PREDICTION OF SEROCONVERSION IN RELATION TO HBsAG QUANTIFICATION

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GOVT. STANLEY MEDICAL COLLEGE & HOSPITAL

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI, INDIA.

AUGUST 2013

CERTIFICATE

This is to certify that the dissertation entitled **"PREDICTION OF SEROCONVERSION IN RELATION TO HBsAG QUANTIFICATION IN CHRONIC HBV PATIENTS "** is the bonafide original work of **Dr.B.HARRIPRASAD** in partial fulfillment of the requirements for **D.M (GASTROENTEROLOGY) BRANCH – IV** Examination of the Tamilnadu Dr. M.G.R. Medical University to be held in August 2013. The period of study was from October 2010 to April 2012.

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DECLARATION

I, **Dr. B.HARRIPRASAD ,** solemnly declare that the dissertation titled, "**Prediction of seroconversion in relation to HBsAg quantification in chronic HBV patients**" is a bonafide work done by me at Govt. Stanley Medical College & Hospital during 2010-2013 under the guidance and supervision of **Dr. A.R.VENKATESWARAN., M.D., D.M,** Professor and Head, Department of Medical Gastroenterology, Stanley Medical College, Chennai-600 001.

The dissertation is submitted to The Tamilnadu Dr. M.G.R. Medical University, towards partial fulfillment of requirement for the award of **D.M Degree (BRANCH – IV) in Gastroenterology.**

Place: Chennai.

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INSTITUTIONAL ETHICAL COMMITTEE, STANLEY MEDICAL COLLEGE, CHENNAI-1

Title of the Work : Prediction of seroconversion in relation with surface Antigen quantification in patients with CHRONIC HBV Infection

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The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 08.11.2011 at the Council Hall, Stanley Medical College, Chennai-1 at 2PM

The members of the Committee, the secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

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INTRODUCTION

There are approximately 400 million hepatitis B virus (HBV) carriers in the world. Till 1981, hepatitis B patients relied on serology assays [1]. E antigen (HBeAg) was a marker of infectivity. Initially assays to quantify HBV DNA polymerase activity was done and later only HBV DNA level estimation could be done. Method used was hybridization techniques. Spontaneous e antigen seroconversion is seen in the course of chronic HBV infection.

Course of B positive individuals had 2 stages as defined initially. First stage has e antigen, and HBV DNA detectable. Second stage does not have HBeAg, immeasurable DNA, and passive liver disease. Second stage patients are "healthy" carriers, who are non replicative

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INTRODUCTION

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There are approximately 400 million hepatitis B virus (HBV) carriers in the world. Till 1981, hepatitis B patients relied on serology assays [(1).] "E" antigen (HBeAg) was a marker of infectivity. Initially assays to quantify HBV DNA polymerase activity was done and later only HBV DNA level estimation could be done. Method used was hybridization techniques. Spontaneous e antigen seroconversion is seen in the course of chronic HBV infection.

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Table 29.1. Patterns of Hepatitis B Virus Infection

Prevalence	High	Intermediate	Low
Carrier rate	8%–20%	3%–7%	0.1%–2%
Geographical distribution	Southeast Asia China Pacific Islands Sub-Saharan Africa Alaska (Eskimos)	Mediterranean basin Eastern Europe Central Asia Japan Latin and South America Middle East	United States and Canada Western Europe Australia New Zealand
Predominant age at infection	Perinatal and early childhood	Early childhood	Adult
Predominant mode of transmission	Maternal–infant Percutaneous	Percutaneous Sexual	Sexual Percutaneous

Our country India lies in intermediate zone with a carrier rate of 3-7 % [(2)]. India presents with HBV in early childhood. Means of transmitting infection by percutaneous method is common like sexual route.

Our study aimed to determine common routes of infection and clinical profile of HBV patients. Various parameters were assessed for e antigen seroconversion and its correlation was analysed. Clinical response was also analysed with the antiviral drug and differences in responses of both e antigen groups were analysed.

AIM

AIM

1. To predict the HBeAg seroconversion in relation with HBsAg quantification in patients with chronic HBV infection with antiviral treatment

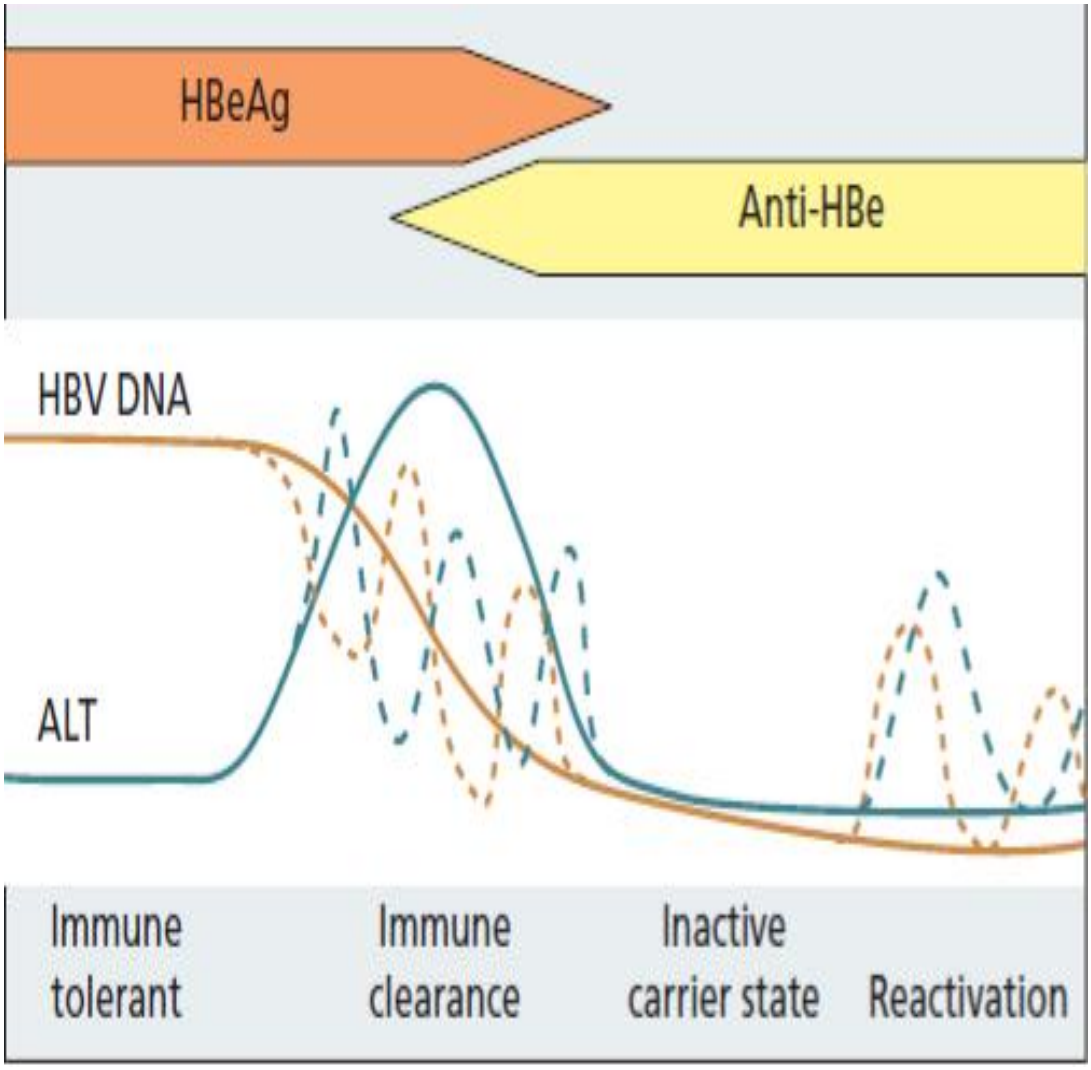
2. Clinical profile of Chronic HBV infection

3. Clinical response of Chronic HBV infection patients with antiviral drug in a Tertiary centre

REVIEW OF LITERATURE

REVIEW OF LITERATURE

HBV INFECTION - Natural history :



4 stages of chronic infection include

1. Tolerance stage - e antigen positive, high hepatitis B deoxy nucleic acid, stable enzymes and stable histology [3]. E seroconversion is limited. Prognosis is good.

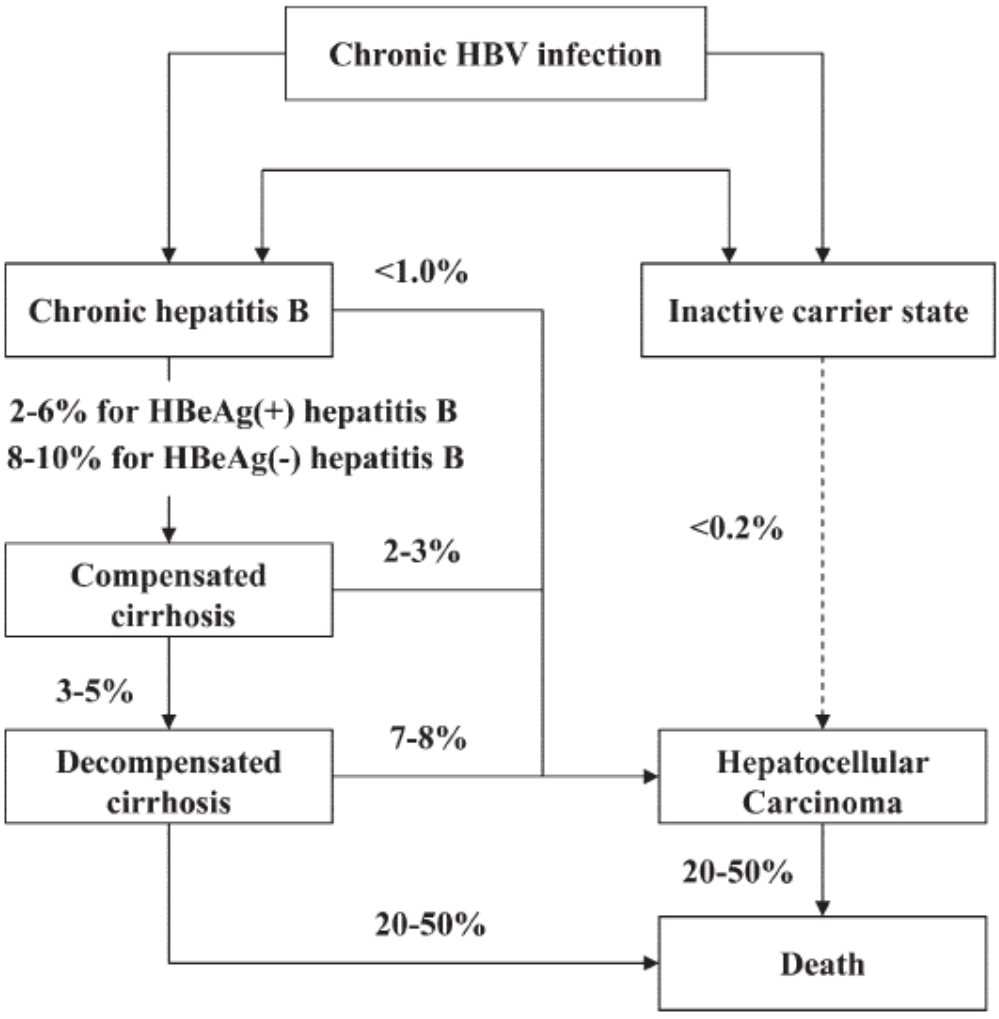
2. Clearance – e antigen positive , alternating HBV deoxyribonucleic acid and dormant inflammation

Rate of spontaneous e antigen clearance is 10 to 20 % [4]

3. Inactive - e antigen negative, antibody to e antigen present, stable ALT and immeasurable Deoxy ribo nucleic acid levels.

4. Fourth stage - e antigen negative , antibody to e antigen positive , measurable DNA levels , increased enzymes and fibrosis.[5]

Cirrhosis is seen in two to six % in e antigen positive. In e antigen negative it is around eight to ten % [6]. High levels of cirrhosis in e negative occur due to elderly age who has progressive liver disease. Advancement to cirrhosis occurs due to alcohol, co infection with other viruses and depending on genotype.



Natural course of HBV infection

CHRONIC HBV INFECTION AND HCC:

HCC incidence is one % for non-cirrhotic carriers and 2% to 3% in patients with cirrhosis.[7]

Other factors which may progress to HCC include

Co-infection with HCV[8],

Family history of HCC[9],

Alcohol intake,

High levels of HBV replication,

And core promoter mutations.[10]

Host Factors	Virus Factors	Environmental Factors
Older age* (longer duration)	High levels of HBV replication*	Concurrent infection (HCV*, HDV, HIV)
Male*	Genotype (C > B)*	Alcohol consumption*
Immune status	HBV variant (core promoter)	Diabetes mellitus†
		Obesity†

Ways and means of Hepatitis B transmitting routes

Ethnicity and high risk behaviour are important routes of transmitting infection.

Knowing of risk factors should be done .

Transmitting routes of infection are :

Blood transfusion

Percutaneous

Sexual [11]

Perinatal [12]

Vaccination against hepatitis B is the mainstay. Universal vaccination to all new born is practised now[13]. HCC is reduced in juvenile group because of vaccination. Vaccination has resulted in a major fall in HCC even in this young age group [14].

Hepatitis B immunoglobulin and vaccine has better efficacy (98%) compared to vaccine alone [15].

Indications for Hepatitis B Vaccine

1. All newborns[a]
2. All children and adolescents not vaccinated at birth
3. High-risk adults:
    a. Health care workers
    b. Men who have sex with men
    c. Persons with multiple sexual partners
    d. Injection drug users
    e. Patients on hemodialysis
    f. Institutionalized patients
    g. Health care workers and public safety workers
    h. Spouse, sexual partners and household members of HBV carriers

Plasma and recombinant are two types of vaccine available. Vaccine is administered intramuscularly 0 , 1 and 6 months . Dose is 10 to 20 microgram for adults.[16]

Vaccine brand	Age group	Dose	Volume	Number of doses
Engerix-B	0–19 years	10µg	0.5mL	3
	≥20 years	20µg	1.0mL	3
Recombivax HB	0–19 years	5µg	0.5mL	3
	≥20 years	10µg	1.0mL	3
(Optional 2 doses)	11–15 years	10µg	1.0mL	2

For haemodialysis patients, recommended dose is 40µg with each dose (Engerix-B 40µg per 2.0mL and Recombivax HB dialysis formulation 40µg per 1.0mL).

Currently available vaccines their dosage and schedule.

Anti HBs level more than ten IU / L is arrived in more than 95 % of recipients[17].

Host factors
Age > 40 years
Obesity
Smoking
Genetics, certain HLA types
Other medical conditions
Diabetes
Cirrhosis
Renal failure
Conditions requiring immunosuppressive therapy
Unrecognized chronic HBV infection
Technical
Subcutaneous administration
Freezing of vaccine

Various factors for failure of vaccine.

Clinical symptoms :

Fatigue is more common than poor appetite and malaise. Right upper quadrant pain is generally but of low grade. Physical examination may reveal hepato splenomegaly . Decompensation progresses to jaundice , ascites and peripheral edema. Serum bilirubin and enzymes are usually normal in inactive carrier state . enzymes become elevated during exacerbations of disease .

Extra hepatic syndromes [(18)] are seen in both acute and chronic forms. They are arthritis , dermatitis , glomerulo nephritis ,polyarthritis

nodosa[19], cryoglobulinemia papular acrodermatitis and polymyalgia rheumatica. They are secondary to circulating immune complexes.

DIAGNOSIS:

	HBsAg	HBeAg	Anti-HBc (IgM)	Anti-HBc (IgG)	Anti-HBs	Anti-HBe	HBV DNA	Interpretation
Acute HBV	+	+	+	-	-	-	+++	Early phase
Infection	-	-	+	+	-	+	+	Window phase
	-	-	-	+	+	+	+/-	Recovery phase
Chronic HBV	+	+	-	+	-	-	+++	HBeAg+ chronic hepatitis or Immune tolerant phase
Infection								
	+	-	-	+	-	+	+/-	Inactive carrier state
	+	-	-	+	-	+	++	HBeAg- chronic hepatitis
	+	+/-	+/-	+	-	+/-	++	Exacerbations of chronic hepatitis

Patients do not have any symptoms until they have been progressed to progressive stage . Screening high risk person is essential for early diagnosis .

Individuals born in areas of high* or intermediate prevalence ratest for HBV including immigrants and adopted children‡§
Asia: all countries
Africa: all countries
South Pacific Islands: all countries
Middle East (except Cyprus and Israel)
European Mediterranean: Malta and Spain
The Arctic (indigenous populations of Alaska, Canada and Greenland)
South America: Ecuador, Guyana, Suriname, Venezuela and Amazon regions of Bolivia, Brazil, Colombia and Peru
Eastern Europe: all countries except Hungary
Caribbean: Antigua and Barbuda, Dominica, Granada, Haiti, Jamaica, St. Kitts and Nevis, St. Lucia, and Turks and Caicos
Central America: Guatemala and Honduras
Other groups recommended for screening
US born persons not vaccinated as infants whose parents were born in regions with high HBV endemicity (≥8%)
Household and sexual contacts of HBsAg-positive persons‡
Persons who have ever injected drugs‡
Persons with multiple sexual partners or history of sexually transmitted disease‡
Men who have sex with men‡
Inmates of correctional facilities‡
Individuals with chronically elevated ALT or AST‡
Individuals infected with HCV or HIV‡
Patients undergoing renal dialysis
All pregnant women
Persons needing immunosuppressive therapy

High risk persons need to be screened

HBsAg is important for the diagnosis . Continuation of positivity even after 6 months denotes chronic infection. C anigen cannot be detected in blood but antibody can be seen. Immunoglobulin G presence presents an idea whether the the person has been recovered or chronically infected .E antigen is derived from precore protein indicating replication and infectivity. Seroconversion is followed by reduction in DNA levels .If it doesn't happen it may be due to precore or core promoter HBV variants [20].

DNA is a marker of viremia which could be done by realtime PCR assays [21]. They identify less than ten international units. Regular monitoring is done to see which phase the patient belongs and to see the response during treatment. Serum HBV DNA levels are expressed in IU/ml to ensure comparability.

PRE THERAPEAUTIC ASSESSMENT :

Assessment of the liver disease needs to be done. HBV serological markers is done for first degree relatives and sexual partners of patients They are vaccinated if tested negative. Normal ALT levels are seen in immune tolerant phase and inactive carriers.E negative people have intermittently normal ALT level. Routine liver function tests are needed to assess the patient .Enzymes are a crucial determinant for starting treatment

while albumin , globulin are predictors to exclude decompensation. A liver biopsy needed to determine the degree of necroinflammation and fibrosis since histology can assist the decision to start treatment. It may rile other cause for liver disease. Adverse effects are very low 1 in four thousand or ten thousand. A liver biopsy is not required with clinical evidence of cirrhosis or in those in whom treatment is indicated irrespective of stage of fibrosis. serum markers and transient elastography can assess hepatic fibrosis and complement or to avoid a liver biopsy. Transient elastography has high diagnostic accuracy.

TREATMENT OF CHRONIC HEPATITIS B :

The aims of treatment of chronic hepatitis B are to achieve

a) continued suppression of HBV replication

b) Remission of liver disease.

They should be decided whether to start or defer treatment .It depends on the grade of liver disease and its future progression to cirrhosis and hepatocellular carcinoma. [22 - 26]. Low risk patients should be monitored at regular intervals.

Algorithm for treatment of CHB

Treatment strongly recommended

- Acute liver failure
- Decompensated cirrhosis and detectable serum HBV DNA
- Compensated cirrhosis and serum HBV DNA > 2000 IU/mL
- Severe exacerbations of chronic hepatitis B

Treatment should be considered

- HBeAg-positive chronic hepatitis, ALT persistently > 2 x ULN and HBV DNA > 20000 IU/mL
- HBeAg-negative chronic hepatitis, ALT persistently > 2 x ULN and HBV DNA > 20000 IU/mL

Treatment should be individualized

- HBeAg-positive, ALT 1–2 x ULN or age > 40
- HBeAg-negative, ALT 1–2 x ULN and/or HBV DNA 2000–20000 IU/mL

Patients in whom treatment can be deferred

- Young patients in the immune tolerance phase or inactive carrier state

ALT, alanine aminotransferase; ULN, upper limit of normal.

Deferred groups for treatment are young patients who are in tolerant phase and inactive carrier phase. These group of patients should br regularly followed up with blood tests. IFNs are given predefined durations, while nucleoside analogues (NA) are usually administered until

certain endpoints are achieved. This occurs due to immunomodulatory effects . For HBeAg-positive patients, viral suppression can be sustained in 50% to 90% patients if treatment is suspended after HBeAg seroconversion is achieved. For HBeAg-negative patients, relapse is common even when HBV DNA has been suppressed to undetectable levels for more than a year; thus, the endpoint for suspending treatment is unclear .

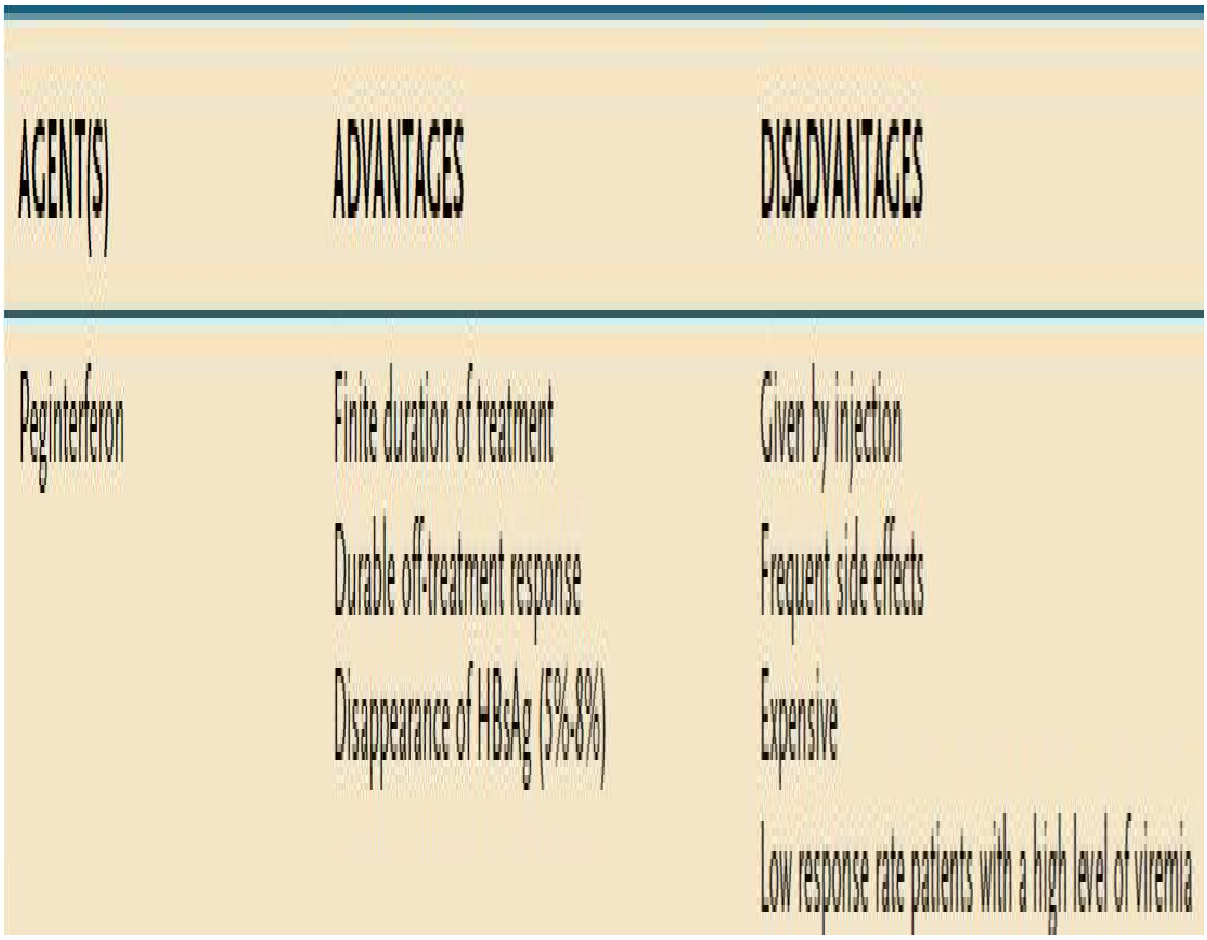
CATEGORY OF RESPONSE	
Biochemical (BR)	Decrease in serum ALT to within the normal range
Virological (VR)	Decrease in serum HBV DNA to $<10^5$ IU/mL and loss of HBeAg in patients who were initially HBeAg positive; undetectable serum HBV DNA ($<10^2$ IU/mL) in patients who were initially HBeAg negative
Histologic (HR)	Decrease in histologic activity index by at least two points compared to pretreatment liver biopsy
Complete (CR)	Fulfill criteria of biochemical and virological response and loss of HBsAg

Both antiviral and immune modulation effect has been seen with interferon[27]. It has been used from 1992 . It is effective even after a short treatment. There is poorer acceptance because of low DNA suppression and adverse effects. IFN-alpha induced HBeAg clearance in e positive appears to be durable in 80% to 90% of patients with a follow-up period of 4 to 8 years[28].

Pegylated interferon is more potent. Attachment of polyethylene glycol reduces absorption. Renal clearance is also reduced thereby prolonging its half life. Results of treatment response ranged from 38% to 90% in treated patients compared with only 0% to 37% of controls [29] e antigen negative patients. It is given for 48 weeks for both e antigen positive and negative patients .Data is not available for increased effectiveness which may be due to effect on viral replication or immune modulatory function [30].

Both Interferons have similar side effect profiles. The most common side effect is influenza-like illness: fever, chills, headache, malaise and emotional lability.

Peg interferon – advantages and diadvantages



AGENT(S)	ADVANTAGES	DISADVANTAGES
Peg interferon	Finite duration of treatment	Given by injection
	Durable off-treatment response	Frequent side effects
	Disappearance of HBsAg (5%-8%)	Expensive
		Low response rate patients with a high level of viremia

Lamivudine was approved by 1998 . Monotherapy has good effect in suppressing replication of the virus and in stopping progression of the liver disease . It is easy to administer and free of side effects. Increment in resistance is seen as duration of treatment progresses . Thirty eight percent at end of 2 years and sixty five percent at 5 years is seen [31]. It is more

common when associated with retro viral patients where treatment would have been started earlier.

Adefovir is acyclic phosphonate nucleotide analog of AMP . Approved in 2002 based on the trials of various continents [32]. E antigen seroconversion and non detectability of DNA is increased during the second year. [33]. Adverse events noted with this drug are

1.Renal impairment

2.Fanconi's anemia [34]

3. Hypophosphatemia

Selective inhibition of replication is seen with entecavir. Approved in 2005 based on results showing better efficacy than lamivudine. It is better than lamivudine in regards to histological improvement, reduction to undetectable HBV DNA, reduction in mean HBV DNA level from baseline , ALT normalization, and HBeAg seroconversion [35]

Telbivudine is an L nucleoside analog of thymidine. Drug has activity against HBV DNA polymerase.It is efficiently phosphorylated by cellular kinases to form the active triphosphate form. Active form has an intracellular half-life of 14 hours. Telbivudine-5'-triphosphate inhibits

HBV DNA polymerase (reverse transcriptase) and thus HBV replicationt is more potent than lamivudine in trials[36] .

YMDD motif is the place where mutations occur . It is well tolerated when single therapy is used. It is used safely. Complaints of myopathy and peripheral neuropathy are reported. Peripheral neuropathy common when telbivudine was used in combination with pegIFN[37] .

TENOFOVIR :

Tenofovir disoproxil fumarate is a nucleotide analogue initially approved for the treatment of HIV infection and later approved for the treatment of chronic hepatitis B in 2008. Tenofovir is structurally similar to adefovir. Similar rates of histologic response and HBeAg seroconversion was seen when compared to adefovir[38]. Dose should be adjusted with creatinine clearance < 50 mL/min. Adverse effect note with tenofovir are

1. Renal impairment
2. Fanconi syndrome
3. Osteomalcia

Approved dose – antiviral agents

Lamivudine	100 mg daily
Adefovir dipivoxil	10 mg daily
Entecavir	0.5 mg daily (1.0 mg daily for patients with lamivudine resistance)
Telbivudine	600 mg daily
Tenofovir disoproxil fumarate	300 mg daily

	Interferon	Nucleos(t)ide analogues
Route of administration	Parenteral	Oral
Duration of treatment	Finite, ~12 months	Indefinite, years
Antiviral activity	Modest, but has immunomodulatory effects	Potent: ETV / TDF / TBV > LAM > ADV
Antiviral resistance	None identified	Yes: LAM > TBV > ADV > ETV / TDF
Side effects	Frequent, may be serious	Negligible ADV / TDF nephrotoxicity TBV myopathy

ADV, adefovir dipivoxil; ETV, entecavir; LAM, lamivudine; TBV, telbivudine; TDF, tenofovir disoproxil fumarate.

Characteristics of Interferon and NA

Resistance is the major concern with oral antiviral agents . In the current time , increased rates of resistance and entecavir and tenofovir offers less resistance. Early manifestation of antiviral resistance is virologic breakthrough . it is mainly due tomedication noncompliance. DNA levels are low initially but compensatory mutations restore replication fitness leading to a progressive increase in serum HBV DNA . Drug having low rate of genotypic resistance should be started and compliance reinforced. Combination therapy has shown good results.

	Incidence of genotypic resistance at year (%)				
	1	2	3	4	5
Nucleos(t)ide naïve patients					
Lamivudine	~20	45	55	71	65
Telbivudine	5–10	10–20	na	na	na
Adefovir dipivoxil	0	3	11	18	29
Entecavir	0	~1	1–2	1–2	1–2
Tenofovir disoproxil fumarate	0	0	0	na	na
Patients with lamivudine resistance					
Adefovir dipivoxil	~5	~20	na	na	na
Entecavir	6	15	36	46	51

na, not available.

In treatment naïve patients , resistance is more seen in lamivudine and it increases every year. While entecavir [(39)]and tenofovir is very less.In patients with resistance to lamivudine entecavir proved good results but resistance increased by years in those patients also[(40)].

Types of resistance	Preferred treatment	Alternative treatment
Lamivudine/ telbivudine	Add or switch to tenofovir	Add adefovir
		Stop lamivudine/ telbivudine, switch to truvada
Adefovir	Switch to or add entecavir	Add lamivudine/ telbivudine
		Stop adefovir, switch to truvada
Entecavir*	Switch to or add tenofovir	Stop entecavir, switch to truvada
Tenofovir*	Switch to or add entecavir	Stop tenofovir, switch to truvada

Truvada, combination pill with emtricitabine and tenofovir, not approved for HBV.
*Limited clinical data.

Rescue therapy for resistance

HBeAg SEROCONVERSION :

E antigen clearance and seroconversion is used for

suppression of HBV,

reduced infectivity

improved clinical prognosis.

E antigen seroconversion is the desirable effect of treatment .Other points in treatment are enzyme normal levels , immeasurable DNA and clearance of e antigen. When treatment is continued for long after e antigen clearance and conversion sustained virological response is good.They should be closely monitored for relapse with follow-up testing of HBV DNA and HBeAg for up to 2 years after discontinuation of NA monotherapy.

Treatment is considered to stop when immeasurable DNA level is documented on two separate occasions with six months apart . Importance of this period of consolidation therapy reduces risk of relapse after HBeAg seroconversion. They may lead to HBsAg seroclearance, which is the most desirable end point closest to a “cure.”

Newer-generation oral NAs provides a finite course of therapy for individuals with HBeAg-positive CHB .E antigen seroconversion with low DNA levels is the ideal goal in the management .

HBsAg QUANTIFICATION :

HBsAg is an important test that marks active infection with HBV and also predict the clinical outcome of the infection. Detection of low HBsAg and HBV DNA levels identify true inactive carriers who need

neither strict follow up nor antiviral treatment. Based on HBsAg quantification, a response-guided therapy in both HBeAg-positive and -negative patients treated with Peg-IFN has been developed. According to the data, therapy can be stopped at week 12 in primary non responders, who become candidate to alternative therapies, such as unlimited suppressive therapy with NA. Decline of serum HBsAg may also assist NA-treated patients, mainly the HBeAg-positive ones, however, according to slower kinetics than those related to Peg-IFN therapy. Because progressive decline of HBsAg heralds clearance of HBsAg in all instances, this may help increasing cost-effectiveness ratio of NA therapy.

MATERIALS AND METHODS

MATERIALS AND METHODS

It is a prospective study conducted between October 2010 and April 2012 where consecutive patients with the diagnosis of Chronic HBV infection undergoing medical treatment with antiviral Telbivudine from our hospital were included. During this period patients started on treatment for compensated CHB infection are included in this study.

A written consent was obtained from all the patients. Institute ethical committee has approved the study. All patients with compensated CHB patients were included in the study. All patients underwent a detailed clinical evaluation at entry, with the following data:

Age, gender, duration of illness, details of treatment prior to registration. Baseline demographic details such as age, gender, literacy, socio economic status, alcohol intake, smoking, religion and occupation were collected. Patient had baseline investigations such as Complete blood count, Liver function test, Prothrombin time, International normalized ratio, renal function test, HBsAg, Anti-HCV, ultra sonogram and endoscopy.

A detailed history about the method of transmission, identification of chronic HBV infection was asked from history .A detailed clinical examination was also performed in all patients which includes pallor,

jaundice, and on per abdomen examination abdominal veins, liver and spleen enlargement and ascites to exclude decompenation.

Upper gastrointestinal endoscopy and grading of the varices was done in all patients. Grading of varices was done by using Sarin's classification.

Exclusion Criteria:

1. Patients with decompensated chronic liver disease
2. Patients who did not fit into the guidelines for treatment of chronic infecton were not included.

Blood tests :

Haematological and biochemical workup included measurement of haemoglobin , total leukocyte count , platelet count, prothrombin time and liver function tests including bilirubin and liver enzymes. Special investigations in relation to chronic HBV infection like HBeAg, HBV DNA quantification, HBsAg quantification , at baseline and at regular intervals at 4,12, 24 and 48 weeks were done for follow up.

Statistical analysis :

Quantitative data were expressed in Mean and Standard deviation. Qualitative data were given in frequencies with their percentage. Differences in clinical response at the end of 48 wks between e antigen positive and negative patients were analyzed by using Pearson Chi square test/ student independent test as appropriate. P value less than 0.05 was taken as statistically significant.

OBSERVATION AND RESULTS

OBSERVATION AND RESULTS

100 patients of chronic HBV infection (76 men, 24 women) were enrolled in the study. Mean age of males who are HBeAg positive are 42.3 yrs and who are e antigen negative are 44.3 years. Mean age of females who are e antigen positive are 37.4 yrs and 41.2 yrs. Mean HBV DNA log 10 IU /ml was 6.25 in e positive and 4.45 in e negative patients . Mean HBsAg log 10 IU/ml was 3.91 in e positive and 3.39 in e negative patients . Mean ALT levels were 75 in e positive and 68 in e negative patients.

Fig 1. Gender distribution :

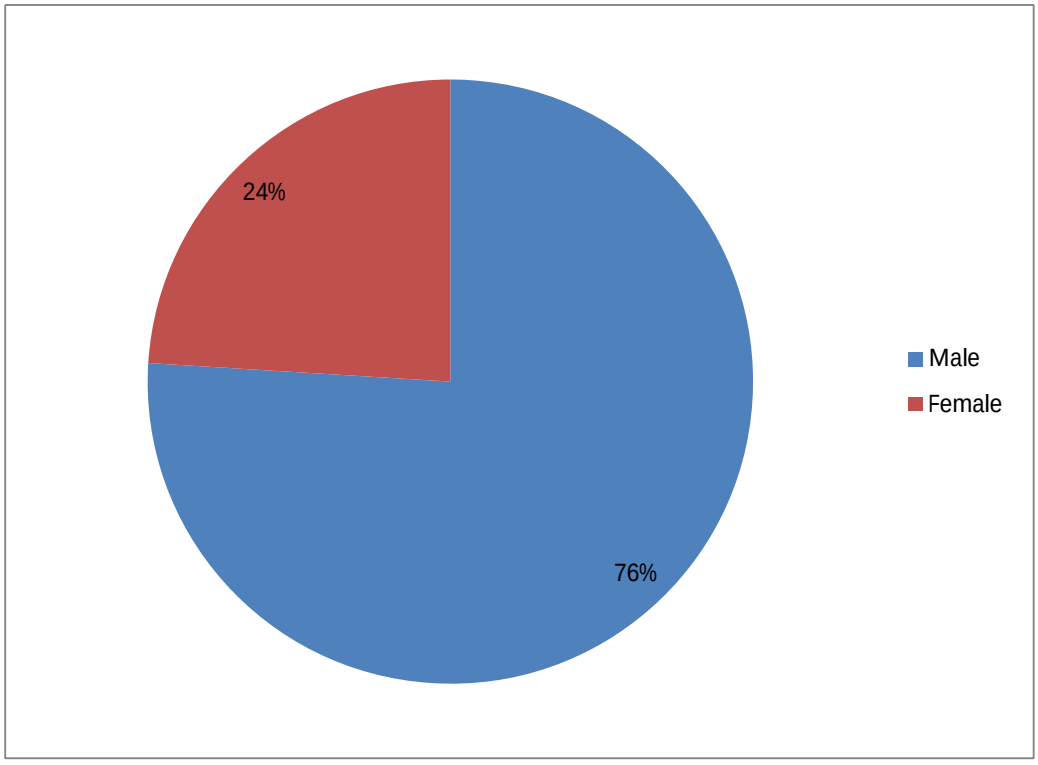


Table 1 : Demographic characteristics of the study population

		e Ag positive	e Ag negative
No. of Pts		48	52
Sex	Male	37 (77%)	39 (75%)
	Female	11 (23%)	13 (25%)
Mean age	Male	42.3 yrs	44.3 yrs
	Female	37.4 yrs	41.2 yrs
Mean HBV DNA log 10 IU/ml		6.25	4.45
Mean HBsAg log 10 IU/ml		3.91	3.39
Mean ALT IU/ml		75	68

Fig 2. SOURCE OF INFECTION:

Unknown causes form in majority (36%) followed by blood transfusion (21%) . Injection use and vertical transmission (16% each) accounts for further transmission .

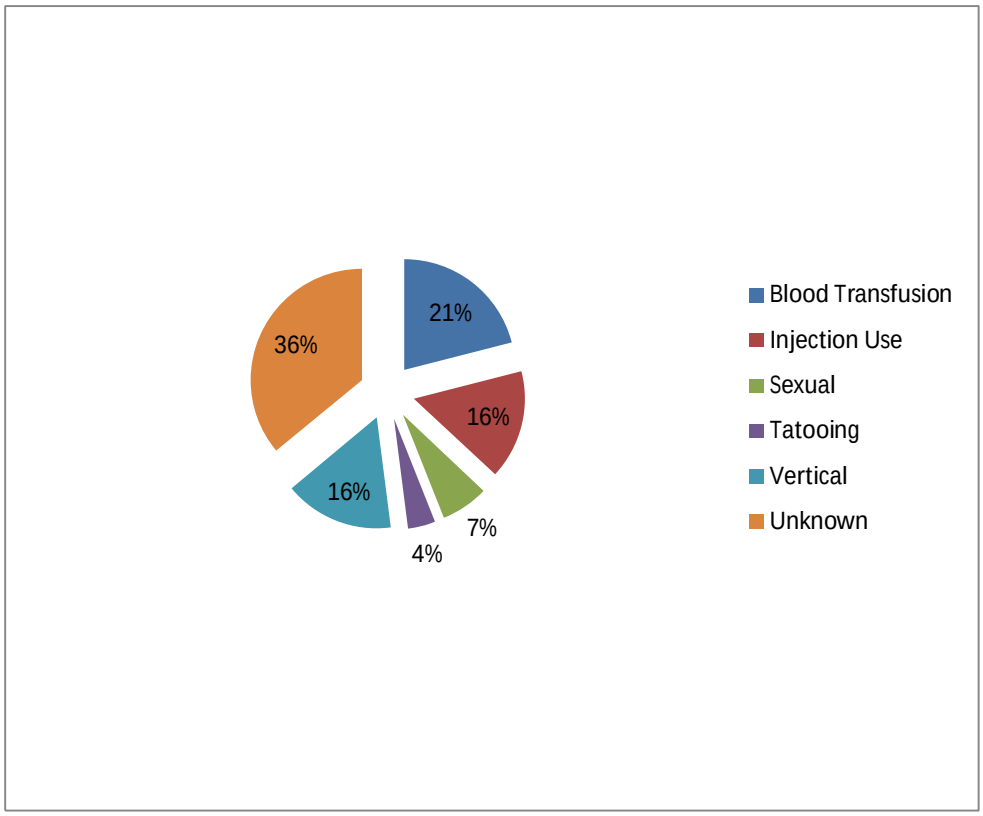


Fig. 3 : Detection of HBsAg

E antigen positivity was seen in 48 patients and e antigen negative status seen in 52 patients.

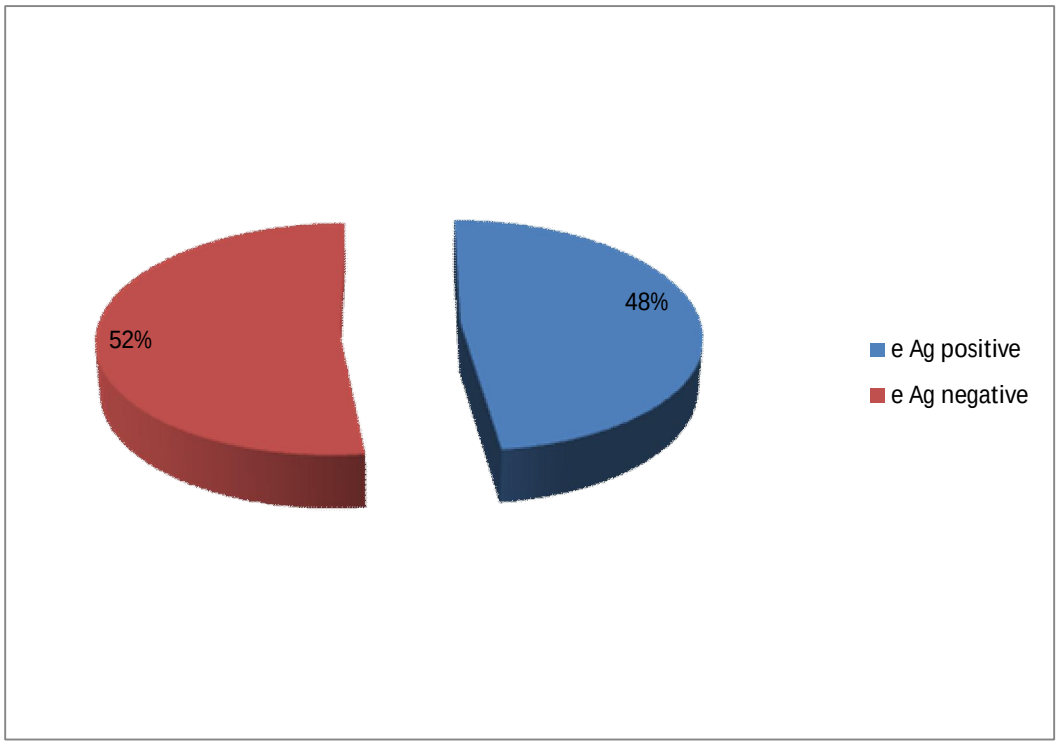


Fig 4 : USG Abdomen :

Patients had normal study in 89% and fatty liver in 11% of patients by ultrasound

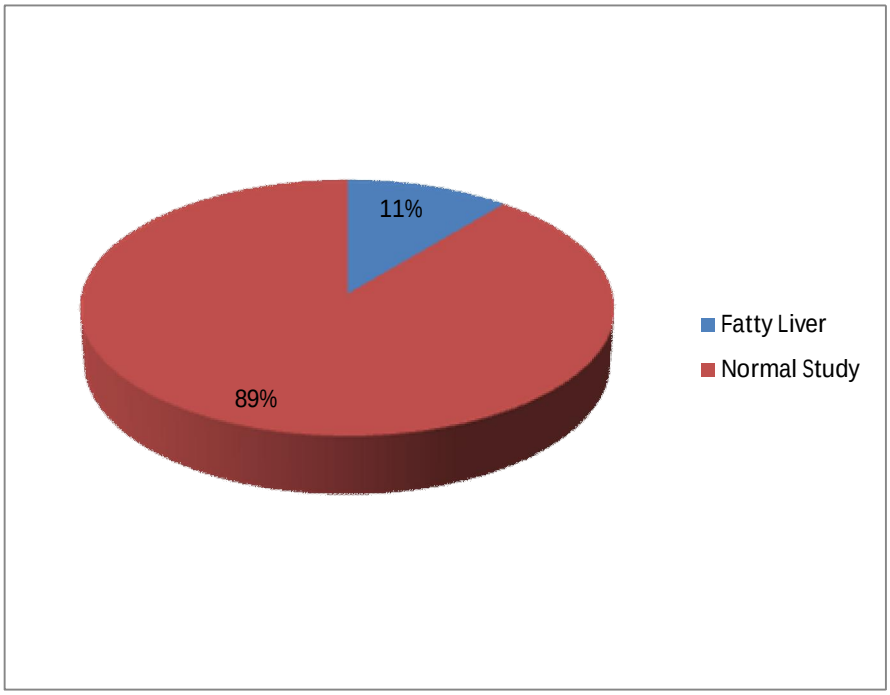


Fig . 5 : Endoscopic findings :

92 % patients had normal study in endoscopy. 6 % had portal hypertensive gastropathy and 2 % had oesophageal varices

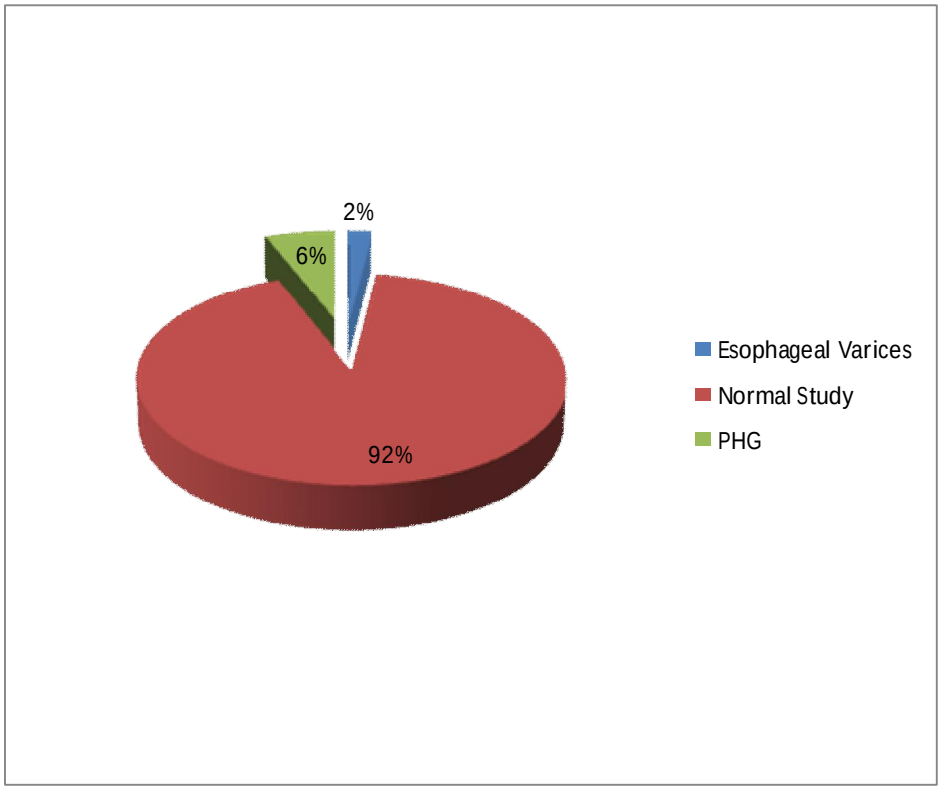
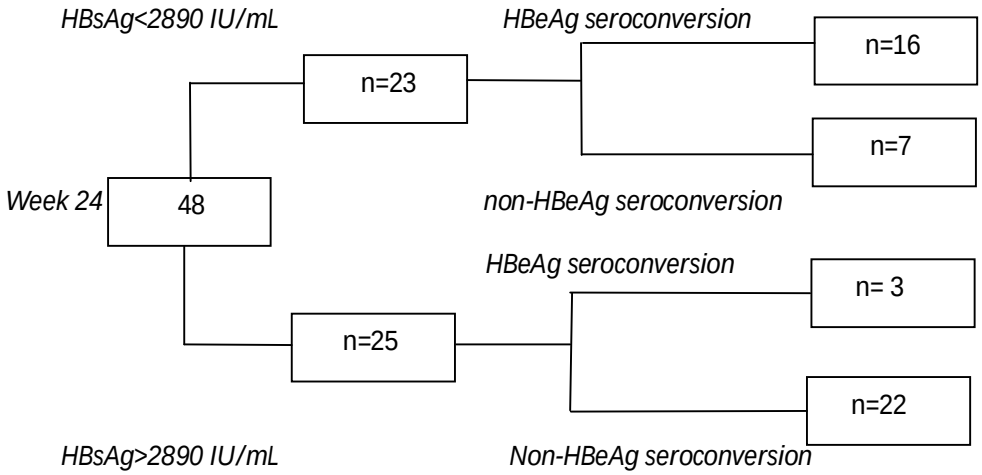


TABLE 1

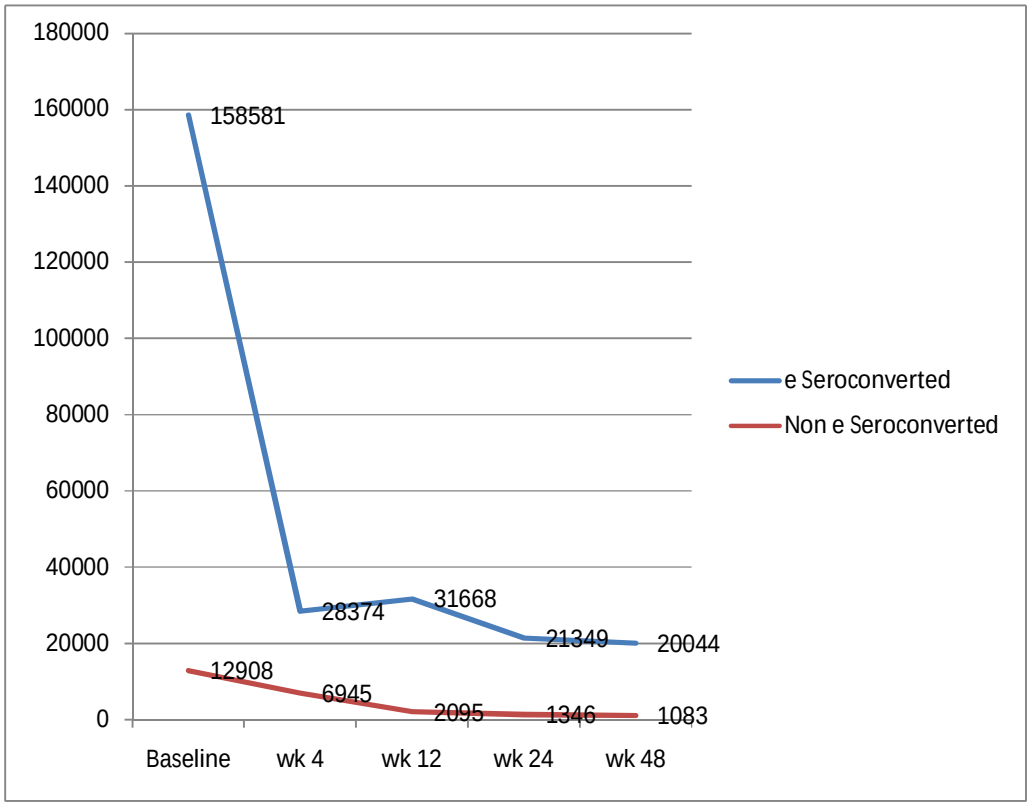
Prediction of HBeAg seroconversion in relation with HBsAg quantification



HBsAg at 24 wk	Seroconverted	Non seroconversion	PPV	NPV	P VALUE
<2890	16	7	0.70	0.88	0.05
>2890	3	22			

HBsAg value at 24 weeks had a significant value at 2890 IU/ ml .Hence patients were randomised to levels below or above 2890 and according to seroconverted or non seroconverted. Among 23 patients with HBsAg levels < 2890 IU/mL at week 24, 68 % had HBeAg seroconversion at the end of follow up. Among 25 patients with HBsAg levels > 2890 IU/ mL at week 24, 13 % had HBeAg seroconversion at the end of follow up (P = 0.05). Positive predictive value was 0.70 and Negative predictive value was 0.88 .

FIG 6 : Mean HBsAg decline in HBsAg patients



Median HBsAg concentrations over time in patients are shown in Figure 7. Among patients who achieved HBeAg seroconversion, HBsAg level decreased consistently during treatment and remained at low levels .Conversely, HBsAg in patients in the non-HBeAg seroconversion group showed a slight decrease in HBsAg levels during therapy.

Other factors in predicting e seroconversion:

		COLUMN		Total	
		1	2		P value
Age >40		14	10	24	0.149
<40		9	15	24	
Vertical		2	16	18	0.132
Other		9	21	30	
ALT >60		16	14	30	0.332
<60		7	11	18	

Various parameters were assessed for e antigen sero conversion. Age, vertical transmission and ALT levels which were proven predictors for e antigen seroconversion had an insignificant p value. P values for age, vertical transmission and ALT levels are 0.149 , 0.132 and 0.332 respectively

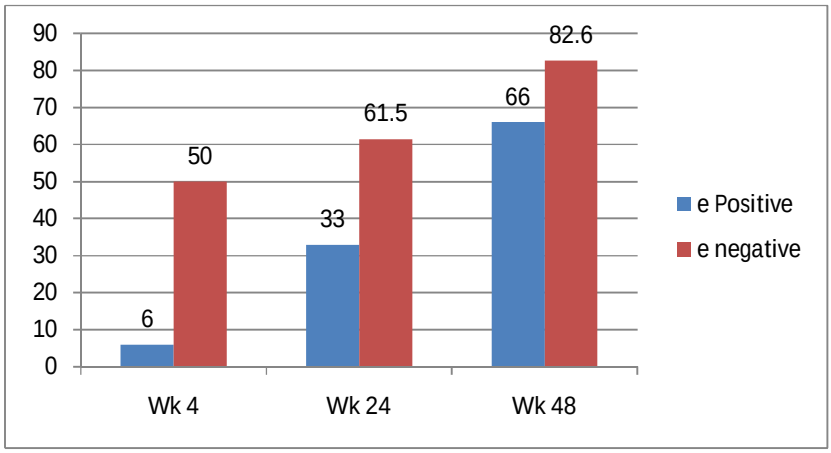
Table 2: Response to Telbivudine in e positive patients:

	Baseline	Wk 4	Wk 12	Wk 24	Wk 48
Mean HBV DNA log 10 iu/ml	6.25	4.15		2.48	1.86
Mean HBV DNA log 10 iu/ml redn		-2.09		-3.77	-4.39
PCR negativity < 300 copies/ml (n / %)		3 (6)		16 (33)	32 (66)
Mean HBsAg log 10 iu/ml	3.91	3.74	3.68	3.48	3.45
Mean HBsAg log 10 iu/ml redn		-0.17	-0.23	-0.43	-0.46
Mean ALT levels	75				44
ALT normalization (n / %)					28 (58)
e Seroconversion (n / %)					19 (39.5)

Table 3 : response to Telbivudine in e negative patients

	Baseline	**Wk 4**	**Wk 12**	**Wk 24**	**Wk 48**
Mean HBV DNA log 10 IU/ml	4.45	2.55		2.01	1.54
Mean HBV DNA log 10 IU/ml redn		-1.9		-2.44	-2.9
PCR negativity < 300 copies/ml (n / %)		26 (50)		32 (61.5)	43 (82.6)
Mean HBsAg log 10 IU/ml	3.39	3.44	3.46	3.31	3.32
Mean HBsAg log 10 IU/ml redn		0.05	0.07	-0.08	-0.07
Mean ALT levels	68				37.6
ALT normalization (n / %)					38 (73)

HBV DNA SUPPRESSION PCR negativity (< 300 cp / ml)



Mean ALT Normalization (< 40 iu/ml) at 48 weeks

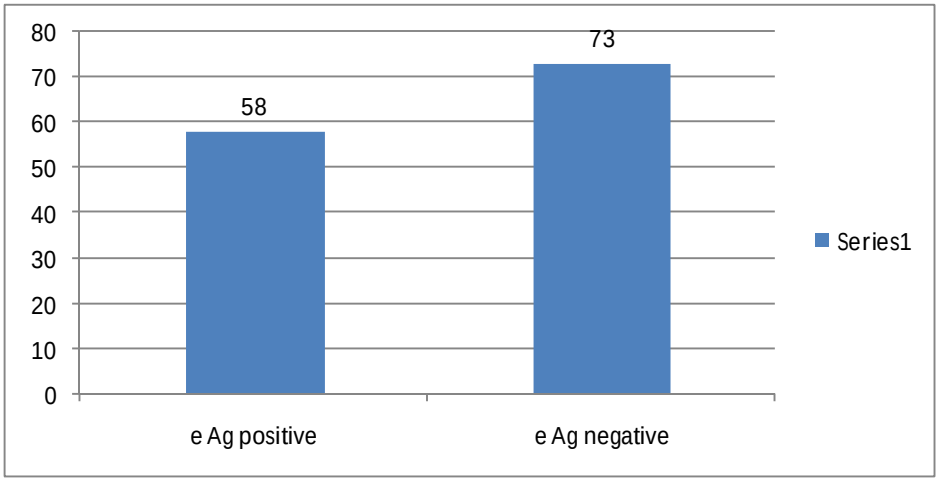
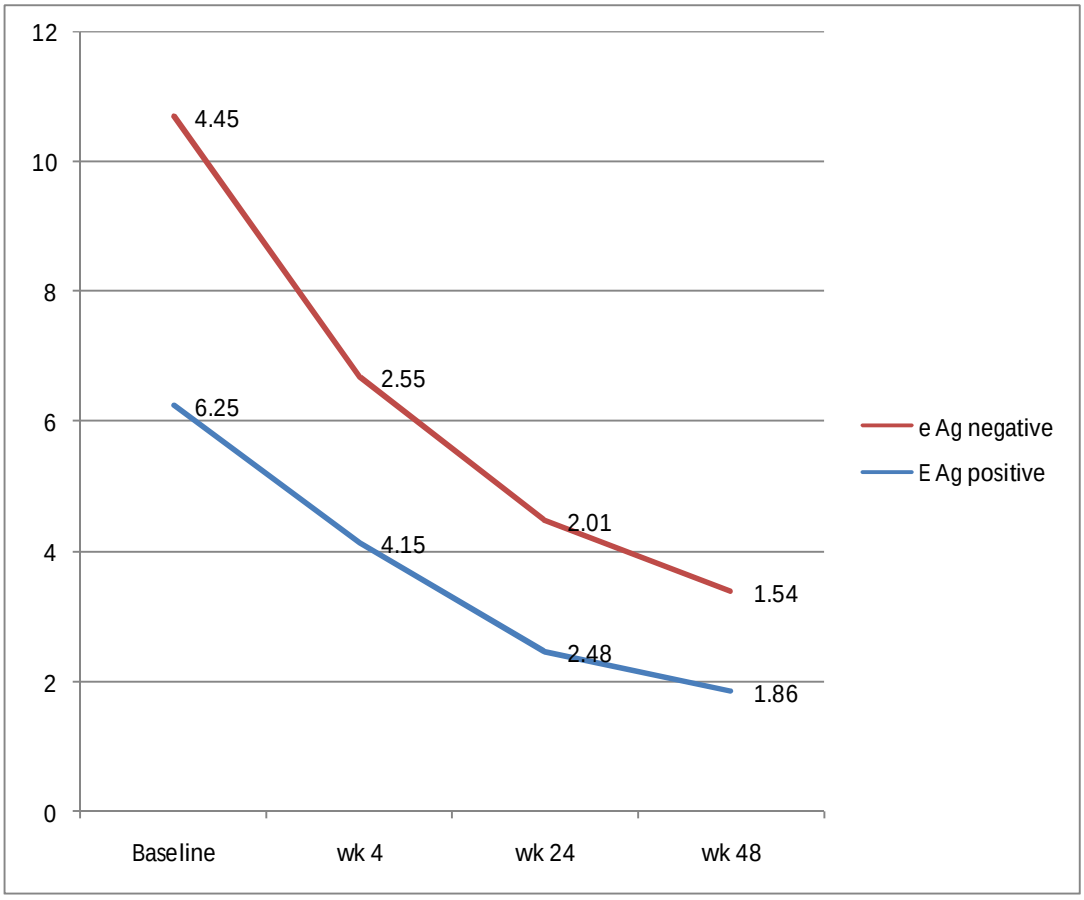


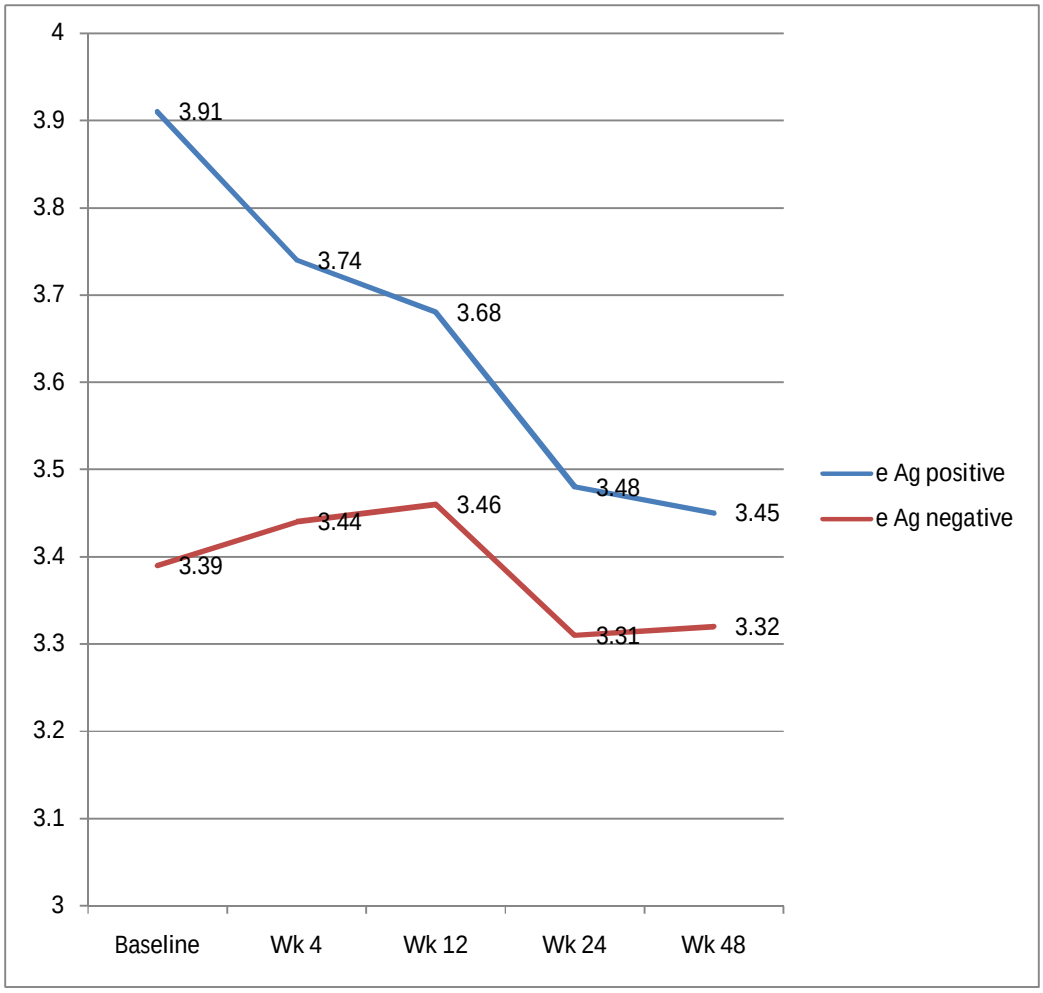
Table 4: response at 48 weeks between e positive and negative

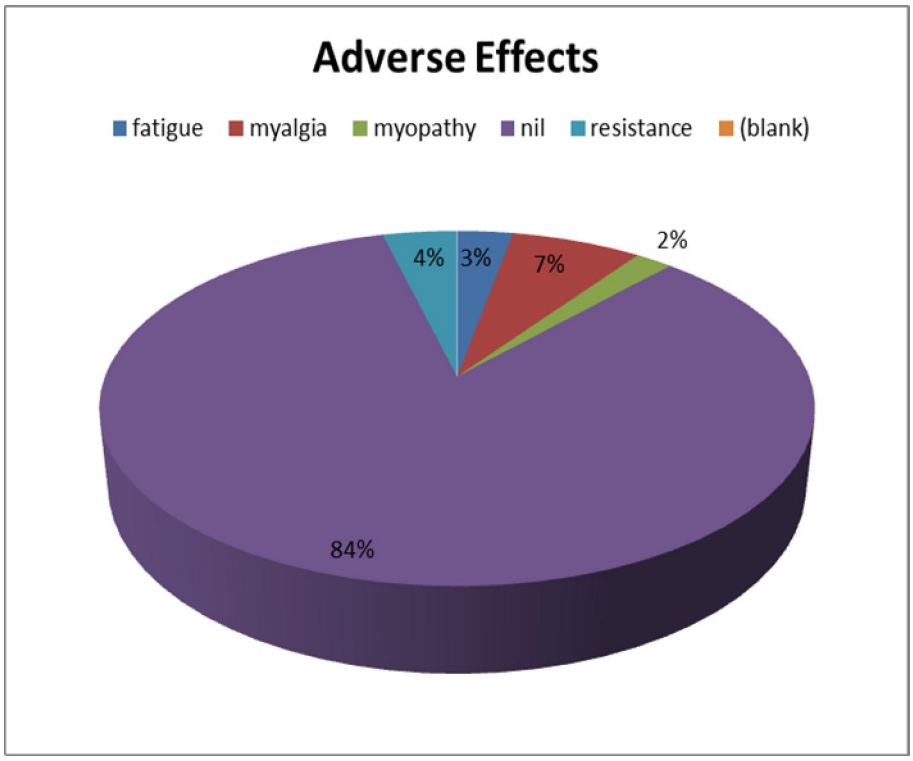
	T	df	Sig. (2-ailed)	Mean Difference	95% Confidence Interval of the Difference	
					Lower	Upper
hbv_48	1.144	98	.256	.292	-.2147	.7989
	1.148	97.967	.254	.292	-.2127	.7968
cp_48	1.230	98	.222	.3140	-.19260	.82058
	1.235	97.932	.220	.3140	-.19043	.81841
hbvred_48	-4.611	98	.000	-1.5268	-2.18382	-.86974
	-4.609	97.137	.000	-1.5268	-2.18425	-.86931
hbsag_48	.823	98	.412	.129	-.1813	.4385
	.819	93.715	.415	.129	-.1831	.4403
hbsred_48	-2.429	98	.017	-.3913	-.71090	-.07163
	-2.398	84.732	.019	-.3913	-.71568	-.06685
alt_48	1.601	98	.113	6.39	-1.533	14.312
	1.592	93.532	.115	6.39	-1.582	14.361

MEAN HBV DNA log 10 IU / ml decline



MEAN HBsAg log 10 IU / ml decline





More patients did not record any adverse effect but minority of patients experienced

Myalgia

Myopathy

Fatigue

resistance

DISCUSSION

DISCUSSION

Chronic HBV infection is major burden to the community with significant changes from simple chronic infection progressing to cirrhosis and liver failure. However this complication primarily occurs in patients who remained e antigen positive for a longer time. Hence treatment for chronic HBV infection occurs is an important option to reduce HBV DNA level and e antigen seroconversion. Few data have been published about predictors of HBeAg seroconversion. In hepatitis B e antigen (HBeAg) positive patients, the strongest predictor of HBeAg seroconversion is the pretreatment alanine aminotransferase (ALT) level. Other factors include high histologic activity index, low HBV DNA level, HBV genotypes A and B . Few studies have been done to study the effect of HBsAg quantification in relation to e antigen seroconversion.

Our study, based on information achieved from 100 patients from chronic HBV infection in a tertiary centre in south India we tried to predict the relation between HBsAg quantification and HBeAg seroconversion .

Clinical profile of chronic HBV patients was done in relation to mode of infection, identification of infection, radiological and endoscopic findings of patients.

In our study, unknown factors were the cause for maximum mode of transfusion followed by blood transfusion. This study was contrary in terms being intravenous drug use being more common in Ko YC, Chung DC et al [41]

Hui Ma et al [42] demonstrated serum HBsAg and HBeAg are strong predictors for sustained HBeAg seroconversion with pegylated interferon. In our study we correlated HBsAG quantification with e antigen seroconversion with telbivudine.

Hui ma et al had demonstrated a cut off value of 2890 IU / ml of HBsAg at week 24 .In our study a statistical significant value was identified as 2890. With cut off value of 2890, e seroconversion was found to have positive predictive value of of 0.70 , negative predictive value of 0.88 with p value of 0.05 . In contrary Hui ma et al demonstrated positive predictive value at 0.40 and negative predictive value of 1 with p value of 0.010 .

In our study HBsAg level decreased consistently during treatment in sero converted group when compared to non seroconverted group.This was consistent with Hui ma et al .

Clinical and virological efficacy endpoints were evaluated separately in the HBeAg-positive and HBeAg-negative patient populations in Globe study. The primary endpoint at week 52 is suppression of HBV DNA to <5 log10 copies/mL in addition with either loss of serum HBeAg or ALT normalized. Secondary endpoints include histological response, ALT normalization.

Response parameter	HBeAg-positive (n = 921)		HBeAg-negative (n = 446)	
	Telbivudine 600 mg (n = 458)	Lamivudine 100 mg (n = 463)	Telbivudine 600 mg (n = 222)	Lamivudine 100 mg (n = 224)
Mean HBV DNA reduction from baseline (log_{10} copies/mL) ± SEM[1,2]	-6.45 (0.11)*	-5.54 (0.11)	-5.23 (0.13)*	-4.40 (0.13)
% Patients HBV DNA negative by PCR	60%*	40%	88%*	71%
ALT normalisation[3]	77%	75%	74%	79%
HBeAg seroconversion[4]	23%	22%	NA	NA
HBeAg loss[4]	26%	23%	NA	NA

Response at 48 weeks

Response parameter	E positive	E negative
Mean HBV DNA log 10 iu/ml redn	- 4.39	-2.9
PCR negativity < 300 copies/ml (/ %)	66%	82.6
ALT normalization (/ %)	58	73
e Seroconversion (/ %)	52	N.A

Our study found that HBsAg reduction at 48 weeks had significant value in both e antigen positive and negative cases .Other values like ALT, HBsAg , HBsAg reduction , HBV DNA copies and HBV DNA reduction was not significant in both groups.

SUMMARY

SUMMARY

In the present study,

1. The most common mode of transmission was unidentified (36%) followed by blood transfusion and vertical modes. (21% and 16 % respectively)

2. HBsAg quantification is an important predictor of e antigen seroconversion with a p value of significance. (p – 0.05)

3. Other factors expected to have importance like age, vertical and ALT levels did not have any statistical significance. (0.14 , 0.13 , 0.332 respectively)

4. Various parameters to assess clinical response at 48 weeks between e antigen positive and negative were assessed. HBsAg reduction at 48 weeks seemed to have statistical significance. (p- 0.019)

CONCLUSION

CONCLUSION

In conclusion, results of our study indicate that HBsAg quantification is a good predictor of HBeAg seroconversion .Values for the HBsAg quantification from this study need to be validated by randomised prospective studies . Other parameters like age , vertical transmission and baseline ALT levels were not significant.

Applying HBsAg quantification though may not be cost effective it appears to be a good predictor for e antigen seroconversion but further randomised studies are needed to evaluate the accurate prediction of e antigen seroconversion in our population .

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42. Quantitative serum HBsAg and HBeAg are strong predictors of sustained HBeAg seroconversion to pegylated interferon alfa-2b in HBeAg-positive patients Hui Ma,1 Rui-feng Yang1 and Lai Wei Peking University People's Hospital,Peking University Hepatology Institute, Beijing, China

ABBREVIATIONS

ABBREVIATIONS

HBV	-	Hepatitis B virus
HBsAg	-	Hepatitis B surface antigen
HBeAg	-	Hepatitis e antigen
NAT	-	Nucleic acid testing
IDU	-	Intravenous drug use
HBIG	-	Hepatitis B Immunoglobulin
NA	-	Nucleoside analogue
RCT	-	Randomised control trials
IFN	-	Interferon
Rt	-	Reverse Transcriptase
HCC	-	Hepatocellular carcinoma
C antigen	-	Hepatitis B virus Core antigen
Anti HCV	-	Antibody to hepatitis C virus
DNA	-	Deoxyribonucleic acid

PROFORMA

PROFORMA

Name: Age: Sex:

MGE No:

D.O.R:

Resident of: Chennai / other city (specify)

Type of house: Pucca/hut/semiPer capita income:

Literacy status: studied up to: no education/I-V/VI-VIII/IX-XII/college/professional/other courses

Occupation (as such):No. of children:

No. of adult family members:

Religion: Hindu /Muslim /Christian/others (specify):

Smoker: - Present/Past/Never Alcohol:- Present/Past/Never

Identity of infection :

Incidental

screening

Source of infection :

vertical

blood transfusion

iv drug abuse

sexual

unknown

O/E

Pallor: Jaundice: Clubbing: Cyanosis:

Fever: Pedal edema: Asterixis:

Liver cell failure features :

Parotidomegaly:

Gynaecomastia:

Spider angioma:

Dupuytran’s contracture:

Palmar erythema:

Testicular atrophy:

Per abdomenVeins

Liver span:Consistency/edges/surfaceSpleen size

Investigations

Total Count:

Haemoglobin:

Platelets:

PT&INR:

Total Bilirubin:

Con.j Bilirubin:

Albumin:

Globulin:

AST

ALT

Alk Phos:

HBsAg:

Anti HCV:

Sugars:

Urea:

Creatinine:

Blood test	baseline	4 weeks	12 weeks	24	48
HBV DNA (Q)					
HBsAg (q)					
HBeAg					
ALT					

USG abdomen:

Endoscopy :

Complications

Fatigue
myalgia
myopathy
resistance

MASTER CHART

CODING FOR MASTER CHART

Sex - 1 – male , 2- female

E antigen - 1-positive , 2- negative

Usg abdomen - 1- normal study , 2 – fatty liver

Endoscopy - 1 – normal , 2 – PHG , 3- esophageal varices

							Baseline										24th Week								48th week												
Sl.No	Name	Hosp.No	Age	Sex	Mode of transmission	HBeAg	ALT	AST	HBV DNA IU/ml	HBV DNA log10 IU/ml	HBV DNA copies/ml	HBV DNA log10 cp/ml	HBsAg	HBsAg log10	HBV	HBV DNA log10	HBV DNA cp/ml	HBV DNA log10 cp/ml	HBV DNA log redn	HBsAg	HBsAg log 10	HBsAg log redn	HBV	HBV log 10	HBV DNA cp/ml	HBV DNA log 10 cp/ml	HBV DNA log redn	HBsAG	HBsAG log 10	HBsAg log redn	ALT	usg abdomen	endoscopy	HBeAg Seroconversion after 48	adverse effects	HBsAg	diagnosis
1	VIJAYALAKSHMI	1684/10		2	unknown	2	38	24	215000	5.33	1247000	6.1	6450	3.81	3000	3.48	17400	4.24	-1.86	5385	3.73	-0.08	2000	3.3	11600	4.06	-2.03	3172	3.5	-0.31	16	1	normal study	negative	nil	positive	incidental
2	JAYADEEPAK	5715/09	21	1	vertical	1	68	42	170000000	8.23	986000000	8.99	4500	3.65	847	2.93	4912.6	3.69	-5.3	5620	3.75	0.1	20	1.3	116	2.06	-6.93	4222	3.63	-0.03	36	1	normal study	positive	nil	positive	screening
3	VEERARAGHAVAN	2117/09	58	1	tatooing	2	64	32	22000	4.34	127600	5.11	12000	4.08	20	1.3	116	2.06	-3.04	19545	4.29	0.21	20	1.3	116	2.06	-3.04	8721	3.94	-0.14	40	1	normal study	negative	nil	positive	incidental
4	GOMATHI	4200/08	36	2	sexual	2	52	32	19446	4.29	112786.8	5.05	3414	3.53	234	2.37	1357.2	3.13	-1.92	5432	3.73	0.2	20	1.3	116	2.06	-2.99	3421	3.53	0	32	1	normal study	negative	nil	positive	incidental
5	SIVAPRAKASAM	1250/10	69	1	unknown	2	72	23	22431	4.35	130099.8	5.11	3437	3.54	20	1.3	116	2.06	-3.05	2103	3.32	-0.21	20	1.3	116	2.06	-3.05	2312	3.36	-0.17	24	2	PHG	negative	nil	positive	incidental
6	PARASURAM	1392/04	44	1	injection use	1	72	45	100929	5	585388.2	5.77	13652	4.14	20	1.3	116	2.06	-3.7	2400	3.38	-0.75	20	1.3	116	2.06	-3.7	1321	3.12	-1.01	32	1	normal study	negative	nil	positive	incidental
7	PREMKUMAR	4630/10	47	1	unknown	1	63	92	23990660	7.38	139145828	8.14	4737	3.68	242	2.38	1403.6	3.15	-5	2000	3.3	-0.37	20	1.3	116	2.06	-6.08	1674	3.22	-0.45	54	1	normal study	negative	nil	positive	incidental
8	RAMAN	4352/10	50	1	unknown	2	82	19	2400	3.38	13920	4.14	1604	3.21	20	1.3	116	2.06	-2.08	1421	3.15	-0.05	6	0.78	34.8	1.54	-2.6	1108	3.04	-0.16	62	2	PHG	negative	nil	positive	incidental
9	RAMAMOORTHY	4701/10	51	1	blood transfusion	2	56	32	4326	3.64	25090.8	4.4	476	2.68	20	1.3	116	2.06	-4.51	1200	3.08	0.4	32000	4.51	185600	5.27	0.87	3211	3.51	0.83	68	1	normal study	negative	myalgia	positive	incidental
10	SAKTHIVEL	1687/10	36	1	blood transfusion	1	58	54	25290	4.4	146682	5.17	4272	3.63	20	1.3	116	2.06	-3.1	12342	4.09	0.46	6	0.78	34.8	1.54	-3.62	12342	4.09	0.46	72	1	normal study	positive	nil	positive	incidental
11	LOGANATHAN	5432/10	30	1	injection use	2	125	37	3781	3.58	21929.8	4.34	15138	4.18	76001	4.88	440805.8	5.64	1.3	951	2.98	-1.2	6	0.78	34.8	1.54	-2.8	8030	3.9	-0.28	32	1	normal study	negative	nil	positive	incidental
12	VASUDEVAN	3851/10	29	1	vertical	2	28	36	11755	4.07	68179	4.83	586	2.77	20	1.3	116	2.06	-2.77	149	2.17	-0.59	6	0.78	34.8	1.54	-3.29	192.7	2.28	-0.48	26	1	normal study	negative	nil	positive	screening
13	ARPUTHAM	5423/10	36	2	unknown	1	36	26	646100	5.81	3747380	6.57	48.61	1.69	20	1.3	116	2.06	-4.51	48.41	1.68	0	6	0.78	34.8	1.54	-5.03	66.96	1.83	0.14	16	1	normal study	negative	nil	positive	incidental
14	MOORTHI.V	4909/07	36	1	unknown	2	54	32	34707080	7.54	201301064	8.3	14973	4.18	24300	4.39	140940	5.15	-3.15	6450	3.81	-0.37	20000	4.3	62	5.06	-3.24	6000	3.78	-0.4	54	1	normal study	negative	nil	positive	incidental
15	SHAHIR	154/10	43	1	unknown	2	59	19	3042	3.48	17643.6	4.25	347	2.54	20	1.3	116	2.06	-2.18	152	2.18	-0.36	6	0.78	34.8	1.54	-2.71	254	2.4	-0.14	26	1	normal study	negative	nil	positive	incidental
16	VARGHEESE	0259/10	50	1	unknown	1	98	112	14999204	7.18	86995383.2	7.94	10135	4.01	6800	3.83	39440	4.6	-3.34	2342	3.37	-0.64	3132	3.5	18162.8	4.26	-3.68	3770	3.58	-0.43	82	2	normal study	positive	resistance	positive	incidental
17	GAJAPATHY RAJA	3540/09	32	1	blood transfusion	2	68	42	6400	3.81	37120	4.57	896	2.95	20	1.3	116	2.06	-2.51	490	2.69	-0.26	20	1.3	116	2.06	-2.51	450	2.65	-0.3	40	1	normal study	negative	myalgia	positive	incidental
18	VIMALANCEMARY	5231/10	45	2	blood transfusion	2	40	43	2742079	6.44	15904058.2	7.2	1956	3.29	20	1.3	116	2.06	-5.14	2462	3.39	0.1	20	1.3	116	2.06	-5.14	1432	3.16	-0.14	20	1	esophageal varices	negative	nil	positive	incidental
19	GANGADHARAN	2062/08	55	1	injection use	2	54	32	5000	3.7	29000	4.46	0.04	-1.4	20	1.3	116	2.06	-2.4	42	1.62	3.02	20	1.3	116	2.06	-2.4	72	1.86	3.26	28	1	normal study	negative	nil	positive	incidental
20	JAYARAJ	2342/10	62	1	unknown	2	84	26	23346	4.37	135406.8	5.13	23635	4.37	20	1.3	116	2.06	-3.07	24741	4.39	0.02	6	0.78	34.8	1.54	-3.59	26738	4.43	0.05	62	1	normal study	negative	nil	positive	incidental
21	JAYASEELAN	3567/11	38	1	blood transfusion	2	56	22	3456	3.54	20044.8	4.3	4210	3.62	20	1.3	116	2.06	-2.24	644.3	2.81	-0.82	6	0.78	34.8	1.54	-2.76	2221.4	3.35	-0.28	24	1	normal study	negative	nil	positive	incidental
22	CHAKRAPPAN	3623/11	25	1	tatooing	1	56	48	20500	4.31	118900	5.08	200	2.3	20	1.3	116	2.06	-3.01	136.68	2.14	-0.17	6	0.78	34.8	1.54	-3.53	188.9	2.28	-0.02	26	1	normal study	negative	nil	positive	incidental
23	MURUGAESAN	0052/10	33	1	injection use	1	45	32	132115736	8.12	76671268.8	8.88	58515	4.77	5150	3.71	29870	4.48	-4.41	41011	4.61	-0.15	2690	3.43	15602	4.19	-4.69	25117	4.4	-0.37	62	1	normal study	positive	nil	positive	incidental
24	SABAPATHY	4922/10	66	1	unknown	1	76	32	29300	4.47	169940	5.23	4117	3.61	20	1.3	116	2.06	-3.01	4500	3.65	-0.05	20	1.3	116	2.06	-3.17	5200	3.72	0.1	32	1	normal study	positive	nil	positive	incidental
25	POORNIMA	3914/10	55	2	sexual	2	46	34	2440	3.39	14152	4.15	503	2.7	20	1.3	116	2.06	-2.09	243	2.39	-0.32	20	1.3	116	2.06	-2.09	246	2.39	-0.31	16	1	normal study	negative	nil	positive	incidental
26	DEEPA	2114/10	21	2	vertical	1	44	37	170000000	8.23	986000000	8.99	125000	5.1	1747	3.24	10132.6	4.01	-4.99	92034	4.96	-0.13	1230	3.09	7134	3.85	-5.14	64799	4.81	-0.29	47	1	normal study	positive	nil	positive	screening
27	BHARATHI	3211/10	37	2	sexual	2	45	22	3500	3.54	20300	4.31	3938	3.6	85	1.93	493	2.69	-1.61	2746	3.44	-0.16	11.5	1.06	66.7	1.82	-2.48	2317	3.36	-0.23	22	1	normal study	negative	nil	positive	incidental
28	BABY	3133/10	49	2	sexual	1	36	26	24032586	7.38	139388998.8	8.14	19280	4.29	20	1.3	116	2.06	-6.08	46.86	1.67	-2.61	6	0.78	34.8	1.54	-6.6	11.47	1.06	-3.23	20	1	normal study	negative	nil	negative	incidental
29	ANUSYA	4122/10	38	2	unknown	2	82	21	2693	3.43	15619.4	4.19	7639	3.88	20	1.3	116	2.06	-2.13	9366.9	3.97	0.09	6	0.78	34.8	1.54	-2.65	6293	3.8	-0.08	18	1	normal study	negative	myalgia	positive	incidental
30	SUNDARI	5433/10	21	2	vertical	1	28	41	30036784	7.48	174213347.2	5.24	8832	3.95	1802	3.26	10451.6	4.02	-4.22	3210	3.51	-0.44	7.35	0.87	42.63	1.63	-6.61	2876	3.46	-0.49	22	1	normal study	negative	nil	positive	screening
31	PERUMAL	0177/08	34	1	injection use	2	92	87	3000	3.48	17400	4.24	2710	3.43	20	1.3	116	2.06	-2.18	2221	3.35	-0.09	6	0.78	34.8	1.54	-2.7	1841.8	3.27	-0.17	68	1	normal study	negative	nil	positive	incidental
32	VIGNESH	6067/10	20	1	vertical	2	65	32	375616	5.57	2178572.8	6.34	21000	4.32	20	1.3	116	2.06	-4.27	31818	4.5	0.18	6	0.78	34.8	1.54	-4.8	23213	4.37	0.04	62	1	normal study	negative	nil	positive	screening
33	SUDHAKARAN	0494/10	45	1	unknown	1	72	23	30000	4.48	174000	5.24	503	2.7	20	1.3	116	2.06	-3.18	202	2.31	-0.4	6	0.78	34.8	1.54	-3.7	186	2.27	-0.43	32	1	normal study	negative	nil	positive	incidental
34	RAMARAJAN	3700/08	60	1	injection use	2	75	43	5400	3.73	31320	4.5	2298	3.36	124	2.09	719.2	2.86	-1.64	2124	3.33	-0.03	6	0.78	34.8	1.54	-2.95	1876	3.27	-0.09	32	1	normal study	negative	nil	positive	incidental
35	MASILAMANI	5911/10	62	1	unknown	2	65	43	230000	5.36	1334000	6.13	876	2.94	422	2.63	2447.6	3.39	-2.74	69093	4.84	1.9	36890	4.57	213962	5.33	-0.79	568	2.75	-0.19	64	1	normal study	negative	nil	positive	incidental
36	SUBRAMANI	5614/10	63	1	blood transfusion	2	46	22	150606	5.18	873514.8	5.94	5700	3.76	20	1.3	116	2.06	-3.88	10324	4.01	0.26	20	1.3	116	2.06	-3.88	8760	3.94	0.19	28	1	normal study	negative	nil	positive	incidental
37	GANESHAN	1899/10	35	1	blood transfusion	1	89	20	25000	4.4	145000	5.16	810	2.91	190	2.28	1102	3.04	-2.12	15621	4.19	1.29	20	1.3	116	2.06	-3.1	16000	4.2	1.3	18	1	normal study	positive	nil	positive	incidental
38	MURALI	1468/06	37	1	injection use	2	49	21	4900	3.69	28420	4.45	155	2.19	20	1.3	116	2.06	-2.39	101	2	-0.19	20	1.3	116	2.06	-2.39	121	2.08	-0.11	22	2	normal study	negative	nil	positive	incidental
39	RANJITH KUMAR	1232/10	18	1	vertical	2	68	34	154027	5.19	893356.6	5.95	4376.8	3.64	20	1.3	116	2.06	-3.89	7428	3.87	0.23	6	0.78	34.8	1.54	-4.41	5570	3.75	0.1	32	1	normal study	negative	nil	positive	screening
40	MOORTHI.K	1432/10	35	1	blood transfusion	2	43	44	2320	3.37	13456	4.13	3678	3.57	20	1.3	116	2.06	-2.06	1349	3.13	-0.44	6	0.78	34.8	1.54	-0.39	1496	3.17	-0.39	32	1	normal study	negative	fatigue	positive	incidental
41	RAMASAMY	6027/10	56	1	unknown	1	82	22	10232863	7.01	59350605.4	7.77	820	2.91	60	1.78	348	2.54	-5.23	825	2.92	0	6	0.78	34.8	1.54	-6.23	842	2.93	0.01	28	1	normal study	negative	nil	positive	incidental
42	PUSHPA	5769/09	25	2	vertical	1	52	42	26230544	7.42	152137155.2	8.18	8974	3.95	58000	4.76	336400	5.53	-2.66	3560	3.55	-0.4	7000	3.85	40600	4.61	-3.57	1300	3.11	-0.84	80	1	normal study	positive	nil	positive	screening
43	DAMODHARAN	6925	55	1	blood transfusion	1	92	46	24000	4.38	139200	5.14	1230	3.09	20	1.3	116	2.06	-3.08	226	3.6	0.51	20	1.3	116	2.06	-3.08	252	2.4	-0.69	18	1	normal study	negative	nil	positive	incidental
44	WAHIDHA	185/06	36	2	unknown	2	38	32	7740	3.89	44892	4.65	10703	4.03	6	0.78	34.8	1.54	-3.11	3968	3.6	-0.43	6	0.78	34.8	1.54	-3.11	3422	3.53	-0.5	15	1	normal study	negative	nil	positive	incidental
45	SELVARAJ	6556/10	44	1	unknown	2	66	32	2456	3.39	14244.8	4.15	13031	4.11	312	2.49	1809.6	3.26	-0.9	47	1.67	-2.44	6	0.78	34.8	1.54	-2.61	14963	4.18	0.06	40	1	normal study	negative	nil	positive	incidental
46	PRAKASH	6026/10	39	1	blood transfusion	2	236	87	740790	5.87	4296582	6.63	71916	4.86	14700	4.17	85260	4.93	-1.7	2320	3.37	-1.49	10980	4.04	63684	4.8	-1.83	1980	3.3	-1.56	76	1	normal study	negative	myopathy	positive	incidental
47	ETHIRAJ	7055/10	47	1	unknown	2	114	49	10400	4.02	60320	4.78	7127	3.85	6	0.78	34.8	1.54	-3.24	1626	3.21	-0.64	6	1.3	116	1.54	-3.24	3907	3.59	-0.26	82	2	esophageal varices	negative	nil	positive	incidental
48	RAMESH	4071/02	36	1	injection use	2	62	36	2500	3.4	14500	4.16	640	2.81	20	1.3	116	2.06	-2.1	1839	3.26	0.46	20	1.3	116	2.06	-2.1	1620	3.21	0.4	32	1	normal study	negative	nil	positive	incidental
49	RAJASEKAR	5149/09	29	1	vertical	1	48	42	8382885	6.92	48620733	7.69	2E+06	6.3	68000	4.83	394400	5.6	-2.09	454	2.66	-3.64	42000	4.62	243600	5.39	-2.3	524	2.72	-3.58	82	1	normal study	positive	nil	positive	incidental
50	BABU	6772/10	28	1	injection use	2	85	31	14860	4.17	86188	4.94	22320	4.35	6	0.78	34.8	1.54	-3.39	4524	3.66	-0.69	6.15	0.79	35.67	1.55	-3.38	5030	3.7	-0.65	25	1	normal study	negative	nil	positive	screening
51	RAMESH	2216/08	30	1	blood transfusion	2	62	42	4200	3.62	24360	4.39	111	2.05	20	1.3	116	2.06	-2.32	54	1.73	-0.31	6	0.78	34.8	1.54	-2.85	77	1.89	-0.16	40	1	normal study	negative	nil	positive	incidental
52	CHANDRA	7405/11	45	2	unknown	2	43	32	329536	5.52	1911303	6.28	37039	4.57	2000	3.3	11600	4.06	-2.22	21502	4.33	-0.24	440	2.64	2552	3.41	-2.87	22562	4.35	-0.22	34	1	normal study	negative	nil	positive	incidental
53	LOGANAYAKI	1022/05	40	2	unknown	2	42	21	26651	4.43	154575.8	5.19	4.64	0.67	4E+08	8.58	2186600000	9.34	4.15	351.27	2.55	1.88	2E+06	6.39	1.4E+07	7.15	1.96	686	2.84	2.17	68	1	normal study	negative	myopathy	positive	incidental
54	KANNAGI	1034/05	30	2	sexual	2	38	24	2440	3.39	14152	4.15	2126	3.33	6	0.78	34.8	1.54	-2.61	1897	3.28	0.05	6	0.78	34.8	1.54	-2.61	169	2.23	-1.1	14	1	normal study	negative	nil	positive	incidental
55	DEIVASIGAMANI	639/10	50	1	unknown	2	52	24	2780	3.44	16124	4.21	939	2.97	20	1.3	116	2.06	-2.14	1246	3.1	0.12	6	0.78	34.8	1.54	-2.67	1022	3.01	0.04	28	1	normal study	negative	nil	positive	incidental
56	RAVI KUMAR	7302/10	45	1	blood transfusion	2	140	40	8000	3.9	46400	4.67	2282	3.36	20	1.3	116	2.06	-2.6	2022	3.31	-0.05	6	0.78	34.8	1.54	-3.12	1824	3.26	-0.1	34	1	normal study	negative	myalgia	positive	incidental
57	KANNAN	7251/10	23	1	vertical	2	40	76	434348	5.64	2519218.4	6.4	117425	5.97	31	1.49	179.8	2.25	-4.15	68373	4.83	-0.23	13.5	1.13	78.3	1.89	-4.51	60000	4.78	-0.29	32	1	normal study	negative	nil	positive	screening
58	JAYASEKARAN	5136/10	42	1	unknown	1	82	43	28000	4.45	162400	5.21	6628	3.82	15.4	1.19	89.32	1.95	-3.26	7452	3.87	0.05	6	0.78	34.8	1.54	-3.67	6500	3.81	-0.01	48	2	normal study	positive	nil	positive	incidental
59	NEDUNCHEZIAN	7538	56	1	unknown	2	62	32	5174757	6.71	30013590.6	7.48	2908	3.46	40.91	1.61	237.278	2.38	-5.1	2630	3.42	-0.04	50	1.7	290	2.46	-5.01	1855	3.27	-0.2	35	1	normal study	negative	nil	positive	incidental
60	THANIGACHALAM	8361/10	45	1	injection use	2	76	28	24000	4.38	139200	5.14	373	2.57	306	2.49	1774.8	3.25	-1.89	124	2.09	-0.48	6	0.78	34.8	1.54	-3.6	387	2.59	0.02		1	normal study	negative	nil	positive	incidental
61	SELVAKUMAR	141/09	29	1	vertical	1	36	29	170000000	8.23	986000000	8.99	125000	5.1	185	2.27	1073	3.03	-5.96	552	2.74	-2.35	6070	3.78	35206	4.55	-4.45	41724	4.62	-0.48	63	1	normal study	positive	fatigue	positive	screening
62	ARJUNAN	329/11	60	1	blood transfusion	1	74	116	321754	5.51	1866173.2	6.27	2898	3.46	6	0.78	34.8	1.54	-4.73	1199	3.51	0.04	1411	3.15	83.8	3.91	-2.36	964.64	2.98	-0.48	24	1	normal study	negative	nil	positive	incidental
63	SUNDARAM	728/10	53	1	injection use	1	48	63	487362	5.69	2826699.6	6.45	1189	3.08	12000	4.08	69600	4.84	-1.61	23000	4.36	1.29	10900	4.04	63220	4.8	-1.65	13141	4.12	1.04	82	1	normal study	positive	resistance	positive	incidental
64	PARIMALA	319/11	60	2	sexual	1	37	32	24582222	7.39	142576887.6	8.15	1017	3.01	5400	3.73	31320	4.5	-3.66	344	2.54	-0.47	20	0.78	34.8	2.06	-6.09	240	2.38	-0.63	18	1	normal study	negative	nil	positive	incidental

65	RAMACHANDRAN	626/11	65	1	unknown	2	45	24	36958	4.57	214356.4	5.33	10295	4.01	240	2.38	1392	3.14	-2.19	7800	3.89	-0.12	20	1.3	116	2.06	-3.27	6824	3.83	-0.18	23	1	normal study	negative	nil	positive	incidental
66	MANOHARAN	264/11	56	1	unknown	2	152	42	10359634	7.02	60085877.2	7.78	10141	4.01	680	2.83	3944	3.6	-4.18	9840	3.99	-0.01	20	1.3	116	2.06	-5.71	6800	3.83	-0.17	68	1	normal study	negative	nil	positive	incidental
67	DHARANI KARASI	932/10	42	2	blood transfusion	1	66	20	533175	5.73	3092415	6.49	4952	3.69	7.57	0.88	43.9	1.64	-4.85	7545	3.88	0.18	6	0.78	34.8	1.54	-4.95	6924.3	3.84	0.15	64	1	normal study	positive	nil	positive	incidental
68	SUBRAMANIYAM	2369/10	60	1	unknown	1	65	50	23177706	7.37	134430694	8.13	1688	3.23	18200	4.26	105560	5.02	-3.1	5453	3.74	0.51	14200	4.15	82360	4.92	-3.21	4045.4	3.61	0.38	58	2	normal study	positive	nil	positive	incidental
69	SURESH KUMAR	1115/11	30	1	injection use	1	212	58	9268972	6.97	53760037.6	7.73	17461	4.24	8.86	0.95	51.38	1.71	-6.02	37130	4.57	0.33	6	0.78	34.8	1.54	-6.19	49436	4.69	0.45	82	1	normal study	positive	nil	positive	incidental
70	RAMADOSS	3575/10	44	1	blood transfusion	1	138	130	129846328	8.11	753108702.4	8.88	125000	5.1	77.6	1.89	450.08	2.65	-6.22	1450	3.16	-1.94	6	0.78	34.8	1.54	-7.34	1000	3	-2.1	32	1	PHG	negative	nil	positive	incidental
71	ARUMUGAM	860/11	28	1	vertical	1	33	50	170000000	8.23	986000000	8.99	121833	5.09	33200	4.52	192560	5.28	-3.71	56923	4.76	-0.33	2340	3.37	13572	4.13	-4.86	48924	4.69	-0.4	38	1	normal study	positive	myalgia	positive	screening
72	GAJENDIRAN	1764/11	52	1	injection use	1	60	36	12395264	7.09	71892531.2	7.86	13816	4.14	6	0.78	34.8	1.54	-6.32	891	2.95	-1.99	6	0.78	34.8	1.54	-6.32	568	2.75	-1.39	26	1	normal study	negative	nil	positive	incidental
73	ANANDHAN	1725/11	65	1	unknown	1	56	42	7086425	6.85	41101265	7.61	781	2.89	2400	3.38	13920	4.14	-3.47	432	2.64	-0.26	20	1.3	116	2.06	-5.55	400	2.6	-0.29	34	1	normal study	negative	nil	positive	incidental
74	SIVA	1012/11	41	1	injection use	1	170	65	5069172	6.7	29401197.6	7.47	1275	3.11	230	2.36	1334	3.13	-4.34	1040	3.02	-0.09	20	1.3	116	2.06	-5.4	820	2.91	-0.19	24	1	normal study	negative	nil	positive	incidental
75	SRINIVASAN	890/11	36	1	unknown	1	82	34	2057013	6.31	11930675.4	7.08	61910	4.79	6950	3.84	40310	4.61	-2.47	23903	4.38	-0.41	420	2.62	2436	3.39	-3.69	32560	4.51	-0.28	62	2	normal study	positive	nil	positive	incidental
76	venkatesan	2191/11	29	1	vertical	1	75	42	102523	5.01	594633.4	5.77	54830	4.74	560	2.75	3248	3.51	-2.26	2690	3.43	-1.31	20	1.3	116	2.06	-3.71	1480	3.17	-1.57	35	2	normal study	negative	nil	positive	screening
77	shanthi	1648/11	39	2	blood transfusion	1	86	21	2689058	6.43	15596536.4	7.19	4602	3.66	60.8	1.78	352.64	2.55	-4.65	40.54	1.61	-2.06	13.9	1.14	80.62	1.91	-5.29	346.11	2.54	-1.12	18	1	normal study	negative	myalgia	positive	incidental
78	kali	275/10	49	1	blood transfusion	1	56	77	15464257	7.19	89692690.6	7.95	4434	3.65	2454	3.39	14233.2	4.15	-3.8	30700	4.49	0.84	20	1.3	116	2.06	-5.89	24500	4.39	0.74	58	1	PHG	positive	nil	positive	incidental
79	N.Govindan	2346/11	50	1	injection use	2	64	101	2488	3.4	14430.4	4.16	330	2.52	1E+05	5.11	747620	5.87	1.71	650	2.81	0.29	3E+05	5.48	1734200	6.24	2.08	265.64	2.42	-0.09	72	1	normal study	negative	resistance	positive	incidental
80	sumathi	6976/10	58	2	unknown	2	61	72	6890	3.84	39962	4.6	43.95	1.64	890	2.95	5162	3.71	-0.89	210	2.32	0.68	20	1.3	116	2.06	-2.54	180	2.26	0.61	28	1	normal study	negative	nil	positive	incidental
81	rajendiran	222/11	42	1	unknown	1	84	62	170000000	8.23	986000000	8.99	125000	5.1	1400	3.15	8120	3.91	-5.08	8200	3.91	-1.18	20	1.3	116	2.06	-6.93	7046.9	3.85	-1.25	68	1	normal study	positive	nil	positive	incidental
82	MURUGADOSS	2135/11	33	1	blood transfusion	2	42	65	8000	3.9	46400	4.76	15512	4.19	6	0.78	34.8	1.54	-3.12	4070	3.61	-0.58	6	0.78	34.8	1.54	-3.12	8697.7	3.94	-0.25	26	1	normal study	negative	nil	positive	incidental
83	rajasekar.m	3089/11	60	1	unknown	1	51	74	28350	4.45	164430	5.39	5818	3.64	6150	3.79	35670	4.55	-0.66	18923	4.28	0.51	350	2.54	2030	3.31	-1.91	12000	4.08	0.31	32	1	normal study	positive	nil	positive	incidental
84	Shahul Hameed	2902/11	29	1	vertical	1	82	42	170000000	8.23	986000000	8.99	125000	5.1	1040	3.02	6032	3.78	-5.21	53591	4.73	-0.37	6.42	0.81	37.2	1.57	-7.42	2576.8	3.41	-1.69	80	1	PHG	positive	fatigue	positive	screening
85	Mallika Begum	2859/11	46	2	unknown	2	60	23	4570	3.66	26506	4.42	2460	3.39	180	2.26	1044	3.02	-1.4	1250	3.1	-0.29	6	0.78	34.8	1.54	-2.88	1100	3.04	-0.35	16	2	normal study	negative	nil	positive	incidental
86	Gunasekaran	2906/11	54	1	unknown	2	82	49	1397652	6.15	8106381.6	6.91	4783	3.68	122	2.09	707.6	2.85	-4.06	2222	3.35	-0.33	20	1.3	116	2.06	-4.84	1800	3.26	-0.42	26	1	normal study	negative	nil	positive	incidental
87	Adhikesavan	3079/11	52	1	tatooing	2	78	32	130	2.11	754	2.88	14231	4.15	6	0.78	34.8	1.54	-1.34	6128	3.79	-0.37	6	0.78	34.8	1.54	-1.34	5860	3.77	-0.39	32	1	PHG	negative	myalgia	positive	incidental
88	Sivakami	3010/11	36	2	unknown	1	52	22	42000	4.62	243600	5.39	4320	4.03	426	2.63	2470.8	3.39	-1.99	2200	3.34	-0.29	20	1.3	116	2.06	-3.32	1800	3.26	-0.38	32	1	normal study	negative	nil	positive	incidental
89	Sathiya	2472/11	25	2	vertical	2	34	45	43363640	7.64	251509112	8.4	55064	4.74	6	0.78	34.8	1.54	-6.86	73084	4.86	0.12	6	0.78	34.8	1.54	-6.86	52000	4.72	-0.02	64	1	normal study	negative	nil	positive	screening
90	Ameen	3099/11	34	1	tatooing	1	92	43	62000	4.79	359600	5.56	5230	3.72	84	1.92	487.2	2.69	-2.87	2450	3.39	-0.33	20	1.3	116	2.06	-3.49	2000	3.3	-0.42	32	1	normal study	negative	nil	positive	incidental
91	Sivachandran	3157/11	25	1	vertical	1	86	52	84445	4.93	489781	5.69	10700	4.03	6	0.78	34.8	1.54	-4.15	22954	4.36	-0.33	4030	3.61	23374	4.37	-1.32	66216	4.82	0.79	68	1	normal study	positive	resistance	positive	screening
92	Mohandass	4177/11	48	1	blood transfusion	2	84	24	2640	3.42	15312	4.19	351	2.55	240	2.38	1392	3.14	-1.04	380	2.58	0.03	20	1.3	116	2.06	-2.12	320	2.51	-0.04	24	1	normal study	negative	nil	positive	incidental
93	Jaykumar	4197/11	46	1	unknown	1	84	42	3620000	6.56	20996000	7.32	1806	3.26	18	1.26	104.4	2.02	-5.3	1773	3.25	-0.01	6	0.78	34.8	1.54	-5.78	1450	3.16	-0.1	36	1	normal study	negative	nil	positive	incidental
94	Ettiyappan	4310/11	46	1	injection use	2	72	23	110000000	8.04	638000000	8.8	41923	4.62	1890	3.28	10962	4.04	-4.76	16068	4.21	-0.42	163	2.21	945.4	2.98	-5.83	33000	4.52	-0.1	35	1	normal study	negative	nil	positive	incidental
95	Sabarish	4885/11	34	1	blood transfusion	1	76	46	48000	4.68	278400	5.44	6280	3.8	250	2.4	1450	3.16	-2.28	2140	3.33	-0.47	20	1.3	116	2.06	-3.38	1890	3.28	-0.52	26	1	normal study	negative	nil	positive	incidental
96	Govindasamy	4510/11	65	1	unknown	1	223	116	110000000	8.04	638000000	8.8	20929	4.32	1200	3.08	6960	3.84	-4.96	2500	3.4	-0.92	280	2.45	1624	3.21	-5.59	2100	3.32	-1	38	1	normal study	negative	nil	positive	incidental
97	Jothi	803/11	47	2	unknown	1	43	29	56000	4.75	324800	5.51	6780	3.83	112	2.05	649.6	2.81	-2.7	3500	3.54	-0.29	20	1.3	116	2.06	-3.45	3800	3.58	-0.25	26	1	normal study	positive	nil	positive	incidental
98	Latha	5453/11	36	2	sexual	1	32	28	124000	5.09	719200	5.86	1136862	6.06	900	2.95	5220	3.72	-2.14	41747	4.62	-1.44	400	2.6	2320	3.37	-2.49	35000	4.54	-1.51	46	1	normal study	positive	nil	positive	incidental
99	Kanniyappan	192/08	38	1	blood transfusion	1	120	50	30004	4.48	174023.2	5.24	4800	3.68	20	1.3	116	2.06	-3.18	2700	3.43	-0.25	20	1.3	116	2.06	-3.19	2450	3.39	-0.29	34	2	normal study	negative	nil	positive	incidental
100	Abdul Jabbar	5540/11	34	1	vertical	1	84	42	120000	5.08	696000	5.84	8760	3.94	20000	4.3	116000	5.06	-0.78	14670	4.17	0.22	12500	4.1	72500	4.86	-0.98	13450	4.13	0.19	72	1	normal study	positive	nil	positive	screening