



Perspective

Alcohol & cancer: Evidence to action

Harmful use of alcohol is associated with morbidity and mortality worldwide alongside many physical and mental disorders including cancer. Numerous studies have indicated a causal association of alcohol consumption with oropharyngeal, laryngeal, oesophageal (squamous cell), colorectal, hepatocellular and female breast carcinoma¹⁻⁵. Despite this well-reported association, public awareness about the risk of alcohol consumption with cancer remains low. The Global Burden of Disease (GBD) 2016 study⁶ reported alcohol to be a major risk factor for deaths and disability-adjusted life years (DALYs) worldwide and accounted for 2.2 and 6.8 per cent of age-standardized female and male deaths, respectively. More importantly, consumption of alcohol was the leading risk factor for death in the 15-49 yr age group globally. 'The per capita alcohol consumption is defined as the amount of alcohol consumed in litres of pure alcohol per person (age >15 yr) in a year after adjusting for tourist consumption'¹. The global per capita alcohol consumption between 1990 and 2017 has increased from 5.9 to 6.5 l and is further expected to reach 7.6 l by 2030⁷.

Epidemiology and pattern of alcohol use in India

There has been a marked increase in alcohol consumption in low- and middle-income countries over the last decade. From 2010 to 2017, India recorded a 38 per cent increase in per capita alcohol consumption⁷. Consumption of country liquor predominates in rural areas, whereas Indian-made foreign liquor is the preferred alcoholic beverage in urban areas. Country liquor is known by various names such as *desi daru*, *tharra*, *toddy*, *tari* and *arrack* and contains about 33 per cent (w/v) ethanol⁸. Traditional rice beer preparations are unique to the North-East of India. Almost every tribe has a unique way of preparing alcoholic beverages using locally available plant components as starter cultures⁹. The prevalence

of alcohol use is high in the age group of 25-34 yr in the northeastern States. Mizoram and Meghalaya have reported a higher prevalence of alcohol use in comparison to other northeastern States as per the fourth round of district-level household survey¹⁰.

The per capita alcohol consumption is higher in India (5.7 l) as compared to the average for Southeast Asian region (SEAR) countries (4.5 l)¹. According to the report on the magnitude of substance use, there are about 160 million alcohol users in India in the 10-75 yr age group. There is a considerable gender difference in the use of alcohol, while 27.3 per cent of men use alcohol, the corresponding figure for women is 1.6 per cent. More importantly, there are about 57 million problem users and 29 million dependent users who require treatment intervention¹¹. A substantial proportion of alcohol users in India (around 43% of all users) consume more than four drinks on a single occasion¹¹. Furthermore, there is a huge treatment gap for alcohol use disorders in our country. According to the National Mental Health Survey of India 2015-2016¹², the treatment gap for alcohol use disorders was 86.3 per cent. For a given level of alcohol consumption, disadvantaged social groups suffer from greater alcohol-attributable harm as compared to individuals from upper socioeconomic strata¹³.

Alcohol and cancer

Alcohol induces carcinogenesis via multiple mechanisms. Acetaldehyde produced during alcohol metabolism is mutagenic to human DNA. The amount of acetaldehyde generated depends on the activity of ethanol-metabolizing enzymes, namely alcohol dehydrogenase and aldehyde dehydrogenase (ALDH)¹⁴. Due to genetic polymorphism, ALDH2 has extremely low activity in 40-50 per cent of Asians, which increases the risk of alcohol-related cancers. The oxidation of ethanol to acetaldehyde by the alternate

microsomal CYP2E1 pathway leads to the generation of reactive oxygen species and mediates DNA damage by lipid peroxidation and DNA adduct formation^{14,15}. Alcohol also causes carcinogenesis through epigenetic alterations. These include activation of oncogenes and inhibition of tumour suppressor genes by aberrant DNA methylation¹⁶. Alcohol consumption increases oestrogen levels by altering the hepatic redox state leading to reduced steroid degradation. In addition, chronic alcohol consumption leads to an increase in aromatase activity in peripheral tissues causing increased conversion of androgens to oestrogen¹⁷. Oestrogen is known to have proliferative effects on breast tissue and excess exposure to oestrogen is known to promote tumour growth¹⁷. Ethanol also has immunomodulatory properties and evidence suggests that it may modify innate immune responses by affecting antigen recognition and intracellular signalling¹⁸. A study¹⁹ from the northeast region of India has suggested that alcohol and tobacco act as important risk factors in the causation of head and neck cancer.

In 2016, 4.2 per cent of cancer deaths globally were attributable to alcohol consumption¹. A study comprising eight European countries from the EPIC cohort showed that 10 [95% confidence interval (CI): 7-13%] and three per cent (95% CI: 1-5%) of all cancer cases in men and women, respectively, were attributable to alcohol consumption and the fractions were highest for cancers of the upper aerodigestive tract and the liver²⁰. The cancer risk attributable to alcohol is also dose dependent. A meta-analysis reported a higher relative risk of cancers of the oropharynx and oesophageal SCC with heavy drinkers as compared to light drinkers and non-drinkers³. This study highlighted that the magnitude of risk varies with the quantity of alcohol consumed as well as the site of cancer. A recent large Australian cohort study reported an increased risk of alcohol-attributable cancers with increasing levels of intake. Consumption of more than 14 drinks per week as compared to less than one drink per week resulted in a higher absolute cumulative risk of 4.4 and 5.4 per cent in men and women, respectively, for alcohol-attributable cancers⁵. Tobacco and alcohol have a synergistic effect on cancers of upper aerodigestive tracts, though studies have clearly shown an independent association between alcohol and cancers of the upper aerodigestive tract after controlling for the effects of tobacco^{21,22}. Alcohol use among women increases the risk of breast carcinoma in a dose-dependent manner^{5,23}. Regular

alcohol consumption for greater than 10 yr increased the risk of breast cancer by threefold among women aged less than 50 yr²⁴.

In 2016, alcohol use contributed 6.6 per cent to the total cancer DALYs in India, second only to tobacco (10.9%), amongst the GBD risk factors²⁵. The WHO Global status report on alcohol and health estimated the alcohol-attributable fractions of cancer in India to be 6.5 and 0.8 per cent amongst males and females, respectively^{1,26}. A recent meta-analysis from India showed consumption of alcohol increases the overall risk of cancer, with an odds ratio (OR) of 2.32 (95% CI: 1.50-3.47) in case-control studies and relative risk of 1.52 (95% CI: 0.97-2.51) in cohort studies²⁷. A significant relationship between oral cancer and alcohol consumption (current and past drinkers) was observed in Kerala²⁸.

Alcohol-related health policies

Numerous studies have demonstrated the effect of alcohol cessation on cancer risk reduction²⁹⁻³¹. A meta-analysis showed that alcohol cessation was associated with an average risk reduction of two per cent per year as compared to 'current drinkers', *i.e.*, those with ongoing alcohol consumption, for pharyngeal and laryngeal cancers²⁹. A multi-country time-series analysis revealed a significant temporal association between alcohol sales and cancer mortality. Countries with increasing, decreasing and stable alcohol consumption over the years observed similar trends in cancer mortality a few years later³⁰. Strengthening alcohol-related policies can reduce cancer mortality attributable to alcohol. A 10 per cent increase in restrictiveness of alcohol-related policies resulted in an 8.5 per cent decrease in cancer mortality due to alcohol in the USA³¹. By 2025, the WHO also targets to reduce the harmful use of alcohol by at least 10 per cent. SAFER is a WHO-led initiative and action package that aims to reduce alcohol-related morbidity and mortality³². It provides five high-impact strategic actions that are practical, are cost-effective and can be incorporated into alcohol control policies by all countries to reduce alcohol-related harm.

In India, alcohol comes under the purview of the State government, and therefore, the laws governing sale, taxation and minimum legal drinking age (MLDA) vary from one State to another. In Tamil Nadu and Kerala, the State government has a monopoly over the sale and distribution of alcohol³³. This system permits the State to control over the pricing,

Box. Suggested strategies to reduce alcohol consumption and the associated harms.

Government monopoly on the sale and distribution of alcohol
 Uniform minimum legal drinking age throughout the country
 Ban on surrogate advertising and strict regulation of sponsorship activities that promote alcoholic beverages
 Increasing tax on alcoholic beverages
 Enforcement of stricter laws against the production of illicit alcohol
 Reduction of timings of sale of alcohol and the density of outlets
 Increasing awareness and community participation in alcohol control measures
 Narrowing the treatment gap by enhancing provision and access to treatment
 Promotion of research on alcohol and cancer in India (calculation of the State-wise alcohol-attributable fraction of various cancers).

safety and quality of alcohol and prevents its illegal sale and unauthorized distribution. The maximum permissible blood alcohol concentration for driving a motor vehicle in India is 0.03 per cent³⁴. There is a complete ban on the sale of alcohol in Bihar, Gujarat, Mizoram, Nagaland and Lakshadweep. Mizoram was a dry State till 2014 when the ban on the sale and consumption of alcohol was lifted. Mizoram has reinstated the ban on the sale and consumption of alcohol since 2019 when the new Mizoram liquor prohibition bill was passed³⁵. Alcohol use is prevalent throughout the country, including the States that have enforced prohibition. Chhattisgarh, Tripura and Punjab are amongst the highest alcohol-consuming States in the country¹¹. Underreporting is a challenge, especially in States that have prohibited alcohol such as Bihar and Gujarat. The MLDA also varies from State to State from 18 to 25 yr³⁴. Delhi has recently lowered the MLDA from 25 to 21 yr³⁶. As per the Cable TV Networks Amendment Bill 2000, liquor and tobacco advertisements are banned in India, but surrogate advertising by alcohol companies remains a major issue. Evidence suggests that alcohol promotion and advertisement increase the likelihood of alcohol use amongst adolescents³⁷. Peer pressure, clever surrogate advertising and innovative targeted marketing of young adults, with the involvement of social media, are thought to be the key factors that trigger the use of alcohol by the youth of our country.

Some strategies to reduce alcohol consumption and the harms associated with it are suggested in the Box.

Overall, consumption of alcohol is causally linked with cancer. The European Code of Cancer and the American Society of Clinical Oncology have also recommend minimizing alcohol consumption for cancer prevention^{38,39}.

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