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Burden of HBV and HIV Co-Infection and Immunological Response in HAART Attendant in Ethiopia: Review

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ABSTRACT

Despite HIV related death was substantially reduced with emergence of ART but, HBV co- infection accelerated the disease progression to AIDS defining events and liver related chronic infection. Since HIV positive individuals especially those that are immune compromised are more susceptible to HBV infection due to common mode of transmission. Earlier screening of HBV infection enhances for proper selection of ART regimens and to reduce transmission of the infection. But, underscoring the need for earlier detection HBV infection and timely treatment initiation may result in irreversible complication of HBV infection. In this review paper we emphasise the burden and immune reconstitution of HBV/HIV co- infected individuals following HART administration.

Keywords: HBV co-infection, Chronic infection, Immune reconstitution, HART administration, ART regimens

INTRODUCTION

Human immunodeficiency virus related mortality has been greatly reduced with expanded and wide use of antiretroviral therapy (ART) but, HBV is an increasing cause of morbidity and mortality among people living with HIV [1]. People living with HIV are frequently susceptible to HBV which leads to continuous non-AIDS defining morbidity and mortality. HIV-HBV co-infected people are treated with HIV antiretroviral therapy but, underlying hepatitis B virus is becoming a major cause of death mainly in resource limited areas [2]. HBV infection and pattern of transmission varies throughout the world [3]. Moreover, Hepatitis B virus is highly endemic in developing regions which accounted 8% and 70% to 95% for chronic carrier and past or current serological markers of HBV infection respectively [4]. HIV-HBV co-infection is not uncommon due to shared risk factors in endemic areas like Ethiopia [5].

The risk of acquiring HBV infection in HIV infected patients was increased by 40% than HIV negative [2]. Likewise, the rate of chronic HBV infection among HIV-HBV co-infected and those infected with HBV alone was 25% and 4% respectively [6]. There are two patterns of HBV infection which are crucial in measuring the occurrence of HBV disease. If HBV infection occurs in early life, most of the infections attributed to chronic infections and results in long term consequences. But, if infection is acquired during childhood, it may result in symptomatic acute infection and fulminant hepatitis [7].

Many HIV positive people are unaware of their infection with HBV and they are at high risk of developing liver related diseases and co-infection increases the causes of mortality and AIDS defining illness [4,8]. Likewise, it increases the progression of cirrhosis with increased risk of HCC and liver related death [9]. There are many research reports for HBV-HIV co-infection in HIV infected individuals in Ethiopia but, it lacks the correlation of the findings with national ART guideline, immunological response failure following treatment and implication of the screening for HBV infection Ethiopia. So, this review paper was present the overall burden and immunological response of HBV-HIV co-infected individuals following combination ART regimens in different ART centers in Ethiopia.

PREVALENCE OF HBV-HIV CO-INFECTION

Approximately 4 million HIV positive individuals are co-infected with HBV worldwide [10]. In Africa it was estimated that 3.4 million people were considered to be co-infected with

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HBV-HIV with proportion of 15% [2].

Moreover, in Ethiopia it was estimated that 718,498 people were living with HIV [11]. Of these, approximately 71,849 HIV infected individual were co-infected with HBV as 10% HIV positive individual were expected at risk of developing HBV infection. The global prevalence of HBV varies greatly and defined by high, intermediate and low with ≥8%, 2-7% and <2% respectively [7,12]. The proportion and risk factors of HBV-HIV co-infection varies widely with geographical distribution and different risk groups [2]. Ethiopia is one of the endemic sub Saharan Africa for HBV infection with a prevalence of 6.2% in general population [5]. Majorities of the previous research findings indicated that the prevalence of HBV-HIV co-infection among HIV positive individuals were ranges from 2% to 11.7% [13-16].

The higher prevalence of HBV-HIV co-infection was observed in eastern Ethiopia which was 11.7% among HIV infected individuals [15]. With this report, HIV positive individuals and positive for HBsAg were taking combination ART regimen with Lamubidine (3TC) only were shown HBV resistance mutation and increased HBV replication despite anti-HBV combination regimen. Slightly higher prevalence of HBV co-infection (8.4%) was reported in ART attendants in Wolaita Sodo [17]. The major predictors for HBV co-infection indicated by majorities of the researchers were having multiple sexual partners, low circulating CD4+ T cells (<200cells/ul), skin piercing and underlying opportunistic infection [17-19]. Likewise, significant proportion of male groups were more likely exposed by HBV infection [9,13,20].

The HBV-HIV co-infection was higher in those who were taking ART regimen with combination 3TC only [18]. Because, 3TC were invariably associated with drug resistance HBV mutation but yet this combination ART regimen was given for HBV- HIV co-infection [15,18,19]. Moreover, HBV co-infections were substantially increased with patients under AZT, 3TC, and EFV combination ART regimen [17,18]. Another interesting report in Amhara, Northern Ethiopia proven that Lamubidine (3TC) combination ART regimen revealed HBV drug resistance mutation and these mutants were tested positive for HBsAg [19]. Additionally, with this findings patient who were taking 3TC combination regimen have shown HBV resistance mutation. The variation of HBV-HIV co-infection with different study was attributed to choose of combination ART regimen and time of screening for HBV infection [15].

IMMUNOLOGICAL RECONSTITUTION

HIV-HBV co-infected individuals frequently expressed an impaired immune response with low CD4+ T cell count than HIV mono-infected [18]. This immune response failure influences the course or control of HIV disease progression [12]. A study in Gondar suggested that HBV-HIV co-infected individuals were at increasing risk of AIDS defining event compared to HIV infected only [21]. Many of the studies indicated that HBV- HIV co-infection was not considered as active infection that recurs spontaneously and results in severe liver disease [14-19]. Moreover, HIV infected individuals were treated with ART without prior screening for HBV infection which leads HBV related liver disease and treatment failure [21]. Individuals with HBV-HIV co-infection were characterized by the presence of immunological response failure with declined CD4+ T cell counts [18,20,21].

HBV co-infection individuals on combination of ART regimen were more likely to express anti HBc sero marker which indicated the recovery or seroconversion [15]. The presence of positive anti-HBc with HBsAg (-) and anti- HBs (+) are indicators of protective immunity to previous HBV infection. But, individuals with anti-HBcAg particularly in HIV positive people are at high risk of the viral reactivation and progression with less spontaneous clearance of the infection [19]. HBV specific antibodies are protective proteins and markers of the disease's progression. Furthermore, anti-HBC is a biological marker for prior HBV infection and are expressed by HIV-HBV co-infected people which could be due to the effect of treatment regimen or natural history of the infection.

Many researchers indicated that HBV-HIV co-infected individuals were expressed low CD4+ T cell counts (<200 cells/ul) [13,15,17,21]. Furthermore, co-infected individuals with immune compromised people were positive for anti-HBc antibody marker ultimately results in HBV reactivation [13]. Because, HBV-HIV co-infected patients have an impaired immune response with declined CD4+ T cells which creates a chance for reverse seroconversion as a result of HBV replication with detectable HBsAg. This leads lower clearance of the infection with accelerated progress of HBV reverse sero conversion. Moreover, immunological response failure was observed in HBV-HIV co-infected patients despite the combination ART regimen [18,21].

A high and sustained serum HBV DNA levels and decreased sero conversion of HBeAg and HBsAg were often seen in HBV-HIV co-infected people [22]. Because, early phase of HBV infection is characterized by the presence of HBeAg and detectable serum HBV DNA level [7]. Following HBV infection, individuals can spontaneously clear the infection by developing anti-HBe protective immunity which achieves a state of non-replicative HBV with low or undetectable serum HBV DNA. Human immunodeficiency virus infective individuals were taking ART regimen with combination of TDF and 3TC were significantly reduced the HBsAg exposure but, patients taking without combination of TDF are more likely exposed to HBV [15,18]. Likewise, patients on combination ART regimen with TDF and 3TC anti-HBV drugs were positive for HBsAg are more likely to express an anti-HBc sero marker (46.7%) which is an indicator for the resolution of the infection [15].

CONCLUSION

The prevalence of HBV-HIV co-infection with different studies in Ethiopia was similar with previous reports in HBV endemic areas. But we have observed that the ranges of HBV co-infections reported was large due to improper administration of combination ART regimen with anti HBV drugs in different ART center. Yet, there is a gap with adherence of the national ART guideline for HIV positive individuals during enrolment and follow. HBV-HIV co-infected individuals were taking combination ART regimen with lamubidine only resulted HBV drug resistance and further reactivation and seroconversion which needs a great concern. Moreover, the current screening strategy for HBV is based the present or absence of circulating HBsAg but, this could be under report or loss of active cases of HBV infection which leads liver related chronic infection and continuous transmission. Therefore, the national HBV testing algorism for HIV positive should be updated for testing HBsAg, HBc Ag and anti HBc antibody which enables to detect low level of circulating HBV DNA level before ART initiation. Ultimately this can also important for the classification HBV infection for proper patient management. Moreover, HBV-HIV co-infected individuals should be treated with TDF containing combination ART regimen for better treatment outcome.

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