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# A study on alcohol consumption on cardiovascular biomarkers: A prospective study.

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**Abstract:**

**Objective: Aim:** An important mechanism responsible for increased cardiovascular risks in chronic excessive alcohol use is the pro-oxidant effects of alcohol. There are some emerging risk factors like: lipoprotein, High-sensitivity C-reactive protein (hs-CRP), Lipid profile, Prothrombotic and pro-inflammatory factors that play an important role in the pathogenesis of atherosclerosis. So we investigated the relation between the levels of cardiovascular biomarkers & the degree of alcohol intake in alcoholic subjects.

**Materials and Methods:** The present study was carried out in the Department of Psychiatry and in association with the Department of Biochemistry, Tertiary Care Teaching Hospital over a period of 6 months. 90 Alcoholic subjects, in the age group 18-60 years, randomly selected from the areas and ward, in and around were included in the study. Estimation of Serum Level of hs-CRP & Lp (a) by turbidimetric immunoassay. Serum Cholesterol by CHOD-POD & Triglycerides by enzymatic colorimetric method. LDL cholesterol was calculated by Friedwald equation.

**Results:** The mean serum Total cholesterol levels showed no significant association across different alcohol drinking groups. The mean TG & LDLc levels were significantly ($p<0.05$) higher in occasional (175.50 ± 62.22), (131.15 ± 12.26) drinkers and heavy drinkers (177.49 ± 21.53), (115.35 ± 16.30) than that of low-moderate (193.47 ± 24.15), (34.46 ± 2.49) & moderate (176.48 ± 21.56), (111.11 ± 14.27) drinkers respectively. In the occasional drinkers (35.23 ± 6.21) the mean serum HDL cholesterol levels were significantly elevated as compared to the low-moderate (34.46 ± 2.49), moderate drinkers (35.30 ± 5.44) and heavy drinkers (31.25 ± 5.02).

**Conclusion:** Our study suggests that heavy drinking may lead to significant dyslipidemia and inflammatory changes and adversely affect the cardiovascular system but has shown a beneficial effect of occasional drinking on HDLc levels and moderate drinking on hs-CRP levels. However a large scale study needs to be done to confirm these beneficial effects of occasional to moderate drinking on the cardiovascular system.

**Keywords:** Alcoholics, Lipid profile, hs-CRP & Lp (a).

## Introduction

Controversy has surrounded the association between alcohol intake and cardiovascular disease (CVD), which remains the leading global cause of death. [1] Observational studies have repeatedly demonstrated a lower risk of CVD with light to moderate alcohol intake compared

with either abstinence or heavy consumption, suggesting J- or U-shaped epidemiologic associations. [2] However, the observed cardiac benefits of alcohol have been hypothesized to be the product of residual confounding because of favourable lifestyle, socioeconomic, and behavioural factors that tend to coincide with modest alcohol intake. [3]

Alcohol use has complex effects on cardiovascular (CV) health. The associations between drinking and CV diseases such as hypertension, coronary heart disease, stroke, peripheral arterial disease, and cardiomyopathy have been studied extensively and are outlined in this review. Although many behavioural, genetic, and biologic variants influence the interconnection between alcohol use and CV disease, dose and pattern of alcohol consumption seem to modulate this most. [4]

Low-to-moderate alcohol use may mitigate certain mechanisms such as risk and haemostatic factors affecting atherosclerosis and inflammation, pathophysiologic processes integral to most CV disease. [5] But any positive aspects of drinking must be weighed against serious physiological effects, including mitochondrial dysfunction and changes in circulation, inflammatory response, oxidative stress, and programmed cell death, as well as anatomical damage to the CV system, especially the heart itself. Both the negative and positive effects of alcohol use on particular CV conditions are presented here. [6]

We aim to assess the relationship between alcohol consumption and adverse health outcomes, including cardiovascular diseases and mortality, in a homogenous population. We used a composite of CVD and total mortality as primary outcomes, to illustrate an overall pattern of alcohol consumption and chronic disease risk, as did previously. [7] As a secondary analysis, associations between alcohol intake and each condition were examined. Our hypothesis was that low to moderate alcohol consumption would be associated with lower risk of major chronic diseases and mortality, compared to none or high alcohol consumption.

## Materials and Methods

The present study was carried out in the Department of Psychiatry and in association with the Department of Biochemistry, Tertiary Care Teaching Hospital over a period of 6 months.

*Inclusion criteria*

90 Alcoholic subjects, in the age group 18-60 years, randomly selected from the areas and ward, in and around were included in the study.

Exclusion criteria

Patients of diabetes mellitus, hypertension, chronic liver diseases, cardiovascular diseases, renal diseases, thyroid dysfunction, Smokers, Pregnant females, Patients on anti-inflammatory drugs, Patients suffering from infectious and inflammatory diseases were excluded from the study.

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Control

Total 40 Age & sex matched nonalcoholic subjects, randomly selected from the areas and wards, in and around, meeting the exclusion criteria.

Study procedure

A detailed history from alcoholic subjects comprising type of alcoholic beverages consumed, amount, frequency and duration of alcohol consumption was recorded on participant preformat. Subjects were classified into different groups based on frequency and amount of alcohol consumption.

After a written informed consent, all patients were subjected to detailed history and thorough clinical examination. Alcoholic subjects were classified into different categories based on their alcohol intake in terms of drinks/week as group I (occasional drinkers, 1-10 drinks/week), group II (low-moderate drinkers, 11-20 drinks/week), group III (moderate drinkers, 21-30 drinks/week) and group IV (heavy drinkers, >30 drinks/week). {*A Standard drink consists of 10-14 gram of ethanol, which is equal to 12 Ounce or 300-360cc of Beer (5-7%), 120-150ml of wine(12%), 30-45ml of hard liquor (40-50% alcohol)}

Taking all aseptic precautions, about 5 ml of blood was drawn by venipuncture from a peripheral vein, with a disposable syringe. Sample for serum hs-CRP, lipoprotein (a) and lipid profile, were collected in plain vials in the morning after an overnight fast & were allowed to stand for 30 minutes at room temperature for the retraction of clot. It was then centrifuged at 3000 revolutions per minute for 10 minutes to separate the serum. The serum was stored at 4°C in the refrigerator for analysis. Care was taken to avoid hemolysis of samples.

Estimation of Serum Level of High sensitivity C-reactive protein & Lipoprotein (a) by turbid metric immunoassay using semi auto analyzer**.** Serum Cholesterol by CHOD-POD & Triglycerides by Enzymatic colorimetric method using (Roche Diagnostics) Roche/Hitachi Cobas c 501 analyzer. LDL cholesterol was calculated by Fried Ewald equation.

Statistical analysis

Using the statistical Package for the Social Sciences (SPSS 25) for windows, to analyze the data for qualitative significance unpaired t test and Duncan Multiple Range Test (DMRT) were used to show the inter-category significance ($p<0.05$).

**Results**

In table 1, maximum was male 87.7% in case group and least were female.

**Table 1: Distribution of gender Between cases and control**

| **Gender** | **Case N=90 (%)** | **Control N=40 (%)** |
|---|---|---|
| **Male** | 79 (87.7%) | 33 (82.5%) |

| | | |
|---|---|---|
| **Female** | 11 (12.2%) | 7 (17.5%) |
| **Total** | 90 (100%) | 40 (100%) |

**Table 2: Distribution of age among the cases and control**

| **Age group (years)** | **Case N=90 (%)** | **Control N=40 (%)** |
|---|---|---|
| 18-30 | 13 (14.4%) | 7 (17.5%) |
| 31-40 | 17 (18.8%) | 9 (22.5%) |
| 41-50 | 29 (32.2%) | 11 (27.5%) |
| 51-60 | 31 (34.4%) | 13 (32.5%) |
| Total | 90 (100%) | 40 (100%) |

In the present study most of the cases were in the age group 51-60 years (34.4%) followed by 32.2% within 41-50 years, 18.8% within 31-40 years and 14.4% within 18-30 years in Table 1

**Table 3: Lipid profile in the studied subjects among the cases and control**

| **Parameter** | **Case Mean ± SD** | **Control Mean ± SD** |
|---|---|---|
| Total cholesterol (mg/dL) | 211.28±27.43 | 151.63± 27.86 |
| TG (mg/dL) | 196.28±21.28 | 136.22±19.33 |
| HDLc (mg/dL) | 37.63±4.98 | 41.13±6.26 |
| LDLc (mg/dL) | 134.39±18.19 | 83.26±17.72 |
| VLDLc (mg/dL) | 39.25±4.25 | 27.24±3.86 |

*Significance level as compared to controls: $p < 0.05$.

The mean total cholesterol & LDLc levels were significantly raised ($p < 0.05$) in cases (211.28±27.43) & (134.39±18.19) as compared to controls (151.63± 27.86), (83.26±17.72) respectively. The mean HDLc level was also significantly decreased ($p < 0.05$) in cases (37.63±4.98) as compared to controls (41.13±6.26) in Table 3.

**Table 4: Serum levels of Lipid Biomarkers in cases according to alcohol intake**

| **Parameters (mg/dl)** | **Degree of alcohol Intake** | | | |
|---|---|---|---|---|
| | **1- 10 drinks/week (n=21) mean ± SD** | **11- 20 drinks/week (n=31) mean ± SD** | **21-30 drinks/week (n=18) mean ± SD** | **>30 drinks/week(n= 20) mean ± SD** |
| **Total cholesterol( mg/dL)** | 201.48 ±31.26 | 193.47±26.15 | 176.48±21.56 | 177.49±21.53 |
| **HDLc (mg/dL)** | 35.23 ±6.21 | 34.46 ±2.49 | 35.30 ± 5.44 | 31.25 ± 5.02 |
| **LDLc** | 131.15 ±12.26 | 125.77±11.2 | 111.11 ±14.27 | 115.35 ±16.30 |

| | | | | |
|---|---|---|---|---|
| **(mg/dL)** | | 0 | | |
| **TG (mg/dL)** | 175.50 ±62.22 | 166.18±14.26 | 150.375±13.25 | 154.43±56.11 |

*Different alphabets shows significance (P<0.05) with each other and same alphabets shows no significant (P>0.05) association with each other.

The mean serum Total cholesterol levels showed no significant association across different alcohol drinking groups. The mean TG & LDLc levels were significantly (p<0.05) higher in occasional (175.50 ± 62.22), (131.15 ± 12.26) drinkers and heavy drinkers (177.49 ± 21.53), (115.35 ± 16.30) than that of low-moderate (193.47 ± 24.15), (34.46 ± 2.49) & moderate (176.48 ± 21.56), (111.11 ± 14.27) drinkers respectively. In the occasional drinkers (35.23 ± 6.21) the mean serum HDL cholesterol levels were significantly elevated as compared to the low-moderate (34.46 ± 2.49), moderate drinkers (35.30 ± 5.44) and heavy drinkers (31.25 ± 5.02) in Table 4

**Table 5: Serum levels of Biomarkers of cardiovascular inflammation in cases and controls**

| **Parameter** | **Cases** (n= 90) **Mean ± SD** | **Control** (n= 40) **Mean ± SD** |
|---|---|---|
| **Serum hs-CRP (mg/dL)** | 0.367±0.18 | 0.23±0.04 |
| **Serum Lp(a) (mg/dL)** | 26.24±2.40 | 20.93±6.26 |

*significance level as compared to controls: p < 0.05

The mean serum hs-CRP & Lp (a) levels were significantly raised (p < 0.05) in cases (0.367 ± 0.18), (26.24 ± 2.40) as compared to the controls (0.23 ± 0.04), (20.93 ± 6.26) respectively in Table 5

**Table 6: Serum levels of Biomarkers of cardiovascular inflammation in cases according to alcohol intake**

| **Parameters** | **Cases** | | | |
|---|---|---|---|---|
| | **1 -10 drinks/week (n=21) mean ± SD** | **11- 20 drinks/week (n=31) mean ± SD** | **21-30 drinks/week (n=18) mean ± SD** | **>30 drinks/week (n= 20) mean ± SD** |
| **Serum hs-CRP (mg/dL)** | 0.324± 0.14 | 0.318± 0.14 | 0.281± 0.15 | 0.272±0.10 |
| **Lp (a) (mg/dL)** | 20.26±2.40 | 22.20±2.43 | 23.46±2.50 | 27.33±3.27 |

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The mean serum hs-CRP level in the moderate drinkers (21-30 drinks/week) (0.281 ± 0.15) and heavy drinkers (>30 drinks/week) (0.272 ± 0.10) was significantly lower ($p<0.05$) as compared occasional drinkers (1-10 drinks/week) (0.32 ± 0.14) and low-moderate drinkers (11-20 drinks/week) (0.318 ± 0.14) respectively. Whereas the mean serum Lp (a) levels in different alcoholic groups did not show anysignificant ($p>0.05$) association. Table 5.

**Discussion**

In this large-scale prospective study including approximately 100,000 Chinese adults, were found that participants who reported consuming 1–150 g/wk. of alcohol had lower risk for CVD, cancer, and mortality, relative to non-drinkers and heavy drinkers. This amount of alcohol intake is equivalent to approximately no more than 10 servings of alcohol/wk. The range identified is consistent with most global dietary guidelines for low-risk drinking cutoffs (100 to 300 g/wk). [8] However, in this Indian cohort the lowest risk was observed among those with ~ 25 g/wk., equivalent to ~ 2 servings per week. Because the mechanism for each CVD disorder or site-specific cancer is different, both individual and composite outcomes should be taken into consideration when developing dietary policy. Currently in India, there is no national policy on alcohol sales restrictions and no dietary guidelines for alcohol containing beverages. This study provides evidence for recommending light consumption of alcohol.

In our study, the mean serum Total cholesterol levels showed no significant association across different alcohol drinking groups. The mean LDLc levels were significantly higher ($p<0.05$) in occasional and heavy drinkers as compared to low-moderate and moderate drinkers (Tables 3 and 4). In our study the mean serum HDL cholesterol levels in the occasional drinkers were significantly elevated as compared to the low-moderate, moderate drinkers and heavy drinkers

Our study in an Asian cohort supports prior observations of a J-shaped association between alcohol consumption and CVD. [9] We found an overall lower CVD risk at consuming 1- 10 drinks/week alcohol/wk. In secondary analyses, we identified different patterns for specific CVD. A J-shaped curve was found for stroke and an almost linear inverse association was found for myocardial infarction and heart failure. As previously suggested, alcohol could impact CVD risk via its favorable effects of raising HDL-C concentration and reducing inflammation, and its unfavorable effect of increasing blood pressure. [10] However, the impact of these risk factors on different CVDs (i.e., myocardial infarction vs stroke) could be different, thus potentially mediating their association with alcohol consumption. For example, the association of HDL-C and myocardial infarction could be stronger than its association with stroke. [11] Further, high blood pressure has consistently been identified as the strongest risk factor for stroke risk. [12] These factors may contribute to the different patterns in the associations between alcohol and myocardial infarction or heart failure, vs stroke.

We found J-shaped association between alcohol consumption and cancer, especially non-alcohol-related cancers. The causal pathway of alcohol is not fully understood for all cancer types. For female breast cancer, for example, alcohol could increase risk by altering levels of

estrogen and estrogen receptors. [13] Hence, the inverse association between light alcohol intake (≤ 25 g/wk) and overall cancer risk was likely driven by the lower risk of non-alcohol-related cancer. However, limited statistical power due to small number of individual non-alcohol-related cancer cases precluded us from addressing this hypothesis.

Our result showed that light to moderate alcohol intake was consistently associated with lower risk of total mortality and CVD- and cancer-specific mortality. The former observation is consistent with the result from a recent meta-analysis of 87 studies which found that compared to non-drinkers or high alcohol intakes, low-volume alcohol consumers (9.1–174 g alcohol/wk) had 14% lower risk of overall mortality. [14]

In other Chinese cohort the association between alcohol consumption and major chronic disease risk was modified by smoking status. Because alcohol consumption and smoking are common addictive behaviors and co-vary, smoking could mask the effect of alcohol alone on health status. [15] As expected, although the protective association of light-to-moderate alcohol to CVD, cancer, and mortality was significant in both smokers and non-smokers, it was stronger in non-smokers. However, even for lung cancer, light alcohol consumption still showed lowest risk, compared to non-drinkers and heavy drinkers. [16]

The potential biological mechanism of the overall beneficial effect of alcohol consumption is not fully understood, but may include altering cholesterol concentrations, especially HDL-C and triglyceride concentrations, improving insulin sensitivity, [17] decreasing the inflammatory process during cell signaling, decreasing platelet aggregation and blood clotting, and interaction with genetic variation in alcohol dehydrogenase polymorphism. [18] Although recent genetic epidemiological studies suggested that drinkers with ALDH2 deficiency had a more favorable profile for CVD risk factors, independent of alcohol consumption, no relation was reported in non-drinkers. [19]

In previous cross-sectional analysis based on Kailuan Study 2014, salt intake was highly correlated with overall diet quality. [16] Alcohol consumption was calculated based on self-report frequency and usual amount of drinking. This could introduce measurement error, which might attenuate or magnify the association. However, drinking habits and amounts are common conversations with family and friends in many areas of India. [17] Therefore, self-reported consumption could be an acceptable measurement of the true intake with low risk of systematic bias, as supported by a significant correlation between self-report alcohol and longitudinal HDL-C concentration in the Kailuan Study. [16]

Of note, HDL-C concentration has been widely used for the validation study of self-report alcohol intake. Genetic variation in ALDH2, and consequent metabolic response to alcohol (e.g., skin flash) were not available. The participants of the Kailuan Study lived in a traditional Indian industrial community, which limits its generalization to other populations. However, the homogenous nature of the study population reduced variance in potential confounding and enhanced internal validity. Finally, due to the nature of Kailuan cohort, women were underrepresented (22.3%), and most women (96.7%) did not report consuming

any alcoholic beverages, which is consistent with Chinese national nutritional survey and other reports. [16]

## Conclusion

In our study demonstrated significant changes in lipid profile (decreased level of serum HDLc, increased level of serum LDLc & Tg) in heavy drinkers (>30drinks/week) and in occasional drinkers (1-10 drinks/week) had significantly high HDLc levels as compared to moderate (21-30 drinks/week) and heavy drinkers. Levels of Lp (a) were significantly elevated in all categories of alcoholics as compared to non-alcoholic controls while hs-CRP level was comparatively less in moderate and heavy drinkers to those of low moderate and occasional drinkers.

Our study suggests that heavy drinking may lead to significant dyslipidemia and inflammatory changes and adversely affect the cardiovascular system but has shown a beneficial effect of occasional drinking on HDLc levels and moderate drinking on hs-CRP levels. However a large scale study needs to be done to confirm these beneficial effects of occasional to moderate drinking on the cardiovascular system.

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