



## AN INTEGRATIVE REVIEW: ALCOHOL INTAKE AND ANTIRETROVIRAL THERAPY AMONG PEOPLE LIVING WITH HIV

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**Abstract:** Endurance rate of peoples living with HIV was improved and HIV/AIDS related deaths were reduced due to the initiation of combination of antiretroviral therapy (cART). The purpose of this review was to explore the effect of alcohol use on adherence to antiretroviral therapy, its effect, and antiretroviral drug toxicity among people living with HIV (PLHIV). Alcohol intake was found as have positive and linear relation with antiretroviral drug adherence. It was also found that exacerbate immune suppression and toxicity of antiretroviral therapy drug as well affects life expectancy. One study realizes that during the intake of alcohol, there has been found to lessen the production of antibodies in response to vaccination and has been related to a more reduction in the number of CD4 cells that constitutes the primary targets of HIV infection prior to antiretroviral therapy (ART) initiation. It is known that as medications can cause a wide range of toxicities; from low-grade intolerance that may be self-limiting to life-threatening drug toxicities. The most common toxicities include: Mitochondrial dysfunction, Lipodystrophy, other metabolic abnormalities, Hematological and Hyper sensitivity. Since it is concluded that alcohol intake can affect medication adherence level, from people started antiretroviral therapy (ART) among peoples living with HIV, those with 40% to 80% of doses taken as ordered/adhered were 3.6 times have probability to develop AIDS compared with people with at least 95% adhered and those with poor ART adherence, less than 40% of doses taken as ordered were 5.9 times more probably to develop the acquired Immune deficiency syndrome (AIDS).

**Keywords:** Alcohol intake, Anti-retroviral therapy, HIV/AIDS.

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**Introduction:** Acquired Immune Deficiency Syndrome is a disease caused by HIV virus which is the virus that destroys the body's immune system and predispose the body to infection and disease, finally lead to death <sup>[1]</sup>. World widely, approximately 36.9 million people were living with HIV in 2014<sup>[2]</sup>, including 2.3 million new HIV infections,

showing a 33% fall of new infections compared to 3.4 million in 2001. Similarly, AIDS related deaths were also declined to 1.6 million AIDS related deaths in 2012 compared to 2.3 million in 2005<sup>[3]</sup>.

Moreover, HIV/AIDS related deaths were reduced due to the launch of the combination of antiretroviral therapy (cART) and survival rate of patients that are infected by HIV were also improved<sup>[4-8]</sup>. Different studies in different study settings have revealed that the combination of antiretroviral therapy (cART) has reduced HIV/AIDS related deaths to almost below rates of non-HIV/AIDS related deaths<sup>[9, 10]</sup>.

The combination of HAART - highly active anti-retroviral therapy has improved HIV care, before the launch of (ART) in the late 1990s. In 1995, annual mortality rate due to HIV/AIDs was approximately 500 per 1,000 person years<sup>[11]</sup> and it was the most predominant cause of death among individuals aged 25-44 in the United States<sup>[12]</sup>. Next to the introduction and dissemination of combined Antiretroviral therapy(ART), deaths due to HIV/AIDS infection were dropped to one fifth of their prior level (i.e., 100 per 1,000 person-years in 2002)<sup>[11]</sup>.

Moreover, the dramatic decrease in HIV/AIDS related death indicates that almost 80 percent of deaths in HIV infected individuals are being prevented by the availability and/or accessibility of Anti-retro viral therapy (ART). As a result, HIV/AIDS disease has changed into a chronic manageable disease with medication<sup>[13]</sup>.

Even if, human immune deficiency virus/ Acquired immune deficiency syndrome (HIV/AIDS) related deaths are dropped sharply to their highest level in the pre ART time, preventable human immune deficiency virus/ Acquired immune deficiency syndrome (HIV/AIDS) related deaths are still common among many patients living with human immune deficiency virus (HIV), who not strictly adhere to their Antiretroviral therapy (ARV) medications. Anti-retroviral therapy (ART) is

normally a complex medical treatment that several medicines must be taken per the instruction at different times daily, and to ensure its effectiveness, at least 95% of medication doses need to be taken exactly as ordered<sup>[13]</sup>. But, different studies states that only 39% to 91% of ART medication doses are taken as directed<sup>[14, 15]</sup> result in reduced treatment effectiveness. Alcohol intake is a strong risk factor for poor ART adherence across a wide spectrum of patient cohorts and health care settings<sup>[16-18]</sup>. Thus, this article review mainly aimed to explore the relation of Alcohol intake and antiretroviral therapy among people living with HIV.

**Method:** For this integrative review of literature on alcohol intake and antiretroviral therapy among people living with HIV, electronic based search strategy was used with limited time period of 1996 to 2015, and key terms ART, PLWHIV, alcohol intake. Then, the appropriately selected studies were exported to data manager endnote 6. To extract the ideas repeated reading was done by the author.

**Issue of Alcohol intake among PLWHIV:**

Alcohol is a kind of drug prepared in the form of, wine beer, gin, whisky and vodka etc<sup>[19]</sup>. Moreover, its action is to relax brain and body. Many people feel that moderate drinking of alcohol (per day to drink a unit or two unit of alcohol helps relieve stress, encourages relaxation and acts as an appetite stimulant. However, its effects can also affect mood and lead to psychological, physical and social problems. NB. a unit = small glass of wine<sup>[19]</sup>.

Even though, no evidence that moderate drinking of alcohol does have harmful effect on people living with HIV, a person who has hepatitis or high levels of blood fats, is advised not to drink alcohol. Moreover, alcohol dependency is common among people living with HIV and heavy drinking affects immune system and slow down recovery from infections. Some studies suggest that, alcohol can interfere with the normal functions of various components of immune system<sup>[19]</sup>.

Further a study conducted on people living with HIV revealed, fifty three percent of the people living with HIV drink alcohol one month prior to the investigation. Moreover, 8% were considered as heavy drinkers<sup>[20]</sup>.

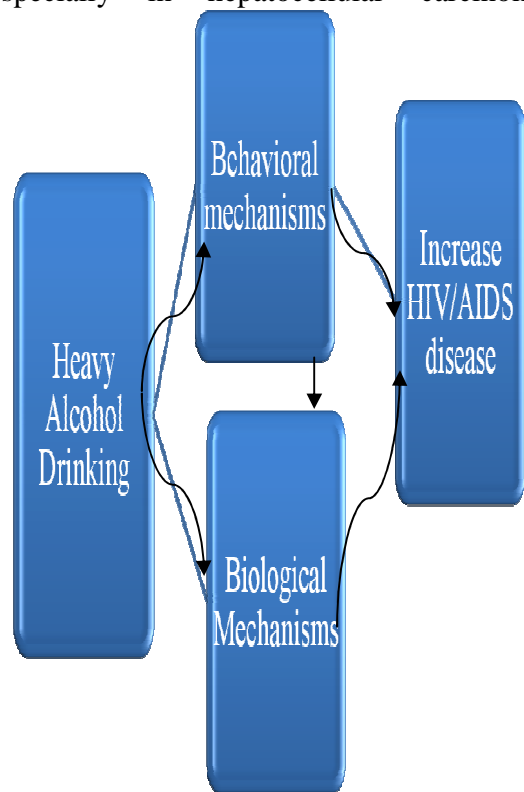
Some studies revealed that levels of hazardous alcohol drinking were found to be almost twice in non-HIV-infected population compared to those people living with HIV. Moreover, studies show that the health of people living with HIV can be affected by alcohol drinking intermittently through: reducing adherence to medications, increasing client's risk of liver damage, reducing the client's ability to practice safer sex, escalating the risk of side effects from medications and shifting how prescribed drugs may work in the body<sup>[21]</sup>.

Moreover, alcohol use can be defined by the amount used or by the consequences of its use. the national institute on alcohol abuse and alcoholism (NIAAA) defined that at-risk use is when a man drinks > 4 on an occasion or >14 in a week and a woman drinks >3 on an occasion and >7 drinks in a week for woman<sup>[22, 23]</sup>. This is to define heavy drinking for those with HIV infection.

Moreover, the relation between alcohol use and HIV is complex; Research shows that alcohol has direct and indirect effect on the development HIV virus and its intensity of causing disease. Further, it increases the growth of the virus HIV in amount (viral load) in the body. Thus, the higher viral load increases the spread of the disease. One study revealed, women taking antiretroviral therapy and moderate level of alcohol drinker had more likely to have higher viral load, which is the ultimate cause of HIV/AIDS related morbidity and mortality and also increases the transmission possibility<sup>[24]</sup>.

Even though, no evidence on moderate levels of alcohol drinking has an effect on the health of people living with HIV, heavy drinking has a significant effect. As, heavy alcohol drinking can affect behaviors like low adherence in HIV care, ART drug, nutritional deficiency and

biological effects like bacterial division in the gut, overlapping pathways of alcohol and ART metabolism. Thus, all the factors described can increase the progression of HIV/AIDS disease<sup>[21]</sup>. Moreover, alcohol consumption has been related susceptibility to infectious diseases like tuberculosis and bacterial pneumonia, increased severity of diseases, especially in viral hepatitis, and increased risk of cancers, especially in hepatocellular carcinoma<sup>[25]</sup>.



**Fig 1: Potential mechanisms alcohol on HIV/AIDS disease progression.**

The other factors that aggravate the above listed disease are vitamin deficiencies, malnutrition, or other substance use. Further, it is a fact that as chronic alcohol intake can lead to liver disease and cirrhosis, which can impact immune competence.

As, animal and human studies revealed, alcohol use has harmful effect on both innate and acquired immunity. Moreover, impaired innate immunity causes vulnerability to infection, while impaired acquired immunity speed up disease progression. In addition, alcohol intake

play a role in translocation of bacteria in the gut which cause immune activation, resulting in increased HIV disease progression.<sup>[26]</sup>

Moreover, alcohol intake increases morbidity among patients that are living with HIV/AIDS through many ways. Among many, some ways are changing the effectiveness of ART medication and the independent effect of alcohol itself, like reducing immune competence and exposing to different infectious disease<sup>[27]</sup>.

#### **Alcohol intake and adherence to ART:**

Ninety five percent adherence to ART drug is required in order to treat the disease, HIV/AIDS successfully and to prevent its resistance<sup>[28]</sup>. However, the lower adherence rates were found among people at any level of drinkers<sup>[29]</sup>.

The strength and consistency of the relation between alcohol intake and adherence of ART were unclear<sup>[30, 31]</sup>. Moreover, due to the use of different drinking variables in most studies a “dose-response” effect has not been systematically evaluated. Some studies revealed that different levels of alcohol use have found that a positive relationship with medication non adherence<sup>[33-35]</sup>. In contrast, others studies revealed that similar adherence rates across modest and high level of alcohol drinkers<sup>[17, 18, and 23]</sup>. Moreover, some studies revealed that alcohol drinking and non-adherence were related with demographic variables<sup>[36, 37]</sup> and how medication adherence is described<sup>[38-40]</sup>.

Even though, there have not been systematic efforts was used to evaluate hypothesized moderators of the alcohol-adherence association, some studies revealed the effect of alcohol in antiretroviral therapy was as follows: Alcohol has a power to add hepatotoxic processes that increase the degree of hepatic inflammation and deterioration of the cell of liver through its digestion process. Thus, it magnifies the toxic effect of ARVs<sup>[41, 42]</sup>. Moreover, one of the main digestive effects of alcohol in the liver is the microsomal ethanol-oxidizing system (MEOS), Which is principally

referred to a family of molecules called cytochrome P450<sup>[43, 44]</sup>.

Further, two studies revealed that degeneration of liver cell in relation to alcohol intake was occurred due to the heavy alcohol consumption leads to extreme stimulation of microsomal ethanoloxidizing system, which ultimately result in the production of reactive oxygen species and oxidative stress. Thus, initiation of microsomal ethanoloxidizing system and augmented oxidative stress were linked as a cause of liver failure. Moreover, because of both alcohol intake and antiretroviral drugs affect the process of MEOS, alcohol intake has confirmed as the potential exacerbate the toxicity of ART drug like injury of mitochondria<sup>[40, 41]</sup>.

#### **Effect of alcohol intake on ART**

**Effectiveness:** The effect of alcohol intake on survival of HIV infected patient is through affecting patient’s adherence behavior on ART drug and its effectiveness. It is the fact that, these effects of alcohol play crucial role in affecting the survival rate of people living with HIV, as at least 95% adherence rate of ART drug were required to ensure its effectiveness<sup>[12]</sup>. Alcohol intake is a basic risk factor for poor adherence of ART. Moreover, its effect also aggravated by alcohol; through increased ART toxicity, skipping ART doses after taking alcohol due to fear of toxic effects or hepatotoxic effects of ART drug. Commonly, non-adherence is the primary cause of ART drug failure, as has been shown in numerous patient groups and health care settings, also the ultimate cause of non adherence to ART drug among people living with HIV is alcohol consumption<sup>[43, 44]</sup>.

Moreover, in the long run, it is fact that non-adherence will not only leads to virological failure, but also increases the probability that the virus becomes resistant to different ARVs, thereby lowers the effectiveness of ART drug<sup>[45]</sup>. The reduced effectiveness of ART drug, gradually amplifies the probability that the patients’ infection will progress to a disease

AIDS. Thus, as studies revealed among people started ART, those with 40% to 80% of doses adhered were 3.6 times have probability to develop the disease AIDS compared with people with at least 95% adhered. On the other hand, those with poor ART adherence less than 40% of doses were 5.9 times more probably to develop AIDS [46].

**Conclusion:** This review concludes that there is no evidence as moderate level of alcohol intake can effect worsening progression of HIV/AIDS disease. However, the heavy level of alcohol intake worsens the progression of the disease, HIV/AIDS through affecting the behavioral and biological mechanism of the person living with HIV/AIDS.

ART drug has an action of declining HIV virus, which result in control of viral load in the blood plasma of the person living with HIV. This incidence gives the opportunity for enhancement of CD4 cell, which ultimately result in resolution of once occurred opportunistic infection and prevent the chance of acquiring new opportunistic infection. However, all ART drug's have their own side effects.

Alcohol intake has a positive relation with antiretroviral drug adherence. However, there are studies revealed that same rate of adherence among moderate and/or high level of alcohol consumers and non alcohol consumers. Moreover, alcohol intake affects the survival rate of people living with HIV, this is through the effect of increases poor adherence to ART drug, increases toxicity of ART drug, and increases an ART drug resistance level, as 95% adherence rate is required in order to ensure its effectiveness.

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