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A retrospective study of maternal and perinatal outcome of seropositive pregnant women attending PPTCT centre at a tertiary care centre

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Abstract
Introduction: Women diagnosed with HIV/AIDS may transmit the infection to their child during pregnancy, childbirth, or breastfeeding. However, the risk of mother-to-child transmission of HIV may be reduced by the use of antiretroviral therapy (ART).
Objective: The main aim of the study is to appreciate the declining trend of HIV in babies with HIV positive mother by implementation of PPTCT services.
Methodology: A retrospective study of detection of HIV positive mothers among all the antenatal patients attending OPD and including the patients coming in Emergency services and delivered at Mahila chikitsalaya, SMS Medical College, Jaipur from July 2008 to Dec 2017 was included in the study. They were screened for HIV status and further management of all HIV positive patients.
Results: Total 220445 patients have attended OPD over 10 years from 2008 to 2017 among which total 150077 patients have tested for HIV (68.07%). Among these 240(0.15%) patients were found HIV reactive. From history, we could elicit sexual contact as a prime mode of infection in these women 198(82.50%), followed by blood transfusion in 31 (12.91%), and through needle injury/sharing in 11(4.58%). The CD4 count was more than 200 in 86% women. In total 240 patients 3 patients were aborted that were excluded. Out of 237 HIV-infected women, 35.02% (83) had a cesarean delivery and vaginal delivery was primary mode of delivery in 154(67.94%). HIV-infected women were more likely to have preterm, IUGR and anemia (16.45, 8.86%, 6.4%). There were no maternal mortality. Mean age of HIV positive women was 24.62±3.6 years. Mean parity was 1.72±0.48. In total 237 deliveries, 60(25.31%) babies were low birth weight. Mean birth weight was 2354.60±499g. Among total 154 vaginal deliveries, only 2 (1.29%) babies were found HIV ELISA positive at 18 months and in 83 LSCS, only 2 babies (2.40%) were found HIV positive. Among 237 deliveries, 229 babies (96.62%) were alive and rest 8 babies (3.37%) were still birth. In total 229 alive babies, 25 babies were admitted in NICU and early neonatal mortality occurs in 8 babies, and late neonatal mortality occurs in 6 babies. Among total alive 229 babies, 160(69.86%) babies were on breastfeed and 69(30.13%) babies were on top feed.
Conclusion: Good antenatal care and multidisciplinary team approach can optimize pregnancy outcomes in HIV-infected women.

Keywords: Human immunodeficiency virus (HIV), antiretroviral therapy (ART), prevention of parent to child transmission (PPTCT), preterm birth, intrauterine growth restriction

Introduction
The human immunodeficiency virus (HIV) is a lent virus that causes HIV infection and over time acquired immunodeficiency syndrome (AIDS) [4, 5]. Infection with HIV occurs by the transfer of blood, semen, vaginal fluid, pre-ejaculate, or breast milk. Infection with HIV/AIDS is not a contraindication to pregnancy. Some women are unaware they have the disease until they become pregnant. In this case, they should begin antiretroviral therapy as soon as possible [1]. With the appropriate treatment, the risk of mother-to-child transmission can be reduced to below 1% [2]. Without treatment, the risk of transmission is 15% - 45% [3]. Perinatal transmission of human immunodeficiency virus (HIV) infection occurs in the absence of any interventions. The benefits of antiretroviral treatment (ART) in decreasing mother to child transmission (MTCT) of HIV infection are largely undisputed [1]. Current practice has adopted the use of highly active antiretroviral therapy (HAART) in an attempt to suppress viral load below detection, to minimize MTCT of HIV.

In India, the program for Prevention of Mother to Child Transmission (PMTCT) of HIV was launched in the year 2002. With effect from 2014, India adopted the World Health Organization (WHO) instigated Option B+ for prevention of MTCT of HIV [1].

Objectives

1. To study the effect of HIV infection on pregnancy and the effect of HAART on pregnancy outcome.
2. To analyze the declining trend of HIV in babies with HIV positive mother by implementation of PPTCT services.
3. To detect the rate of transmission according to method of delivery and treatment received during pregnancy.

Material and Method

A retrospective study of detection of HIV positive among all the antenatal patients attending ANC and including the patients coming in Emergency services and delivered in Department of Obstetrics and Gynecology at Mahila chikitsalaya, SMS Medical College, Jaipur from July 2008 to Dec 2017 were included in the study. They were screened for HIV status and further management for all HIV positive patients done. Total 240 HIV infected women were included in the study over 10 years. Among these, 3 women undergoing abortion were excluded.

Results

Table 1: Comparison between different years and the trend of HIV positive cases as evident from data over 10 years

Year	Total Antenatal OPD	Total Tested	HIV Reactive
2008	14850	1902(12.80%)	4(0.21%)
2009	16226	8143(50.18%)	9(0.11%)
2010	16379	13223(80.73%)	17(0.13%)
2011	16569	11014(66.47%)	27(0.24%)
2012	14621	10499(71.81%)	16(0.15%)
2013	20380	12135(59.54%)	23(0.19%)
2014	28902	21026(72.75%)	35(0.16%)
2015	28337	24394(86.05%)	40(0.16%)
2016	32229	23661(73.41%)	31(0.13%)
2017	31952	24080(75.36%)	38(0.15%)
Total	220445	150077(68.07%)	240(0.15%)

Total 220445 patients have attended OPD over 10 years from 2008 to 2017 among which total 150077 patients have tested for HIV (68.07%). Among these 240(0.15%) patients were found HIV reactive. The PPTCT program has significantly improvised its ANC OPD burden from 14850 in 2008, 20380 in 2013 to 31952 in 2017 among those for HIV screening as in Table 1. Out of them total of 1902 were tested in 2008 and 12135 in 2013 and 24080 in 2017. It implies the efficacy of effective implementation of PPTCT program.

Table 2: Mode of transmission of HIV among antenatal women

Year	Total	Sexual Transmission	Blood / Blood Products Transfusion	Needle Sharing / Injury
2008	4	2	1	1
2009	9	4	4	1
2010	17	9	5	3
2011	27	23	4	0
2012	16	13	1	2
2013	23	19	3	1
2014	35	32	2	1
2015	40	39	1	0
2016	31	26	4	1
2017	38	31	6	1
Total	240	198(82.5%)	31(12.91%)	11(4.58%)

In 240 patients sexual contact was the prime mode of transmissions in 198 (82.50%), second mode of transmission was blood transfusion in 31 (12.91%), and through needle injury/infected syringe sharing in 11(4.58%).

Table 3: Mode of delivery in HIV reactive antenatal women

Year	Total Deliveries	Vaginal Deliveries (In %)	LSCS (In %)
2008	4	3 (75%)	1 (25%)
2009	9	6 (66.66%)	3 (33.33%)
2010	17	15 (88.24%)	2 (11.76%)
2011	26	21 (80.77%)	5 (19.23%)
2012	16	11 (68.75%)	5 (31.25%)
2013	23	16 (69.56%)	7 (30.44%)
2014	34	21 (61.76%)	13 (38.24%)
2015	39	20 (51.28%)	19 (48.72%)
2016	31	17 (54.84%)	14 (45.16%)
2017	38	24 (63.16%)	14 (36.84%)
Total	237	154(64.97%)	83(35.02%)

In total 240 patients 3 patients were aborted that were excluded. In total 237 patients, vaginal delivery was main mode of delivery in 154(67.94%), LSCS occurred in 83(35.02%) patients. Earlier LSCS was promoted for delivery in case of HIV positive patients but Now-a-days according to recent guideline, Elective LSCS is not recommended.

Table 4: Rate of transmission based on mode of delivery

Year	Total Vaginal Deliveries	Reactive Babies In Vaginal Delivery	Total LSCS	Recative Babies In LSCS
2008	3	0	1	0
2009	6	0	3	0
2010	15	0	2	0
2011	21	2	5	1
2012	11	0	5	1
2013	16	0	7	0
2014	21	0	13	0
2015	20	0	19	0
2016	17	0	14	0
2017	24	0	14	0
Total	154	2(1.29%)	83	2(2.4%)

Among total 154 vaginal deliveries, only 2 (1.29%) babies were found HIV ELISA positive at 18 month follow up and in total 83 LSCS, only 2 babies (2.40%) were found HIV positive.

Table 5: Perinatal morbidity and mortality

YEAR	Total No. Of Deliveries	Alive Babies	Still Birth	Nicu Admission	Early Neonatal Mortality	Late Neonatal Mortalty
2008	4	4	0	0	0	0
2009	9	9	0	1	0	1
2010	17	17	0	2	1	2
2011	26	24	2	2	1	1
2012	16	15	1	1	0	0
2013	23	22	1	2	2	1
2014	34	32	2	3	1	1
2015	39	39	0	5	0	0
2016	31	30	1	4	0	0
2017	38	37	1	5	3	0
Total	237	229(96.62%)	8(3.37%)	25	8	6

Among total 237 deliveries, 229 babies (96.62%) were alive and rest 8 babies (3.37%) were still birth. In total 229 alive babies, 25 babies were admitted in NICU and early neonatal mortality occurs in 8 babies, and late neonatal mortality occurs in 6 babies.

Table 6: Low birth weight babies among total deliveries

Year	Total Deliveries	Lbw Babies (In %)	Preterm	IUGR
2008	4	2 (50%)	1	1
2009	9	2 (22.22%)	1	1
2010	17	4 (23.53%)	2	2
2011	26	6 (22.22%)	4	2
2012	16	3 (18.75%)	2	1
2013	23	3 (13.04%)	2	1
2014	34	16 (45.71%)	10	6
2015	39	11 (27.5%)	7	4
2016	31	5 (16.13%)	4	1
2017	38	8 (21.05%)	6	2
Total	237	60(25.31%)	39(65%)	21(35%)

In total 237 deliveries, 60(25.31%) babies were low birth weight, among all these low birth weight babies 39(65%) were due to preterm birth and 21(35%) were due to IUGR. Mean birth weight was 2354.60±499g.

Table 7: Feeding pattern among babies of HIV positive mother

Year	Total Deliveries	Breast Feed	Top Feed
2008	4	4	0
2009	9	7	2
2010	17	13	4
2011	24	16	8
2012	15	12	3
2013	22	14	8
2014	32	22	10
2015	39	24	15
2016	30	20	10
2017	37	28	9
Total	229	160(69.86%)	69(30.13%)

Among total alive 229 babies, 160(69.86%) babies were on breastfeed and 69(30.13%) babies were on top feed. This is because majority of women belonged to low or middle socio-economic status.

Discussion

Total 220445 patients have attended antenatal OPD over 10 years from 2008 to 2017 among which total 150077 patients have tested for HIV ELISA (68.07%). Among these 240(0.15%) patients were found HIV reactive. In total 240 patients 3 patients were aborted that were excluded. Out of 237 HIV-infected women, 83.96% (199) delivered after 37 completed weeks of gestation, 35.02% (83) had a cesarean delivery and vaginal delivery was primary mode of delivery in 154 (67.94%). HIV-infected women were more likely to have preterm, IUGR and anemia (16.45, 8.86%, 6.4%). There were no maternal mortality. One woman had postpartum hemorrhage but did not require blood transfusion. 3 had wound infection managed with dressing and antibiotics and 4 had febrile morbidity. There were 2 instances of needle prick to health professionals all received post-exposure prophylaxis and are negative for HIV on follow-up. Majority of women, 160(69.86%) opted to breastfeed their babies.

Mean age of HIV positive women was 24.62±3.6 years. The majority of women belonged to low or middle socio-economic status. Of the total, 36% of women were referred to us after diagnosed with HIV infection. Primi parity and multiparity were equally distributed. Mean parity was 1.72±0.48. About 12% women had a previously infected child. Of the total women, 187 (77.91%) were diagnosed in index pregnancy, the remaining 53 were already on HAART at the time of conception.

From history, we could elicit sexual contact as a prime mode of infection in these women 198 (82.50%), followed by blood transfusion in 31 (12.91%), and through needle injury/sharing in 11 (4.58%). The CD4 count was more than 200 in 86% women. The most common route of infection is sexual transmission more commonly through male to female w.r.t female to male. So the fetus becomes the innocent bearer of the disease. Majority, 72.5% of the women booked with us before 28 weeks and they received more than 4 weeks of ARV drugs for prophylaxis, 8 women did not receive any ARV treatment. Single dose NVP was given to 41 (17.08%), ZDV or ZDV+3TC to 62 (25.83%) and HAART (Tenofovir 300 mg + Lamivudine 300 mg + Efavirenz 600 mg) to 137 (57.08%) HIV-infected women.

In total 237 deliveries, 60(25.31%) babies were low birth weight, among all these low birth weight babies 39(65%) were due to preterm birth and 21(35%) were due to IUGR. Mean birth weight was significantly lower in neonates of HIV-infected women (2354.60±499g) [P-value<0.05]. HIV-infected women on ART had decreased incidence of PTB and IUGR.

Among total 154 vaginal deliveries, only 2 (1.29%) babies were found HIV ELISA positive at 18 months. Among total 83 LSCS, only 2 babies (2.40%) were found HIV ELISA positive. These children were called at 6weeks, 6 months and 18 months for follow up. Out of 4, one mother received HAART for prevention of perinatal transmission and 3 didn't receive any prophylaxis and all babies received formula feeds except one. Among 237 deliveries, 229 babies (96.62%) were alive and rest 8 babies (3.37%) were still birth. In total 229 alive babies, 25 babies were admitted in NICU (indications were: low birth weight, transient tachypnea of newborn-2, respiratory distress-5, sepsis-3 and

others -5). and early neonatal mortality occurs in 8 babies, and late neonatal mortality occurs in 6 babies.

HIV-infected women who were on HAART had a lower risk of PTB compared to women receiving sdNVP or no drugs, and this was statistically significant (P value<0.05). Antenatal care was important as those not having received any antenatal care prior to deliver were at increased risk of having a pre-term delivery.

It was because of novel approach of NACP and PPTCT counselling enabling the antenatal women to be diagnosed earlier. In 2008 only 4 patients were found to be reactive w.r.t 2017 there were 38 patients who were reactive at our institute.

Most of the patients are getting delivered at a tertiary care center, thus ensuring Prophylactic and Postnatal care of the mother and baby. The risk of vertical transmission of HIV from mother to baby ranges from 7% - 40%. Maternal HIV transmission is the primary means by which infant become infected. Hence prevention of maternal HIV transmission is of paramount importance. According to Kesho Bora study, Infants of mothers with undetectable virus levels after being given Triple ARVs at time of delivery has only 2.7% risk of HIV infection at the end of one year. So initiation of ARVs early in pregnancy and to all women who require ART irrespective of CD4 count as per 2013 guidelines significantly eliminate risk of Mother to Child HIV Transmission.

In accordance to NACO and PPTCT, Tablet NVP 200 mg should be given 2 hours before planned delivery or at onset of labour. The newborn should be given Nevirapine suspension. Now, it has been changed to TLE Regimen to mother for at least 24 weeks & NVP to baby. For preventing MTCT, Triple ART should be started irrespective of CD4 count and clinical stage.

The 2006 guidelines recommended starting lifelong ART for pregnant women with a CD4 count equal to or below 200 cells/mm3, usually the stage at which the immune system is no longer strong enough to prevent opportunistic diseases.

The 2010 revised PMTCT guidelines refer to the following two key approaches:

1. Lifelong ART for HIV-infected women (irrespective of gestational age) in need of treatment for their own health, which is also safe and effective in reducing mother to child transmission of HIV (MTCT).
2. Short-term ARV prophylaxis to prevent MTCT during pregnancy, delivery and breastfeeding for HIV-infected women not in need of treatment.

Eligibility for treatment: The 2010 guidelines promote starting lifelong ART for all pregnant women with severe or advanced clinical disease (stage 3 or 4), or with a CD4 count at or below 350 cells/mm3 regardless of symptoms. The new ART eligibility criteria, which are the same as those for adults in general, emphasize the need for access to CD4 testing. In both sets of guidelines, the timing of ART initiation for HIV-positive pregnant women is the same as for non-pregnant women, i.e. as soon as the eligibility criteria are met.[5]

The better outcome in this cohort is explained by regular antenatal care, majority of women diagnosed in pregnancy were asymptomatic and others were already on HAART. Pregnancy outcome is affected by many factors. The adverse outcome in women from developing countries could be because of the poor socio-economic status of these women, marginalized population because of stigmata of HIV and poor access to antenatal care. Women who were asymptomatic or on treatment are likely to have a better outcome.

The type of antiretroviral (ARV) prophylaxis women received for prevention of perinatal transmission depended on the time period of the study. From 2002-2006 women received either single dose nevirapine (sdNVP) intrapartum or sdNVP tailed with 7 days of zidovudine and lamivudine (ZDV± 3TC) and the newborn was given sdNVP 2 mg/kg. In years 2007-2010 women were advised ZDV 300 mg BD from 28 weeks gestation. Due to financial constraints, women opted for ZDV+3TC from 28 weeks onwards that they received free from ART clinic as ZDV alone was not available in ART clinic. Newborns received sdNVP or ZDV 2 mg/kg for 7 days. Following the new WHO guidelines, from 2010, women are receiving triple-drug ART (Tenofovir 300 mg+Lamivudine 300 mg +Efavirenz 600 mg) for MTCT. The Government of India rolled out WHO B+ from 2014.

According to recent guideline, Elective LSCS is not recommended. Women were counseled about the benefits and risks of elective cesarean delivery and formula feeding, the majority opted for cesarean delivery and exclusive breastfeeding to prevent perinatal transmission. Since the implementation of WHO B+ option, we are encouraging women for vaginal delivery and exclusive breastfeeding.

Conclusion

Pregnancy in HIV infected women is associated with adverse maternal and neonatal complications. Pregnant HIV-positive women should be followed in high-risk health care centers.

With good antenatal care HIV-infected women can have good pregnancy outcome. There may be at increased risk of an adverse outcome like PTB, IUGR, and anemia, which may be due to disease or ART. A multidisciplinary team approach to management involving an HIV physician, experienced obstetrician, and neonatologist are essential to optimize maternal and fetal outcome.

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