### **Original Research Article**

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# Blood pressure profile in freshly diagnosed alcohol dependence syndrome patients

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#### **ABSTRACT**

**Background:** Alcohol consumption and raised Blood pressure (BP) are among the top five risk factors responsible for the growing global non-communicable diseases (NCD) burden. The present study was undertaken to study the relationship between alcohol dependence syndrome (ADS) and hypertension and the effect of reduction in alcohol consumption on BP.

**Methods:** A prospective observational study was conducted at a tertiary care hospital over a period of 02 years from 08 Oct 2016 to 02 Oct 2018. A total of fifty freshly diagnosed ADS patients with BP in the hypertensive range after the withdrawal subsided, were recruited into the study. The study group was subjected to repeated BP measurements, serum Gamma glutamyl transferase (GGT) measurements and status of alcohol consumption at 03, 06, 09 and 12 monthly intervals. The data was analyzed with ANOVA, Post-hoc Bonferroni and Pearson's correlation tests.

**Results:** There was a statistically significant mean decrease in systolic and diastolic blood pressure from the baseline till 03 months and between 03 months and 06 months of follow-up. The correlation between GGT levels and systolic and diastolic BP at different time intervals showed that there was a statistically non-significant weak positive correlation at baseline (r value=0.125) (p value=0.38). During follow-up period there was a negative correlation between GGT and systolic BP at 12 months (r value=-0.40), which was statistically significant. The correlation between alcohol consumption and BP at different time intervals showed a moderate positive correlation at baseline with systolic BP(r value=0.478), which was statistically significant.

**Conclusions:** This study evaluated changes in blood pressure occurring during Alcohol dependence syndrome treatment. Observed decreases in systolic and diastolic blood pressure were substantially accounted for by reductions in alcohol consumption and occurred largely in the first 03 months of treatment. There was no significant fall in systolic blood pressure between 06 months and 01-year duration of follow-up.

Keywords: Alcohol dependence syndrome, Blood pressure, GGT

#### INTRODUCTION

Alcohol dependence Syndrome (ADS) is a chronic disease with many medical complications and up to 40% of hospitalized patients with ADS receives treatment for the same. Individuals consuming an average of 03 or more

units of alcohol per day have 3-4 times the prevalence of hypertension as compared to control subject.<sup>2</sup>

Hypertension is the most common diagnosis in OPD and alcohol is a cause in a significant number of patients, which is often overlooked and underreported. Although,

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the exact pathophysiology for alcohol induced Hypertension remains undefined, the various proposed mechanisms are alcohol causing dysfunction of baroreceptors, sympathetic dysregulation leading to discharge of sympathetic amines, dysregulation of Renninangiotensin-aldosterone system, increased cortisol level, endothelial and oxidative stress.<sup>3-5</sup>

Multiple studies have confirmed the association between heavy drinking and development of hypertension.<sup>6-8</sup>

Based on the available literature, guidelines for clinical management of hypertension from the National institute for Health and Care Excellence, recommends that all patients undergoing assessment or treatment for hypertension should receive initial and periodic lifestyle advice regarding reduced intake of alcohol. The American Heart Association guidelines for the prevention and treatment of high Blood pressure (BP) recommend limiting daily alcohol intake to 02 or less drinks for men and 01 or less drinks for women.<sup>9,10</sup>

Moderation of alcohol to less than two standard drinks per day (one drink equals 12 oz of beer, 5 oz of wine, or 2 oz of liquor) has been included as a beneficial lifestyle change in the treatment of hypertension.<sup>11</sup>

Although it is well established that heavy alcohol consumption increases the risk of hypertension, there is limited research about the effect of reduction of alcohol intake on blood pressure. A systematic review and meta-analysis including 36 trials with 2865 participants revealed that reduction in alcohol intake was not associated with a significant reduction in blood pressure in people who drank two or fewer drinks per day. However, in people who drank more than two drinks per day, a reduction in alcohol intake was associated with greater blood pressure reduction. <sup>13</sup>

The present study was undertaken to study the BP in freshly detected ADS patients and to study the BP profile of these patients for 01 year thereafter. It is intended to bring forth the relation between ADS and hypertension and the effect of reduction in alcohol consumption on BP.

#### **METHODS**

This was a prospective observational study in which fifty freshly diagnosed ADS patients in our hospital, over a period of 2 years from 08 October 2016 to 02 October 2018 were included. The study population consisted of serving male defence personnel, who were diagnosed as alcohol dependence syndrome belonging to different geographical areas of India.

#### Inclusion criteria

Freshly diagnosed patients of alcohol dependence syndrome.

#### Exclusion criteria

The subjects who were on drugs of addiction (other than alcohol), hypertension due to secondary causes and the subjects of ADS who had a relapse.

After Hospital Ethics committee approval, all consecutive fresh cases of alcohol dependence syndrome admitted in the Psychiatry department of the hospital were included in the study. Patients with BP in the hypertensive range (>140/90 mm of Hg) were included int he study. Subjects were included in the study after at least 10 days of stopping alcohol intake and after the features of alcohol withdrawal had subsided. The period of follow- up was 01 year. Thorough history, physical examination and laboratory evaluation were undertaken and patients complications of alcohol or hypertension or other significant co-morbidities were excluded from the study. Patients with history of other addictive drugs were also excluded. All the subjects included in the study were assigned to Motivational enhancement therapy (MET) for ADS in addition to anti-craving medications. 13 Reduction in average self-reported alcohol intake was used to assess follow-up. This was supported by follow-up GGT values.

A well-maintained, properly calibrated and validated electronic BP machine was used for measurement of BP. BP was measured after a period of rest in a quiet room for 15 minutes. Patient should not have had consumed coffee or tea or had a meal in the last half an hour prior to the measurement. Patient should have emptied their bladder before the measurement of BP. The BP was measured in the sitting position with the arm supported at the level of the heart, back supported and legs rested flat on the ground and uncrossed. BP measurements were taken in the upper arm and on both arms in the first visit. It was ensured that the cuff of the bladder encompasses two-thirds of the arm circumference. Three BP readings were taken at oneminute interval between the individual readings and the average calculated. Clothing from the arm was removed before taking the BP measurement. Neither the patient nor the observer talked during the measurement.

All possible causes of secondary hypertension were ruled out with the help of USG abdomen, renal doppler study, 2D-echocardiography, thyroid function test and biochemical investigations. All such patients who were found to have any secondary causes of hypertension were excluded from the study.

Patients were also interviewed regarding the history of any comorbid conditions like cerebrovascular accidents, pre-existing hypertension, ischemic heart disease, diabetes mellitus or any other chronic illness. Patients with the above comorbidities other than hypertension were excluded from the study. Those with known hypertension and on antihypertensive medication were included in the study.

Assessment of Alcohol consumption- The Quantity-Frequency (QF) method was used to assess alcohol consumption. The patients were asked to report the number of days per week they drank, how much they typically consumed on a given drinking day and the type of alcoholic beverage that they drank. The total quantity of alcoholic beverage consumed was divided by total number of days (7 days) to obtain the average quantity of a particular alcoholic beverage per day. Based on the percentage of alcohol content in the type of alcohol beverage consumed, the average quantity of pure alcohol consumed (in mL) per day was calculated. Given the specific weight of alcohol is 0.793 g/mL, the quantity of alcohol consumed in grams was calculated by multiplying with 0.793. One standard drink is equivalent to 14 grams of pure alcohol (ethanol). The number of standard drinks per day was calculated by dividing the average quantity of pure alcohol consumed per day (grams) by 14. This provided the number of standard drinks consumed per day by the patient in the study.

The quantity of pure alcohol consumed was calculated by the following formula:

Quantity of pure alcohol consumed per day (in mL)=Quantity of a particular type of alcohol beverage consumed per day (in mL) X The conversion factor for the particular type of alcoholic beverage

The quantity of pure alcohol consumed in grams per day = Quantity of alcohol consumed in mL X 0.793.

Number of standard drinks was calculated by the formula:

Number of standard drinks consumed per day = Quantity of pure alcohol consumed per day (in grams) /14.

Drinking was estimated by self-reporting on the basis of a questionnaire -Alcohol use disorder identification test-C (AUDIT-C), a three- question test adapted from the original AUDIT developed by the World Health Organization specifically for use in primary health care.<sup>14</sup>

Initial GGT values were recorded from laboratory reports of the patients during his initial admission as a fresh case of ADS. These values of GGT were later correlated with the reduction in BP values to look for a possible association between the two variables.

Serial BP recordings were made at 3 monthly intervals for duration of 01 year from the baseline for all the subjects. The patients were followed up for one year while they were on treatment for ADS.

#### Statistical method and data analysis

Database was created in MS Excel (Version 2007) and analyzed using IBM SPSS (Statistical Package for Social Sciences) statistics software version 22. Data was presented in numbers, percentages and mean + SD. Other

statistical methods used in the data analysis were analysis of variance (ANOVA), Post-hoc Bonferroni and Pearson's correlation as per the nature of data. For statistical significance p value was considered at 5% level (p<0.05).

#### **RESULTS**

The mean  $\pm$  SD age of the patients was 35.62 $\pm$ 6.2 years with a range from 26-52 years. The mean $\pm$  SD BMI was 18.6 $\pm$ 2.64. The mean $\pm$ SD number of drinks per day was 3.5 $\pm$ 1.21 with a range of 1.5-5.5 drinks/day. The mean $\pm$ SD value of initial GGT was 106.12 $\pm$ 68.97 with a range from 18.0-305.

Table 1: Conversion factor to calculate the quantity of pure alcohol consumed based on the alcohol by volume percentages of different types of alcoholic beverages.

Type of alcohol beverage	Percentage of alcohol	Conversion factor to calculate quantity of pure alcohol consumed (in ml)
Rum, Whiskey, Brandy	42.8	0.428
Vodka	37.5	0.375
Beer	08	0.08

The mean  $\pm$  SD initial systolic and diastolic BP in study population was  $143.34\pm6.56$  mm Hg and  $94.4\pm5.29$  mm Hg respectively. The mean  $\pm$  SD systolic and diastolic BP at 03 months follow-up was  $133.94\pm6.72$  and  $89.06\pm4.86$  mm Hg. The mean  $\pm$  SD systolic and diastolic BP at 06 months follow-up was  $131.26\pm6.75$  and  $87.02\pm5.34$  mm Hg. The mean  $\pm$  SD systolic and diastolic BP at 09 months follow-up was  $130.48\pm8.31$  and  $87.16\pm5.53$  mm Hg. The mean  $\pm$  SD systolic and diastolic BP at 12 months follow-up was  $130.82\pm8.87$  and  $88.04\pm6.37$  mm Hg.

## Comparison of the systolic BP from baseline with various follow-up stages (at 03, 06, 09 and 12 months)

The mean difference of systolic BP from the baseline at 3 months was 9.4 (p=0.00), at 06 months 12.08 (p=0.00), at 9 months 12.86 (p=0.00), and at 12 months 12.52 (p=0.00).

The mean difference of systolic BP from 03 months at 06 months was 2.68 mm Hg (p=0.00), 09 months was 3.46 mmHg (p=0.00), at 12 months was 3.12 mm Hg (p=0.00).

The mean difference of systolic BP from 06 moths at 09 months was 0.78 (p=0.782, at 12 months was 0.44 (p=1.0).

The mean difference of systolic BP from 09 months at 12 months was -0.340 (p=1.0) (Table 2).

The comparison of the systolic blood pressure using repeated measures ANOVA had 'F' value of 105.166 (p<0.05).

### Comparison of the diastolic BP from baseline with various follow-up stages

The mean difference of diastolic BP from the baseline at 03 months was 5.34 (p=0.00), 06 months was 7.38 (p=0.00), at 09 months was 7.24 (p=0.00), and at 12 months was 6.36 (p=0.00).

The mean difference of diastolic BP from 03 months at 06 months was 2.04 mm Hg (p=0.00), 09 months was 1.90

mmHg (p=0.00), and at 12 months was 1.02 mm Hg (p=0.00).

The mean difference of diastolic BP from 06 moths at 09 months was - 0.14 (p=1.0) and at 12 months was 1.02 (p=0.427). The differences were not statistically significant (as p>0.05). The mean difference of diastolic BP from 09 months at 12 months was 0.88 (p=0.686) (Table 3).

Table 2: Post-hoc bonferroni- comparison of the systolic BP from baseline with various follow-up stages.

Time interval	Time interval	Mean Difference	Std. Error	P value
Baseline	3 months	9.400*	0.826	0.000*
	6 months	12.080*	0.971	0.000*
	9 months	12.860*	1.104	0.000*
	12 months	12.520*	0.211	000*
3 months	6 months	2.680*	0.328	0.000*
	9 months	3.460*	0.494	0.000*
	12 months	3.120*	0.583	0.000*
6 months	9 months	0.780	0.434	0.782
	12 months	0.440	0.497	1.000
9 months	12 months	-0.340	0.369	1.000

Table 3: Post-hoc bonferroni-comparison of the diastolic BP from baseline with various follow-up stages.

Time interval	Time interval	Mean Difference	Std. Error	P value
Baseline	3 months	5.34	0.77	0.00*
	6 months	7.38	0.84	0.00*
	9 months	7.24	0.94	0.00*
	12 months	6.36	0.94	0.00*
3 months	6 months	$2.040^{*}$	0.230	0.000*
	9 months	1.900*	0.472	0.002*
	12 months	1.020	0.591	0.905
6 months	9 months	-0.140	0.364	1.000
	12 months	-1.020	0.490	0.427
9 months	12 months	-0.880	0.473	0.686

The comparison of the diastolic blood pressure using repeated measures ANOVA had 'F' value of 43.27 (p<0.05).

## Correlation between GGT levels and systolic and diastolic blood pressure at various follow-up stages

There was a very weak positive correlation between GGT levels at baseline and SBP (r value = 0.125), which is not statistically significant, at baseline. There was a very weak negative correlation of GGT values with SBP and DBP at 3 months, which was not statistically significant. There was a very weak negative correlation between GGT at baseline and SBP and DBP at 6 months, which was statistically significant. There was a moderate negative correlation between GGT at baseline and SBP and DBP at 12 months, which was statistically significant (Table 4).

# Correlation between alcohol consumption and systolic and diastolic blood pressure at different time intervals

There was a moderate positive correlation between alcohol consumption and systolic BP at baseline (r value= 0.478), which is statistically significant (p=0.00) indicating that the baseline BP was higher in the subjects consuming higher amount of alcohol. There was a weak negative correlation between the alcohol consumption and diastolic BP at baseline (r value= - 0.23) (p= 0.1).

At 3 months, there was a moderate positive correlation between alcohol consumption and systolic BP (r value= 0.564) (p=0.00) whereas there was a moderate negative correlation between alcohol consumption and diastolic BP (r value= -0.45) (p= 0.001).

At 6 months there was a moderate positive correlation between alcohol consumption and systolic BP (r value= 0.54), which was statistically significant. There was a weak negative correlation between alcohol consumption and diastolic BP (r value= - 0.33) at 06 months (p=0.012).

Table 4: Correlation between GGT levels and systolic and diastolic blood pressure at different time interval.

		r value	P value
GGT *	SBP	0.125	0.38
baseline	DBP	0.138	0.33
<b>GGT</b> * 3	SBP	-0.19	0.18
months	DBP	-0.19	0.18
<b>GGT</b> * 6	SBP	-0.32	0.02*
months	DBP	-0.29	0.04*
<b>GGT</b> * 9	SBP	-0.39	0.004*
months	DBP	-0.46	0.001*
GGT * 12	SBP	-0.40	0.004*
months	DBP	-0.23	0.105

Table 5: Correlation between alcohol consumption and systolic and diastolic blood pressure at different time intervals.

		r value	P value
Alcohol	SBP	0.478	0.00*
consumption at baseline*	DBP	-0.23	0.1
Alcohol	SBP	0.564	0.00*
consumption at 03 months	DBP	-0.45	0.001*
Alcohol	SBP	0.54	0.00*
consumption at 06 months At *6	DBP	-0.35	0.012*
Alcohol	SBP	0.387	0.005*
consumption at 09 months	DBP	-0.28	0.04*
Alcohol consumption at 12 months	SBP	0.39	0.005*
	DBP	-0.17	0.227

At 09 months there was a weak positive correlation between alcohol consumption and systolic BP (r value= 0.387) (p=0.005) and a weak negative correlation between alcohol consumption and diastolic BP (r value= -0.28) (p= 0.04).

There was a weak positive correlation between alcohol consumption and SBP at 12 months (r value= 0.39) (p = 0.005). The r value is 0.39 at 12 months which is less than the r value at baseline of r = 0.478 indicating that the reduction in systolic blood pressure over 1 year is more in those with higher alcohol intake prior to the onset of the study. There was a very weak negative correlation between alcohol intake and diastolic BP at 12 months (r value= -0.17) (p= 0.227).

### Correlation between alcohol consumption and initial GGT levels

The correlation between amount of alcohol consumption and the GGT values was very weak positive correlation (r value =0.114), which was not statistically significant (p=0.431).

#### **DISCUSSION**

Epidemiological, preclinical and clinical studies have established the association between excess alcohol consumption and hypertension. Studies have shown that a reduction in alcohol intake is effective in lowering the blood pressure both in hypertensive and normotensives. <sup>12</sup> This study was undertaken to study the relationship between reduction in alcohol intake and reduction in BP over a follow up period of 1 year while the patients were on treatment for alcohol dependence syndrome.

In current study, there was a mean decrease in systolic blood pressure from the baseline till 3 months of follow-up period of 9.4 mm Hg that was statistically significant. There was a fall in systolic blood pressure between 3 months and 6 months averaging 2.68 mm Hg that was again statistically significant. However, there was no significant fall in systolic blood pressure between 6 months till 01-year duration of follow-up duration (Table 2). These findings were in concurrence with a meta-analysis of randomized controlled trials, which reported that alcohol reduction was associated with a significant reduction in mean systolic and diastolic blood pressures.<sup>15</sup>

There was a mean reduction in diastolic BP in the first 3 months from the baseline of 5.34 mm Hg and 2.04 mm Hg from 3 months to 6 months duration of follow-up and both these were statistically significant (Table 3). However, there was no statistically significant difference in Diastolic BP from 6 months to 12 months. This indicates that upon reduction in alcohol intake, both the systolic and diastolic BP show reduction in the initial 6 months, however, there was no significant change in BP from 06 months to 12 months of follow-up duration. This observation was again in consonance with available literature and re-affirms the recommendation for reduction in alcohol intake during management of hypertension.<sup>2</sup>

The correlation between GGT levels and systolic and diastolic BP at different time intervals showed that there was a statistically non-significant weak positive correlation at baseline (r value=0.125) (p value= 0.38). However, post alcohol reduction, there was a negative correlation between GGT and systolic BP at 12 months (r value=-0.40), which was statistically significant. This may be because of a greater reduction in systolic BP in those subjects with higher initial GGT values. This is in concurrence to a study, which examined the reduction of BP during treatment of alcohol dependence using alcohol biomarkers of Carbohydrate deficient transferrin (CDT) and GGT.<sup>16</sup>

The correlation between alcohol consumption and BP at different time intervals showed a moderate positive correlation at baseline with systolic BP (r value= 0.478) which was statistically significant indicating that the systolic BP was higher in those consuming higher amounts of alcohol. At 12 months, there was a weak positive (r = 0.39) correlation (p<0.005), indicating that the overall fall in systolic BP at 01 year was greater in those subjects who had a greater alcohol intake before the study onset. This was in consonance with a recent systematic review and meta-analysis, which reported that upon abstinence (partial/complete), reduction of blood pressure was greatest in subjects who consumed excess (≥06 drinks/day) amounts of alcohol compared to those who would typically drink ≤02 drinks/day.

The strengths of the study included repeated and detailed assessment of daily alcohol use over time, repeated blood pressure measurement and adequate representation of several ethnic groups. The limitations of the study were a relatively smaller number of subjects. Further research with a larger population would be required in future to confirm the findings.

#### **CONCLUSION**

This study evaluated changes in blood pressure occurring during Alcohol dependence syndrome treatment. There was definite decline in systolic and diastolic blood pressure upon reduction in alcohol consumption especially in the first 3 months of treatment. There was no significant fall in systolic and diastolic blood pressure between 6 months till 01-year duration of follow-up. Also, the fall in systolic BP at 01 year was greater in those subjects who had a greater alcohol intake before the study onset.

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Institutional Ethics Committee

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