DISSERTATION

on

Study of Hepatitis-B and Hepatitis-C co-infection in HIV Positive Patients of Government General Hospital and Madras Medical College, Chennai

M.D., DEGREE EXAMINATION

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DECLARATION

I solemnly declare that this Dissertation entitled "Study of Hepatitis-B and Hepatitis-C co-infection in HIV positive patients of Government General Hospital and Madras Medical College, Chennai" was done by me at Madras Medical College and Government General Hospital during 2004-2007 under the guidance and supervision of **Prof. K. RAGHAVAN.** This dissertation is submitted to the Tamil Nadu Dr. M.G.R. Medical University towards the partial fulfillment of requirements for the award of **M.D., Degree in General Medicine, Branch-I.**

Place :

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CERTIFICATE

This is to certify that the Dissertation entitled "Study of Hepatitis-B and Hepatitis-C co-infection in HIV positive patients of Government General Hospital and Madras Medical College, Chennai" is a bonafide work done by **Dr. SREEJESH. B,** at Madras Medical College, Chennai in partial fulfillment of the University rules and regulations for award of **M.D., Degree in General Medicine** under my guidance and supervision during the academic period from May, 2004-2007.

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ABBREVIATION

A

AIDS	→	Acquired Immuno-Deficiency Syndrome
ALP	→	Alkaline Phosphatase
ALT	→	Alanine Amino Transferase
ANC	→	Ante Natal Case
ART	→	Anti Retroviral Therapy
AST	→	Aspartate Amino Transferase

B

b-DNA	→	Branched Deoxy ribo Nucleic Acid
BIR	→	Barnard Institute of Radiology

C

CD	→	Cluster of Differentiation
CDC	→	Centre for Disease Control and Prevention
CM	→	Centi metre
CMV	→	Cyto Megalo Virus
CNS	→	Central Nervous System

D

DNA	→	De Oxy Ribo Nucleic Acid

E

E/R/S	→	Elisa / Rapid / Simple
EDTA	→	Ethylene Diamine Tetra Acetic Acid
ELISA	→	Enzyme Linked Immuno-Sorbent Assay
EMC	→	Essential Mixed Cryoglobulinemia

G

GGH	→	Government General Hospital
GGT	→	Gamma Glutamyl Transpeptidase
GOI	→	Government of India

H

HAV	→	Hepatitis A Virus
HBc Ag	→	Hepatitis B core Antigen
HBe Ag	→	Hepatitis B e Antigen
HBsAg	→	Hepatitis B Surface Antigen
HBV	→	Hepatitis B Virus
HCV	→	Hepatitis C Virus
HIV	→	Human Immuno Deficiency Virus

I

i.e.	→	That is
IFNα	→	Interferon Alpha
IU	→	International Units

K

Kbp	→	Kilo Base Pair

L

LKM	→	Liver kidney Microsomal

M

μL	→	Micro litre
ML	→	Milli litre

N

NANB	→	Non A Non B
NM	→	Nano Metre
NNRTI	→	Non Nucleoside Reverse Transcriptase Inhibitor
NRTI	→	Nucleoside Reverse Transcriptase Inhibitor

P

PAN	→	Poly Arteritis Nodosa
PCR	→	Polymerase Chain Reaction
PI	→	Protease Inhibitor

R

RIBA	→	Recombinant ImmunoBlot Assay

RNA	→	Ribo Nucleic Acid
Rt PCR	→	Reverse transcriptase Polymerase Chain Reaction.

S

SEAR	→	South East Asian Region
SGOT	→	Serum Glutamate - Oxaloacetate Transaminase
SGPT	→	Serum Glutamate Pyruvate Transaminase

U

US	→	United States of America

W

WHO	→	World Health Organization

CONTENTS

INTRODUCTION

Hepatitis B virus, Hepatitis C virus and Human Immuno Deficiency virus have in the recent years posed significant challenges to the health care system. These viruses have a marked ability to spread from one person to another by parenteral route especially sexual contact. Eventhough blood transfusion is the most effective method of transmission for all these viruses, introduction of stringent measures in the recent times have reduced this method of transmission to a considerable extent. Concomitant infection of these viruses leads to higher frequency of carrier state and severe manifestations of the disease.

Whereas 40 million individuals are estimated to be infected with HIV worldwide, nearly 400 million people are chronic HBV carriers. There is no doubt regarding the fact that HBV is more infectious than HIV. Data from different regions in the world give highly variable prevalence rates for the co-infection of HBV and HCV in HIV patients. Even reports published from various parts of India give different prevalence rates for these co-infections.

This depends a lot on geographical distribution of study as well as the group of people under study. For example various reports from the state of Manipur and other north eastern states in India showed a high prevalence of HBV and HCV co-infection. In many studies where the study population was mainly injection drug users a high prevalence of HBV and HCV is reported as in the case of North eastern States where IDU is the main mode of transmission [31,32] .

Liver disease caused by chronic Hepatitis B virus infection is currently an important cause of morbidity and mortality among HIV infected patients in Western world, where classical complications of severe immunodeficiency have declined dramatically as a result of widespread use of potent anti retroviral therapies. With the availability of these potent anti retroviral drugs in this part of world, the same scenario is bound to happen here also[1].

The presence of HIV infection increases the risk of chronicity after exposure to HBV. Moreover it reduces the rate of spontaneous HBs Ag and HBeAg seroconversion. The prevalence of HBeAg negative chronic hepatitis B, as well as the HBV inactive carrier state tend to be lower in HBV/HIV

co-infected individuals. Several clinical studies have shown that the risk of end stage liver disease is significantly increased in HIV infected patients with chronic Hepatitis B.

HIV infection appears to speed the rate of progression of chronic hepatitis C to end stage liver disease. But this accelerated progression has not been observed in all studies[1].

The co-infection of HBV or HCV in HIV patients warrants special care while initiating anti retroviral therapy for HIV. This prompts the physician to take decisions regarding the choice of drugs as well as treating those co-infections whenever necessary.

Although the impact of HIV on HBV and HCV is established by many studies, it is not known whether HCV or HBV accelerate the progression of HIV[2,20].

In the light of above facts, the need for study regarding co-infection of Hepatitis B and Hepatitis C in HIV positive patients of Government General Hospital and Madras Medical College was felt and hence this study was undertaken.

REVIEW OF LITERATURE

HISTORICAL ASPECTS

AIDS was first recognised in 1981 in the United States. In 1983, human immuno deficiency virus was isolated. In 1984 it was established as the cause of AIDS. In the year of 1985, a sensitive enzyme linked immunosorbent assay was developed for the detection of HIV[35].

In the case of Hepatitis B virus, in the year of 1969, Blumberg and co-workers reported a protein antigen in the serum of an Australian aborgine which gave a clearly defined line of precipitation with sera from two hemophiliacs, who had received multiple transfusions. This antigen was called Australia antigen. In the year 1968, this antigen was shown to be associated with hepatitis and was subsequently shown to be the surface component of the hepatitis B virus. The 32nm particle which is the complete hepatitis B virus was first described by Dane and colleagues in 1970[37].

Hepatitis C virus came to the light with experimental transmission of infection from cases of post transfusion

hepatitis to Chimpanzees. Till then this organism was grouped under non A non B (NANB) hepatitis agent [37].

ETIOLOGICAL AGENTS

HIV- Acquired Immuno Deficiency Syndrome (AIDS) is caused by Human Immuno Deficiency Virus (HIV). It belongs to the family of retroviruses and sub family of lenti viruses. 2 types of HIV are identified, HIV-1 and HIV-2. HIV-1 is a more virulent pathogen than HIV-2. HIV-1 virus is reported more in India. This virus is found in all body fluids and organs. But they are present in very large numbers in semen, vaginal & cervical secretions and blood. The central nervous system, testis and lymph nodes act as reservoir of HIV. But highest concentration of HIV among body fluids is found in cerebrospinal fluid. HIV genome is 9.2 kbp in size [26].

HBV: Hepatitis B virus is a DNA virus belonging to the family hepadna virus and is classified as Hepadna virus type-I. Hepatitis B isolates fall into atleast 8 sub types and 7 genotypes A-G. Types A&D predominate in US and Europe, while B&C in Asia. Genotype B is associated with less rapidly progressive liver disease. HBV is also present in all secretions. HBV DNA codes for four sets of viral products.

They are 's', 'c', 'p' and 'x'. Envelope protein HBs Ag is the product of 's' gene of HBV. Nucleocapsid proteins are coded for by the 'c' gene and antigen expressed on the surface of the nucleocapsid is referred to as Hepatitis B core antigen (HBcAg). The corresponding antibody is anti HBc. HBcAg remains in the hepatocyte and do not circulate in the serum. Third Hepatitis B virus antigen is Hepatitis B e antigen(HBeAg). This denotes high level of replication and infectivity. Antibody to HBeAg when it appears may be a harbinger of clinical improvement. DNA polymerase directs replication and repair of HBV DNA. The 'x' gene codes for HBxAg and it effects Calcium release. Its genome size is 3.2 kbp [34].

HCV : Hepatitis C before its identification was labelled as non A, non B hepatitis. It is a linear single strand RNA virus. HCV is the only member of hepaci virus in the family flavi-viridae. The replication rate of HCV is very high 10^{12} virions per day. But its half life is 2.7 hours. Atleast six distinct genotypes as well as sub types within genomes of HCV have been identified by nucleotide sequencing. The genotypic and quasi-species diversity of HCV, resulting from its high mutation rate interferes with effective humoral

immunity. Though neutralising antibodies to HCV have been demonstrated they tend to be short lived. Its genome size is 9.5 kbp [34,4].

MODES OF TRANSMISSION

All three viruses spread mainly through parenteral route.

TABLE-1: Characteristics of HIV transmission

S.No.	Modes of Transmission	Efficacy	Source of Infection
1	Sexual intercourse, homosexual, heterosexual	0.1 to 1.01	80-85%
2	Blood transfusion	90 to 95%	3-5%
3	Perinatal	20 to 40%	2-3%
4	Injection drug user	0.5 to 1%	3-5%
5	Needle stick exposure	<0.1%	-

(26)

Regarding sexual intercourse, the receiving partner is at a greater risk than the insertive partner. Anal sex carries a higher risk than vaginal sex.

In the case of perinatal / ante natal transmission, the risk is about 23-30% before birth, 50-65% during birth and 12-20% via breast feeding.

HBV : Transmission is mainly by percutaneous route. This virus is highly infectious and very minute amounts of some carrier sera as little as 0.000001 ml can transmit the disease. Therapeutic and diagnostic procedures, tattooing, accupuncture, ritual circumcision, nose and ear piercing, sharing of razors and needles, sexual intercourse and kissing apart from blood transfusion can spread the virus. Perinatal transmission from mother to child is another important mode of transmission. But patients infected through male homosexual contact tend to show the highest rates of transmission along with injection drug users[38].

HCV: Hepatic C virus was mainly transmitted through blood transfusion of contaminated blood and blood products until a few years ago. But with the stringent screening measures taken this has come down to a great extent. This virus is now transmitted through other means like sharing of needles in injection drug users, tattoing and scarification and traditional circumcision with contaminated instruments. The risk of sexual and perinatal transmission is small [38].

EPIDEMIOLOGY

HIV infection is a global pandemic with an estimated population of ~37 million world wide, two thirds of whom are in subsaharan Africa. An estimated 2.5 millon children below the age of 15 are living with HIV/AIDS. Now it is the fourth leading cause of mortality.

INDIA HIV estimates in India is close to 5.3 million in the age group of 15-49 years. Almost 89% cases are in the age group of 15-44 years. Of these 73% are men and 27% are women. Its prevalance varies from State to State.

States are classified into 3 groups

Group-I High prevalence states: States with 1% or more of ante natal women, like Maharashtra, Karnataka, Andhrapradesh, Manipur, Mizoram, Dadar and Nager Haveli. Tamil Nadu was previouly in this group, but of late antenatal case prevalence dropped to 0.63 in 2004.

Group-II: In these states HIV infection has crossed 5% or more among high risk groups but less than 1% in antenatal women.

Eg: Gujarat, Rajasthan, Kerala & Goa.

Group-III : Remaining states are with <5% prevalences in high risk groups and <1% in ANC [26].

HBV : It is estimated that there are around 400 million chronic HBV carriers. Infection with HBV is a major cause of morbidity and mortality is SEAR, were more than one third of population is estimated to be infected with HBV. In western countries the prevalence of chronic HBV infection is overall 10 fold higher among HIV positive individuals than general population. Serological evidence of previous exposure to HBV is found in more than 80% of HIV +ve patients[2].

Based on the different HBsAg carrier rates, countries in the South east asian region/South asian region can be classified into 3 epidemiological patterns.

Type-I Carrier rate 0.9-1% --> Nepal and Sri Lanka

Type-II Bhutan, India, Indonesia, Maldives — carrier rate 5-7%.

In India alone an estimated 43-45 million HBsAg carriers are present.

Type-III The carrier rate is 9-12% .

Countries like Myanmar, Thailand, Bangladesh, Korea included in this group [38].

Hepatitis 'C': WHO estimates that 3% of world population is infected with HCV and around 170 million individuals are chronic carriers at risk of developing liver cirrhosis and liver cancer. Numerous studies have documented a high rate of HCV co-infection among HIV infected injection drug users and persons with hemophilia. In India it is estimated that 2% of general population is infected with HCV [38].

Pathogenesis

HIV/AIDS: The natural history of HIV infection begins as soon as the virus enters the body of a susceptible host. HIV predominently infects the helper CD4 lymphocytes. As the numbers and function of CD4 cells decline immune deficiency sets in and this will in turn lead to opportunistic infections and maligancies. By this time CD4 counts fall below a critical level below 200 cells/μl and reach the stage of advanced HIV disease. Dissemination of virus to lymphoid organs is a major factor in the establishment of chronic and persistent infection. Despite the robust cellular and humoral immune

response against the primary infection, the virus succeeds in escaping the immune mediated clearance and is virtually never eliminated completely from the body in all HIV infected individuals. There exists a pool of latently infecting resting CD4 T Cells that serve as one of the persistent reservoirs of viruses. One other striking feature of HIV infection is that, clinical latency is not accompanied by microbiologic latency as some degree of virus replication invariably occurs [35].

Hepatitis B: The existence of inactive hepatitis B carriers with normal liver histology and function suggests that the virus is not directly cytopatic. Patients with defects in cellular immune competence are more likely to remain chronically infected rather than to clear virus is cited to support the role of cellular immune responses in the pathogenesis of Hepatitis-B related liver injury. Although the precise mechanisms of liver injury in HBV infection remains elusive, studies of nucleocapsid protiens have revealed profound immunological tolerance to HBV, in babies born to mothers with highly replicative chronic HBV infection [34].

Hepatitis C: Cell mediated immune responses and elaboration by T cells, of antiviral cytokines contribute to

containment of infection and pathogenesis of liver injury by Hepatitis C. HCV infection of lymphoid cells may play a role in moderating immune responsiveness to the virus. The role of virus activated CD4 helper T cells that stimulate, via the cytokines they elaborate, HCV specific CD8 cytotoxic T cells is supported by many studies. Cross reactivity between viral and host auto antigens has been invoked to explain the association between Hepatitis C and a subset of patients with autoimmune hepatitis and antibodies to liver kidney microsomal antigen (LKM) [34].

HIV/Hepatitis B Co-infection: The risk of HBV associated end stage liver disease, seems to be increased in the setting of HIV co-infection. The presence of HIV infection increases the risk of chronicity after exposure to HBV. It reduces the rate of spontaneous HBsAg and HBeAg sero conversion. Thus the prevalence of HBeAg negative chronic hepatitis B as well as the HBV inactive carrier state tends to be lower.

Despite a higher serum HBV-DNA level seen in HIV patients, hepatic necro inflammation tends to be milder in HIV/HBV co-infected individuals. However the enhanced replication levels of HBV in HIV co-infected patients may

result paradoxically in the progression of more severe liver fibrosis [1].

HIV/Hepatitis C Co-infection: HIV-I infection appears to speed the progression of chronic hepatitis C to end stage liver disease to as little as 10 years after exposure. The average risk of progressive liver disease is 2.9 times higher among HCV/HIV-1 co-infected persons than among persons infected only with HCV. Evaluation of liver histology indicates the presence of more extensive fibrosis as well as a greater rate of fibrosis progression among HCV/HIV-1 co-infected than among those with HCV infection alone [2].

Clinical manifestations:

HIV: After entry of HIV, the HIV replication will be going on in the body. Antibodies useful in detection of HIV will be in low titres and will not be detectable during this period. However the patient will be in a carrier state capable of transmitting the disease. This stage lasts for 6 weeks – 12 weeks. This phase is known as window period.

Acute HIV Syndrome: It is estimated that 50-70% people with HIV infection experience an acute clinical

syndrome approximately 3-6 weeks after primary infection. The typical clinical features occur along with a burst of plasma viremia. Symptoms usually persist for one to several weeks. The clinical findings include fever, pharyngitis, lymphadenopathy, head ache, retro orbital pain, arthralgia, myalgia, lethargy, malaise, anorexia, weight loss, nausea, vomiting and diarrhoea. Neurological manifestations may include meningitis, encephalitis, peripheral neuropathy and myelopathy. Dermatological manifestations include mucocutaneous ulcerations and erythematous maculopapular rash.

Asymptomatic stage: Following acute HIV syndrome the patient may enter a stage of clinical latency i.e., the asymptomatic stage. HIV disease with active virus replication is ongoing and progressive during this phase. The average rate of CD4 cell decline is 50 cells/μl/year. When the CD4 cell count is less than 200/μl the resulting state of immunodeficiency puts the patient at a high risk for opportunistic infections and neoplasms.

Persistent generalised lymphadenopathy: This is indicated by the presence of enlarged lymph nodes more than 1 cm in

length in two or more extra inguinal sites for more than 3 months without any obvious cause. It is actually an immunological response by the reticuloendothelial system to HIV infection with an attempt to arrest the virus in the lymph nodes.

Symptomatic Disease: Diagnosis of AIDS is made in any one with HIV infection and CD4 count <200/µl and in any one with HIV infection who develops one of the HIV associated diseases considered to be indicative of severe defect in cell mediated immunity.

1993 revised classification system for HIV infection and expanded AIDS surveillance case definition for adolescents and adults.

Table-II

CD4 categories	Asymptomatic Acute HIV/PGL	Symptomatic but not A or C	AIDS indicator condition
>500/µl	A_1	B_1	C_1
200-499/µl	A_2	B_2	C_2
<200/µl	A_3	B_3	C_3

Clinical Categories

Category-A : One or more conditions of the following in an HIV +ve who is more than 13 years of age

(1) Asymptomatic HIV infection

(2) Persistent generalised lymphadenopathy

(3) Acute HIV infection

with accompanying illness or history of acute HIV infection.

Category-B : Symptomatic conditions not included in clinical category C and that meet atleast one of the following.

(1) The conditions are attributed to HIV infection or are indicative of defect in cell mediated immunity.

(2) The conditions are considered to have a clinical course or require management that is complicated by HIV infection.

Eg:
- Bacillary angiomatosis
- Oropharyngeal & Vulvo vaginal candidiasis
- Cervical dysplasia (moderate or severe) / Cervical carcinoma insitu
- Constitutional symptoms like fever ≥38.5°C or Diarrhoea for more than one month.

- Oral hairy leukoplakia

- Herpes Zoster which is either multidermatomal or atleast two distinct episodes.

- Idiopathic thrombocytopenic purpura

- Listeriosis

- Pelvic inflammatory disease, particularly if complicated by tubo ovarian abscess.

- Peripheral neuropathy.

Category-C : AIDS defining illness

- Candidiasis of trachea, bronchi or lungs.

- Esophageal candidiasis

- Invasive cervical cancer

- Coccidioidomycosis (disseminated or extra pulmonary)
- Cryptococcosis (extra pulmonary)
- Cryptosporidiosis (chronic intestinal > 1 month)
- Cytomegalo virus disease (other than spleen, liver or nodes)
- CMV retinitis (with loss of vision)
- HIV related encephalopathy
- Herpes simplex : chronic ulcers > 1 month or bronchitis, pneumonia or esophagitis
- Histoplasmosis : Disseminated or extrapulmonary
- Isosporiasis (chronic intestinal > 1 month)
- Kaposi's sarcoma

- Burkitt's lymphoma & primary CNS lymphoma

- Mycobacterium Avium complex or Mycobacterium Kansasii – Disseminated or extra pulmonary

- Mycobacterium, other species or unidentified species (disseminated or extra pulmonary)

- Pneumocystis carinii pneumonia

- Recurrent pneumonia

- Progressive multifocal leuko encephalopathy

- Salmonella septicemia

- Toxoplasmosis of brain

- Wasting syndrome due to HIV [26, 35]

Hepatitis B and Hepatitis C

Acute Viral Hepatitis: Usaually the incubation period of Hepatitis-B extends from 30-180 days and Hepatitis-C, 15-160 days. In the case of HBV, the onset can be acute or insidious and for Hepatitis-C it is usually insidious. Prodromal symptoms of acute viral hepatitis are systemic and quite variable. Constitutional symptoms are anorexia, nausea, vomiting, fatigue, malaise, arthralgias, myalgias, head ache, photophobia, pharyngitis and coryza which may precede the onset of jaundice by 1 to 2 weeks. Patients are usually afebrile unless in the case of Hepatitis-B, if heralded by serum sickness like syndrome. Then there is the phase of clinical jaundice which is followed by recovery.

Extra Hepatic manifestations : Serum sickness like syndrome can complicate acute hepatitis due to Hepatitis-B. In chronic hepatitis B glomerulonephritis with nephritic syndrome is occasionally observed. Poly arteritis nodosa develops in considerably fewer than 1% patients with chronic HBV infection, but 20-30% with PAN have HBsAg in serum. A substantial proportion of essential mixed cryoglobulinemia cases is associated with hepatitis C virus infection. This is less common with hepatitis B. Immune complex glomerulo nephritis is another recognised extra hepatic manifestation of chronic hepatitis C infection.

Co-infection with HIV increases chronicity of infection for both Hepatitis B and Hepatitis C. Unusual histologic pattern of fibrosing cholestatic hepatitis may occur in patients with severe immuno suppression with concomitant HBV infection.

DIAGNOSIS :

HIV: HIV infection is diagnosed by detecting antibodies or / and antigens in the body.

HIV Antibody Tests:

1. **ELISA tests:** It is a standard screening test for HIV infection (enzyme immuno assay). This solid phase assay is an extremely good screening test with a sensitivity more than 99.5%.

2. **Rapid Test:** It is a quick test and results could be obtained in 30 minutes.

3. **Western Blot Test:** It is a confirmatory test and is more specific. Confirmation can also be done by using results from two or three consecutive different ELISA/Rapid test kits.

HIV Antigen Tests:

1. RT-PCR for viral RNA
2. b-DNA test (branch-b)

   The above PCR (polymerase Chain Reaction) tests become positive after 72 hours of infection.

Viral load assessment tests like NASBA become positive after 72 hours of infection.

P24 antigen becomes positive after 2 weeks of infection.

HIV Testing Strategies: WHO/GOI have developed these strategies.

Strategy-I: Used for ensuring donation safety by using ELISA/RAPID/Simple tests for HIV once. If results are negative, serum is considered free of HIV. If serum is positive, the unit of blood is discarded and donor sent for VCTC. This strategy is used in blood banks .

Strategy-II : Used for surveillance and for diagnosis of HIV infection only if some AIDS indicator disease is present. If the first ELISA is negative, the serum sample is considered negative. If the first ELISA is positive, the serm is subjected to a second ELISA. If the second confirms the report of the first, the serum sample is considered positive.

Strategy-III : It is used to diagnose HIV infection in asymptomatic individuals indulged in high risk behaviour. It is similar to strategy II, but with an added confirmation of a third reactive ELISA test, for a positive reported sample by the two previous ELISAs.

Supplementary/Confirmatory tests are used in problem cases, eg: in cases of indeterminate / discordant results E/R/S. [26, 35, 1].

HBV : A diagnosis of HBV infection in the setting of acute Hepatitis-B is made by detection of HBsAg in serum. Sometimes it may be low but diagnosis can be established with the help of IgM anti HBc.

Commonly Encountered Scrologic Patterns of Hepatitis B Infection:

Table-III

S.No.	HBsAg	AntiHbs	Anti HBc	HBeAg	AntiHBe	Interpretation
1	+	-	IgM	+	-	Acute hepatitis B with infectivity
2	+	-	IgG	+	-	Chronic hepatitis B high infectivity
3	+	-	IgG	-	+	1. Late acute / chronic hepatitis B 2. HBeAg negative precore mutant Hepatitis B chronic or rarely acute
4	+	+	+	+/-	+/1	1. HBsAg of one sub type and hetero typic anti-HBs. 2. Process of seroconversion from HBsAg to anti HBs
5	-	-	IgM	+/-	+/-	1. Acute hepatitis B 2. Anti HBc "window"
6	-	-	IgG	-	+/-	1. Low level hepatitis B carries 2. Hepatitis B in remote part
7	-	+	IgG	-	+/-	Recovery from hepatitis
8	-	+	-	-	-	Immunisation (after vaccination) Hepatitis B in the remote past , false positive

- HBV DNA by PCR: This test can detect as few as 100 or 1000 virions / ml.

The persistance of HBeAg beyond 3 months or HBsAg beyond 6 months after acute hepatitis signifies establishment of chronic hepatitis.

Hepatitis-C : Specific diagnosis is possible by demonstrating presence of anti HCV in serum by 2nd or 3rd generation assays that detect antibodies to non structural or nucleocapsid proteins in upto 90-95% cases of acute Hepatitis-C and is >95% cases with chronic hepatitis C. A recombinent immunoblot assay can be used to establish viral proteins (RIBA). Assay for HCV RNA are the most sensitive tests for HIV infection and represent the "gold standard" in establishing the diagnosis.

Hepatitis 'C' RNA : Three diagnostic assays have been approved for qualitative detection of HCV RNA. Two of the assays use RT-PCR and have a lower limit of detection of 50-100 IU/µl. 3rd one uses transcription mediated amplification and has a lower limit of detection of 10 IU/µl. Quantitative tests for HCV RNA include quantitative RT-PCR or branched DNA signal amplification assays (1).

In HBV/HIV Co-infection: Isolated anti-hepatitis B core antigen is frequently recognised, particularly among patients with more severe immuno deficiency (2).

Treatment : HIV/AIDS - These include psychosocial support, ongoing counselling, patient education, prevention of transmission, prevention and treatment of opportunistic infections and anti retroviral therapy.

Anti – retroviral therapy :

Aims :

1. To prolong life and improve quality of life.
2. Reduction of viral replication as much as possible to halt disease progression and to prevent and reduce drug resistant variants.
3. To achieve immune reconstitution and thus to prevent opportunistic infections and malignancies .
4. To achieve reduction in HIV transmission.

DRUGS:

- ❒ Nucleoside reverse transcriptase inhibitors
- ❒ Non nucleoside reverse transcriptase inhibitors
- ❒ Protease inhibitors – Most potent drugs.
- ❒ Fusion / Entry inhibitors – Inhibit HIV fusion with CD4 membrane.

Antiretroviral Drugs
Table-IV

NRTI	NNRTI	PI	Fusion Inhibitors
- Zidovudine	- Delavirdine	- Indinavir	Enfuvirtide
- Didanosine	- Nevirapine	- Ritonavir	
- Stavudine	- Efaviren z	- Nelfinavir	
- Lamivudine		- Lopinavir	
- Zalcitabine		- Saquinavir	
- Abacavir		- Amprenavir	

Recommended Regimens:

1. 2 NRTIs + 1 NNRTI
2. 2 NRTIs + 1 PI
3. 3 NRTIs
4. 2 NRTIs + P1 Boosting (2 PIs)

Guidelines for starting ART
Table-V

Category	CD4 count/μl	Recommendation
Symptomatic HIV	any value	treat
Asymptomatic HIV	<200	treat
Asymptomatic HIV	>200	Consider treatment based on CD4 count, Rate of CD4 decline, Viral load >50,000 to 1,00,000 copies. Take into consideration

		- Adherence issues - Potential drug interation - Risk for adverse effects.

Hepatitis B & Hepatitis C :

— Acute Hepatitis B
- Because 99% of patients spontaneously recover no treatment is usually required.

— Acute Hepatitis C
- As it is sure that the condition progresses to chronic form in most of the patient's treatment is mandatory, preferably with long acting pegylated interferon + nucleoside analogue ribavirin.

Chronic Hepatitis B : Interferon α was the first approved drug for therapy. Other drugs useful are lamivudine, Adefovir and Tenofovir which are primarily used against HIV infection. Other drug is emtricitabine. Entecavir and telbivudine can reduce HBV DNA levels and are useful in treatment.

Patients who are candidates for antiviral therapy in chronic Hepatitis B. [34].

Table-VI

S.No.	Clinical features	Interferon	Lamivudine	Adefovir
1	Detectable markers HBV replication	Yes	Yes	Yes
2	Normal ALT activity	No	No	No
3	ALT < 2 x upper limit of Normal	No	No	No
4	ALT > 2 x upper limit of Normal	Yes	Yes	Yes
5	Immuno competent	Yes	Yes	Yes
6	Immuno compromised	No	Yes	Yes
7	Adult acquisitional	Yes	Yes	Yes
8	Childhood acquisition	No	Yes	Yes
9	Compensated liver disease	Yes	Yes	Yes

10	Decompensated liver disease	No	Yes	Yes
11	HBeAg reactive	Yes	Yes	Yes
12	HBeAg(-) chronic Hepatitis	Yes	Yes	Yes
13	Interferon refractory	No	Yes	Yes

(34).

For chronic hepatitis C treatment is with ribavirin and pegylated interferon.

HBV/HIV Co-infection:

For hepatitis B treatment is indicated in presence of HIV in the following scenarios.

1. For active HBV replication.
2. HBeAg positive / HBV DNA > 10^5 copies / ml.
3. 2 x upper limit of Alanine Aminotransferase.

Scenario-1 : Indications are there to begin treatment for HIV but not for HBV.

1. Consider withholding Tenofovir / Emtricitabine / Lamivudine for future use.
2. Avoid using Lamivudine or Tenofovir as a single drug with anti HBV activity.

Scenario-2 : When indications are present there for initiating treatment for HBV but not for HIV. Use interferon (pegylated) or Adefovir. Do not use Lamivudine / Emtricitabine / Tenofovir.

Scenario-3: When indications are there to begin therapy against both HIV & HBV.

- Lamivudine / Emtricitabine + Tenofovir. Here two drugs with action against both HIV & HBV, these viruses are initiated with a third agent Efavirenz (1).

HIV/HCV Co-infection : Persons susceptible to Hepatitis A virus infection should get vaccination against HAV (2 doses) because of increased risk of fulminant hepatic failure in these patients.

All patients with evidence of chronic hepatitis C in the form of who have detectable HCV RNA levels on qualitative assay, persistently elevated ALT levels > 2 times upper limit of normal and liver biopsy suggestive of portal or bridging

fibrosis and moderate inflammation should receive treatment with pegylated interferon and Ribavirin apart from ART [1].

Prevention: Vaccine is available only against hepatitis B but not against Hepatitis C or HIV. Practising safe sex, maintaining universal precautions while handling infective material practising post exposure prophylaxis in case of accidental exposure to infective materials are important. Mother to child transmission is reduced by Nevirapine / Zidovudine prophylaxis.

AIMS AND OBJECTIVES

1. To find out the prevalence of Hepatitis B virus and / or hepatitis C virus co-infection in HIV patients of Government General Hospital and Madras Medical College, Chennai.
2. To find out the main modes of transmission / acquisition for HIV, HBV & HCV infections in the same population.
3. To know the impact of co-infection on liver function.
4. To determine the impact of HBV/HCV co-infection on HIV disease progression and vice versa.

MATERIALS AND METHODS

The study was carried out at Government General Hospital and Madras Medical College, Chennai. This study was made possible with the help of anti-retroviral treatment centre, Voluntary Counselling and Testing Centre, Department of Microbiology, Institute of Sexually Transmitted Diseases, Barnard Institute of Radiology and Central Research Unit of Government General Hospital & Madras Medical College.

A simple observational study (prevalance study; cross sectional study) was carried out over a period of one year from June,2005 to June, 2006. Altogether one hundred HIV positive patients visiting GGH were selected for the study. Sampling was done by simple random sampling. Informed consent was taken before testing of HIV at VCTC, Governent General Hospital and Madras Medical College.

Inclusion Criteria: HIV positive individuals.

Exclusion Criteria :

- All HIV negative persons
- Persons in the paediatric age group
- Persons in the geriatric age group
- Ante natal women
- Those who are already on anti retroviral therapy.
- Those who are known to be cases of alcoholic decompensated liver disease.
- Those who present with altered level of sensorium or decreased level of consciousness.
- More than one member from the same family.

Parameters considered for analysis:

1. Age, 2. Sex, 3. Educational Status, 4. Marital Status
5. HIV – Serology status of spouse / partner
6. Probable route of transmission of HIV divided under the following categories.
   a) Sexual → Hetero / Homosexual
   → Contact with commercial sex worker
   → Multiple sex partners
   b) Injection drug user.

c) Blood transfusion

d) Iatrogenic

e) Unknown

7. History of regular alcohol intake.
8. CD4 count.
9. WHO staging
   i) Weight loss — a) +/- b) if + > 10% / <10%
   ii) Activity → number of days inactive the previous month
   iii) Persistent generalised lymphadenopathy
   iv) Acute HIV syndrome.
   v) Oral candidiasis
   vi) AIDS defining illness

10. Liver Function Tests — including
    a) Serum Bilirubin (SBb)
    b) Alanine Aminotransferase (ALT, SGPT)
    c) Aspartate amino transferase (AST/SGOT)
    d) Alkaline Phosphatase (ALP)
    e) Gamma Glutamyl Transpeptidase (GGT)

11. Ultra Sonography of abdomen
    a) Liver : Size & echoes
    b) Portal vein – size
    c) Spleen – size & splenic vein
    d) Ascites
    e) Venous Collaterals

WHO – Clinical Groups:

1. Clinical Group-I
   → Acute HIV infection, persistent generalised lymphadenopathy.
   → Asymptomatic normal activity.
2. Clinical Group-II (early stage disease)

   → Weight loss, but less than 10%
   → Mucocutaneous problems.
   → Herpes Zoster
   → Recurrent upper respiratory tract infection.
   → Normal Actvity
3. Clinical Group-III (intermediate Stage Disease)

- → Weight loss more than 10%
- → Chronic diarrhoea (>1 month)
- → Prolonged fever (>1 month)
- → Oral candidiasis
- → Oral hairy leukoplakia
- → pulmonary tuberculosis
- → severe bacterial infection
- → Bed ridden but less than 50% of day the previous month.

4. Clinical Group-IV (late stage disease)
   - → Definitive or presumptive diagnosis of any AIDS defining disease.
   - → Bed ridden for more than 50% of day the previous month.

[26].

Patients were tested for HIV by ELISA at VCTC after counselling and getting informed consent. Positive results were confirmed by following strategy-II recommended by WHO / GOI. ELISA was done with kit Microlisa using 96 plate titer well.

CD4 count was estimated by facs count. For this 2 ml of venous blood was collected into EDTA containing vacutainers.

About 5 ml of venous blood was collected from each patient and transferred into test tubes. These test tubes were centrifuged at a speed of 4000 rotations per minute in an electric centrifuge for 5 minutes and serum was separated.

For HBsAg rapid test card from Intec products (XIAMEN) was used first and followed it up with microwell ELISA test (HEDALISA).

Fo anti-HCV Biozyme one step anti HCV test, with a sensitivity of 99% and specificity of 97-99% was used.

Serum Bilirubin was estimated by Jendrassik method. For alanine aminotransferase and Aspartate aminotransferase kit from "autopak" was used. For GGT and alkaline phosphatase also kits from "autopak" was used and analysed with ERBA-CHEM-5plus semi-auto analyser.

Following are the normal ranges for these tests.

1. SGOT (AST) - 11-47 IU/ml
2. SGPT (ALT) - 7-53 IU/ml
3. GGT Males : 11-50 IU/ml
   Females : 7-32 IU/ml
4. Alkaline Phosphatase : 38 – 126 IU/ml

For all the tests manufacturer's instructons were strictlty followed.

Ultra sound abdomen was done at BIR, GGH. Following parameters were looked at.

Liver : Size & Echoes:

Size in mid clavicular line

Normal 1. < 13 cm (cranio-caudal)
2. < 15 cm (depending on body habitus)

Marginal Angle
<30° (left hepatic lobe, lateral)
< 45° (right hepatic lobe, caudal)

Portal Vein : Luminal Width
<1.3 cm → normal
>1.5 cm → portal hypertension

Spleen : Maximum size
<11.0 cm (length)
<7.0 cm (width)
<4.0 cm (depth, measured between splenic hilum and surface.

Splenic Vein : <1.0 cm – Normal
>1.2 cm – portal hypertension

Presence of Ascites / Venous collaterals :

Ultra sound scan was performed with ALOKA B mode Ultra sound scanner.

Statistical Analysis was done with SPSS V6. The characteristics of HIV positive patients with hepatitis co-infection and those without co-infection were compared. With categorical variables the chi-square test was applied. To find out the association between liver enzymes with other variables like alcoholism, co-infection, CD4 count logistic regression was used.

RESULTS

Table-VII
Age and Gender wise distribution of study population

Age	Male	Female	Total
<30	19	10	29%
31-40	46	11	57%
>40	10	4	14%
TOTAL	75	25	100%

The youngest in the study population was 23 years of age and oldest was 54 years of age. The mean age of the study population was 34.79. Highest number of individuals belonged to 31-40 years of age group followed by ≤ 30 years age group.

There were 75 males and 25 females in the study population.

Table-VIII
Educational/Literacy Status of study population

Educational Qualification	Frequency	Percentage
Illiterate	2	2%
Lower primary school Education	15	15%
Upper primary school Education	23	23%
High School Education	41	41%
Higher Secondary School	6	6%
Above Higher Secondary School	13	13%
TOTAL	100	100%

Among the study population there were only 2 illeterates.

Table-IX
Marital Status of Study population

Marital Status	Men	Women
Married	57	25
Unmarried	18	0

Out of the 75 males, 57 were married and 18 were unmarried. But all the 25 women in the study were married.

Table-X
HIV Status of Spouse / Partner

HIV Status of spouse / partner	Married Men	Married Women
Positive	19	24
Negative	33	1
Not known	5	0

Thus out of 25 females, 24 had their husbands tested as positive for HIV. But of 57 males, 19 of them had their wives tested positive for HIV. There were 33 men with their wives' HIV status as negative and 5 of them don't know the HIV status of their wives.

Table-XI
Distribution of Study Population by CD4 count

CD4 count	Frequency	Percentage
≥ 500	3	3
200 – 499	33	33
50 – 199	52	52
<50	12	12
TOTAL	100	100

Thus the majority of individuals i.e. 52 of them had their CD4 count between 50-199/μl and 12 below 50 / μl. There were 3 individuals with their CD4 counts above 500/μl and 33 people with CD4 counts in between 200-499.

Table-XII
Distribution of Study Population by WHO Staging

WHO Stage (Clinical)	Frequency	Percentage
I	17	17
II	33	33
III	41	41
IV	9	9
TOTAL	100	100

There were 9 people belonging to clinical stage IV, but the maximum number of individuals i.e.41 individuals belonged to clinical Stage-III. There were 17 people in Stage-I and 33 in clinical Stage-II.

Table-XIII

Distribution of Study Population by modes of transmission / acquisition

Mode of Transmission	Frequency of HIV +ve
Hetero sexual	93
Homo sexual	0
Injection Drug user	5
Blood/Blood related products	1
Iatrogenic	0
Not known	1
TOTAL	100

Majority in the study population, 93 of them had HIV through the hetero sexual mode. All the men who were tested HIV positive in this group had history of sexual contact with commercial sex workers. All the 24 women who were tested positive for HIV in this group had their husbands already tested positive for HIV. There were no homosexuals in the study population. The next highest share is by injection drug users, all males. One person got the infection through probably, blood transfusion. One person was not sure of the mode of acquisition.

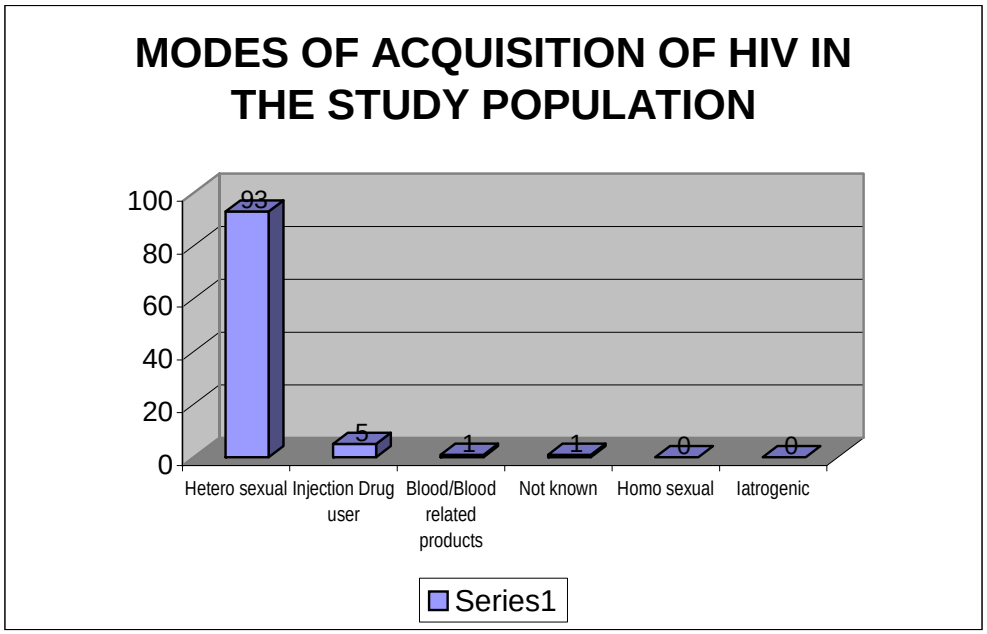
MODES OF ACQUISITION OF HIV IN THE STUDY POPULATION
100
80
60
40
20
0
93
5
1
1
0
0
Hetero sexual
Injection Drug user
Blood/Blood related products
Not known
Homo sexual
Iatrogenic
Series1

Table-XIV

Hepatitis-B surface antigen and Anti HCV prevalence in study population

Serum	Positive	Number examined	Percentage
HBsAg	8	100	8%
Anti HCV	4	100	4%
HBsAg and Anti HCV	1	100	1%

So, out of 100 persons, 8 tested positive for HBsAg and 4 tested positive for anti HCV. Out of the 100 persons only one had evidence of positivity for both HBsAg and anti HCV.

Table-XV
Age related prevalence of HBV / HCV

Age group	Total examined	HBsAg+	Anti HCV+	Both HBsAg+ Anti HCV+	% HBsAg+	%Anti HCV+	Both HBsAg+ Anti HCV+
≤30	29	4	1	1	13.8%	3.4%	3.4%
31-40	57	4	3	-	7%	5.26%	-
>40	14	-	-	-	-	-	-

All the HBS Ag +ve / Anti HCV + were in the age group ≤40 years

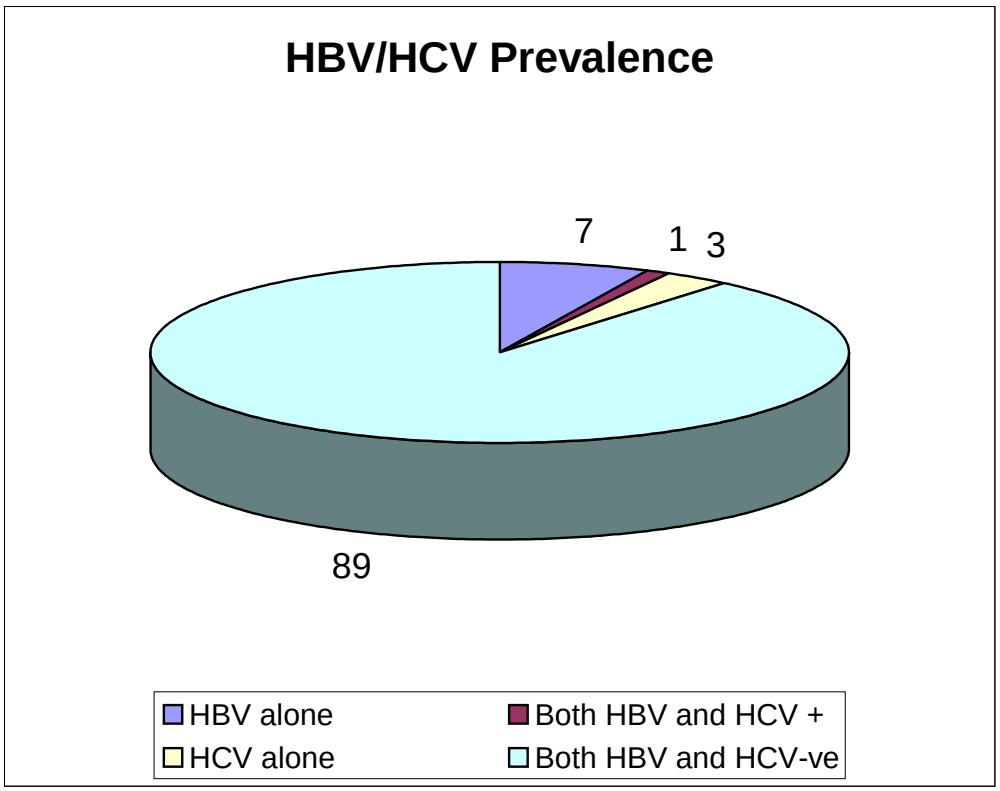
HBV/HCV Prevalence
7
1
3
89
HBV alone
Both HBV and HCV +
HCV alone
Both HBV and HCV-ve

Table-XVI

Sex related prevalence of HBV / HCV

Sex	No. examined	HBsAg +	Anti HCV+	HBsAg + anti HIV+	% HBsAg +	% anti HCV+	% HBsAg + anti HCV+
Male	75	7	3	1	9.3%	4%	1.3%
Female	25	1	1	0	4%	4%	-

Out of the 8 individuals who were tested positive for Hepatitis B surface antigen 7 were males and one was a female. Percentage being 9.3% and 4% respectively.

Out of the 4 individuals who were tested positive for anti HCV, 3 were males and one was a female. Prevalence being 4% in men and women. The only individual in whom both HBsAg and anti HCV were tested positive was a male. Percentage being 1.3% of total male population.

Table-XVII

Mode of transmission/acquisition for HBV / HCV

Mode	Total	HBsAg+	Anti HCV+	Both HBsAg+ Anti HCV+	HBsAg%	Anti HCV+ %	Both HBsAg+ anti HCV+ %
Heterosexual	93	6	1	-	6.5%	1.1%	-
Injection drug user	5	2	3	1	40%	60%	20%
Blood / Blood related products	1	-	-	-	-	-	-
Not known	1	-	-	-	-	-	-

1. Thus out of 8 cases of HBsAg+ve persons, 6 acquired the infection through heterosexual route and the remaining two through injection drug use. That means 75% of cases through hetero sexual route and 25% through injection drug use.

2. But only 6.5 % among heterosexually exposed group turned out to be positive for HBsAg. Meanwhile 40% of injection drug uses were tested positive for HBsAg.

   *p value > 0.05**

3. Injection drug users accounted for 3 out of 4 anti HCV positive cases thus comprising 75 % and one case , 25% acquired the infection through heterosexual route.
4. Thus 60% of injection drug users and 1.1% heterosexual group tested positive for anti HCV.

   *p value < 0.001**

Table-XVIII

HBV / HCV Distribution based on CD4 count

CD4 count	Total No.	HBsAg+	Anti HCV+	Both HBsAg+ Anti HCV+	HBsAg%	Anti HCV+ %	Both HBsAg+ anti HCV+ %
>500	3	-	-	-	-	-	-
200-499	33	1	-	-	3%	-	-
50-199	52	6	2	-	11.5%	3.84%	-

<50	12	1	2	1	8.3%	16.7%	8.3%

- Out of the 8 persons with HBsAg positivity, 7 had CD4 counts below 200 and one had CD4 count more than 200. The only one person with HBsAg positivity with CD4 count below 50 had associated HCV co-infection.

  p value > 0.05.*

- Out of the 4 persons with anti HCV positivity all the four were having CD4 counts below 200 and two among them having CD4 counts below 50. It has to be noted that one person with CD4 count below 50 who was tested positive for anti HCV had HBsAg positivity also.

  *p value >0.05**

Table-XIX

HBV / HCV Distribution based on WHO stage

WHO Stage	Total No.	HBsAg+	Anti HCV+	Both HBsAg+ Anti HCV+	HBsAg%	Anti HCV+ %	Both HBsAg+ anti HCV+ %
I	17	1	-	-	5.9%	-	-
II	33	3	-	-	9.1%	-	-
III	41	3	1	-	7.3%	2.4%	-
IV	9	1	3	1	11.1%	33.3%	14.3%

- Thus out of the 8 HBsAg+ve patients, 3 each were in clinical stage II and III and one each in clinical stage I & IV.

  *p value >0.05**

- Of the 4 anti HCV+ve individuals, there were three in clinical Stage IV and the remaining one patient in Stage III.

  *p value <0.001**

- The only one patient with HBV/HCV/HIV co-infection was in Stage IV.

  *p value <0.01**

Table-XX
Elevated transaminase level in the study population

Serology status	Total	Normal SGOT/SGPT	High SGOT/SGPT	% of High SGOT/SGPT
HBsAg+/anti HCV-	7	4	3	42.9%
HBsAg-/anti HCV+	3	1	2	66.7%
HBsAg+/anti HCV+	1	-	1	100%
HBsAg-/anti HCV-	89	78	11	12.4%

- When only HBV co-infection was associated with HIV there was an increased level of transaminases in three out of seven cases i.e.42.9% *p value <0.01**
- When only HCV co-infection was associated with HIV infection there was an increased level of transaminases in 2 out of 3 cases i.e. 66.7%. *p value <0.01**
- When both HBV and HCV co-infections were there with HIV infection, there was an increased level of transaminases in all the cases / case i.e. 1 out of 1 (100%). *p value <0.01**
- Multivariate logistic regression was performed to know the effect of age, sex and alcohol on liver enzymes in co-infected patients but was found to be statistically insignificant.

Table-XXI

Alkaline Phosphatase levels with WHO stage.

WHO Stage	Normal value	High Value
I	14	3
II	21	12
III	19	22
IV	1	8

High Alkaline Phosphatase levels were seen with worse WHO clinical stages. Out of 9 persons in WHO clinical stages IV, there were 8 persons with increased alkaline phosphatase levels while in clinical Stage III, 22 out of 41, in II, 12 out of 33 and in Stage I, 3 out of 17 had higher values.

*p value < 0.01**

Table-XXII

Alkaline phosphatase levels with CD4 count

CD4 count	Normal	High value
> 500	3	-
200-499	26	7
50-199	24	28
<50	2	10

With decreasing CD4 count higher number of increased alkaline phosphatase levels were observed. *p value < 0.001**

Table-XXIII

G.G.T. values with clinical stages of HIV

WHO Stage	Normal range	High values
I	16	1
II	32	1
III	33	8
IV	6	3

*p value < 0.05**

Table-XXIV

G.G.T. values with CD4 counts

CD4 counts	Normal range	High values
>500	3	-
200-499	33	-
50-199	42	10
<50	9	3

*p value < 0.5**

In most of the patients with increased alkaline Phosphatase level there was a high proportion of raised GGT levels. It co-related with worse stages of HIV infection and lower CD4 counts which were significant statistically.

Serum Bilirubin : Serum Bilirubin was within normal limits for all the patients.

Ultrasound Abdomen : None of the patients co-infected with HBV had abnormality in their ultrasonogram. Only one among the four HCV co-infected patients had increased liver echoes which was not statistically significant.

**p values* : Level of Significance

>0.05 – statistically not significant at 5% level
<0.05 – statistically significant at 1-5% level
<0.01 – statistically significat at 1% and below.

DISCUSSION

1. AGE AND SEX DISTRIBUTION

Most of the patients in the study were in their twenties and thirties which is the economically productive age group. The mean age of the study group was 34.79 and Male: Female ratio was 3:1. It is estimated that in India HIV / AIDS cases reported consist of approximately 73% men and 27% women with 89% of reported cases in the age group of 15-44 years [26].

2. PREVALENCE

Of the 100 HIV infected patients, 8 were found to have positivity for Hepatitis B surface antigen (8%), 4 were found to have positivity for anti HCV (4%) and one was found to have positivity for both HBS Ag and anti HCV. Thus a total of 8% in this study population have co-infection with Hepatitis B, 4% with Hepatitis C Virus and 1% has co-infection with both Hepatitis B and Hepatitis C virus.

The prevalence of Hepatitis co-infection with HIV varies widely across different studies.

TABLE-XXV
Prevalence of HBV/HCV co-infection in HIV patients - studies in India.

Sl.No.	Study By	HIV + HBV	HIV + HCV
1	Padmapriyadarsini etal: [7] (Chennai)	6.4%	2.1%
2	Rogers etal [5, 7]	4%	3%
3	Ramanamma etal [21]	14.3	-
4	Tankhivale SS etal [11] (Maharashtra)	30.4%	7.27
5	Shazia M Ahson etal [3] (Mumbai)	3.5%	8%
6	Dhan Vijay etal [28]	28%	
7	K.Agarwal etal [6] (Delhi)	13%	

TABLE-XXVI
HBV / HCV co-infection - Foreign Studies

Sl.No.	Study By	HBV%	HCV%
1	Petrus Uchenna Inyama [8] (Nigeria)	-	5.7%
2	J.Ockenga etal [17, 29]	9%	23%
3	Saillour F etal [22]	6.9%	42.5%
4	Dimitrakopoulos [23]	67.4%	13.8%
5	Treilinger etal [24]	3.1%	54.7%
6	C.Larsen etal [9]	7%	24.3%

Sl.No.	Study By	HBV%	HCV%
1	Present Study	8%	4%

A cluster survey conducted in randomly selected districts of Tamilnadu showed that the overall community prevalence of Hepatitis B as 5.3% [27]. It is estimated that in India prevalence of Hepatitis B virus infection is 5% and Hepatitis C virus infection is 2% [30] [19]. There is another report available which puts the sero prevalence in India for Hepatitis B as 3% (HBS Ag.) and 1-1.5% for anti HCV (Hepatitis.C) [15]. The prevalence in this study is higher than these statistics, the reason being the high risk behaviour in the study group. The slightly higher prevalence rates in this study when compared to two other studies conducted in Chennai [7,5] may be due to variation in the institution where the studies were conducted or distribution of risk factors among the selected study group. The high variation in prevalence of co-infection of HBV or HCV in HIV reported from different parts of world and India may again be due to distribution of risk factors, geographic location, etc., of the study population.

MODE OF TRANSMISSION / ACQUISITION

Out of 8 HBS Ag positive persons there were 6 persons who acquired the infection through hetero sexual mode. The rest of them, 2 in number, acquired the infection through injection drug use. But only 6.5% among the hetero sexually exposed group turned out to be positive for HBS Ag, but 40% of injection drug users tested positive for HIV. But these were found to be statistically insignificant.

While, in the case of Anti HCV positivity, of the 4 anti HCV positive patients there were 3 persons who got the infection through injection drug use and one through probably hetero sexual mode i.e., 75% by injection drug use and 25% by heterosexual route. Thus 60% of injection drug users and 1.1% of heterosexually exposed group had evidence of Hepatitis C co-infection. This observation showed statistical significance.

TABLE-XXVII
Some of the studies conducted in India and other countries on injection drug users.

Sl. No.	Study By	Co-infected HBV	Co-infected HCV
1	Baveja etal [14] 2003	39.5%	36.45%
2	Sunil Solomen [16] etal	12%	85.2%
3	Decarvalho etal [33]	75%	75%
4	Saha mk etal [31]	100%	92%
5	Perdas etal [32]	20%	

Thus all these studies prove a higher incidence of HIV, HBV, HCV Co-infection in this particularly high risk group of injection drug users.

EFFECT OF CO-INFECTIONS ON IMMUNE STATUS

Out of the 8 HBS Ag positive people 7 had their CD4 counts below 200, of them one with CD4 count below 50. One had CD4 count in between 200 and 499. These observations were not statistically significant. But all the HCV infected persons had CD 4 counts below 200 / μL. Out of them two had CD 4 counts below 50. Whether HCV accelerates progression of HIV-I disease is unknown. But many recent studies have reported that HCV infection might accelerate progression of HIV-I infection. But it is not sure whether HCV

co-infection worsens the immunological dysfunction already present in the host.

The majority of studies conducted so far on the effect of HBV co-infection on the course of HIV progression have given conflicting results. Thus no definitive proof for role of HBV on HIV disease progression has been reported so far [1]. The finding regarding HBV co-infection on HIV in this study was also statistically insignificant.

Of the 8 persons infected with hepatitis B in the present study, there were 3 persons each in clinical stage II and III and one person each in WHO clinical stages I and IV. These observations were shown insignificant by statistical analysis.

But of the 4 persons found to be co-infected with Hepatitis C virus, 3 persons were in clinical stage IV and the remaining one patient in Stage III. So in this study all the HCV co-infected patients had poorer clinical stages and lower CD4 counts suggestive of poor immune status. The correlation between HCV co-infection and poor WHO clinical stage was statistically significant ($P<0.0001$).

The only patient with HBV, HCV co-infection; with HIV was also in clinical stage IV and was also having CD4 count below 50. Though the association between HBV Co-infection

and lower CD4 count was found to be statistically insignificant, the association with worse WHO clinical stage was statistically significant

IMPACT OF CO-INFECTION ON LIVER FUNCTION

The impact of co-infection on liver function was also analysed. This was done by looking at elevated transminase levels (ALT or AST). It was shown in the study that 42.9% of cases with Hepatitis B co-infection alone had a rise in transaminase levels. In those with evidence of Hepatitis C co-infection alone had a rise in transminase level in 66.7% of cases and in the case of Hepatitis B and C co-infection had a rise in 100% case (one out of one). These associations were proved significant statistically. Logistic regression was used to analyse the impact of the other obvious, hepatotoxic agent, alcohol on transminases in patients with co-infection and was found insignificant.

Hepatitis B virus is a non-cytopathic virus that causes liver damage mainly through immune mediated mechanisms. But the risk of HBV associated end stage liver disease seems to be increased in the setting of HIV co-infection. This is because the presence of HIV infection increases the risk of

chronicity of HBV infection, as well, reduces the rate of spontaneous HBS Ag seroconversion. Despite the proposed milder hepatic necro inflamation in HBV co-infected HIV patients, in agreement with the postulated immune mediated pathogenicity, there are reports of enhanced HBV replication levels leading on to progression of more severe liver disease [1].

HIV I infection appears to speed the rate of progression of chronic hepatitis C to end stage liver disease to as little as 10 years after exposure. However, this accelerated progression has not been observed in all studies. Data from a meta analysis indicate that the average risk for progressive liver disease is 2.9 times higher among HCV / HIV - I co-infected persons than among persons infected only with HCV [2] [25].

A study from Mumbai (3) showed higher serum transaminase levels in most of the HCV co-infected persons but there was no evidence of elevated transminases in Hepatitis B co-infection group. But a study from Chennai [7] recorded higher transaminase values for those co-infected with HBV when compared to non HBV group of HIV +ve patients.

HIV & ALKALINE PHOSPHOTASE LEVELS

The effect of HIV infection on the level of alkaline phosphatase was studied in the population. In the study group a higher proportion of patients with elevated alkaline phosphatase levels were seen in worse WHO clinical stages as well as in patients with low CD4 counts. These findings were significant on statistical analysis also. HIV infection is known to cause a rise in alkaline phosphatase levels [7]. This has been linked to the progression of disease as well. Those patients with increase alkaline phosphatase level had either high normal values of GGT or abnormally high GGT values which also showed correlation with worse stages of HIV infection, which were significant statistically also.

This study has its share of limitations as well. This data may have underestimated the true prevalence of HBV co-infection. Atypical serum HBV markers are a problem among some HIV infected individuals as in some of them isolated anti-hepatitis B core antigen is recognised, particularly among patients with severe immune deficiency [1, 13].

The underestimation may have also occurred in the case of Hepatitis C co-infection as well because at least 4% of HIV -

HCV co-infected patients have no detectable anti HCV antibodies in the presence of HIV viremia (16, 12). Also HCV RNA could not be tested which is considered as the gold standard in the diagnosis of Hepatitic C infection. But the test performed in this study has a sensitivity of 99% and specificity of 97%.

CONCLUSIONS

The prevalence of HBV co-infection was found to be 8% in HIV patients in this study.

The prevalence of HCV co-infection in HIV patients in the study population was 4%.

The prevalence of HBV, HCV co-infection in the study population was 1%.

The majority of Hepatitis B co-infections were acquired through heterosexual route. But 40% of injection drug users were co-infected with HBV. But these observations are not statistically significant.

Injection drug use accounted for 75% of cases of Hepatitis C infection and 60% of injection drug users had Hepatitis C co-infection, making injection drug use the main mode of transmission for this co-infection. This observation is significant statistically also.

Both Hepatitis B and Hepatitis C co-infection caused statistically significant elevation of transaminase levels thus predicting on going liver damage. While Hepatitis B co-infection did not produce statistically significant impact on HIV disease progression, hepatitis C co-infection caused statistically significant impact on HIV disease progression with lower CD 4 counts and worse WHO clinical stages.

There was significant association between HIV disease progression and level of alkaline phosphatase. Serum GGT also showed a similar trend with worse WHO clinical stages and lower CD4 counts.

The prevalence of Hepatitis B and Hepatitis C co-infection is fairly high in HIV infected population of Government General Hospital and Madras Medical College supporting the use of more careful screening for these viruses in this institution. Particularly in injection drug users screening for Hepatitis B and C should be undertaken.

SUMMARY

Hepatitis B virus, Hepatitis C virus and Human immuno deficiency virus have in the recent years posed significant challenges to the health care system.

The aim of this study was to know the prevalence and impact of Hepatitis B virus and Hepatitis C virus co-infection in HIV patients of Madras Medical College and Government General Hospital.

Altogether one hundred HIV positive patients in Government General Hospital and Madras Medical College were selected by random sampling and were screened for Hepatitis B surface antigen and anti HCV. Liver function tests and ultra sonography of abdomen were done. Statistical analysis was done and *p values* were estimated wherever necessary.

Results showed that prevalence of Hepatitis B co-infection as 8%, Hepatitis C co-infection as 4% and Hepatitis B and Hepatitis C co-infection together as 1% in HIV

population. There was significant elevation of liver enzymes with co-infection.

On the basis of higher prevalence rates for Hepatitis B and Hepatitis C co-infection routine screening for these viruses is necessary in HIV positive population.

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LIST OF TABLES

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PROFORMA

1. Name
2. Age
3. Sex
4. Occupation
5. Education
6. Marital Status
7. HIV diagnosed on
8. Mode of Acquisition

   a) Sexual → Hetero/Homosexual

   → Contact with commercial sex worker

   → Multiple sex partners

   b) Injection drug user.

   c) Blood transfusion

   d) Iatrogenic

   e) Unknown
9. Alcoholic intake
10. HIV status of partner / Spouse
11. CD4 count
12. WHO clinical stage

    - Weight loss - a) Yes / No

    - b) Weight loss, if there - >10% of <10%

- Activity - Limited / Normal

- No. of days inactive the previous month

- Persistent generalised lymphadenopathy +/-

- Acute HIV syndrome - Yes / No

- Oral candidiasis - Yes / No

- AIDS defining illness

- Pulmonary tuberculosis

13. Liver function test

- Serum Bilirubin

- AST / SGOT

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- GGT

- S.Alkaline phosphatase

14. Ultrasonogram - Abdomen

- Liver - Size / echoes

- Spleen / Splenic vein

- Portal vein

- Ascites

- Venous collalevals.

Sl.No.	Number IP/OP	Age	Sex	Education	Marital Status	HIV Status of Spouse	Mode of Transmission	Alcohol intake	CD4 Count	WHO Stage	HBs Ag	Anti HCV	LFT					USG
													SBb	SGOT	SGPT	GGT	ALP	
1	844/06	37	M	U.P.School	Married	-ve	Heterosexual	Yes	254	II	-ve	-ve	1.0	24	26	32	78	N
2	753329	35	M	U.P.School	Married	+ve	Heterosexual	No	109	III	-ve	-ve	0.8	24	22	25	72	N
3	113228	40	M	U.P.School	Married	N K	Heterosexual	Yes	45	III	-ve	-ve	0.8	38	31	40	136	Fatty Liver
4	141280	33	M	SSLC	Married	N K	Heterosexual	No	148	III	-ve	-ve	0.9	32	32	30	98	N
5	56945	54	M	L.P. School	Married	-ve	Heterosexual	No	94	III	-ve	-ve	1.1	32	30	28	84	N
6	122329	26	M	SSLC	Not Married	-	Heterosexual	No	340	I	-ve	-ve	0.6	28	26	28	58	N
7	143790	48	F	U.P.School	Married	+ve	Heterosexual	No	178	IV	-ve	-ve	1	30	41	20	84	N
8	165865	40	M	Hr.Secondary	Married	+ve	Heterosexual	Yes	86	III	+ve	-ve	1.2	59	49	48	98	N
9	103411	28	M	SSLC	Not Married	-	Heterosexual	No	235	III	-ve	-ve	1.2	32	30	30	68	N
10	17973	35	M	SSLC	Married	+ve	Heterosexual	Yes	40	III	-ve	-ve	0.9	58	28	52	186	N
11	38774	40	M	High School	Married	N K	Heterosexual	Yes	45	IV	-ve	-ve	0.8	58	28	39	180	N
12	120146	40	M	High School	Married	+ve	Heterosexual	No	230	II	-ve	-ve	0.8	34	32	28	70	N
13	40631	31	M	U.P.School	Married	+ve	Heterosexual	No	58	III	-ve	-ve	0.6	32	30	36	132	N
14	77268	24	M	SSLC	Not Married	-	IVDU	No	39	IV	+ve	+ve	1.2	85	80	52	163	N
15	140179	32	M	SSLC	Married	-ve	Heterosexual	Yes	146	III	-ve	-ve	1.1	24	26	38	138	N
16	122743	26	M	Diploma	Married	+ve	Heterosexual	No	181	II	+ve	-ve	0.9	25	25	42	176	N
17	158548	38	M	SSLC	Married	-ve	BT	Yes	206	II	-ve	-ve	0.5	108	51	42	356	Fatty Liver
18	101645	39	M	SSLC	Not Married	-	Heterosexual	Yes	231	I	-ve	-ve	0.6	21	28	31	65	Fatty Liver
19	35802	26	M	U.P.School	Not Married	-	Heterosexual	No	49	III	-ve	-ve	0.9	20	18	34	165	N
20	121318	45	M	L.P. School	Married	-ve	Heterosexual	Yes	69	IV	-ve	-ve	1.2	58	28	48	188	Fatty Liver
21	96804	40	F	L.P. School	Married	-ve	Heterosexual	No	11	IV	-ve	-ve	0.5	23	16	28	168	N

Sl.No.	Number IP/OP	Age	Sex	Education	Marital Status	HIV Status of Spouse	Mode of Transmission	Alcohol intake	CD4 Count	WHO Stage	HBs Ag	Anti HCV	LFT					USG
													SBb	SGOT	SGPT	GGT	ALP	
22	131631	35	F	High School	Married	+ve	Heterosexual	NO	430	II	-ve	-ve	0.7	28	22	21	97	N
23	102404	32	M	Diploma	Not Married	-	Heterosexual	NO	642	I	-ve	-ve	1	40	58	30	122	N
24	37518	38	F	High School	Married	+ve	Heterosexual	NO	35	III	-ve	-ve	0.8	25	19	20	105	N
25	234197	34	M	High School	Married	-ve	Heterosexual	NO	8	IV	-ve	-ve	0.8	32	30	40	220	N
26	1432/06	29	M	SSLC	Not Married	-	Heterosexual	YES	160	III	-ve	-ve	0.6	26	30	24	104	N
27	110125	35	M	Diploma	Married	-ve	Heterosexual	NO	136	II	-ve	-ve	0.7	24	16	28	106	N
28	154574	48	F	L.P.School	Married	-ve	Not known	NO	72	II	-ve	-ve	0.9	29	30	22	98	Fatty liver
29	107645	40	F	L.P.School	Married	+ve	Heterosexual	NO	53	III	-ve	-ve	0.8	33	44	28	151	N
30	113812	33	M	No	Not Married	-	IVDU	YES	178	III	-ve	+ve	1	38	36	44	110	N
31	124935	29	F	U.P.School	Married	+ve	Heterosexual	NO	158	I	+ve	-ve	0.6	87	42	71	153	N
32	141280	33	M	SSLC	Married	-ve	Heterosexual	NO	256	II	-ve	-ve	0.9	29	33	24	110	N
33	43720	35	M	SSLC	Married	+ve	Heterosexual	YES	118	III	-ve	-ve	0.7	29	33	28	156	N
34	131601	27	M	U.P.School	Married	N K	Heterosexual	YES	122	III	-ve	-ve	0.9	46	38	26	97	N
35	169198	30	M	High School	Married	-ve	Heterosexual	YES	96	III	-ve	-ve	0.8	33	36	30	126	N
36	136689	35	F	High School	Married	+ve	Heterosexual	NO	28	IV	-ve	+ve	1.7	180	148	68	300	N
37	160139	28	F	L.P.School	Married	+ve	Heterosexual	NO	260	I	-ve	-ve	0.8	48	37	24	120	N
38	101686	36	M	U.P.School	Married	-ve	Heterosexual	YES	120	III	-ve	-ve	1.1	56	49	34	89	N
39	97676	30	M	High School	Not Married	-	Heterosexual	YES	68	III	-ve	-ve	1.2	59	49	30	91	N
40	1603/05	29	M	Hr.Secondary	No	-	Heterosexual	NO	182	II	+ve	-ve	1.1	38	44	36	133	N
41	155710	38	F	L.P.School	Yes	+ve	Heterosexual	NO	280	I	-ve	-ve	0.8	24	34	29	168	N
42	146103	36	F	High School	Married	+ve	Heterosexual	NO	380	I	-ve	-ve	0.6	22	28	26	76	N

Sl.No.	Number IP/OP	Age	Sex	Education	Marital Status	HIV Status of Spouse	Mode of Transmission	Alcohol intake	CD4 Count	WHO Stage	HBs Ag	Anti HCV	LFT					USG
													SBb	SGOT	SGPT	GGT	ALP	
43	133817	32	M	High School	Married	-ve	Heterosexual	YES	82	III	-ve	-ve	1.1	29	34	28	183	Fatty liver
44	802283	30	M	U.P. School	Married	-ve	Heterosexual	YES	120	III	-ve	-ve	1	49	40	38	150	N
45	68721	35	F	High School	Married	+ve	Heterosexual	NO	48	III	-ve	-ve	1	32	27	20	81	N
46	136102	35	M	High School	Married	-ve	Heterosexual	NO	110	II	-ve	-ve	0.8	27	26	26	199	N
47	209070	28	M	SSLC	Not Married	-	Heterosexual	NO	192	II	-ve	-ve	0.8	46	37	38	261	N
48	100536	35	M	High School	Married	-ve	Heterosexual	YES	220	II	-ve	-ve	0.9	35	26	34	136	N
49	815145	30	M	L.P. School	Married	-ve	Heterosexual	YES	192	II	-ve	-ve	0.8	34	24	38	140	N
50	1250106	30	F	L.P. School	Married	+ve	Heterosexual	NO	220	I	-ve	-ve	0.8	29	23	20	67	N
51	2557/05	44	M	U.P. School	Married	+ve	Heterosexual	YES	220	II	-ve	-ve	0.9	26	18	30	126	N
52	19455	34	M	Diploma	Married	-ve	Heterosexual	NO	140	III	-ve	-ve	0.9	33	28	38	150	N
53	33274	46	M	U.P. School	Married	-ve	Heterosexual	NO	230	II	-ve	-ve	0.8	34	38	40	184	N
54	176059	27	F	High School	Married	+ve	Heterosexual	NO	320	I	-ve	-ve	0.8	35	27	20	126	N
55	188505	35	M	High School	Married	+ve	Heterosexual	YES	110	III	-ve	-ve	0.9	28	21	32	95	N
56	179727	29	M	U.P. School	Not Married	-	Heterosexual	NO	180	II	-ve	-ve	0.9	32	26	24	98	N
57	57845	24	F	L.P. School	Married	+ve	Heterosexual	NO	360	I	-ve	-ve	0.8	21	20	18	87	N
58	113830	33	M	High School	Married	+ve	Heterosexual	YES	122	III	+ve	-ve	0.8	29	28	26	92	N
59	33643	28	M	High School	Not Married	-	Heterosexual	NO	210	II	-ve	-ve	1	26	29	38	166	N
60	213410	32	M	U.P. School	Married	-ve	Heterosexual	NO	140	III	-ve	-ve	1.1	30	32	38	180	N
61	115841	23	F	High School	Married	+ve	Heterosexual	NO	268	I	-ve	-ve	1	18	16	16	33	N
62	148149	34	M	U.P. School	Married	+ve	Heterosexual	NO	88	III	+ve	-ve	1.2	48	54	51	166	N
63	48617	26	M	U.P. School	Not Married	-	Heterosexual	NO	116	III	-ve	-ve	0.7	29	26	43	180	N

Sl.No.	Number IP/OP	Age	Sex	Education	Marital Status	HIV Status of Spouse	Mode of Transmission	Alcohol intake	CD4 Count	WHO Stage	HBs Ag	Anti HCV	LFT					USG
													SBb	SGOT	SGPT	GGT	ALP	
64	215043	30	M	B.A.	Not Married	-	Heterosexual	NO	176	II	-ve	-ve	0.6	28	20	29	114	N
65	99602	38	F	Not educated	Married	+ve	Heterosexual	NO	320	I	-ve	-ve	0.9	28	23	26	131	N
66	31541	35	F	U.P. School	Married	+ve	Heterosexual	NO	180	III	-ve	-ve	0.7	23	20	28	161	N
67	35921	42	M	High School	Married	+ve	Heterosexual	YES	226	II	-ve	-ve	0.9	28	26	30	112	N
68	35929	36	M	High School	Married	-ve	Heterosexual	YES	520	I	-ve	-ve	0.6	24	26	26	113	N
69	701104	38	M	B.A.	Married	-ve	Heterosexual	NO	163	II	-ve	-ve	0.8	23	25	22	75	N
70	1392156	45	F	L.P. School	Married	+ve	Heterosexual	NO	92	III	-ve	-ve	0.6	26	22	20	80	N
71	1392182	25	F	U.P. School	Married	+ve	Heterosexual	NO	420	I	-ve	-ve	0.6	21	29	20	91	N
72	138968	40	M	U.P. School	Married	NA	IVDU	YES	260	II	+ve	-ve	0.8	23	42	38	107	N
73	38474	36	M	B.A.	Married	-ve	Heterosexual	NO	160	III	-ve	-ve	1.4	77	81	52	114	N
74	430011	32	M	Hr.Secondary	Married	-ve	Heterosexual	YES	210	II	-ve	-ve	1.1	54	26	30	80	N
75	40531	31	M	High School	Married	-ve	Heterosexual	NO	210	II	-ve	-ve	1	16	18	24	115	N
76	182549	35	M	SSLC	Married	-ve	Heterosexual	YES	128	II	-ve	-ve	1.1	44	32	30	119	N
77	147512	39	M	B.A.	Married	-ve	IVDU	NO	96	IV	-ve	+ve	0.9	55	59	61	176	N
78	135052	41	M	L.P. School	Married	+ve	Heterosexual	YES	204	III	-ve	-ve	0.7	21	28	20	78	N
79	138553	40	M	B.A.	Married	- ve	Heterosexual	NO	648	I	-ve	-ve	0.7	30	25	22	79	N
80	203499	50	M	L.P. School	Married	- ve	Heterosexual	NO	214	II	-ve	-ve	0.6	18	16	20	72	N
81	826733	30	M	High School	Not Married	- ve	Heterosexual	YES	62	III	-ve	-ve	0.8	38	23	56	289	N
82	144517	44	M	b.a.	Married	- ve	Heterosexual	YES	186	II	-ve	-ve	0.8	24	32	30	108	N
83	97314	43	F	L.P.. School	Married	+ ve	Heterosexual	NO	220	III	-ve	-ve	1	30	28	22	88	N
84	56656	38	F	High School	Married	+ ve	Heterosexual	NO	316	I	-ve	-ve	1.1	23	20	22	114	N

Sl.No.	Number IP/OP	Age	Sex	Education	Marital Status	HIV Status of Spouse	Mode of Transmission	Alcohol intake	CD4 Count	WHO Stage	HBs Ag	Anti HCV	LFT					USG
													SBb	SGOT	SGPT	GGT	ALP	
85	106410	33	M	Hr.Secondary	Married	- ve	Heterosexual	NO	88	III	-ve	-ve	0.8	20	20	56	158	N
86	126420	36	M	High School	Married	+ ve	Heterosexual	YES	114	III	-ve	-ve	0.9	29	25	52	138	N
87	968103	32	M	U.P. School	Not Married	-	Heterosexual	YES	312	II	-ve	-ve	1	30	28	28	90	N
88	286105	50	M	U.P. School	Married	- ve	Heterosexual	NO	172	II	-ve	-ve	0.9	19	22	58	209	N
89	954105	33	M	B.A.	Married	- ve	Heterosexual	YES	220	II	-ve	-ve	1.1	35	37	41	168	N
90	130046	38	M	High School	Married	- ve	Heterosexual	YES	160	II	-ve	-ve	1	43	40	32	98	N
91	122327	30	F	U.P. School	Married	+ ve	Heterosexual	NO	46	III	-ve	-ve	0.9	26	27	31	189	N
92	98184	47	M	High School	Married	- ve	Heterosexual	YES	118	II	-ve	-ve	0.8	24	28	26	101	Fatty Liver
93	70618	28	F	High School	Married	+ ve	Heterosexual	NO	80	III	-ve	-ve	1.1	36	33	52	275	N
94	52810	38	M	Diploma	Married	+ ve	Heterosexual	NO	110	II	-ve	-ve	0.8	17	19	38	133	N
95	127188	26	M	High School	Not Married	-	IVDU	NO	260	II	-ve	-ve	1.1	22	29	28	76	N
96	202105	35	M	B.A.	Married	+ ve	Heterosexual	NO	68	III	-ve	-ve	0.9	30	32	62	232	N
97	173105	32	M	L.P. School	Married	+ ve	Heterosexual	YES	130	III	-ve	-ve	1.3	41	52	42	141	N
98	1175/05	36	M	Hr.Secondary	Married	+ ve	Heterosexual	NO	38	IV	-ve	-ve	0.9	36	35	42	172	N
99	120414	25	F	U.P. School	Married	+ ve	Heterosexual	NO	342	I	-ve	-ve	0.9	20	21	24	84	N
100	171402	35	M	Hr.Secondary	Married	+ ve	Heterosexual	NO	132	III	-ve	-ve	0.9	22	28	42	143	N

NK = Not Known