

Pregnancy Outcome in HIV-Positive Pregnant Women at Tertiary Care CenterMandeep Kaur¹, Parneet Kaur², Anju Gupta³, Tarvinderjit Khurana⁴, Gurdip Kaur⁵, Satinder Pal Kaur⁶¹Senior Resident, Department of Obstetrics & Gynaecology, GMC, Patiala²Professor & Head of Department, Department of Obstetrics & Gynaecology, GMC, Patiala³Associate Professor, Department of Obstetrics & Gynaecology, GMC, Patiala⁴Assistant Professor, Department of Medicine, Adesh Medical College and Hospital, Mohri, Shahabad, Haryana⁵Former Professor, Department of Obstetrics & Gynaecology, GMC, Patiala⁶Associate Professor, Department of Obstetrics & Gynaecology, GMC, Patiala

Received: 30-05-2023 / Revised: 30-06-2023 / Accepted: 30-07-2023

Corresponding author: Dr. Tarvinderjit Khurana

Conflict of interest: Nil

Abstract:**Introduction:** The Human Immunodeficiency Virus remains a major public health issue in developing countries and it has great impact on pregnant mothers and birth outcomes. Thus, it is very important to identify, estimate CD4 count and treat all pregnant women with HIV infection to reduce mother to child transmission, morbidity and mortality.**Aims and Objectives:** To study pregnancy outcomes, prevalence of co-infections and ART practices in HIV positive pregnant women at tertiary care centre.**Material and Methods:** The study was a prospective observational study conducted in Department of Obstetrics and Gynaecology, Government Medical College and Rajendra Hospital, Patiala for a period of one and a half years. All the pregnant females presenting with HIV positive status or diagnosed as HIV positive in our Gynaecology Department for were taken up for study. All women were followed till delivery for development of any complications. Maternal and fetal outcome was noted. The data was collected and analysed statistically.**Result:** During the study period 70 subjects with HIV positive status were enrolled for study. Complications in pregnant women including anemia (p-value -0.0001), preterm labour (p-value -0.044) and gestational diabetes mellitus (p-value - 0.0338) were significantly more in the study group as compared to the control group. Neonatal outcomes in HIV positive mothers included fetal growth retardation (p-value -0.00036), low birth weight (p-value -0.0012) and NICU admissions (p-value -0.00036). Major risk factor for mother was positive status of the husband (82.8%). Other risk factors included the previous history of unsterile nasal or ear piercing (11.4%), IM/IV injections from RMP in village (14.3%) and blood transfusion (17.1%). Coinfections like HCV (p-value -0.0062) and Candidiasis (p-value - 0.0026) were prevalent in the study group as compared to controls.**Conclusion:** The accumulated data shows a positive correlation between HIV infection and anemia, preterm labour, GDM, LBW, NICU admissions and coinfections like HCV and candidiasis as compared to controls. It was observed that with increasing awareness, pregnant females had started ART pre-pregnancy and in 1st trimester. In our study, ART was taken for more than 24 weeks by majority of the subjects, which is in accordance with NACO guidelines for the prevention of MTCT.**Keywords:** HIV (Human immunodeficiency Virus), ART (Antiretroviral Therapy), TLE regimen (Tenofovir + Lamivudine + Efavirenz), TLD regimen (Tenofovir + Lamivudine + Efavirenz), LBW (Low birth weight), FGR (Fetal growth retardation), IUD (Intrauterine Death), PPRM (Preterm premature rupture of membranes).This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.**Introduction**

The first case of Human immunodeficiency Virus (HIV) in India was diagnosed among female sex workers in 1986 in Chennai. According to the United

Nations Program on HIV and AIDS (UNAIDS), in 2020, there were 37.7 million people who were HIV positive globally. India is facing the third largest

epidemic worldwide. [1] There has been a rapid decline in HIV related morbidity and mortality due to the wider availability of affordable, more efficacious and less toxic Antiretroviral (ARV) drugs over the last two decades.

HIV belongs to retroviridae family and subfamily lentiviridae. There are two types of HIV viruses, HIV1 and HIV2. [2] HIV1 is more common than HIV2.

Rate And Mode Of Transmission: HIV virus infects all irrespective of age, sex or race. The transmission rate from male to female is 1.9 times more than female to male transmission.[3] The mode of transmission of HIV includes unprotected sexual intercourse, both homosexual and heterosexual, vertical transmission, blood and blood products transfusion, needle prick injury and intravenous drug abusers.[4]

Effect Of Disease On Pregnancy: Several studies conducted in developing nations concluded that there are several adverse outcomes occurring in HIV infected pregnant women. Both early and late pregnancy outcomes are associated with maternal HIV infection.[1] These include –

- There is an increased risk of anemia [5], spontaneous abortion, ectopic pregnancies, preterm labour [1], premature rupture of membranes and abruptio placenta [6] in HIV positive women as compared to HIV uninfected women.
- Fetal adverse outcomes like preterm birth, small for gestational age babies, still birth, low birth weight and low APGAR [7] more common in HIV positive women.
- Coinfections like tuberculosis [8], other systemic infections, genital tract infections [1] and opportunistic infections [8] are also more common in these females.

Prevention of Mother to Child Infection: Mother-to-child transmission is a major route of HIV infection. According to World Health Organization, there were 15 to 45 % chances of HIV infected women transmitting the virus to their children because of limited access to antiretroviral drugs (ART) in the past.[9] The transmission rate can be reduced to less than 5% with effective intervention during pregnancy, labour, delivery and breastfeeding.[10]

In 2013 WHO Consolidated guidelines on the use of antiretroviral drugs: They recommended ART for all pregnant and breastfeeding women irrespective of clinical eligibility.

In 2019 WHO further updated ART guidelines: They recommended dolutegravir, a new antiretroviral medication, as the preferred first-line and second-line HIV treatment for all populations.[11] So instead of TLE now TLD regimen is recommended.

ART can reduce the risk of vertical transmission to 1-2% or lower if maternal viral load < 1000 copies/ml.[12] Perinatal HIV transmission may be significantly reduced in breastfeeding populations through a combination of behavioural interventions that encourage exclusive breastfeeding and the use of antiretrovirals for mothers and/or their infants.[13] The present study has been conceptualized to assess the outcome of pregnancy in HIV-positive pregnant women and to see the effect of ART. It is now being given irrespective of gestational age and CD4 count to prevent mother to child transmission.

Aims and Objectives: To study pregnancy outcomes, prevalence of co-infections and ART practices in HIV positive pregnant women at tertiary care center.

Material and Methods

The present study was a prospective observational study conducted in the Department of Obstetrics and Gynaecology, Govt. Medical College and Rajendra Hospital, Patiala during year 2020-2021 for a period of 1.5 year. All the pregnant females presenting with HIV positive status or diagnosed as HIV positive in our department were taken up for study. Pregnant women opting for medical termination of pregnancy were excluded. 50 pregnant females who were not HIV positive were taken as control. History was obtained in detail after informed, written consent and filled-in pre-designed proforma. General physical examination, systemic examination and obstetrical examination was done on each patient. All women were followed till delivery for development of any complication. Maternal and fetal outcome was noted. Data was collected and analysed.

Statistical Analysis: Descriptive and inferential statistics were carried out in the present study. Result was presented as number or percentage for categorical variables, while they were presented using Mean \pm SD for quantitative variables. Level of significance was fixed at $P = 0.05$ and any value less than or equal to 0.05 was considered to be statistically significant. First, we applied normality test, we found that our data was not followed normality test (Kolmogorov Smirnov & Shapiro wilk test). So, we used Chi-square test. The data were analysed using statistical software (Statistical Package for Social Sciences; version 25) & data enter in Excel 2019.

$$x_1 = \sum xi/n_1 = \text{mean of sample}$$

$$s = \sqrt{\sum (x_1 - \bar{x})^2 / n_1} = \text{Standard deviation of sample}$$

$$\chi^2 = \sum_{i=1}^n (O - E)^2 / E$$

Observations

During the study period 70 subjects with HIV positive status were enrolled for study. 50 pregnant females

who were not HIV positive were taken as control. In our study the majority of the subjects (study group = 48.6% and control group = 46%) belonged to the age

group of 20-25 years and were literate in both study (82.9%) and control (92%) groups. In both groups majority of subjects were housewives.

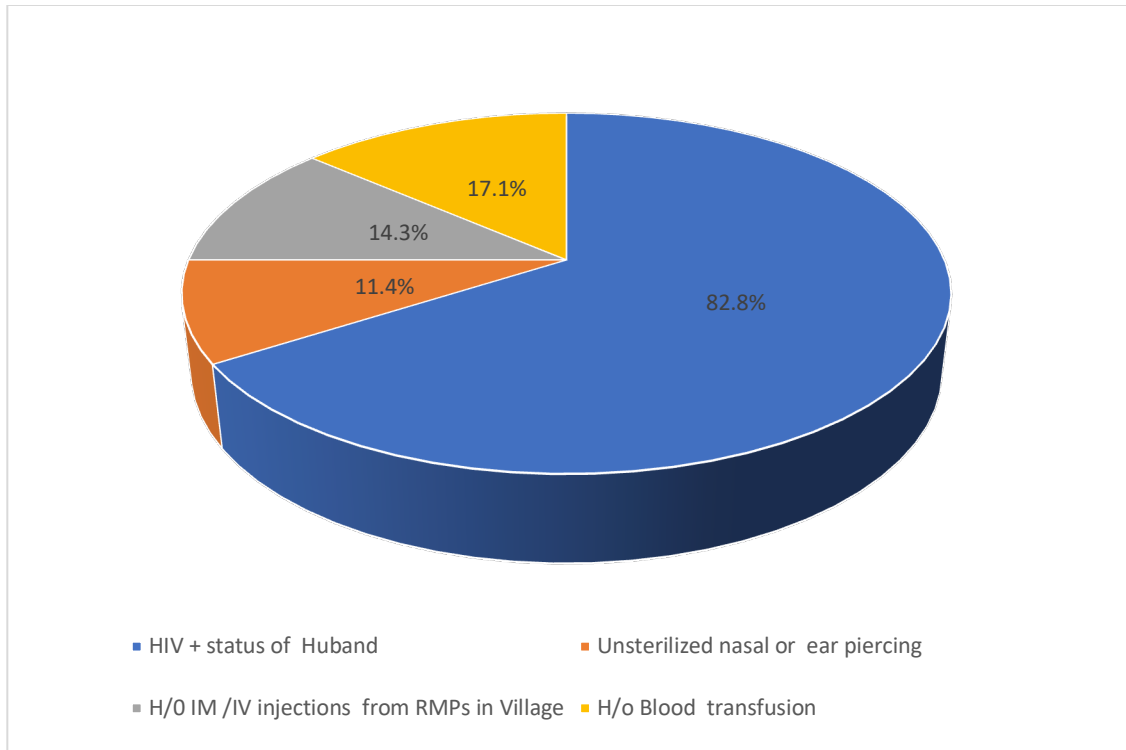


Figure 1: Showing risk factors for HIV infection

Among the risk factors for the mothers 82.8 % of subjects had h/o positive status of the husband. Other risk factors included the previous history of unsterile nasal or ear piercing (11.4%), IM/IV injections from RMP in the village (14.3%) and blood transfusion (17.1%) (Figure No. 1)

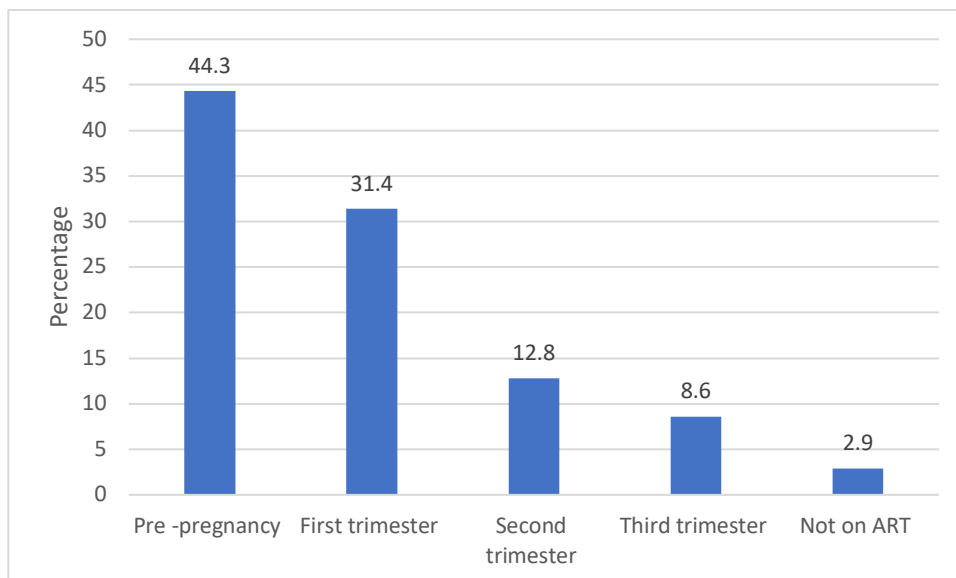


Figure 2: Time since start of ART

In our study, most of the subjects were already on antiretroviral therapy before pregnancy (44.3%), while others started early in the first trimester (31.4%). However, there were 2 subjects who were not on ART and referred from the

peripheral centre after diagnosis for delivery and were started ART immediately. A positive finding was that most of the mothers were on ART before conceiving (44.3%) thus reducing the chances of mother to Child Transmission (MTCT). (Figure No. 2)

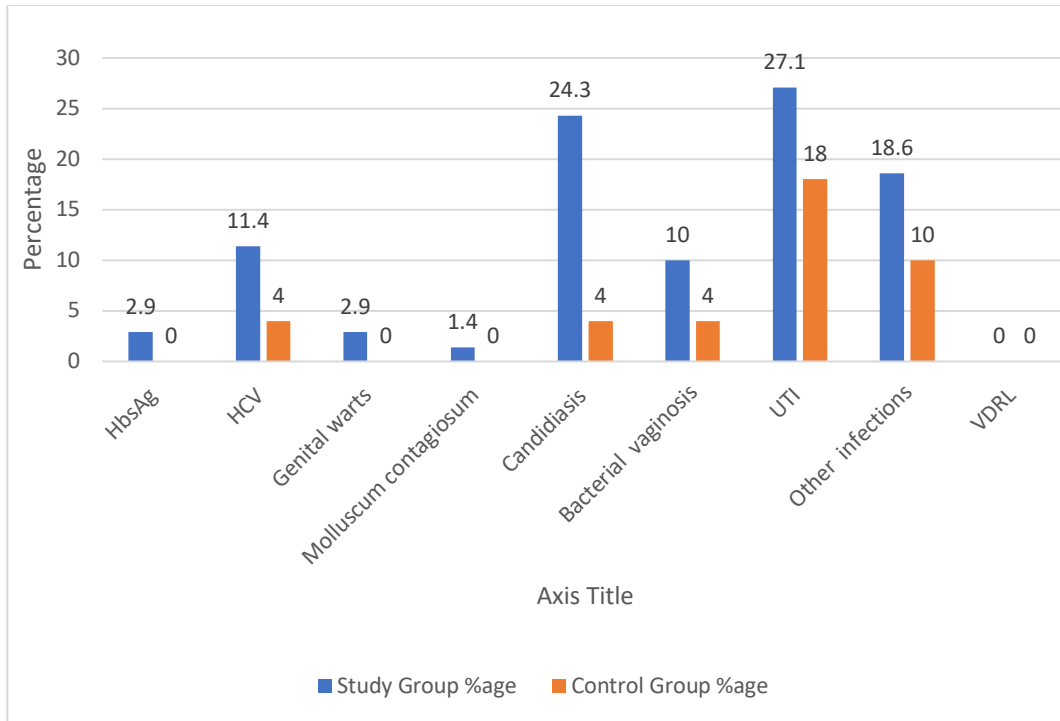


Figure 3: Distribution according to prevalence of Co-infection

Among Co-infections, candidiasis (p-value - 0.0026) and HCV (p-value - 0.0062) were significantly more in the study group as compared to the control group. Infections like genital warts, molluscum contagiosum, bacterial vaginosis and UTI were more in the study group as compared to the control group but were not statistically significant. (Figure No. 3)

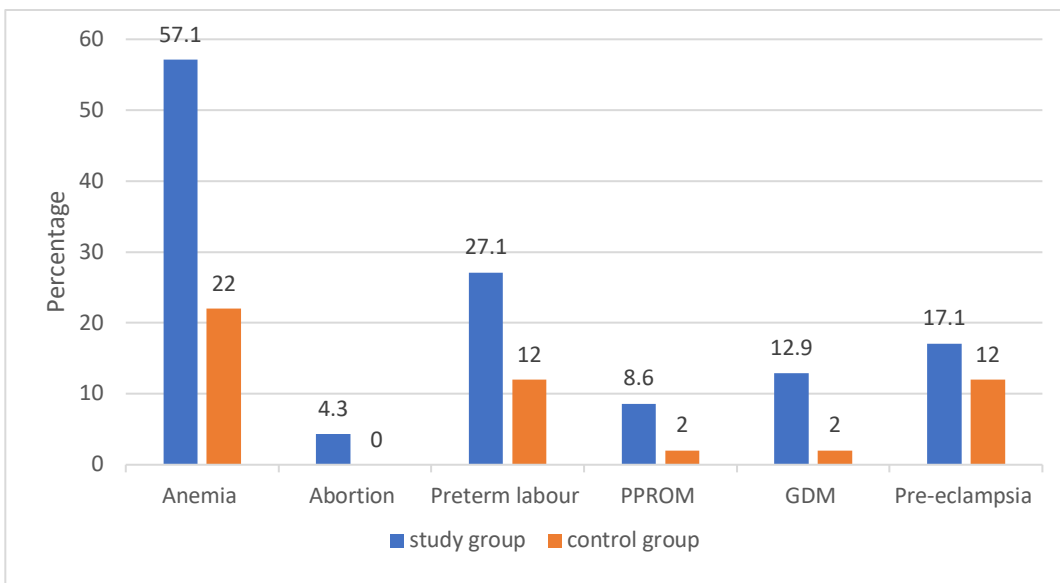


Figure 4: Distribution according to maternal complications

Complications in pregnant women included anemia (p-value -0.0001), Preterm labour (p-value -0.044) and

Gestational diabetes mellitus (p-value - 0.0338) were significantly more in the study group as compared to

the control group. Spontaneous abortion was observed in 3 subjects(4.3%) among the study group.(Figure No. 4)
 Most of the patients had vaginal delivery in both study (62.7%) and control (58%) groups. C-sections were

done in the study group due to obstetric indications. Only a single subject in the study group underwent vaginal birth after a caesarean. And 65 babies (97%) out of 67 were born alive.

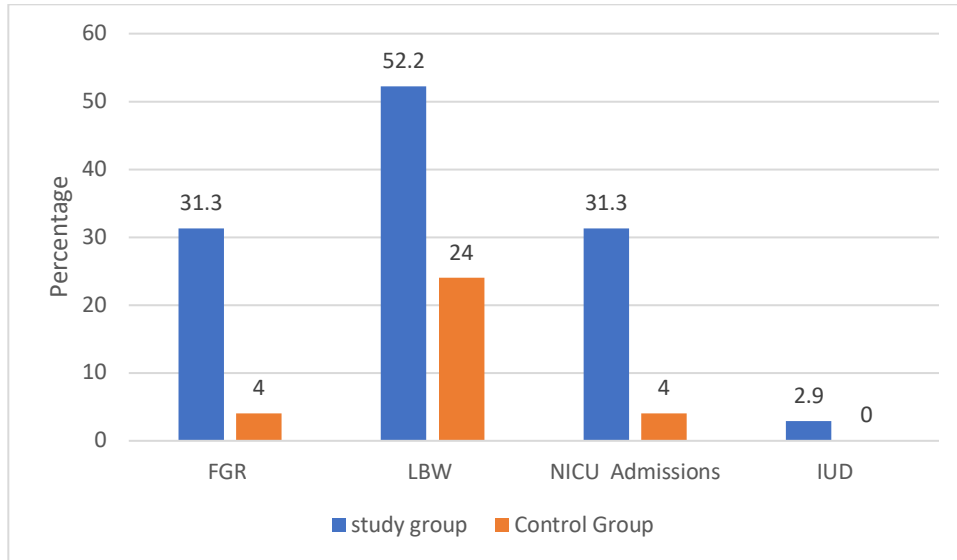


Figure 5: Distribution according to neonatal outcome

Neonatal outcomes in HIV positive mothers included fetal growth retardation (p-value -0.00036), Low birth weight (p-value -0.0012) and NICU admissions (p-value -0.00036) which were significantly seen in the study group as compared to the control group.(Figure No. 5)

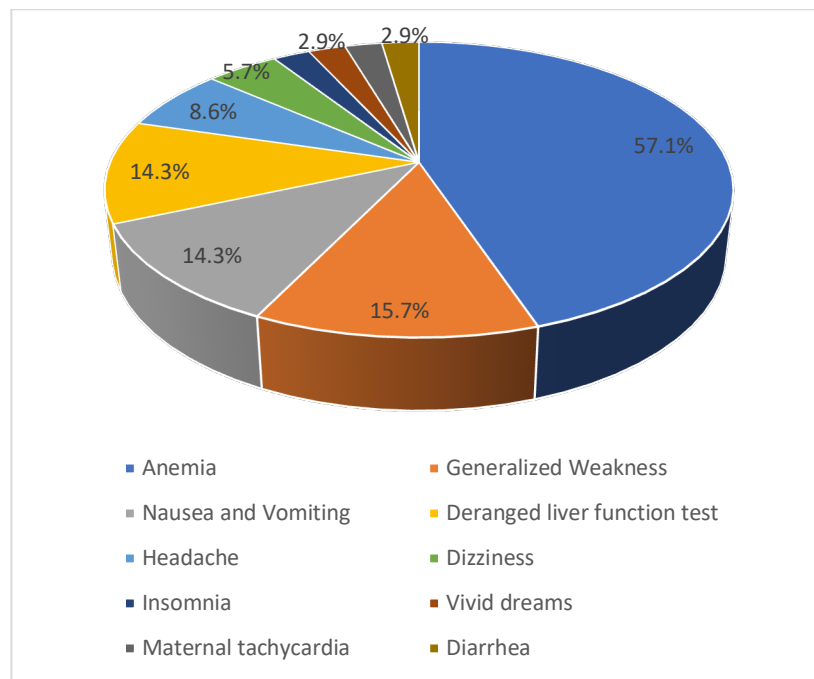


Figure 6: Side effects of Antiretroviral Therapy

Common side effects of antiretroviral therapy such as anemia (57%), Generalized weakness (15.7%), Nausea

and vomiting (14.3%), deranged liver function test, including hyperbilirubinemia (14.3%), Headache

(8.6%) were also reported in pregnant women. (Figure No. 6)

In our study, babies of 92.3% of subjects were started on formula feed, and only 7.7% opted for breastfeeding. All babies were started on nevirapine prophylaxis. All-inclusive counselling and wilful testing are recommended for all pregnant women early in pregnancy to decrease mother to child transmission of HIV infection and also complications of pregnancy.

Discussion

Stigmatization towards HIV in our communities can impact multiple facets of life for an HIV positive individual. This is especially true for pregnant mothers as there are two lives at stake. In the present study, the majority of the subjects (study group = 48.6% and control group = 46%) belonged to the age group of 20-25 years. A similar finding was seen in the study conducted by Akabuike JC et al. (2010) [14] in South-Eastern Nigeria, where the majority of the patients (68%) belonged to the peak reproductive age group of 20-29 years. The study and control groups in our study were mainly referred cases from peripheral centres (study group-55.7% and control group - 60%) with a small proportion of un-booked cases (study group-4.3% and control group 4%). In contrast to this, Pooli R et al. (2016) [15] discovered that the majority of HIV seropositive women were un-booked cases (55%) and the majority of seronegative constituted booked registration category (57%).

The current study showed that the majority of women in the study group were literate (82.9%). This reflects awareness about the disease and treatment-seeking behaviour among them. However, Desai RS et al. (2018) [16], who conducted a prospective cohort study in Bangalore Medical College Hospitals to study obstetric and newborn outcomes in HIV-infected pregnant women, observed that majority of the women reporting to the hospital were illiterate (51.6%).

Subjects in our study (study - 97.2% and control - 96%) were housewives. Similarly, Desai RS et al. (2018) [16] in her study found the majority of the participant (80%) to be housewives.

It was seen in our study that 65.7% and 72% of subjects were multigravidas in the study and control group, respectively. Dhadwal V et al. (2017) [5] in their study to find pregnancy outcomes in 212 HIV-infected women as compared to 238 HIV-uninfected controls, had a similar finding that out of 212 women, 111 (52.4%) were multiparous.

The present study showed that most of the subjects were already on antiretroviral therapy before pregnancy (44.3%) while others started early in first

trimester (31.4%). However, there were 2 subjects who were not on ART and referred from the peripheral centre after diagnosis for delivery and were started on ART immediately. Early initiation of ART can help to prevent perinatal transmission of HIV. [17] Moore BM et al. (2017) [7] also observed that out of 290 mothers, 198 (2.3%) had started ART in their pre-pregnancy period.

Mean CD4 counts in current study subjects were 349.04 ± 128.125 . 45.8% subjects had CD4 counts between 350-500 cells/mm³ and 40% had CD4 count between 200-350 cells/mm³. Similarly, Theron G et al. (2021) [18] in his study on adverse pregnancy outcomes in a randomized trial on isoniazid preventative therapy among women living with human immunodeficiency virus, found the mean CD4 count at baseline was 494 cells/mm³.

In the present study, the most common risk factor was HIV positive status of the husband (82.8%). Other risk factors included the previous history of unsterile nasal or ear piercing (11.4%), IM/IV injections from RMP in the village (14.3%) and blood transfusion (17.1%). In a study by Naicker N et al. (2015) [19] on South African women found that 18-24 years had the highest HIV and were almost three times more likely to acquire HIV compared to women 25 years and older. Also, women having multiple sex partners had more than twice the risk of acquiring HIV when compared to women who had no partner or who had a husband or figure partner. Although in our study none of the subjects gave a history of multiple sexual partners but three of them had remarriage.

In the present study, HIV-positive patients were significantly associated with HCV coinfection in study group (11.4%) as compared to the control group (4%), but Hepatitis B coinfection did not show statistical significance. Sharma V et al. (2018) [20] suggested that both HCV and Hepatitis B coinfection were significant in HIV-positive patients (p value < 0.001) were significantly higher in HIV-positive subjects as compared to HIV-negative.

Pregnant women in the current study reported common side effects of antiretroviral therapy such as anaemia (57.1%), Generalized weakness (15.7%), Nausea and vomiting (14.3%), deranged liver function including (14.3%) and Headache (8.6%). A study by Delicio AM et al. (2018) [21] on a cohort of 793 pregnant women infected with HIV at the CAISM/UNICAMP Obstetric Clinic from 2000 to 2015 showed maternal adverse effects were: dyslipidaemia (82%), anaemia 48 (56%), liver function test abnormalities (54.5%), including hyperbilirubinemia (11.6%), fasting glycemia alteration (19.2%), thrombocytopenia (14.1%), and allergic reaction (2.7%). Our study also showed that

two subjects had tachycardia who were investigated, but the specific cause of tachycardia could not be found out, but tachycardia settled 4-6 weeks after initiation of ART.

Most of the patients in the present study had vaginal delivery in both study (64.2%) and control (58%) groups. Caesarean section was done in 35.8% of subjects in the study group (due to obstetric indication only) and 42% of subjects in the control group. Similarly, in a study conducted by Aho I et al. (2018) [22] in Finland, it was reported that 74.5% of births were vaginal, 12.8% elective Caesarean, and 12.8% emergent Caesarean. Also, in this study, it was reported that elective caesarean section is preferred when the Viral Load is $\leq 1,000$ copies/ml.

The present study revealed that fetal growth retardation (p-value -0.00036), Low birth weight (p-value -0.0012) and NICU admissions (p-value -0.000168) were significantly more in the study group as compared to the control group. Similarly in a study by Tukei, VJ et al. (2021)[23] comparing a total of 614 HIV-positive and 390 HIV-negative pregnant women with delivery information on 571 (93.1%) and 352 (90.3%) respectively found that in comparison with their HIV-negative counterparts, a higher proportion of HIV-positive women experienced an intrauterine death (miscarriage or stillbirth), 7.1% versus 2.3% (P = 0.002), low birth weight delivery, 13.2% versus 7.9% (P = 0.010) and preterm delivery, 7.4% versus 3.8% (P = 0.046). Contrary to this, a study by Halli SS et al. (2015) [24] in a large sample of HIV-positive women in India reported pregnancy wastage in 17% of mothers, including stillbirths (3.8%), spontaneous abortions (13.7%) and induced abortions (2.8%). By reducing the social stigma associated with HIV and improving ART knowledge, the outcome of pregnancy among HIV-positive women can be improved. Integration of HIV and maternal health services may reduce adverse maternal and neonatal outcomes. In our study, as per protocol option of top feeding was offered. Out of 65 live births, 7.7% of subjects opted for breastfeeding. Mebratu L et al. (2020) [25] conducted a facility-based cross-sectional study with quantitative approaches through an interviewer-administered questionnaire from April 8 to May 10, 2019 among 209 participants and found that 81.6% (95% CI: 75.8–86.5) practised exclusive breastfeeding and 18.4% (95% CI: 13.5–23.7) practised mixed feeding.

Conclusion

The accumulating data shows a positive correlation between HIV infection and anemia, preterm labour, GDM, LBW, NICU admissions and coinfections like HCV and candidiasis as compared to controls. It was

observed that with increasing awareness, pregnant females had started ART pre-pregnancy and in 1st Trimester. In our study, ART was taken for more than 24 weeks by the majority of the subjects, which is in accordance with NACO guidelines for the prevention of MTCT.

References

1. Manogna D, Nooyi SC, Murthy NS. Outcome of pregnancy among HIV infected women: a retrospective cohort study in a tertiary care hospital in Bangalore, India. *Community Med.* 2017;8(6):343-8.
2. van Heuvel Y, Schatz S, Rosengarten JF, Stitz J. Infectious RNA: Human Immunodeficiency Virus (HIV) Biology, Therapeutic Intervention, and the Quest for a Vaccine. *Toxins.* 2022; 14(2):138.
3. Duriux-Smith A, Tw E, Goodman JT. Comparison of female to male and male to female transmission of HIV in 563 Figure couples. *BMJ.* 1992 Mar 28; 304:809.
4. M Tebit D, Ndemi N, Weinberg A, E Quinones-Mateu M. Mucosal transmission of human immunodeficiency virus. *Curr HIV Res.* 2012 Jan 1;10(1):3-8.
5. Cohen MS, Hellmann N, Levy JA, DeCock K, Lange J. The spread, treatment, and prevention of HIV-1: evolution of a global pandemic. *J Clin Invest.* 2008 Apr 1;118(4):1244-54.
6. Dadhwal V, Sharma A, Khoiwal K, Deka D, Sarkar P, Vanamail P. Pregnancy outcomes in HIV-infected women: experience from a tertiary care center in India. *Int J MCH AIDS.* 2017; 6(1):75.
7. Galvin SR, Cohen MS. The role of sexually transmitted diseases in HIV transmission. *Nat Rev Microbiol.* 2004 Jan;2(1):33-42.
8. Moore BM, Tobin-West CI. Pregnancy outcome of HIV-infected women on antiretroviral therapy in a treatment centre in Port Harcourt, Nigeria: a retrospective analysis. *Niger Heal J.* 2017;17(1).
9. McIntyre J. Mothers infected with HIV: reducing maternal death and disability during pregnancy. *Br Med Bull.* 2003 Dec 1;67(1):127-35
10. McGowan JP, Shah SS. Prevention of perinatal HIV transmission during pregnancy. *J Antimicrob Chemother.* 2000 Nov 1;46(5):657-68.
11. Kassa GM. Mother-to-child transmission of HIV infection and its associated factors in Ethiopia: a systematic review and meta-analysis. *BMC Infect Dis.* 2018 Dec;18(1):1-9.
12. Lyerly AD. Dolutegravir: advancing ethical research in pregnancy. *The Lancet.* 2019 Nov 30;394(10213):1972-4.
13. Silverman NS. ACOG Committee Opinion Number 751 Labor and Delivery Management of

- Women with Human Immunodeficiency Virus Infection. *Obstet Gynecol.* 2018;132(3): E131–7.
14. Slater M, Stringer EM, Stringer JS. Breastfeeding in HIV-positive women: What can be recommended? *Paediatr Drugs.* 2010 Feb;12(1):1-9.
 15. Akabuiké JC, Ikechebelu JI, Mbachu II, Eke NO, Ugboaja JO, Akabuiké MN. Pregnancy outcome in HIV seropositive women booked at a tertiary healthcare institution in southeastern Nigeria. *Afrimed J.* 2010;1(2):28-33.
 16. Pooli R, Devi J, Rani S. Comparative study of pregnancy and its outcome between HIV positive and HIV negative pregnant woman. *Int J STD AIDS.* 2016 Feb22; 5:717-21.
 17. Desai RS, Shivamurthy G, Desai S. Obstetric and newborn outcome in HIV infected pregnant women: a prospective cohort study in Bangalore Medical College Hospitals, India. *Int J Gynaecol Obstet.* 2018 Nov 1;7(11):4445-51.
 18. National AIDS Control Organization. National Technical Guidelines on Anti-Retroviral Treatment. *Naco2018;* 148:3–5.
 19. Theron G, Montepiedra G, Aaron L, McCarthy K, Chakhtoura N, Jean-Philippe P, et al. Individual and Composite Adverse Pregnancy Outcomes in a Randomized Trial on Isoniazid Preventative Therapy Among Women Living with Human Immunodeficiency Virus. *Virus. Clin Infect Dis.* 2021 Jun 1;72(11): e784-90.
 20. Naicker N, Kharsany A, Werner L, van Loggerenberg F, Mlisana K, Garrett N, et al. Risk factors for HIV acquisition in high risk women in a generalised epidemic setting. *AIDS Behav.* 2015 Jul;19(7):1305-16.
 21. Sharma V, Ramachandran VG, Mogha NS, Bharadwaj M. Hepatitis B & C virus infection in HIV seropositive individuals & their association with risk factors: A hospital-based study. *Indian J Med Res.* 2018 Jun;147(6):588.
 22. Delicio AM, Lajos GJ, Amaral E, Lopes F, Cavichioli F, Myioshi I, et al. Adverse effects of antiretroviral therapy in pregnant women infected with HIV in Brazil from 2000 to 2015: a cohort study. *BMC Infect Dis.* 2018 Dec;18(1):1-4.
 23. Aho I, Kaijomaa M, Kivelä P, Surcel HM, Sutinen J, Heikinheimo O, et al. Most women living with HIV can deliver vaginally—National data from Finland 1993–2013. *PLoS One.* 2018 Mar 22;13(3): e0194370.
 24. Tukei VJ, Hoffman HJ, Greenberg L, Thabelo R, Nchephe M, Mots'oane T, et al. Adverse pregnancy outcomes among HIV-positive women in the era of universal antiretroviral therapy remain elevated compared with HIV-negative women. *Pediatr Infect Dis J.* 2021 Sep;40(9):821.
 25. Halli SS, Khan CG, Shah I, Washington R, Isac S, Moses S, Blanchard JF. Pregnancy wastage among HIV-infected women in a high HIV prevalence district of India. *BMC Public Health.* 2015 Dec;15(1):1-9.
 26. Mebratu L, Mengesha S, Tegene Y, Alano A, Toma A. Exclusive Breast-Feeding Practice and Associated Factors among HIV-Positive Mothers in Governmental Health Facilities, Southern Ethiopia. *J Nutr Metab.* 2020; 2020:7962054.