High body mass index and alcohol intake increase deaths due to liver disease

Hart CL, Morrison DS, Batty GD, Mitchell RJ, Smith GD. (Public Health and Health Policy, Division of Community Based Sciences; Faculty of Medicine, University of Glasgow, Glasgow; Medical Research Council Social and Public Health Sciences Unit, Glasgow; Department of Social Medicine University of Bristol, Brisol, UK.) Effect of body mass index and alcohol consumption on liver disease: Analysis of data from two prospective cohort studies. *BMJ* 2010;340:c1240. doi:10.1136/bmj.c1240.

**SUMMARY**

An analysis of data from 2 prospective cohort studies among general and working Scottish men aged 18–92 years was done to ascertain whether alcohol and increased body mass index (BMI) act in conjunction to increase the risk of liver disease.

The 2 studies, Main (1965–68) and Collaborative (1970–73) were part of the Midspan studies.1 There were 9772 participants at baseline, of whom, after exclusion, 9559 participants were eligible. The mean (SD) age at screening was 47.3 (9.55) years. The participants were followed up till death or 31 December 2007, and were censored upon embarkation from the UK.

The 2 exposure variables, viz. weekly alcohol consumption and BMI were recorded at baseline. BMI was then categorized into under-weight (<18.5), normal weight (18.5 to <25), over-weight (25 to <30) and obese (≥30). Under-weight and normal weight categories were clubbed together for analysis. Alcohol consumption was categorized into non-drinkers, 1–7, 8–14, 15–21, 22–34 and ≥35 units of alcohol consumed per week. One unit of alcohol was equal to 8 g of ethanol. For calculation of BMI, height and weight were self-reported in the Main study, and were measured in the Collaborative study. Relative rate (RR), adjusted for age and study, of liver disease mortality and morbidity by BMI and alcohol consumption was estimated; under-weight/normal weight category and non-drinkers were taken as reference (RR=1).

The total number of deaths with liver disease as the main cause and with liver disease as a contributing cause was 80 and 146, respectively. BMI was strongly associated with mortality from liver disease. With liver disease as the main cause of death, the RR of mortality for over-weight and obese men was 1.78 (1.10–2.90) and 5.07 (2.57–10.0), respectively. With liver disease as the main cause of death, the RR of mortality for weekly alcohol consumption of 15–21 units, 22–34 units and ≥35 units was 5.61 (2.54–12.4), 7.35 (3.40–15.9) and 11.5 (5.31–25.0), respectively. Mortality due to liver disease was not associated with weekly alcohol consumption of <14 units.

An analysis of mortality due to liver disease by BMI and alcohol consumption showed that heavy drinkers (≥15 units per week) who were obese were at highest risk (RR 18.7 [6.91–50.7]) followed by over-weight (RR 7.35 [3.20–16.9]) and under-weight/normal weight (RR 3.43 [1.41–8.37]) men consuming the same level of alcohol. Obese men consuming even 1–14 units of alcohol in a week were also 5-times (RR 5.44 [1.40–21.1]) more likely to die from liver disease. Similar results were seen after combined analysis of morbidity and mortality among men in the Collaborative study.

All the above associations were also significant with death from liver disease as a contributing cause, and even after adjusting for various covariates such as social class, smoking, systolic blood pressure, height, bronchitis, FEV1, angina, ischaemia on electrocardiogram and diabetes; however, little attenuation was observed in most situations.

To observe the biological interaction, BMI and weekly alcohol consumption were categorized as dichotomous variables: Baseline, high BMI and high alcohol. High BMI was defined as being over-weight or obese, and high alcohol consumption as drinking >15 units of alcohol per week, respectively. The relative risk due to high BMI was 1.29 (0.60–2.80), whereas for high alcohol consumption was 3.66 (1.74–7.71). The relative excess risk due to interaction and synergy index calculated by Andersson method2 was 5.58 (1.09–10.1) and 2.89 (1.29–6.47), respectively. Thus, alcohol had a greater effect on mortality due to liver disease than high BMI, and they synergistically increased the risk more than their individual additive effect, showing an interaction between high BMI and high alcohol in causing mortality from liver disease.

**COMMENT**

The available evidence suggests a strong association of liver diseases with BMI and alcohol intake.3,4 This study adds that men having both high alcohol intake and high BMI are at a higher risk for morbidity and mortality due to liver disease, than expected by the two factors individually. This suggests that a targeted intervention is required to simultaneously limit both risk factors as a strategy for the primary prevention of liver disease. This is especially important as liver disease is often advanced by the time it is diagnosed.

The main strength of this study was that it was a large prospective cohort study comprising both the working and general population with a long follow up (median 27.3 years). Adjustments were made for known confounders.

However, a critical analysis of the study raises several methodological issues. The first is that the outcome, i.e. liver disease was not excluded in the participants at the beginning of the study, which is a thumb rule of a prospective cohort study. Since the Midspan studies were not conducted with this objective in mind, liver disease was not excluded by any means at the beginning of the study. Another limitation was that BMI was self-reported in one of the two studies rather than being measured. Alcohol intake was self-reported. No intermediate survey was conducted during the long follow up period to estimate the changing level of exposure with time. It has been reported elsewhere that reporting of alcohol consumption can be considered to be reliable, and the intake was stable over the years for 2686 men screened twice.5 However, misclassification bias cannot be ruled out completely for alcohol intake.

This study showed that liver disease mortality started increasing with weekly alcohol consumption of ≥15 units. Moreover, any level of alcohol intake was harmful in obese individuals; consumption of even 1–14 units of alcohol in a week was associated with mortality due to liver disease in them. However, it has been reported from a prospective cohort study that all cause mortality increases with weekly alcohol consumption of ≥22 units.6 A Working Group of the Royal College of Physicians, Psychiatrists and General Practitioners has endorsed that the ‘sensible’ limit of alcohol consumption for men is 21 units per week.4 Maybe, the ‘sensible’ limit of alcohol consumption for obese individuals needs to be revisited.

The findings of this study are useful in the Indian setting as well. The prevalence of alcohol intake in adult Indian men has been reported to be 32%.7 In India, the estimated total alcohol consumption (in litres of absolute alcohol) has been reported to be 12.9 per adult drinker per year.8 The prevalence of over-weight/obesity in adult Indian men has been reported to be 9.2%.7 Obesity is a known risk factor for non-alcoholic fatty liver disease (NAFLD). In a study in western India, the prevalence of

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*SELECTED SUMMARIES*

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NAFLD based on ultrasound in persons >20 years of age was 18.9%.
A hospital-based study in northern India reported an overall prevalence of NAFLD of 32.2%; the subjects with NAFLD had significantly higher values of BMI. Two-thirds of the subjects with NAFLD had BMI of >25.

In a study of 324 patients with hepatocellular carcinoma in a tertiary care hospital in India, alcohol was found to be the sole aetiology in 6% of cases; patients with alcohol-related hepatocellular carcinoma had poorer survival than those in which the carcinoma was associated with viral hepatitis. A history of significant intake of alcohol (>80 g/day for more than 5 years) was present in 14%, with a mean intake of 86 g/day and median duration of 17.5 years (range 0–40).

In a hospital-based study in northern India among 194 patients with cirrhosis, the aetiology for the liver disease was autoimmune, alcohol or cryptogenic in 27.8% of patients. It has also been shown that adult Indian men in England are at a higher risk of dying from alcoholic liver disease and other liver diseases than their English counterparts and natives of Bangladesh and Pakistan staying in the West, showing a higher risk in Indians. In a study of 1230 autopsies in western India, the overall prevalence of fatty liver was 15.8%, and alcohol was its most common risk factor.

Thus, the current literature suggests that the prevalence of liver disease, high BMI and alcohol consumption in India warrants public health action. The simultaneous presence of both exposures, viz. high BMI and high alcohol intake, increases the risk of liver disease morbidity and mortality beyond their individual risks. Both exposures are modifiable and amenable to interventions that target lifestyle changes.

REFERENCES


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