



Research Article

**ANTENATAL COMPLICATIONS AND PREGNANCY OUTCOME AMONG HIV POSITIVE PREGNANT WOMEN AT TERTIARY CARE HOSPITAL: ELEVEN YEARS RETROSPECTIVE STUDY**

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**ABSTRACT**

Acquired immunodeficiency syndrome (AIDS) first case was reported in 1986 and now there are an estimated 21.17 lakhs people living with HIV/AIDS in India of which 6.54% are children (<15 years) with an adult prevalence of 0.26% in 2015. Aim of this study was to know antenatal complications and pregnancy outcome in HIV infected pregnant women. This retrospective study conducted from September 2005 to July 2016, carried at G.S.V.M. Medical College, Kanpur U.P. Hospital records of all HIV infected pregnant women collected including medical conditions, antenatal complications and pregnancy outcomes. Out of 34924 women registered, 102 women were found HIV seropositive. Majority were multiparous (62.7%), registered in third trimester (58.8%) and had CD4 count <350 (43.1%). 5.9% women were not on any Antiretroviral therapy (ART). Although incidence of gestational diabetes (8.8%), hypertension (5.8%) and fetal growth restriction (6.9%) were low but anemia (76.5%) and preterm births (23.5%) were more and 3 antenatal mortality were also noted. 65% women delivered vaginally, rest by caesarean section. This study suggests link between HIV infection and adverse maternal outcome in form of anemia, preterm births and mortality. To conclude, good maternal outcome can be achieved by effective counseling, adequate antenatal care and ART.

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**INTRODUCTION**

The first AIDS case was reported in India in 1986 and now India has third largest number of estimated people living with HIV/AIDS. There are an estimated 21.17 lakhs people living with HIV/AIDS of which 6.54% are children (<15 years) with an adult prevalence of 0.26% in 2015. HIV prevalence has declined consistently over last one decade from 0.4% in the year 2000 to 0.26% in 2015. This decline reflects impact of scaled up HIV prevention interventions under the National AIDS control programme (NACP) through PMTCT (Prevention of mother to child transmission) services<sup>1</sup>.

According to HIV sentinel surveillance 2014-15 by the NACO, overall HIV prevalence is 0.29% among antenatal clinic attendees<sup>1</sup>. Young adults especially women of reproductive age group and children are mainly affected<sup>2</sup>. Mother to child transmission of HIV is a major route of new infection in children<sup>3,4,5</sup>.

While the effect of HIV infection of maternal morbidity, mortality and vertical transmission to her off spring are well established, controversy exist on the relationship between maternal HIV infection and the adverse pregnancy outcomes of miscarriage, prematurity, stillbirth and IUGR<sup>6,7</sup>. Several

studies done to resolve the controversy by studying obstetrics and perinatal outcome but still several questions remain unanswered<sup>8-13</sup>.

Although well designed studies from developed countries fails to show significant adverse effect of HIV infection on pregnancy<sup>11,12,13</sup>; while some studies from developing countries reported association between maternal infection and adverse pregnancy outcome<sup>8,9,10,14,15</sup>.

Both maternal and fetal outcome can be improved by increasing awareness and effective implementation of PMTCT programme which includes HIV testing facility to all pregnant women with provision of counseling, ARV prophylaxis and adequate antenatal care. So in this study we tried to reflect the effect of HIV infection on pregnancy and maternal outcome in past eleven years in tertiary care hospital of northern India.

**MATERIAL AND METHODS**

This retrospective study conducted from September 2005 to July 2016, carried out at G.S.V.M. Medical College, Kanpur U.P. Out of 34924 women registered, 102 women were found seropositive for HIV infection. The hospital records of all HIV infected pregnant women were collected. Data on

demographic profile, CD4 count, medical co-morbidities, antepartum and intra-partum complications such as preterm birth (defined as birth<37 weeks gestation), gestational diabetes (diagnosed by having an abnormal result from a 2-hour glucose tolerance test), hypertension (diagnosed as blood pressure 140/90 in pregnancy after 20 weeks of gestation or preexistinghypertension), fetal growth anomalies (defined as growth less than 10<sup>th</sup> percentile growth for gestational age by ultrasound assessment) and mode of delivery; were obtained and analyzed. For HIV positive women detected for the first time and for those who were not on ART during September 2005 to February 2014; single dose Nevirapine 200 mg were given during labour and 2 mg /kg to the neonate soon after the delivery. If she was already on treatment then ART was continued.From the year October, 2012 to July 2016 for HIV positive women ART (triple drug regimen- Tenofovir 300 mg, Lamivudine 300 mg and Efavirenz 600 mg) was started at 14 wks of gestation or whenever she was diagnosed.Nevirapine was given to neonate according to birth weight up to 6 weeks.

Statistical analysis done by mean and percentage.

## RESULTS

In this study among seropositive, 59.8% women were in age group 21 –30 years. Majority of women were literate (90.1%), from rural area (67.6%), belongs to low socio-economic status (62.7%) and housewife by occupation (89.2%).Main occupation of husbands of seropositive women was labourers (29.4%) followed by drivers (22.5%) and 55.9% husbands were also found positive for HIV infection. During counseling, heterosexual contact (92.2%) was found to be main route of transmission (Table 1).

**Table 1** Demographic Profile of Hiv Positive Pregnant Women (N=102)

Sl.No.	Factors	No. of seropositives (n=102)	Percentage
1.	Age	<20	4 3.9%
		21-30	61 59.8%
		>30	37 36.3%
2.	Marital status	Married	102 100%
		Unmarried	0
3-	Education	Illiterate	10 9.8%
		Literate	92 90.2%
4.	Habitat	Rural	69 67.6%
		Urban	33 32.4%
5.	Socio-economic status	Upper	10 9.8%
		Middle	28 27.5%
		Lower	64 62.7%
6.	Occupation of wife	Housewife	91 89.2%
		Labourer	6 5.9%
		Service	5 4.9%
		Driver	23 22.5%
7.	Occupation of husband	Labourer	30 29.5%
		Farmer	19 18.6%
		Business	10 9.8%
		Pvt. Job	20 19.6%
8.	HIV status of husband	Reactive	57 55.9%
		Non reactive	30 29.4%
		Not Obtained	15 14.7%
9.	Probable route estimated for transmission	Heterosexual contact	94 92.2%
		Blood	6 5.9%
		Needle contamination	2 1.9%

Most of the women were multigravida (62.7%) and registered in third trimester (58.8%). CD4 count of 43.1% women was less than 350 out of which 13.7% had CD4 count of less than 200. Six out of 102 women (5.9%) were neither on ART nor got Nevirapine prophylaxis. 3 women delivered in vehicle, 2 at home and 1 women was prescribed ART in antenatal period

but she died before it could started. Rest women were either on ART or got Nevirapine prophylaxis (Table 2)

**Table - 2** Antenatal Status of HIV Positive Pregnant Women (N=102)

1.	Gravidity	Primigravida	38	37.3%
		Multigravida	64	62.7%
2.	Gestational Age at time of registration	Ist trimester	16	15.6%
		IInd trimester	26	24.4%
		IIIrd trimester	60	58.8%
3.	CD4 count	Not known	6	5.9%
		<200	14	13.7%
		<350	30	29.4%
4.	ART status (* 83 women)	>350	52	50.9%
		Not on ART/ARV		
		ART/ARV started before pregnancy	6	7.2%
		ART/ARV started during pregnancy	26	31.3%
			51	61.15%

\* Excluding 11 abortions, 4 lost to follow up, 4 delivered outside town

87 women (85.3%) had co-morbidities, the most common being anemia (76.5%) followed by tuberculosis 3(2.9%) and hepatitis (2.9%). (Table 3)

**Table 3** Medical Comorbidities In Hiv Sero Positive Pregnant Women (N=102)

Medical comorbidities	No	Percentage
Anemia	78	76.5%
Tuberculosis	3	2.9%
Hepatitis-B/C	3	2.9%
Secondary infection	2	1.9%
Varicella	1	0.9%

The mean gestational age at delivery was 37.4 weeks. Preterm birth rate was 23.5%. Out of 24 preterm deliveries,21 were spontaneous and 3 were induced. Causes for preterm induction were PPROM in 2 patients and IUGR in one woman.9women (8.8%) had GDM, all were controlled on diet al one. 6 women (5.8%) had hypertension, one had pre-existing hypertension, rest had gestational hypertension and only two patients were needed antihypertensive therapy. 4 women had APH (3.9%), in which 3 had abruption and one was placenta previa. IUGR was found in 7 (6.9%) cases in which one had severe IUGR. Congenital anomaly was not found in any case. Postpartum hemorrhage occurred in 6 women (5.9%) which did not require surgical intervention and was managed conservatively. 3 women expired in antenatal period. (Table 4).

**Table 4** Obstetric Complications In Hiv Seropositive Pregnant Women (N-102)

Obstetric Complications	No.	Percentage
Preterm	24	23.5%
PROM	18	17.6%
APH	4	3.9%
GDM	9	8.8%
PIH	6	5.9%
IUGR	7	6.9%
PPH	6	5.9%
Maternal Mortality	3	2.9%

6 women had abortions and 5 women opted for MTP after counseling at gestational age less than 13 weeks. 10 women (9.8%) had early preterm and 14(13.7%) had late preterm births. 56women (64.6%) delivered at term. Out of 80 deliveries, 75 occurred in hospital, 3 in vehicle and 2 at home. 52 babies (65%) were born by vaginal delivery and 28 (35%) by caesarean section. 75/80 (93.8%) delivered at our hospital

but 3 women delivered in vehicle and 2 women at home and so could not get Nevirapine prophylaxis (Table 5).

**Table - 5** Birth Outcome of Hiv Seropositive Pregnant Women

	Birth Outcome	No.	Percentage
Gestational age (n=91) <sup>#</sup>			
1.	MTP	6	6.5%
	Abortion	5	5.4%
	<34 weeks	10	9.8%
	34- 37 weeks	14	13.7%
	>37 weeks	56	64.6%
Mode of delivery(n=80) <sup>s</sup>			
2.	Vaginal	52	65.0%
	LSCS	28	35.0%
Place of delivery (n=80)			
3.	Hospital	75	93.8%
	Vehicle	3	3.7%
	Home	2	2.5%

# = excluding 4 lost to follow up, 4 delivered outside, 3 antenatal mortality

S = excluding 4 lost to follow up, 4 delivered outside, 3 antenatal mortality, 11 abortion +MTP)

## DISCUSSION

In this 11 years retrospective study, 102 pregnant women were found seropositive with prevalence of 0.3%. Mean age in this study was 25.2 years which is comparable to study done by Prameela *et al*<sup>16</sup> in which mean age was 23 years, while mean age was 30 years in study done by Ezechi *et al*<sup>2</sup>. 67.6% women belonged to rural area similar to study done by Prameela *et al* (68.6%)<sup>16</sup>. In this study 55.9% husbands were HIV positive while in study done by Malik *et al*<sup>17</sup> and Prameela *et al*<sup>16</sup>, 44% and 44.3% spouses were found positive. Heterosexual contact was found main route of transmission of infection (92.2%). In discordant couple sexual promiscuity (73.3%) among women was main cause. In contrast study done by Malik *et al*<sup>17</sup>, heterosexual contact contributed 52% risk factor for transmission.

In this study, 62.7% women were multigravida while in study by Prameela *et al*<sup>16</sup>, 59.3% were primigravida. Ezechi *et al*<sup>2</sup> also reported mean parity  $1.7 \pm 1.1$  in seropositive women. Most of women registered in 3<sup>rd</sup> trimester even some in labour also, in contrast 68% women registered in 1<sup>st</sup> trimester in study done by Malik *et al*<sup>17</sup>. 13.7% women had CD4 count less than 200 cells/mm<sup>3</sup>, while in study done by Gautam *et al*<sup>18</sup>, Malik *et al*<sup>17</sup>, Prameela *et al*<sup>16</sup> and E. Azria<sup>19</sup> *et al* 15.4%, 24%, 26.9% and 12.6% women had CD 4 count less than 200 respectively. It is noticeable that majority of women got nevirapine prophylaxis, only 7.2% women were not on any ART/ARV prophylaxis which is lower than study done by Prameela *et al*<sup>16</sup> and Malik *et al*<sup>17</sup> in which percentage was 10.2% and 16%.

78 (76.5%) women had anemia in which (18.9%) women had severe anemia and required blood transfusion. According to ICMR, NFHS 2 and 3, prevalence of anemia in pregnancy in India is >70%<sup>20</sup>. So in this study, incidence of anemia was slightly raised in HIV positive women. 3 women had pulmonary tuberculosis and prescribed ATT. The rate of GDM was low in our cohort that is 8.8%. All women controlled with diet alone. The effect of ART on glucose metabolism and insulin resistance among pregnant women remains poorly understood and protease inhibitors are mainly associated with glucose intolerance. There is conflicting results in the literature with respect to the risk of gestational

diabetes in HIV positive women<sup>21,22,23</sup>. Similarly, 6% women had gestational diabetes in study done by Yudin *et al*<sup>24</sup>. Recent data on the prevalence of GDM in our country was 16.55% by WHO criteria of 2 hr P  $\geq 140$  mg/dl<sup>25</sup>.

Observational and cohort studies evaluating the risk for hypertension disorders in pregnancy complicated by HIV have suggested that the risk is increased<sup>26</sup>, while maternal cohort studies from Canada and United State have not demonstrated this increase<sup>27,28</sup>. In the current study, 6 (5.8%) women developed hypertension, similar to study by Yudin *et al* (5%)<sup>24</sup> and Ezechi *et al*<sup>2</sup> (4.1%). In India, pregnancy induced hypertension is seen in approximately 10-20% of all pregnant women, according to ICMR<sup>29</sup>.

In our study, spontaneous abortion rate was 5.9% while in study by Ezechi *et al*, it was 3.2%. Approximately 15% of recognized pregnancy result in spontaneous abortion in general population<sup>30</sup>. 24 women delivered preterm (<37 wks). Most common cause of preterm was PROM (75%). It is possibly subclinical chorio-amnionitis may more common in HIV infected mothers and this could cause preterm labour and perinatal hypoxia<sup>6,31</sup>. Preterm deliveries were 1.8% in study by Prameela *et al*<sup>16</sup>, 4% by Malik *et al*<sup>17</sup>, 13.1% by Ezechi *et al*<sup>2</sup> and 19% by Yudin *et al*<sup>24</sup>. but in our study preterm birth rate was 23.5% which is higher than national average in general population of approximately 21%<sup>32</sup>.

In this study, APH was found in 4 women (3.9%) similar to Ezechi *et al*<sup>2</sup> (3.9%). In study by Ezechi *et al*; rates of spontaneous abortions, severe anemia and preterm delivery were found significantly higher in HIV positive women compared to their HIV negative counterparts; while there was no difference in between two groups regarding rates of obstetric hemorrhage and pregnancy induced hypertension<sup>2</sup>. Fetal growth restriction was also less in present study (6.6%). In an American prospective observational study, HIV severity was associated with an increased risk of fetal growth abnormalities after adjusting for socio-demographic variables, medication use and disease severity; ART use was not associated<sup>33</sup>. In a Canadian matched cohort study, there was no difference in the risk of growth restriction between HIV positive women and an HIV negative matched control group<sup>27</sup>. Studies have shown an association between maternal HIV status and preterm labour<sup>34</sup>, IUGR<sup>35,36,37</sup> and APH<sup>38</sup>. Current study also demonstrated increase incidence of anemia and preterm births whereas incidence of APH, hypertension and GDM remained low. Lower socio-economic status, late registration and poor antenatal care could also be confounding factors. Adverse maternal outcome may be associated with HIV-positivity, combination or specific antiretroviral drugs use, or the presence of confounding factors.

Most of the women delivered vaginally (65%) as in our hospital LSCS in HIV positive women is done for obstetrics indication only. Similarly in study done by Gautam *et al*<sup>18</sup>, Prameela *et al*<sup>16</sup> and Kale *et al*<sup>39</sup>, 70.8%, 73.7% and 64% women delivered vaginally respectively. In contrast to E. Azria<sup>19</sup> *et al* study 55% required LSCS.

Unfortunately, in our study there were 3 antenatal mortality in which one patient was HIV positive prior to pregnancy with low CD4 count, had fulminant tuberculosis and patient died at 6<sup>th</sup> months of gestation at TB and chest hospital. Another patient developed fulminant measles with high grade fever at

8<sup>th</sup> month of pregnancy and died. The third one had undiagnosed abdominal pregnancy with severe anemia and patient expired after 12 hours of operation due to excessive blood loss intra-operatively and baby was also still born. Globally in 2011, HIV related causes contributed to 6-20% of maternal deaths<sup>40</sup> and TB is a leading cause of maternal mortality in settings with high HIV burden.

Both maternal mortality and morbidity can be prevented by timely intervention and effective implementation of PPTCT services. According to NACO also, adequate antenatal care and triple drug therapy should be given to all HIV positive pregnant females irrespective of their CD4 count.

Limitation of this study was being retrospective as these studies are limited by their reliance on data extraction from previous records. Study is from a single center and study population mostly belonged to lower socio-economic status and may not fully representative of entire population and there were many lost to follow up cases. Finally, there was no control groups to compare outcomes.

## CONCLUSIONS

As previous studies found an association between HIV infection and adverse pregnancy outcomes, in our study also link between HIV infection and adverse maternal outcome in form of anemia, preterm births and mortality was found. To conclude, maternal morbidity, adverse pregnancy outcome and overall PTCT can be prevented by timely detection, effective counseling, adequate antenatal care, ART irrespective of CD4 count.

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