



# A Case Control Study on Alcohol Consumption and Pancreatitis

Keyur Surati<sup>1</sup>, Jainam Shah<sup>2</sup>, Yogesh Modiya<sup>3</sup>, Jatin Modi<sup>4</sup>, Kushal Prajapati<sup>5</sup>, Aneri Shah<sup>6</sup>

<sup>1</sup>AMCMET College and L.G. Hospital, Ahmedabad, Gujarat, India

<sup>2</sup>NHL Municipal Medical College, Ahmedabad, Gujarat, India

<sup>3</sup>NHL Municipal Medical College, Ahmedabad, Gujarat, India

<sup>4</sup>AMCMET College and L.G. Hospital, Ahmedabad, Gujarat, India

<sup>5</sup>AMCMET College and L.G. Hospital, Ahmedabad, Gujarat, India

<sup>6</sup>AMCMET College and L.G. Hospital, Ahmedabad, Gujarat, India

## ABSTRACT

**Introduction:** In Western population, a threshold of 5 drinks per day may exist for alcohol to increase pancreatitis risk. Given ethnic differences in alcohol metabolism, we examined the associations between smoking, alcohol, and pancreatitis in Western Indians.

**Methods:** A case control study was conducted in a surgery department of a hospital in western India. Information on drinking was collected by in-person interview. Baseline characteristics and alcohol consumption was compared between cases of pancreatitis and control (without pancreatitis).

**Results:** Baseline characteristics of cases and control are Among 4% of the cases and 2% of the control, bile stone was found to be present and this difference was also statistically not significant. Alcohol use was associated with pancreatitis in a dose-dependent way. Those who were taking heavy amount of alcohol had more than five and half-time risk of developing pancreatitis compared to those who are not taking alcohol.

**Conclusions:** Indians are more prone to alcohol-related pancreatitis than Westerners, and alcohol consumption is the leading cause of pancreatitis in India.

**Key Words:** Alcohol drinking, pancreatitis, case control

## INTRODUCTION

Acute pancreatitis (AP) can result in local complications, organ failure, and even death.<sup>1</sup> Chronic pancreatitis (CP) is characterized by repeated or persistent pancreatic injuries that result in chronic pain, malabsorption, and diabetes mellitus, all of which have a substantial medical and social impact.<sup>2</sup> AP and CP are typically thought to be independent entities, however new research suggests that they are both expressions of the same illness spectrum, with CP being the continuous disease process and AP being a distinct occurrence along the way.<sup>3,4</sup> In recent years, there has been a significant increase in hospital ad-

missions for pancreatitis throughout the world<sup>5</sup>, highlighting the urgent need for a better knowledge and control of pancreatitis risk factors to reverse this trend.

Heavy drinking (>5 drinks per day) increases the incidence of AP<sup>9</sup> and CP,<sup>6,7</sup> according to population-based cohort and case-control studies in Western populations. However, the link between alcohol and pancreatitis has not been well investigated in India, and it is unknown if a comparable threshold exists for alcohol to enhance pancreatitis risk in the Indian population.

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**Correspondence:** Dr. Jatin Modi (Email: pkushal89.kp@gmail.com)

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Because of genetic variations in the metabolism of these components, the health consequences of alcohol in India and the Western population may differ. Indian genetic variants increase acetaldehyde buildup following alcohol consumption,<sup>8,9</sup> suggesting that Indians are more prone to alcohol-induced pancreatitis. We used case-control research to look at the links between alcohol use and pancreatitis in the Indian population.

## MATERIALS AND METHODS

A case control study was assembled using participants from a hospital in western India. In-person interview was used to collect information on health status, health behaviour, and medical care use in survey participants.

Those who attended the surgery department of the hospital with complain of pain in abdomen were included in the study. After in-depth evaluation those who were having pancreatitis were included in the case group and among those who were free from pancreatitis were included in the control group. However, considering the large number of patients without pancreatitis, controls were taken into proportion of 2:1 with cases. During the whole year we 50 cases were recruited and matched 100 controls were included in the study.

Detailed information on alcohol use and other covariate information were collected by in-person interview at baseline. Alcohol consumption was classified into never, low (less than once per week), moderate (once per week or more but not to the extent of being intoxicated), or heavy (once per week or more and to the extent of being intoxicated).

Potential confounders considered in the analysis included age, education (lower than primary, Primary and high school, and graduate or higher level), physical activity (with or without regular activity), and gall stone/bile duct stone.

### Ascertainment of Pancreatitis and Gall Stone/Bile Duct Stone

A standard hospital protocol was followed for the diagnosis of pancreatitis. Ultrasound and its correlation with clinical findings were the main investigations for diagnosis of Pancreatitis. CT scan was used in some cases were recommended by experts. Because gallbladder/bile duct stone is also an important risk factor for pancreatitis, we identified whether the participants had the diagnosis of gallbladder stone and bile duct stone in inpatient and outpatient medical records during the follow-up period.

Statistical Analysis: Cox proportional hazards model was used to analyze the associations among smoking, alcohol drinking, and pancreatitis. The proportional

hazards assumption was checked by examining the cumulative hazard function in different groups of alcohol exposure. We used age as the time scale and adjusted for known risk factors of pancreatitis as potential confounders.

All statistical tests were 2 sided with an  $\alpha$  level of 0.05. All confidence intervals (CIs) were 95%. The data management and statistical analyses were performed with SPSS. Permission was obtained from institutional review board.

## RESULTS

Baseline characteristics of cases and control are described in Table 1. As mentioned in the table the mean age of cases was 43 years while it was 41 years. However, the difference was statistically not significant. There are 32% female in case group and 38% female in controls. The difference in sex ration was also statistically not significant similarly there was no significant difference in education income and physical activity in cases and control. Among 4% of the cases and 2% of the control, bile stone was found to be present, and this difference was also statistically not significant.

**Table 1: Baseline Characteristics of Pancreatitis cases and control**

	Case (%)	Control (%)	P value
Sample size n	50	100	-
Mean age (SD), yr	43.1±16.8	41.2±17.4	0.524
Female, n (%)	16 (32)	38 (38)	0.485
Education (%)			
Belo primary	6 (12)	13 (13)	0.921
Primary to high school	27 (54)	51 (51)	
Graduate and above	17 (34)	36 (36)	
Low income, %*	12 (24)	20 (20)	0.572
Physical activity	13 (26)	32 (32)	0.449
Biliary stone, %#	2 (4)	2 (2)	0.473

\*Household income less than INR10,000 per month.

#Gallbladder or bile duct stone.

**Table 2: Univariate Analysis of Drinking and Pancreatitis**

Alcohol intake	OR (95 % CI)	P
Never	1	
Low	1.08 (0.56–2.08)	0.81
Moderate	2.08 (1.13–3.83)	0.018
Heavy	5.50 (3.00–10.09)	<0.001

Table 2 shows univariate regression analysis of alcohol intake and pancreatitis. Those who had never taken alcohol were taken as a reference group for calculating risk of pancreatitis. Low alcohol consumer has 1.08 times risk of developing pancreatitis which was statistically not significant. However moderate drinkers has slightly raised risk compared to the never smoker. Those who are taking moderate

amount of alcohol had two times more risk of developing pancreatitis compared to those were not taking alcohol and this difference was statistically significant ( $p < 0.05$ ). Those who were taking heavy alcohol have much higher risk of developing pancreatitis compared to those who are not taking alcohol. Those who were taking heavy amount of alcohol had more than five and half-time risk of developing pancreatitis compared to those who are not taking alcohol.

## DISCUSSION

In this case control among Indian population, we found that alcohol use was associated with pancreatitis in a dose-dependent way. These results are in sharp contrast with studies conducted in Western population and lend support to significant ethnic differences in the risk of alcohol-related pancreatitis.

This study discovered that the Indian population appears to be more prone to alcohol-related pancreatitis than the Western population. Although it is necessary to consume more than 4 to 5 drinks per day (i.e., extremely heavy drinking) to increase the risk of pancreatitis in the Western population,<sup>6,7,10</sup> In our study, the risk of pancreatitis was raised at all levels of alcohol use, with a clear dose-response relationship. Many Indians carry variant alleles of the aldehyde dehydrogenase-2 gene (ALDH2\*2) and alcohol dehydrogenase-1B gene (ADH1B\*2), whereas whites seldom do.<sup>11</sup> These genetic variants are linked to the formation of acetaldehyde after consuming alcohol, which might explain the discrepancy. Alcohol dehydrogenase converts alcohol to acetaldehyde dehydrogenase-2 (ALDH2) into acetic acid, which is then metabolized by aldehyde dehydrogenase.<sup>8</sup>

Acetaldehyde is poisonous and can cause pancreatic stellate cell activity/fibrosis as well as the production of harmful free radicals.<sup>12,13</sup> After drinking, heterozygotes and homozygotes of ALDH2\*2 had 5 times and 18 times greater blood acetaldehyde levels,<sup>14</sup> resulting in the typical "Asian flush" (facial flushing, nausea, and tachycardia)<sup>8,9</sup>. Asians are more susceptible to alcohol-related malignancies. ADH1B\*2 enhances acetaldehyde build up after drinking by facilitating alcohol to acetaldehyde conversion (homozygote with 40 times higher  $V_{max}$ ).<sup>15</sup> More research is needed to confirm if ALDH2\*2 and ADH1B\*2 increase the incidence of alcohol-related pancreatitis and can explain why our group is more susceptible to alcohol. Meanwhile, because ALDH2\*2 and ADH1B\*2 are also found in other Asian nations, such as Japan and Korea, it will be crucial to learn more about the role of alcohol in pancreatitis in these populations.

Our findings reveal a large pancreatitis disease burden in our community, which may be due to rising alcohol intake and vulnerability to alcohol-related pancreatitis. In India, alcohol consumption and the prevalence of alcoholism have skyrocketed, with per capita average yearly consumption increasing by a

factor of ten. Our data suggest that alcohol is a major risk factor for pancreatitis in our community, and that control measures are urgently needed to prevent additional disease burden rises.

Our research offers various advantages. The high quality of the interviews, as well as extensive information on sociodemographic and behavioural characteristics, allowed for the correction of possible confounders.

The research includes flaws as well. In mild and early Chronic Pancreatitis, functional and structural abnormalities of the pancreas might be inconspicuous, eluding clinical identification and diagnosis.<sup>2</sup> In research on the incidence and prevalence of Chronic pancreatitis, under-detection is a prevalent flaw. Second, the amount of alcohol drunk was not measured by the number of drinks drunk, making it impossible to compare our findings to those of other research and to determine the precise shape of the alcohol-pancreatitis dose-response relationship.

## CONCLUSION

In conclusion, Indians are more prone to alcohol-related pancreatitis than Westerners, and alcohol consumption is the leading cause of pancreatitis in India. To prevent additional increases in the disease burden of pancreatitis in our society, control measures to curb growing alcohol use are required. Identification of high-risk people and effective preventative actions may be made easier if the mechanism of increased sensitivity to alcohol-related pancreatitis is understood.

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