Research Article

Impact of Alcohol Consumption on Tuberculosis Progression and Treatment Response

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ABSTRACT

According to WHO tuberculosis is one of the top causes of death, and the leading cause from single infectious agent (above HIV/AIDS) millions of people continue to fall sick with disease each year. Alcohol is considered as major risk factor for death and holds 5th rank of 67 leading risk factor in 2010. The primary objective of this study is to identify potential mechanisms by which alcohol impacts on tuberculosis progression and treatment response. This Study involves systemic review of observational and experimental studies. Daily consumption of 40g ethanol increases the risk of resistance of pathogens towards the regimen. It alters the pharmacodynamic and pharmacokinetic parameters of the drugs. The consumption of alcohol affects the pulmonary immunity and makes them more susceptible for getting infections. Alcohol consumption only deteriorates the effectiveness of tubercular antibiotics and paves the way for multidrug resistance TB.

Keywords: Alcoholism, Tuberculosis, MTB, Tuberculosis therapy.

INTRODUCTION

TB is an infectious disease caused by the bacillus *Mycobacterium tuberculosis*. It typically affects the lungs (pulmonary TB), but can also affect other sites (extra pulmonary TB). The disease is spread when people who are sick with pulmonary TB expel bacteria into the air, for example by coughing.

According to WHO tuberculosis is one of the top causes of death, and the leading cause from single infectious agent (above HIV/AIDS) millions of people continue to fall sick with disease each year. Tuberculosis affects all countries and all age groups. 2017 estimates showed that 90% of cases were adults (aged ≥15 years). 64% were male, 9% were people living with HIV (72% of them in Africa) and two third were in 8 countries. India (27%), China (9%), Indonesians' (8%), Philippines (6%), Pakistan (5%), Nigeria (4%), Bangladesh (4%), South Africa (3%). Only 6% of cases were WHO region of the America, each of which had 3% of cases.[1]

About 10% of tuberculosis deaths globally have been attributed to alcohol as a risk factor.

MAJOR RISK FACTORS OF TUBERCULOSIS

	Relative risk of Active tuberculosis	Global prevalence rate (total population)	Population attributable factor (total population*)
HIV infection	26.7	0.8†	11.0
Malnutrition	3.2	16.7	26.9
Diabetes	3.1	5.4	7.5
Alcohol use >40g/day	2.9	8.1‡	9.8
Smoking	2.0	26.5‡	15.8
Indoor air pollution	1.5	71.2	22.2
Population attributable factor (percentage of tuberculosis cases attributable to the risk factor) †for 15-19 year age group. ‡for adults.			

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Alcohol is considered as major risk factor for death and holds 5th rank of 67 leading risk factor in 2010. [2] Alcohol abuse and alcoholism are major health problem that affect both men and women. Men are showing higher prevalence in alcoholism even though women are at high risk in alcohol related bodily damage. [3] It has been shown in many studies that the patients do consume alcohol especially those who engages in heavy episodic drinking than the patient do not consume alcohol have a delayed culture conversion, peak risk of treatment failure and pave the way to death

Alcoholism during the tuberculosis treatment affects the outcome and major influence on the pharmacokinetic and pharmacodynamic parameters of the drug.[4]

Research had conducted in mouse shows, rat which consumed ethanol produce a large mycobacterial burden, as well as impaired response to BCG vaccine. [5] Alcohol imparts alteration in the intestinal absorption of second line anti tubercular drugs. It also interferes with the metabolic pathways and protein binding of the regimen.[6,7] In the STG's published by WHO includes a target "strengthen the prevention and treatment of substance abuse, including narcotic drug abuse and harmful use of alcohol. The primary objective of this study is to evaluate major articles explaining the alcohol consumption and its effect on tuberculosis treatment and point out the negative effects create by alcohol in the outcome of therapy.

DISCUSSION

In the article of Meyers et. Al. a study protocol has studied about the alcohol consumption interfere with the patient adherence towards tubercular regimen. Their aim is Tuberculosis Treatment and Alcohol Use Study (TRUST).

The alcohol use also affects the first pass metabolism of the drugs. Studies on the impact of alcohol on Isoniazid are contrary. Then they conducted several studies in patients showing slow clinical response, those who failed in or early relapse found that alcohol cause higher levels of serum concentration of rifampicin. The TRUST then designed to improve the approach of regimen of tuberculosis for those who have co- morbid problem alcohol use. And for instance they found that high dose of Isoniazid and rifampicin found to be well tolerated in clinical trials. So they prefer the further studies to conduct regarding the pharmacokinetic and delayed absorption of these drugs in alcohol users. In such conditions substitution of drugs such as fluroquinolones to the patient and they are non – inferior to standard therapy. [4]

S. Imtiaz et. Al. conducted a Meta analysis in which alcohol consumption as a risk factor for tuberculosis. [8]As alcohol is one among the major risk factor for the occurrence of tuberculosis. They conducted the Meta analysis of alcohol consumption, alcohol related problems by means of questionnaires. Nonetheless there is some evidence to suggest that alcohol consumption impacts tuberculosis treatment compliance, leading to acquired drug resistance. This article gives crystal clear explanation about how alcohol affects tuberculosis by explaining two pathways. The consumption of alcohol terribly affects our immune system so that the patient becomes more susceptible to the tuberculosis. By through the alcohol consumption the ability of macrophage to detect new mycobacterium gets compromised.[9] In normal conditions the mycobacteria are easily removed by these macrophages. Alcohol consumption also decreases the cytokine production of monocyte that regulates the inflammation.[10,11] By affecting the macrophages the phagocytosis and superoxide production got impaired.[12,13] These all factors contribute to the immune system both acquired and innate. So easily they can get affect. [8]

A large acquisition of drug resistance has observed I patients have problem alcohol use primarily Isoniazid and rifampicin resistance. There is 8 fold increment of drug resistance to tubercular patient who have problem alcohol disorder. This alcohol disorder also leads to multiple drug resistant tuberculosis. The study conducted in rat shows increased acetylation / metabolic rates of tubercular drug in presence of ethanol. [2]

Lonnroth et. Al. in his studies shows alcohol use as a risk factor for tuberculosis. The risk of getting tuberculosis gets doubled to the patients who consume 40g ethanol per day and those have alcohol use disorder. Alcohol mainly renders the immune system and the host becomes more susceptible to tuberculosis.[14,15] The alcoholic consumption will favor the bacteria to became more resistant to drug mainly Isoniazid and rifampicin this will lead to MDRTB . Because of alcoholic consumption these drugs fail to obtain optimal drug levels. Alcohol may reduce the NO system response to mycobacterial infection, which may prevent the destruction of mycobacteria.[16] Studies have shown that alcohol consuming mice show significant higher pulmonary MTB burden.

According to pincock et. Al. shows that the importance of alcohol impact in tuberculosis patients. Alcohol get intoxicate the patients and become more susceptible to bacillus thereby resistant to therapy. This study unequivocally shows that alcoholism is a serious and frequent complication. [17]

According to Ashoka kumar et. Al. In many research studies heavy alcohol consumption repairs the immune system of individual and reactivation of tuberculosis.[18,19] Finally the alcohol exposure adversely affects the antigen specific T cell, so that the humoral immunity dominates the cell mediated immunity which is responsible for overcoming tuberculosis infection. By the consumption of alcohol hepatic damage, nutritional deficiency or hygiene factors etc. does happen. However, by whatever mechanism alcohol has a bad impact on reactivation of tuberculosis.[20] In addition alcohol has been shown to reduce the macrophage response to immune system modifiers like cytokines including IL-6, TNF, IL-8 and prevents the protection effect exerts by them.[22]

Robin room et. Al. shows that there is relation between alcohol consumption and tuberculosis risk. Alcohol consuming host are considered as immunocomprimised, because the incidence and severity of occurring disease in them are faster than abstainers. Macrophages in a healthy host are capable of killing 90% of inhaled mycobacteria.[23] If not happen so the bacteria itself grow in macrophage. In vivo and invitro studies shows that alcohol hinders antimycobacterial defense by diminishing mobilization, adherence, phagocytosis, and superoxide production of alveolar macrophage.[24,25] It is often more difficult to treat tuberculosis in HIV patients especially in terms of

pharmacological interactions. Because the concomitant administration of rifampin and protease inhibitors, both of them are sharing the CYP450 pathway leads to alterations in pharmacokinetics. Tuberculosis therapy lowers the serum concentration of protease inhibitors like lopinavir/ ritonavir and atazanavir.[26] Likely the commonly used TB antibiotics like rifampicin and rifabutin lowers the serum concentration of Nevirapine, Efavirenz and Delaviridine to sub therapeutic level. Sub therapeutic level of this antivirals leads to HIV resistance.[27] Alcohol mainly metabolize via oxidative and non- oxidative pathway. Primary steps involve the conversion of alcohol to aldehyde. Alcohol dehydrogenase is the enzyme catalyses the reaction, the microsomal ethanol oxidizing system involves several CYP450 isoenzymes. It has been shown that alcohol even in small concentration taken along with therapies results interactions and leads to toxicity.[28] This can be explained that the ethanol shows synergism to xenobiotics metabolized by CYP2E1.

According to Ping zhang et. Al. reported that alcoholic consumption will terribly affect the lung immunity. The immunity in the sense, alcohol spoils the sterility of the lungs. It is easy to occur infectious disease for those who consume alcohol. Bacterial pneumonia also can be easily propagated. The alcohol consumption affects both innate immunity and acquired immunity.[29]

Mycobacterial infections are more commonly observed in alcohol consumers. A lot of studies are conducted regarding this topic and found out the fact that alcohol impacts a 3 fold increase in the occurrence of pulmonary mycobacterial infections.[30-34] alcohol remains independent risk factors regardless the presence of other factors.[35, 36.] Antibiotic therapy becomes more crucial due to the presence of drug resistant microbes. In early clinical studies conducted in alcoholics, observed that no extensive disease progression in alcoholic patient than in non-alcoholics, but later on this get changed like they got more extensive disease progression, longer treatment course and are more likely to be non-compliant.[37] In 1964 Green et. Al. reported that alcohol suppress the pulmonary clearance of bacteria. IL-10 is an anti-inflammatory cytokine responsible for pro inflammatory cytokine expression and other aspects related to immune response.[38, 39] It has been found that alcohol enhances the production of IL-10. This is the one mechanism left behind all immunosuppressive properties of alcohol.[40]

Munk Me et. Al. reports that there is residence to associate gamma/ delta T cells with anti-mycobacterial immunity such as their preferential accumulation in inflammatory lesions, in necrotic areas of tubercular lymphadenitis and potent invitro stimulations by mycobacterium tuberculosis component. [41]

Tuberculosis mainly shows inflammation, proliferative inflammation and productive inflammation depending on the severity. The first process is the T cell recognition of antigen within the infected lung then differentiation occurs. NK cells are innate lymphocytes which are first line of defense against mycobacterial infection. Human alveolar macrophages and monocytes can serve as antigen presentation cells for delta gamma T cells. [42]

The increase of alcohol consumption has contributed to a dramatic rise in TB deaths between 1992-1995.[43] Mason et. Al. [16] in his studies reported that chronic alcohol consumption adversely affect the multiple function of CD4+ lymphocytes. CD8+ lymphocytes cells help to control over the mycobacterial cells.[44]

CONCLUSION

Alcohol remains as a major risk factor to tuberculosis, hence anyone continue to consume alcohol during the course of treatment only worsens the conditions. . Daily consumption of 40g ethanol increase the risk of resistance of pathogens towards the regimen The alcohol mainly affect the immunological response of a person , the ability of our immunity to fight against the newly entering pathogens especially the mycobacterium strains. Mainly the alcohol ruins the phagocytic capability of macrophage. Growth of Mycobacterium tuberculosis within the macrophage gets enhanced in the exposure of alcohol. Alcohol consumption only deteriorate the effectiveness of tubercular antibiotics and paves the way for multidrug resistance TB. Several research studies had shown the impact of alcohol among Isoniazid and rifampicin.

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