# **Original Research Article**

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# Epidemiological correlates with communicable viral co-infections of hepatitis B and hepatitis C and non-communicable diabetes among HIV ART naïve rural patients of Kanchipuram district: a prospective cohort study

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#### **ABSTRACT**

**Background:** The objectives of the study were to study the epidemiological correlates of ART Naïve HIV cases; to study the incidence of co–infections among them; to find the incidence of onset of diabetes among them. Concomitant infection of hepatitis B virus, hepatitis C virus viruses leads to higher frequency of carrier state and severe manifestations of the disease in HIV patients. There is general agreement that the traditional risk factors for DM (increasing age, minority race, obesity) are still responsible for most of the increased risk in the HIV infected population.

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**Methods:** This study was designed as a prospective cohort study and was done at the Meenakshi Medical College & Research institute, an academic and Tertiary medical centre in Kanchipuram, Tamil Nadu, South India. The study duration was from June 2004 to June 2010. SPSS 13 was used in the calculation of chi-square and percentages.

**Results:** Among 207 participants, mean age is 36.04 and the SD is 10.895. There is significant difference between the incidence of viral co-infections like hepatitis B and hepatitis C (p<0.001). There is significant difference between the incidence of onset of diabetes (p<0.001). The HbsAg and HCV co infection was comparatively lower than the urban population. Among the 50 HIV reactive, non diabetic patients without risk factors, only one found to be Diabetic and another found to be Pre diabetic after 6 months follow-up.

**Conclusions:** The cost of treatment escalates, when PLHA is co-infected either with viral infections or diabetes, and also their quality of life becomes poor. So, monitoring of CD4 and CD8 should be done as a routine and screening and early treatment should be made mandatory.

Keywords: Epidemiological correlates, CD4 count, Co-infection, Diabetes

# **INTRODUCTION**

Hepatitis B virus, hepatitis C virus and human immune deficiency virus are big challenges to the health care system. These viruses have the ability to spread from one person to another by parenteral route especially sexual

contact. Even though blood transfusion is the most effective method of transmission for all these viruses, introduction of stringent measures have reduced this method of transmission to a certain extent. Concomitant infection of these viruses leads to higher carrier state and severe manifestations of the disease.<sup>1</sup>

#### HbsAg and HCV co- infection

Globally an estimated 350-400 million people are chronically infected with hepatitis B virus (HBV), 190 million are chronically infected with hepatitis C virus (HCV) and 33 million are living with HIV infection today. As a result of shared routes of transmission, the HIV, HBV and HCV epidemics overlap, with around 10% of the HIV infected population estimated to have chronic HBV infection and around one- third estimated to have chronic HCV infection.<sup>2</sup> The clinical management of HIV infected individuals co infected with HCV or HBV is challenging and HIV infection is known to have a negative impact on the outcome of HCV and HBV infections. Although whether or not HCV directly impacts upon HIV disease progression remains controversial, the complex interactions between HIV/HCV co infection and HAART use and the indirect effect of these on HIV disease progression are increasingly apparent.3-5

#### Modes of transmission

Irrespective of the route of infection, transmission depends on factors like HIV-1 concentration in the relevant body fluid and susceptibility of the naive host in addition to virus specific determinants. The heterosexual route of transmission accounts for 50% of infections spread in Asia, Sub-Saharan Africa and Latin America (including the Caribbean).

# Alcoholism and HIV

According to MAC's longitudinal design, among men already at high risk for HIV infection, heavy alcohol consumption, moderate to heavy drug use and younger age further increased their seroconversion by the follow-up visit.<sup>7</sup>

# Aim and objectives

- To study the epidemiological correlates of ART Naïve HIV cases.
  - To ascertain the modes of transmission among the rural population with the available history and evidence.
  - To assess the correlation between the alcohol and smoking behavior with the HIV reactive status.
- To study the incidence of co –infections among them.
  - To correlate with CD4 count.
- To correlate with incidence of diabetes among the same.

#### **METHODS**

This study was designed as a prospective cohort study and was done at the Meenakshi Medical College and Research institute, an academic and tertiary medical centre in Kanchipuram, Tamil Nadu, South India. The study duration was from June 2004 to June 2010. The study was approved by the institutional review board of MAHER University, Chennai. The study population was drawn from the population of newly diagnosed HIV infected ART naïve rural people receiving care at the hospital. The study subjects met the following eligibility criteria.

#### Inclusion criteria

Inclusion criteria were patients with rural background and HIV Reactive serum, which is confirmed by 3 serological test kits with different principles; visit the hospital ICTC for diagnosis and counseling; not on antiretroviral therapy; consented for testing.

#### Exclusion criteria

Exclusion criteria were patients or their attendants who did not give informed consent to participate were excluded; HIV reactive patients with urban background were not included.

Only 50 reactive eligible patients in the age group of 13-40 years were selected and informed consent obtained for the research. Patients proforma were collected including the age, sex, stage of the disease and the clinical Parameters. The reactive patients were also tested for co infections like HbsAg and HCV. At the time of follow up visit the venous plasma glucose levels were measured during fasting at least 8 hours and postprandial state i.e., 2 hours after meal from 50 reactive and diabetes risk free ART- naïve patients and the WHO criteria followed

SPSS 13 is used in the calculation of chi- square and percentages.

#### **RESULTS**

The current investigation includes the study of rural HIV infected patients and their problems. The positive cases confirmed for HIV was 207 (1.59%) among the total 12971 patients screened, in which 3 were antenatal cases. Male cases were more prominent than female patients in the rural population. The sexually active age group 20-50 was the commonly infected. HIV 1 was the most common type in rural setup. Many patients preferred to take native drugs immediately after the diagnosis. Most of the patients were detected at the final stages like stage 3 or 4. The common mode of transmission was heterosexual. Not even a single case with homosexual transmission was reported. The study shows there was an association between the smoking and alcohol intake with the HIV infection probably because of the risk taking behavior. The HbsAg and HCV co infection was comparatively lower than the urban population. Among the 50 HIV reactive, non-diabetic patients without risk factors, only one found to be diabetic and another found to be pre diabetic after 6 months follow-up.

Table 1: Age distribution of PLHA.

Age group in years	Frequency	Percentage (%)	P value
Up to 12	6	2.9	
13-40	143	69.1	<0.001**
Above 40	58	28.0	<0.001***
Total	207	100.0	

Mean age was 36.04 and the SD is 10.895\*\*- most significant. 69.1% of the people are in the reproductive age group (Table 1). Male cases were more prominent than female patients in the rural population accounting for 69.6%. None were transgenders (Table 2).

Table 2: Sex distribution of PLHA.

Sex	Frequency	Percentage (%)	P value
Male	144	69.6	
Female	63	30.4	<0.001**
Total	207	100.0	

Table 3: Marital status of PLHA.

Marital status	Frequency	Percentage (%)	P value
Married	187	90.3	
Unmarried	20	9.7	<0.001**
Total	207	100.0	

Table 4: Occupation of PLHA.

Occupation	Frequency	Percentage (%)	P value
Driver	9	4.3	
Cooly/daily wages worker	83	40.1	
Self employed	34	16.4	
Farmer	16	7.7	<0.001**
Labour	23	11.1	
House wife	25	12.1	<0.001
CSW	7	3.4	
Unemployed	7	3.4	
Govt. employee	3	1.4	
Total	207	100.0	

Table 5: HbsAg infection.

Hbs Ag infection	Frequency	Percentage (%)	P value
No	193	93.2	
Yes	14	6.8	<0.001**
Total	207	100.0	

There is significant difference between married and unmarried on the PLHA status (Table 3). Cooly/daily

wage worker contributes to 40.1% suggesting that PLHA is common among lower socio-economic group in the rural people (Table 4).

Table.6. HCV infection.

HCV infection	Frequency	Percentage (%)	P value
No	204	98.6	
Yes	3	1.4	<0.001**
Total	207	100.0	

There is significant difference among the PLHA, in the incidence of co- infections with communicable viral co-infections like, hepatitis B virus and hepatitis C virus.

#### CD4 count

All participants were ART-naive by self-report. The mean CD4 counts in this group was 286 cells/mm<sup>3</sup> with a median value of 256 cells/mm<sup>3</sup>. The CD4 counts in this group ranged from 70–726 cells/mm<sup>3</sup>.

Table 7: CD4 Count.

CD4 count	Frequency	Percentage (%)	P value
Up to 200	36	17.4	
201-350	71	34.3	<0.001**
Above 350	100	48.3	
Total	207	100.0	

CD4 Mean=404, SD=231, CD8 Mean=402, SD=300.

#### Modes of transmission

In this study, the heterosexual transmission was the predominant mode of transmission with 96.6% followed by the mother to child transmission with 2.6%. Only 0.5% of the study population found to be transmitted through blood and there was not even a single patient with H/O of homosexual exposure.

# HIV and diabetes

From the 50 reactive patients who were eligible and selected from the whole reactive group i.e., 207, only 2% developed type 2 diabetes and another 2% developed impaired glucose tolerance during the 6 months follow-up. Males were 38 and female 12 in number. One male and no female became pre diabetic after 6 months. Similarly, one male and no female became diabetic after 6 months. Mean age was 32 years.

# HIV and association of smoking and alcohol

Among the total number of 207 PLHA, 95 (45.9%) patients were non alcoholics, based on the history and the

remaining 112 (54.1%) patients were alcoholics (p=0.237). On the whole, the smokers were higher in number than non-smokers comparatively. Of the total, 108 (52.2%) persons were smokers and the 99 (47.8%) persons were non-smokers (p=0.532).

Table 8: Fasting blood sugar.

Fasting blood sugar	Frequency	Percentage (%)	P value
Below 110	49	23.7	
110-124	1	0.5	
Total	50	24.2	<0.001**
Others	157	75.8	
Total	207	100.0	

Mean FBS=86, SD=9.29, \*\*=Most significant.

Table 9: Post prandial blood sugar.

Post prandial blood sugar	Frequency	Percentage (%)	P value
Below 140	48	23.2	
140-200	1	0.5	<0.001**
Above 200	1	0.5	
Total	50	24.2	
Others	157	75.8	
Total	207	100.0	

Mean PPBS=133, SD=23.3; Significant no of people with PLHA became diabetics.

#### **DISCUSSION**

#### HIV and diabetes

Adeel et al determined the relationship between HIV infection and other risk factors for prevalent diabetes in one of the largest prospective cohorts of HIV infected persons and HIV uninfected controls and found that HIV infection *per se* was not associated with a higher risk of DM. In fact, the risk of DM at baseline was lower in the HIV infected (OR 0.84, 95% CI 0.72-0.97) compared with HIV uninfected persons. While HIV infected persons may have higher levels of high sensitivity C-reactive protein levels, those with HCV/HIV co infection have lower levels than uninfected persons. How these interact in a given patient to determine the net risk of diabetes requires further study. HOV

#### HCV and diabetes

It was found that HCV infection is associated with a higher risk of DM in the HIV infected group, and demonstrated a similar trend in the uninfected group in multivariable analysis (Although this trend did not reach statistical significance, the effect size was similar). This confirms the suggestion from some previous studies that HCV affects the risk of DM in a complex manner, and such risk is influenced significantly by other more traditional risk factors. <sup>11,12</sup> Insulin resistance and higher levels of inflammatory cytokines are also seen in patients

with chronic HCV (but not with HCV/HIV co infection) and may be one common pathway leading to a higher risk of DM. <sup>13-16</sup>

#### Diabetes and co-infections

Although the optimal method and frequency of screening for diabetes and insulin resistance among those infected with HIV have not yet been determined, research and clinical practice in both HIV and diabetes has provided some insight for designing a basic template for screening. In 2002, recommendations of the International AIDS Society-USA Panel for the management of metabolic complications associated with antiretroviral therapy for HIV-1 infection were published.<sup>17</sup> This 12-member panel developed guidelines that were meant to assist physicians in the management of glucose, lipid and body fat distribution abnormalities and bone disease.

Brar et al findings did not suggest an increased prevalence of DM in ART naive HIV infected patients. Although there was a trend toward increased prevalence of DM in HIV-HCV-co infected patients, dominant risk factors associated with DM among ART-naive HIV-infected adults mirrored those of the general population. In our study, the new onset of diabetes during follow-up was only 2% which is minimal comparing to the CPCRA clinical trials and the NHANES which showed 3.3% and 4.8%.

The role of HCV co infection in HIV infected persons is also unclear. In the FIRST study, HCV co infection was associated with a higher risk of DM in the antiretroviral-naive HIV infected population who were <50 years old, while no increased risk was found in the Swiss HIV cohort study or an urban cohort of HIV infected persons in New York city. In our current study, there was no direct relationship with HCV for diabetes was found. But, since it was a small group of patients and short duration of follow-up, we could not have directly correlated the results.

In the present study, one patient with HbsAg co infection found to be present with impaired glucose tolerance. Very few studies have analyzed the HIV and HbsAg co infection and association of type 2 diabetes, which did not revealed any direct relationship. Butt et al suggested that the HIV infected veterans should be screened regularly for diabetes, especially those who are older, are from a minority race, or have HCV co infection.

# Modes of transmission

The three documented routes of transmission of HIV-1 can be classified into sexual, vertical and percutaneous routes. Irrespective of the route of infection, transmission depends on factors like HIV-1 concentration in the relevant body fluid and susceptibility of the naive host besides virus specific determinants. The heterosexual route of transmission accounts for over 50% of infections spread in Asia, Sub-Saharan Africa and Latin America

(including the Caribbean).<sup>21</sup> The risk of maternal to foetal transmission is 13-40% and can be reduced by treatment of the mother and infant before and after delivery, respectively.<sup>22</sup> Postpartum transmission occurs by breast feeding and is associated with a transmission rate of 16%.<sup>23</sup> HIV-1 transmission has also been associated with transfusion of infected blood and blood products and reuse of contaminated needles.<sup>24</sup>

According to NACO 2009-10 Annual Report, the mode of transmission were as follows: heterosexual (87.4%), mother to child (5.4%), IDU (1.6%), MSM (1.5%) and Blood and blood products (1%).<sup>25</sup> In our study also, the major route of transmission was heterosexual (96.6%) followed by mother to child 2.6% and percutaneous 0.5%. Sexual transmission among homosexual men is still a significant part of epidemic spread in United States and Europe.<sup>26</sup>

The overall HIV prevalence among different population groups in 2008-09 continues to portray the concentrated epidemic in India, with a very high prevalence among HRGs – IDU (9.19%), MSM (7.3%), FSW (4.94%) and STI clinic attendees (2.46%), and low prevalence among ANC attendees (0.48%).<sup>27</sup> Korzeniewska-Kosela et al in their study found that 30 (75%) were heterosexual, 6 (15%) were homosexual and used intravenous drugs, 2 (5%) just used intravenous drugs, and 1 (2%) had heterosexual contact with prostitutes; for the remaining subject the risk factor for HIV infection was not established.<sup>28</sup>

In our study, the heterosexual transmission was the predominant mode of transmission with 96.6% followed by the mother to child transmission with 2.6%. Only 0.5% of the study population found to be transmitted through blood. In our findings, FSW (3.4%), ANC (1.4%), IDU (0%) and MSM (0%) were identified. There was no report of Injecting drug users or homosexual transmission in our group. Probably, the drug injecting users, transgenders and homosexuals were very low in number due to the cultural influences in the rural area or may be migrated to the urban setup.

#### Association of smoking and alcohol with HIV

According to MAC's longitudinal design, among men already at high risk for HIV infection, heavy alcohol consumption, moderate to heavy drug use and younger age further increased their seroconversion by the follow-up visit. Another study's data suggests heavy drinking, moderate to heavy use of drugs and younger age were significantly related to seroconversion.<sup>29</sup>

Six studies were identified with HIV seroconversion as an outcome measure. Five of these indicated that smoking tobacco was an independent risk factor after adjusting for important confounders with adjusted odds ratios ranging from 1.6 to 3.5. Totally, ten studies were identified using progression to AIDS as an end point of which nine found no relation with tobacco smoking.

Tobacco smoking may be an independent risk factor for HIV infection although residual confounding is another possible explanation. Smoking did not appear to be related to progression to AIDS although this finding may not be true in developing countries or with the longer life expectancies seen with highly active antiretroviral therapy.<sup>30</sup>

#### **CONCLUSION**

The cost of treatment escalates, when PLHA is coinfected either with viral infections or diabetes, and also their quality of life becomes poor. So, monitoring of CD4 and CD8 should be done as a routine and screening and early treatment should be made mandatory.

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Institutional Ethics Committee

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