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RESEARCH ARTICLE

HIV IN PREGNANCY: DO COUNTS REALLY COUNT?

***Dr. Rupali Bhatia, Dr. Sumita Mehta, Dr. Nalini Mittal and Dr. Anshul Grover**

Obstetrics and Gynaecology Department, BabuJagjivan Ram Memorial Hospital, Jahangir Puri, Delhi, India

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**Corresponding author*

ABSTRACT

Background: HIV screening in antenatal women is being conducted routinely in most countries today. It is necessary to identify the infection to start antiretroviral drugs as soon as the diagnosis is confirmed. The antiretroviral treatment helps to reduce the risk of mother-to-child HIV transmission (MTCT) as well as prevent maternal morbidity. In present study we aim to identify the relevance of measuring CD4 counts in respect to perinatal transmission and risk of maternal tuberculosis in HIV infected antenatal women. **Methods:** In an observational study, 64 antenatalHIV positive women on antiretroviral therapy were studied for their demographic profile, the CD4 counts, mode of delivery and presence of concomitant pulmonary tuberculosis, over 3 years (2014-2016). HIV status of the newborns was then confirmed by dried blood spot test at the end of 18 months.

Results

- MTCT risk was not significantly higher in women with low CD4 counts as compared to women with high counts (p=0.69).
- HIV positive women with lower CD4 counts were at risk of having concomitant pulmonary tuberculosis at rates similar to those with higher counts.(p=0.85)

Conclusion: Routine measurement of CD4 counts during antenatal period in HIV positive women may be omitted owing to their doubtful role in determining perinatal transmission or maternal immune response to occurrence of tuberculosis. In countries with low resource settings and restricted infrastructure the omission may prove beneficial in reducing treatment cost especially when the counts do not dictate even the commencement of antiretroviral therapy in affected individuals.

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INTRODUCTION

HIV screening in antenatal women is being conducted routinely in most countries today. It is necessary to identify the infection to start antiretroviral drugs as soon as the diagnosis is confirmed. The antiretroviral treatment helps to reduce the risk of mother-to-child HIV transmission (MTCT) as well as prevent maternal morbidity. During evaluation of HIV infected antenatal women, a CD4 count is done along with other relevant investigations. CD4 cells also known as T-helper cells are leucocytes that contribute largely to cellular immunity of the body. The normal count of CD4 cells ranges from 500 cells/mm^3 to 1,600 cells/mm^3 in a healthy individual. Higher the CD4 count, the greater is the ability of immune system to combat HIV and other infections and hence lower the risk of perinatal HIV transmission (Moore, 2007). Opportunistic infections occurring as a result of weakened immune response, pose a great deal of morbidity and mortality for both mother and the foetus. Tuberculosis (TB) is the most commonly reported opportunistic infection among HIV-infected individuals in many countries throughout the world, including India (Giri *et al*., 2013; Wondimeneh *et al*., 2012; Kufa *et al*., 2014; Gao *et al*., 2013). Few years back the levels of CD4 countin HIV positive women served an important criterionin initiation of antiretroviral treatment; however since 2013WHO (Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection:, 2013; Global Health Sector Strategy for HIV 2016–2021) and many other organizations (Centers for Disease Control and Prevention, 2016; Joint United Nations Programme on HIV/AIDS (UNAIDS). 2014) recommend anti-retroviral therapy (ART) for all HIV positive women irrespective of their CD4 counts. But these counts are still being measured routinely in many countries as they are believed to indicate risk of opportunistic infections in mother and perinatal transmission of HIV. Therefore in present study we aim to identify the relevance of measuring CD4 counts in HIV infected antenatal women.

Objectives

- To assess mother to child HIV transmission risk in relation to maternal CD4 counts.

- To study the association of CD4 counts with risk of developing concomitant tubercular infection in HIV positive women.

MATERIALS AND METHODS

An observational study was conducted in BJRM hospital in which 6950 antenatal women were screened for HIV infection over 3 years (2014-2016). Out of those, 64 women who tested HIV positive were initiated on WHO recommended antiretroviral therapy (Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection, 2013) and further studied for their demographic profile, the CD4 counts and the mode of delivery. Presence of concomitant pulmonary tuberculosis in such women was also recorded(In suspected cases presence of tuberculosis was confirmed by sputum culture positivity). All the new-borns were followed for 18 months and their HIV status was then confirmed by dried blood spot test (DBS). The statistics were performed using SPSS.

All 64 HIV positive females were categorized into 3 groups based on the level of CD4 counts (Fig.1):

- Group 1 – CD4 counts < 200 / mm^3
- Group 2 - CD4 counts 200-500 / mm^3
- Group 3 - CD4 counts > 500 / mm^3

RESULTS

28% (18/64) women enrolled in our study had CD4 counts of less than 200, 39% (25/64) had counts between 200 and 500, rest 33% (21/64) had more than 500 counts. All these women delivered through normal vaginal delivery and the mode of feeding adopted by them was exclusive breastfeeding. Most of the women (59.3%) belonged to the age group of 25 to 35 years. Amongst all the women, 47% were first or second gravida and rest 53% were of higher gravida. The husbands of 36% of these women were diagnosed as HIV positive (Table 1). The rate of mother to child transmission of HIV was 10.9% (7/64). Among women with CD4 counts of less than 200, it was 16.6% (3/18), 8% (2/25) in women with counts between 200 and 500, and 9.5% (2/21) in women with counts more than 500 (Fig.2, Table 2). Statistically no significant difference was observed in MCT HIV risk in women with CD4 counts less than 200/mm^3 as compared to women with higher counts (p=0.69). We also observed the risk of developing tubercular infection in HIV positive antenatal women. It was 11% (2/18) in women with CD4 counts less than 200, 8% (2/25) in women with counts between 200 and 500, and 4.7% (1/21) in women with counts more than 500 (Fig.3, Table 3). No statistically significant difference was found in these rates of contracting TB with respect to maternal CD4 counts (p=0.85). Therefore, HIV positive women with CD4 counts less than 200/mm^3 were at risk of having concomitant tuberculosis at rates similar to those with higher counts.

DISCUSSION

New interventions are being constantly implemented for prevention of parent to child transmission of HIV. However, for interventions to be effective we need to identify the factors

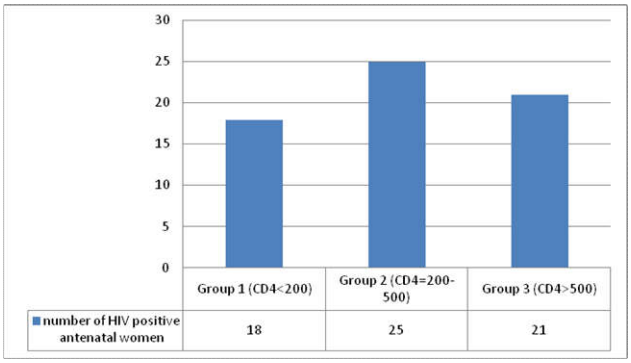

Figure 1. Categorization of cases based on CD4 count (cells/mm^3)

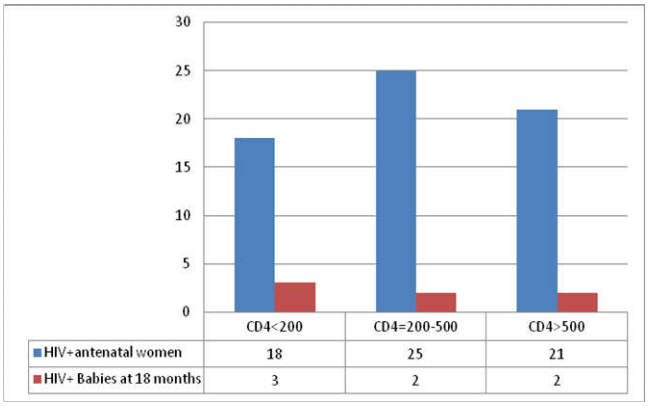

Figure 2. Mother to child HIV transmission risk in relation to maternal CD4 count (cells/mm^3)

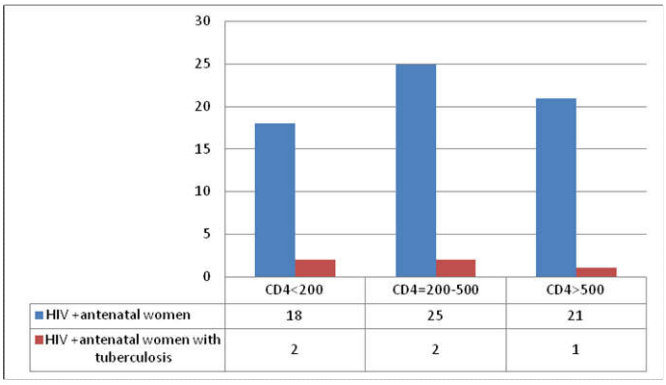

Figure 3. Association of CD4 count (cells/mm^3) with risk of developing concomitant tubercular infection in HIV positive women

Table 1. Demographic profile of cases

N = 64		Number	Percentage
Maternal age	Less than 25 years	20	31.2%
	25 to 35 years	38	59.3%
	More than 35 years	8	12.5%
Parity	0 or 1	30	46.9%
	More than 1	34	53.1%
Spouse HIV status	Positive	23	35.9%
	negative	41	64.1%

Table 2. Mother to child HIV transmission risk in relation to maternal CD4 counts

Cd4 count (cells/mm^3)	< 200	200-500	>500	P-value
Hiv + cases	18	25	21	0.69
Hiv + babies	3	2	2	

Table 3. Association of CD4 counts with risk of developing concomitant tubercular infection in HIV positive women

CD4 count (cells/mm^3)	< 200	200-500	>500	p-Value
HIV + CASES	18	25	21	0.85
HIV and TB + CASES	2	2	1	

involved in transmission of the infection. One such factor considered is the maternal CD4 counts. In our study we found no positive association between maternal CD4 count and perinatal transmission. Similar results were observed in a study conducted by Nyamagoudar *et al*. (2016) in 2016.They observed that mother to child HIV transmission was 3.6 % (1/28) and 4.5% (1/22) among antenatal women with CD4 count above and below 350cells/mm^3 respectively, deducing no statistically significant association between maternal CD4 count and vertical transmission of HIV. Also evidence showed by other studies (Guyatt *et al*., 2011; Guyatt *et al*., 2011) emphasized the importance of providing antiretroviral therapy to all pregnant women lifelong, irrespective of their CD4 count, for both the long-term health benefits of the mother and to prevent HIV transmission to the child. In our study, we also correlated risk of tubercular infection and CD4 count. It was observed that incidence of pulmonary tuberculosis was similar in all groups with varying CD4 counts. Contrarily, a study conducted in 2009 by Ghate *et al* (Ghate *et al*., 2009) reported a ten times greater risk of contracting tuberculosis at CD4 count of <200 than at >350 but the result was not significant**.** Wondimeneh *et al*. (2012) too found mean CD4 count in HIV infected individuals to be 296 ± 192 Cells/mm^3 as compared to mean count of 199 ± 149 Cells/mm^{3}in tuberculosis-HIV co-infected cases with p value of 0.007.

Recent observational studies and randomized controlled trials (Sterne *et al*., 2009; Althoff, 2010; Antiretroviral Therapy, 2009) indicated that initiation of ART irrespective of CD4 counts reducesthe incidence of HIV associated complications such as cardiovascular disease, kidney disease, liver disease, cancer , neurological sequel and improves survival; however no concrete evidence was given regarding occurrence of tuberculosis. Data analysis from another randomized controlled trial (HIV-CAUSAL Collaboration, 2011) also suggested that starting ART at a CD4 count >500 cells/mm^3, in the absence of other treatment indications, leads to less severe AIDS related morbidity (opportunistic infections and combined outcome of death) compared with treatment initiation at a CD4 count at or below 500 cells/mm^3, inferring that CD4 counts do not influence the occurrence of concomitant infections like tuberculosis in HIV infected individuals. Establishment of tubercular infection is mainly dependant on amount of viral load in HIV positive individuals. It may occur over a wide range of CD4 counts, unlike other opportunistic infections such as cryptococcal meningitis, candidiasis or toxoplasmosis, which occur at very low CD4 counts (Cheryl, 2008).

Conclusion

The use of antiretroviral drugs in antenatal women and the neonate is the most important intervention for prevention of mother-to-child transmission during antepartum, intra-partum, and early postpartum periods. CD4 counts neither govern the initiation of the therapy nor do they play a significant role in determining the risk of HIV transmission from mother to child, as is observed in our study.

These counts serve as a means to assess damage caused to the immune system by HIV, and can therefore indicate risk of other infections. However, occurrence of primary tubercular infection or activation of latent tuberculosis in antenatal HIV positive women is not dependent on CD4 counts. Therefore, routine measurement of CD4 counts during antenatal period in HIV positive women may be omitted owing to their doubtful role in determining perinatal transmission or maternal immune response to occurrence of tuberculosis. In countries with low resource settings and restricted infrastructure the omission may prove beneficial in reducing treatment cost especially when the counts do not dictate even the commencement of antiretroviral therapy in affected individuals.

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