was expressed in terms of percentage positivity rate and 95% confidence level. Incidence rates and odds ratio with 95% confidence interval were calculated. Odds ratios were computed instead of relative risk since the primary endpoint was outcome of pregnancy and associated events in the mothers and newborns of both cohorts. The differences in mean values between the groups were tested for statis-

tical significance by applying the student "t"-test. Differences in median were tested using the Mann Whitney U Test. Similarly, to test for differences in the positivity rate between different groups of women, Chi-square test of significance was employed. Fischer's Exact Test was used when values in cells were less than five. P-value <0.05 was considered for statistical significance. Multiple logistic regression was employed to identify significant independent outcomes associated with HIV positive pregnancy.

RESULTS

A total of 158 women, 79 HIV infected subjects and 79 age and parity matched HIV non-infected subjects, were recruited as exposed cohort and non-exposed cohort, respectively. We observed that the mean age was 25.17 years (SD 4.11 years), ranging between 18 and 39 years, with 43.1 % of the women being aged between 25 and 29 years. 48% of the

women under study were primigravidae. Mean gravidity was observed to be 1.96 (SD 1.13).

Quantitative variables consisting of maternal haemoglobin and weight prior to delivery as well as neonatal hospitalization in the HIV positive and HIV negative cohorts have been summarized in Table 1.

Univariate analysis of the various maternal and neonatal outcomes of pregnancy in the exposed and non-exposed cohort has been summarized in Table 2. It demonstrated significant association of HIV positive pregnancy with maternal infections in the antenatal period, incidence of caesarean section, incidence of low birth weight babies, post partum maternal infections and incidence of neonatal complications. In order to find the independent outcomes amongst the above mentioned outcomes, a multiple logistic regression was done considering HIV positives as exposed cohorts and HIV negatives as non-exposed cohorts.

Table 1- Characteristics of haemoglobin level, maternal weight prior to delivery and duration of neonatal hospitalization in the exposed and non-exposed cohort

Variable	Exposed Mean (SD) g/dL	Non-Exposed Mean (SD) g/dL	"P" Value
Haemoglobin	10.82 (1.54)	11.50 (1.63)	0.011
Weight	59.50 (8.95)	65.02 (10.56)	0.003
Duration of neonatal hospitalization Median (IQR) in days	6 (3-58)	4 (1-51)	0.000

Table 2- Maternal and neonatal outcomes of pregnancy in HIV positive and HIV negative cohorts

Outcome	Exposed (%)		Non Exposed (%)		OR(95% CI)	aOR (95% CI)	P value
	Yes	No	Yes	No			
Outcomes in past pregnancy(s)							
Previous abortions (n=41)*	19 (46.3)	22 (53.7)	20 (48.8)	21 (51.2)	0.91 (0.38-2.16)		0.996
Previous still-births (n=41)*	8 (19.5)	33 (80.5)	3 (7.3)	38 (92.7)	3.07 (0.75-12.53)		0.105
Outcomes in present pregnancy							
Positive syphilis serology†	3 (4.3)	67 (95.7)	1 (1.4)	71 (98.6)	3.18 (0.32-31.32)		0.297
Hyperemesis Gravidarum (n=79)	5 (6.3)	74(93.7)	1 (1.3)	78 (98.7)	5.27 (0.60-46.18)		0.096
Ante-natal Infections (n=79)	10 (12.7)	69 (87.3)	3 (3.8)	76 (96.2)	3.67 (0.97-13.89)		0.043
Preterm Delivery (n=79)	11 (13.9)	68 (86.1)	10 (12.7)	69 (87.3)	1.12 (0.45-2.80)		0.815
Caesarean Section (n=79)	73 (92.3)	6 (7.7)	21 (26.6)	58 (73.4)	33.6 (12.73-88.69)	35.71 (12.57-100.55)	0.000
Post-partum Hemorrhage(n=79)	7 (8.9)	72 (91.1)	2 (2.5)	77 (97.5)	3.74 (0.75-18.61)		0.086
Post-partum Infections (n=79)	15 (19)	64 (81.0)	4 (5.1)	75 (94.9)	4.46 (1.41-14.14)		0.007
Neonatal Outcomes							
Low Birth Weight‡n=81)	28 (34.6)	53 (65.4)	14 (17.3)	67 (82.7)	2.74 (1.26-5.93)		0.009
NICU Admission‡n=81)	24 (29.6)	57 (70.4)	22 (27.2)	59 (72.8)	1.13 (0.57-2.24)		0.727
Neonatal Jaundice§	22 (28.2)	56 (71.2)	23 (31.1)	51 (68.9)	0.78 (0.38-1.58)		0.482
Neonatal Complications	17 (21.5)	62 (78.5)	5 (6.4)	73 (93.6)	3.95 (1.38-11.32)	5.41 (1.06-41.62)	0.007

Note: Statistically significant "P" values have been highlighted in bold and underlined.

OR=Odds Ratio by Univariate Analysis; aOR=Adjusted OR by Multivariate Analysis

*38 subjects in each group were primigravidae and hence could not be included in the testing for outcomes in past pregnancy (ies)

†Due to non-availability of information in the records, there were 9 and 7 missing values among exposed and non-exposed cohorts, respectively

‡Although 79 subjects were included in each study group, we studied 81 neonates in each group since 1 exposed cohort gave birth to triplets and 2 non-exposed cohorts delivered twins

§Data of 3 neonates of exposed cohort and 7 neonates of non-exposed cohort was not available in the records and therefore, 78 and 74 neonates were tested in the exposed and non-exposed cohort groups, respectively

||Data of 2 neonates of exposed cohort and 3 neonates of non-exposed cohort was not available in the records and therefore, 79 and 78 neonates were tested in the exposed and non-exposed cohort groups, respectively

The analysis revealed 2 factors, namely incidence of caesarean section, with odds ratio of 35.71 and 95% confidence level, 12.57-100.55 and incidence of neonatal complications, with odds ratio of 5.41 with a 95% confidence interval of 1.06-41.62, as the significant outcomes.

DISCUSSION

In many societies, HIV/AIDS is more than just a disease; it is a stigma. Being HIV positive can affect multiple dimensions of an individual. This is more important in the case of a pregnant woman because there are two individuals at stake.

Although studies found an association between HIV infection in pregnancy and previous spontaneous abortions and previous still-births, our study did not yield a statistically significant difference between exposed and non-exposed cohorts in either of the above.^{2,4,11} Since 38 out of 79 subjects in each group were pregnant for the first time, they were excluded in the testing of the above mentioned outcomes. A larger number of subjects could be required in order to demonstrate a statistical significance. In addition to this, the hospital in which the study was carried out is a tertiary referral hospital and hence, in spite of matching for age and parity, few of the subjects of the unexposed cohort were also considered high-risk pregnancies.

We saw a significant association between HIV positive maternal status and incidence of infections in the antenatal period. Pregnancy and HIV are both, individually, states of immune-suppression and may even exert a synergistic effect together. Several other studies have also demonstrated similar results.^{3,4} We observed that 4.3% of the HIV positive women were reactive for VDRL while only 1.4% of the HIV negatives had positive syphilis serology. A study from South-Africa reported that 33% of HIV-positive pregnant women had a concurrent infection with syphilis.⁴

We found that anaemia is significantly associated with HIV positive pregnancy. Women who were HIV positive had significantly lower haemoglobin values in comparison with their HIV negative counterparts (10.82 g/dL versus 11.5 g/dL; p-value=0.011). This was consistent with the findings of several previous studies.^{11, 12} HIV, by itself, results in decreased RBC production, increased destruction of RBCs and in some cases, even blood loss. These can contribute to anaemia directly. Next, zidovudine is known to produce bone marrow suppression and thus, may result in anaemia. An indirect cause of anaemia in HIV positive women could be that they are stigmatized in the society and thereby, nutritional deficiencies are more frequent in them.

A statistical association was also established in our study between HIV in pregnancy and poor weight gain during pregnancy. Higher energy expenditure associated with HIV infection and neglected nutritional status of HIV positive women could contribute to lower weight gain among these women.

Opportunistic infections in HIV positive women predisposes to preterm births. Numerous studies have concluded that HIV positive pregnancy can result in pre-term labour.^{2, 6, 12} Though our study did find a higher incidence of preterm delivery in HIV positive subjects than in HIV negative analogues (13.9 % versus 12.7 %), we did not find a statistical significance. This could be due to high risk pregnancy among a few members of the non-exposed cohort in our centre of study. In Ghana, preterm delivery was reported to be higher among HIV positive mothers (24.4% versus 13.6%) with statistical significance.⁶

A considerable number of cases of vertical transmission of HIV from mother to child occur due to fetal exposure to the virus during labour and delivery. Hence, caesarean section has been considered to be a safer mode of delivery in HIV positive pregnant women. Thus, it is not surprising that 92.3% of HIV positive subjects included in our study underwent caesarean section as opposed to 26.6% of the HIV negative women (p-value=0.000). Multiple logistic regression was done and the odds ratio was found to be 35.71 at 95% confidence interval and caesarean delivery was found to be a significant outcome. A South-Nigerian study, in like manner, reported that while 46.9% of HIV positive women underwent a caesarean section, 27.3% of HIV negative women had a caesarean section.²

We found a significant (p-value=0.007) association between maternal HIV infection and low birth weight in the neonate. HIV positive women were 2.74 times more likely to give birth to a low birth weight baby than the HIV negatives. Numerous other studies have produced results coherent with the above.^{6,12-14} Poor maternal nutritional status in HIV positive pregnancy plays a crucial role in causation of low birth weight as do other factors like the negative influence of HIV on maternal immunity and higher incidence of other infections.

Many studies have looked into the incidence of postnatal complications in HIV positive pregnancies, few of which concluded that HIV pregnant women had a greater risk of developing postpartum haemorrhage (PPH).¹⁵ The reasons for the same are poor wound healing and HIV-related thrombocytopenia. In our study, we observed a higher incidence of PPH in the exposed cohort (8.9% vs 2.5%). However, a statistical significance was not obtained. We found a statistically significant association ($P=0.006$) in case of postpartum

infections with the risk being 4.64 times higher in the HIV positive cohort.

Past studies concluded that maternal HIV infection was an important determinant of stillbirth and early neonatal mortality.¹⁴ In our study, however, we observed that there were no stillbirths and neonatal deaths during the period of hospitalization. One of the reasons for this may be the availability of tertiary level obstetric care and neonatal intensive care unit (NICU) facilities in our centre.

We observed that newborns of HIV positive women required a longer duration of hospitalization and the difference was statistically significant ($P=0.000$). Neonates of HIV positive women had greater rates of NICU admission compared to those of HIV negative subjects, though not statistically significant. Few studies found a higher rate of admission in newborns of HIV positive women in comparison with those of HIV negative analogues.² Since HIV positive pregnant women are more likely to go into preterm labour, these newborns require NICU admission for preterm care. Additionally, neonates of HIV positive pregnancy are more susceptible to developing complications during the neonatal period, also necessitating NICU care.

Several studies have established a higher incidence of adverse neonatal outcome in HIV positive pregnancy.^{2,8} In our study, 22.1% of the newborns of HIV positive women developed one or more complications during the hospital stay compared to a small proportion of neonates of HIV negative pregnant women. The neonatal complications in the exposed cohort included congenital pneumonia, transverse tachycardia of newborn, hypoglycaemia, grade 3 germinal matrix bleed, congenital anomalies in the form of accessory nipple and cleft palate, sepsis and labial cellulitis, ocular infection, cutaneous infection, heart disease in the form of situs solitus, tricuspid regurgitation and patent ductus arteriosus, candidiasis, abdominal distension, excessive crying, sacral swelling, staphylococcal sepsis and gastroenteritis.

The implications of our study are several. The medical line of care for the HIV positive pregnant woman and her newborn will differ from that provided to an uninfected woman. In view of this, it is important that the woman and her family be informed and counseled about these differences. Pregnancy makes a good entry point to the diagnosis and management of HIV. Awareness among health personnel about adverse outcomes of HIV positive pregnancy will aid in better anticipation and management of complications and institution of measures to reduce transmission of infection to neonate and increase neonatal survival. Increasing awareness among women about the effects of HIV infection in pregnancy will lead to better health-

seeking behavior, including HIV screening and better compliance to antenatal care.

A larger sample size and a prospective cohort study would probably strengthen the findings of our study further and throw more light on the challenges of a pregnancy complicated by HIV.

CONCLUSION

Maternal HIV status is a vital determinant of the outcome of pregnancy. This study established a significant positive association between HIV infection and anaemia, infections in the ante partum period, maternal weight gain prior to delivery, incidence of caesarean section, postpartum infections, birth weight of the neonate and duration of neonatal hospitalization. HIV positive women also had a higher incidence of previous stillbirths, concurrent positive syphilis serology, preterm labour, postpartum haemorrhage and neonatal admission to the neonatal intensive care unit. Caesarean section and ante partum infections influenced the pregnancy outcome the most.

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