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ORIGINAL RESEARCH

In India, alcohol consumption is correlated with impaired β-cell function independent of body mass index

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ABSTRACT

Type 2 diabetes is linked to alcohol consumption. The link between alcohol consumption and β-cell function, on the other hand, is still unknown. The purpose of this study is to look at the link between them. 675 Indian men between the ages of 20 and 75 were enlisted. The participants were first categorised into four categories: never drinkers, abstainers, light drinkers (0.1-19.9 g/day), moderate drinkers (20.0-39.9 g/day), and heavy drinkers (≥40.0 g/day), and then into two subgroups based on their body mass index (BMI) (BMI< 25kg/m^2 and BMI ≥25kg/m^2). Confounders such as age, smoking status, BMI, waist circumference (WC), blood pressure, lipids, and blood uric acid were used to adapt the analysis process.Alcohol intake was linked to lower homeostasis model assessment of β-cell function (HOMA-β) scores when compared to never drinkers, regardless of BMI. In the BMI<25kg/m^2 group, the homeostasis model assessment of insulin resistance (HOMA-IR) was strongly connected with alcohol consumption history, and in the BMI≥25kg/m^2 group, it was significantly correlated with alcohol consumption. The findings imply that alcohol intake is linked to β-cell dysfunction in Indian community-dwelling men, regardless of BMI.

Keywords: Alcohol consumption, β-cell function, Body mass index, Indian men

INTRODUCTION

Indian economic progress has resulted in a steep increase in alcohol use [1], as well as a significant increase in the prevalence of diabetes. According to Sethuram et al.'s study [2], in 15 Indian states, the total prevalence of diabetes was 73% (95 percent confidence interval: 70%-75%). Type 2 diabetic patients' β-cell function is compromised earlier and more prominently in Indian Americans [3]. Alcohol consumption has been linked to insulin resistance (IR) and obesity in previous research [4-7], but the effect of alcohol consumption on β-cell secretion is unknown. The goal of this study was to see if alcohol consumption was linked to β-cell function, although the link could be muddled further by an increase in obesity among community-dwelling men in Indiancities.

METHODS

SUBJECT

The study sample was selected from the central population registry (five years) of people aged 20 to 75 living in Bhubaneshwar, India. We chose 1865 people at random to participate in a face-to-face investigation. Participants were informed about the study's goal and procedures.

Self-reported history of diabetes, cardiovascular illness, pancreatitis, liver, or kidney disease were all exclusion factors, and because the prevalence of alcoholics among women was low, we only included men in our study. In the end, 675 males were successfully recruited for the study.

ASSESSMENTS OF ALCOHOL CONSUMPTION

A standardised questionnaire was used to collect data on alcohol consumption, including drinking history (years), drinking frequency (days or months), and average intake of each type of beverage (beer, wine, hard liquor (>38 percent v/v), and light liquor (≤38 percent v/v). According to the Indian Food Composition Table 2004, daily alcohol intake was calculated in grams by adding monthly ethanol intake of each type of beverage and then dividing by 30.5 with the following content: 50mL of hard liquor, 21.85g; 50mL of light liquor, 15.75g; one 640mL bottle of beer, 31.36g; and 50 mL of wine, 5.2g[8].

All subjects were separated into five groups: never, abstain (>0.5 year) [9], light (0.1-19.9 g/day), moderate (20.0-39.9 g/day), and heavy drinkers (≥40 g/day) [10], and then into overweight (BMI ≥25 kg/m^2) and non-overweight (BMI<25 kg/m^2) groups [11].

EVALUATION OF RISK FACTORS

Clinical questionnaires were used to collect data on demographic variables and risk factors. Before the exam, all subjects were instructed to fast for at least 12 hours and refrain from drinking, smoking, or engaging in strenuous physical activity. A qualified medical professional used a standardised technique to gather anthropometric data and fasting blood samples. The participants' body weight, height, waist circumference (WC), and blood pressure were all measured. Weight (kg)/ $height^2$ was used to compute BMI (m2). An automatic biochemical analyzer was used to measure the plasma levels of fasting blood glucose (FBG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C), triglyceride (TG), and blood uric acid. Radioimmunoassay was used to measure fasting insulin (Fins).The homeostasis model used Levy's computer model to calculate the β-cell function (HOMA-β) and insulin resistance (HOMA-IR). (HOMA-IR= FBG×FIns/22.5; HOMA-β =20×FIns/FBG-3.5; HOMA-β =20 FIns/FBG-3.5).

STATISTICAL ANALYSIS

SPSS17.0 was used to conduct the statistical analysis. The mean±standard deviation was used to express all of the data. Variance, chi-square, and covariance were used to compare study characteristics between alcohol intake categories. For FBG, HOMA-β, and HOMA-IR of

participants categorized by BMI, multiple regression analysis was employed to assess the contribution of each confounding factor. A $p<0.05$ value was considered significant. Multiple testing was corrected using the Bonferroni adjustment.

RESULTS

Table 1: Characteristics of study participants according to alcohol consumption

	Abstainers	**Current drinkers**			**Never drinkers**	**P-value**
N	35	213	123	61	243	
Age(year)	52 ±13	50 ±13	44 ±11	36 ±12	44 ±15	<0.001
WC(cm)	91.7 ±9.70	88.45 ±8.57	90.07 ±8.84	87.9 ±11.38	87.53 ±9.76	0.069 0.180
TG(mmol/L)	1.65 ±0.70	1.76 ±1.75	2.31 ±1.85	1.87 ±1.50	1.60 ±1.12	0.006 0.035
FBG(mmol/L)	5.56 ±0.96	5.24 ±0.71	5.89 ±1.93	5.56 ±1.65	5.29 ±0.8	<0.001 <0.001
TC(mmol/L)	5.39 ±1	5.26 ±0.95	5.65 ±0.93	5.10 ±1.10	5.10 ±0.87	<0.001 0.018
LDL-C(mmol/L)	3.50 ±0.89	3.26 ±0.75	3.50 ±0.80	3.16 ±0.86	3.25 ±0.73	0.013 0.168
HDL-C(mmol/L)	1.33 ±0.26	1.41 ±0.30	1.45 ±0.32	1.41 ±0.29	1.36 ±0.26	0.033 0.049
BMI(kg/m^2)	26.34 ±4.29	25.63 ±3.19	26.47 ±3.07	25.44 ±3.16	25.52 ±3.89	0.164 0.205
Uric(μmol/L)	348.1± 90	343±74.53	354.04 ±88.44	338.45 ±63.78	331.9±67.9	0.155 0.387
Fins(mmol/L)	9.19 ±5.59	8.76 ±5.9	8.9 ±5.7	8.4 ±4.7	10.8 ±15.1	0.159 0.316
HOMA-IR	2.29 ±1.5	2.09 ±1.4	2.30 ±1.6	2.13 ±1.59	2.65 ±4.7	0.343 0.584
HOMA-β	98.30 ±58.04	110.5 ±71.05	90.92 ±67.53	94.07 ±57	126.7 ±128.19	<0.001 0.001
DBP(mmHg)	84 ±11.39	82.59 ±10.69	83.13 ±10	79.04 ±10.77	80.11 ±10.19	0.006 0.136
SBP(mmHg)	128.90 ±20	125.87 ±16	124.65 ±17.7	120.11 ±15.9	122.36 ±14.7	0.005 0.206

Table 1 shows the characteristics of the participants. Current drinkers accounted for 58.8% of the participants, with 15.4% consuming more than 40 g of alcohol each day. Young guys made up the majority of the heavy drinkers (average age of 37 years). Nonsmokers accounted for 48.7%, former smokers for 12.9 percent, and current smokers for 38.4%. In the mild, moderate, and heavy groups, the percentage of current smokers was 46.5 percent, 53.7 percent, and 36.1 percent, respectively. There were notable variances between the groups. FBG levels were greater among moderate-to-heavy drinkers after controlling for age and

smoking. Moderate drinkers had higher TG and TC levels. In moderate-to-heavy drinkers, HOMA- β was lower.

The abstainers (22.9 percent) had the highest proportion of FBG≥6.1mmol/L [13] and the light drinkers had the lowest (8.9 percent). Moreover, half of the subjects (58.1%) were overweight, and moderate drinkers had more overweight subjects than never drinkers (69.1 percent vs. 53.1 percent). The connection between alcohol and FBG, HOMA-IR, or HOMA-β, grouped by BMI, was shown, excluding abstainers. The FBG was found to be higher in moderate-to-heavy drinkers for total and BMI≥25 kg/m2 subjects after adjusting for age and smoking. HOMA-IR was shown to be lower in drinkers than in never drinkers, although there was no statistically significant difference. HOMA-β was found to be lower in all alcohol consumption groups, regardless of BMI. When controlled for multiple testing, there was still a significant difference in most comparisons, especially between never and heavy drinkers ($p<0.0083$).

Factors	**BMI<25 (kg/m^2)**		**BMI=Total**		**BMI≥ 25(kg/m^2)**	
	β	p	β	p	β	p
Age(year)	0.007	0.005	0.07	0.051	0.037	0.442
Uric(μmol/L)	0.030	0.630	-0.065	0.085	-0.089	0.062
Alcoholhistory(year)	0.097	0.115	0.031	0.466	0.035	0.485
TC(mmol/L)	0.132	0.011	0.244	<0.001	0.277	<0.001
TG(mmol/L)	0.099	0.095	0.152	<0.001	0.169	<0.001
Alcoholconsumption(never/abstainer/light/moderate/heavy)	0.100	0.085	0.060	0.049	0.065	0.188
Constant	4.191	<0.001	3.759	<0.001	3.710	<0.001
Smoke(never/past/current)	0.024	0.686	-0.055	0.150	-0.049	0.330
R^2	0.084	<0.001	0.10	<0.001	0.096	<0.001
WC(cm)	0.043	0.466	0.045	0.220	0.019	0.330

Table 2 Multiple regression analysis of various confounding factors for FBG by BMI

Tables 2 show the results of multiple stepwise regression analysis with FBG, HOMA-IR, and HOMA-β as objective variables and numerous confounding variables as explanatory variables. In all BMI≥25kg/m^2 participants, TG and TC were substantially and independently linked with higher FBG. In patients with a BMI of less than 25 kg/m^2, age and TC were linked to higher FBG. In all BMI<25 kg/m^2 people, alcohol history was significantly and independently linked with lower HOMA-IR, whereas alcohol consumption was significantly and independently associated with decreased HOMA-IR in the BMI≥25 kg/m^2 subjects. WC was significantly and independently associated with increased HOMA-IR in all and BMI≥25 kg/m^2 subjects. Uric was significantly and independently associated withHOMA-IR. Alcohol consumption and age were correlated with decreased HOMA-β and WC was correlated with increased HOMA-β independent of BMI.

Table 3: Multiple regression analysis of various confounding factors for HOMA-IR and HOMA-β by FBG

Factors	HOMA-IR				HOMA-β			
	FBG ≥ 6.1mmol/L (N=77)		FBG<6.1mmol/L (N=598)		FBG≥6.1mmol/L (N=77)		FBG<6.1mmol/L (N=598)	
	β	p	β	p	β	p	β	p
Age	-0.21	0.002	-0.05	0.219	-1.28	<0.001	-1.37	<0.001
TG (mmol/L)	0.02	0.873	0.07	0.055	0.07	0.086	0.08	0.052
Alcohol history	-0.02	0.881	-0.08	0.001	-0.02	0.911	-0.01	0.909
Smoke (never/past/current)	-0.15	0.211	-0.04	0.343	0.03	0.506	0.01	0.870
BMI (kg/m^2)	0.20	0.059	0.21	<0.001	9.30	<0.001	0.12	0.782
TC (mmol/L)	-0.05	0.689	0.02	0.648	-0.02	0.838	-0.02	0.646
Alcohol consumption	-1.20	0.039	-0.03	0.448	-8.89	<0.001	-9.25	<0.001
BMI (kg/m^2)	0.20	0.059	0.21	<0.001	9.30	<0.001	0.12	0.782
Uric (μmol/L)	0.12	0.234	0.003	<0.001	0.06	0.187	0.07	0.094
R^2	0.14	0.004	0.26	<0.001	0.21	<0.001	0.18	<0.001
WC (cm)	0.16	0.137	0.12	0.115	0.12	0.071	3.12	<0.001
Constant	17.39	<0.001	-3.79	<0.001	-51.02	0.040	-83.81	0.006

Table 3 shows the results of multiple stepwise regression analysis with HOMA-IR and HOMA-β as objective variables and numerous confounding factors as explanatory variables, all of which were classified by FBG. Alcohol use and age were significantly and separately linked with decreased HOMA-IR and HOMA-β in the person with FBG≥6.1mmol/L, but BMI was significantly and independently associated with increased HOMA-β. Alcohol history (year) and alcohol intake were linked to lower HOMA-IR and HOMA-β, respectively, in subjects with FBG n<6.1mmol/L, but BMI and WC were linked to higher HOMA-IR and HOMA-β, respectively.

DISCUSSION

In the development of type 2 diabetes, β-cell dysfunction is important [14]. The study's key conclusion is that HOMA-β levels fell at all levels of alcohol consumption, and the link between them was irrespective of body mass index. The HOMA-IR and alcohol intake were found to have a U-shaped association, with a low mark in light drinkers.

Pulsatile insulin secretion, hyperglycemic clamp, intravenous glucose tolerance test, oral glucose tolerance test (OGTT), and other procedures are being used to measure and evaluate β-cell function. However, because these procedures are more sophisticated and involve large numbers of patients, they are not suitable for large-scale clinical trials [15].

FBG is far more convenient to evaluate because it is intimately linked to β-cell functions

[16]. Piche's [17] study found that participants with increased fasting glucose levels had reduced insulin production and lower insulin sensitivity, even after controlling for age, sex, BMI, and WC. Increased fasting plasma glucose levels were also found to signal gradual disintegration of β-cell functions in India [18] and could be utilised to guide clinical treatment strategy. This suggests that FBG is a useful indicator for assessing β-cell function.

In this study, 11.4 percent of the participants had high FBG levels (≥6.1mmol/L), with more than half of them being current drinkers. Light drinkers had the lowest proportion of individuals with FBG≥6.1mmol/L. Alcohol use, TG, and TC were the most important risk variables for impaired FBG in the multiple regression analysis, although the R2 was only 0.109, suggesting that additional risk factors such as genetics, environment, and lifestyle may have a greater impact on FBG.Similarly, a Korean study found that not only moderate but also heavy drinking in Korean men was associated with impaired fasting glucose or type 2 diabetes [15]. The FBG level of heavy drinkers was lower than that of moderate drinkers in this study, although there was no statistical difference. The reason for this could be that the number of strong drinkers was limited, and the majority of heavy drinkers were young.

Meanwhile, light drinkers had reduced FBG, TG, TC, HOMA-IR, and HOMA-β levels, but moderate-to-heavy drinkers had the opposite. This suggested that moderate drinking could help to improve metabolic markers. There were few investigations on the link between alcohol use and β-cell dysfunction at the time. This study found that, regardless of BMI, the HOMA-β level was lower in the four categories of drinkers than in the never drinkers, indicating that alcohol use may have an impact on β-cell secretion. Alcohol use was also a key determinant in β-cell dysfunction, regardless of BMI, according to the multiple regression analysis. After correcting for age, sex, race, diet, body weight, and sports, Crandall's study [19] found that increased alcohol consumption was related to reduced insulin secretion at all levels of insulin sensitivity.These findings backed up our research. Alcohol intake was also highly related to β-cell dysfunction in those with FBG6.1mmol/L when categorised by FBG. This shows that alcohol may have a role in the progression of pre-diabetes to diabetes. The following are some of the proposed mechanisms by which alcohol use causes β-cell dysfunction: 1) Chronic alcohol consumption is a risk factor for chronic pancreatitis, with chronic pancreatitis being reported in 50 to 70% of patients [20]; 2) Chronic alcohol consumption accelerates pancreatic fibrosis [21]; 3) Chronic alcohol consumption may cause some optical and structural abnormalities in β-cells[22], which may contribute, at least in part, to β-cell functional disturbance. Of course, further human research is required.

The link between alcohol use and IR type 2 diabetes has raised a lot of eyebrows. There was a "U" or "J" association between them in several research [23]. However, the "U" or "J" curve was not observed in another research [16-18]. Alcohol consumption and its health consequences are more complicated. Chronic excessive alcohol consumption degraded insulin-stimulated glucose uptake and increased insulin resistance by up-regulating Gs in isolated rat skeletal muscle [9] and down-regulating GLUT4 expression in rat cardiac muscle [20], as well as affecting adipokine contents in both VAT and sera in a dose-response manner [1].It's unclear how alcohol can help people with insulin resistance. Alcohol may impede gluconeogenesis in the liver by increasing the NADH (reduced form of nicotinamide adenine dinucleotide)/NAD (nicotinamide adenine dinucleotide) ratio and the lactate/pyruvate ratio,

according to one idea [22].

The HOMA-IR level was lowest in light drinkers in this study, which showed a "U" shape, but no statistical difference was found. Our multiple regression analysis revealed that among overweight men, HOMA-IR was adversely linked with alcohol dose, whereas in non-overweight men, alcohol history played a larger effect. Previous research has only looked at the influence of alcohol dose on HOMA-IR, ignoring the impact of alcohol history (length). All of them, we believe, were essential elements in the development of HOMA-IR. Increased BMI was found to be a significant predictor of insulin resistance [23]. We also discovered that people with a BMI≥25kg/m^2 had a higher level of HOMA-IR (Fig. 2) and that subjects with a BMI≥25kg/m^2 had more heavy drinkers than subjects with a BMI<25kg/m^2 (16.6 percent vs. 14.1 percent). As a result, the effect of drinking dose on HOMA-IR is more significant, whereas the change in HOMA-IR in participants with a BMI<25kg/m2 requires a longer time to notice.

Obesity, in addition, is a separate risk factor for IR [13]. After accounting for alcohol intake, smoking, blood lipids, and uric acid, this study found that WC was still significantly related to higher IR. Over half of the participants were overweight, with moderate-to-heavy drinkers being the most overweight. This could mean that alcohol intake has a significant impact on Indian men's obesity. Considering that WC [14] was a stronger indication of visceral fat, this finding suggested that alcohol may worsen insulin resistance in overweight adults by increasing visceral fat.

Finally, among Indian men, a roughly U-shaped relationship between alcohol consumption and HOMA-IR was discovered. When age, smoking, lipids, and blood uric acid levels were taken into account, alcohol intake and obesity were found to be significant risk factors for β-cell dysfunction. Because β-cell dysfunction plays a critical role in the development of type 2 diabetes [15], it may be more useful to focus on the link between alcohol consumption and insulin secretion.

Obviously, this research had certain limitations. First, this study relies on self-reporting of alcohol consumption, disease history, and other factors, which could lead to errors and bias. Second, numerous additional variables, such as the type of binge, the diet, and family history of diabetes, have yet to be investigated. Third, there were not many strong drinkers. Fourth, as with other studies, the cross-sectional study design reduced the ability to investigate the causal association between alcohol and β-cell activity. Prospective population-based research must be conducted.

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