Original Article

Treatment outcome of different antiretroviral drug regimens in HIV-positive pregnant women

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Abstract

Objective: The objective of the study was to compare the maternal and fetal outcomes of currently preferred tenofovir-based regimen with previous zidovudine-based regimen and also to determine whether the time of starting antiretroviral therapy (ART), whether it can affect the pregnancy and fetal outcome.

Materials and Methods: Pregnant patients prescribed any of the above regimens were followed up every month till delivery and newborns for initial 6 months. Maternal endpoints were body weight, hemoglobin, and CD4 count, whereas fetal endpoints were birth weight, Apgar score, body weight, and HIV status at 6 months. Data were analyzed using ANOVA and unpaired *t*-test. $P < 0.05$ was considered statistically significant.

Results: A significant increase in CD4 count was observed in patients treated with both the regimens at 12 months as compared to baseline ($P < 0.001$ and 0.05). Moreover, a significant increase in CD4 count was observed at 12 months as compared to baseline, whether treatment was started before or after the diagnosis of pregnancy ($P < 0.05$ and 0.001). A significant difference in mean body weight at the end of 9 months was observed in patients wherein ART was started before or after the diagnosis of pregnancy ($P < 0.005$). Majority of patients had a favorable maternal outcome, while fetal birth weight, Apgar score, body weight, and HIV status were comparable at 6 months irrespective of treatment and time of starting ART.

Conclusion: All ART regimens are equally effective in terms of increase in CD4 count, gestational gain in body weight, and pregnancy and fetal outcome. Furthermore, there is no significant difference in efficacy, pregnancy, and fetal outcome in women who were already on ART when diagnosed pregnancy or who were started ART later in antenatal period.

Keywords: Antiretroviral therapy, CD4 count, HIV, pregnancy

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INTRODUCTION

The prevention of parent-to-child transmission of HIV/AIDS is an integral component of the AIDS control program since mother-to-child transmission (MTCT) of HIV/AIDS accounts for over 90% of new infections in children.[1] This, also referred to as "vertical transmission," occurs during pregnancy, at the birth time, or through breastfeeding. According to the National AIDS Control Organization, about 30,000 infants are estimated to acquire HIV infection each year in India.[2] In the absence of any

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intervention, transmission rates range from 15% to 45%. However, it can be reduced to below 5% with effective interventions during the periods of pregnancy, labor, delivery, and breastfeeding. The target of the Global Plan 2016 is to reduce MTCT rate to 5% or less among breastfeeding women and to 2% or less among nonbreastfeeding women.[3]

The drug treatment of HIV-positive pregnant patients and newborns has undergone a lot of twists and turns since 1990. Physiological changes may require dose modification or adjustment in pregnant HIV mothers.[4] Since 2006, zidovudine (AZT)/lamivudine (3TC) with a nonnucleoside reverse-transcriptase inhibitor or a protease inhibitor was the recommended combination regimen in antiretroviral therapy (ART)-naive pregnant women. However, due to safety issues (AZT-induced anemia and nevirapine (NVP)-induced fatal skin reactions), AZT has been replaced by tenofovir (TDF)-based regimen as preferred treatment in HIV-positive pregnant patients.[1]

Since January 2014, the recommended first-line regimen for HIV-infected pregnant women has been TDF (300 mg) + 3TC (300 mg) + efavirenz (EFV) (600 mg) at any gestational age and preferred to previous AZT + 3TC + NVP regimen. However, very few data are available for comparison of pregnancy and fetal outcome in patients treated with different regimens and whether the time of starting ART, can affect the pregnancy and fetal outcome is not known.

MATERIALS AND METHODS

This was a continuous, longitudinal, prospective, and retrospective, observational, single-center study conducted over a period of 27 months (January 2016–March 2018) in HIV-positive pregnant patients receiving antiretroviral (ARV) drugs at an ART center, Civil Hospital, Ahmedabad. The study protocol was approved by the Institutional Ethics Committee (Reference number-EC/Approval/23/17/dated 04/04/2017) and Gujarat State AIDS Control Society (Reference number-2017-18/1/6258-59).

Known cases of HIV-positive pregnant women treated with ARV drug/regimen, who were >18 years of age and willing to participate in the study and give written informed consent, were included in the study. Patients who did not want to participate in the study and refused to give informed consent were excluded.

All HIV-positive pregnant patients receiving treatment from an ART center, Ahmedabad, and who met the inclusion and exclusion criteria were enrolled in the study. Pretreatment/prepregnancy assessment data of pregnant patients such as demographic details, baseline CD4 count, WHO stage, clinical history, obstetric history, family history, and laboratory investigations were obtained from the records retrospectively. Patients prescribed first-line regimen TDF (300 mg) + 3TC (300 mg) + EFV (600 mg) (TLE) once daily by a consultant physician. While patients who were stable on AZT (300 mg) + 3TC (150 mg) + NVP (200 mg) (ZLN) twice daily regimen or tablet TDF (300 mg) + 3TC (300 mg) + atazanavir (300 mg) + ritonavir (100 mg) (TL Atz/r) once daily were continued the same regimen. The details of study method are shown in Figure 1.

An attempt has been made to analyze the data according to treatment regimen, already on ART at the time of diagnosis of pregnancy and ART started in antenatal period after the diagnosis of pregnancy.

The sample size of 55 was calculated considering power of study as 95% and level of significance 0.05%. The data were recorded in Microsoft Excel® worksheet 2010 and analyzed using frequency and percentage analyses, Student's *t*-test, ANOVA, and Chi-square test. Student's *t*-test and ANOVA were used for comparison of parametric data, and Chi-square test was used for comparison of nonparametric data between the groups. $P < 0.05$ was considered statistically significant.

RESULTS

Of 87 patients, 84 completed the study, whereas 3 were lost to follow-up. Baseline demographic details are mentioned in Table 1. The analysis was done as per treatment regimen and as per time of starting ART.

Data analysis as per treatment regimen

The patients were treated with three different regimens as prescribed by the consultant physician. Of 87 patients, 53 received TLE regimen, 28 received ZLN regimen, and 6 received TL Atz/r regimen.

Efficacy analysis

CD4 count

Baseline CD4 count in patients with all the three regimens was comparable ($P = 0.54$). A significant increase in CD4 count was observed in patients taking TLE regimen at 12 months as compared to baseline and 6 months ($P < 0.001$ and $P < 0.01$) [Table 2]. Similarly, a significant increase in CD4 count was observed at 12 months of treatment in patients treated with ZLN regimen as compared to baseline ($P < 0.05$) [Table 2]. However, there was no significant change in CD4 count in HIV-positive patients with TL Atz/r regimen at 6 or 12 months as compared to baseline [Table 2].

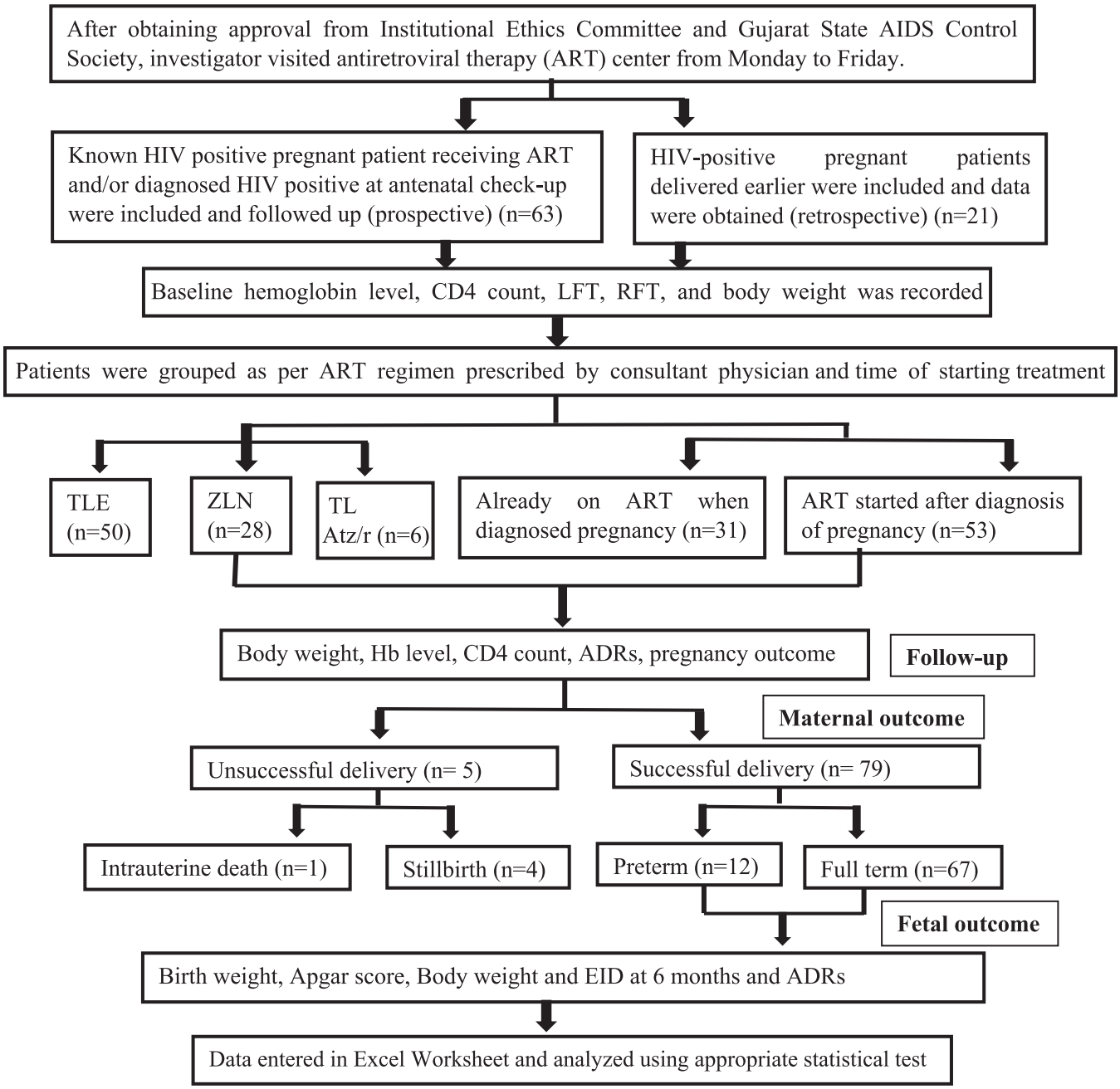

Figure 1: Details of the study design. LFT = Liver function test, RFT = Renal function test, ADRs = Adverse drug reactions, EID = Early infant diagnosis, Tenofovir (300 mg) + Lamivudine (300 mg) + Efavirenz (600 mg) OD, Zidovudine (300 mg) + Lamivudine (150 mg) + Nevirapine (200 mg) BD, and Tenofovir (300 mg) + Lamivudine (300 mg) + Atazanavir (300 mg) + ritonavir (100 mg) OD

Hemoglobin level

No significant change in hemoglobin was observed in patients treated with all the three regimens.

Body weight

Mean increase in body weight in HIV-positive pregnant patients with TLE, ZLN, and TL Atz/r regimens during pregnancy was 5.02 ± 3.16 kg, 6.40 ± 3.59 kg, and 7.56 ± 4.62 kg, respectively.

Pregnancy and fetal outcome

Of total 84 HIV-positive pregnant patients, majority had the favorable outcome (79, 94.04%), i.e. either full term (67) or preterm (12) delivery. However, four patients had stillbirths (one in TLE regimen and three in ZLN regimen) and one had intrauterine death (TLE regimen) [Table 3].

Interestingly, there was no significant difference in mean birth weight, of in infants born to patients treated with

all the three regimens similarly. Mean increase in body weight at 6 months was almost same (2.88 ± 0.10 kg and 2.86 ± 0.29 kg) in patients treated with TLE and TL Atz/r regimens, respectively. At 6 weeks and 6 months, early infant diagnosis (EID) was negative in all infants born to patients with TLE, ZLN, and TL Atz/r regimens.

Data analysis as per time of starting antiretroviral therapy treatment

Of 87 patients, 32 were already on ART when diagnosed pregnancy, whereas 55 were diagnosed HIV positive at antenatal checkup, and treatment was started thereafter.

Efficacy analysis

CD4 count

A significant increase in CD4 count was observed at 12 months as compared to baseline and 6 months in women who were already on ART ($P < 0.05$) [Table 2]. However, in patients where ART was started after being diagnosed pregnancy (antenatal period), a significant increase in CD4 count was observed at 6 months of ART as compared to baseline ($P < 0.05$) and at 12 months as compared to baseline and 6 months ($P < 0.001$ and $P < 0.005$) [Table 2].

Table 1: Demographic details and clinical presentation of HIV-positive pregnant women in the study

Parameters	TLE (*n*=53)	ZLN (*n*=28)	TL Atz/r (*n*=6)
Mean age (years)±SD	26.16±4.55	27±5.17	25.33±2.73
Baseline mean body weight (kg)	50.66±10.91	51.48±10.07	47.76±7.89
Education			
Illiterate	25	13	6
Primary school	18	8	-
Secondary school	3	4	-
College	7	3	-
Occupation			
Homemaker	48	27	6
Service	5	1	-
Mode of transmission			
Unknown	18	15	3
Sexual	27	8	-
Blood transfusion	8	5	3
Entry point			
PPTCT	29	17	2
VCT	15	7	1
Private	9	1	-
ICTC	-	3	1
IPD	-	-	2
Start of ART			
First trimester	25	19	5
Second trimester	19	3	1
Third trimester	9	6	-
WHO clinical staging			
Stage 1	53	28	6
Stage 2	-	-	-
HIV 1/2			
HIV 1	53	28	5
HIV 2	-	-	1

TLE=Tenofovir + lamivudine + efavirenz, ZLN=Zidovudine + lamivudine + nevirapine, TL Atz/r=Tenofovir+lamivudine + atazanavir + ritonavir, PPTCT=Prevention of parent-to-child transmission of HIV, VCT=Voluntary counseling and testing center, ICTC=Integrated counseling and testing center, IPD=Inpatient department, ART=Antiretroviral therapy, SD=Standard deviation

Hemoglobin level

No significant change in hemoglobin level was observed in both the groups of patients irrespective of time of starting ART.

Body weight

A significant difference was observed in increase in mean body weight at the end of 9 months in patients where ART was started before and after the diagnosis of pregnancy ($P < 0.005$) [Figure 2].

Pregnancy and fetal outcome

Majority of HIV-positive pregnant patients delivered at full term. Mean birth weight of all newborns was almost same in patients who were on ART at pregnancy or who started ART in antenatal period. The Apgar score of all newborns was between 8 and 10 in both the groups irrespective of time of starting ART. At 6 weeks and 6 months, EID was negative in all infants born to patients in both the groups.

Safety analysis

During the study period, 101 adverse drug reactions (ADRs) were reported. Of 101 ADRs, 97 were reported in HIV-positive women and 4 in infants.

Adverse drug reactions in HIV-positive women

Of 97 ADRs, 80 were reported in TLE regimen, 9 in TL Atz/r regimen, and 8 in ZLN regimen.

System organ involvement

The most common body systems involved were

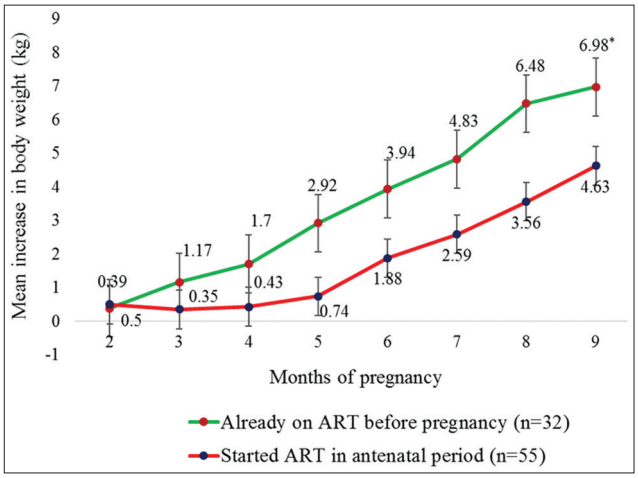

Figure 2: Mean increase in body weight of patients starting antiretroviral therapy at different time intervals ($n = 87$). *$P < 0.005$ as compared to antiretroviral therapy started after pregnancy

Table 2: Comparison of mean CD4 count in HIV-positive pregnant women treated with different ARV regimens (*n*=87)

CD 4 count (cells/mm^3)	Baseline	6 months	12 months
TLE (95% CI) (*n*=53)	445.96±41.73 (360.74-531.19)	511.91±37.83 (435.78-588.06)	679.43±38.10 (602.63-756.24)*,@
ZLN (95% CI) (*n*=28)	508.22±50.94 (403.48-612.96)	561.84±43.08 (472.92-650.76)	610.85±53.49 (500.66-721.05)#
TL Atz/r (95% CI) (*n*=6)	543.25±105.17 (208.59-877.91)	605.6±81.98 (378.01-833.19)	683.5±118.92 (377.75-989.25)
Already on ART before pregnancy (*n*=32)	536.93±39.25 (456.78-617.09)	529.93±39.58 (448.86-611.0)	626.11±47.63 (528.69-723.53)†
Started ART in antenatal period (*n*=55)	403.48±47.21 (306.78-500.18)	534.04±38.40 (456.64-611.45)†	669.86±39.77 (589.61-750.12)$,α

*$P<0.001$ compared to baseline, @$P<0.01$ compared to 6 months, #$P<0.05$ compared to baseline, †$P<0.05$ as compared to baseline and 6 months, $$P<0.005$ as compared to 6 months, α$P<0.001$ as compared to baseline. Paired *t*-test was used for comparing with baseline and 6 months. Data are expressed in mean±SEM. TLE=Tenofovir + lamivudine + efavirenz, ZLN=Zidovudine + lamivudine + nevirapine, TL Atz/r=Tenofovir + lamivudine + atazanavir + ritonavir, ART=Antiretroviral therapy, SEM=Standard error of mean, CI=Confidence interval

Table 3: Mode, term at delivery, and health status of newborns in patients treated with different ARV regimens

Parameters	TLE (*n*=48)	ZLN (*n*=25)	TL Atz/r (*n*=6)	*P*
Mode of delivery				
Normal delivery	37	20	4	0.78
LSCS	11	5	2	
Term at delivery				
Preterm	7	5	0	0.46
Full term	41	20	6	
Mean birth weight (kg±SEM)	2.58±0.07	2.53±0.11	2.92±0.20	0.26
Mean birth weight (95% CI)	2.43-2.73	2.30-2.77	2.35-3.49	
Number of LBW infants (<2.5 kg)	19	11	2	0.87
Apgar score				
8-10	48	25	6	
4-7	0	0	0	
0-3	0	0	0	

TLE=Tenofovir + lamivudine + efavirenz, ZLN=Zidovudine + lamivudine + nevirapine, TL Atz/r=Tenofovir + lamivudine + atazanavir + ritonavir, SEM=Standard error of mean, CI=Confidence interval, LBW=Low birth weight, LSCS=Lower segment caesarian section

neurological (37.11%) and gastrointestinal (37.11%) disorders followed by psychiatric disorders (15.46%) [Figure 3]. The most common presentation in neurological disorders was vertigo (66.66%), While vomiting was most common in gastrointestinal disorders (58.33%) [Table 4].

Causality, preventability, and severity assessment

Forty-three ADRs were categorized as possible (44.32%) and 54 as probable (55.67%) as per the Naranjo's algorithm, whereas WHO-Upsala Monitoring Center scale showed a possible causal relation of ADRs with drug therapy. Of 98 ADRs, 39 (39.79%) were probably preventable, whereas 59 (60.2%) were not preventable. Majority of ADRs were mild in nature (96, 97.95%), whereas 2.04% were moderately severe in nature.

Time relationship of adverse drug reaction with drug therapy and duration of adverse drug reaction

Majority of the ADRs (58, 59.18%) were observed on the 1st day of treatment. Most of the ADRs (82, 83.67%) resolved within 1 month, whereas 12.24% ADRs were recovering after 1 month.

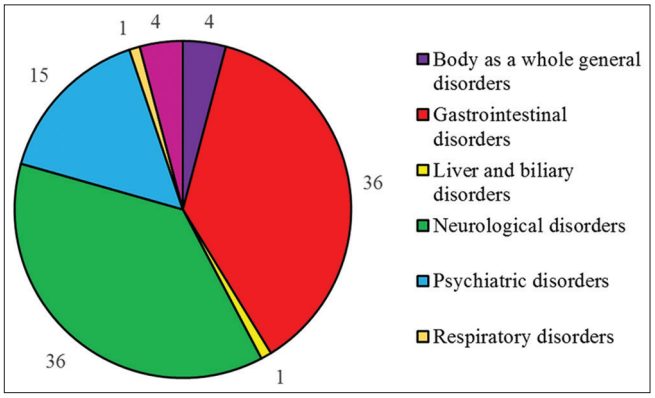

Figure 3: Body system affected by different antiretroviral therapy regimens in HIV-positive pregnant patients in the study (*n* = 97)

Seriousness

Majority of the ADRs (95, 96.93%) were not serious in nature.

DISCUSSION

Immune functions are suppressed in both HIV-infected and uninfected women in pregnancy. In addition, the presence of HIV infection in pregnancy accelerates the progression of the disease.[5] The CD4 + T-cell count is one of the best indicators of the immunologic competence of the patient with HIV infection, which determines the extent of damage and disease progression. It has been mentioned that in ART-naïve HIV-infected women, CD4 counts are lower with no significant difference during pregnancy as compared to prenatal or postpartum periods,[6] while in our study, CD4 count increased during pregnancy in HIV-positive pregnant patients treated with all the three ARV regimens. Interestingly, a significant increase in CD4 count was observed during pregnancy in patients who started ART in antenatal period; however, it was not observed in patients who were already on ART before conception. This indicates that patients who were already on ART (before pregnancy) were stable, and ARV drugs had maximally increased CD4 count. On the other hand, patients who started ART late (antenatal) had active disease and low CD4 count, and subsequent to starting ART, CD4 count increased as expected.

Table 4: Clinical presentation of adverse drug reactions by different ARV regimens in HIV-positive women in the study (*n*=97)

Body system affected	Clinical presentation
Neurological disorders (36)	Vertigo (24)
	Headache (4)
	Giddiness (4)
	Dizziness (3)
	Syncope at night (1)
Gastrointestinal disorders (36)	Vomiting (21)
	Nausea (6)
	Abdominal pain (2)
	Gastric burning (2)
	Constipation (1)
	Diarrhea (1)
	Dry mouth (1)
	Stomach fullness (2)
Psychiatric disorders (15)	Sleeplessness (4)
	Nightmares (3)
	Sleepiness (2)
	Mental imbalance (2)
	Bad dreams (1)
	Bad thoughts (1)
	Forgetfulness (1)
	Restlessness (1)
Respiratory disorders (2)	Breathlessness (2)
Skin and appendage disorders (4)	Itching (2)
	Rash (2)
Body as a whole general disorder (4)	Edema legs (2)
	Edema face (1)
	Weakness (1)
Liver and biliary disorders (1)	Increased serum bilirubin (1)

ARV drugs, especially AZT, have been reported to cause anemia.[1] However, in our study, there was no change in hemoglobin level in patients treated with AZT-based regimen. Recently, it has been reported that ARV therapy may have a positive impact on hemoglobin level with at least 6 months of usage.[7] Thus, it seems that ARV therapy certainly increases the resolution of anemia, and this might be due to the effects of ARV drugs on inflammation and chronic infection. However, it can be argued that pregnant women treated with ARV drugs also receive iron, folic acid, multivitamin, and other nutritional supplements, which may have an overall positive impact on health. Furthermore, the change in dietary patterns during pregnancy may have a positive effect on hemoglobin levels.

Interestingly, mean increase in body weight was more in patients already on ART as compared to patients who started ART later in antenatal period ($P < 0.005$). This could be due to the fact that pregnant patients who were already on ART were more vigilant and stable. Second, the records of body weight were readily available from ART center from day 1.

Furthermore, a higher rate of spontaneous abortion and delivery of low birth weight (LBW) infants may exist in women with advanced HIV disease.[8] Moreover, there is a risk of maternal anemia and adverse pregnancy outcomes such as stillbirth, LBW, and preterm newborns; HIV-infected women have increased chances of abortion than HIV-uninfected women.[9] Our study observed no difference in frequency of preterm in patients treated with TDF-based or AZT-based therapy which is similar to a study done by Pintye *et al*.[10] Furthermore, our study observed no difference in rate of premature delivery in patients initiating treatment before or after pregnancy. A systematic review and meta-analysis observed that ART initiation before conception has been associated with significantly higher risk of prematurity than ART initiation after conception. Moreover, the magnitude of these associations was highest in studies done in low- and middle-income countries, where background rates of preterm delivery and low birth weight are already higher than high-income countries.[11] Li *et al*. also observed a higher risk of preterm delivery in women initiating Highly Active Antiretroviral Therapy (HAART) before pregnancy (84, 14%) as compared to women initiating HAART in antenatal period (41, 8%).[12] Probably, pregnant patients while on ART were older, likely to be multigravida with advanced HIV infection as compared to patients starting ART in antenatal period who were younger, healthier primigravidae.[11]

Birth weight of newborns delivered at full term by Indian mothers is around 2.8–3.0 kg.[13] While our study observed the birth weight of newborns from 2.58 kg to 2.92 kg with no significant difference between the three regimens. A study done by Nachega *et al*. also found no significant difference in mean birth weight and LBW infants born to mothers receiving TDF-based ART compared to those born to mothers receiving non-TDF-based ART during pregnancy [Table 5].[14,15]

Table 5 shows comparison of pregnancy and fetal outcome in hivpositive pregnant patients treated with different arv regimens in various studies.[16-18]

Although the use of ART in pregnancy presents unquestionable benefits in preventing MTCT of HIV, it is not free from adverse effects. We observed significant rates of ADRs in HIV-positive pregnant patients, albeit rather of low severity. In the present study, the most common body systems involved were neurological and gastrointestinal disorders followed by psychiatric disorder. However, a study by Agu and Oparah reports that the most common systemic presentations of ADRs were skin and appendage disorders, followed by neurological disorders.[19] The difference could be due to variation in ART regimens. In the present study, most of the ADRs were categorized as possible followed by probable in nature. Similar results were found in the study of Sadiq *et al*.[20] ARV regimens are administered as

Table 5: Comparison of pregnancy and fetal outcome in HIV-positive pregnant patients treated with different ARV regimens in various studies

Parameters	Our study (*n*=87)	Moodley *et al*., 2016 (*n*=2726) (South Africa)[16]	Zash *et al*., 2016 (*n*=2221) (Boston)[17]	Akinbami *et al*., 2015 (*n*=143) (Nigeria)[18]	Nachega *et al*., 2017[14]
Preterm (%)	Tenofovir-based ART (14.59) Zidovudine-based ART (20)	Tenofovir-based ART (21.1) Zidovudine-based ART (20.12)	Tenofovir-based ART (21.8) Zidovudine-based ART (22.06)	-	Tenofovir-based <nontenofovir-based ART (RR: 0.90)
Stillbirth (%)	Tenofovir-based ART (2.08) Zidovudine-based ART (12)	Tenofovir-based ART (2.22) Zidovudine-based ART (1.75)	Tenofovir-based ART (2.7) Zidovudine-based ART (4.1)	-	Tenofovir-based <nontenofovir-based ART (RR: 0.60)
Vaginal delivery (%)	Tenofovir-based ART (77.08) Zidovudine-based ART (80)	-	-	52.7	-
Cesarean delivery (%)	Tenofovir-based ART (22.92) Zidovudine-based ART (20)	-	-	47.3	-
LBW (%)	Tenofovir-based ART (39.58) Zidovudine-based ART (44)	Tenofovir-based ART (13.4) Zidovudine-based ART (15.3)	-	-	No significant difference Tenofovir-based and nontenofovir-based ART (RR: 0.91)

ART=Antiretroviral therapy, LBW=Low birth weight

fixed dose combination. Thus its difficult to pinpoint any single drug resulting in to possible category. In addition pregnancy itself can cause gastrointestinal symptoms.

Like any other study, there were few limitations. We did not have access to viral load during pregnancy as it was not done. Second, the data of AZT-based therapy were obtained retrospectively. Thus, we could not obtain details of gain in infant body weight at 6 months and ADRs occurred in those patients, if any. However, the strength of data collection and analysis leads to valid important conclusion.

Hence, to conclude, all the three ART regimens are equally effective in terms of increase in CD4 count, gestational gain in body weight, and pregnancy and fetal outcome. Furthermore, there is no significant difference in efficacy, pregnancy, and fetal outcome in women who were already on ART when diagnosed pregnancy or who started ART later in antenatal period. Hence, ART should be started as early as possible when diagnosed with HIV as it is highly effective in preventing MTCT of HIV and Results into favorable pregnancy and fetal outcomes.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. NACO, Government of India; Ministry of Health and Family Welfare. Prevention of Parent to Child Transmission (PPTCT) of HIV using Multi Drug Anti-retroviral Regimen in India. NACO, Government of India; Ministry of health and family welfare; New Delhi: 2013. Available from: https://ksaps.gov.in/pdfs/pptct_natiionalguideline.pdf. [Last accessed on 2019 Jan 20].
2. Ministry of Health and Family Welfare Govt of India. India HIV Estimation 2015; Technical Report; National AIDS Control Organization and National Institute of Medical Statistic. Ministry of Health and Family Welfare Govt of India; 2015. p. 12-3. Available from: http://www.naco.gov.in/upload/2015%20MSLNS/HSS/India%20HIV%20Estimations%202015.pdf. [Last accessed on 2019 Jan 20]
3. UNAIDS. Global plan 2016; On the Fast Track to An AIDS Free Generation. Joint United Nations Programme on HIV/AIDS. Geneva: UNAIDS; 2016. p. 32. Available from: http://www.unaids.org/sites/default/files/media_asset/GlobalPlan2016_en.pdf. [Last accessed on 2019 Jan 20]
4. Desai M, Iyer G, Dikshit RK. Antiretroviral drugs: Critical issues and recent advances. Indian J Pharmacol 2012;44:288-98.
5. Scott GB, Fischl MA, Klimas N, Fletcher MA, Dickinson GM, Levine RS, *et al*. Mothers of infants with the acquired immunodeficiency syndrome. Evidence for both symptomatic and asymptomatic carriers. JAMA 1985;253:363-6.
6. Heffron R, Donnell D, Kiarie J, Rees H, Ngure K, Mugo N, *et al*. A prospective study of the effect of pregnancy on CD4 counts and plasma HIV-1 RNA concentrations of antiretroviral-naive HIV-1-infected women. J Acquir Immune Defic Syndr 2014;65:231-6.
7. Tunkyi K, Moodley J. Anaemia in pregnancy in a setting of high HIV prevalence rates. S Afr J Infect Dis 2017;32:138-41.
8. Johnstone FD, MacCallum L, Brettle R, Inglis JM, Peutherer JF. Does infection with HIV affect the outcome of pregnancy? Br Med J (Clin Res Ed) 1988;296:467.
9. González R, Rupérez M, Sevene E, Vala A, Maculuve S, Bulo H, *et al*. Effects of HIV infection on maternal and neonatal health in southern mozambique: A prospective cohort study after a decade of antiretroviral drugs roll out. PLoS One 2017;12:e0178134.
10. Pintye J, Baeten JM, Celum C, Mugo N, Ngure K, Were E, *et al*. Maternal tenofovir disoproxil fumarate use during pregnancy is not associated with adverse perinatal outcomes among HIV-infected East African women: A Prospective study. J Infect Dis 2017;216:1561-8.

11. Uthman OA, Nachega JB, Anderson J, Kanters S, Mills EJ, Renaud F, *et al*. Timing of initiation of antiretroviral therapy and adverse pregnancy outcomes: A systematic review and meta-analysis. Lancet HIV 2017;4:e21-e30.
12. Li N, Sando MM, Spiegelman D, Hertzmark E, Liu E, Sando D, *et al*. Antiretroviral therapy in relation to birth outcomes among HIV-infected women: A Cohort study. J Infect Dis 2016;213:1057-64.
13. Krishnan KD, Avabratha KS, D'Souza AJ. Estimation of average birth weight in term newborns a hospital-based study in coastal Karnataka. Int J Contemp Pediatr 2017;1:156-9.
14. Nachega JB, Uthman OA, Mofenson LM, Anderson JR, Kanters S, Renaud F, *et al*. Safety of tenofovir disoproxil fumarate-based antiretroviral therapy regimens in pregnancy for HIV-infected women and their infants: A systematic review and meta-analysis. J Acquir Immune Defic Syndr 2017;76:1-2.
15. Mofenson LM, Baggaley RC, Mameletzis I. Tenofovir disoproxil fumarate safety for women and their infants during pregnancy and breastfeeding. AIDS 2017;31:213-32.
16. Moodley T, Moodley D, Sebitloane M, Maharaj N, Sartorius B. Improved pregnancy outcomes with increasing antiretroviral coverage in South Africa. BMC Pregnancy Childbirth 2016;16:35.
17. Zash R, Souda S, Chen JY, Binda K, Dryden-Peterson S, Lockman S, *et al*. Reassuring birth outcomes with tenofovir/Emtricitabine/Efavirenz used for prevention of mother-to-child transmission of HIV in Botswana. J Acquir Immune Defic Syndr 2016;71:428-36.
18. Akinbami AA, Gbadegesin A, Ajibola SO, Uche EI, Dosunmu AO, Adediran A, *et al*. Factors influencing CD4 cell count in HIV-positive pregnant women in a secondary health center in Lagos, Nigeria. HIV AIDS (Auckl) 2015;7:115-8.
19. Agu KA, Oparah AC. Adverse drug reactions to antiretroviral therapy: Results from spontaneous reporting system in Nigeria. Perspect Clin Res 2013;4:117-24.
20. Sadiq S, Gupta S, Khajuria V, Tandon VR, Mahajan A, Gupta M. Adverse drug events due to antiretroviral therapy in a Northern Indian tertiary care institution. Natl J Physiol Pharm Pharmacol 2016;6:205-8.