Original Research Article

Effect of antenatal retroviral therapy on feto-maternal outcome in human immunodeficiency virus seropositive patients

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Received: 08 April 2020
Accepted: 30 May 2020

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ABSTRACT

Background: To study the effect of HIV and duration of ART on term of delivery, newborn birth weight and adverse fetal outcomes.

Methods: Prospective comparative study of 40 HIV seropositive pregnant females with varying duration of ART (tenofovir 300 mg + lamivudine 300 mg + efavirenz 600 mg) and HIV seronegative pregnant females attending ANC and delivering in department of obstetrics and gynecology at S. M. S. Medical College, Jaipur, Rajasthan, India.

Results: Most HIV seropositive patients were in age group 25 to 30 years and more number were booked in comparison to unbooked. Adverse fetal outcomes were seen more in HIV seropositive patients and they were found to be statistically significant (p=0.029). No relationship could be derived of duration of ART on either the birth weight or term of delivery or adverse fetal outcomes.

Conclusions: Maternal HIV infection was significantly found associated with adverse fetal outcome and this was not affected by the use of ART.

Keywords: Adverse fetal outcomes, ART, Human immunodeficiency virus, Term of delivery

INTRODUCTION

AIDS (acquired immune deficiency syndrome), sometimes called wasting disease or slim disease is a fatal illness caused by a retrovirus known as the “human immunodeficiency virus” (HIV) which breaks down the body’s immune system, leaving the victim vulnerable to be a host of life threatening opportunistic infections, neurological disorders and unusual malignancies. AIDS being the end stage of HIV infection.¹

The causative virus is transmitted from person to person most frequently through sexual activity. HIV can also be transmitted by contaminated blood, injection drug abusers and from an infected mother to her baby (through the placenta or during delivery or by breast feeding). HIV infected people are more prone to infect others in early stages before antibody production i.e. during the “window period” and when the infection is well advanced, because level of virus is highest in blood at these times.¹

HIV infection/AIDS is a pandemic with cases reported from virtually every country. Recognised as an emerging disease in early 1980′s, AIDS has rapidly established itself throughout the world. India has the 3rd largest HIV epidemic in the world. As per the recently released, India HIV Estimation 2017 report, National adult (15-49 years) HIV prevalence in India is estimated at 0.22% (0.16%-0.30%) in 2017. Estimated number of people living with HIV/AIDS in India is 2.11 million with 0.29% being antenatal clinic attendees.²⁻⁵
METHODS

This is prospective-comparative study 40 HIV seropositive and 40 seronegative pregnant women attending ANC and delivering in the department of obstetrics and gynecology at S. M. S. Medical College and attached hospitals, Jaipur, Rajasthan, from May 2018 to November 2019.

Inclusion criteria

- Women delivering in study hospital with regular ANC visits (Both HIV seropositive and negative)
- Patients giving consent for study and willing for follow up of mother and child
- HIV positive females (both on ART/ not on ART)
- Patients with period of gestation (POG) >28 weeks.

Exclusion criteria

- Individuals refusing for HIV testing
- Other immunodeficiency disorder
- IUGR for other causes
- Severe anaemia, HDP, thyroid disorders.

Pregnant females attending ANC for regular check-up were evaluated after written informed consent. HIV testing done and the patients were divided into two groups after application of inclusion and exclusion criteria:

Group A - seronegative pregnant females
Group B - seropositive pregnant females.

Detailed history was taken and physical examination done. Baby parameters (weight, Apgar, etc) were obtained. Biochemical investigations were done for both mother and baby.

Statistical analysis

A pre structured proforma was used to collect patient data. Analysis was done using unpaired t test, chi square test and fisher exact test. MEDCALC software was used for all statistical analysis.

RESULTS

In Table 1, most of the subjects in sero-positive (case) group were in age group 25 to 30 years (42.5%) while most of the subjects in sero-negative (control) group were in the age group <25 years (55%). The differences in age distribution were not found to be statistically significant (p=0.153).

As shown in Table 2, among the seropositive group i.e. cases, 65% patients were booked and 35% were unbooked. While in the control group i.e. seronegative, 70% patients were booked and 30% unbooked. The difference was not found to be statistically significant (p=0.811).

Table 1: Age distribution of study groups.

| Age group (years) | Case | Control | Total |
|------------------|------|---------|-------|
| < 25             | 16   | 22      | 38    |
| 25-30            | 17   | 16      | 33    |
| >30              | 7    | 2       | 9     |
| Total            | 40   | 40      | 80    |

Chi-square = 3.755 with 2 degrees of freedom; p=0.153 (NS).

Table 2: Distribution of study groups according to booking status.

| Booking status | Case | Control | Total |
|----------------|------|---------|-------|
| Booked         | 26   | 28      | 54    |
| Un-booked      | 14   | 12      | 26    |
| Total          | 40   | 40      | 80    |

Chi-square = 0.057 with 1 degree of freedom; p = 0.811 (NS).

Table 3: Term of delivery among study groups.

| Term of delivery | Case | Control | Total |
|------------------|------|---------|-------|
| Term             | 36   | 39      | 75    |
| Preterm          | 4    | 1       | 5     |
| Total            | 40   | 40      | 80    |

Fisher exact test - p = 0.359 (NS).
In Table 3, among the seropositive group, 4 patients (10%) had preterm delivery i.e. <37 weeks while in the control group, 1 patient (2.5%) had preterm delivery. Though the difference in the two group are evident but the results are not statistically significant (p=0.359).

The given Table 4 depicts the term of delivery in relation to duration of ART. Of 29 seropositive patients on ART for < 9 months, 3 (10.3%) had preterm delivery and 26 (89.7%) were delivered at term. While the other group with 11 patients on ART for >9 months, 1 (9.1%) patient had preterm delivery. The differences in the results were not found to be statistically significant (p=1.000).

As per Table 5, in the seropositive mother group/cases, 8 babies born of 40 had weight < 2.5 kg i.e. LBW (low birth weight) while in the seronegative mother group/control, 9 babies born of 40 were LBW. The differences were not found to be statistically significant (p=0.486).

Table 4: Term of delivery in relation to duration of ART.

| Term of delivery | ART <9 months | ART >9 months | Total |
|------------------|---------------|---------------|-------|
| N                | %             | N             | %     | N     | %     |
| Preterm          | 3             | 10.3%         | 1     | 9.1%  | 4     | 10%   |
| Term             | 26            | 89.7%         | 10    | 90.9% | 36    | 90%   |
| Total            | 29            | 100%          | 11    | 100%  | 40    | 100%  |

Table 5: New born birth weight among study groups.

| Birth weight (kg) | Case N | Case % | Control N | Control % | Total N | Total % |
|-------------------|--------|--------|-----------|-----------|---------|---------|
| <2.5 kg           | 8      | 20%    | 9         | 22.5%     | 17      | 21.25%  |
| ≥ 2.5 kg          | 32     | 80%    | 31        | 77.5%     | 63      | 78.75%  |
| Total             | 40     | 100%   | 40        | 100%      | 80      | 100%    |

Mean±SD = 2.73±0.09 kg
2.81±0.47 kg

Chi-square = 0.000 with 1 degree of freedom, p=1.000 (NS), t = -0.699 with 78 degrees of freedom; p=0.486 (NS).

Table 6: New born birth weight in relation to duration of ART.

| Birth weight (kg) | ART <9 months N | ART <9 months % | ART >9 months N | ART >9 months % | Total N | Total % |
|-------------------|----------------|----------------|----------------|----------------|---------|---------|
| <2.5 kg           | 6              | 20.7%          | 2              | 18.2%          | 8       | 20%     |
| ≥ 2.5 kg          | 23             | 79.3%          | 9              | 81.8%          | 32      | 80%     |
| Total             | 29             | 100%           | 11             | 100%           | 40      | 100%    |

Fisher exact test - p = 1.000 (NS).

Table 7: Adverse fetal outcome among study groups.

| Fetal outcome     | Case N | Case % | Control N | Control % | Total N | Total % |
|-------------------|--------|--------|-----------|-----------|---------|---------|
| Favourable        | 32     | 80%    | 39        | 97.5%     | 71      | 88.75%  |
| Adverse           | 8      | 20%    | 1         | 2.5%      | 9       | 11.25%  |
| Total             | 40     | 100%   | 40        | 100%      | 80      | 100%    |

Fisher exact test - p = 0.029 (NS).

Table 8: Adverse fetal outcome in relation to duration of ART.

| Fetal outcome     | ART <9 months N | ART <9 months % | ART >9 months N | ART >9 months % | Total N | Total % |
|-------------------|----------------|----------------|----------------|----------------|---------|---------|
| Favourable        | 23             | 79.3%          | 9              | 81.8%          | 32      | 80%     |
| Adverse           | 6              | 20.7%          | 2              | 18.2%          | 8       | 20%     |
| Total             | 29             | 100%           | 11             | 100%           | 40      | 100%    |

Fisher exact test - p = 1.000 (NS).
Table 6 predicts the relationship of new-born birth weight with respect to duration of ART. In this study, 29 seropositive patients (mothers) were on ART for <9 months, of which 20.7% gave birth to babies <2.5 kg i.e. LBW and 79.3% had babies ≥2.5 kg. Of the remaining 11 patients on ART for >9 months, 18.2% had LBW babies and 81.8% had babies ≥2.5 kg. The differences in birth weight in the two groups were not found to be statistically significant (p=1.000).

Table 7 compares adverse fetal outcomes in terms of IUD, still birth and preterm birth in the two study groups. Of the 40 seropositive cases, 8 (20%) fetal outcomes were adverse while in the seronegative control group, 1 (2.5%) of 40 fetal outcome was adverse. The result was found to be statistically significant with p-value <0.05, (p=0.029).

Table 8 illustrates the adverse fetal outcome in relation to the duration of ART. Among 29 patients with duration of ART <9 months, 6 babies (20.7%) had adverse outcomes in terms of IUD, still birth and Preterm birth; while in the other group where patients were on ART > 9 month, out of total 11 babies born, 2 (18.2%) had adverse outcome with 9 being favourable/uneventful. The difference in results of adverse outcome with duration of ART were not found to be statistically significant (p=1.000).

DISCUSSION

The mean age of HIV seropositive patients was 26.16 years with maximum number of patients lying in the age group 25 to 30 years (42.5%). Mean age in study done by Dwivedi et al was found to be 25.2 years which is comparable; while in study done by Prameela et al and Ezechi et al, the mean age were 23 years and 30 years respectively.6-8 The mean age of HIV seronegative patients in this study was 24.5 years with more number of patients in age <25 years (55%).

More number of patients in both HIV seropositive and HIV seronegative group were booked 65% and 70% respectively. The difference is not significant. This could be attributed to easy accessibility of health services and ART centres at various places for HIV seropositive patients under NACO’s initiative.

The mean birth weight in HIV seropositive group was 2.73±0.09 kg and that in HIV seronegative was 2.81±0.47 kg. 20% babies born in HIV seropositive group were LBW (birth weight <2.5 kg) while in HIV seronegative group 22.7% were LBW. The differences were not statistically significant. Also, there was no significant relationship of duration of ART with birth weight of the baby/ LBW. Among seropositive group, 10% patients delivered preterm while in seronegative group preterm deliveries were only 2.5%. The differences were not statistically significant. Also, there was no relationship of preterm delivery with maternal duration of ART. The inference of the above observations may be due to improved infrastructure of health care bringing about earlier detection of HIV disease, awareness among the ‘at risk’ population, availability of HAART and active government policies to cater the diseased effectively. Similar results were found in study done by Schulte et al, who reported a decline in the rates of low-birth-weight infants and preterm infants.9 Also all women in this study were asymptomatic and diagnosed in early stages which decreased the incidence of preterm labour and low birth weight as was found in study done by Coley et al, in Tanzania which suggested that although HIV infected asymptomatic women did not have a higher risk of having LBW infants compared with uninfected women, symptomatic HIV-infected women (who were in stage 2 or higher according to the WHO staging system) had about 2-times higher risks for low birth weight and prematurity compared with HIV-uninfected ones.10 This is consistent with the finding of Buccheri et al, and Muhangi et al.11,12 Brocklehurst et al, reported that the increasing risks of LBW and PTD were associated with maternal HIV infection.13 Xiao PL et al, concluded that maternal HIV infection increased the risks of both LBW and PTD.14 Townsend et al also concluded that HAART was associated with PTD.15 ARVs might be responsible for adverse pregnancy outcomes such as LBW and PTD, but its high effectiveness in the prevention for mother to child transmission outweighed its risk of LBW/PTD suggested by Santini et al.16 This could be explained by the fact that protease inhibitor based ART when used, it lowered the level of progesterone resulting in preterm labour and low birth weight. Papp et al, suggested that protease inhibitor (PI)-based ART could increase the risk of adverse pregnancy outcomes mainly due to lower level of progesterone, which was significantly associated with fetal weight.17 Sibude et al also found that ARVs and, particularly, with the initiation of ritonavir-boosted PI therapy during pregnancy were correlated with PTD in HIV infected women.18 Xiao PL et al, in their study found that HAART or other regimens of antiretroviral therapy (ART) had no obvious effect on the associations between maternal HIV infection and LBW/PTD; intraterine ARVs exposure did not decrease or increase the risk of LBW or PTD in HIV infected women.14 And this is consistent with the findings reported by Van der Merwe et al and Townsend et al.19,20

There was an increased incidence of adverse fetal outcomes in terms of IUD, still birth and preterm birth - 20% in HIV seropositive patients in contrast to 2.5% in HIV seronegative pregnancies. The differences were found to be statistically significant (p=0.029). Kennedy D et al, found a still birth rate of 1.7/1000 births in HIV seropositive population compared to 8.3/1000 in HIV seronegative population.21 Kumar et al from India, matched 160 HIV infected pregnant women with uninfected control and found that HIV infection had a detrimental effect on pregnancy in terms of abortion, prematurity, intrauterine fetal death and maternal and neonatal mortality.22 Similar results were found in various studies done by Ezechi et al, Ellis et al,
Brocklehurst et al and Dwivedi et al,6,8,13,23 In India, studies done by Gautam S et al and Prameela et al found still birth rate to be comparatively less 3.1% and 3.9% respectively.7,24

In this study authors found no relationship of duration of ART on adverse fetal outcomes. Similar results were found in study by Haeri et al, which compared 151 HIV infected women on HAART and 302 HIV uninfected women. Neonatal outcomes were similar, HAART did not increase maternal complications. On the contrary studies by Parisaei et al, Patil S et al and Fekadu M et al reported adverse perinatal complications in women who received ART.26-28

CONCLUSION

Despite the social stigma regarding HIV, a greater number of HIV seropositive patients are getting themselves booked due to better availability of health services and easy accessibility to ART centres. In this study authors found that neither HIV infection nor ART (irrespective of duration) had any detrimental effect on term of delivery or birth weight of baby. HIV infected women have been found to have more adverse fetal outcomes in comparison to HIV uninfected women. Since all patients in this study were on ART, it becomes difficult to analyse whether the adverse outcomes were due to ART or due to HIV infection.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Trivedi S, Nagar O, Trivedi S, Rastogi P. Effect of antenatal retroviral therapy on feto-maternal outcome in human immunodeficiency virus seropositive patients. Int J Reprod Contracept Obstet Gynecol 2020;9:2364-9.