

Research Article

Human Immunodeficiency Virus in Pregnancy a Retrospective Study on Maternal and Perinatal Outcomes

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Abstract

Objective: To assess the maternal and perinatal outcome in pregnant women with HIV infection and the role of Antiretroviral therapy in reducing complications of pregnancy.

Methods: A retrospective analysis was conducted on data from HIV-positive mothers receiving antenatal care at a tertiary care center between February 2015 and January 2020. The study examined various adverse pregnancy outcomes in relation to antiretroviral treatment. Statistical analysis employed chi-square and Fisher's exact tests to determine differences in distribution proportions of patients on ART versus those not on ART across various antenatal and neonatal complications, with significance attributed to p-values <0.05.

Results: A total of 155 patients were found to be HIV positive. Out of this 58 were diagnosed before pregnancy and 97 during pregnancy. Miscarriage was seen in one (0.6%) patient on ART and two (1.2%) not on treatment (p-value 0.6). Sixteen (10.3%) patients underwent medical termination of pregnancy (MTP); all were HIV-positive and they were all on ART (p-value <0.001). Anemia was seen in eighteen (11.6%) patients out of which 14(9%) were on ART (p-value 0.01). One (0.64%) woman had thrombocytopenia and she was on ART (p-value 1). Two (1.2%) patients on ART had diabetes mellitus (p-value 0.4). One (0.64%) patient who was on ART developed polyhydramnios (p-value 1). A total of 8 (5.16%) women had hypertensive disorders; out of which 4(2.58%) were on ART (p-value 1). 11(7.09%) patients who were on ART and 6(3.8%) not on ART had preterm labor (p-value 0.2). 12(7.74%) patients who were not on ART had intrauterine growth restriction (IUGR) and 2(1.29%) on ART had IUGR. A total of 6(3.87%) patients had Intrauterine fetal demise (IUID), of which 3(1.93%) were on ART and 3(1.93%) were not (p-value 1). Pre-labour rupture of membranes (PROM) was observed in 2(1.29%) women on ART and 11(7.09%) patients not on ART (p-value 0.004). All women (100%) had CD4 counts more than 500. All (100%) babies delivered at our center received antiretroviral therapy with oral Nevirepine. Almost half the women (51.6%) had vaginal delivery. Almost one-fourth, 41(26.4%) had a cesarean section. All caesareans were done given obstetric indications. There were no instrumental deliveries. Our study had a total of 122 live births. All 122(100%) babies were exclusively breastfed. None of the babies delivered in our center developed HIV on follow up which was done at 6 weeks and 6 months. Nine (5.8%) patients had infections. None of these women were on ART(p-value < 0.001).

Conclusion: HIV infection during pregnancy is associated with various adverse outcomes, but ART plays a crucial role in mitigating these risks and preventing mother-to-child HIV transmission. Initiating ART in all HIV-positive mothers and their infants is essential regardless of HIV status.

Keywords: anemia, ART, HIV, MTP, Perinatal outcome, PROM.

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INTRODUCTION

Human immunodeficiency virus (HIV) in pregnancy is a topic of significant importance, affecting both the present and future generations. Globally, an estimated 1.3 million women living with HIV become pregnant each year¹. The prevalence of HIV infection in pregnant women in India has ranged from 0.7% to 1.2%². In India, the

prevalence of HIV infection in pregnant women has ranged from 0.7% to 1.2%. In Karnataka, the estimated adult HIV prevalence declined from 0.81% in 2006 to 0.47% in 2017, with a corresponding decrease in prevalence among antenatal clinic attendees from 1.12% to 0.38% during the same period³. Often, the diagnosis of HIV is first made during pregnancy. Currently, there is no cure or vaccine for HIV. Women

with HIV who become pregnant or acquire the infection during pregnancy are at risk of both maternal and fetal complications, particularly if the virus is poorly controlled. There is also a risk of vertical transmission to the fetus during pregnancy, labor, and postpartum⁴. Without intervention, this risk ranges from 15% to 45%.¹

Several studies have shown that untreated maternal HIV infection increases the risk of stillbirth, premature rupture of membranes and preterm delivery, low birth weight, and small-for-gestational-age infants⁵. These complications not only lead to poor obstetric outcomes but also increase the risk of mother-to-child transmission of HIV. Addressing this issue is crucial but challenging, requiring substantial efforts from policymakers, healthcare workers, and patients alike.

HIV remains a significant public health concern globally, affecting both developing and developed countries. HIV in pregnancy is particularly complex as it directly impacts the health of future generations. However, antiretroviral therapy has shown promise in reducing obstetric complications and the transmission of HIV from mother to child. Our study aims to assess maternal and perinatal outcomes in pregnant women with HIV infection and evaluate the role of antiretroviral therapy in reducing pregnancy complications.

METHODS

This was a retrospective study for which ethical committee clearance was obtained. Data concerning HIV-positive mothers receiving antenatal care at a tertiary care center in Mangaluru, India, from February 2015 to January 2020 (spanning 5 years) were collected from the medical records of both mothers and babies. The center was selected as the study setting due to its status as a referral center for high-risk pregnancies. Data collected included the status of HIV infection, whether diagnosed pre-conceptionally or antenatally, the status of antiretroviral therapy (ART), occurrences of medical termination of pregnancy (MTP), maternal and fetal complications during the antenatal period, mode of delivery, neonatal conditions at birth such as APGAR scores, the need for NICU admission, the status of HIV infection in babies at 6 weeks and 6 months, ART administration to babies, and breastfeeding status up to 6 months. All necessary measures were taken to

maintain patient confidentiality. The collected data were entered into MS Excel and analyzed using SPSS V 22.0. Categorical variables, such as the presence of various antenatal complications like miscarriages, MTP, and polyhydramnios, along with current ART status, were expressed as frequency and percentage. The chi-square test of association and Fisher's exact test were employed to determine differences in the proportion of distribution between those currently on ART and those not across various antenatal and neonatal complications, with statistical significance attributed to a p-value <0.05.

RESULTS

A total of 155 patients were found to be HIV positive during the study duration and all of them were included in the study. Out of this 58 were diagnosed before pregnancy and 97 during pregnancy. Among them, 78(50.3%) were on antiretroviral therapy (ART) and 77(49%) were not on ART. Of these 78, 58(37%) were on ART before pregnancy and in 20 (12.9%) initiation of ART was done after pregnancy.

Miscarriage was seen in one (0.6%) patient on ART and two (1.2%) not on treatment (p-value 0.6). Sixteen (10.3%) patients underwent medical termination of pregnancy (MTP); all were given HIV-positive status and they were all on ART (p-value <0.001). Anemia was seen in eighteen (11.6%) patients out of which 14(9%) were on ART (p-value 0.01). One (0.64%) woman had thrombocytopenia and she was on ART (p-value 1). Two (1.2%) patients on ART had diabetes mellitus (p-value 0.4). One (0.64%) patient who was on ART developed polyhydramnios (p-value 1). A total of 8 (5.16%) women had hypertensive disorders; out of which 4(2.58%) were on ART (p-value 1). About 11(7.09%) patients who were on ART and 6(3.8%) not on ART had preterm labor (p-value 0.2). Almost 12(7.74%) patients who were not on ART had intrauterine growth restriction (IUGR) and 2(1.29%) on ART had IUGR. A total of 6(3.87%) patients had Intrauterine fetal demise (IUFD), of which 3(1.93%) were on ART and 3(1.93%) were not(p-value 1). Pre-labour rupture of membranes (PROM) was observed in 2(1.29%) women on ART and 11(7.09%) patients not on ART(p-value 0.004). All women (100%) had CD4 counts more than 500.

Twenty-four (15.48%) babies were low birth weight babies of these 10(66.6%) were on ART. Of these 24 low birth weight babies, 14(9.03%) had

IUGR. It was found that, ⁶ (3.87 %) babies had low APGAR at 1 minute, of which 4(2.58%) mothers were not on ART(p value 0.4). One (0.64%) baby was admitted to NICU given low APGAR and later died on the 5th post-natal day. There were no maternal deaths reported during the study period. All (100%) babies delivered at our center received antiretroviral therapy either with oral Nevirepine. None of the babies delivered in our center developed HIV on follow up which was done at 6 weeks and 6 months. Almost half the women (51.6%) had vaginal delivery. Almost

41(26.4%) had a cesarean section. All caesareans were done given obstetric indications. There were no instrumental deliveries. Our study had a total of 122 live births. All the 122(100%) babies were breastfed. As per the medical records, all were exclusively breastfed without any reports of mixed feeding.

Nine (5.8%) patients had infections. 4 women had tuberculosis, One had chicken pox and Vaginal infection and malaria were seen in three and one patient respectively. None of these women were on ART (p-value < 0.001).

Table 1. Antenatal Complications in Pregnancies with HIV (N=155)

Complications	On ART (n=78) (%)	Not on ART (n=77) (%)	Total (%)	P value(by Chi-square / Fisher exact test)
Miscarriage	1(0.6)	2(1.2)	3(1.8)	0.6
MTP*	16(10.3)	0	16(10.3)	<0.001
Anemia*	14(9)	4(2.5)	18(11.6)	0.01
Thrombocytopenia	1(0.64)	0	1(0.64)	1
Gestational diabetes	2(1.2)	0	2(1.2)	0.4
Polyhydramnios	1(0.64)	0	1(0.64)	1
Hypertension	4(2.58)	4(2.58)	8(5.16)	1
Preterm labour	11(7.09)	6(0.38)	17(10.8)	0.2
Pre-labour rupture of membranes*	2(1.29)	12(7.7)	14(9)	0.004
Intrauterine fetal demise	3(1.9)	3(1.9)	6(3.8)	1
Various maternal Infections*	0	9(5.8)	9(5.8)	<0.001
CD4 count less than 500	0	0	0	

MTP: Medical termination of pregnancy, *statistically significant. Figures in parenthesis indicate the percentage of N

Table 2. Neonatal Parameters (N=155)

Complications	On ART (n=78)(%)	Not on ART (n=77)(%)	Total (%)	P value(by Chi-square / Fischer exact test)
Low APGAR	2(1.2)	4(2.58)	6(3.8)	0.4
NICU admission	0	1(0.6)	1(0.6)	0.4
Neonatal death	0	1(0.6)	1(0.6)	0.4
Babies developing HIV	0	0	0	

Figures in parenthesis indicate the percentage of N

DISCUSSION

HIV continues to be a significant health burden in many countries, impacting both developed and developing nations alike. Our study was retrospective in nature, aiming to analyze maternal and perinatal outcomes in pregnancies among mothers with HIV. Of the patients included in our study, 98 (63.3%) were first diagnosed during pregnancy. While an opt-out method is typically employed when offering diagnosis during the antenatal period, it is important to recognize that actively providing counseling sessions at the time of diagnosis can encourage patients to undergo testing. This proactive approach can significantly

reduce the number of undiagnosed and missed cases. This finding aligns with previous studies on the subject.⁶ Undiagnosed cases pose a huge threat to public health including neonatal health as it may lead to HIV propagation⁷.

In this study, approximately half (50.3%) of the HIV-positive women were already on ART. These women maintained good general health and quality of life. Conversely, an equal number of women commenced ART only after pregnancy diagnosis. ART plays a crucial role in preventing mother-to-child transmission of HIV, although this was not statistically significant in our findings. Nevertheless, our results are supported by recommendations from the Panel on Treatment

of HIV During Pregnancy and Prevention of Perinatal Transmission⁸. In contrast to the old recommendation, all pregnant women are now advised to start ART as soon as pregnancy is diagnosed, and should be done irrespective of CD4 or viral RNA levels.

HIV exerts a significant psychosocial impact on women, as evidenced by the observation that 16 women (10.3%) opted for termination of pregnancy due to HIV, all of whom were on ART. This finding was statistically significant (p -value <0.001). Similar findings and suggestions were reported in a previous study.⁹ Personalized psychological counseling sessions could potentially reduce these numbers by assisting women in overcoming their fears of transmitting HIV to their babies.

HIV is not a common etiological factor for miscarriage. It has been observed in various studies such as those, that miscarriages are more common than the general population in women with HIV¹⁰. Our study made similar observations. However, infection in general is an established cause for miscarriage. So HIV as an infection could cause miscarriage. In our study three women had miscarriages. Among these, two women were not on ART and the remaining woman was on ART. Although these findings are not statistically significant, this hints about the protective role of ART in preventing miscarriages and stresses the significance of starting ART at the earliest.

In our study 17(10.9%) women had preterm labour, mostly late preterm labour. Among these 11(7%) patients were not on ART and 6(3%) on ART. HIV is known to cause preterm labor. Most of these are iatrogenic preterm labor. About 13(8.3%) women had Pre labor rupture of membranes (PROM). Almost 11 (7%) of these women were not on ART whereas 2 (1.2%) women developed PROM despite being on ART. Our study had more preterm labor and pre-labour rupture of membranes in women who did not receive ART. This finding was statistically significant (p -value 0.01). Similar observations were made in their study on pregnancy complications in HIV-positive women¹¹. These findings in our study go a long way in emphasising the importance of ART in women with HIV.

Twenty-four babies (15.4%) were born with low birth weight. Among these, 14 (9%) had mothers who did not receive ART, while 10 (6.4%) had mothers who were on ART and still delivered low birth weight babies. However, these findings did not reach statistical significance. Intrauterine

growth restriction was identified as the cause of low birth weight in all babies whose mothers did not receive ART. These findings suggest a potential protective effect of ART against low birth weight and intrauterine growth restriction. Similar conclusions were drawn in another study on HIV in pregnancy. Conducting further research could provide more precise data on this matter¹².

Low APGAR at 1 minute was seen in about 6 babies, out of which 4 mothers were not on ART. Among this one baby was admitted to NICU in view of low APGAR and later died on 5th postnatal day. As this finding did not show statistical significance, it may be difficult to draw a conclusion that ART would help preventing babies with low APGAR. However it is highly probable that ART is efficacious in preventing babies with low APGAR and further studies would be required to establish this. These findings were similar to a study conducted by Yang et al about impact of maternal HIV infection on pregnancy outcomes in China¹³.

A total of 6 patients had intrauterine fetal demise. Out of which 3(1%) were on ART and 3(1%) were not on ART. Although, this finding is not statistically significant, it is possible that ART doesn't have an impact on reducing intrauterine fetal demise. A study made similar observations¹⁴. It is also important to keep in mind that intrauterine fetal demise is multifactorial. This confounding effect by other factors might skew the data and make it difficult to draw a conclusion. Further research in this area is warranted.

In our study, eight (5%) women had hypertensive disorders. Out of this, 4(2.5%) were on ART and remaining 4 (2.5%) were not on ART. Women with HIV in pregnancy were found to have slightly higher incidence of hypertensive disorders of pregnancy¹⁵. Similar to the aforementioned discussion, our data indicates that ART does not appear to impact the occurrence of hypertensive disorders in pregnancy. Although this finding did not reach statistical significance (p -value 1), it is important to note that most ART medications have adverse effects on liver function, which could potentially lead to hypertension and elevated liver enzymes. Consequently, there may be an increased likelihood of misdiagnosing severe forms of hypertension in pregnancy such as HELLP syndrome and preeclampsia. This is in contradiction to a study which concluded long term ART could be protective in hypertensive disorders in pregnancy¹⁶. Unfortunately, there is a lack of data on the type of hypertension and

severity because of the retrospective nature of study. Further studies on this are strongly recommended.

Anemia was seen in eighteen (11.6%) patients. Out of this, 14(9%) were on ART. This observation is statistically significant(p value 0.01). Thrombocytopenia developed in One (0.6%) woman. She was on ART. Both anemia and thrombocytopenia could be due to the myelosuppressive effect of ART. This was in accordance with a study by Dennis El Jacobson where he suggested that anemia could be a complication of ART¹⁷. Hemoglobin levels of pregnant women on ART should be maintained well above normalcy during pregnancy. Stringent monitoring of hemoglobin and cell counts are advised.

Diabetes was diagnosed in two (1.2%) women on ART. A patient who had diabetes and was on ART developed polyhydramnios. These findings were not statistically significant. Nonetheless a study came up with similar findings¹⁸. This could be attributed to the fact that ART drugs lead to deranged glucose metabolism. Another aspect to consider is the occurrence of gestational diabetes due to the hyperglycemic effect of human placental lactogen (HPL). However, management of diabetes irrespective of its etiology remains the same. At the same time we must give due consideration to multidisciplinary management with special stress on ART dose modification.

Almost half the women (51.6%) had vaginal delivery. Caesarean section was done in 41(26.4%). All caesareans were done in view of obstetric indications. None of the caesareans were performed to prevent mother to baby transmission. Similar observations were made in a study at Finland¹⁹. However it is advisable to make a conscious effort to avoid emergency caesarean sections as it may accentuate mother to baby transmission as well as put the staffs at risk of blood splashes and needle stick injuries. This shows that route of delivery was mainly determined by obstetric condition of the mother and fetus. There were no instrumental deliveries. This is in accordance with the latest guidelines stating to avoid instrumental deliveries to prevent accelerated mother to baby spread of HIV infection¹.

All babies delivered in our study were exclusively breastfed. The practice of discontinuing breastfeeding to prevent mother-to-baby transmission is considered outdated. Breastfeeding should be encouraged, particularly

when both babies and mothers are receiving ART coverage. However, mixed feeding, involving episodes of formula feeding alongside breastfeeding, should be strongly discouraged. An article strongly advocates for counseling HIV-positive mothers to breastfeed their babies, provided they are on AR.²⁰

All babies delivered in our center received antiretroviral therapy with oral Nevirepine. None of the babies delivered in our center developed HIV on follow-up at 6 weeks and 6 months. This explains the importance of administering ART to all babies without fail. An article also reiterates the same²⁰.

Various infections were reported in 9 (5.8%) mothers, including tuberculosis, chickenpox, malaria, and vaginal infections. An intriguing observation is that none of these women were on ART. This finding was statistically significant (p-value 0.001), clearly indicating that ART improves immunity in pregnant women with HIV and helps prevent maternal infections. Opportunistic infections have been shown to increase the risk of mother-to-child transmission, as found in previous studies.²¹ However in our study, none of the babies were found to be HIV positive at 6 weeks and 6 months follow up; prime reason for this being the administration of ART. Studies such as those emphasise on the role of ART in preventing maternal infections and mother-to-child transmission of HIV; and this is in agreement with our findings^{22,23}. This strategy is further emphasized in other studies and editorials advocating for universal screening for HIV and the use of ART to prevent vertical transmission²⁵.

STRENGTH of the STUDY

The study spanned a period of five years, affording a substantial follow-up duration. The meticulous maintenance of medical records facilitated comprehensive data collection concerning HIV-positive mothers and their babies.

LIMITATIONS of the STUDY

It was a retrospective study.

CONCLUSION

HIV during pregnancy can lead to various adverse pregnancy outcomes. However, antiretroviral therapy (ART) is highly effective in mitigating

these complications and reducing the risk of mother-to-child transmission of HIV. ART should be initiated in all mothers with HIV and their babies irrespective of their HIV status.

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