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REVIEW ARTICLE

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Alcohol and Noncommunicable Diseases: Part I Cardiovascular Diseases, Obesity, Respiratory Diseases, Depression, Liver Diseases

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Abstract

Alcohol is a popular drink and is consumed globally. It has received considerable scrutiny in its effect on health. Although its relationship with most cardiovascular diseases is J/U shaped, in general, alcohol intake can increase the risk of several diseases. Heavy intake may induce weight gain. Although no definite relationship has been noted with COPD, asthma, and lung cancer, it does appear to increase the propensity for the development of pneumonia. Its use is strongly related to chronic liver disorders. Its relationship with depression is bidirectional, and deleterious for both conditions. In general, alcohol intake of 2 drinks per day for men and 1 drink per day for women appears to be relatively safe.

Keywords: alcohol, non-communicable diseases, cardiovascular diseases, respiratory diseases, COPD, obesity, depression, liver diseases

1 | INTRODUCTION

Non-communicable diseases (NCD) are chronic and may lead to prolonged disability and premature death[1,2]. It is estimated that NCDs are responsible for over 70% of total global deaths each year[3]. The majority of these occur in low- and middle-income countries[4] and a severe financial burden[5]. The Sustainable Development Goals hope to reduce by 2030 (relative to 2015 levels) premature mortality from NCDs by one third[6].

The effects of alcohol on health can vary depending on the amount and pattern of intake[7–9]. In the United States, a standard drink contains 12–15 g of pure ethanol and this is present in 100–125 ml of wine, 240–300 mL of beer, and 30–37.5 mL of spirits[10]. Moderate alcohol intake is considered as two standard drinks a day for men and one standard drink a day for women[11,12]. Heavy drinking is defined as, high-dose intake, of >60 g/day in men and >40 g/day in women, usually taken over long term[13]. Binge drinking is considered as 4 or more drinks for women and 5 or more drinks for men over a 2-hours or in

one sitting[14,15]. Compulsive excessive alcohol intake may lead to alcohol use disorder (AUD)[16]. The National Institute on Alcohol Abuse and Alcoholism defines AUD as "a chronic relapsing brain disease characterized by an impaired ability to stop or control EtOH use despite adverse social, occupational, or health consequences"[17]. Although low to moderate alcohol intake may have some beneficial effects, alcohol consumption, in general, is associated with several negative health consequences[18]. Besides its impact on diseases mentioned in this manuscript, alcohol intake can cause cancers of the breast, mouth, throat, esophagus, liver, and colon[19], learning and memory difficulties (including dementia)[20,21], and mental health disorders, such as depression and anxiety[20,22]. Alcoholics tend to be more prone to trauma[20,23] and more likely to be involved in homicide, suicide, sexual assault, and violence[24–27]. Drinking alcohol during pregnancy can be extremely dangerous, and can increase the risk of miscarriage, stillbirth, or fetal alcohol disorder[28–30]. Alcohol poisoning is a medical emergency and is associated with extremely high blood alcohol levels[31]. The World Health Organization estimated that, in 2018, around 5% of global deaths were attributable to alcohol consumption[32].

The health effects of alcohol on NCDs are discussed in this two-part manuscript. Part I discusses the relationship between alcohol intake and cardiovascular diseases (CVD), chronic obstructive pulmonary disease (COPD), depression, and liver diseases. Part II discusses its impact on cancer, diabetes mellitus, kidney diseases, Alzheimer's disease, and arthritis.

Supplementary information The online version of this article (10.52845/CMI/2021-2-3-5) contains supplementary material, which is available to authorized users.

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2 | DISCUSSION

Cardiovascular diseases (CVDs) are an array of diseases that affect the cardiovascular system[33]. They include hypertension (HTN), coronary heart disease (CHD), stroke, heart failure (HF), cardiac arrhythmias, congenital heart disease, peripheral artery disease (PAD), vasculogenic erectile dysfunction (ED), and venous thromboembolism (VTE)[33]. They cause considerable morbidity and are the number one cause of mortality worldwide[34,35]. Almost one-third of all worldwide deaths are attributable to CVDs[36]. In 2016, chronic respiratory diseases were responsible for 7% of all global deaths[37,38]. Community-acquired bacterial pneumonia, although not an NCD, is strongly associated with alcoholism[39]. Pulmonary tuberculosis is also deleteriously affected by alcoholism40. Overweight refers to a BMI of 25–29.9 kg/m^2 while obesity exists when the BMI is $\geq$30 kg/m$^{2.41}$. Obesity affected 42.4% of the US population in 2017–2018[42]. Obesity is associated with several NCDs[43,44], especially type 2 diabetes mellitus (DM) and CVDs[45]. Depression is a common cause of emotional suffering[46]. It is closely associated with anxiety[47], dementia[48], DM[49], CHD[50], Parkinson's disease[51], epilepsy[52], pain[53], several cancers[54], osteoporosis[55], and irritable bowel syndrome[56]. Chronic liver pathologies are also common[57]. The major chronic diseases affecting the liver are hepatitis B virus (HBV)[58] and hepatitis C virus (HCV) [59]infections, steatohepatitis due to non-alcoholic fatty liver disease[60], alcoholic liver disease[61], hepatic cirrhosis[62], and primary hepatocellular carcinoma[63].

The development and progression of NCDs are dependent on several modifiable and non-modifiable risk factors. Non-modifiable risk factors include heredity, age, race, and gender. Socioeconomic, cultural, political, and environmental factors may also play a role. The major modifiable factors include diet, obesity, physical activity, and non-smoking. Alcohol consumption is also a modifiable factor that impacts NCDs and is discussed in this manuscript.

2.1 | CARDIOVASCULAR DISEASES

Light to moderate alcohol intake has been associated with a lower risk of cardiovascular disease[64]. Heavy consumption has been associated with deleterious CV outcomes including increased mortality[65]. Studies have established that alcohol consumption and CVD have a J- or U-shaped relationship[66]. Harmful CVD effects are also noted with binge drinking[67] and alcohol use disorder[68]. About 5% to 24% of hypertension cases are associated with ethanol consumption[69,70]. It is estimated that intake of 3 to 4 drinks per day raises the prevalence of hypertension by 50%, when compared with non-drinkers, while an intake of 6 to 7 drinks per day, increases the prevalence by 100%[71]. Binge drinking, in the short term, raises the blood pressure from 4 to 7 mmHg systolic and 4 to 6 mmHg diastolic[72−74]. Reduction in alcohol intake to <2 alcoholic drinks per day helps reduce the blood pressure in a dose-response manner[75]. Most studies indicate that alcohol consumption between 2.5 g/day and 30 to 60 g/day (mild to moderate drinking) is cardioprotective for both CV mortality and CHD mortality[76]. In a meta-analysis done by Bagnardi and colleagues, the risk of CHD was higher in binge and heavy drinkers, when compared with non-drinkers[77]. A similar pattern has been noted between alcohol intake and stroke[78]. Larsson et al in a systemic review and meta-analysis of 27 prospective studies concluded that light to moderate alcohol consumption (1-2 drinks/day) was associated with a lower risk of ischemic stroke, whereas heavy drinking (>2-4 drinks/day) was associated with an increased risk, especially of hemorrhagic stroke[78]. HF also appears to be less in individuals consuming <7 drinks/week[79]. Wannamethee et al. found that heavier drinking (≥5 drinks/day or ≥35 drinks/week) significantly increased the risk for HF[80]. Heavy alcohol intake may also induce alcoholic cardiomyopathy[81]. The causal relationship between alcohol intake and atrial fibrillation has also been known for a long time[82]. In a recently published study of 107,485 subjects followed for nearly 14 years, Csengeri et al. found that alcohol increased the risk of developing atrial fibrillation by16%, irrespective of the type of beverage consumed[83]. According to Koskinen and group, 5%-10% of all new episodes of atrial fibrillation are related to alcohol use[84]. Alcohol also plays a significant role in sudden cardiac death (SCD)[85]. In a study of the Finnish population, 4 of 10 victims of unexpected SCD exhibited evidence of alcohol intake before the fatal event[86]. Drinking during pregnancy is also harmful to the offspring, who may be born with congenital anomalies such as aberrant great vessels, atrial septal defects, and ventricular septal defects[87,88]. High levels of alcohol intake are also associated with an increased risk of PAD[89]. Wang et al, in a metanalysis, determined that light to moderate alcohol intake (<21 drinks/week) correlated with a decreased risk of erectile dysfunction[90]. Alcohol is also associated with many other CVD risk factors, such as sleep disorders[91], chronic kidney disease[92], weight gain[93], depression[94], and smoking[95]. The beneficial effects of alcohol are related to several actions[96−104]. Alcohol intake has an inverse association with T2DM (low to moderate intake)[96] and tends to increase HDL-C and apolipoprotein A-I[97−99] – these effects are CVD protective. Alcohol helps alter the atherosclerotic plaque composition and provides stabilization[100]. Alcohol also exerts several effects on factors involved in hemostasis, such as inhibition of platelet aggregation[101], lowering of fibrinogen levels[102] and plasma viscosity[103], as well as increasing levels of tissue plasminogen activator[104].

2.2 | OBESITY

The relationship between alcohol intake and obesity has been well studied[105,106.] Several studies have however produced conflicting findings[105,107]. Since alcohol provides extra calories (1 gram of alcohol provides 7.1 kcal (29 kJ), its intake with a regular diet may lead to a positive energy balance, and weight gain[108]. It is estimated that in the US, 16% of adult drinkers' total energy intake comes from alcohol[109]. However, alcohol's relationship with obesity is not that simple[110−112]. Several studies show that light-to-moderate alcohol intake is not associated with weight gain[105,108]. Moderate drinkers are more likely to follow healthier lifestyles, such as exercising regularly and eating fruits and vegetables, which tends to prevent weight gain[107,113]. Heavy drinking does tend to be associated with an increased risk of obesity[107].

A recent study confirmed that high alcohol consumption, especially binge drinking, was associated with higher risks of obesity in Korean men[114]. The increased tendency for men to gain weight with excessive alcohol drinking may be because they tend to drink about three times the amount of alcohol consumed by women and are more likely to drink beer and spirits[115]. Beer is rich in carbohydrates and may provide more calories[108,116.] Women tend to drink more wine, which is more likely to protect against weight gain[105]. Many other factors like socioeconomic status[117], behavioral changes[118], metabolic effects[119], etc. may also play a role. The available data, however, does not conclusively confirm a positive association between alcohol consumption and weight gain[105,120].

2.3 | RESPIRATORY DISEASES

There is no definitive association between alcohol intake and COPD, or lung cancer[121−123]. The association between alcohol abuse and pneumonia is, however, strong[124−126]. Although not an NCD, this association will be briefly discussed. AUD individuals are often affected by bacterial pneumonia with Streptococcus pneumoniae and Klebsiella pneumoniae[127,128]. These patients are more prone to bacteremia, sepsis, septic shock[126,129], and adult respiratory distress syndrome (ARDS)[130]. ARDS is almost four times more likely to occur in AUD patients than nonalcoholic patients[131,132]. Its presence is associated with poorer outcomes, including persistent hospitalization and death[133]. Abusers of alcohol are not only less likely to receive preventive antipneumococcal vaccination[134] but may also experience a less protective response[135]. Individuals with AUD are also more likely to develop tuberculosis (TB)[136] and respiratory syncytial virus infection[137]. Acute lung injury is also seen more commonly in alcoholics after major trauma, such as a motor vehicle accident, gunshot wound, or burns[138,139]. Excessive alcohol consumption increases susceptibility to pneumonia through multiple mechanisms[140−143]. These include a reduced immunity[140], altered microbial composition in the lung passages and alveoli[141], and an increased risk of aspiration[142]. Several other factors are also known to play a deleterious role[143].

2.4 | DEPRESSION

Alcohol misuse and depression commonly co-occur[144,145]. AUD individuals are many times more likely to have suffered from major depressive disorder[146,147]. Depression may also lead to alcohol abuse in some individuals[148]. The alcohol–depression relationship appears to be curvilinear, with alcohol abstinence and heavy drinking both being associated with a higher risk of depression[149,150]. Both conditions are interlinked and co-existence results in greater severity and a worse prognosis for both disorders than either condition independently[151−154]. Data indicates that men usually develop AUD before depression, while women develop depression and then progress on to AUD[155,156]. Patients who abuse alcohol may also exhibit more depression and tend to be not adherent to treatment[157]. Alcohol abstinence appears to significantly improve depressive symptoms in depressed individuals[158]. Antidepressants may be useful for the treatment of depression, alcohol dependence, or both, concurrently. Behavioral treatments are also effective in both[159−161.]

2.5 | LIVER DISEASES

Alcohol-related hepatoxicity appears to be the "oldest form of liver injury known to humankind"[162,163]. Alcohol-related damage to the liver is broadly called alcoholic liver disease (ALD) and includes alcoholic fatty liver, alcoholic hepatitis, and alcoholic cirrhosis[164]. About 90% of alcoholics develop alcoholic fatty liver (steatosis), about 25% develop alcoholic hepatitis, about 15% develop alcoholic cirrhosis, and about 10% develop hepatocellular carcinoma (HCC)[165−168]. Continued alcohol consumption usually leads to progression from alcoholic fatty liver to hepatitis and then on to cirrhosis. Alcoholic steatosis is usually asymptomatic (although some nausea, anorexia, and vomiting may be present)[169] and these patients exhibit mild elevations of gamma-glutamyl transpeptidase (GGT), aspartate aminotransferase (AST), and alanine aminotransferase (ALT) levels[170]. There is no abnormality of the serum bilirubin, International Normalized Ratio (INR), or albumin level. On liver biopsy, there

is microvesicular and macrovesicular fat accumulation within hepatocytes, minimal inflammatory reaction, and no hepatic fibrosis[171]. Abstinence will often revert these changes[172]. Patients with alcoholic hepatitis may have jaundice, pyrexia, unintentional weight loss, malnutrition, and an enlarged, tender liver[173]. There are moderate elevations in GGT, AST, and serum bilirubin[174]. Typically, the AST:ALT ratio is $\geq$ 2:1 in these patients[175]. The liver biopsy usually shows neutrophilic infiltration, hepatocyte necrosis, steatosis, and the presence of Mallory bodies[176]. Patients with alcoholic cirrhosis may also exhibit gynecomastia, palmar erythema, spider angiomata, testicular atrophy, parotid gland enlargement; signs of portal hypertension, and Dupuytren's contracture[177]. Laboratory findings often include hypoalbuminemia, hyperbilirubinemia, thrombocytopenia, and prolonged prothrombin time, and increased INR[173]. The liver biopsy usually reveals bridging fibrosis and regenerating nodules, and these are uniformly sized and micronodular[178]. In Western countries, alcohol is responsible for up to 50% of end-stage liver disease[179]. It is estimated that almost 50% of all deaths from cirrhosis in the world are related to ALD[180]. Potentiating factors for ALD include metabolic syndrome[181], diabetes[182], smoking[183], obesity[184], iron overload[185], and chronic viral hepatitis B or C[186,187.] Genetic factors may also play a role[188]. Although abstinence markedly reduces mortality[189], the only definitive treatment for ALD remains liver transplantation[190−193]. Alcohol abuse in patients with hepatitis B or HCV infection will often hasten the development of cirrhosis and its complications including HCC[194]. Alcohol abuse is reported to be responsible for approximately 15%–30% of HCC[195,196].

3 | CONCLUSION

Alcohol drinking is popular all over the world. This manuscript focuses on the relationship between alcohol intake and cardiovascular diseases, obesity, respiratory diseases, depression, and liver disorders. Alcohol consumption is generally safe, provided the consumption is in low to moderate amounts. It appears to be beneficial in these amounts for CVDs. However higher levels of alcohol consumption are harmful. Alcohol intake of more than 3 drinks per day in men and more than 2 drinks in women, should be avoided.

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