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Alcohol use disorder and risk of sensitization to environmental allergens in Sub-Continental Asian Indian males

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ABSTRACT

Alcohol is known to cause elevation of serum total IgE (tIgE). Whether it can predispose to allergic disorders, however, is not clear. To assess whether alcohol can cause sensitization to allergens, we analyzed 100 individuals with alcohol use disorder (AUD) and 50 matched healthy controls. Serum tIgE and specific IgE against environmental allergens were measured. We found 93% of individuals with AUD had raised tIgE compared to only 48% of healthy controls ($p < 0.0001$). Sensitization to aeroallergens was noted in 68% drinkers compared to 24% of controls ($p < 0.0001$). The degree of sensitization was directly proportional to the amount and duration of alcohol intake. There is a possibility of a link between alcohol abuse and allergic sensitization.

KEYWORDS

Alcohol use disorder; aeroallergens; total IgE; specific IgE

Introduction

Alcohol use disorder (AUD) in India is rising and emerging as a significant health problem. It includes both dependence and harmful consumption of alcohol.^{1,2} According to recent data, nearly 30% of the Indian population, drinks alcohol, and in the last 10 years per capita consumption has increased from 1.6 to 2.2 liters.³ Among those with AUD, more than half fall into the criteria for hazardous drinking characterized by bingeing and solitary intake to the point of intoxication.¹ Also, a significant quantity of alcohol consumed in India is traditionally brewed (called *desi daru* or *sharab*) from a variety of locally available starch or sugar-containing raw materials, e.g., cereals, sugarcane, fruits, etc. In the Northern part of India, it is obtained from rectification of molasses or by wheat husk fermentation and sold with brand names like *Santra* and *Rocket*. Such form of liquor usually contains 28.5–42.8% of alcohol, but it may go up to 95% in a few inferior and illegally prepared liquors.⁴ Chances of alcohol-related health problems, i.e., liver, digestive, cardiac or neurological illnesses,

and a defective immune system, and behavioral and mental problems, therefore, are likely to be more in these individuals.^{1,3}

Alcohol can induce allergic symptoms, particularly in asthmatics and is known to be associated with higher levels of circulating total IgE (tIgE).^{5–7} Nevertheless, studies favoring a link between alcohol, sensitization to environmental allergens, and allergic disorders are very few and inconclusive. Linneburg et al. followed 1200 adults with AUD (>14 drinks per week) from the age of 40 to 60 years and found that AUD was significantly associated with the prevalence of aeroallergen sensitization and atopic disease.⁸ Another study on 1469 individuals between 20 and 60 years of age showed alcohol consumption to be significantly associated with sensitization to aeroallergen *D. ferinae*.⁹ A Danish study, in contrast, did not find any relationship between AUD and risk of allergic disease despite an association with high plasma tIgE levels.¹⁰ Sensitization to cross-reactive carbohydrate determinants in drinkers can also occur and may cause false-positive results or interference with the interpretation

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of in-vitro allergy tests.^{11,12} Because of such conflicting results, more studies are required to conclude a true relation between alcohol and allergic diseases. India is home to one-sixth of the world's population with high prevalence of both AUD and allergic diseases.¹³ A study of a representative cohort from such population is therefore ideal and may help in better understanding the relationship between the two, if any.

Methods

In a cross-sectional study, 100 volunteers from the general population of Chandigarh city located in the Northwest region of India were recruited. The investigators visited households within the health care area of School of Public Health, Post Graduate Institute of Medical Education and Research. The volunteers consuming alcohol regularly for at least 6 months and fulfilling at least 2 of 11 criteria recommended by “Diagnostic and Statistical Manual of Mental Disorders, 5th edition” for a diagnosis of AUD were selected by the process of simple randomization. A medical/research officer offered all the participants a pre-designed questionnaire including 10 point Alcohol Use Disorders Identification Test (AUDIT) score sheet that followed an interview. Information related to age at the onset of alcohol consumption, duration, and severity of AUD, confounding factors like dietary and smoking habits, parasitic and other infections particularly of the respiratory tract, associated co-morbidities and any sign and symptoms of allergy was collected. AUDIT score was calculated to assess the physical dependency. Thereafter, tIgE and allergen-specific IgE (spIgE) levels were measured in serum samples using an immunoassay analyzer (Phadia 100; Thermofisher Scientific, Sweden) and ready to use reagents and kits. The spIgE was measured against a battery of respiratory allergens grouped together as house dust (dust mite and cockroach), molds (*Penicillium chrysogenum*, *Cladosporium herbarum*, *Aspergillus fumigatus*, *Alternaria alternata*), trees (Mountain juniper, Oak, Elm, Cottonwood, Mesquite), and weeds (Ragweed, Mugwort, Plantain, Goosefoot, Saltwort). The cutoff value for tIgE was ≥ 100 IU/ml, and individuals with spIgE levels >0.35 IU were labeled as positive.

Liver enzymes, e.g., aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase, and albumin levels were also analyzed to evaluate alcohol-induced liver damage, if any.

Fifty age-matched, nondrinker, healthy adults from hospital staff were recruited as controls and were randomly selected to avoid selection bias. Besides tIgE assay, ImmunoCAP Phadiatop (Thermofisher Scientific, Sweden) was used for determination of IgE antibodies specific to inhalant allergens in these subjects. Written consent for participation and prior ethical approval was obtained from the institutional human ethics committee before the commencement of the study.

Statistical analysis

Statistical analysis was performed with SPSS version 20 (SPSS, Chicago, IL). Association between AUD and categorical variables, i.e., tIgE and spIgE levels, were analyzed by Independent t-test and Fisher's exact test. Mean, range, and standard deviation were used for nonparametric variables. A p -value <0.05 was considered statistically significant.

Results

The study group consisted of males only. The age of the participants ranged from 16 to 70 years with a mean age of 39.5 and 36.8 years and SD ± 12.3 and ± 12.1 in cases and controls, respectively. Six cases were <20 years old, 41 between 20 and 39 years and 53 aged 40 or above. Majority of the individuals with AUD (96%) belonged to the lower socioeconomic group and were non-vegetarian (95%). Fourteen percent had a chronic illness, i.e., hypertension or diabetes mellitus and were on regular treatment. None of the participants reported any symptom of allergic reaction. The majority were heavy drinkers consuming more than 100 ml/day (>6 ounces of liquor/day or 35–70% alcohol by volume) for more than 2 years. All except five had an AUDIT score of 8 or more suggesting hazardous drinking, and 58% were probably categorized as a severe AUD (Table 1). Most were consuming liquor with high

Table 1. Comparison of different parameters analyzed in individuals with AUD.

Variables	AUD (n = 100)	tIgE, mean $\pm$ SD	AUD with raised tIgE, number (%)	AUD with positive spIgE, number (%)	Percentage of individuals positive for spIgE for different groups of allergens			
					House dust	Tree	Weed	Mold
Age								
<20	6	954 $\pm$ 1055	6 (100)	4 (67)	66	66	50	16
20–39	41	1072 $\pm$ 1464	40 (97)	28 (68)	58	44	51	19
$\geq$ 40	53	1512 $\pm$ 1668	47 (88)	43 (81)	64	47	51	36
Diet								
Non-vegetarian	95	1344 $\pm$ 1566	89 (94)	65 (68)	68	53	57	36
Vegetarian	05	425 $\pm$ 960	01 (20)	03 (60)	20	40	40	20
Smoking								
No	81	883 $\pm$ 1533	75 (93)	59 (73)	64	51	54	28
Yes	19	934 $\pm$ 1610	18 (95)	09 (47)	58	53	47	21
Frequent infections								
>1 episode/year	08	1415 $\pm$ 821	08 (100)	05 (62)	62	62	50	12
1 episode/year	10	1070 $\pm$ 1597	08 (80)	03 (30)	70	50	70	30
No information	82	–	–	–	–	–	–	–
Type of liquor								
English liquor	37	904 $\pm$ 1320	34 (92)	22 (59)	51	51	40	19
Desi daru/Tharraa	18	2824 $\pm$ 1623	16 (89)	13 (72)	67	39	55	33
All types	45	1546 $\pm$ 1647	40 (93)	33 (73)	69	47	45	33
Amount of drink/day								
<100 ml	04	774 $\pm$ 985	04 (100)	02 (50)	50	50	50	0
100–250 ml	27	896 $\pm$ 1440	26 (96)	15 (55)	52	44	44	30
250–500 ml	55	887 $\pm$ 1485	50 (91)	40 (73)	67	45	51	25
>500 ml	14	939 $\pm$ 2018	13 (93)	11 (78)	64	57	57	43
Duration of drinking								
$\leq$ 2 years	08	698 $\pm$ 798	07 (100)	03 (37)	25	37	25	25
$\leq$ 10 years	42	1215 $\pm$ 1575	40 (95)	17 (40)	62	48	52	21
$\leq$ 20 years	24	1761 $\pm$ 1648	24 (100)	18 (75)	71	42	58	42
>20 years	26	1213 $\pm$ 1526	21 (81)	18 (69)	65	42	46	31
AUDIT score								
<16	42	887 $\pm$ 1636	38 (90)	27 (64)	55	45	43	26
$\geq$ 16	58	924 $\pm$ 1487	55 (95)	41 (71)	67	48	55	29
Total IgE levels								
$\leq$ 100	07	–	–	0	0	0	0	0
101–500	40	–	–	21 (52)	40	30	20	30
501–5000	43	–	–	37 (86)	84	58	80	42
>5000	10	–	–	10 (100)	100	100	100	100
Total	100	–	–	68 (68)	62	49	47	30

^aFollowing brand names of locally brewed alcohol were used: Santra ($n = 15$) and Rocket ($n = 3$).

AUD, alcohol use disorder; tIgE, total IgE; spIgE, specific IgE; AUDIT, alcohol use disorder identification test.

alcohol content, e.g., 35–50% in the form of whiskey or *desi daru*.

Ninety-three percent of the cases had raised tIgE levels with a mean value of 1299 IU/ml (median = 532 IU/ml; range 8.7 to >5000 IU/ml; SD $\pm$ 1562; odds ratio 12.5 and CI 0.23–673). In contrast, 48% (24/50) of controls were found to have increased tIgE with mean levels 348.7 IU/ml (median = 84.5 IU/ml; range 2.0–701 IU/ml; SD $\pm$ 220; Figure 1). Fisher's exact test analysis showed a statistically significant difference in tIgE levels in two groups ($p = 0.0001$).

Sixty-eight percent of individuals with AUD had positive spIgE against one or more allergens (odds ratio 40.2 and CI 2.2–731.3). The positivity for single, two, three, or all four allergen groups was 19, 22, 21, and 38%, respectively. The sensitization was most common against house dust

(94%) followed by weed (75%), tree (69%) and molds (41%). The amount and duration of alcohol intake were found to be directly proportional to the degree of sensitization for different aeroallergens. The relation was further supported by a higher AUDIT scores in these individuals (Table 1). Very high tIgE level was associated with more chances of sensitization as 100% of AUD cases with tIgE levels >5000 IU/ml (10/10) were positive for all the aeroallergens while those with normal levels were all negative. Liver enzymes (AST and ALT) although abnormal in 19% of heavy drinkers did not correlate with tIgE or spIgE.

In contrast, only 24% (12/50) controls had a positive spIgE (Figure 1). Fisher's exact test revealed a significant p -value ($p = 0.0001$) when compared to the AUD group. None of these positive individuals were earlier investigated for any

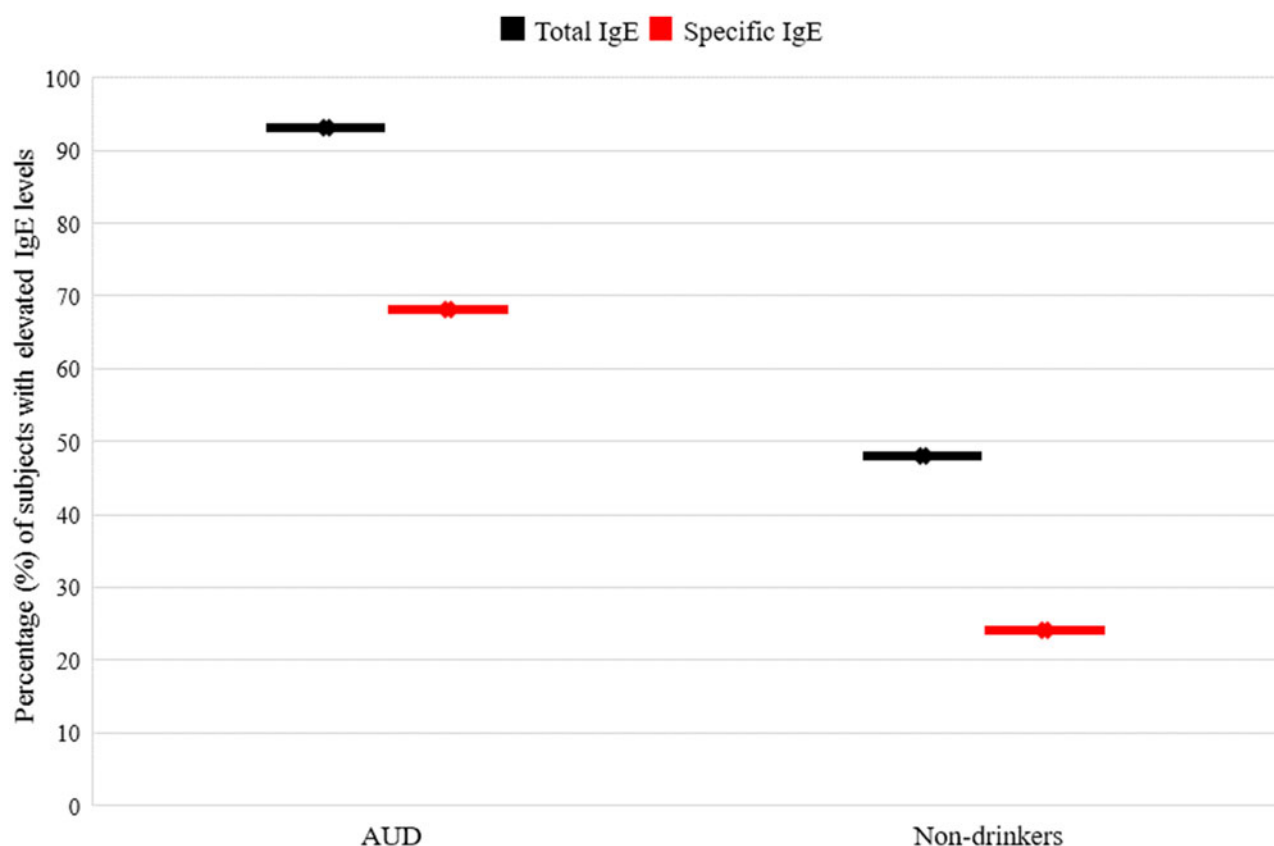


Figure 1. Box and Whisker plot showing individuals with AUD and nonalcoholic individuals (in %) with raised tIgE and positive for allergen-specific IgE.

allergic disorders or were aware of any such disease. However, on a further interview, two of them were found to be symptomatic and were episodically taking treatment for bronchial asthma.

Discussion

Whether AUD can induce changes in spIgE levels and sensitization to environmental allergens has not been well studied.¹⁴ In the present study, compared to controls, we observed significantly raised tIgE as well as spIgE levels in chronic drinkers consuming moderate to a heavy amounts of alcohol. Both tIgE and spIgE levels, however, were unrelated to any symptoms of allergy or any liver injury as reflected by normal liver enzymes in the majority of these individuals.

Though there are no Asian data for comparison, few studies on European subjects with AUD tried to demonstrate increased sensitization to different inhalant allergens. Vidal et al. found 54% of 325 allergic patients taking a moderate amount of alcohol (average consumption of 30 g/

week) and positive spIgE for house dust and grass pollen.¹⁵ In another study on 720 Spanish alcoholic adults, a skin prick test against 13 aeroallergens showed sensitization to pollens only.⁶ A Danish study reported a statistically significant association of moderate to heavy alcohol intake with aeroallergen sensitization, which was independent of alcohol type.¹⁶ Eight-year follow-up of the same population further confirmed this association though it was only of borderline significance. We, in contrast, have found frequent sensitization to molds also in addition to house dust and pollens in individuals with AUD.

Alcohol has a significant impact on the immune system, although that depends on the amount consumed, drinking patterns, beverage type, gender differences, and nutritional status. Chronic alcohol intake can directly suppress immune responses and may be associated with frequent infections.¹⁷ It causes alteration in serum levels of immunoglobulins, i.e., IgG, IgA, IgM and may promote the development of liver-specific autoantigens leading to alcohol-related

liver damage. It induces a pro-inflammatory response, impairs anti-inflammatory cytokines and T cell functioning. It also disrupts the balance between B and T cell subsets as well as changes in cell surface markers. Elevated immunoglobulins and a state of immunodeficiency probably result in Th1/Th2 imbalance and polarization towards an excess of Th2 functions.^{18–20} In a previous study, we also identified raised levels of serum IgG, IgA, and IgM immunoglobulins along with reduced levels of IgM in a few subjects with AUD.⁷

It is well documented that alcohol is more toxic in older subjects because of aging, changed metabolism, and vulnerable immune system.²¹ In the present study we also found the levels of tIgE and spIgE were higher in older individuals compared to younger cases of AUD.

A balanced diet gives strength to the immune system. Though controversial, it is believed that individuals practicing strict dietary patterns (e.g., vegans) are more prone to infections or allergic diseases due to an imbalanced intake of nutrients.²² Though we noticed a proportionate relation between tIgE and degree of sensitization in non-vegetarians, this finding needs verification in a larger cohort of patients of AUD. Also, it is stated that allergy decreases with increasing age.²³ However, in the present study allergic sensitization was found to be more common in older population. This could be either due to effect of alcohol or an age biased selection process.

Although the study suggests a link between AUD and allergen sensitization, its relevance is dampened by small sample size. Another limitation is use of a self-reported questionnaire. Even though it is reliable and easy to understand it can affect the significance of outcome if there is a faulty or erroneous interpretation of questions by the illiterate participants or concealment of information under the influence of alcohol or due to poor memory in these individuals. Also, no physical examination was carried out to exclude allergic disease and allergy screening was done only for common environmental allergens. Thus, the possibility of sensitization to other allergens has not been excluded in those with a negative spIgE. Another shortcoming was the selection of an exclusively male cohort because females neither

revealed nor volunteered for participation in the study. Tobacco use was another confounding factor not excluded. Also, there is strong genetic influence both in AUD and in allergic diseases that was not addressed in this study.

However, we feel that despite the above limitations, the study has clinical significance as it is a pioneer work that reports an association between alcohol and abnormal total and spIgE levels for the first time in an Asian population. Also, the fact that the cohort selected belonged to a lower socio-economic class, which otherwise is expected to have a lower frequency of allergic sensitization, provides added strength to the results. Larger follow-up studies with a long-term allergic outcome and an emphasis on interfering factors, immune mechanisms of alcohol-induced allergic sensitization, e.g., Th2 polarization and role of T cell-related transcription factors are required to identify the exact nature of the relationship between AUD and allergic sensitization observed in our study.

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Disclosure statement

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