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Full Length Research Paper

Prevalence of HBV/HIV co-infection and effect of HAART on HBSAg seroreactivity in Ayder Referral Hospital, Mekelle, Tigray, Ethiopia

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Hepatitis B virus (HBV) co-infection with HIV is becoming a major challenge due to shared routes of transmission. Therefore screening HBV in HIV infected individuals should be a routine clinical practice. In Ethiopia practice of routine HBV screening, Use of HAART regimens with dual Anti HIV/HBV action & their effect on HBSAg sero reactivity is not well studied. To determine the sero prevalence of HBSAg in HIV infected patients, Pattern of HAART use in Co infected patients and Effect of HAART on HBSAg serore activity. A Six years Retrospective review of HIV infected patients for whom HBSAg testing was done previously was taken by reviewing the medical records of 424 patients following in ART clinic of Ayder referral hospital from January 1,2009 – January 15, 2016. The prevalence of HBV in HIV infected patients is found to be 10%. Among co infected patients 81.8% of patients were put on HAART regimens with two agents active against HIV & HBV which is in line with international guidelines. HBSAg Sero Conversion rate was found to be 63.6% in co infected patients who took HAART for more than one year. HIV/HBV Co infection rate in Ayder hospital is comparable with the previously done studies & Practice of HAART use in ARH is in accordance with International HIV & HBV treatment guidelines recommendations. All of the seroconverted patients were taking Tenofovir, Lamivudine, Efavirenz regimen proving the importance of this regimen on co infected patients.

Key words: Hepatitis B virus (HBV), highly active anti-retroviral treatment (HAART), hepatitis B surface antigen (HBSAg), prevalence, Ayder.

INTRODUCTION

Approximately 350 million people (5 to 7% of the world's population) are chronically infected with the hepatitis B virus (HBV), and 600,000 (0.2%) die each year of HBV-related disease and hepatocellular carcinoma (Lai et. al., 2003; Christopher and Alan, 1997; Susan et al., 2005). Perinatal transmission predominates in East and Southeast Asia; in Africa, most HBV transmission occurs before the age of 5 years, through close contact within households, medical procedures, traditional scarification and possibly additional unidentified mechanisms (Paniz et al., 2022; Vardas et al., 1999). In high-endemicity areas of Africa and Asia, most HBV infections occur in the first 5 years of life. The prevalence of HBV carriers varies from 0.1 to 2% in low prevalence areas (United States, Canada, Western Europe, Australia and New Zealand), to 3 - 5% in intermediate prevalence areas

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(Mediterranean countries, Japan, Central Asia, Middle East, and Latin and South America), to 10 to 20% in high prevalence areas (Southeast Asia, China, sub-Saharan Africa) (Maynard, 1990; Alter et al., 1990). In 2012, an estimated 35.3 million people were living with Human Immunodeficiency Virus (HIV). Sub-Saharan Africa, especially southern Africa has the highest global burden of HIV (70.8%) (UNAIDS, 2013). HIV is a major contributor to the global burden of disease. In 2010, HIV was the leading cause of disability-adjusted life years worldwide for people aged 30 – 44 years and the fifth leading cause for all ages (Ortblad et al., 2013). HIV and HBV are often diagnosed in the same patient because they share similar routes of transmission and Chronic HBV affects approximately 10% of HIV-infected patients worldwide (Puoti et al., 2002). The rates of HIV/HBV co infection vary according to geographic region and are highest in sub-Saharan Africa and Asia, where most transmission occurs perinatally (Scott et al., 2003). The risk of HBV infection may be higher in HIV-infected adults, and therefore all persons newly diagnosed with HIV should be screened for Hepatitis B surface Antigen (HBSAg) and anti-HBs to identify those with Chronic hepatitis B infection, and vaccinated if non-immune (Ni et al., 2013). HIV co infection has been shown to have a profound impact on almost every aspect of the natural history of HBV infection and includes more rapid progression to cirrhosis and Hepatocellular Carcinoma (HCC), higher liver-related mortality, and decreased treatment response compared with persons without HIV co infection (Hoffmann and Thio, 2007; Easterbrook et al., 2012; Collin et al., 1999; Konopnicki et al., 2005; Puoti et al., 2000; Hawkins et al., 2013; Wandeler et al., 2013; Zollner B et al., 2004; Benhamou et al., 1999). Other challenges with co infection include cross-resistance between HIV and HBV drugs (Zollner B et al., 2004; Benhamou et al., 1999).

Increased liver injury, either due to direct hepatotoxicity (Nunez, 2010; Labarga et al., 2007) or ART-related immune-reconstitution hepatitis, with elevation of ALT and even fulminant hepatitis can occur if ART does not cover both HIV and HBV infections adequately (De Simone, 2000; Shelburne et al., 2002; Lacombe and Rockstroh, 2012).

MATERIALS AND METHODS

Study design

A retrospective cohort analysis to assess "The prevalence of HBV/HIV co infection, type of Highly Active Antiretroviral Treatment (HAART) used in Co-infected pts and the effect of HAART on HBSAg positivity in HIV Infected patients in Ayder referral Hospital.

Study period

Data was collected from patients Medical records. The study participants are HIV-infected patients for whom HBSAg was done previously and who took ART for more than one year. The study was conducted from January 2015 to April 2015.

Study area

Mekelle University (Ayder Referral) Hospital is found in Tigray region, Mekelle town in the Northern part of Ethiopia 780 Km away from the capital Addis Ababa. It was started as a referral and specialized medical center in 2008 to 8 million population in its catchment areas of Tigray, northern Afar, and north-eastern part of Amhara regional states. It is the second largest hospital in the nation and has 500 inpatient beds in the four major departments and other specialty units. The Anti-Retroviral Therapy (ART) clinic in Ayder Referral Hospital was started in January 2009, currently till January 2015 a total of 1055 HIV patients are in the ART clinic; of these, 1007 are taking ART and 51 patients are on Pre- ART program.

Patient selection

Medical records of 424 HIV patients who are following in ARH-ART clinic were evaluated for HBSAg test results,128 patients who have HBSAg test results were found, Of these 18 patients were excluded from the study for various reasons (Age < 18 Years, Incomplete medical records, ART duration < 1year) and a total of 110 patients are included in the study.

Study procedure

The Medical records of all 110 patients were evaluated for Sociodemographic data, previous HBSAg test result, type of HAART regimen they are taking and duration of HAART based on structured check list. Those patients who were co infected with HBV/HIV undergo repeat rapid HBSAg test and liver enzyme determination was taken after informed consent was taken from patients.

Statistical analysis

Data was entered, Cleaned and analysed using SPSS version21 software. Descriptive statistical procedures are used to see the frequencies of the variables. Univariate and Bivariate analysis was performed using Chi square and Binomial statistical analysis to ascertain the association between the dependent variable and the covariates.

RESULTS

Socio-demographic characteristics of study population

From a total of 110 patients included in the study 60 patients (54.5%) are females and 50 (45.5%) are males. 86 patients (78.2%) came from Mekelle City and 24 patients (21.8%) came from areas out of Mekelle. All 110 patients are above 18 years of age, of this 16(14.5%) are 18 to 30 years, 44 (40%) 31 to 40, 31 (28.2%) 41 to 50, 14 (12.7%) 51 to 60, 5 (4.5%) >60 years of age (Figure 1).

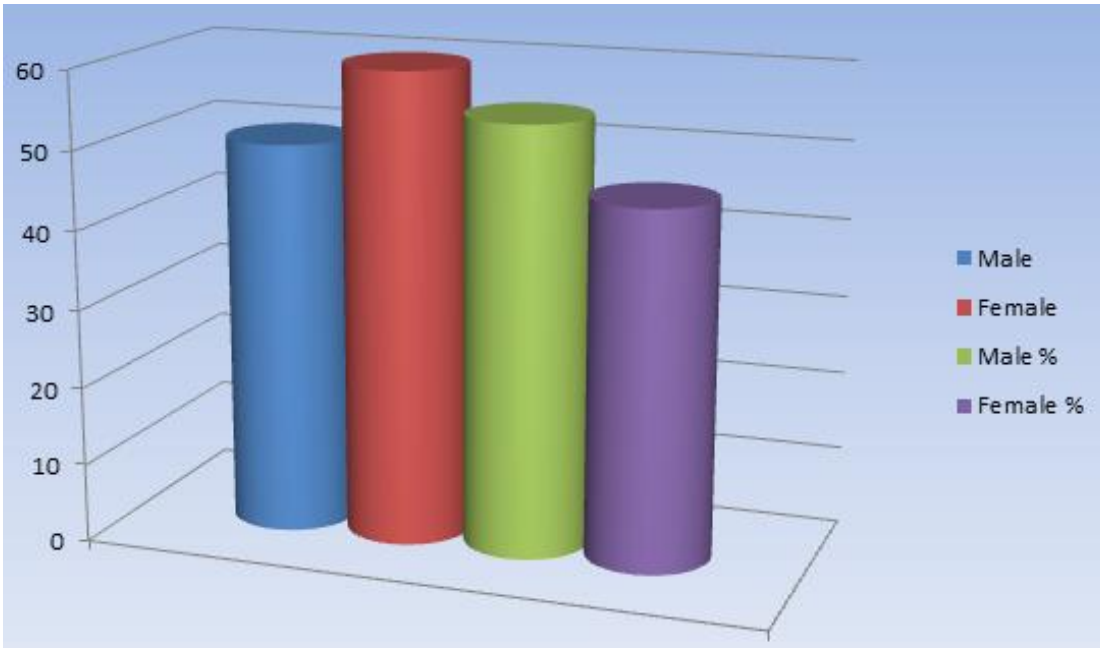

Figure 1. Distribution of study Patients based on gender.
Source: Author

HBSAg sero prevalence

Based on HBSAg test done previously 11(10%) patients are found to be HBSAg Positive. The HBSAg sero prevalence is further analyzed for its association with gender, age group and area of residence. There is no significant difference among Male and Female study subjects (p = 0.543), there was no statistically significant difference among the different Age groups for HBV infection (P = 0.58). Then the HBSAg positive patients are further analyzed for repeat HBSAg tests and lLiver transaminases determinations. From the 11 patients who were retested for HBSAg 7 (63.6%) patients are found to be HBSAg Negative and 4 (36.3%) patients are found to be HBSAg positive based on rapid HBSAg testing (Figure 2).

Liver enzyme levels

All HIV/HBV Co infected patients undergo Liver enzyme determinations to assess the activity of Hepatitis Virus infection; all the 11 Patients for whom Liver enzymes were determined have Liver enzymes below 2X the upper limit of Normal including those patients who have Persistence of HBSAg reactivity

Type of HAART used

From all 110 patients involved in the study, 70 (63.6%) patients are taking Tenofovir (TDF), Lamivudine (3TC), EFV; 24(21.8%) patients are taking Zidovudine (AZT), 3TC, Nevirapine (NVP) and 16 (14.5%) patients are taking AZT, 3TC,EFV HAART regimens, There was no statistically significant difference in the HAART choice among study subjects (P = 0.412). Patients who were initially HBSAg positive are also analyzed for the type of HAART used and its association with HBSAg seroconversion. Among the co infected patients 9 (81.8%) patients were taking TDF, TC, EFV, 1 (9.1%) is taking AZT, 3TC, NVP, 1 (9.1%) is taking AZT,3TC,EFV HAART regimens. Among 7 patients who sero convert, all of them were taking TDF, 3TC, EFV HAART regimen. Of the 4 patients who remain HBSAg sero positive, 2 patients were taking AZT, 3TC, NVPand the other 2 patients were on TDF, 3TC, EFV HAART regimens. There was no statistically significant difference in the HAART choice in HIV/HBV co infected patients (P= 0.57) (Table 1).

DISCUSSION

Although different guidelines recommend routine Hepatitis B screening in HIV infected patients, In this retrospective study the practice of routine Hepatitis B screening is poor in ART clinic, from 423 patients initially evaluated for HBSAg test results, only 128 patients had HBSAg done till the study period. A study of 16,248 HIV-infected patients in the United States found the prevalence of chronic HBV was 8% among unvaccinated

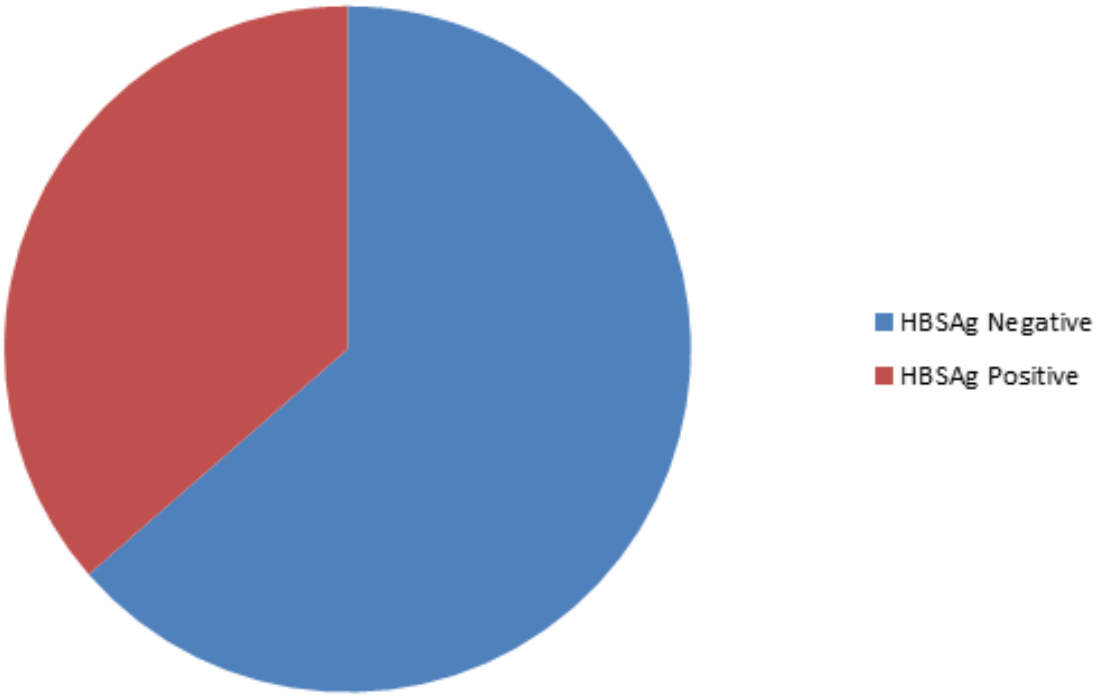

Figure 2. HBSAg sero prevalence in the study patients.
Source: Author

Table 1. Type of HAART regimen used in study patients.

Type of ART	Frequency	Percent
AZT,3TC,NVP	24	21.8
AZT,3TC,EFV	16	14.5
TDF,3TC,EFV	70	63.6
TOTAL	110	100

Source: Author

participants (Christopher and Alan, 1997). In a study done in Nigeria which assesed the Immunological and Biochemical tests in Nigerian HIV/HBV co infected patients on HAART found that HBSAg sero prevalence rate to be 13.8% (Lawal et al., 2020). This study found 10% HIV/HBV co infection rate which is slightly higher than the study done in USA and it was consistent with worldwide prevalence. Several observational studies from the United States and Europe suggest that HIV/HBV co infected patients may have faster rates of Liver fibrosis progression and an increased risk of cirrhosis, end-stage liver disease, and HCC than patients with HBV infection alone (Colin et al., 1999; Di Martino et al., 2002). HCC also occurs at an earlier age among patients who are HIV-infected compared with HIV-seronegative patients (Bräu et al., 2007). Effect of HBV on HIV progression is controversial, one study of 1302 HIV-infected patients and 262 HIV/HBV-co infected patients in Nigeria found that high levels of HBV replication were associated with lower Cluster of Differentiation (CD4) cell counts at ART initiation (Idoko et al., 2009); however, two longitudinal studies and one retrospective study did not show any impact of HBV co infection on CD4 depletion, progression to AIDS or AIDS related mortality (Scharschmidt et al., 1992; Nikolopoulos et al., 2009). HAART is a double-edged sword in patients with HIV-HBV co infection: by restoring innate and adaptive immunity, it can induce anti–hepatitis BS and/or anti–hepatitisB seroconversion with or without flares of necroinflammatory activity (Puoti et al., 2006). Three antiretroviral - Lamivudine, Tenofovir, and Emtricitabine- have “dual” Anti HIV/HBV activity and are able to suppress both HIVand HBV replications. Their use as components of HAART has been associated with prevention of new infections, histological improvement, and prevention of hepatitis B progression toward cirrhosis and hepatocellular carcinoma (Puoti et al., 2006). The

HAART regimen in co infected patients should include at least 2 agents active against both HIV and HBV. The 2013 World Health Organization's (WHO) HIV treatment guideline recommends initiation of HAART in co infected patients when there is evidence of severe Chronic liver disease regardless of the CD4 Count and when the CD4 count <500/mm^3 regardless of the severity of Liver disease (WHO, 2013). It was recommended in many treatment guidelines that HBV/HIV co infected patients should be put on HAART regimens containing at least two Antiretroviral drugs with dual anti HBV and HIV activity.

In this study, 9 (81.8%) patients were taking TDF, 3TC, EFV regimens which contains two (TDF and 3TC) Antiretroviral drugs active against HBV, 2 (18.2%) patients were put on regimens which contain only one Antiretroviral drug active against HBV. Though a huge number of patients are on HAART regimens with dual anti HBV/HIV activity there is still a gap noticed in adhering to the standard treatment guidelines. A tenofovir-based regimen is the recommended therapy, which should include tenofovir/lamivudine, or tenofovir/ emtricitabine (provided there is no contraindication to tenofovir), together with a third drug efavirenz, to prevent the selection of HIV-resistant mutants. Tenofovir is available co-formulated with lamivudine or emtricitabine and efavirenz (WHO, 2015). This treatment strategy has achieved high rates of HBV DNA suppression (90%), Hepatitis B envelope Antigen (HBeAg) loss (46%) and HBsAg loss (12%) in HBeAg-positive patients after 5 years of treatment, without evidence of resistance, and reduced progression to cirrhosis with no significant differences in response in those with or without HIV co infection (de Vries-Sluijs et al., 2010). Among the co infected patients who were retested for HBSAg in this study, 7(63.6%) patients were seroconverted and all of them were put on TDF, 3TC, EFV regimen which is the regimen with dual antiviral activity and the first line of HAART regimens in both HBV infected and noninfected HIV patients; this result is consistent with the guidelines recommendations that HAARTs with dual antiHIV/HBV action are effective in co infected patients. Although in this study there was no statistically significant difference on the choice of HAART and its effect on HBSAg sero reactivity, the fact that all patients who seroconverted were taking TDF, 3TC, EFV regimen suggest that HAARTs with dual anti HIV/HBV action are effective in treatment of both infections.

Strength and limitations

The strength of the study is the first of its kind in ARH to show the seroprevalence of HBSAg in HIV infected individuals, evaluate the practice of HBSAg testing, and HAART use in co infected individuals and adherence to the currently available Guidelines. The limitations of the study are: (i) It's a retrospective study so it may be difficult to generalize the findings to the general population (ii) Most of the patients following in our the ART clinic do not have HBSAg testing which may be due to availability of the test or lack of awareness that HBSAg testing should be done routinely in HIV infected individuals. The other problem is unavailability of confirmatory ELISA HBSAg testing creates difficulty in the diagnosis of HBV infection with certainty.

Conclusions

This study assesses the prevalence of HIV/HBV co infection in Ayder referral Hospital, Practice of routine HBSAg screening in HIV patients in ART clinic, adherence to HIV treatment guidelines in choice of HAART in co infected patients and effect of HAART on HBS Ag seroreactivity in coinfected patients. This study shows the seroprevalence of HBSAg in HIV patients is comparable with the previously done studies and use of HAARTs with dual antiviral activity has important clinical benefit in HBSAg seroconversion.

Recommendations

The prevalence of HIV/HBV co infection is very high as it is revealed in this study as well as previously done studies, therefore routine screening of all HIV infected patients for HBV and all HBV infected individuals for HIV should be practiced. HIV infected patients without HBV infection should also be advised about the risk of HBV infection and its possible adverse consequences and should be encouraged to take the possible prevention methods. Also, the use of HAART in HIV/ HBV Co infected patients should be practiced in line with the currently available recommendations, and should contain agents active against both HIV and HBV. Serial Monitoring of Co infected patients with Liver enzymes, HBeAg and HBSAg to evaluate for the progression of liver disease anddisappearance of HBV infection should be practiced in our hospital.

CONFLICT OF INTERESTS

The author has not declared any conflict of interest.

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