DISSERTATION ON

THE IMPACT OF HIV ON VARIOUS SEXUALLY TRANSMITTED INFECTIONS

Submitted in partial fulfilment of

Requirements for

M.D. DEGREE BRANCH I GENERAL MEDICINE

OF

THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY, CHENNAI

INSTITUTE OF INTERNAL MEDICINE

MADRAS MEDICAL COLLEGE

CHENNAI – 600 003

APRIL – 2011

CERTIFICATE

This is to certify that this dissertation entitled **"THE IMPACT OF HIV ON VARIOUS SEXUALLY TRANSMITTED INFECTIONS"** submitted by **Dr. THYAGARAJAN. N.** appearing for Part II M.D. Branch I General Medicine Degree examination in April 2011 is a bonafide record of work done by him under my direct guidance and supervision in partial fulfillment of regulations of the Tamil Nadu Dr. M.G.R. Medical University, Chennai. I forward this to the Tamil Nadu Dr.M.G.R. Medical University, Chennai, Tamil Nadu, India.

The Professor,
Institute of Internal Medicine,
Madras Medical College,
Government General Hospital.

The Director and Professor,
Institute of Internal Medicine,
Government General Hospital,
Chennai – 600 003.

The Dean,
Madras Medical College,
Government General Hospital
Chennai – 600 003.

DECLARATION

I solemnly declare that the dissertation titled **"THE IMPACT OF HIV ON VARIOUS SEXUALLY TRANSMITTED INFECTIONS"** is done by me at Madras Medical College & Govt. General Hospital, Chennai during 2009-2010 under the guidance and supervision of Prof. R. SUKUMAR, M.D.

The dissertation is submitted to The Tamilnadu Dr. M.G.R. Medical University towards the partial fulfillment of requirements for the award of M.D. Degree (Branch I) in General Medicine.

Place:

Date:

Dr. THYAGARAJAN N.
M.D. (General Medicine),
Postgraduate Student,
Institute of Internal Medicine,
Madras Medical College.

ACKNOWLEDGEMENT

I would like to thank my beloved Dean, Madras Medical College **Prof. J. Mohana Sundaram, M.D., Ph.D., DNB.,** for his kind permission to use the hospital resources for this study.

I would like to express my sincere gratitude to my beloved Professor and Director, Institute of Internal Medicine, **Prof. C. Rajendiran, M.D.,** for his guidance and encouragement.

With extreme gratitude, I express my indebtedness to my beloved Chief and teacher **Prof. R. Sukumar, M.D.,** for his motivation, advice and valuable criticism, which enabled me to complete this work.

I would like to express my sincere thanks to our **Prof. Raghunanthanan, M.D.,** for permitting me to do my study in ART clinic.

I am extremely thankful to Assistant Professors of Medicine **Dr. S. Deepa, M.D., and Dr. R. Sharmila, M.D.,** for their co-operation and guidance.

I thank the entire **ART team** for their extreme cooperation extended to me without whom the study would not have been possible. I especially like to thank **Dr. S. Sekar**, senior medical officer, ART centre for his co-operation and guidance.

I would always remember with extreme sense of thankfulness for the co-operation and criticism shown by my Postgraduate colleagues.

I am immensely grateful to the generosity shown by the patients who participated in this study. If at all, this study could contribute a little to relieve them from their suffering I feel that I have repaid a part of my debt.

I am extremely thankful to my family members for their continuous support. Above all I thank my God Almighty for His immense blessings.

CONTENTS

INTRODUCTION

HIV infection/AIDS is pandemic, with cases reported from nearly every country in the world. Unlike other epidemics, AIDS falls most heavily on young adults in their prime, posing a grave challenge in the areas of health, social and economic development .

Demographically, being the second largest country in the world, India also has the third largest number of people living with HIV/ AIDS. As per the Annual HIV Report of NACO -2010, there are an estimated 22.7 lakh people living with HIV/ AIDS in India[1,2,3]. The HIV prevalence in the country is 0.29 % and most infections occur through heterosexual route of transmission.

Modes of transmission of HIV

By far, sexual route is the commonest mode of transmission of HIV worldwide; heterosexual being more common than the homosexual route[5,7]. The presence of other sexually transmitted diseases has been strongly associated with susceptibility to infection and infectivity with micro-organisms like Treponema pallidum, Hemophilus ducreyi, Herpes simplex virus type 2, etc.

HIV can also be transmitted to individuals who receive HIV-tainted blood transfusion, blood products or transplanted tissues as well as to intravenous drug

users (IDUs), who are exposed to HIV while sharing injections, needles, syringes, water in which drugs are mixed, cotton through which drugs are filtered, etc. Subcutaneous and intramuscular injections can transmit HIV as well.

Occupational exposures can spread HIV to health care workers via percutaneous injuries or contact of mucus membrane or non-intact skin with blood, tissue, or other potentially infectious body fluids.

Also, HIV infection can be transmitted from an infected mother to her fetus during pregnancy, delivery or breast feeding. Most commonly maternal transmission to the fetus occurs in the perinatal period[10]

Routes of transmission	Percentage
Heterosexual	87.1 %
Parent to Child	5.4 %
Intravenous Drug user	1.6 %
Homosexual	1.5 %
Blood and Blood products	1.0 %
Unknown	3.3 %

HIV and other Sexually transmitted infections (STIs)

The knowledge of coinfection of STIs with HIV is essential in making syndromic approach in the management of STIs and changes in the highly active

anti-retroviral therapy (HAART) in specific situations as in herpes simplex virus type 2, hepatitis B and C coinfections.

HBV and HCV co-infections in HIV positive individuals is of utmost importance due to the underlying consequences such as the hepatological problems associated with these viruses, which have been shown to decrease the life expectancy in the HIV-infected patients. Co-infections of hepatitis-B (HBV), hepatitis-C (HCV) and syphilis are a major concern in HIV/AIDS patients. HIV, HBV and HCV share modes of transmission and hence co-exist in the same host at significantly high rates. Enormous evidences are available indicating that syphilis increases the risk of HIV infection. [4,6]

The prevalence of co-infection with HIV varies widely across different studies within India and outside. Therefore, it is important to find out regional prevalence of these co-infections. Moreover, co-infections with the HIV have become a major health care catastrophe. Hence, it is important to identify them early to reduce the morbidity, delay mortality and improve quality of life in HIV/AIDS patients. According to HIV prevalence rates in adult population, the state of Jammu and Kashmir in India has been placed in low prevalence state. However, in this state the disease has begun to show its ugly face in the recent time and there is a dearth of such data of co-infection in HIV/AIDS patients.

This is a prospective study to find out associated infections like, HBV, HCV, syphilis in HIV/AIDS patients.

Worldwide, most adults acquire atleast one STI and many remain at risk for complications including genital neoplasms; certain STIs such as syphilis, gonorrhea, HIV infection, hepatitis B and C and chancroid are most concentrated within core populations characterized by high rates of partner change, multiple concurrent partners or highly connected sexual networks – e.g. involving prostitutes and their clients, some homosexual men and persons involved in the use of illicit drugs.

The initial rate of spread of any STI within a population depends on three factors – rate of sexual exposure to infectious people, efficiency of transmission per exposure and duration of infectivity of those infectivity. Among STIs, HIV has become the leading cause of death in some developing countries and HPV and hepatitis B viruses remain important causes of cervical and hepatocellular carcinoma respectively – two of the most common malignancies in the developing world.

Sexually transmitted HSV infections now cause most genital ulcer disease throughout the world and an increasing proportion of cases of genital herpes in developing countries, with HIV epidemics.

The coincidence of syphilis with HIV and the probable resurgence of syphilis in these patients is also being noted worldwide, more so in the developing countries. The presence of genital ulcers is likely to increase the transmission of other STIs, including HIV, in such patients.

The common manifestations of STIs are urethritis, epididymitis, vulvovaginal infections including trichomoniasis, bacterial vaginosis, mucopurulent cervicitis, pelvic inflammatory disease, genital ulcer, proctitis, enteritis, etc.

AIMS AND OBJECTIVES

- To study the prevalence of co-infection of HIV patients with syphilis, herpes simplex-2, hepatitis B and hepatitis C.
- To study the demographic profile of these four STIs in HIV patients.
- To study the clinical profile of these four STIs in HIV patients.
- To study the impact of these STIs in HIV patients in various laboratory parameters like CD4, liver function tests and ultrasonography of abdomen.

REVIEW OF LITERATURE

INDIAN EPIDEMIOLOGY OF HIV/STI CO-INFECTION

An emerging epidemic of human immunodeficiency virus (HIV) infection in India has made sexually transmitted infection (STI) control as one of the strategies imperative and probably the most important one to decrease HIV transmission[8]

Sexually transmitted Diseases particularly genital ulcer diseases are major public health problem in India. They play an important role in the transmission of HIV & two have been observed to be interrelated from September 2002 to January 2003, 331 patients who were confirmed cases of HIV were included in the study group(Screening for HIV was done by ELISA, those who were found positive were tested by repeat ELISA utilizing another blood sample & considered HIV seropositive only if both samples were found to be positive). All the serum samples were then subjected to VDRL and confirmed by TPHA for serodiagnosis of Syphilis. Of 331 HIV positive patients,15 (4.57%) were found to be VDRL reactive. ALL the VDRL reactive patients had high titres. Twelve of the patients were also found to be TPHA positive thus confirming the diagnosis of Syphilis in these patients. Mean age of patients was 30.1 years and most of these patients were asymptomatic and might be having early Syphilis at the time of screening. Thus routine surveillance for Syphilis should be carried out in HIV infected individuals

particularly to diagnose asymptomatic Syphilis so that appropriate interventions can be taken to prevent the disease

Test	Positive No (%)	Negative No (%)
VDRL	10 (4.34)	220 (95.66)
Anti-HSV-2	20 (8.68)	210 (91.32)
HBsAg	8 (3.4)	222 (95.62)
Anti-HCV	0 (0)	230 (100)

The prevalence of HSV-2 and syphilis was 10.1% and 1.7%, respectively. Geographic differences in HSV-2 prevalence were significant, while for syphilis it was comparable. Urban–rural differences in prevalence were only seen for syphilis. For both infections, the prevalence between males and females was not significantly different. In males and females, HSV-2 prevalence increased significantly with increasing age; for syphilis, a slight trend was seen only in females. In a multivariable analysis, HSV-2 infection in males and females was associated with site, religion and testing positive for syphilis, in addition to reporting ≥2 lifetime partners in the previous year among males and being ever married or having had sex with a non-regular partner in the last year among females.

In Asia, HSV seroprevalence studies are sparse and they have recorded lower prevalence of HSV infection, especially HSV-2[9] study included 135 consecutive STD cases having history of ulcerative or non-ulcerative STD in the present or in the past 5 years and 135 age and sex-matched controls. Diagnostic serology was done for HSV-1 and HSV-2 using type specific IgG by indirect immunoassay using ELISA. The results were analyzed utilizing Chi- square test. Amongst 135 STD clinic cases, 106 cases were males and 29 cases were females with male to female ratio of 3.65:1. The mean age was 32.2 years (range 16-65 years). Among study group cases, 112 (82.9%) cases were co-infected with HSV-1 and HSV-2, 11 (8.1%) cases were seropositive for HSV-1 alone and 3 (2.2%) cases were seropositive for HSV-2 alone. In the control group, 112 (82.9%) cases were co-infected with HSV-1 and 2, 12 (9.6%) for HSV-1 alone and 1(0.8%) for HSV-2 alone. Correlation of HSV-1 and HSV-2 serology with various demographic and behavioral factors was statistically insignificant.: Seroprevalence of HSV-1 and HSV-2 in STD clinic cases and control group is high, similar to that recorded in sub-Saharan Africa. Thus, serological studies for HSV-1 and HSV-2 cannot be taken as a marker of sexual behavior in our set of population

HIV/AIDS cases were diagnosed as per the NACO, 2000 criteria. The following screening tests were used to evaluate associated infections, HBsAg micro screen ELISA Test Kit (for hepatitis B); HCV micro ELISA

(3 rd generation): for detection of antibodies to Hepatitis C virus in human serum/plasma and Rapid plasma reagin test (RPR Test) for rapid serological diagnosis of syphilis.

Among 230 HIV/AIDS patients enrolled, HBsAg was positive in eight cases (3.47%); anti Hepatitis C antibody was present in none of the cases. Ten (4.34%) out of 230 cases were positive for VDRL

CD4 count was less than 200 mm^3 in 73 patients in HIV alone, , six in HBV and five patients in syphilis co-infection group. Sixty patients recorded absolute TLC less than 1200/cm^2 in HIV alone group. Whereas three and four patients recorded absolute TLC less than 1200 mm^3 in, HBV and syphilis co infection groups respectively. All HBV patients were asymptomatic and syphilis was diagnosed in only 10 patients after performing VDRL in all the HIV diagnosed patients. All diagnosed patients were of primary syphilis. Among the total diagnosed patients with syphilis were treated with Benzathine penicillin G, 2.4 MU IM in a single dose.

This study documents fairly high rates of HBV and syphilis co-infection among HIV infected persons. Thus, it should be mandatory to screen every HIV/AIDS patient for co-infection and vice-versa for early detection and a

simultaneous treatment besides HIV infection management to combat the menace of this dreadful disease.

2456 adults were surveyed in Hyderabad, Bangalore and Chandigarh in India. Socio-demographic and lifestyle characteristics were obtained through a questionnaire, and a dried blood spot (DBS) was collected from all individuals aged 18 years and over; sexual behaviour was collected from those aged 18–49 years. DBS samples were tested for HSV-2 and syphilis serology. The association between HSV-2 and syphilis infections with socio-demographic and behavioural variables was analysed using multivariable logistic regression.

SYPHILIS

Syphilis is a sexually transmitted disease caused by the spirochetal bacterium Treponema pallidum subspecies pallidum. The route of transmission of syphilis is almost always through sexual contact, although there are examples of congenital syphilis via transmission from mother to child in utero or at birth.

HIV AND SYPHILIS

The interaction of syphilis and HIV infection is complex. Epidemiological studies demonstrate that STIs, including syphilis, are associated with an increased risk for HIV infection among both homosexual and heterosexual persons. [11],[12] Presumably sexual behaviours that increase the risk for acquiring STIs also increase the risk for HIV transmission. Furthermore, ulcerations and inflammation caused by STIs are implicated as the cofactors for acquiring HIV infection. Recent data suggest that in the presence of other STIs, individuals are three to five times more likely to acquire HIV if exposed to the virus through sexual contact. [3]

The diagnosis of syphilis may be more complicated in the HIV-infected patients. Unusual serological responses have been reported in syphilis, namely, higher than expected serologic VDRL titers. But false positive results have been reported in HIV-infected patients with syphilis and specific tests like Fluroscent

Treponemal Antibody Absorption test (FTA-ABS) or Treponema pallidum hemagglutination Assay (TPHA) would be beneficial.

Proper treatment of syphilis will go long way in preventing HIV infection. Hence the study was undertaken to determine the prevalence of syphilis in HIV-seroreactive patients with high-risk behaviour and to correlate age, sex and clinical presenting complaints with HIV seroprevalence and prevalence of syphilis

The course of syphilis in HIV-positive patients with depressed immune function is thought to differ from that in HIV-negative patients. Animal models suggest that cell-mediated immunity plays a role in clearing *Treponema pallidum* infections; lack of such immunologic control may prevent complete eradication of infection, particularly at sanctuary sites such as the central nervous system (CNS) or the eye. HIV coinfection has been associated with a higher titer Rapid Plasma Reagin (RPR), multiple primary chancres, more rapid progression to tertiary manifestations, increased frequency of ocular disease, delay or failure of titer decline following treatment, and predilection for development of the Jarisch-Herxheimer reaction compared with syphilis infection alone[14 15 16] Coinfected patients may also experience slower resolution of primary chancres, and, in cases of neurosyphilis, of cerebrospinal fluid (CSF) pleocytosis, protein elevation and Venereal Disease Research Laboratory (VDRL) titer.[19 21 24] Several reports indicate

that HIV-coinfected patients may be at higher risk for syphilis relapse than are HIV-negative patients.[19-21.22,25], Features of secondary syphilis may be particularly pronounced in HIV-coinfected patients.

.CLINICAL MANIFESTATIONS:

The numerous manifestations of neurosyphilis are highly variable, ranging from ocular syphilis (most commonly uveitis) to meningovascular disease (manifesting as stroke), to tabes dorsalis (a disease of the posterior columns of the spinal cord and nerve roots). Neurologic manifestations are generally classified as "early" or "late." Early manifestations, which affect tissues derived from mesodermal structures, include syphilitic meningitis, meningovascular disease, labyrinthitis, meningomyelitis, and cranial nerve palsies. Late manifestations, which affect sites of ectodermal origin, include tabes dorsalis, general paresis, CNS gumma, and other parenchymal diseases. Late manifestations generally occur 5 to 15 years from the date of infection but may be accelerated in patients with HIV disease[16,17,20,22,28,29]. Ophthalmic disease (e.g., uveitis, keratitis, optic neuritis, conjunctivitis, optic atrophy, or chorioretinitis) is particularly common in HIV-coinfected individuals. In a study of 46 patients with neurosyphilis, Katz and colleagues reported ophthalmologic abnormalities in 42% of 24 HIV-positive patients compared with 14% of 22 HIV-negative individuals. [22] Patients with

neurosyphilis presenting with eye disease may be otherwise asymptomatic. Nonetheless, all patients with ocular syphilis should undergo LP and should be treated with a standard neurosyphilis regimen. The purpose of LP in these patients is to establish whether CSF abnormalities are present; if so, a follow-up CSF exam is indicated 6 months after treatment to establish resolution of these findings. Failure to see either a reduction in pleocytosis or clearance of CSF-VDRL should prompt repeat therapy.

FREQUENCY OF NEUROSYPHILIS IN HIV-INFECTED PATIENTS:

HIV infection may increase the frequency or accelerate the development of neurologic sequelae of syphilis, including early pathologies such as acute syphilitic meningitis and late pathologies such as CNS gummatous lesions. Berger reported 2 HIV-infected patients (CD4 counts, 274 and 10 cells/mm^3) who presented with seizures and who were each found to have an enhancing lesion on head imaging. Toxoplasma serologies and bacterial, fungal, and mycobacterial CSF cultures were all negative; syphilis serologies were positive; biopsy material was consistent with gumma formation; and clinical/radiographic response to intravenous penicillin therapy was seen.[20] In 1 patient, contact tracing revealed exposure to syphilis only 6 months earlier. Horowitz and colleagues described a similar case treated for primary syphilis who presented 4 years later with CNS gumma (CD4 count, 9

cells/mm^3). Such rapid progression to previously regarded "late" complications of neurosyphilis was largely unprecedented in the pre-HIV era.

DIAGNOSIS

The lack of a practical and readily available gold-standard test makes the diagnosis of neurosyphilis challenging. Diagnosis relies on integrated findings of positive serum non-treponemal and confirmatory antibody in conjunction with neurologic or ophthalmic symptoms, CSF pleocytosis or elevated protein, and/or a reactive CSF-VDRL. In the HIV-infected population, diagnosis may be further challenged by atypical serologic tests (unusually high, low, or fluctuating titers). [18, 30] False-positive RPR and treponemal confirmatory tests can occur due to concomitant cross-reacting infections or HIV-related B-cell dysfunction[23]

Waning serum treponemal antibody titers can be seen with AIDS, and false-negative CSF-VDRL results can occur in 20% to 70% of patients with CNS disease. False-positive CSF-VDRL is an infrequent occurrence, but can be seen when blood contaminates the CSF.[15], [27] Microhemagglutination *T. pallidum*(MHA-TP) and fluorescent treponemal antibody absorption (FTABS) tests have been used on CSF samples and are thought to be less specific than CSF-VDRL, though significantly more sensitive. Use of these confirmatory tests in the CSF is therefore regarded as having a high negative predictive value for

neurosyphilis -- some experts contend that a negative CSF FTA-ABS may exclude this diagnosis.[27, 30] The CSF abnormalities commonly seen with HIV disease make mild pleocytosis or elevated protein very challenging to interpret and present the greatest challenge to current diagnostic schema for neurosyphilis

HERPES SIMPLEX VIRUS TYPE 2

Sexually transmitted infections (STIs) are markers of high risk sexual behaviour in an individual/spouse/sexual partner. Infections due to herpes simplex virus (HSV) are extremely common. While most infections are asymptomatic or mild, some can be transmitted to neonates and are associated with other STIs and cervical neoplasia. HSV-2 may contribute more to human immunodeficiency virus (HIV) infection because of its higher frequency than other STIs. Thus, because of the recurrence of genital herpes, high prevalence of genital herpes in populations at risk for HIV infection and large number of herpes infected persons who continue their sexual activities despite being infectious, genital herpes is a risk factor for acquisition of HIV-1 infection. HSV-2 infection is also significantly associated with syphilis. Considering that herpes is a life long infection, not cured by antimicrobial treatment, HSV-2 antibodies are a much more reliable indicator of risky behaviour than than T.PALLIDUM antibodies. However, a large number of genital infections are also caused by HSV-1. The present study was thus

undertaken for finding IgM antibodies against HSV-1 and HSV-2, antibodies to HIV-1 and 2 and screening for syphilis in STD patients

Out of 250 STD patients, 136 (54.4%) were males while 114 (45.6%) were females. Forty-four of these (17.6%) were positive for HSV-1 and 2 IgM antibodies. Out of these, 25 (56.8%) were males and 19 (43.2%) were females. Eleven of 44 (25%) patients were positive for HIV-1 and 2 and 10/44 (22.7%) were reactive to VDRL antigen and TPHA positive. HSV seropositive persons had mixed clinical feature while most HIV reactive or VDRL reactive persons had genital ulcers with or without other features. Seven of 44 (15.9%) patients were reactive to both HIV-1 and 2 antibodies and VDRL antigen. In the asymptomatic group, 12/50 (24%) women were positive for HSV, while none was reactive to HIV antibodies or VDRL antigen. Highest HSV seroprevalence in STD patients was in the age group of 21-30 years (45.5%) and who were of young age at first sexual contact, i.e., 15-25 years (97.7%). Prevalence was also high in housewives (40.9%), patients with non-specific discharge (50%) and genital ulcers (34.1%). Prevalence in bad obstetric history (BOH) and mouth ulcer cases was 1/44 (2.27%) each. Prevalence was also high in illiterate patients (70.4%) and those with multiple partners (56.8%). Co-infection with HSV and HIV was found in 11/44 (25%) patients. Ten out of 44 (22.7%) persons were reactive to both HSV antibodies and VDRL antigen. The three STIs (HSV, HIV and syphilis) were

present in 7/44 (15.9%) patients. In the control group, seropositivity was high in the age group of 21-30 years (50%) and in those who were of young age (15-25 years) at first contact (91.6%).

HSV seropositivity was highest in the young age group of 21-30 years because of their sexually active life [31, 32] Adolescents are known to be at increased risk of acquiring STIs because of fewer protective antibodies and increased susceptibility of cervix.[32] Seropositivity was more in housewives as most women have little awareness of sexual and reproductive life and symptoms are generally ignored.[33] Also, transmission of HSV-2 is more efficient from men to women compared with women to men.[33] Seropositivity was high in illiterate persons because of ignorance and in persons with multiple partners because of high risk behaviour. High seropositivity was also seen in persons with non-specific discharge and genital ulcers. [34, 35] Regarding prevalence in BOH cases, [36] HSV is one of the TORCH organisms and infection in pregnancy accounts for half of the morbidity and mortality among neonates. [37] It may also lead to abortion/prematurity/intrauterine growth retardation and disseminated infection of neonates.[36,38] HSV predisposes to other STIs as it causes mucosal erosions and may increase the concentration of HIV and other STIs in semen and vaginal fluids. In the control group, a seropositivity of 12/50 (24%) for HSV-1 and 2 was seen. Women are more vulnerable to STIs as they have less say in the contraception

methods, less opportunity for early diagnosis and treatment and are more prone to infections because of procedures like MTP, IUD insertions etc. [39]. Asymptomatic shedding can infect their neonates and they themselves are at more risk to develop cervical cancer,[40] therefore, it is important to screen them.

In summary, this study shows that genital herpes infection is a risk factor for acquisition of HIV and other STIs and the study of seroprevalence of HSV in STD patients is important to plan STI control strategies which may help keeping the HIV status at a low level.

Herpes simplex virus (HSV) infections are among the most common infections worldwide and cause recurrent infections throughout life. Transmission is facilitated by the frequent recurrence of infectious episodes of sub-clinical viral shedding. Moreover, there is increasing evidence that HSV-2 infection could significantly enhance the rates of sexual transmission and acquisition of HIV.

Increasing evidence demonstrates a substantial link between the epidemics of sexually transmitted HIV-1 and herpes simplex virus (HSV)-2 infection. More than 30 epidemiologic studies have demonstrated that prevalent HSV-2 is associated with a 2- to 4-fold increased risk of HIV-1 acquisition. Per-sexual contact transmission rates among couples from Rakai, Uganda indicate that at all levels of plasma HIV-1 RNA in the source partner, HSV-2-seropositive HIV-1-

susceptible persons have a 5-fold greater risk of acquiring HIV-1 compared with HSV-2-negative persons. In vitro and in vivo studies suggest that mucosal HIV-1 shedding is more frequent and in greater amounts during mucocutaneous HSV-2 replication, including subclinical mucosal reactivations. Most HIV-1-infected persons are coinfected with HSV-2, and most experience frequent subclinical and clinical reactivations of HSV-2. Subclinical HSV reactivation elevates serum HIV-1 RNA levels, and daily therapy with acyclovir appears to reduce plasma HIV-1 RNA. These data show that greater attention to the diagnosis and treatment of HSV-2 among HIV-1-infected persons is warranted, especially those who continue to be sexually active, those not on antiretroviral therapy, or those whose disease is not well suppressed by antiretrovirals.

Persons 15-49 years old from 32 rural and 34 urban clusters were sampled using a stratified random method to represent adults in the high HIV prevalence Guntur district in Andhra Pradesh state. Interviews were conducted and dry blood spots were collected on 12,617 study participants. Testing for HSV-2 and syphilis was performed.

Adjusted HSV-2 and syphilis seroprevalence rates were 4.70% and 2.08% for men and 7.07% and 1.42% for women. For men, tattooing, >3 lifetime sex partners, tobacco use, and sex with men in the past 6 months were associated with HSV-2 or syphilis (ORs, 1.66-2.95, $p < 0.05$). Male circumcision was positively

associated with HSV-2 infection (OR, 1.37, p = 0.028) though this could be due to residual confounding. In women, greater than one lifetime partner remained significantly associated with HSV-2 in multivariate analysis (OR, 2.61; 95% CI, 1.39-4.87). Among all behavioral risk factors and other covariates in women and men, HIV infection exhibited the strongest association with HSV-2 and syphilis (ORs, 8.2-14.2, p < 0.001). The proportion of individuals with HSV-2 who were HIV infected was less than the proportion with syphilis who were HIV infected (11.8% vs. 22.7%; p = 0.001).

HEPATITIS B

Hepatitis B virus is an hepadnavirus—hepa from hepatotrophic and dna because it is a DNA virus—and it has a circular genome composed of partially double-stranded DNA. The viruses replicate through an RNA intermediate form by reverse transcription, and in this respect they are similar to retroviruses.

Epidemiology of HIV and hepatitis B co infections.

Co infection with human immunodeficiency virus (HIV) and hepatitis B virus (HBV) is common due to shared routes of transmission. In areas of low endemicity, such as North America, Australia and Europe, HBV and HIV infection are usually acquired in adulthood through sexual or percutaneous transmission. In areas of low endemicity, the prevalence of chronic co infection is around 5-7% among HIV-infected individuals [41] In countries with intermediate and high HBV endemicity, the main routes of transmission of HBV are perinatal or in early childhood; in these countries HBV co infection rates are 10-20% [60, 61]

Impact of co infection on the natural history of HBV and HIV

The rate of progression and complications from viral hepatitis are accelerated in patients with HIV co infection [62,63]. After acquiring HBV infection, HIV infected individuals are 6 times more likely to develop chronic hepatitis B

than HIV negative individuals [44] .This was more likely to occur in HIV infected men with lower CD4 cells [44] .Decreased rates of clearance of HBeAg and increased HBV replication are also seen, with higher HBV DNA viral load [46] .In addition, HIV infected individuals are more likely to lose previously developed protective anti-HBs antibody and develop acute hepatitis B infection; this risk is also associated with lower CD4 counts [43, 58] . Following initiation of antiretroviral therapy (ART), immune reconstitution inflammatory syndrome (IRIS) may occur which can lead to worsening liver disease including hepatic decompensation [49]. In addition, after discontinuation of an ART regimen containing anti-HBV agents, reactivation of hepatitis B can occur: ALT elevations occurred in 29% of 147 patients within 6 months of withdrawal[42]. If reactivation occurs, resuming an agent that is active against HBV is required.

HIV also hastens the progression of HBV related liver disease. Cirrhosis is more common despite lower ALT levels than in HBV mono-infection and is also more common with lower CD4 counts [46, 47] . HIV-HBV co-infected men are greater than 17 times more likely to die of liver related causes compared to those mono-infected with HBV [67]. The impact of co infection is especially important in regions with widespread use of ART [54]. As the use of ART becomes more prevalent in parts of the world with high HBV endemicity and long term survival increases, it is likely that liver disease from chronic hepatitis B in HIV-infected population may

emerge as a greater public health problem than before [53] . It is unclear at present if the risk of hepatocellular carcinoma (HCC) is increased, but there is some evidence that HIV infected individuals with lower CD4 counts are at greater risk of developing HCC [45] For individuals on ART, co infection with chronic hepatitis B increases the risk of hepatotoxicity from ART three-fold to five-fold [63,66]

Assessing for HBV and its sequelae in HIV co infection

Accurate assessment of HBV infection in HIV co-infected individuals is necessary in order to base therapeutic decisions [67] .WHO advocates HBsAg testing especially in areas of high HBV prevalence (WHO, 2006) but additional testing for HBV markers such as HBeAg and HBV DNA and to assess stage of liver disease (e.g. liver enzymes, liver biopsy, etc) may not be widely available in many resource limited countries. For HIV infected individuals with chronic HBV, additional screening for co infection with HCV is recommended; hepatocellular carcinoma screening with alpha fetoprotein and imaging of liver every 6 months is being suggested by some but the cost Benefit of one or both tests as well as the frequency of monitoring in various health Economies remain to be assessed. Liver biopsy remains the gold standard for assessing disease severity in HIV-HBV co infection . Non-invasive markers are also available but none have been widely studied in co-infected patients. Hoffman and Thio provide management

recommendations for use in areas with limited resources They recommend that HBsAg and liver enzymes be tested before ART, with liver enzymes being repeated once or twice during the first 3 months after commencing ART. Detection of HBV DNA is helpful but may not be available. Chronic HBV carriers with HBeAg positivity may benefit from starting anti-HB therapy early.

Transmission

Transmission of hepatitis B virus results from exposure to infectious blood or body fluids containing blood. Possible forms of transmission include sexual contact, blood transfusions, re-use of contaminated needles & syringes, and vertical transmission from mother to child during childbirth. Without intervention, a mother who is positive for HBsAg confers a 20% risk of passing the infection to her offspring at the time of birth. This risk is as high as 90% if the mother is also positive for HBeAg. HBV can be transmitted between family members within households, possibly by contact of nonintact skin or mucous membrane with secretions or saliva containing HBV.However, at least 30% of reported hepatitis B among adults cannot be associated with an identifiable risk factor.

HEPATITIS C

Hepatitis C is an infectious disease affecting the liver, caused by the hepatitis C virus (HCV). The infection is often asymptomatic, but once established, chronic infection can progress to fibrosis and cirrhosis which is generally apparent after many years. In some cases, those with cirrhosis will go on to develop liver failure or other complications of cirrhosis, including liver cancer

Although injection drug use is the most common route of HCV infection, any practice, activity, or situation that involves blood-to-blood exposure can potentially be a source of HCV infection. The virus may be sexually transmitted, although this is rare, and usually only occurs when an STD that causes open sores and bleeding is also present and makes blood contact more likely.[14]

Sexual activities and practices were initially identified as potential sources of exposure to the hepatitis C virus. More recent studies question this route of transmission. Currently, heterosexual vaginal intercourse is thought to be a rare means of transmission of hepatitis C infection.

In 2005, G8 leaders promised that by 2010 Universal Access to HIV prevention, treatment, care and support would be widely available. Since then, much has been accomplished and over 2 million people are now on anti-retroviral treatment. However, as people with HIV live longer, opportunistic and related

illnesses that threaten their health are exposed. Whilst Hepatitis C is an adjunctive rather than opportunistic disease, there is growing awareness that co-infection with the Hepatitis C virus (HCV) is an important issue in HIV prevention, treatment, care and support. Thus, for universal access to be fully realized, HIV/HCV co-infection must be addressed.

To date, research on the extent of HIV/HCV co-infection is scarce. This lack of research data is particularly profound in developing countries, where practical methods to address these dual threats are limited. What is known, however, is that many of those infected with HCV are also co-infected with HIV and dealing with its impact.[68] This combination creates a terrible synergy. Co-infection can worsen the effects of both diseases. For example, if co-infected with HCV and HIV, the chances of developing liver disease are much higher and decisions around appropriate treatment for both diseases becomes far more complicated. It is clear that a comprehensive approach is essential [69,70,71,72]. As such, HIV advocates and professionals must be educated about HIV/HCV co-infection and must address this dual challenge in their future efforts.

Until 1989 Hepatitis C, a viral infection that affects the liver, was referred to as 'non A, non B hepatitis . The WHO estimates that 3% of the world's population (approx. 170 million people) is living with HCV. The medications used in HCV

treatment, pegylated interferon and ribaviron, are costly and may need to be administered for up to a full year[74, 76, 78]. Side effects often make adherence to treatment challenging. The resulting liver disease caused by hepatitis is becoming a major cause of illness and death among those infected with HIV.

HCV is also the most common virus affecting the world's 16 million injection drug users (IDUs). It's estimated that close to 3 million IDUs are living with HIV and some studies indicate that over 90% of IDUs infected with HIV are also infected with HCV.

Although there are similarities between HCV and HIV transmission, there are differences in transmission efficiencies. Rates of transmission where recipients receive blood or blood products that are infected with HCV are close to 100%. HCV is very easily transmitted through sharing equipment used for injecting, smoking or snorting drugs (needles, syringes, pipes and straws) and exposure to injection-related paraphernalia, such as cotton, water, tourniquets, swabs and spoons ('cookers') can also result in transmission [81,82,83,84]. Other objects that are easily contaminated with blood such as piercing and tattoo equipment and ink, razors, toothbrushes and unsterilized medical equipment, are also implicated in transmission.

Although HCV can be transmitted sexually and vertically (from mother to child), until recently these kinds of exposures were thought to be insignificant. However, recent research suggests that outbreaks of acute HCV among HIV-positive gay and bi-sexual men who have unprotected anal intercourse are related to sexual transmission.

Hepatitis C virus infection may remain asymptomatic for long periods of time, and liver damage that occurs during this period may eventually lead to chronic liver disease which may progress to liver failure. Due to the fact that 10 to 20 years can elapse between infection and the onset of liver disease, those who are HCV-positive may unknowingly be spreading the disease. In the instance of HIV/HCV co-infection, liver damage due to HCV tends to occur faster than in HIV-negative people.

Although treatments are available, their effectiveness ranges from 40% to 80%, depending on the genotype (or strain) of HCV. It's important to note that these rates are for those who are dealing with HCV alone. Unfortunately, treatment success is reduced amongst those who are co-infected.

There is no vaccine to prevent HCV infection and researchers face formidable challenges in vaccine development because of the virus' propensity for mutation.

HIV and HCV Co-infection

As noted above, HCV/HIV co-infection compromises immunity, making HCV more likely to be transmitted and more difficult to treat. While there is no proof that people with HCV are more susceptible to HIV infection, it is clear that AIDS is complicated by the liver symptoms associated with HCV[79,80]. Treatment presents additional challenges as many anti-retroviral drugs are cleared from the body by the liver. Depression is another complication of HCV treatment and adds an extra burden for those living with HIV who are already dealing with HIV-related psychosocial and economic challenges.

In this co-infection,spontaneous viral clearance and clearance with treatment occur less frequently. They are also more likely to develop fibrosis or other symptoms than mono-infected patients. They are more than twice as likely as mono-infected patients to develop it much more rapidly –in as few as ten years after infection. They may also be at greater risk for liver cancer than mono-infected patients. Their risk is six times greater for hepatic decompensation develops is significantly shorter.

HIV/Hepatitis C co-infection in the developing nations

Current data about co-infection in the developing world is inadequate. A limited number of reviews provide some information about mono-infection in the general population and among people who use drugs. The following sections give a regional overview of HCV infection and HCV/HIV co-infection prevalences.

South East Asia: The HCV prevalence rate for South-East Asia as a whole was reported as 2.15% in a 1999 review by the WHO. A recent global review of HCV among IDUs reported rates as high as 90% in Indonesia, India, Thailand, Viet Nam and Bangladesh. HIV/HCV co-infection rates were also extremely high in China (99.3%) and Chang Mai, Thailand (100%). Injection drug use in these regions is increasing. Harm reduction, at least in theory, is becoming more accepted. In practice, however, only 3% of people who inject drugs in South Asia and 8% in East Asia currently have access to harm reduction and many countries - Thailand, Viet Nam and Indonesia among them - continue to criminalize drug use.

Eurasia: The countries of Central and Eastern Europe and Central Asia experienced the fastest growing HIV epidemic globally, after a rapid rise in drug use in the 1990s. HCV was of less concern, with rates of only 2% in 1999. Rates of HCV infection, as well as HIV/HCV co-infection, are now consistently between

50% and 90% among IDUs in almost all countries in this region. End-stage liver disease has become a major cause of mortality in Eurasia. Over two million people inject drugs in Russia, which likely has more co-infected people than any other country, particularly among the prison population. Harm reduction supported by the Global Fund to Fight AIDS, Tuberculosis and Malaria has been successful in the Ukraine, and countries with membership in the European Union have also promoted the approach. Many people, however, lack access to harm reduction, in particular, prisoners, street youth and sex workers.

1999, rates of 30% to over 70% among people who inject drugs have recently been reported in Brazil, Argentina and Mexico. Co-infection with HIV is over 90% in Puerto Rico, and over 80% in Argentina and Brazil. ***:*** While overall HCV prevalence in these regions was estimated at less than 2% in Latin American countries and very few Caribbean countries have harm reduction programs. Drug use is criminalized in many countries and prisoners are often denied access to condoms.

North Africa and the Middle East: While HCV prevalence was low in 1999, more recent studies from North Africa and the Middle East now show HCV infection rates of 50% to 60%. HCV prevalence among people who inject drugs in Iran is reported as being as high as 80% and HIV/HCV co-infection as high as 87%. Drug

use, as well as opposition to drug use, is on the rise and drug related offenses bring severe penalties. While Iran and seven other countries have adopted and put into place harm reduction pilot projects, the number of people reached remains insufficient to stop the spread of co-infection.

Sub-Saharan Africa: In 1999, sub-Saharan Africa had the highest global prevalence of HCV infection among the general population; over 5% of Africans were estimated to be HCV-infected. There is limited data as to how HCV is spread in Africa, but it is assumed that health service acquired (nosocomial) infection, and transmission through non-sterile tattooing, circumcision and female genital mutilation (FGM) equipment are underlying factors. There is also little data on injection drug use in Africa, but if injection drug use does grow, it could fuel a serious HIV/HCV epidemic in countries that already have high HIV prevalence.

South Africa, Mauritius, Kenya, Nigeria and Tanzania are reporting increased numbers of IDUs. In one study, Kenya was reported to have HCV rates of over 40% among people who inject drugs. Only Mauritius and South Africa have harm reduction programs. There is no information available on HIV/HCV co-infection, but some better-resourced HIV treatment programs have begun to screen for HCV.

MATERIALS AND METHODS

STUDY POPULATION:

A total of 100 newly diagnosed HIV patients were enrolled in the study from whom attended the ART clinic in Madras Medical College and Government General Hospital. Screening for HIV was done by ELISA, those who were found positive were tested by repeat ELISA utilizing another blood sample & considered HIV seropositive only if both samples were found to be positive

Patients selected for the study satisfied all the inclusion and exclusion criteria; written consent was obtained from all patients participating in the study.

STUDY DURATION:

The study was conducted over a period of 1 year from October 2009 to October 2010.

STUDY DESIGN:

A single center cross-sectioned descriptive study design was chosen.

METHODS:

Detailed clinical history was taken from each patient and complete review of their case notes was performed. A complete examination was undertaken from each patient.

INVESTIGATIONS:

For ALL PATIENTS, the following investigations were done:

- Complete Blood Count
- CD4 count
- Screening of syphilis by VDRL
- HBsAg / Anti-HCV
- Anti-HSV-2-IgG in all patients

For SELECTED patients

- TPHA in patients who are VDRL reactive
- LFT and Ultrasonography of abdomen for those who are positive for Hepatitis virus co-infection

Inclusion criteria:

- Newly detected HIV patients
- Patients yet to be initiated on Highly Active Anti-Retroviral Therapy
- Those who are willing for the study

Exclusion criteria:

- Patients already on HAART therapy
- Known cases of liver disease
- Previously diagnosed syphilis / hepatitis / herpes on treatment

OBSERVATION AND RESULTS

PROFILE OF 100 HIV PATIENTS IN THE STUDY

Male	Female	Transgender
62	36	2

Age<12	12-35	>35
4	46	50

Rural	Urban
42	58

Illiterate	School	College
55	41	4

CD4<200	200-350	>350
36	30	34

Sexual route	Blood transfusion	IDU	Vertical
71	11	13	5

Figure 1. 50% of patients were asymptomatic and 50% were symptomatic on presentation. Symptomatic were in primary stage of infection. Asymptomatic ones probably in the early stages of infection

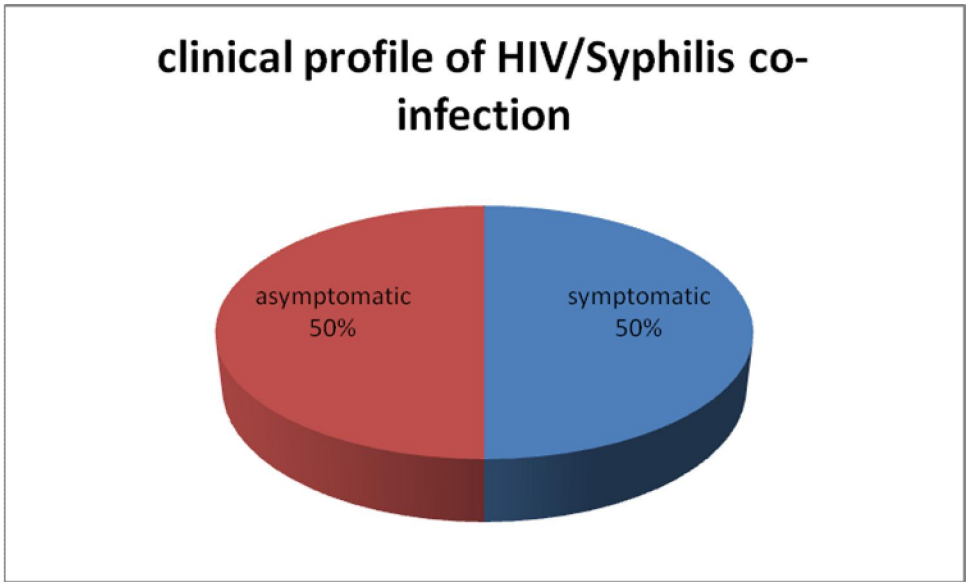


Figure 2. VDRL titres were positive in 9 patients and TPHA positivity was seen only in 6 patients (67%); High VDRL titres has not been noted in HIV / Syphilis in our study.

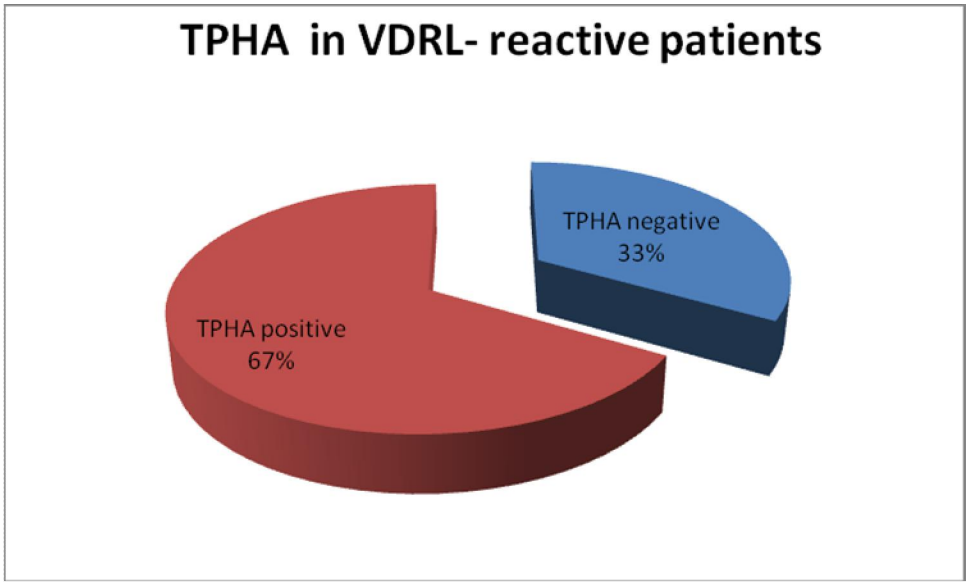


Figure 3. Sexual route is the commonest mode of transmission. In our study, we found 1 case of syphilis in an IDU probably related to the use of blood-tainted shared syringes.

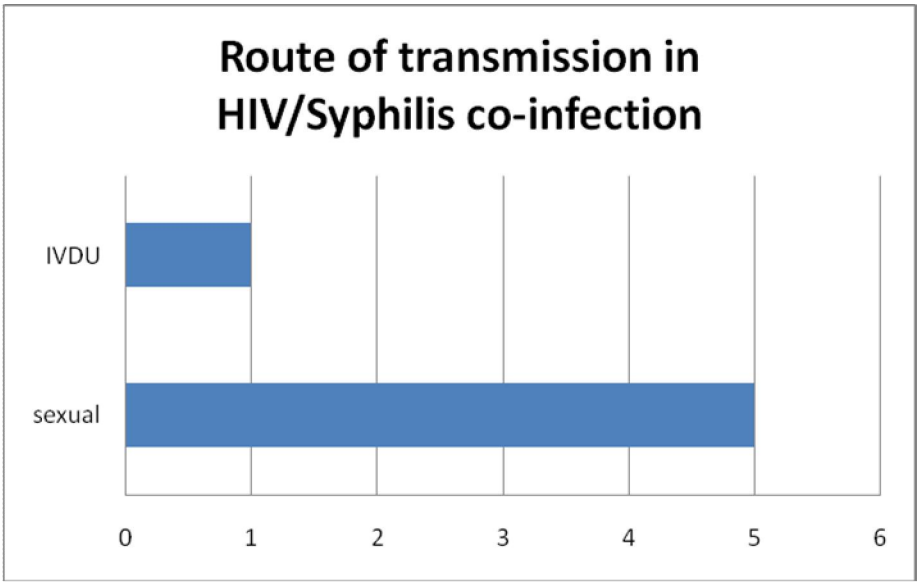


Figure 4. Most patients with syphilis (83%) have CD4 counts >200.

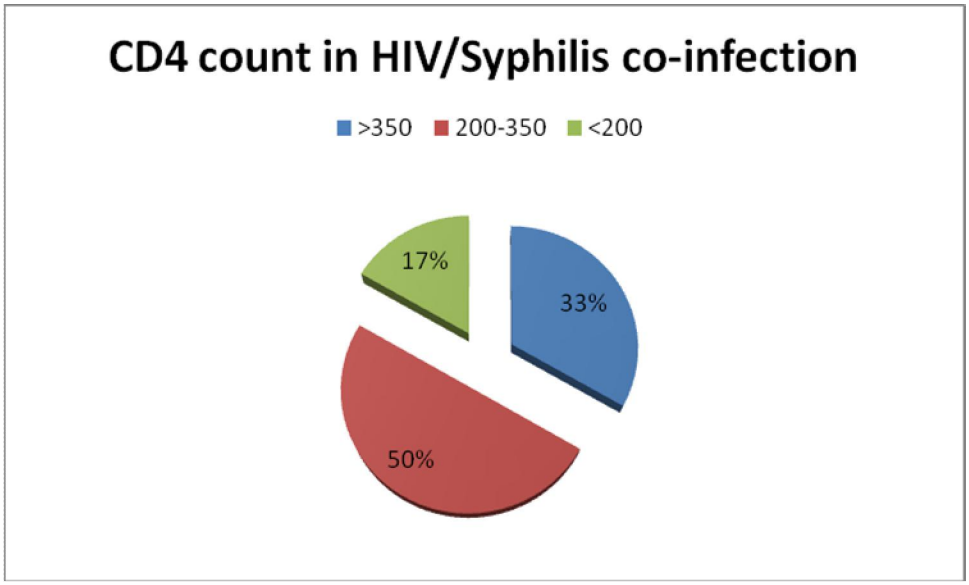


Figure 5. 15% of HIV patients were found to be infected with HSV-2.

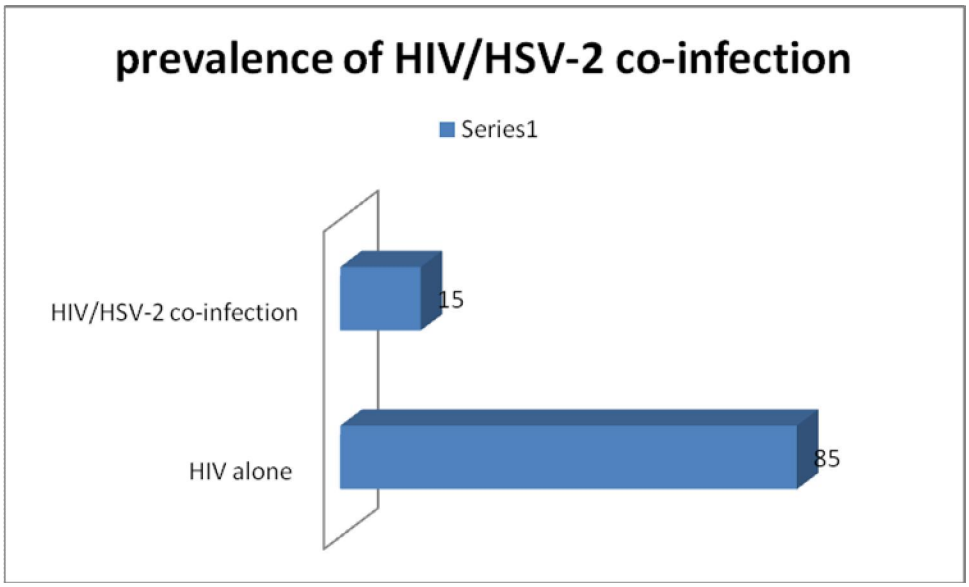


Figure 6. Around three fourths of the patients were asymptomatic. The symptomatic patients presented with painful genital ulcers.

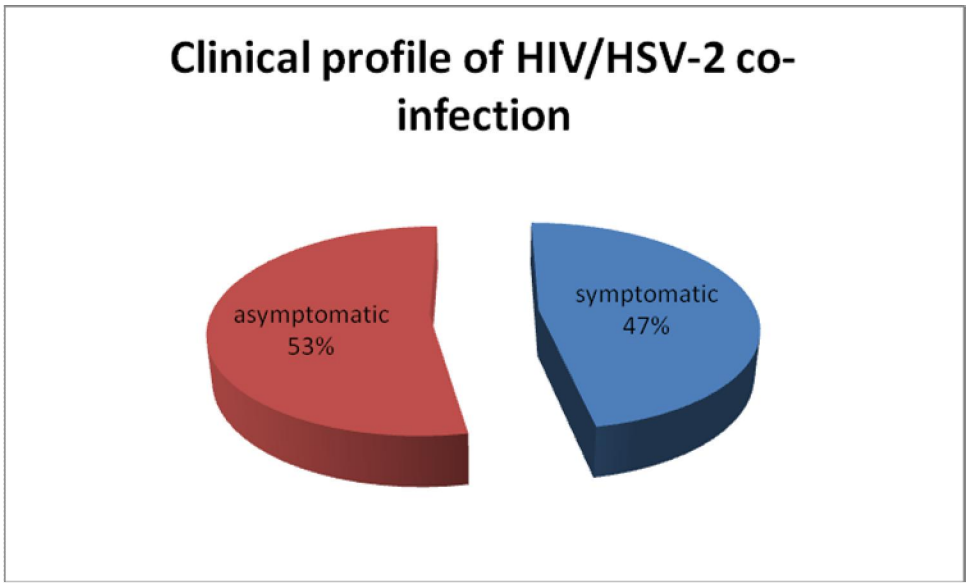


Figure 7. ONE out of FIFTEEN cases was transmitted through blood transmission and all others were transmitted sexually.

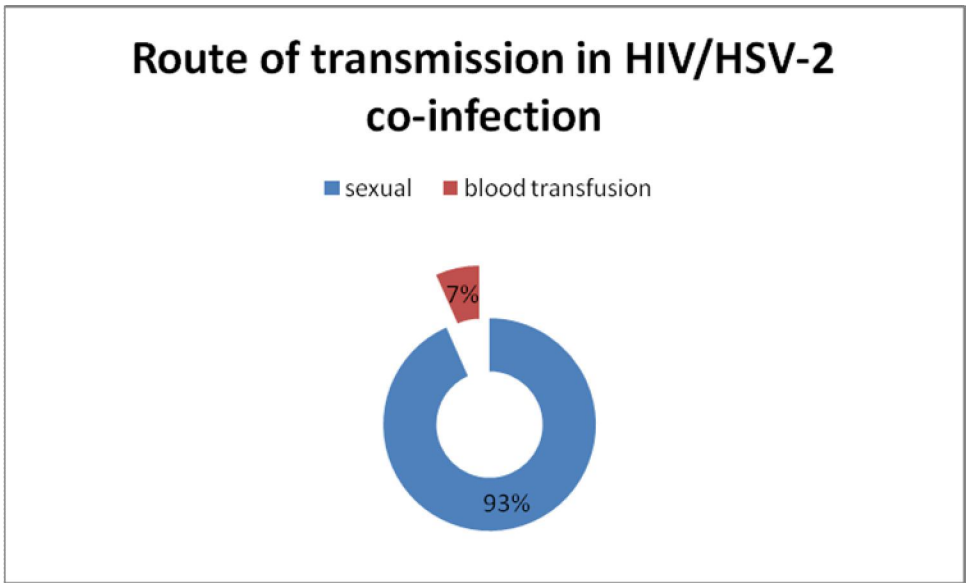


Figure 8. HSV-2 infection was associated with low CD4 counts (<200).

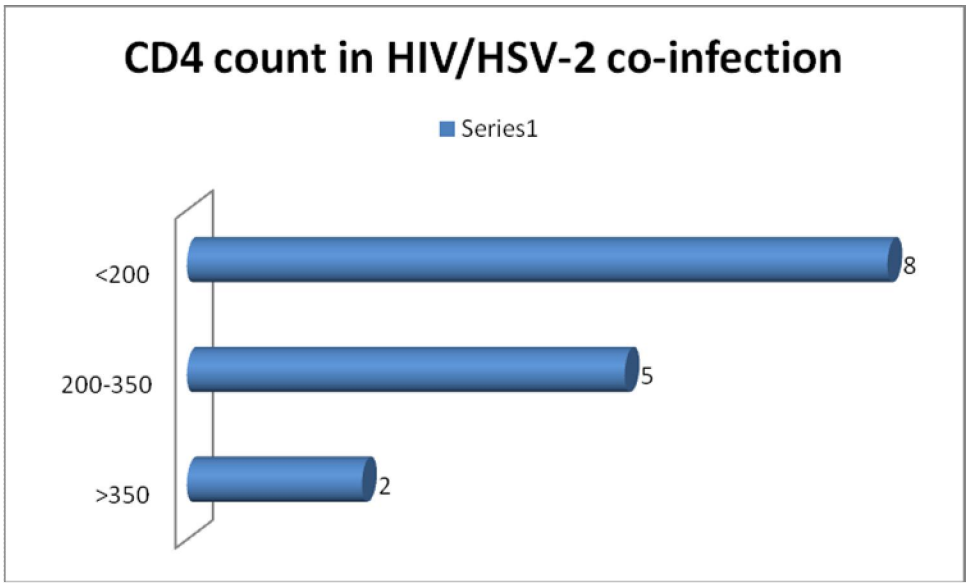


Figure 9. 40% cases were symptomatic and they presented to us with features of decompensated liver disease and portal hypertension.

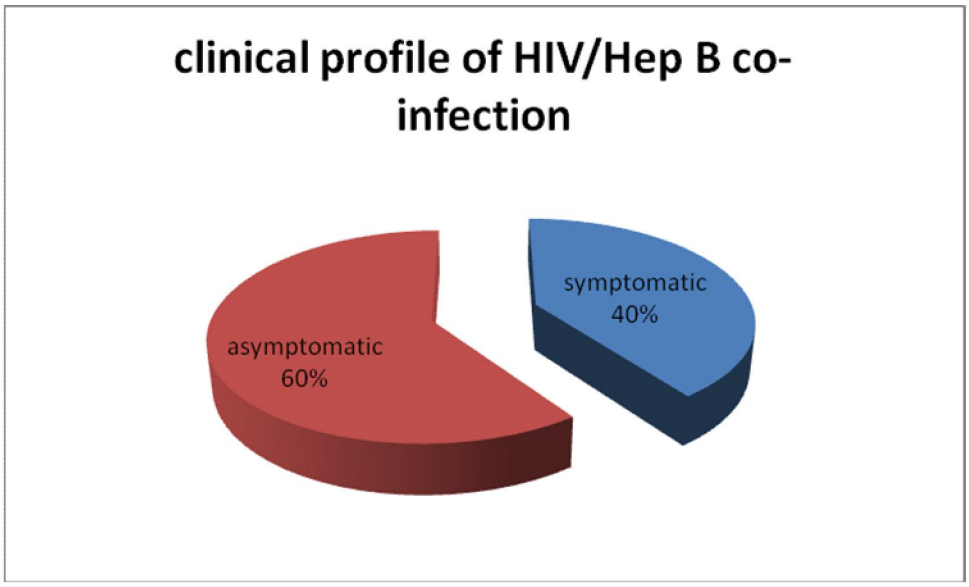


Figure 10. Three out of five cases acquired the disease sexually; 1 out of 5 was an IDU; the other patient has acquired it probably through blood transfusion done per operatively during mitral valve commisurotomy, three years back.

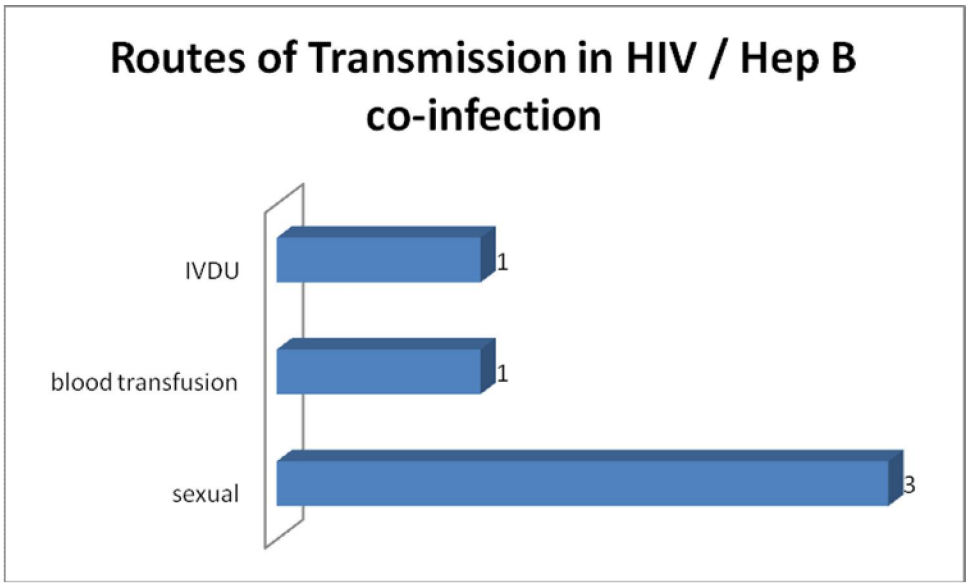


Figure 11. Elevated ALP was seen in 80% of patients (4 in number; Out of them, two were symptomatic).

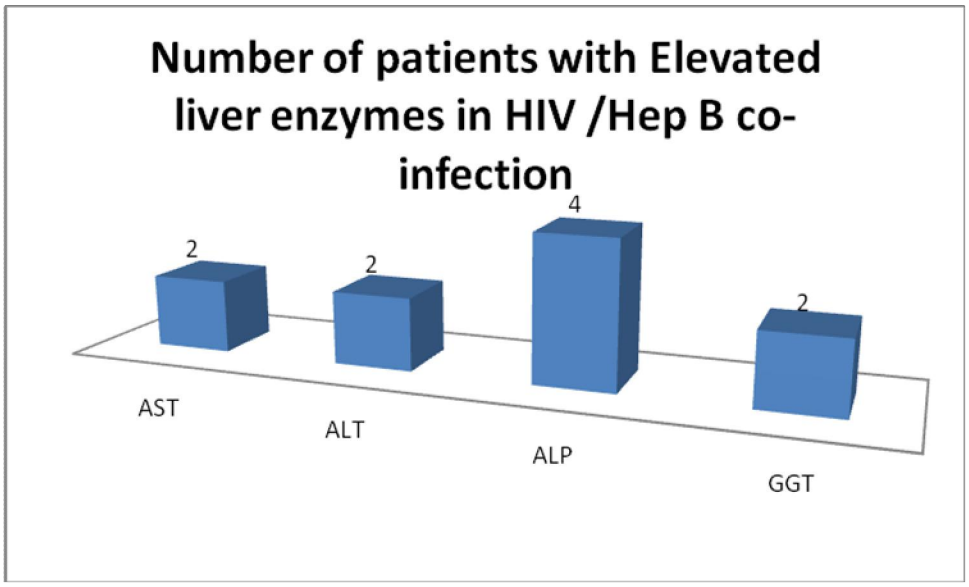


Figure 12. CD4 count was low in 60% of patients.

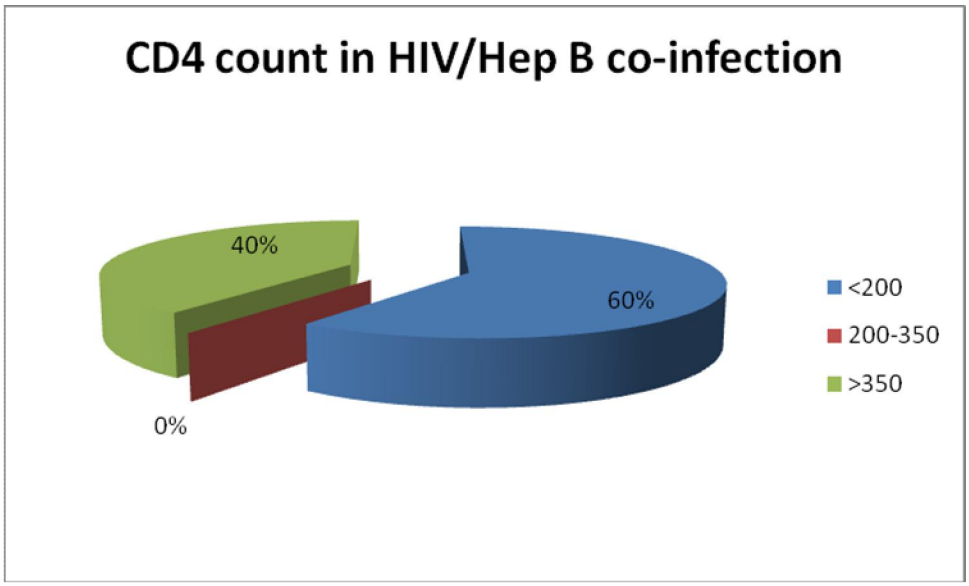


Figure 13. Elevation of liver enzymes was not related to CD4 counts.

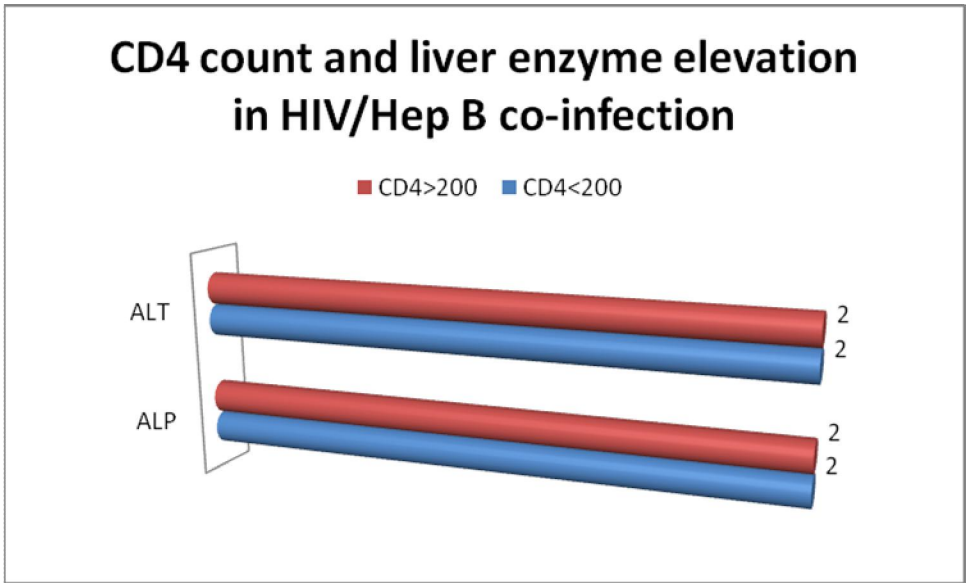


Figure 14. Two symptomatic patients who had features of DCLD with portal hypertension had findings in USG abdomen.

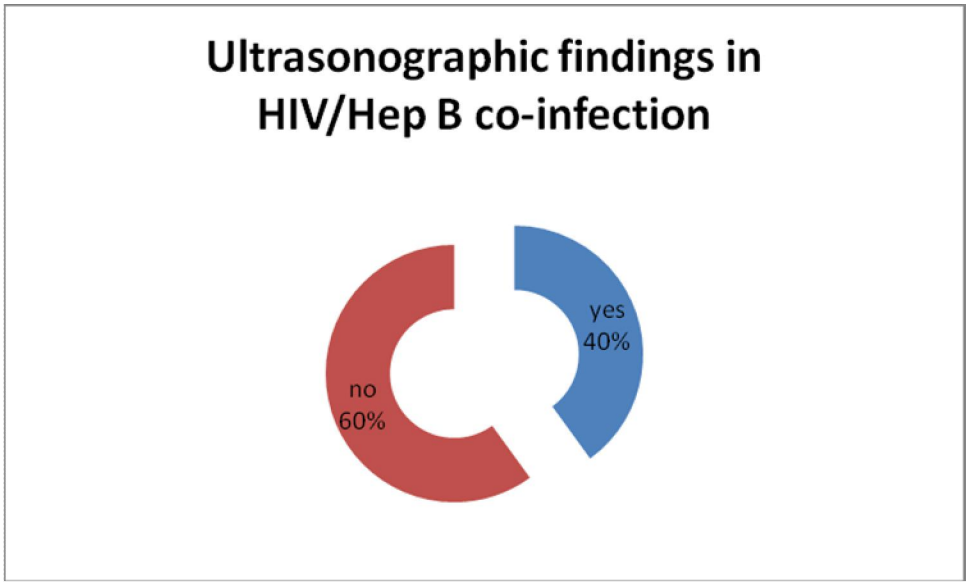


Figure 15. All the patients were asymptomatic.

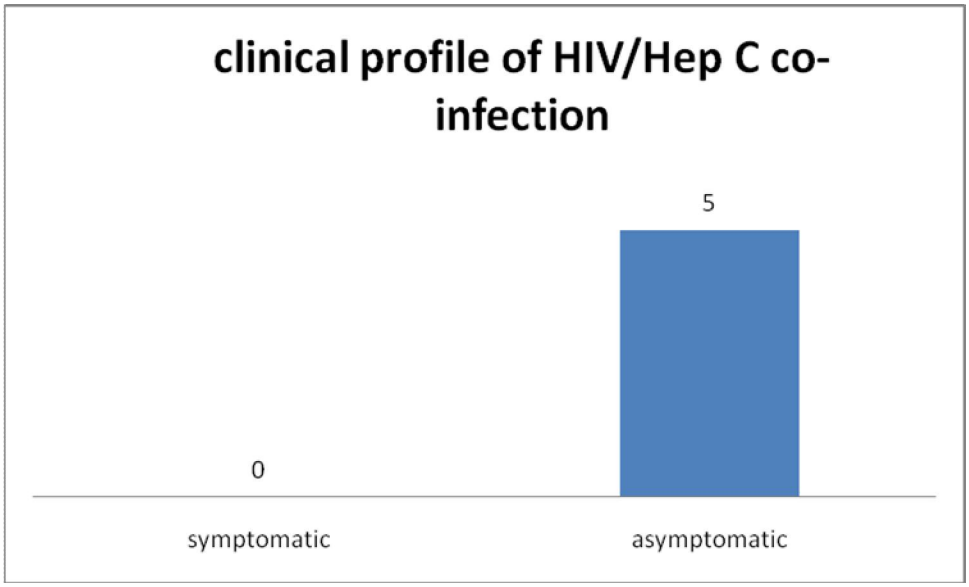


Figure 16. Four out of five patients were IDU. 1 patient has acquired via blood transfusion done for appendicectomy 3 years back.

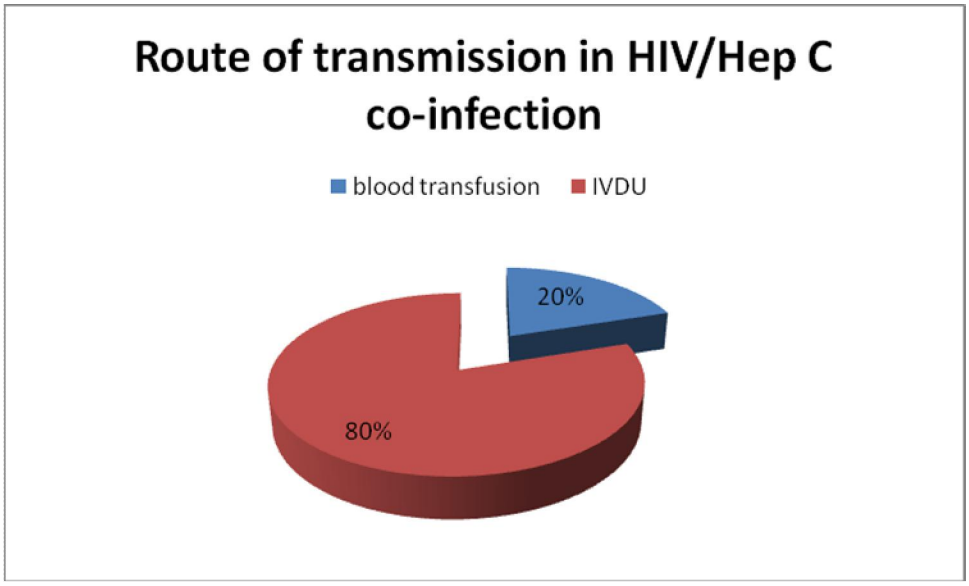


Figure 17. CD4 count was <200 in 80% of patients.

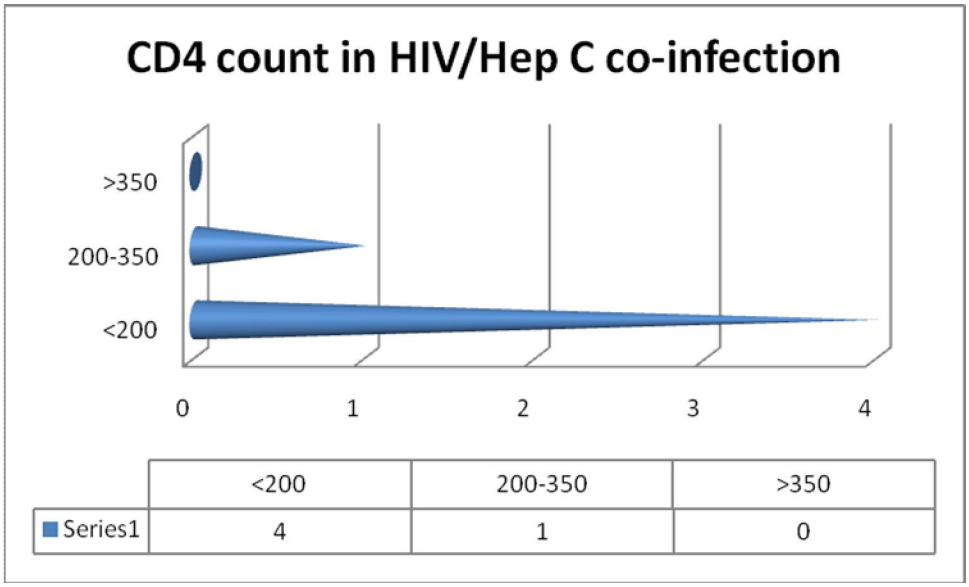


Figure 18. Elevated ALT and ALP was seen in 60% of patients.

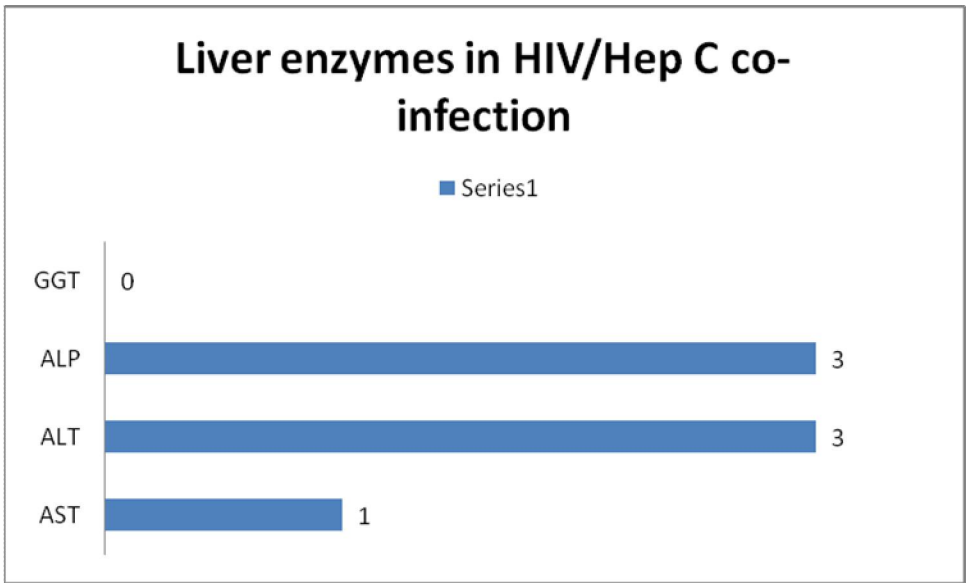


Figure 19. CD4 count was virtually low in all patients with elevated ALT (100%) rather than elevated ALP (60%).

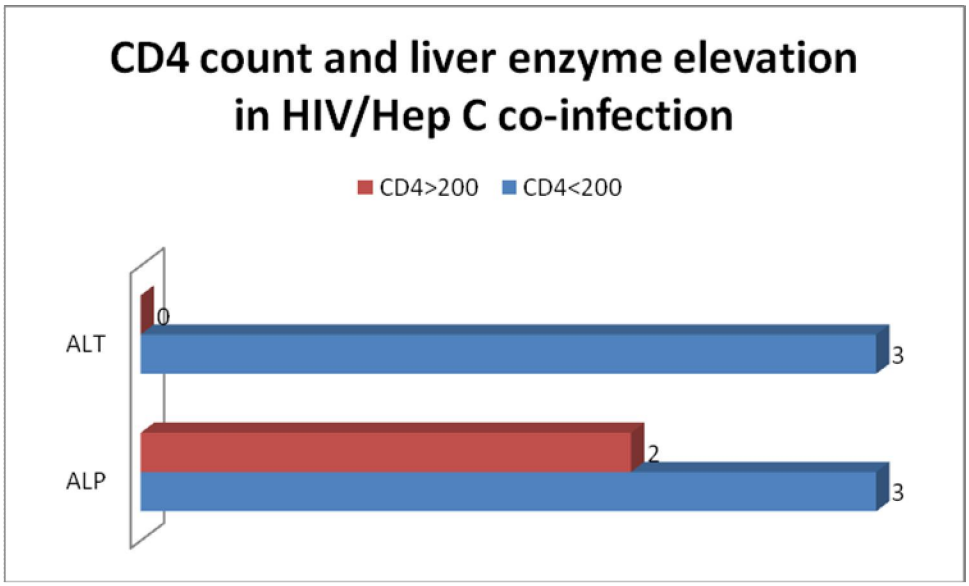


Figure 20. USG abdomen was normal in all cases.

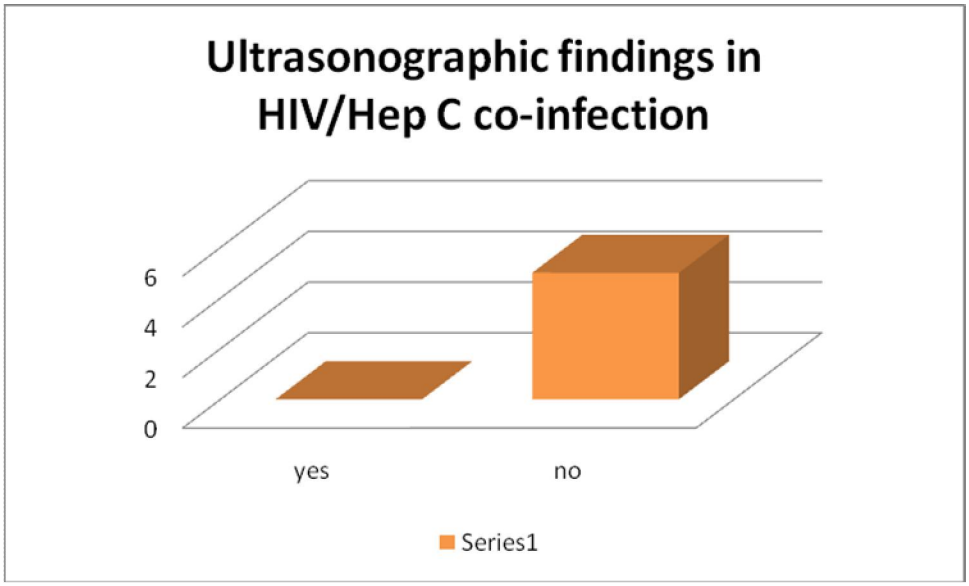


Figure 21. HSV (15%) was the commonest STI associated with HIV followed by syphilis (6%), hepatitis B (5%) and hepatitis C (5%).

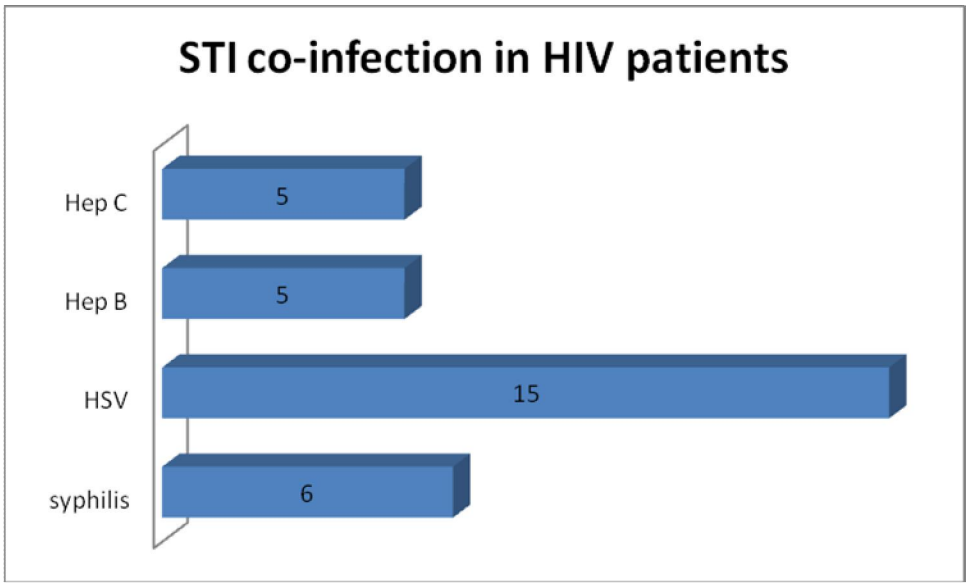


Figure 22. Most of the STIs were asymptomatic, highest noted in hepatitis C infection (100%), followed by HSV-2 infections (33%), syphilis (50%) and hepatitis B (66%).

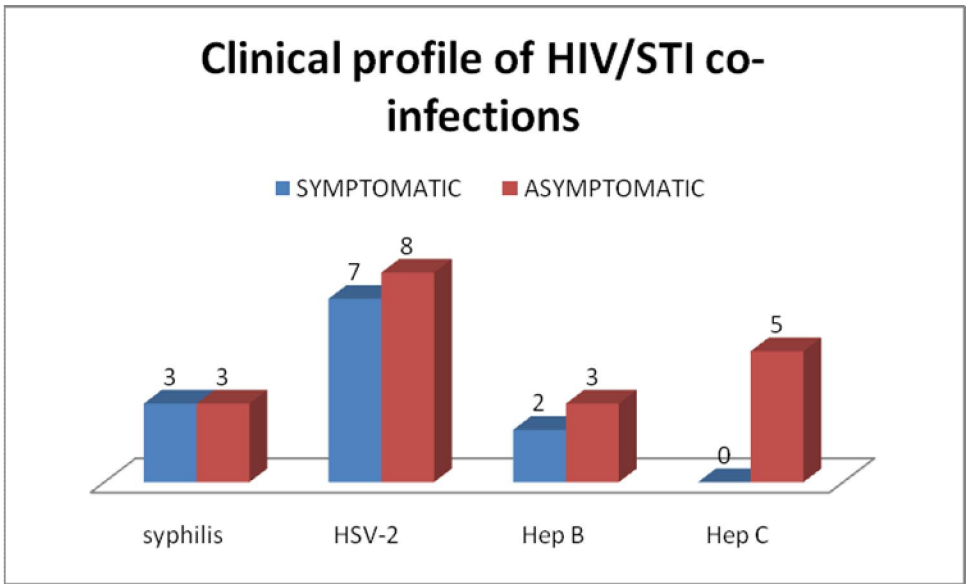


Figure 23. Shows an overall predominance of HIV/STI coinfections, hepatitis C noted only in males; Both the transgenders in our study showed evidence of HSV-2 infection.

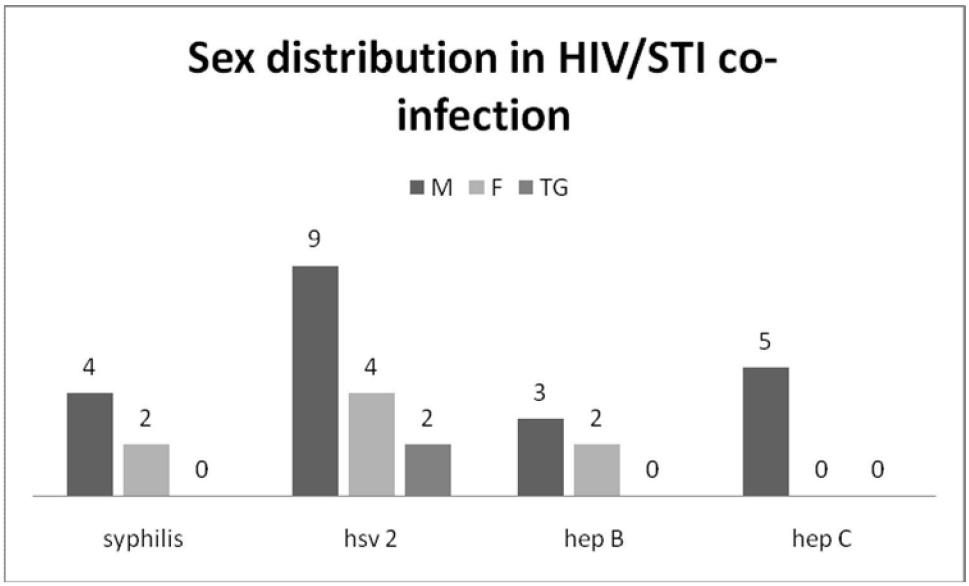


Figure 24. Genito-ulcerative diseases showed no age preponderance, whereas hepatitis infections were noted mostly in patients aged more than 35 years (80%).

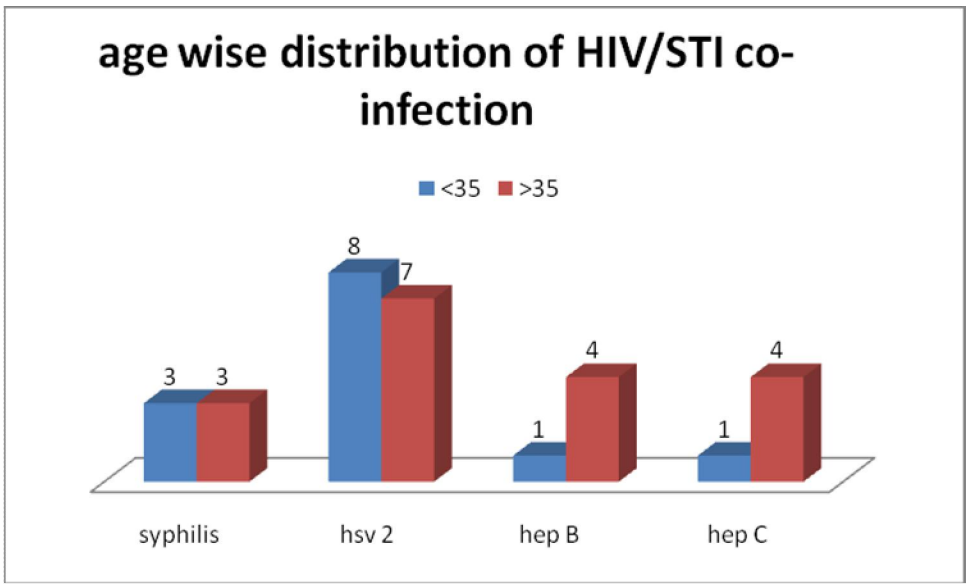


Figure 25. Genito-ulcerative diseases were more common in the rural people (66%) than the urban people, however hepatitis C infection has been noted in more in the urban community (80%).

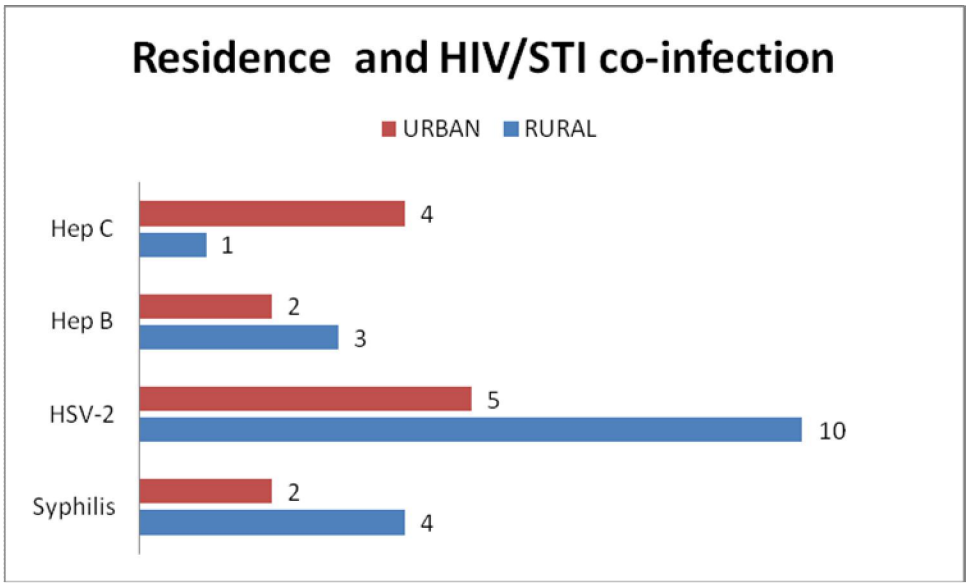


Figure 26. Genito-ulcerative diseases were found in very high percentages (64%) in illiterate people, whereas blood borne infections were common in the literate (66%).

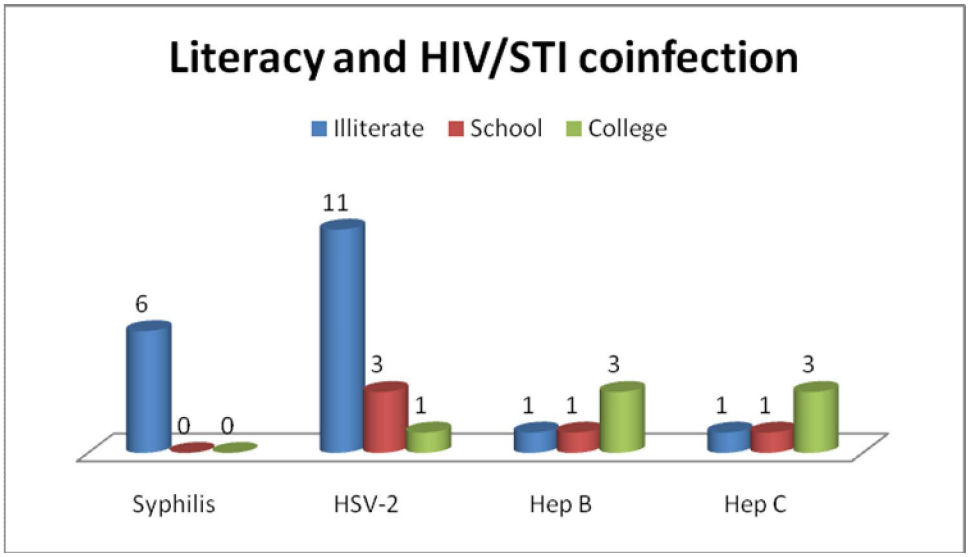


Figure 27. Sexual route of transmission has been the commonest mode of acquisition of ulcerative lesions, though we detected two cases which were blood borne. Hepatitis B infection was mostly sexually transmitted in our study, whereas hepatitis C was only blood borne.

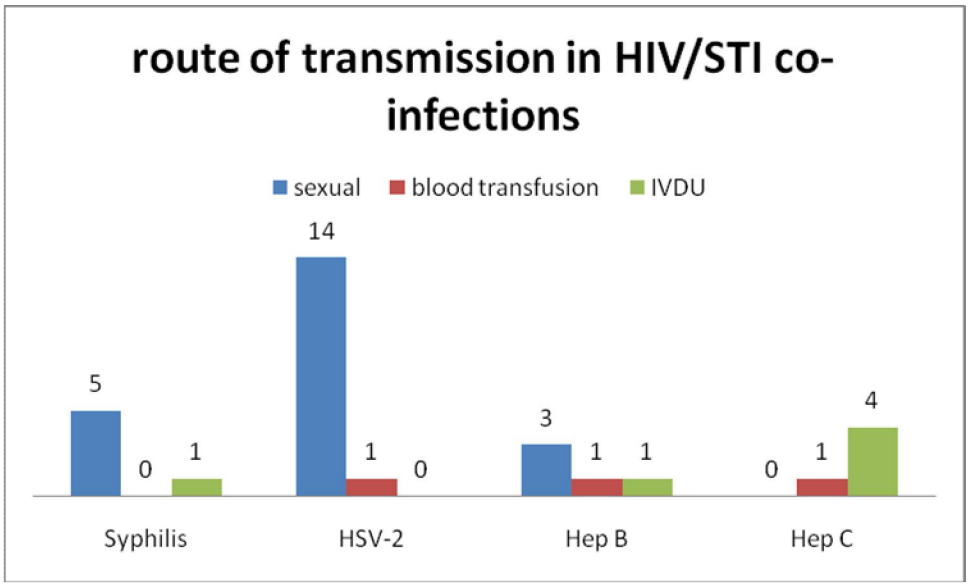


Figure 28. Shows the routes of transmission of HIV in the study population. Sexual transmission (71%) includes homosexual route of transmission (2%).

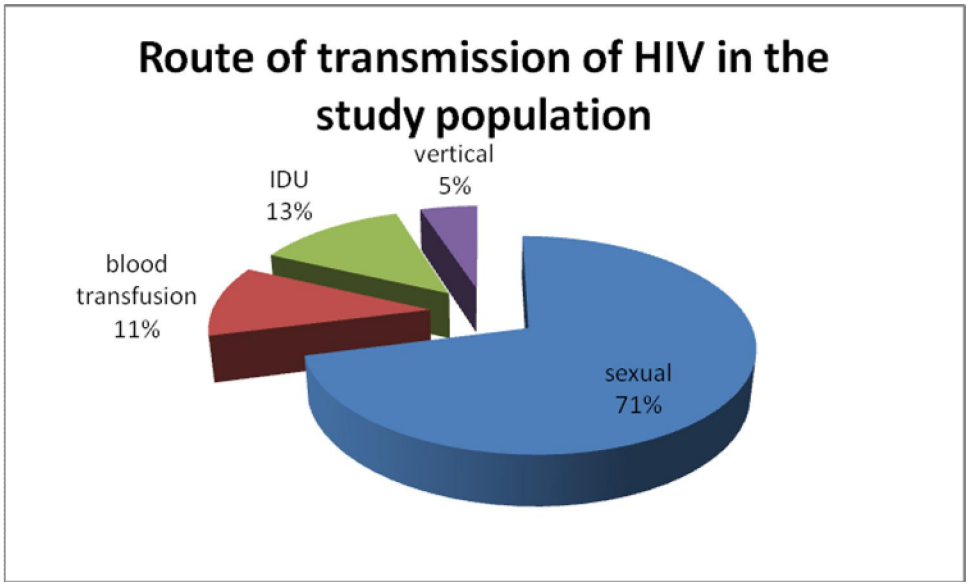
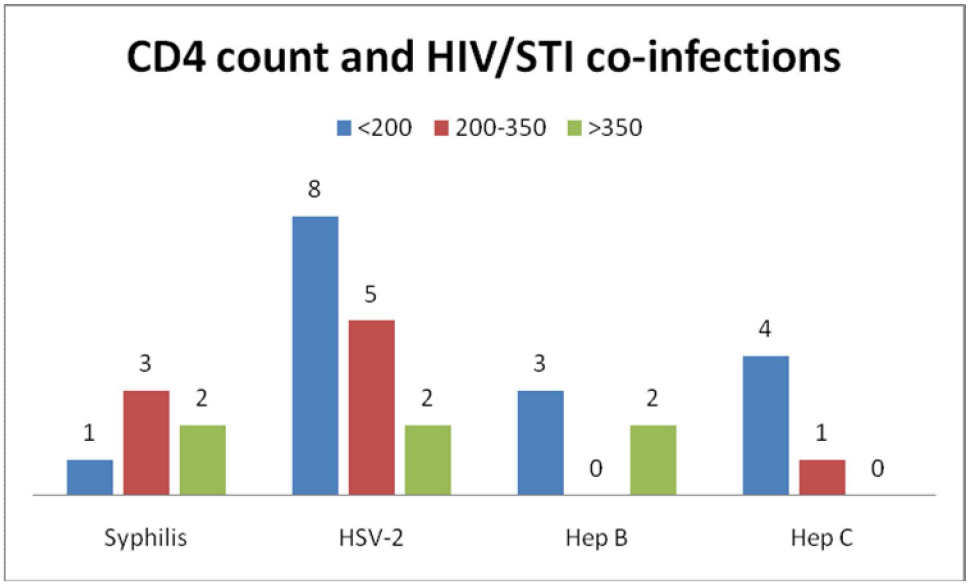


Figure 29. Shows low CD4 counts (<200) associated with HSV-2 and hepatitis C infections.



DISCUSSION

In our study, we intended to analyse 100 newly diagnosed HIV patients, who attended our ART clinic in Madras Medical College and Government General Hospital. All those who took part in our study fulfilled the inclusion criteria. Patients on ART and other hepatotoxic drugs were excluded, as these may interfere with the CD4 counts and liver function test of these patients. Patients who were treated previously for the STIs may have altered clinical features and interference with investigations, so were excluded from the study.

A complete demographic, clinical profile of these patients was taken. Complete blood counts, liver function tests and investigations for Syphilis (VDRL screening and TPHA confirmation for VDRL reactive), Herpes Simplex 2 (anti HSV-2 IgG ELISA), Hepatitis B,(HBsAg), Hepatitis C(anti-HCV) were done in all patients. Ultrasonography was done for those who tested positive for co-infected with hepatitis B or C infections, irrespective of their symptomacy.

Out of the 100 HIV positive patients studied, males accounted to 62% of the cases, a preponderance as shown in many other previous studies. Most of those in the study were urban residents (56%), probably due to study being conducted in a tertiary care center. The literacy rate among the studied population was 45% (who has their schooling was 41%, degree holders were 4%). Most of the IDU patients

were literate. Sexual route of transmission was seen in 28% of among literates and 44% among illiterates.

The commonest route of transmission was found to be sexual (71%), followed by IDU (13%), blood transfusion (11%), and vertical (5%). In contrast to other studies wherein IDU made 2-5% of all cases, we had high percentage of IDU (13%). This is probably due to an increased addressing of IDUs in Chennai and also, Tamil Nadu being identified to harbor the maximum number of IDUs living with HIV infection.[85]

A symptom analysis was done in all the 100 patients for the four STIs (syphilis, HSV-2, hepatitis B and hepatitis C) in detail. Symptoms of genital ulcers were given by 10% and clinical examination revealed features of primary chancre in 3% and herpes genitalis in 7%. However, all hundred patients were subjected to VDRL and anti-HSV-2 IgG antibody detection. VDRL was reactive in 9 patients, out of which three were symptomatic. We did not find high VDRL titres in our study, in contrast to few other previous studies. These patients were subjected to TPHA confirmation and we found it to be positive in six out of those nine. All of these confirmed cases , THREE were in primary stage of syphilis and all three symptomatics had multiple chancres; the other three asymptomatic TPHA positive patients, were probably in early stages of syphilis. Hence, the distribution of HIV/syphilis coinfection was 6%, out of which 60% were males with no age

prelidiction, 66% being rural residents, CD4 counts were more than 350 in most patients.

Patients with symptoms and signs suggestive of herpes genitalis proved to have multiple tender genital ulcerations. In HIV/HSV-2 coinfections, tenderness and necrosis of ulcers was found to be more severe than in HSV-2 infections alone. All the patients in the study were analysed for anti-HSV-2 IgG antibodies.Among the fifteen patients who tested. positive for anti-HSV-2 IgG,, of which seven were symptomatic and eight were asymptomatic. In the asymptomatic group with HIV/HSV-2 coinfection, 50% of the patients gave past history of similar complaints. Analysis of the fifteen who turned positive for anti-HSV-2 IgG antibodies, revealed that nine out of fifteen were males; ten out of fifteen were residents of rural areas/outskirts of the city, eleven out of fifteen were illiterates. Two transgenders included in the study tested positive for HIV/HSV-2 coinfection and were asymptomatic.

Symptoms of hepatitis were asked to all the 100 HIV patients. Among them two patients presented with the history of gradually progressive abdominal distension, one among the two gave history of hematemesis and malena of recent onset. All the other 98 patients showed no symptoms of hepatitis either in the present or in the past. All of them were screened for HBsAg and anti-HCV antibodies.

HBsAg was found to be positive in 5% of individuals (five in number); two of them presented to us with features of decompensated chronic liver disease and portal hypertension. The other three of them were completely asymptomatic. Out of the five patients with this coinfection, there were three males; three were urban residents; four were literate. The mean CD4 counts in these coinfected patients was found to be 297 cells/mm^3. The route of transmission was sexual in three out of five (60%). Liver enzymes were elevated in two patients who had features of DCLD. Ultrasonography showed findings of cirrhotic liver and portal hypertension only in the symptomatic group. Liver was normal in the asymptomatic HIV/hepatits B coinfected patients.

Hepatitis C screening done in 100 patients showed prevalence of 5% in our study, out of which IDU was the most common route of transmission (80%) and 20% was transmitted through blood transfusion. All of them were males[86,87]; 80% were literates; and 80% were urban residents. HIV/hepatitis C coinfection was 100% asymptomatic. Liver enzymes were elevated even in asymptomatics (60%). CD4 counts were virtually low in all patients with elevated ALT. CD4 counts were less than 200 in 80% of individuals with this coinfection. There was no patient co-infected with both Hepatitis B and Hepatitis.C.

Ultrasonography of abdomen was normal in all the patients with HIV/hepatitis C coinfection. The results of HIV/Hepatitis co-infection were in concordance with the studies done by Padmapriyadarshini et al[84]

Overall, analysis of all the 100 HIV patients studied, HSV-2 was the commonest STI associated. Most cases were asymptomatic, CD4 counts were low in most patients with this co-infection; genital ulcers were more tender and necrotic in many patients.

Syphilis was the second most common co-infection with HIV, all of them found to be in primary stage of infection. Like other studies, we also found multiple chancres in few patients, but we never found very high VDRL titres in patients with this co-infection.

Hepatitis B and C infections formed 5% each in being co-infected with HIV. Hepatitis C remained completely asymptomatic in all the patients. Even then, liver enzymes were elevated in majority of the patients with normal ultrasonographic findings. CD4 counts were profoundly low (less than 200/mm^3) in those with elevated liver enzymes in HIV/hepatitis C co-infection rather than HIV/hepatits B co-infection.

We had two patients presented as DCLD, found to have HIV/hepatitis B co-infection. Mode of transmission was sexual in (60% of this co-infection). This was

in contrast to HIV/hepatitis C co-infection where transmission was through IDU and blood transfusion.

The mean age of HIV co-infected[84] with Syphilis was 40 years, hepatitis B – 40 years, hepatitis C – 37 years, HSV-2 – 30 years. CD4 counts remained unaltered with HIV/syphilis or HIV/hepatitis B co-infection. While counts remained low in case of HIV/hepatitis C and HIV/HSV-2 co-nfections. Most patients with these co-infections were asymptomatic and hence mandatory screening may be essential for these co-infections in all HIV patients.

CONCLUSION

In this study, it is clearly shown that, out of 100 HIV patients

- Sexual route of transmission was found to be lesser (71% vs 87%) and IDU was found to be higher (13% vs 2%) than that of national average.
- HIV/STI co-infection was common in males than females.
- Genito-ulcerative diseases were common in the illiterate and rural population, whereas predominantly blood borne infections were common in the literate and urban population.
- HIV/STI co-infections were overall higher in people >35 years of age.
- In all the four STIs studied, asymptomatic infections were higher (highest in hepatitis C(100%), followed by Hepatitis B(60%), HSV-2(53%) and syphilis(50%)
- HSV-2 infection remains the most common STI associated with HIV, many of them being asymptomatic.
- Prevalence rate of HIV/HSV-2 co-infection is higher than that studied elsewhere in Asia and in other states of India.
- Prevalence of HIV/syphilis co-infection is higher (6%) than the Indian average of 4.34%, all of them were in early/primary stage of syphilis.
- Hepatitis C infection was asymptomatic in all those found to be positive.

- Atypical presentation was noted in syphilis (as multiple primary chancres), herpes simplex 2 (has more tender, necrotic ulcers)
- Five patients had HIV/Hepatitis B co-infection (two out of them presented as DCLD with portal hypertension).
- Low CD4 counts were associated with hepatitis C and herpes simplex 2 infections whereas such a correlation was not seen with syphilis and hepatitis B.

PROFORMA

Name: Age: Sex: OP.NO:

Occupation: Income:

Education: Socioeconomic status:

Marital status:

Migration characteristics:

Address: Ph.No:

PRESENTING COMPLAINTS:

Fatigability: Fever:

Jaundice: Abdominal distension:

Lymphadenopathy: Skin changes:

Pedal Edema: Loss of Wt:

Loss of Appetite: Bleeding Tendency:

Altered sensorium:

HISTORY:

H/O IV Drug use:

H/O Previous Blood transfusion:

Sexual history:

HIV status of father / mother / spouse / child:

H/O solid organ transplant/ hemodialysis:

H/O sharing razors:

H/O occupational exposure:

H/O vaccination for hepatitis B

Co Morbid Illness:

EXAMINATION:

GENERAL EXAMINATION:

VITAL SIGNS:

EXAMINATION OF ORAL CAVITY:

EXAMINATION OF ABDOMEN:

EXAMINATION OF GENITALIA:

OTHER SYSTEMS EXAMINATION:

INVESTIGATIONS

COMPLETE BLOOD COUNT:

LIVER FUNCTION TESTS:

CD-4 COUNT:

HBS Ag :

ANTI-HCV ANTIBODY:

USG ABDOMEN(for those who have HIV/Hepatitis co-infection):

VDRL:

TPHA (For those who are VDRL reactive):

Anti HSV-2 IgG antibodies:

FINAL IMPRESSION:

IPNo	PatientName	Age	Sex	Residence	Education	Hepatitis	Syphilis	HSV	Route	TLC	CD4	Bilirubin	ALP	AST	ALT	GGT	HBsAg	AntiHCV	VDRL	TPHA	AntiHSV	USG
1	Stephen	37	M	Urban	S	A	A	A	IVD	6500	161	N	R	N	N	N	-	+	R-	-	-	AN
2	Suresh	38	M	Urban	I	A	A	A	IVD	5000	148	N	N	N	N	N	-	-	R-	-	-	AN
3	Raja	24	M	Urban	C	A	A	A	IVD	7300	102	N	R	R	R	N	-	+	R-	-	-	AN
4	Govindasamy	44	M	Urban	I	A	A	A	Blood	4900	552	N	R	N	N	N	+	-	R-	-	-	AN
5	Banu	33	F	Urban	S	A	A	A	Blood	7800	338	N	N	N	N	N	-	-	R-	-	-	AN
6	Vinitha	28	T	Urban	I	A	A	S	Sexual	5300	275	N	N	N	N	N	-	-	R-	-	+	AN
7	Swapna	28	T	Urban	I	A	A	S	Sexual	4900	168	N	N	N	N	N	-	-	R-	-	+	AN
8	Selvam	40	M	Rural	I	A	S	A	Sexual	5400	297	N	N	N	N	N	-	-	R+	+	-	AN
9	Ramanammal	30	F	Rural	I	A	A	A	Sexual	4700	471	N	N	N	N	N	-	-	R-	-	-	AN
10	Ramakrishnan	38	M	Rural	S	A	A	A	Sexual	5200	468	N	N	N	N	N	-	-	R-	-	-	AN
11	Jayanthi	41	F	Urban	S	A	A	A	Sexual	4800	575	N	N	N	N	N	-	-	R-	-	-	AN
12	Mohan Das	31	M	Rural	S	A	A	A	Sexual	5400	303	N	N	N	N	N	-	-	R-	-	-	AN
13	Anwar	42	M	Urban	S	A	A	A	Sexual	5400	479	N	N	N	N	N	-	-	R+	-	-	AN
14	Selvam	23	M	Urban	I	A	A	A	Sexual	5300	290	N	N	N	N	N	-	-	R-	-	-	AN
15	Ravi	43	M	Urban	I	A	A	A	Sexual	5200	340	N	N	N	N	N	-	-	R-	-	+	AN
16	Robert Singh	33	M	Urban	I	A	A	A	Sexual	4200	175	N	N	N	N	N	-	-	R-	-	-	AN
17	Balasubramani	34	M	Rural	I	A	A	A	Blood	6200	166	N	N	N	N	N	-	-	R-	-	-	AN
18	Arun Raj	24	M	Urban	S	A	A	A	Sexual	7200	338	N	N	N	N	N	-	-	R-	-	-	AN
19	Sooriya Kumar	37	M	Urban	S	A	S	A	Sexual	4200	238	N	N	N	N	N	-	-	R+	-	-	AN
20	Munusamy	39	M	Rural	I	A	A	A	Sexual	3400	543	N	N	N	N	N	-	-	R-	-	-	AN
21	Elangovan	37	M	Urban	I	A	A	A	IVD	3400	154	N	N	N	N	N	-	+	R-	-	-	AN
22	Ravishankar	33	M	Urban	I	A	A	A	IVD	5200	152	N	N	N	N	N	-	-	R-	-	-	AN
23	Manohar	4	M	Urban	NA	A	A	A	Blood	4600	563	N	N	N	N	N	-	-	R-	-	-	AN
24	Jegan	32	M	Urban	I	A	A	A	IVD	4200	166	N	N	N	N	N	-	-	R-	-	-	AN
25	Kamalakannan	45	M	Rural	I	A	S	A	Sexual	6200	261	N	N	N	N	N	-	-	R+	+	-	AN
26	Usha	26	F	Urban	S	A	A	S	Blood	5200	261	N	N	N	N	N	-	-	R-	-	-	AN
27	Dasarathan	38	M	Rural	S	A	A	A	Sexual	4600	490	N	N	N	N	N	-	-	R-	-	-	AN

IPNo	PatientName	Age	Sex	Residence	Education	Hepatitis	Syphilis	HSV	Route	TLC	CD4	Bilirubin	ALP	AST	ALT	GGT	HBsAg	AntiHCV	VDRL	TPHA	AntiHSV	USG
28	Nagammal	47	F	Urban	I	A	A	A	Sexual	5200	504	N	N	N	N	N	-	-	R-	-	-	R=
29	Mahesh	31	M	Urban	I	A	A	A	Sexual	1200	19	N	N	N	N	N	-	-	R-	-	+	AN
30	Kavatha	49	F	Rural	I	A	A	A	Blood	1200	43	N	N	N	N	R	-	-	R-	-	-	AN
31	Babu	30	M	Rural	I	A	A	A	IVD	6800	684	N	N	N	N	N	-	-	R-	-	-	AN
32	Vijayalakshmi	36	F	Rural	I	A	A	A	Blood	4200	120	N	N	N	N	N	-	-	R-	-	-	AN
33	Suresh	29	M	Urban	S	A	A	A	Sexual	8000	38	N	N	N	N	N	-	-	R-	-	-	AN
34	Anjalai	29	F	Urban	S	A	A	A	Blood	4200	240	N	N	N	N	N	-	-	R-	-	-	AN
35	Anbalagan	39	M	Rural	S	A	A	A	Sexual	6700	484	N	N	N	N	N	-	-	R-	-	-	AN
36	Krishnakumari	10	F	Urban	S	A	A	A	Vertical	4200	240	N	N	N	N	N	-	-	R-	-	-	AN
37	Rajendran	42	M	Rural	S	A	A	A	Blood	4200	340	N	N	N	N	N	-	+	R-	-	-	AN
38	Kadhar Moideen	40	M	Urban	I	A	A	A	IVD	6100	473	N	N	N	N	N	-	-	R-	-	-	AN
39	Manimegalai	34	F	Rural	I	A	A	A	Sexual	5200	472	N	N	N	N	N	-	-	R-	-	-	AN
40	Rajendran	35	M	Urban	S	A	A	A	IVD	2600	159	N	N	N	N	N	+	-	R-	-	-	AN
41	Nithya	10	F	Rural	I	A	A	A	Vertical	5200	1951	N	N	N	N	N	-	-	R-	-	-	AN
42	Naveen Kumar	5	M	Urban	NA	A	A	A	Vertical	6200	360	N	N	N	N	N	-	-	R-	-	-	AN
43	Meena	16	F	Rural	S	A	A	A	Vertical	4200	357	N	N	N	N	N	-	-	R-	-	-	AN
44	Rajeshwari	38	F	Rural	S	A	A	A	Blood	1200	82	N	N	N	N	N	-	-	R-	-	-	AN
45	Prakash	22	M	Rural	S	A	A	A	IVD	2100	150	N	N	N	N	N	-	-	R-	-	-	AN
46	Edward	40	M	Urban	S	A	A	A	IVD	7900	327	N	R	N	N	N	-	+	R-	-	-	AN
47	Ramadoss	45	M	Rural	S	A	A	A	Blood	6900	490	N	N	N	N	N	-	+	R-	-	-	AN
48	Selvi	35	F	Rural	S	A	A	A	Sexual	4200	80	N	N	N	N	N	-	-	R-	-	-	AN
49	Kuppusamy	38	M	Urban	S	A	A	A	Sexual	4200	519	N	N	N	N	N	-	-	R-	-	-	AN
50	Meena	16	F	Rural	S	A	A	A	Vertical	6400	240	N	N	N	N	N	-	-	R-	-	-	AN
51	Prakash	38	M	Rural	S	A	A	A	IVD	3300	543	N	N	N	N	N	-	-	R-	-	-	AN
52	Chinnasamy	50	M	Urban	I	A	A	A	Sexual	4300	239	N	N	N	N	N	-	-	R-	-	-	AN
53	Ponnurangan	45	M	Rural	I	A	A	S	Sexual	9400	310	N	R	N	N	N	+	-	R-	-	-	AN
54	Tamilarasi	30	F	Urban	S	A	A	A	Sexual	2400	381	N	N	N	N	N	-	-	R-	-	-	AN

IPNo	PatientName	Age	Sex	Residence	Education	Hepatitis	Syphilis	HSV	Route	TLC	CD4	Bilirubin	ALP	AST	ALT	GGT	HBsAg	AntiHCV	VDRL	TPHA	AntiHSV	USG
55	Ravikumar	29	M	Urban	S	A	A	A	Sexual	1200	508	N	N	N	N	N	-	-	R-	-	-	AN
56	Geetha	28	F	Urban	S	A	A	A	Sexual	2200	268	N	N	N	N	N	-	-	R-	-	-	AN
57	Vasantharani	29	F	Rural	I	A	A	A	Sexual	3300	154	N	N	N	N	N	-	-	R-	-	-	AN
58	Babu	32	M	Urban	I	A	A	A	Sexual	4400	299	N	N	N	N	N	-	-	R-	-	-	AN
59	Sowrirajan	58	M	Urban	I	A	A	A	Sexual	1200	93	N	N	N	N	N	-	-	R-	-	-	AN
60	Jayanthi	46	F	Urban	I	A	A	A	Sexual	3100	120	N	N	N	N	N	-	-	R-	-	+	AN
61	Krishnaveni	40	F	Urban	I	A	A	A	Sexual	1200	432	N	N	N	N	N	-	-	R-	-	-	AN
62	Musha	32	M	Rural	I	A	S	A	Sexual	3300	320	N	N	N	N	N	-	-	R+	+	-	AN
63	Sumathi	35	F	Rural	I	A	A	A	Sexual	1700	373	N	N	N	N	N	-	-	R-	-	-	AN
64	Vetrivendhan	32	M	Urban	S	A	A	A	Sexual	1200	354	N	N	N	N	N	-	-	R-	-	-	AN
65	Vijayasarathi	26	M	Urban	S	S	A	A	Sexual	4200	589	R	N	N	N	N	-	-	R-	-	+	AN
66	Veeralakshmi	29	F	Rural	S	A	A	A	Sexual	3100	316	N	N	N	N	N	-	-	R-	-	-	AN
67	Murugesan	52	M	Urban	I	A	A	A	Sexual	2100	631	N	N	N	N	N	-	-	R-	-	-	AN
68	Krishnan	32	M	Urban	I	A	S	A	Sexual	3100	267	N	N	N	N	N	-	-	R+	-	-	AN
69	Rajesh	34	M	Urban	I	A	A	S	Sexual	1500	93	N	N	N	N	N	-	-	R-	-	-	AN
70	Vijayalakshmi	23	F	Urban	I	A	A	A	Sexual	2300	654	N	N	N	N	N	-	-	R-	-	-	AN
71	Murugan	28	M	Urban	S	A	A	A	Sexual	1400	860	N	N	N	N	N	-	-	R-	-	-	AN
72	Dhanasekar	41	M	Rural	I	A	A	A	Sexual	1800	32	N	N	N	N	N	-	-	R+	+	-	AN
73	Rajesh	34	M	Urban	S	A	A	A	Sexual	3100	93	N	N	N	N	N	-	-	R-	-	-	AN
74	Malar	32	F	Rural	I	A	S	A	Sexual	1200	438	N	N	N	N	N	-	-	R+	-	-	AN
75	Prema	28	F	Rural	I	A	A	A	Sexual	1200	420	N	N	N	N	N	-	-	R-	-	-	AN
76	Shabana Begam	26	F	Rural	S	A	A	A	Sexual	3500	243	N	N	N	N	N	-	-	R-	-	+	AN
77	Younus Khan	30	M	Urban	S	A	A	A	Sexual	1400	283	N	N	N	N	N	-	-	R-	-	-	AN
78	Sekar	54	M	Urban	S	A	A	A	Sexual	4800	235	N	N	N	N	N	-	-	R-	-	-	AN
79	Aruna	35	F	Rural	I	A	A	A	Sexual	1200	52	N	N	N	N	N	-	-	R-	-	-	AN
80	Sandhyagu	32	M	Urban	C	A	A	A	Sexual	1400	110	N	N	N	N	N	-	-	R-	-	+	AN
81	Roslin Amutha	32	F	Urban	S	A	A	A	Sexual	1400	122	N	N	N	N	N	-	-	R-	-	-	AN

IPNo	PatientName	Age	Sex	Residence	Education	Hepatitis	Syphilis	HSV	Route	TLC	CD4	Bilirubin	ALP	AST	ALT	GGT	HBsAg	AntiHCV	VDRL	TPHA	AntiHSV	USG
82	Senthil	22	M	Rural	I	A	A	A	Sexual	1400	282	N	N	N	N	N	-	-	R-	-	+	AN
83	Malarkodi	32	F	Urban	I	A	A	A	Sexual	1400	154	N	N	N	N	N	-	-	R-	-	-	AN
84	Edward	43	M	Urban	S	A	A	A	Sexual	4800	336	N	N	N	N	N	-	-	R-	-	-	AN
85	Sathyamoorthy	42	M	Urban	S	A	S	A	Sexual	1400	409	N	N	N	N	N	-	-	R+	-	-	AN
86	Amsa	40	F	Rural	I	S	A	A	Sexual	6300	194	R	R	R	R	R	+	-	R-	-	+	N
87	Kanniyammal	47	F	Rural	I	S	A	A	Sexual	10600	369	R	R	R	R	R	+	-	R+	+	-	N
88	Leela	40	F	Urban	I	A	A	A	Sexual	600	307	N	N	N	N	N	-	-	R-	-	-	AN
89	Balu	38	M	Rural	I	A	A	A	Sexual	4200	449	N	N	N	N	N	-	-	R-	-	+	AN
90	Santhosam	33	M	Urban	I	A	S	A	Sexual	1400	120	N	N	N	N	N	-	-	R+	+	-	AN
91	Uma	34	F	Rural	I	A	A	A	Sexual	5600	238	N	N	N	N	N	-	-	R-	-	-	AN
92	Mallika	35	F	Rural	I	A	A	S	Sexual	1400	320	N	N	N	N	N	-	-	R-	-	+	AN
93	Arumugam	37	M	Rural	I	A	A	S	Sexual	1400	110	N	N	N	N	N	-	-	R-	-	+	AN
94	Perumal	50	M	Rural	S	A	A	A	Sexual	1400	304	N	N	N	N	N	-	-	R-	-	+	AN
95	Parvathi	48	F	Rural	I	A	A	A	Sexual	1200	309	N	N	N	N	N	-	-	R-	-	-	AN
96	Raghu	40	M	Urban	I	A	A	A	Sexual	1200	208	N	N	N	N	N	-	-	R-	-	-	AN
97	Rekha	34	F	Urban	S	A	A	A	Sexual	25000	187	N	N	N	N	N	-	-	R-	-	-	AN
98	Selvam	45	M	Rural	I	A	A	A	Sexual	11100	12	N	N	N	N	N	-	-	R-	-	-	AN
99	Anbalagan	40	M	Rural	I	A	A	A	Sexual	2700	96	N	N	N	N	N	-	-	R-	-	-	AN
100	Mariyammal	40	F	Rural	I	A	A	A	Sexual	7200	368	N	N	N	N	N	-	-	R-	-	-	AN

I-Illiterate S-school c-college N-Normal R+ REACTIVE R- NON-REACTIVE AN-nil abnormality N-ABNORMAL

BIBLIOGRAPHY

1. AIDS Epidemic Update. Joint United Nations Program on HIV/ AIDS (UNAIDS) and World Health Organization (WHO), 2007.

2. UNGASS Country Progress Report on HIV/AIDS 2008: India. National AIDS Control Organisation, Ministry of Health and Family Welfare Government of India, New Delhi.

3. HIV/AIDS in India.. Available from: http://www.worldbank. org.com. [accessed on 2009 Jul 25].

4. Subramanian T, Gupte MD, Paranjape RS, Brahmam GN, Ramakrishnan L, Adhikary R, *et al*. HIV, sexually transmitted infections and sexual behaviour of male clients of female sex workers in Andhra Pradesh, Tamil Nadu and Maharashtra, India: Results of a cross-sectional survey. AIDS 2008;Suppl 5:S69-79.

5. Kumar R, Jha P, Arora P, Mony P, Bhatia P, Millson P, *et al*. Trends in HIV-1 in young adults in south India from 2000 to 2004: A prevalence study, Lancet 2006;367:1164-72.

6. Ray K, Bala M, Gupta SM, Khunger N, Puri P, Muralidhar S, *et al*. Changing trends in sexually transmitted infections at a Regional STD Centre in north India. Indian J Med Res 2006;124:559-68.

7. Talsania NJ, Rathod D, Shah R, Patel Y, Mathur N. STI/ HIV prevalence in Sakhi Swasthya Abhiyan, Jyotisangh, Ahmedabad: A clinico-epidemiological study. Indian J Sex Transm Dis 2007;28:15-8.

8. Malodia L. Prevalence and trend of STI and HIV among FSW of Ahmadabad, AMC AIDS Control Society, 2004.

9. Setia MS, Lindan C, Jerajani HR, Kumta S, Ekstrand M, Mathur M, *et al*. Men who have sex with men and transgenders in Mumbai, India: An emerging risk group for STIs and HIV. Indian J Dermatol Venereol Leprol 2006;72:425-31.

10. Dandona L, Lakshmi V, Kumar GA, Dandona R. Is the HIV burden in India being overestimated?*BMC Public Health.* 2006;6:308

11. *Primary and secondary syphilis -- United States, 2000-2001.MMWR Morb Mortal Wkly Rep* 2002 Nov 1; 51:971-3.

12. *Primary and secondary syphilis among men who have sex with men -- New York City, 2001. MMWR Morb Mortal Wkly Rep* 2002 Sep 27; 51:853-6.

13. Centers for Disease Control and Prevention. *The national plan to eliminate syphilis from the United States, 1999. Public Health Service. Washington, DC: US Government Printing Office, 1999* .

14. Workowski KA and Berman SM. *CDC sexually transmitted diseases treatment guidelines. Clin Infect Dis* 2002 Oct 15; 35:S135-7.

15. Singh AE and Romanowski B. *Syphilis: Review with emphasis on clinical, epidemiologic, and some biologic features. Clin Microbiol Rev* 1999 Apr; 12:187-209.

16. Estanislao LB and Pachner AR. *Spirochetal infection of the nervous system. Neurol Clin* 1999 Nov; 17:783-800.

17. Hook EW III and Marra CM. *Acquired syphilis in adults. N Engl J Med* 1992 Apr 16; 326:1060-9.

18. Holtom PD et al. *Prevalence of neurosyphilis in human immunodeficiency virus-infected patients with latent syphilis. Am J Med* 1992 Jul; 93:9-12.

19. Rolfs RT et al. A randomized trial of enhanced therapy for early syphilis in patients with and without human immunodeficiency virus infection. *The Syphilis and HIV Study Group. N Engl J Med* 1997 Jul 31; 337:307-14.

20. Berger JR et al. *Syphilitic cerebral gumma with HIV infection.Neurology* 1992 Jul; 7:1282-7.

21. Gordon SM et al. *The response of symptomatic neurosyphilis to high-dose intravenous penicillin G in patients with human immunodeficiency virus infection. N Engl J Med* 1994 Dec 1; 331:1469-73.

22. Horowitz HW et al. *Cerebral syphilitic gumma confirmed by the polymerase chain reaction in a man with human immunodeficiency virus infection. N Engl J Med* 1994 Dec 1; 331:1488-91.

23. Katz DA et al. Neurosyphilis. *A comparative study of the effects of infection with human immunodeficiency virus. Arch Neurol* 1993 Mar; 50:243-9.

24. Gourevitch MN et al. *Effects of HIV infection on the serologic manifestations and response to treatment of syphilis in intravenous drug users. Ann Intern Med* 1993 Mar 1; 118:350-5.

25. Marra CM et al. *Resolution of serum and cerebrospinal fluid abnormalities after treatment of neurosyphilis. Influence of concomitant human immunodeficiency virus infection. Sex Transm Dis* 1996 May-Jun; 23:184-9.

26. Berry CD et al. *Neurologic relapse after benzathine penicillin therapy for secondary syphilis in a patient with HIV infection. N Engl J Med* 1987 Jun 18; 316:1587-9.

27. Zunt HR and Marra CM. *Cerebrospinal fluid testing for the diagnosis of central nervous system infection. Neurol Clin* 1999 Nov; 17:675-89.

28. Carmo RA et al. *Syphilitic meningitis in HIV-patients with meningeal syndrome: Report of two cases and review. Braz J Infect Dis* 2001 Oct; 5:280-7.

29. Aldave AJ et al. *Ocular syphilis. Curr Opin Ophthalmol* 2001 Dec; 12:433-41.

30. Workowski KA and Levine WC. *Sexually transmitted diseases treatment guidelines -- 2002. MMWR Morb Mortal Wkly Rep* 2002 May 10; 51(RR06):1-80.

31. Venkitaraman AR, Seigneurin JM, Lenoir GM, John TJ. Infections due to the human herpes-viruses in southern India: A seroepidemiological survey. *Int J Epidemiol* 1986;**15(4)**:561-566.

32. Agarwal N, Gupta S. Reproductive tract infection in adolescent females. *Obs Gynae Today* 2000;**5(7)**:410-412.

33. Malkin JE, Morand P, Malvy D, Ly TD, Chanzy B, Labareyre CD, Hasnaoui AE, Hercberg S. Seroprevalence of HSV-1 and HSV-2 infection in the general French population. *Sex Transm Infect* 2002;**78**:201-203.

34. Mbizvo EM, Sia EM, Pedersen BS, Chirenje MZ, Munjome M, Hussain A. Association of herpes simplex virus type 2 with the human immunodeficiency virus among urban women in Zimbabwe. *Int J STD AIDS* 2002;**13**:343-348.

35. Legori M. Prevalence of sexually transmitted infections and HBsAg among female sex workers of Thiruvananthapuram, Kerala, India. *J Acad Clin Microbiol* 2001;**3(1)**:5-9.

36. Mookherjee N, Gogate A. Incidence of HSV infection in bad obstetrics history (BOH) cases. *Indian J Med Microbiol* 1994;**12(1)**:60-64.

37. Turbadkar D, Mathur M, Rele M. Seroprevalence of TORCH infection in bad obstetric history. *Indian J Med Microbiol* 2003;**21(2)**:108-110.

38. Kumar A, Gupta N, Sharma JB. Genital Herpes-A Reappraisal. *Obs Gynae Today* 2000;**5(7)**:426-428.

39. Pandey SN, Joshi JV, Vaidya RA, Vaidya AB. Reproductive tract infection. A scourge for women's health. *J Obst Gyn India* 2001; **51(1)**:71-77.

40. Shukla A, Das K, Mathur A, Mehra P. Herpes simplex virus type-2 in carcinoma cervix: A controlled serological study. *J Obst and Gynae India* 1984;**34(2)**:315-318.

41. Alter MJ. Epidemiology of viral hepatitis and HIV co infection. J Hepatol 2006;44(1 Suppl):S6-9.

42. Bellini C, Keiser O, Chave JP et al. Liver enzyme elevation after lamivudine withdrawal in HIV-hepatitis B virus co-infected patients: the Swiss HIV cohort study. HIV Med 2009;10:12-18.

43. Biggar RJ, Goedert JJ, Hoofnagle J. Accelerated loss of antibody to hepatitis B surface antigen among immnodeficient homosexual men infected with HIV. N Engl J Med 1987;316:360.

44. Bodsworth NJ, Cooper DA, Donovan B. The influence of human immunodeficiency virus virus type 1 infection on the development of the hepatitis B carrier state. J Infect Dis 1991;163;1138-40.

45. Clifford GM, Rickenbach M, Polesel J et al. Influence of HIV-related immunodeficiency on the risk of hepatocellular carcinoma. AIDS 2008;22:2135-

46. Colin JF, Cazals-Hatem D, Loriot MA et al. Influence of human immunodeficiency virus infection on chronic hepatitis B in homosexual men. Hepatol 1999;29:1306-10.

47. DiMartino V, Thevenot T, Colin JF et al. Influence of HIV infection on the response to interferon therapy and the long term outcome of chronic hepatitis B. Gastroenterol 2002;123:1812-22.

48. Diop-Ndiaye H, Toure-Kane C, et al. Hepatitis B, C seroprevalence and delta virus in HIV-1 Senegalese patients at HAART initiation (retrospective study). J Med Virol 2008;80:1332-6.

49. Drake A, Mijch A, Sasadeusz J. Immune reconstitution hepatitis in HIV and hepatitis B co infection, despite lamivudine as part of HAART. Clin Infect Dis 2004;39:129-132.

50. Gatanaga H, Yasuoka A, Kikuchi Y, Tachikawa N, Oka S. Influence of prior HIV-1 infection on the development of chronic hepatitis B infection. Eur J Clin Microbiol Infect Dis 2000; 19:237-9.

51. Gilson RJ, Hawkins AE, Beecham MR et al. Interactions between HIV and HBV in homosexual men: effects on the natural history of infection. AIDS 1997;11:597-606.

52. Hadler SC, Judson FN, O'Maeely PM et al. Outcome of hepatitis B virus infection in homosexual men and its relation to prior human immunodeficiency virus infection. J Infect Dis 1991;163:454-9..

53. Hoffman CJ, Thio CL. Clinical implications of HIV and hepatitis B co infection in Asia and Africa. Lancet Infect Dis 2007;7:402-9.

54. Hoffmann CJ, Charalambous S, Martin DJ, Innes C et al. Hepatitis B virus infection and response to antiretroviral therapy (ART) in a South African ART Program. Clin Infect Dis 2008;47:1479-85.

55. Hoffman CJ, Seaberg EC, Young S et al. Hepatitis B and long-term HIV outcomes in co infected HAART recipients. AIDS 2009;23 [EPub].

56. Hoffman CJ, Charalambous S, Martin DJ et al. Hepatitis B virus infection and response to antiretroviral therapy (ART) in a South African ART Program. Clin Infect Dis 2009;47:1479-85.

57. Krogsgaard K, Lindhardt BO, Nielsen JO et al. The influence of HTLV-lll infection on the natural history of hepatitis B virus infection in male homosexual carriers. Hepatol 1987;7:37-41.

58. Laukamm-Josten U, Muller O, Bienzle U et al. Decline of naturally acquired antibodies to hepatitis B surface antigen in HIV-1 infected homosexual men. AIDS 1988;2:400-1.

59. Livry C Binquet C. Sgro C et al. Acute liver enzyme elevations in HIV-1 infected patients. HIV Clin Trials 2003;4:400-10.

60. Lee HC, Ko, NY, Lee NY et al. Seroprevalence of viral hepatitis and sexually transmitted disease among adults with recently diagnosed HIV infection in southern Taiwan, 2000-5: upsurge in hepatitis C virus infections among injection drug users. J Formos Med Assoc 2008;107:404-11.

61. Nyirenda M, Beadsworth MB, Stephany P et al. Prevalence of infection with hepatitis B and C virus and co infection with HIV in medical inpatients in Malawi. J Infect 2008;57:72-77.

62. Puoti M, Spinetti A, Ghezzi A et al. Mortality for liver disease in patients with HIV infection: a cohort study. J Acquir Immune Defic Syndr 2000;24:211-7.

63. Puoti M, Torti C, Ripamonti D et al. Severe hepatotoxicity during combination antiretroviral therapy treatment: incidence, liver histology, and outcome. J Acquir Immune Defic Syndr 2003;32:259-67.

64. Puoti M, Cozi-Lepri A, Paraninfo G et al. Impact of lamivudine on the risk of liver-related death in 2,041 HBsAg and HIV- positive individuals: results from and inter-cohort analysis. Antivir ther 2006;11:567-74.

65. Puoti M, Torti C, Bruno R, Filice G et al. Natural history of chronic hepatitis B in co-infected patients. J Hepatol 2006;44:S65-70.

66. Sulkowski MS, Thomas DL, Chaisson RE, Moore RD. Hepatotoxicity associated with antiretroviral therapy in adults infected with human immunodeficiency virus and the role of hepatitis C or B virus infection. JAMA 2000;283:74-80.

67. Thio, C. Hepatitis B and Human Immunodeficiency Virus Co infection. Hepatol 2009;49:S138-145.

68 FrançaisAceijas, Carmen and Rhodes, Tim. 2007. Global estimates of prevalence ofHCV infection among injecting drug users. Drug Policy. 18 (5). 352-358.

69 Aidsmap. 2007. International panel issues new HIV/HCV co-infection guidelines.http://www.aidsmap.com/en/news/AE8EFA66-1BE6-47BE-94A2-8430634114A5.asp

70 Canadian Centre on Substance Abuse. Harm Reduction.http://www.ccsa.ca/ENG/TOPICS/HARMREDUCTION/Pages/default.aspx

71 Canadian Centre on Substance Abuse. 2005. Hepatitis C virus (HCV) infection and illicit drug use.http://www.ccsa.ca/2005%20CCSA%20Documents/ccsa-004030-2005.pdf

72 International Harm Reduction Association. http://www.ihra.net/Whatisharmreduction

73 Cook, Catherine and Kanaef, Natalya . 2008. The Global State of Harm Reduction 2008: Mapping the response to drug-related HIV and hepatitis C epidemics. International Harm Reduction Association.

74 Laurent, C et al. 2001. Seroepidemiological survey of hepatitis C virus among commercial sex workers and pregnant women in Kinhasa, Democratic Republic of Congo. International Journal of Epidemiology. 30: 872-877.

75 Mathers, Bradley M et al. 2008. Global epidemiology of injecting drug use and HIV among people who inject drugs: a systematic review. The Lancet.http://www.who.int/hiv/topics/idu/LancetArticleIDUHIV.pdf

76 Public Health Agency of Canada. Hepatitis C. http://www.phac-aspc.gc.ca/hepc/index-eng.php

77 Rockstroh, J et al. 2005. Influence of hepatitis C virus infection on HIV-1 disease progression and response to highly active anti-retroviral therapy. Journal of Infectious Diseases. 192: 992-1002.

78 Soriano et al. 2007. Care of patients co-infected with HIV and hepatitis C virus. 2007 updated recommendations from the HCV-HIV International Panel. AIDS 21: 1073-1089.

79 Swan, Tracy. 2006. Care and Treatment for Hepatitis C and HIV Co-infection. U.S. Department of Health and Human Services, Health Resources and Services Administration, HIV/AIDS Bureau.

80 Treatment and Therapeutic Research Lobby Group. 2007HCV-HIV Co-infection : What are the issues for social science scientists? http://www.trt-5.org/IMG/ppt/AIDSImpact2007_-_Presentation_du_TRT-5_sur_la_coinfection_VIH_VHC.ppt

81 WHO. October 2000. Hepatitis C. http://www.who.int/mediacentre/factsheets/fs164/en

82 WHO, UNAIDS & UNODC. 2009. Technical guidance countries for countries to set national targets for Universal Access to HIV prevention, treatment and care for injecting drug users.

83 WHO, UNAIDS & Unicef. 2008. Towards Universal Access: Scaling up priority HIV/AIDS interventions in the health sector.

84 **Padmapriyadarsini C**, Chandrabose J, Victor L, Hanna LE, Arunkumar N, Swaminathan S. Hepatitis B or hepatitis C co-infection in individuals infected with human immunodefi ciency virus and effect of anti-tuberculosis drugs on liver function. *J Postgrad Med* 2006; **52**: 92-96

85. Turbadkar D, Mathur M, Gaikwad S. Prevalence of syphilis among HIV-seroreactive patients. Indian J Sex Transm Dis 2007;28:91-3

86. **Gupta S**, Singh S. Hepatitis B and C virus co-infections in human immunodeficiency virus positive Indian patients. *World J Gastroenterol* 2006; **12**: 6879-6883

87 **Poudel KC**, Jimba M, Okumura J, Wakai S. Emerging coinfection of HIV and hepatitis B virus. *Trop Doct* 2006; **36**: 186-187