RISK FACTORS ASSOCIATED WITH HUMAN IMMUNODEFICIENCY VIRUS (HIV) TRANSMISSION TO UNINFECTED MARRIED PARTNER

CERTIFICATE

This is to certify that the dissertation entitled ***"Risk factors associated with Human Immunodeficiency Virus (HIV) transmission to uninfected married partner"*** is the bonafide original work of Dr. Alice Joan Mathuram submitted in partial fulfillment for the M.D. Branch-1 (General Medicine) Degree Examination 2008 of the Tamil Nadu Dr. M.G.R Medical University, Guindy, Chennai , TamilNadu.

Signature:

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ACKNOWLEDGEMENTS

It gives me immense pleasure to express my heartfelt and profound sense of gratitude to my respected teacher and guide, **Prof. Dilip Mathai** for his valuable suggestions, meticulous guidance, support and encouragement in doing this study.

I am also grateful to **Prof. O.C.Abraham , Prof.Anand Zachariah, Dr.Anand Manoharan** and all my teachers in the **Department of Medicine** for all the support guidance and valuable suggestions received in preparing this dissertation and throughout my three year course in General Medicine.

I am extremely grateful to the social workers and HIV counselors, **Mrs.Joyce Rajan Mr.Govindan , Mr.Peace, Mr.Jacob Matthew** and all the **staff at the Dr.Benjamin M Pulimood Laboratories for Infection and Immunity** for their assistance in the conduct of this study.

I would also like to thank **Mrs. Vishali Jeyaseelan** (Department of Clinical Epidemiology) who helped me with the analysis of data.

I am grateful to **my parents-Dr.Samuel Mathuram and Mrs.Gracie Mathuram** and **my husband-Dr.Manasseh Nithyananth** for their moral support and encouragement throughout this study.

I thank all my **patients** for their co-operation in this study.

Above all, I thank the **Lord Almighty** for all His grace, mercy ,strength and guidance that He gives me in full everyday.

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1. ACRONYMS AND ABBREVIATIONS

HIV	–	Human Immunodeficiency Virus
STI	–	Sexually Transmitted infection
NACO	–	National Aids Control Organization
AP	–	Andhra Pradesh
HLA	–	Human Leukocyte Antigen
RNA	–	Ribonucleic acid
MSM	–	Males who have Sex with males
CCR5	–	Chemokine (C-C motif) receptor 5
HSV 2	–	Herpes Simplex Virus 2
CD4	–	Cluster of Differentiation 4 (glycoprotein)
NRTI	–	Nucleoside Reverse Transcriptase Inhibitors
NNRTI	–	Non-nucleoside Reverse Transcriptase Inhibitors
NtRTI	–	Nucleotide Reverse Transcriptase Inhibitors
Th1	–	T Helper 1
CTL	–	Cytotoxic T Lymphocyte
MHC	–	Major Histocompatibility Complex
YRG CARE	-	Y.R. Gaitonde Centre for AIDS Research and Education
ART	–	Anti-Retroviral Therapy

2. ABSTRACT

Sexual transmission is the major route of HIV transmission among partners. Despite living in partnership about 44% of couples in South India are serodiscordant for HIV infection. This case control study was therefore done to identify factors influencing HIV transmission among couples in whom both or either partner was HIV infected. Newly detected HIV infected patients and their partners who were either seroconcordant or discordant were included from South India. Details of social and sexual behavioural practices which could possibly affect HIV transmission were collected by a standard interview to each individual partner. Each partner was examined and staged clinically according to the WHO classification.CD4 counts were enumerated and partners were counseled on safe sexual practices. The factor which had a statistically significant increased risk for HIV transmission was a CD4 lymphocyte count < 350 cells/mm^3 .Alcohol consumption, smoking, increased frequency of sexual intercourse, genital ulcer disease and urethro-vaginal discharge are associated with an increased risk for transmitting HIV to uninfected partner. Regular condom use, abstinence and male circumcision protect seronegative partners from HIV acquisition. Lesser frequency of sexual intercourse prior to serodetection, increased condom use after serodetection and CD4 lymphocyte counts > 350 cells/mm protect against transmission even after l0 years of living as partners. Therefore counseling of partners who are discordant for HIV infection should be intensified on safe sex practices. ART should be initiated early in such patients to prevent HIV transmission

3. AIM

To identify the risk factors associated with transmission of human immunodeficiency virus (HIV) to uninfected married partner.

4. OBJECTIVES

1. To identify social risk factors involved in HIV transmission to uninfected partner.
2. To assess sexual behaviour pattern in uninfected partner.
3. To correlate the clinical stage of HIV disease associated with transmission.
4. To correlate the immunological stage of HIV disease with transmission

5.0 REVIEW OF LITERATURE

5.1 INTRODUCTION

HIV prevalence in India is 1.7% among adults [1] with the highest prevalence in Andhra Pradesh (A.P) – 3.3% [2].Sexual route is responsible for 85% of the route for HIV transmission[.3] .

Till recently the National AIDS Control Organization (NACO) has calculated the annual burden of HIV by sentinel surveillance in the public sector such as antenatal and STI clinics at medical colleges or district head-quarter hospitals and high risk groups like female sex workers, intravenous drug users and males who have sex with males (MSM). This data cannot be directly extrapolated to the general population as the prevalence of HIV. Therefore population based prevalence estimates are required. A large population based prevalence study done in Guntur district of AP compared population based prevalence data with data from sentinel surveillance .This study found that sentinel surveillance data over-estimated the HIV prevalence by 2.5 times[.1]

HIV concordance (i.e. both partners being positive) in South Indian population is estimated to be 56% and the remaining 44% are discordant [4.] Thus there exists an equally large number of HIV discordant couples. HIV transmission per coital act is 0.0001-0.0020[. 5-8.] Several factors have been implicated that facilitate virus transmission and several that protect persons from HIV acquisition. (Table 1 and 2).

This study was therefore done to study behavioural and social factors implicated in HIV transmission and also to see whether clinical and immunological stage of the disease had any influence on HIV positive serodiscordance or concordance. This study differs from the one done by YRG CARE, Chennai [4] in that, this covers a rural and semi-urban population of South India compared to the urban population enrolled in the former study. There may therefore be differences between these 2 groups of the population with regard to behavioural practices, lifestyle, education etc. which may affect HIV transmission. Also, this study was done to study HIV transmission only in married couples who reside together.

5.2 **TABLE 1** SHOWS FACTORS FOUND TO FACILITATE HIV TRANSMISSION

1. High HIV viral load and advanced stage of disease.[9-12]
2. High risk behaviour (exposure to commercial sex workers or multiple heterosexual or homosexual partners).[4,12,14]
3. Presence of other sexually transmitted diseases.[15-24]
4. Characteristics of the virus like syncytia inducing capability.[25]
5. Certain HLA subtypes.[26]

5.3 **TABLE 2** SHOWS FACTORS FOUND TO PROTECT AGAINST TRANSMISSION

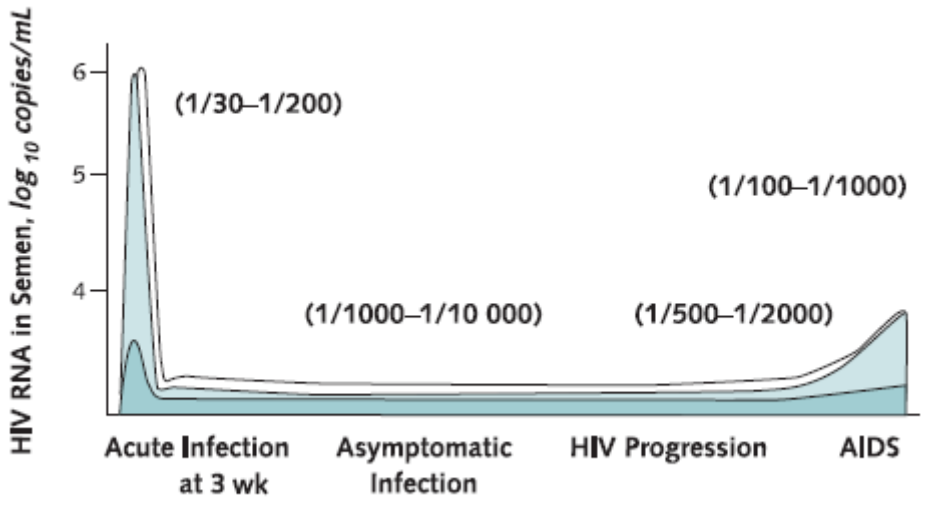
1. Barrier contraception and abstinence.[4,6,12,14,27]
2. Male circumcision.[28-33]
3. Use of anti-retroviral therapy.[34-46]
4. Homozygosity for CCR5 mutation in the chemokine receptor gene.[47]
5. Cell mediated immune responses and cytotoxic T lymphocyte activity.[48-55]
6. Antibody directed against gene products of the major histocompatability complex.[56-58]

5.2 FACTORS FACILITATING HIV TRANSMISSION:-

5.2.1 HIV VIRAL LOAD AND ADVANCED STAGE OF DISEASE

Several studies have demonstrated that transmission of HIV among partners is correlated with higher HIV viral load. In a large cohort study in Uganda ,HIV transmission among initially discordant couples occurred in those who had higher HIV-1 RNA levels (90,254 copies per ml vs. 38,029 copies per ml).For each log increment in viral load the rate ratio for the risk of transmission was 2.45 [9].

A similar but smaller cohort in Italy showed higher HIV-1 RNA copies among index cases who transmitted infection when compared to index cases who did not (46,200 – 3,42,000 vs. 16,500 – 41,870 copies/ml.) [10] . High HIV viral loads are found in both the early acute phase and more advanced stages and transmission occurs at both these times.



[*The numbers in parentheses suggest the probabilityof HIV transmission per episode of penile–vaginal intercourse*].[11]

It is easy to understand that sexual behavioural practices decline in patients with advanced stage of disease due to their morbid state. However, the heterosexual HIV transmission study, New Jersey showed that people with a more advanced HIV stage did not have any significant difference in sexual behavioural practices from those with less advanced HIV disease [12].This was in terms of practice of anal sex, condom use or abstinence.

5.2.2 HIGH RISK BEHAVIOUR

Results of the heterosexual HIV transmission study showed that before knowledge of HIV seropositivity (a) men among discordant couples had fewer life-time sexual

partners than in concordant couples. (b) frequency of vaginal sex before knowledge of the male partner's seropositivity was not significantly different between concordant and discordant couples. (c) Over 80% of the couples never used condoms during vaginal sex and condom use was similar in both discordant and concordant couples. (d) frequency of anal sex was significantly higher among concordant than discordant couples. (e) there were no differences in the frequency of vaginal intercourse during menstruation, fellatio or cunnilingus among discordant and concordant couples.

After HIV status was known , it was found that concordant and discordant couples differed in the proportions that abstained from sex (13% concordant vs. 17% discordant), using condoms at least some of the time (60% vs. 72%) and in never using condoms (27% vs. 10%) [12].

In another cross-sectional study [4] done in Chennai, the rates of abstinence were significantly higher compared to the American study (39% concordant and 49% discordant).

A 7- year cohort study done in four African cities showed duration of marriage to be another risk factor that co-related with HIV positive concordant serostatus [13].

A cross-sectional study of HIV concordant and discordant partners in Uganda showed that living together is another factor associated with HIV positive concordance[14].

5.2.3 SEXUALLY TRANSMITTED DISEASES

Herpes Simplex virus 2 (HSV-2) is the primary cause for genital herpes. Infection with HSV-2 has been shown to increase susceptibility to HIV by disturbing the mucosal barrier [15] and by the inflammatory changes which increase recruitment of HIV target cells to the ulcer [15, 16]. But genital ulcer disease may also be a symptom of acute seroconversion illness[17]. It has been reported by 15% of individuals during the seroconversion illness. It is also found to be more common in patients prevalent with HIV [18, 19].

Therefore, there are questions as to whether genital ulcer disease actually precedes HIV seroconversion or occurs during or after seroconversion. This was addressed in a nested case control study in Rakai,Uganda [20] where participants in the longitudinal cohort who were initially HIV seronegative where questioned about genital ulcer disease ,prior to HIV sero-conversion, at sero-conversion and 10 months post-seroconversion. HSV-2 serology testing was done. They were compared with participants who did not HIV seroconvert. This study showed that prevalence of symptomatic genital ulcer disease is increased both during the period of HIV seroconversion and after HIV acquisition and this increase is mainly observed among HSV-2 seropositive individuals [20]. Reactivated ulcerative herpes could account for the increase in genital ulcer disease after HIV acquisition. This has been shown among pregnant women who acquire HIV-1[21].

Also HSV-2 induced asymptomatic micro-ulceration could contribute to increased risk of HIV infection. Once HIV is acquired, the immunosuppression

caused by HIV could exacerbate the ulcer and cause symptomatic genital ulcer disease.

HSV-2 also upregulates HIV replication, causing higher viral loads for a short-term. This leads to increased rates of transmission and faster progression to AIDS[5, 22, 23,24] .

A cross-sectional study done in four cities in sub-Saharan Africa to study factors influencing HIV concordance among married couples showed in multivariate analysis, that HSV-2 seropositivity was the only factor influencing concordance [13].

5.2.4 PRESENCE OF CERTAIN HLA SUBTYPES

In an observational study among hemophiliacs in Italy it was found that HLA A2 was significantly associated with HIV seropositivity whereas HLA types BW52 and DR4 were negatively associated with seroconversion [26].

5.3 PROTECTIVE FACTORS

5.3.1 BARRIER CONTRACEPTION AND ABSTINENCE

Although barrier contraception has been proven to decrease HIV transmission [27,6]a study among discordant couples in south India showed no statistically significant difference in the concordance rates with condom use [4]. This study also showed that the reported frequency of intercourse did not influence concordance and discordance. But abstinence was quite common after the diagnosis of HIV infection (39% among concordant and 49% among discordant couples).

A Ugandan study however showed an increased risk of 2.4 for women who had not used condoms during their last exposure[14].

The Heterosexual HIV transmission study showed a 70% protective effect for abstinence and condom use on HIV transmission. [12].

5.3.2 CIRCUMCISION

Most cases of primary HIV infection involve HIV binding to the CD4 and CCR5 receptors found on antigen presenting cells-macrophages,Langerhan's cells and dendritic cells in the genital and rectal mucosa. About 70 % of men infected with HIV acquire the virus through vaginal sex and a smaller number from insertive anal intercourse [28].

The uncircumcised penis consists of the penile shaft, glans, urethral meatus, inner and outer surface of the fore-skin and the frenulum (the thin band connecting the inner foreskin to the ventral aspect of the glans). A keratinized stratified squamous epithelium covers the penile shaft and outer surface of the fore-skin. This provides a protective barrier against HIV infection. In contrast, the inner mucosal surface of the fore-skin is not keratinized [29] and is rich in Langerhan's cells[30], making it susceptible to the virus. During heterosexual intercourse, the fore-skin is pulled back down the shaft of the penis and the whole inner surface of the fore-skin is exposed to vaginal secretions, providing a large area where HIV transmission could take place. The epithelium of the glans in circumcised and uncircumcised men is equally keratinized. In circumcised males, only the distal penile urethra is lined with mucosal epithelium. However this is

unlikely to be a common site of infection because it contains comparatively few Langerhan's cells [30].

Ulcerative or inflammatory lesions of the penile urethra, fore-skin, frenulum or glans that are caused by other sexually transmitted infections may provide additional potential routes for HIV transmission. In uncircumcised males , the highly vascular frenulum is particularly susceptible to trauma during intercourse and lesions produced by other STI's commonly occur there. Thus male circumcision further reduces the risk of infection by reducing the synergy that normally exists between HIV and other STI's [16].

Several observational studies and a large cohort study in Uganda had earlier shown significant protective effect of male circumcision on HIV transmission [31,32.] However randomized controlled trials were lacking. Therefore this could not be recommended as a preventive measure for the general population. Recently 2 randomized controlled trials in Kenya and Uganda showed 53% and 48% reduction of risk of HIV acquisition among HIV negative men who were at high risk and were circumcised [33].

5.3.3 USE OF ANTIRETROVIRAL THERAPY

ART has been shown to reduce HIV RNA concentrations in blood, seminal plasma [34], female genital tract secretions [35] and rectal secretions [36]. Therefore ART is expected to reduce infectiousness when used for treatment. Penetration of antiviral agents into genital tract secretions is dictated by the degree of protein binding. Highly protein bound drugs are found in lesser concentrations in the genital tract.

Fusion inhibitors < Protease inhibitors < NNRTI's < NRTI's or NtRTI's.

Retrospective and prospective evaluation of HIV transmission in sero-discordant couples has shown decreased risk of transmission for those on ART. Risk of transmission decreased by 50% in a study by Musico et al [37] and by 86% in a study by Castilla and colleagues [38]. Similar findings were also reported by others [39, 40].

On analysis of population trends, Porco et al found a 60% reduction in anticipated cases of HIV among a homosexual cohort in SanFrancisco [41].Similar results were found by Fang et al in Taiwan [42] – 53% reduction in expected cases and Montaner et al in British Columbia [43] – 50% reduction in expected cases by ART.

However other ecologic studies have shown disappointing results [44, 45]. The patients in these studies who received anti-retroviral therapy had an increased incidence of other STI's. This indicated ongoing risk taking behaviour in these patients. This could suggest that the availability of effective HIV treatment increased high risk sexual behaviour in this populations studied and may be attributed to the possible feeling of well – being experienced by patients on anti-retroviral therapy.

The degree to which ART will reduce infectivity at the individual level is also not known [46].

5.3.4 HOMOZYGOSITY FOR CCR5 MUTATION IN THE CHEMOKINE RECEPTOR GENE

The CCR5 gene serves as a secondary receptor on CD4 T lymphocytes for certain strains of HIV-1.The CCR5 gene was mapped to human chromosome 3p21.A 32 base pair

deletion allele (CCR5Δ32) was identified. This is present at a frequency of 0.10 in the Caucasian population of the United States.

On examining 1955 patients enrolled in 6 cohort studies it was found that among 612 exposed but HIV negative individuals, 17 were homozygous for CCR5Δ32.This deletion was not found at all among the 1343 who were HIV infected.

This indicates that homozygosity for CCR5Δ32 might confer resistance to HIV acquisition [47].

5.3.5 CELL MEDIATED IMMUNE RESPONSES – CYTOTOXIC T LYMPHOCYTE ACTIVITY

Cellular immune responses have been postulated to confer protection from HIV infection in persons at increased risk due to sexual behaviour [48,49]occupational exposure [50], IV drug use [51], perinatal exposure [52,53]and prostitution [54].

The theory which evolved from these studies suggested that strong cell mediated immune responses induced by a predominance of Th1 cytokines would enhance protective immunity or favorably modulate established infections.

In a study done on 11 discordant heterosexual and homosexual couples, cytotoxic T lymphocyte activity (CTL) was assessed in the seronegative partner by generating effector cells against the primary isolates to which that person had been exposed. These effector cells were tested against CD4 and CCR5 transfected autologous target B cell lines that were infected with a panel of viruses consisting of the primary isolate and laboratory isolates. Virus production was measured by p24 antigen.

Production of p24 from infected B cell lines was lower than from infected autologous phytoagglutinin stimulated blasts but the lysis observed in many assays suggested that sufficient antigen was present for processing and presentation of T cells. Cytotoxic T cell activity against primary viruses were detected in 5(46%) of 11 exposed un-infected subjects and there was good concordance between lysis of

transfected B cell lines and autologous CD4 cells. But among these 5 in whom cytotoxic T lymphocyte activity was detected, 4 had partners with undetectable viral loads and all infected partners were on anti-retroviral therapy. Three reasons have

been proposed for the presence of cytotoxic T lymphocyte activity in partners of these patients on ART and with low viral loads.

1. It is possible that these patients who are serpositive would have transmitted sufficient viral antigen / virus (potentially replication deficient variant) to their negative partner to stimulate CTL.
2. CTL may have been generated during a previous greater risk relationship and been maintained through low grade continuous exposure.
3. In persons with greater CD4 counts and lower viral loads, the stimulatory capacity of the infected CD4 cells would be greater compared to those with advanced disease in whom CD4 cells should be lower[55.]

5.3.6 ANTIBODY DIRECTED AGAINST GENE PRODUCTS OF THE MHC OR MHC DISCORDANCE

It has also been proposed that relative resistance to HIV-1 infection may be mediated by antibody directed against the gene products of the major histocompatability complex. This has been shown to protect macaques from simian immunodeficiency virus [56, 57].

In babies born to HIV-1 infected mothers, protection from perinatal infection is strongly associated with Class 1 MHC discordance between the mother and child[58]. However in a small study with 11 serodiscordant partners, resistance to transmission

did not significantly co-relate with the degree of MHC discordance between sex partners[55].

Thereby, many behaviour related and molecular factors have been shown to influence transmission of HIV among heterosexual partners.

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6.0 MATERIAL AND METHODS

6.1 Study setting:

This study is done in the Christian Medical College Hospital Vellore and its satellite clinic at the Low Cost Effective Care Unit. Eligible patients were enrolled from both the in and out-patient sections.

6.2 Study period:

June 2006 to July 2007 (13 months).

6.3 Study design:

This is an unmatched case-control study of couples.

6.4 Subjects:

The patients were enrolled as couples in whom HIV infection was newly detected in either male partner or female partner or in both.

Cases: HIV concordant couples. Defined as both married partners being positive.

Controls: HIV discordant couples. Defined as only one married partner being positive.

Index or transmitting partner: Defined as the partner acquiring HIV infection first and transmitting the virus to the other partner. The probable index partner among the concordant couples was determined by looking at 3 criteria – namely: presence of risk factors for HIV acquisition, levels of CD4 counts and advanced clinical stage of disease (WHO clinical stage 3 and 4). If one of such partners had any two out of these three criteria fulfilled, he or she would be considered the index or transmitting partner. In the serodiscordant group, the positive partner was the transmitting partner.

Unsure transmission: Defined as the concordant couples in whom the probable transmitting partner could not be ascertained.

Inclusion criteria:

The subjects were from rural and sub-urban South India. They should be living together as married partners.

Exclusion criteria:

1.Subjects from other parts of India.

2.Married partners who were not living together.

3.Unmarried partners.

HIV serostatus was confirmed by doing a dually reactive ELISA or by rapid testing using a simple ELISA test on serum. If one of the partners was seronegative, rapid test for HIV was repeated at 3 months.

6.5 Enrollment of cases:

Eligible subjects were interviewed by a standard questionnaire (see proforma). Informed consent was obtained from each partner separately .They were interviewed on sexual behaviour, high risk practices, use of alcohol, smoking, intravenous drug use, condom use before and after knowledge of HIV status, genital ulcers, urethro-vaginal discharge, diagnosed sexually transmitted diseases and circumcision among males. Demographic data was also obtained. Interviews on sexual behaviour and high risk sexual practices

were done. The patients underwent physical examination and were staged clinically according to the WHO staging system (Appendix 1).VDRL test for syphilis was done.

Blood was drawn for CD4 counts. The CD4 lymphocyte counts were enumerated at the Benjamin Pulimood Laboratory for Infection and Immunity by BD FACSCount system of flowcytometry. This flowcytometer uses a single platform methodology to determine absolute CD4 lymphocyte counts. The BD FACSCount system is designed to use unlysed whole blood, collected in liquid EDTA.When whole blood is added to the tubes of a sample reagent pair, the flurochrome-labeled antibodies bind specifically to antigens on the surface of lymphocytes. The BD FACSCount instrument detects two fluorescent colours and measures relative cell size. CD3 cells fluoresce red and CD4 and CD8 cells fluoresce yellow when analysed on the BD FACSCount instrument. A known number of reference beads is contained in each reagent tube and functions as fluorescence and quantitation standard for calculating the absolute counts for CD4+, CD8+ and CD3+ T lymphocytes. Fixative solution is added to the stained samples prior to analysis to preserve the integrity of the antibody binding. No lysing is necessary. When the sample tubes are run on the system, analysis is automatically completed by the system with no user intervention. The automated analysis is done in 5 steps. First the threshold is positioned to eliminate small signal events, such as debris, erythrocytes, platelets, monocytes and granulocytes. Then a fixed number of events is acquired. Second, the bead and cell populations are located in two dimensions: red vs. yellow. Third, ellipses are placed around the cell and bead populations, with the control run providing the starting point. The ellipses optimize their position based on the

centre of each population. Fourth, an orbital region is placed around each ellipse. Lastly, additional events are collected, up to 30,000 per sample, so that precision of the measurement is not limited by statistical sampling variation. The data is then processed and reported. Absolute counts are determined by a simple ratio:

Observed counts from the population of interest ⁄ Observed reference bead counts * Reference bead count⁄µl whole blood.

6.6 Variables studied:

The demographic variables studied were age, occupation, education, income per month, domicile, duration of marriage and number of children. Variables studied regarding sexual behaviour patterns were the number of sexual partners other than spouse, duration since last sexual exposure to any person other than spouse, receipt of any blood transfusion, intravenous drug abuse, cigarette smoking, alcohol consumption, frequency per month of sexual intercourse before knowledge of HIV serostatus and after, frequency of condom use per month, use of other contraceptive practices, previous and current genital ulcers, previous and current urethro-vaginal discharge, diagnosis of previous or current sexually transmitted disease, circumcision in the male partner. Clinical stage of HIV disease, CD4 lymphocyte counts and VDRL test results were recorded.

6.7 Sample size calculation:

Sample size was estimated according to the following formula:

$$n = \frac{\left[Z_{\alpha/2}\sqrt{2\overline{P}(1-\overline{P})} + Z_{1-\beta}\sqrt{P_1(1-P_1)+P_2(1-P_2)_1}\right]^2}{\left(P_1 - P_2\right)^2}$$

P2 is the proportion of "never used condoms" among the concordant couples

P1 is the proportion in the discordant couples

$Z_{\alpha/2}$ is 1.96 at 5% alpha level

$Z_{1-\beta}$ is 1.282 for 90% power

The required sample size was calculated as 109 cases and 109 controls with a 5% alpha level and 90% power.

6.8 Statistical analysis:

All statistical analysis was done using the Statistical Package for the Social Sciences (SPSS) software version 15. Chi-square test was used for comparison of categorical variables. Odds Ratio (OR), confidence intervals were calculated and a 'p' value less than 0.05 was considered statistically significant. All reported p values are two-sided. Univariate logistic regression models were constructed with sero-concordance as the dependent variable to determine the risk of transmission. Variables with $p < 0.20$ in the

univariate model were entered in the multivariate model. Also those variables that could possibly be significant were used in the multi-variate analysis.

HIV concordant and discordant couples were compared for each of these variables and the risk of transmission for each variable calculated using odds ratio's. Their significance was determined using p values and 95% confidence intervals.

Analysis was also done according to the possible mode of transmission of HIV (that is male to female or female to male). were classified as unsure transmission and analysed separately.

6.9 Funding:

This study was approved and funded by the Fluid Research Committee (No 5905) dated 20.6.06 of Christian Medical College, Vellore.

6.10 Ethical clearance:

Ethics committee clearance was not obtained as this study did not involve any intervention. However all patients signed informed consent documents individually.

7.0 RESULTS

7.0 RESULTS

A total of 224 patients that included 112 married couples living together since either partner was detected to be infected with HIV, were enrolled. Among these 224, 168 were HIV infected of which 112(i.e. 56 couples had HIV concordance).In the remaining 112 patients, 56 were HIV seronegative and they had HIV infected partners(i.e.56 couples were serodiscordant) .

7.1 DEMOGRAPHY

7.1.1 AGE:

The mean age of the males were 37.6 and 39.3 years in the concordant and discordant groups respectively. The mean ages of the females were 30.7 and 32.2 among concordant and discordant groups respectively.

Figure 1: shows the age distribution of 112 male partners

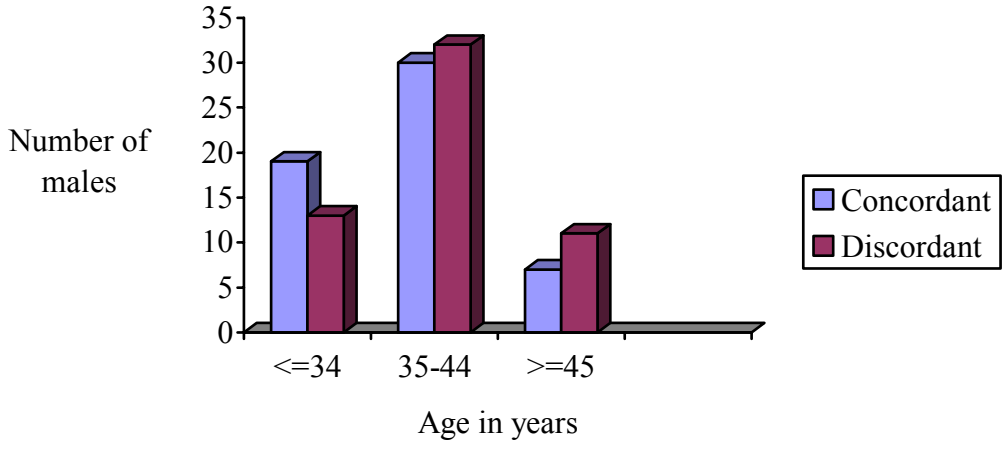
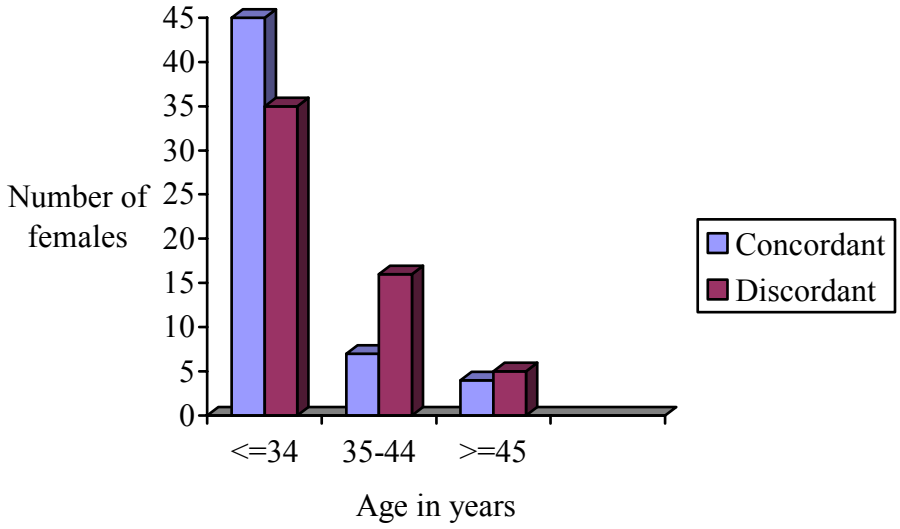


Figure 2: shows the age distribution of 112 female partners



7.1.2 DOMICILE:

Patients from TamilNadu constituted 66.1%. Patients from Andhra Pradesh 31.2% and Karnataka 2.7%.

Figure 3: shows the distribution of domicile of 56 concordant couples

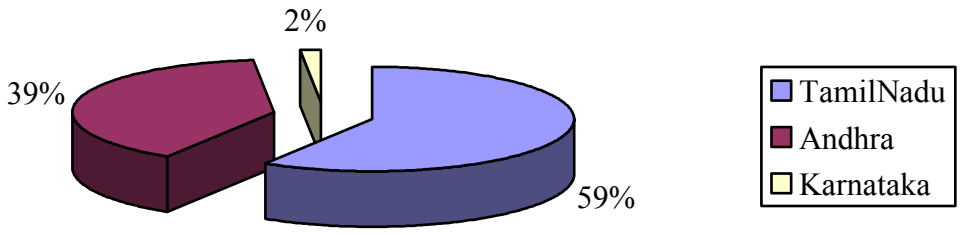
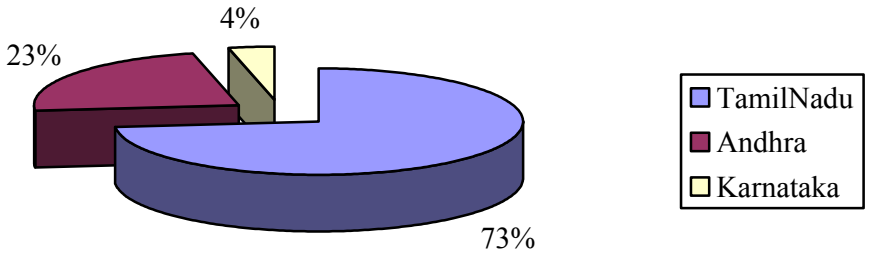


Figure 4: shows the distribution of domicile of 56 discordant couples



7.1.3 OCCUPATION:

Figure 5: shows the distribution of occupation of 112 males

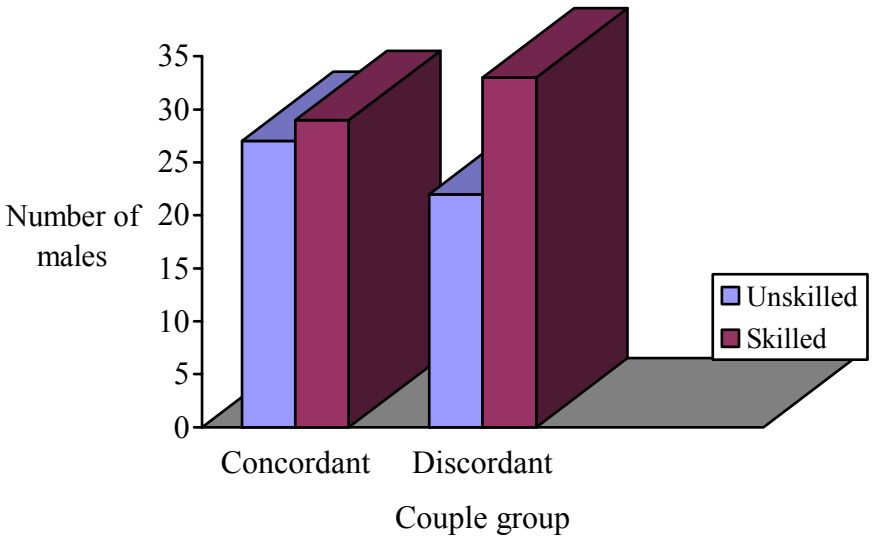
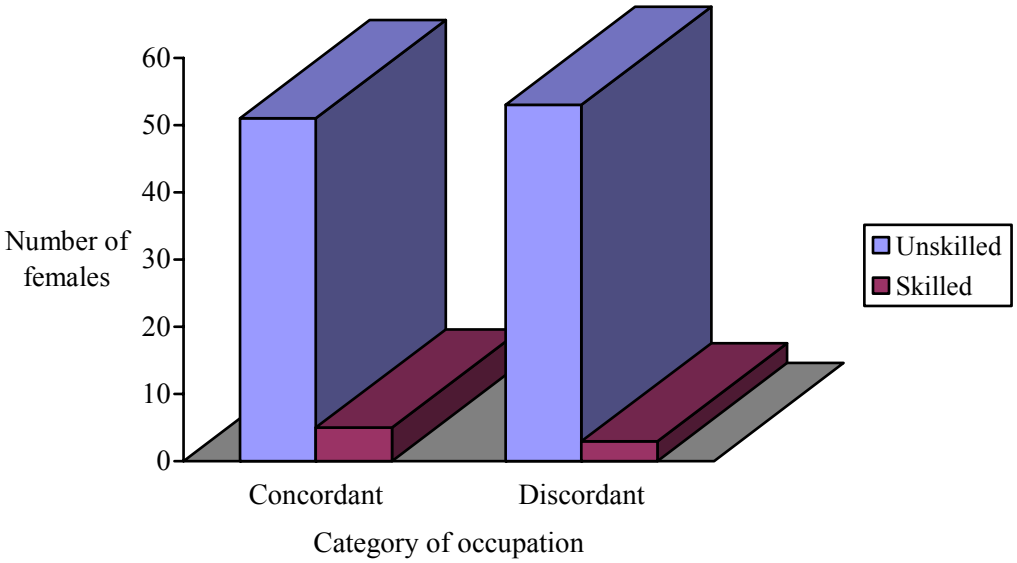


Figure 6: shows the distribution of occupation of 112 females



7.1.4 EDUCATION:

87.7% of the men and 84.8% of the women were educated.

Figure 7: shows the distribution of educational qualification of 112 males

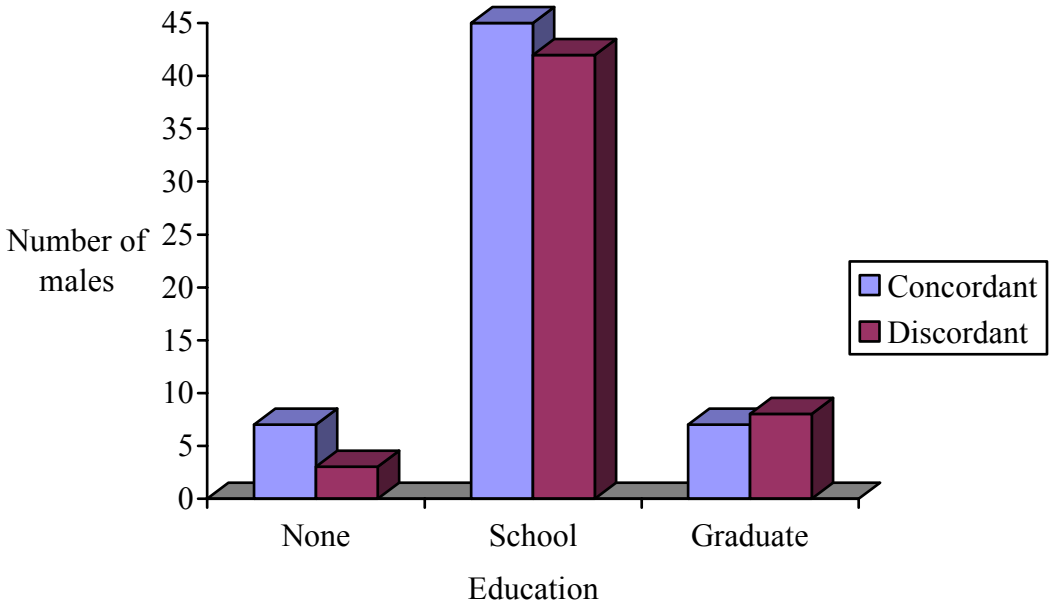
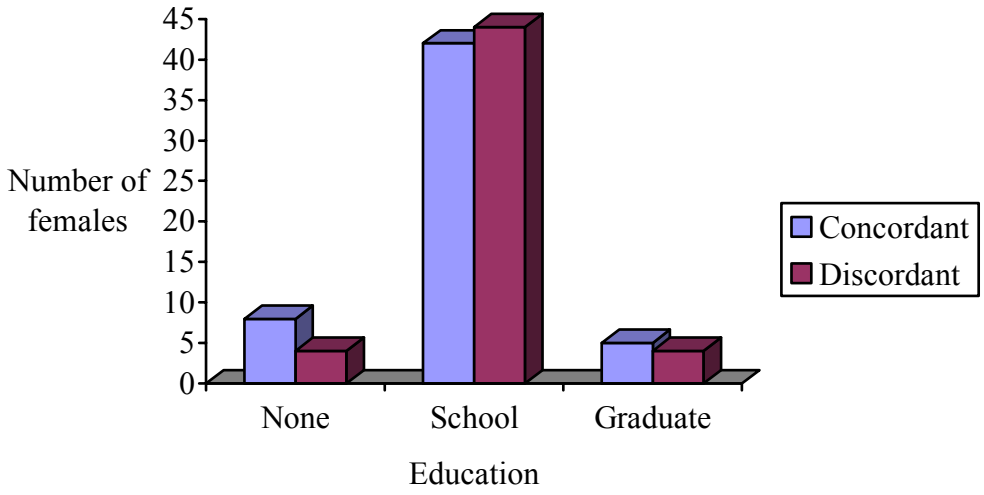


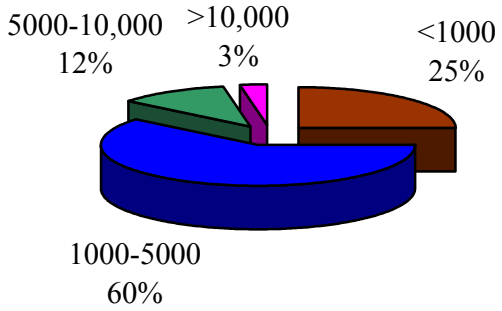
Figure 8: shows the distribution of educational qualification of 112 females



7.1.5 SOCIO-ECONOMIC STATUS:

83.9% of families with discordant couples and 87.5% with concordant couples belonged to the lower socio-economic category, their income being < Rs.5000/month Among the women who worked, 66.7% earned <Rs.1000/month.

Figure 9: shows the income distribution of 112 families



7.1.6 YEARS OF LIVING TOGETHER AS MARRIED COUPLES:

65.3% of the couples had been married for 10 years or less.

TABLE 3: SHOWS THE DISTRIBUTION OF DEMOGRAPHIC CHARACTERISTICS OF 56 CONCORDANT AND 56 DISCORDANT COUPLES

Serial No.	DEMOGRAPHIC VARIABLES	DISCORDANT MALES n=56 (%)	DISCORDANT FEMALES n=56 (%)	CONCORDANT MALES n=56 (%)	CONCORDANT FEMALES n=56 (%)
1	**Age**				
	<=34	13(23.2)	35(62.5)	19(33.9)	45(80.3)
	35-44	32(57.1)	16(28.6)	30(53.6)	7(12.5)
	>=44	11(19.6)	5(8.9)	7(12.5)	4(7.1)
2	**Occupation**				
	Unskilled	22(39.3)	53(94.6)	27(48.2)	51(91.1)
	Skilled	33(58.9)	3(5.4)	29(51.8)	5(8.9)
3	**Education**				
	None	3(5.3)	4(7.1)	7(12.5)	8(14.3)
	School	42(75)	44(78.6)	45(80.3)	42(75)
	Graduate/postgraduate	8(14.3)	4(7.1)	4(7.1)	5(8.9)
4	**Income**				
	None		45(80.3)		43(76.8)
	<1000	12(21.4)	7(12.5)	16(28.6)	9(16)
	1000-5000	35(62.5)	4(7.1)	33(58.9)	4(7.1)
	>5000	9(16)		7(12.5)	
5	**Domicile**				
	TamilNadu	41(73.2)		33(58.9)	
	AndhraPradesh	13(23.2)		22(39.3)	
	Karnataka	2(3.6)		1(1.8)	
6	**Number of children**				
	None	9(16.1)		12(21.4)	
	1	9(16.1)		11(19.6)	
	2	24(42.9)		25(44.6)	
	>2	14(25)		8(14.3)	

TABLE 4: SHOWS THE DISTRIBUTION OF FACTORS INFLUENCING TRANSMISSION AMONG 56 DISCORDANT AND CONCORDANT COUPLES (n=224)

Serial No.	FACTORS AFFECTING TRANSMISSION	DISCORDANT MALES n=56 (%)	DISCORDANT FEMALES n=56 (%)	CONCORDANT MALES n=56 (%)	CONCORDANT FEMALES n=56 (%)
1	**Duration of marriage**				
	<2 years	2(3.6)		4(7.1)	
	2-5	6(10.7)		6(10.7)	
	6-10	17(30.3)		21(37.5)	
	>10	31(55.3)		25(44.6)	
2	**Other sex partners**				
	None	15(29.4)	4(80)		
	1	13(25.5)	1(20)		
	>1	23(45.1)			
3	**Duration since last exposure**				
	None	20(35.7)	55(98.2)	17(30.3)	54(96.4)
	<6 months	1(1.8)		1(1.8)	2(3.6)
	7-12 months	5(8.9)		0	
	>1 year	30(53.6)	1(1.8)	38(67.8)	
4	**Clinical stage**				
	1	20(35.7)	1(1.8)	25(44.6)	45(80.3)
	2	3(5.3)	2(3.6)	3(5.3)	1(1.8)
	3	18(32.1)	1(1.8)	24(42.8)	4(7.1)
	4	9(16)	0	4(7.1)	
5	**CD4 count**				
	<200	20(35.7)	1(1.8)	28(50)	15(26.8)
	200-350	11(19.6)	1(1.8)	16(28.6)	11(19.6)
	>350	16(28.6)	2(3.6)	6(10.7)	22(39.3)
6	**Anti-retroviral use**				
	No	49(87.5)	4(7.1)	53(94.6)	55(98.2)
	Yes	2(3.6)	1(1.8)	3(5.4)	1(1.8)
7	**Condom use**				
	absent	52(92.8)		53(94.6)	
	present	4(7.2)		3(5.4)	
8	**Blood transfusion**				
	No	54(96.4)	53(94.6)	54(96.4)	54(96.4)
	Yes	2(3.6)	3(5.4)	2(3.6)	2(3.6)
9	**IV drug use**				
	No	56(100%)	56(100)	54(96.4)	56(100)
	Yes	0		2(3.6)	
10	**Smoking**				
	No	38(67.9)	56(100)	30(53.6)	56(100)
	Yes	18(32.1)		26(46.4)	

TABLE 4: SHOWS THE DISTRIBUTION OF FACTORS INFLUENCING TRANSMISSION AMONG 56 DISCORDANT AND CONCORDANT COUPLES (n=224) (CONTD)

Serial No.	FACTORS AFFECTING TRANSMISSION	DISCORDANT MALES n=56 (%)	DISCORDANT FEMALES n=56 (%)	CONCORDANT MALES n=56 (%)	CONCORDANT FEMALES n=56 (%)
11	**Alcohol**				
	0	30(53.6)	56(100)	22(39.3)	56(100)
	1-2/week	12(21.4)		10(17.8)	
	3-5/week	5(8.9)		10(17.8)	
	daily	9(16)		14(25)	
12	**Past genital ulcers**				
	9.	41(73.2)	51(91)	36(64.3)	44(78.6)
	Yes	15(26.8)	5(8.9)	20(35.7)	12(21.4)
13	**Present genital ulcers**				
	No	50(89.3)	55(98.2)	53(94.6)	54(96.4)
	Yes	6(10.7)	1(1.8)	3(5.4)	2(3.6)
14	**Past urethro-vaginal discharge**				
	No	50(89.3)	48(85.7)	44(78.6)	40(71.4)
	Yes	6(10.7)	8(14.3)	12(21.4)	16(28.6)
15	**Present urethro-vaginal discharge**				
	No	55(98.2)	51(91.1)	56(100)	46(82.1)
	Yes	1(1.8)	5(8.9)	0	10(17.9)
16	**Past STI**				
	None	53(94.6)	56(100)	52(92.8)	54(96.4)
	Herpes			3(5.4)	1(1.8)
	Syphilis	3(5.4)		1(1.8)	
	Candida				1(1.8)
17	**Present STI**				
	None	54(96.4)	55(98.2)	54(96.4)	53(94.6)
	Herpes	1(1.8)	1(1.8)	1(1.8)	
	Syphilis	1(1.8)			
	Candida				3(5.4)
	Warts			1(1.8)	
16	**VDRL**				
	Reactive	2(3.6)		1(1.8)	1(1.8)
	Non-reactive	33	32	36	38
17	**Circumcision**				
	yes	3(5.4)		2(3.6)	
	no	53		54	

7.2 FACTORS AFFECTING TRANSMISSION:

7.2.1 AGE:

Husband's age being ≤34 years is associated with an OR 2.30 (95% CI 0.71-7.49; p=0.17) for the couple being HIV concordant.

Wife's age ≥35 years is associated with an odds 2.18 (95% CI 0.93-1.02; p=0.33) for the couple being concordant.

7.2.2. OCCUPATION:

Having an unskilled occupation is associated with an OR 1.40 (95% CI 0.66-2.96; p=0.38) in men and OR 0.42 (95% CI 0.16-1.15; p=0.09) among women for HIV transmission.

7.2.3. INCOME:

The risk of HIV transmission for those who earned <Rs.1000/month is OR 0.7 (p=0.36) and is 1.7 (p=0.38) for those who earned between Rs.1000 and 5000 /month.

7.2.4. EDUCATION:

School educated males have a risk of HIV transmission OR 4.66 (95% CI 0.77-28.45; p=0.09).Graduates and post-graduates have an OR 2.14 (95% CI 0.60 –

7.64; p=0.24). A similar increased risk 1.60 (95% CI 0.27-9.28; p=0.6) is found among females who were school educated. Female graduates and post-graduates have an OR 0.76 (95% CI 0.19-3.03; p=0.70) for transmission.

7.2.5. YEARS OF LIVING TOGETHER:

The risk of acquiring HIV infection is 0.97 (95% CI 0.93-1.02; p=0.27) for each additional year of living together.

7.2.6. NUMBER OF CHILDREN:

In couples who had one child the OR for transmission is 0.91(95% CI 0.26-3.14; p=0.89). Couples who have two children or more have a risk of 0.78 (95% CI 0.27-2.18; p=0.63) and 0.42 (95% CI 0.12-1.45; p=0.17) for transmission.

7.2.7. OTHER SEX PARTNERS:

The risk for reported intercourse with partners other than spouse is 0.84 (95% CI 0.49-2.49; p=1.09) for men and 2.03(95% CI 0.18- 23.13; p=0.57) for women.

7.2.8 LAST EXPOSURE:

Male patients who had their last sexual exposure with a person other than spouse more than a year ago have a risk of 1.11(95% CI 0.85-1.45; p=0.45) for HIV concordance compared to those who had their last exposure outside marriage less

than a year ago. Females have an OR 0.83 (95% CI 0.24- 2.84; p=0.76) for transmission if their last exposure outside marriage was more than one year ago.

7.2.9 BLOOD TRANSFUSION:

Previous blood transfusion in males and females is associated with an OR 1 (95% CI 0.14-7.36; p=1.0) and 0.65 (95% CI 0.11-4.07; p=0.65) respectively for HIV transmission.

7.2.10 IV DRUG USE:

Only 2 men among concordant couples reported IV drug use. OR 2E+009; p=0.99

7.2.11 SMOKING:

Smoking in the husband was associated with a risk of 1.83 (95% CI 0.85-3.95; p=0.12) for HIV transmission.

7.2.12 ALCOHOL:

Fewer males among discordant couples [26 (46.43%)] consumed alcohol than concordant couples [34 (60.71%)]. Consumption of 3 or more drinks per week and drinking daily were associated with a risk of 2.72(95% CI 0.82-9.11; p=0.10) and 2.12(95% CI 0.78-5.78; p=0.14) for HIV transmission.

7.2.13 CLINICAL STAGING:

Males who had a WHO clinical stage of 3 and 4 have a risk of 1.08(p=0.83) for transmitting HIV compared to males in stages 1 and 2

7.2.14 CD4 LYMPHOCYTE COUNT:

Males whose CD4 lymphocyte counts were < 200/mm^3 and 200-350/mm^3 have an OR 3.73 (p=0.02) and 3.88 (p=0.03) for HIV transmission respectively.

Females whose CD4 lymphocyte counts were < 200/mm^3 and 200-350/mm^3 have an OR 1.36 (p=0.80) and 1 (p=1.0) for HIV transmission respectively.

7.2.15 ANTI-RETROVIRAL USE:

Males who were not on ART had a risk of 1.38 (95% CI 0.22-8.65; p=0.73) for HIV transmission. The risk was 0.07 (95% CI 0.00-1.39; p=0.08) in females who were not on ART.

7.2.16 FREQUENCY OF INTERCOURSE PRIOR TO SERODETECTION:

An increase in the frequency of sexual intercourse by 1/month increased the risk of HIV transmission by 1.042 (95% CI 0.999-1.087; p=0.05).

7.2.17 FREQUENCY OF INTERCOURSE AFTER SERODETECTION:

Decreased frequency of intercourse of < 2/month was associated with a 36% lower chance of HIV transmission. Increased frequency of intercourse ≥ 2/month was associated with a risk of 1.39 (p=0.37) for transmission.

7.2.18 CONDOM USE:

Condom use lowered the risk of HIV transmission by 35% (95% CI 0.17-2.45; p=0.52).

7.2.19 OTHER CONTRACEPTIVES:

Use of other non-barrier contraceptive methods had a protective effect of 32% on transmission.

Table 5 shows the number of patients using contraceptives other than condoms

	Frequency (%) Concordant	Frequency (%) Discordant
Tubectomy	7(46.7)	8(53.3)
OCP's	0	1(100)
Copper T	1(33.3)	2(66.7)

7.2.20 PREVIOUS GENITAL ULCERS：

History of previous genital ulcers is associated with an OR 1.52 (95% CI 0.68 – 3.40; p=0.31) for transmission in males and an OR 2.78 (95% CI 0.91-8.51; p=0.07) for transmission in females.

7.2.21 CURRENT GENITAL ULCERS：

Presence of genital ulcers in the male at the time of detection of HIV infection is associated with a risk of 0.47 (95% CI 0.11-1.99; p=0.31) for transmission. The risk of

transmission in females who had active genital ulcer disease is 2.04 (95% CI 0.18 – 23.13; p=0.57).

7.2.22 PREVIOUS URETHRO – VAGINAL DISCHARGE：

Previous urethral discharge in males is associated with a risk of 2.27 (95% CI 0.79-6.56; p=0.13) for transmission. The risk of HIV transmission in females with urethral or vaginal discharge is 2.40 (95% CI 0.93-6.18; p=0.07).

7.2.23 CURRENT URETHRO – VAGINAL DISCHARGE：

Current active UV discharge in the female is associated with an increased risk of 2.22 (95% CI 0.71-6.97; p=0.17) for HIV transmission.

7.2.24 PREVIOUS SEXUALLY TRANSMITTED DISEASE:

Presence of syphilis in the husband is associated with a risk of 0.34 (p 0.36) for transmission.

7.2.25 CURRENT SEXUALLY TRANSMITTED DISEASE:

Active genital herpes is associated with a risk of 1(95% CI 0.06-16.40; p=1.0) for transmission.

7.2.26 VDRL POSITIVITY：

Only one concordant couple and 2 males among the discordant couples had a positive VDRL test. Being VDRL non-reactive has a 54% protective effect from HIV transmission.

7.2.27 CIRCUMCISION：

Males who were circumcised have a 35% lesser chance of transmitting HIV infection than whose who did not (95% CI 0.11-4.07; p=0.65).

MULTIVARIATE ANALYSIS

On multivariate analysis, the only variable that affected transmission significantly was the CD4 count of the husband. A CD4 count of < 200 was associated with an odds ratio of 4.24 (95% CI 1.20-14.93; p=0.02) .A CD4 count between 200 – 350 was associated with an odds ratio of 4.15 (95% CI 1.05 -16.40; p=0.04).

Table 6 Data of multivariate analysis

VARIABLES	**Odds ratio**	**P value**	**95% CI**
IV drug use husband	7E+008	0.99	0.00
Smoking-husband	2.21	0.09	0.88-5.59
CD4 husband<200	**4.24**	**0.02**	**1.20-14.93**
CD4 husband 200-350	**4.15**	**0.04**	**1.05-16.40**
Age husband	0.97	0.63	0.86-1.09
Age wife	1.01	0.86	0.90-1.13
Present discharge husband	0.00	1.00	0.00
Present discharge wife	1.21	0.80	0.28-5.20
Present STI wife	1.85	0.32	0.55-6.26
Present STI husband	1E+009	0.99	0.00

TABLE 7: DISTRIBUTION OF FACTORS INFLUENCING TRANMISSION AMONG 56 DISCORDANT AND CONCORDANT COUPLES BASED ON THE PROBABLE MODE OF TRANSMISSION:

Serial No.	FACTORS INFLUENCING MODE OF TRANSMISSION	DISCORDANT MALE PARTNER + (n=51) (%)	DISCORDANT FEMALE PARTNER + (n=5) (%)	CONCORDANT M→F (n=33) (%)	CONCORDANT F→M (n=7) (%)
1	**Duration of marriage**				
	<2 years	3(5.8)	0	1(3)	0
	2-5	6(11.7)	0	3(9)	0
	6-10	16(31.3)	1(20)	12(36.3)	4(57.1)
	>10	26(50.9)	4(80)	17(51.5)	3(42.9)
2	**Other sex partners**				
	None	15(29.4)	4(80)	7(21.2)	6(85.7)
	1	13(25.5)	1(20)	10(30.3)	1(14.3)
	>1	23(45.1)		16(48.5)	
3	**Clinical stage**				
	1	21(41.2)	2(40)	4(12.1)	1(14.3)
	2	3(5.9)	2(40)	3(9.1)	0
	3	18(35.3)	1(20)	22(66.7)	2(28.6)
	4	9(17.6)	0	4(12.1)	4(57.1)
4	**CD4 count**				
	<200	20(39.2)	1(20)	24(72.7)	7(100)
	200-350	11(21.6)	1(20)	6(18.2)	0
	>350	16(31.4)	2(40)	0	0
5	**Past ulcers transmitting partner**				
	absent	36(70.6)	5(100)	25(75.8)	2(28.6)
	present	15(29.4)	0	8(24.2)	5(71.4)
6	**Past ulcers acquiring partner**				
	absent	46(90.2)	5(100)	29(87.9)	2(28.6)
	present	5(9.8)	0	4(12.1)	5(71.4)
7	**Present ulcers transmitting partner**				
	absent	45(88.2)	5(100)	32(97)	6(85.7)
	present	6(11.8)	0	1(3)	1(14.3)
8	**Present ulcers acquiring partner**				
	absent	50(98)	5(100)	32(97)	6(85.7)
	present	1(2)	0	1(3)	1(14.3)

Serial No.	FACTORS INFLUENCING MODE OF TRANSMISSION	DISCORDANT MALE PARTNER + (n=51) (%)	DISCORDANT FEMALE PARTNER + (n=5) (%)	CONCORDANT M→F (n=33) (%)	CONCORDANT F→M (n=7) (%)
9	**Past discharge transmitting partner**				
	absent	46(90.2)	5(100)	27(81.8)	3(42.9)
	present	5(9.8)	0	6(18.2)	4(57.1)
10	**Past discharge acquiring partner**				
	absent	43(84.3)	5(100)	26(78.8)	4(57.1)
	present	8(15.7)	0	7(21.2)	3(42.9)
11	**Present discharge transmitting partner**	.			
	absent	50(98)	5(100)	33(100)	4(57.1)
	present	1(2)	0	0	3(42.9)
12	**Present discharge acquiring partner**				
	absent	46(90.2)	5(100)	29(87.9)	7(100)
	present	5(9.8)	0	4(12.1)	0
13	**Anti-retroviral therapy**	2(3.9)	1(20)	1(3)	0
14	**VDRL reactive**	2(3.9)	0	1(3)	0
15	**Circumcision**	2(3.9)	1(20)	2(6)	0
16	**Previous STI**				
	Syphilis	3(5.9)	0	1(3)	0
	Genital herpes	0	0	2(6)	0
	Vaginal candidiasis	0	0	1(3)	0
17	**Present STI**				
	Syphilis	1(2)			
	Genital herpes	1(2)		1(3)	
	Vaginal candidiasis			1(3)	1(14.3)

TABLE 8: SHOWS THE DISTRIBUTION OF FACTORS INFLUENCING TRANSMISSION IN 16 COUPLES IN WHOM TRANSMISSION WAS UNSURE

Serial No.	VARIABLE	CONCORDANT TRANSMISSION UNSURE-MALE	CONCORDANT TRANSMISSION UNSURE-FEMALE
1	**Duration of marriage**		
	<2 years	3	
	2-5 years	3	
	6-10 years	6	
	>10 years	4	
2.	**Other sex partners**		
	None	8(50)	16(100)
	1	0	0
	>1	8(50)	0
3.	**Clinical stage**		
	1	14(87.5)	13(81.3)
	2	0	0
	3	2(12.5)	2(12.5)
	4	0	1(6.2)
4.	**CD4 count**		
	<200	3(18.8)	6(37.5)
	200-350	6(37.5)	5(31.2)
	>350	4(25)	3(18.8)
5.	**Past genital ulcers**		
	absent	9(56.2)	13(81.2)
	present	7(43.8)	3(18.8)
6.	**Present genital ulcers**		
	absent	15(93.8)	16(100)
	present	1(6.2)	0
7.	**Past discharge**		
	absent	13(81.2)	11(68.8)
	present	3(18.8)	5(31.2)
8.	**Present discharge**		
	absent	16(100)	13(81.2)
	present	0	3(18.8)
9.	**Previous STI**		
	Herpes	1(6.2)	1(6.2)
10.	**Present STI**		
	Warts	1(6.2)	
	Candidiasis		1(6.2)
11.	**Anti-retroviral therapy**	2(12.4)	1(6.2)
12.	**VDRL reactive**	0	0
13.	**Circumcision**	0	0

Longer duration of marriage was associated with higher rates of HIV transmission. But there was an equally large number of patients who had been married for >10 years in the group that had not yet transmitted the infection.

The risk of HIV transmission from male to female among those with clinical stage 3 and 4 compared to 1 and 2 was 2.17(95% CI 1.07-4.40) .

The risk of HIV transmission from female to male was 3.42 (95% CI 0.61-19.22) for those with stage 3 and 4 compared to stage 1 and 2.

Among the concordant group, 5 were asymptomatic transmitting partners (4 male and 1 female).Among the discordant group,22 were asymptomatic transmitting partners (21 male and 1 female).

None had a clinical stage of 1 or 2 along with a CD4 count of >350, used condoms and yet transmitted infection. However, 21(**37.5%**) of the index partners had a clinical stage of 3 or 4 along with a CD4 count of <350, never used condoms and did not transmit the infection.

The number who had blood transfusion alone as the sole mode of transmission was **1 in the concordant group** (where the probable mode of transmission was from male to

female) and **4 in the discordant group,** one in which the male was the index partner and three where the female was the index partner.

7.3 FACTORS ASSOCIATED WITH HIV SERODISCORDANCE

7.3.1 SOCIAL FACTORS:

7.3.1.1 ALCOHOL:

Alcohol consumption is significantly lower in the discordant group 42.4% compared with 57.6% in the concordant group and lesser alcohol consumption has an odds of 1.2 for discordance.

7.3.1.2 SMOKING:

The number of males who smoked is lower in the discordant group 40.9% vs. 59.1% in the concordant group. Lesser smoking had odds of 1.2 for discordance.

7.3.2 BEHAVIOURAL FACTORS:

7.3.2.1 DURATION OF MARRIAGE:

The number of discordant couples who were married for <5 years are more than the number of concordant couples married for the same duration 69.2% vs. 30.8% but this does not have a significant effect on transmission (OR 0.85 ; 95% CI 0.56-1.28).

7.3.2.2 PREVIOUS GENITAL ULCERS:

This is associated with an OR of 0.9 for discordance.

7.3.2.3 CURRENT GENITAL ULCERS:

The OR for discordance is 0.7

7.3.2.4 PREVIOUS URETHRO-VAGINAL DISCHARGE:

Past discharge is associated with an odds of 1.3 for non-transmission.

7.3.2.5 PRESENT URETHRO-VAGINAL DISCHARGE:

This has an OR 0.6 for HIV discordance

7.3.2.6 CLINICAL STAGE OF DISEASE:

Stage of disease of 1or 2 is associated with an OR 1.5 for discordance.

7.3.2.7 CD4 COUNT:

CD 4 count > 350 is associated with an OR of 1.9 for discordance.

We found that 30 couples who were HIV serodiscordant had lived together for more than 10 years and yet not transmitted HIV to the uninfected partner. To study the factors which protected them from such transmission, they were compared with 24 HIV seroconcordant couples who had also lived as partners for more than 10 year duration. There was a lower frequency of sexual intercourse prior to serodetection(i.e

<5 episodes per month) in the discordant group compared to concordant [73% vs.50%] and an increase in condom use after serodetection [23.3% vs.8.4%].23.1% of the serodiscordant males had CD4 lymphocyte counts more than 350 cells compared to 12.5% of the concordant males.

8.0 DISCUSSION

HIV transmission is known to be affected by several factors. There are a large number of HIV sero-discordant partners in whom transmission does not occur despite several years of living in partnership. In a cross-sectional study done in Chennai, this number was reported to be 44%.[4]

This study was there-fore done to identify the risk factors for HIV transmission and to identify factors which protect against transmission by comparing the group in which transmission has already occurred (concordant) with the group in which transmission to the spouse has not yet occurred.

Social factors:

Regular alcohol consumption was associated with an increased the risk of HIV transmission. This has been shown before in several studies. For men, heavier alcohol use is known to be associated with having multiple sex partners in the past month, less condom use, and having a history of sexually assaulting women. [59, 60].

Smoking is also associated with an increased risk of HIV transmission. Lesser alcohol consumption and smoking had a protective effect of 12% for discordance.

Intravenous drug use is not prevalent in this cohort of patients studied as only 2 males who were in a seroconcordant partnership had been abusing IV drugs. The female was the probable index partner in one such partnership and in the other, we are unsure of the probable mode of transmission.

Sexual behavioural patterns:

The women who had other sex partners outside the marital relationship had an increased risk of HIV acquisition. This was probably due to the greater chance of acquiring the disease in women due to the favourable large surface area of the vaginal

mucosa which contains more number of host cell macrophages ,Langerhan's and dendritic cells needed for the virus to be transmitted[8] and the presence of a low pH which is favourable for virus replication.[61]

Risk of HIV seroconversion was higher for those who had their last sexual exposure with a person other than spouse more than a year ago. The risk of HIV acquisition did not significantly increase with the duration of living in partnership or with more number of children. Increased frequency of intercourse increased the risk of HIV transmission and use of condoms regularly had a 35% protective effect.

Previous genital ulcers in both partners and current ulcers in females was associated with an increased risk for transmission. Similarly, urethro-vaginal discharge in both partners had an increased risk for transmission. However, the number of diagnosed STI's were low. Therefore these ulcers could represent those due to trauma or other causes and not necessarily implicate an STI.

Circumcision in the male partner provided a 35% protective effect from acquiring HIV.

Clinical stage of HIV disease:

Increased transmission occurred at advanced clinical stage of disease (WHO stage 3 and 4 compared to 1 and 2). Stage 3 and 4 disease is the group in which we expect the viral loads to be higher and therefore facilitate transmission.

CD4 lymphocyte counts:

This study found that CD4 counts <350 in male partners were significantly associated with risk of acquiring HIV. This could indirectly reflect the fact that higher viral loads present in such people with low CD4 counts influences transmission. This

supports the current recommendation that ART be initiated at CD4 lymphocyte counts < 350 cells/mm^3.

Use of antiretroviral agents:

Only 4 patients -3 discordant and 1 concordant were on ART. This was because many of the patients were recently detected to be HIV infected and had not been initiated on ART. Also, around 50% of the patients had an early stage of HIV disease. Therefore, they were not initiated on ART.

This study was limited by the numbers of couples included. Many of the factors were not statistically significant because of the lesser numbers studied. It is therefore planned to continue the study to enroll 109 concordant and 109 discordant couples.

The main implication of this study is to prevent HIV transmission by counseling partners on safe sexual practices, regular use of barrier contraceptives-mainly condoms, lesser indulgence in alcohol, identification of genital ulcers and seeking appropriate medical help. Also, early initiation of antiretroviral therapy at CD4 lymphocyte counts < 350 cells/mm^3 would prevent HIV transmission to the un-infected partner.

9. 0 CONCLUSION

9.1 The social factor affecting HIV transmission is alcohol consumption in the male.

9.2 The sexual behaviour factors affecting transmission were sex with partners other than spouse, past or present genital ulcer disease and urethro-vaginal discharge.

9.3 The risk of transmission increased with an advanced clinical and immunological stage of disease.

9.4 Lower frequency of sexual intercourse, regular use of barrier contraception prevented HIV transmission among those serodiscordant couples living together for a period of more than 10 years. Therefore, counseling on safe sexual practices including reduction of frequency of intercourse and regular use of condoms should be intensified.

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11.0 PROFORMA

COUPLE NAME:

COUPLE HOSPITAL NUMBER:

QUESTIONNAIRE ADMINISTERED TO MALE / FEMALE PARTNER:

Name-

Age -

Sex -

Occupation-

Education- none / school / graduate / post-graduate.

Income per month - <1000 / 1000-5000 / 5000-10,000 / >10,000

Address-

Living together or not- Yes/No

No. of years of living together-

No of children-

HIV status of patient-

Time since detection of serostatus-

Any other sexual partners till date-

Number of other sexual partners till date-

Time since last sexual exposure
outside this relationship - <6 months/7 months -1 year/>1 year.

Any blood transfusions-

Any IV drug use-

Smoking - present/absent.

Alcohol- (number of drinks per week) - 1-2 / 3-5 / drinks everyday.

Clinical staging of disease-

CD 4 count-

Any anti-retro viral medications taken-

FREQUENCY OF SEXUAL INTERCOURSE BEFORE HIV STATUS KNOWN-

No. of episodes of sexual intercourse per month-

No. of episodes in which condoms were used per month-

FREQUENCY OF SEXUAL INTERCOURSE AFTER HIV STATUS IS KNOWN-

No. of episodes of sexual intercourse per month-

No. of episodes in which condoms were used per month –

Any other contraceptive practices followed- Yes/No

If yes, what - OCP's / barrier methods / spermicides

Presence of ulcerative genital lesions in the past-

Presence of ulcerative genital lesions at present –

History of urethral/vaginal discharge in the past-

History of urethral/vaginal discharge at present-

Any particular diagnosis made for the previous STI-

History of treatment received for the same-

Diagnosis of current STI-

VDRL status-

Circumcision in male partner-

No. of joint counseling sessions-

12. APPENDIX

12.1 APPENDIX 1: WHO CLINICAL STAGING OF HIV DISEASE

Primary HIV Infection

Asymptomatic

Acute retroviral syndrome

Clinical Stage 1

Asymptomatic

Persistent generalized lymphadenopathy

Clinical Stage 2

Moderate unexplained weight loss (<10% of presumed or measured body weight)

Recurrent respiratory infections (respiratory tract infections, upper respiratory infections, sinusitis, bronchitis, otitis media, pharyngitis)

Herpes zoster

Minor mucocutaneous manifestations (angular cheilitis, recurrent oral ulcerations, seborrheic dermatitis, prurigo, papular pruritic eruptions, fungal fingernail infections)

Clinical Stage 3

Conditions for which a presumptive diagnosis can be made on the basis of clinical signs or simple investigations

Severe weight loss (>10% of presumed or measured body weight)

Unexplained chronic diarrhea for >1 month

Unexplained persistent fever for >1 month (intermittent or constant)

Oral candidiasis (thrush)

Oral hairy leukoplakia

Pulmonary tuberculosis within the last 2 years

Severe presumed bacterial infections (eg, pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteremia)

Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis

Conditions for which confirmatory diagnostic testing is necessary

Unexplained anemia (hemoglobin <8 g/dL)

Neutropenia (neutrophils <500 cells/μL)

Thrombocytopenia (platelets <50,000 cells/μL)

Clinical Stage 4

Conditions for which a presumptive diagnosis can be made on the basis of clinical signs or simple investigations

- HIV wasting syndrome, (involuntary weight loss >10% of baseline body weight) associated with either chronic diarrhea (≥2 loose stools per day ≥1 month) or chronic weakness and documented fever ≥1 month
- Pneumocystis jiroveci (formerly carinii) pneumonia
- Recurrent severe or radiologic bacterial pneumonia
- Chronic herpes simplex infection (oral or genital, or anorectal site) for >1 month
- Esophageal candidiasis
- Extrapulmonary tuberculosis
- Kaposi sarcoma
- Central nervous system toxoplasmosis
- HIV encephalopathy

Conditions for which a confirmatory diagnostic testing is necessary

- Cryptococcosis, extra pulmonary
- Disseminated nontuberculosis *Mycobacteria* infection
- Progressive multifocal leukoencephalopathy
- *Candida* of the trachea, bronchi, or lungs
- Cryptosporidiosis
- Isosporiasis
- Visceral herpes simplex infection, cytomegalovirus infection (retinitis or organ other than liver, spleen, or lymph node)
- Any disseminated mycosis (eg, histoplasmosis, coccidioidomycosis, penicilliosis)
- Recurrent nontyphoidal Salmonella septicemia
- Lymphoma (cerebral or B-cell non-Hodgkin)
- Invasive cervical carcinoma
- Visceral leishmaniasis

12.2 APPENDIX 2: GLOSSARY TO MASTER CHART

Occupation

1-unskilled labourer

2-housewife

3-skilled labourer

4-police/army

5-professional

6-businessman

7-unemployed

Education

1-none

2-school

3-graduate

4-postgraduate

Address

1-TamilNadu

2-AndhraPradesh

3-Karnataka

HIV status

1-positive

2-negative

Any sexual partners outside marital relationship

0-no

1-yes

Time since last sexual exposure outside marriage

0-none

1-< 6 months

2-7-12 months

3->12 months

Blood transfusions, intravenous drug use, smoking

0-no

1-yes

Alcohol

0-none

1-1-2 per week

2-3-5 per week

3-drinks daily

ART use

0-no

1-yes

Condom use

0-none

1-occasionally

2-always

Other contraceptives

0-none

1-tubectomy

2-oral contraceptive pills

3-copper T

Presence of genital ulcers or urethro-vaginal discharge

0-no

1-yes

Diagnosis of previous or current STI

0-none

1-syphilis

2-herpes

3-candida

4-viral warts

VDRL status

0-nonreactive

1-reactive

Male circumcision

0-no

1-yes

12.3 MASTER CHART OF DISCORDANT COUPLES IN THE STUDY

12.4 MASTER CHART OF CONCORDANT COUPLES IN THE STUDY