Original Article

Family Loading and Morbidity Risk of Attention-deficit Hyperactivity Disorder in Patients with Alcohol-dependence Syndrome

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ABSTRACT

Background: Attention-deficit hyperactivity disorder (ADHD) and substance-use disorders often co-occur. **Aim:** Aim of this study was to look at the family loading of ADHD (in adults and children) in patients with alcohol-dependence syndrome (ADS) along with the estimation of morbidity risk (MR) for developing ADHD. **Methods:** Thirty-five male patients with ADS along with their 369 first-degree relatives (FDRs) – both children and adults – were recruited. **Results:** ADHD and residual ADD (ADDRT) were significantly more common in the early-onset (EO) ADS group and their FDR. In ADHD children, high MR (27.27%) for developing EO of ADS was noted. **Discussion:** Findings from this study raise an avenue for research in the Indian population about the shared risk between ADS and ADHD.

Key words: *Attention-deficit hyperactivity disorder, alcohol-dependence syndrome, family loading, morbidity risk*

INTRODUCTION

Attention-deficit hyperactivity disorder (ADHD) is one of the common comorbidities in patients with substance-use disorders (SUDs). A recent meta-analysis of 29 studies reported that the prevalence of ADHD in SUDs is approximately 23%.[1] Our previous study in a treatment cohort from India suggested that the rates of comorbidity of ADHD and SUD are around 21.7%.[2] Another study from our center found that there were higher odds of ADHD in individuals with early onset (EO) of alcohol-dependence syndrome (ADS) defined as ADS established by the age of 25 years or earlier.[3] Furthermore, the SUD and related problems are severe, and outcomes are poorer in individuals with ADHD than those without ADHD.[4,5] The population-based study done by Skoglund *et al.* found a strong familial association between ADHD and SUD.[6] They also found that pure ADHD in probands could predict pure SUD in relatives, and this supported the hypothesis of shared familial risk factors for the co-occurrence of the two disorders. The

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consistent association between ADHD and SUD was also hypothesized to be mediated by an independent transmission of these disorders.[7]

The increasing evidence of ADHD and SUD along with the familial propensity of these disorders, and the dearth of literature from the Indian subcontinent supporting this evidence, prompted us to study: (1) the family loading of ADHD in patients with ADS and (2) the morbidity risk (MR) of development of ADHD in the children and the first-degree relatives (FDRs) of the patients with early- and late-onset (LO) ADS.

METHODOLOGY

The study was conducted at the Centre for Addiction Medicine, National Institute of Mental Health and Neuro Sciences, Bangalore, India. Figure 1 describes the methodology with a flowchart. Men fulfilling the ICD 10 criteria for ADS were recruited along with their children and FDRs. Patients with comorbid psychotic or mood disorders as well as independent anxiety disorders and with the other substances of abuse except tobacco were excluded. Stratified random sampling method was used for the recruitment. Informed consent was obtained from the patients and their FDRs participating in the study. Two trained interviewers performed the interviews of the patients and FDRs. For triangulating information from the index patients and their adult FDRs, their mother and at least one of the older siblings were also interviewed along with them. For FDRs who are children, their parents and one another family member were interviewed. The information collected was used to generate the best diagnosis on discussion with two independent consultant psychiatrists.

Instruments

First, the information was gathered from the patient. The Schedule for Clinical Assessment in Neuropsychiatry[8] was used in the index subject to diagnose alcohol dependence and exclude other psychiatric disorders. The severity of alcohol dependence in patients was assessed using the Severity of Alcohol Dependence Data Questionnaire.[9] The family history of psychiatric disorder in the FDRs was ascertained using the Family Interview for Genetic Studies (FIGS).[10] Furthermore, two or more FDRs were interviewed by FIGS, to increase the accuracy and reliability of the information. The residual ADHD in patients was assessed with the ADHD checklist (ADHD-CL).[11] The retrospective information about the childhood ADHD in patients was collected from parents using the Parents Rating Scale (PRS) (modification of Conner's Abbreviated Teachers Rating Scale).[12]

Later, the information about the FDR was collected. In the siblings of the patient, ADHD-CL and PRS were used to assess for adult residual ADHD and prior ADHD in childhood, respectively. Children (<16 years of age) were interviewed using the Diagnostic Interview for Children and Adolescents-Parents version.[13] Other available records with the patients such as old hospital papers were also used as a source of information.

The MR was calculated separately for all the FDRs (father, mother, brother, and sister) using the Weinberg's abridged method[14,15] with the help of following formula:

$$\text{Morbidity risk} = \frac{a}{b - bo - \frac{bm}{2}} \times 100$$

Where a is the number of affected individuals, b is the total number of individual studied, b_o is the number

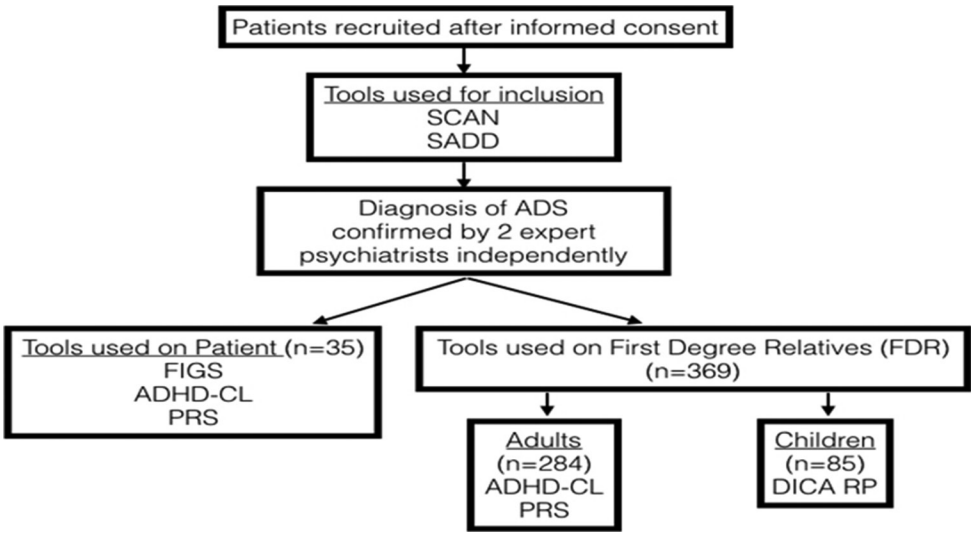

Figure 1: A flowchart describing the method used in the study. SCAN – Schedule for Clinical Assessment in Neuropsychiatry, SADD – Severity of Alcohol Dependence Data, FIGS - Family Interview for Genetic Studies, ADHD-CL – Attention Deficit Hyperactivity Disorder Checklist, PRS – Parents rating scale, DICA RP – Diagnostic Interview for Children and Adolescents – Parents version

of individuals who have not reached the manifestation period, and b_m is the number of individual passing through the risk period.

RESULTS

Attention-deficit hyperactivity disorder in patients

Thirty-five male patients with alcohol dependence were included in the study. As per the age of onset of alcohol dependence, their data were divided into two groups: The Early Onset (EO) group with the onset of alcohol dependence before 25 years of age (n = 18) having a mean age of 34.89 years and the Late Onset (LO) group with the onset of alcohol dependence after 25 years of age (over 30 years to avoid overlap) (n = 17) having a mean age of 40.47 years. Ten individuals (28.4%) in total had ADHD/residual ADD (ADDRT), of which the significant overrepresentation was by the EO group (50%) compared to the LO group (6%) ($t = 2.13$, $P < 0.05$). The odds for developing the EO of alcohol dependence were 16 times more in the individuals who had ADHD/ADDRT than the others.

Attention-deficit hyperactivity disorder in first-degree relative

A total of 369 FDRs (85 children and 284 adults) were studied. The total number of FDR of the EO group patients was 187 and that in the LO group was 182. Thirty (male = 28, female = 2) alcohol-dependent FDRs were identified. Alcohol dependence was significantly more prevalent in the family members of the EO group compared to the LO group ($t = 4.32$, $P < 0.001$). The EO of alcohol dependence was also significantly higher among the FDRs of the EO group compared to the LO group ($t = 4.2$, $P < 0.001$). Conversely, there was a more modest clustering of the LO form of dependence among the LO relatives ($t = 2.08$, $P = 0.047$). In total, 25% of FDR children were diagnosed as ADHD. It was significantly more represented among the children of the EO group individuals (38%) than the children of the LO group individuals (12%) ($t = 2.81$, $P < 0.01$). Similarly, 16% of adult FDRs of EO patients had a history of ADHD in childhood or ADDRT in adulthood. Moreover, only 6% of FDR of LO patients had the same.

Morbidity risk

The MR for developing alcohol dependence among FDR of EO patients was 17.51%, of which the morbidity for developing EO of alcohol dependence in FDR was 11.72% and for developing LO of alcohol dependence was 1.84% [Table 1]. The MR for developing alcohol dependence in FDR of LO patients was 10.68%, of which developing EO of alcohol dependence was 2.91% and that of LO was 8.73%. Overall in FDR, father and brothers had higher MR of developing alcohol dependence compared to sisters and mothers.

Table 1: Morbidity risk of Alcohol Dependence Syndrome and Attention Deficit Hyperactive Disorder in the first-degree relatives of alcohol-dependent individuals

Morbidity risk in FDR	ADS (%)	ADHD (%)
Overall	14.52	11.11
EO group	17.51	16.0
LO group	11.73	5.74

FDR – First-degree relative; ADS – Alcohol-dependence syndrome; ADHD – Attention-deficit hyperactivity disorder; EO – Early onset; LO – Late onset

The MR of ADHD/ADDRT in FDR of patients was 11.11%, of which the FDR of EO patients had 16.00% and that of LO patients had 5.74%. The MR of developing ADHD in children of the EO group (50%) was higher than the children of the LO group (15.5%). The MR for developing EO alcohol dependence in ADHD children of individuals with alcohol dependence was 27.27%.

DISCUSSION

The finding which needs to be highlighted is that ADHD and ADDRT were significantly more common in the EO group and their FDRs. This replicates similar findings from our previous studies on ADHD and SUD.[2,3] The MR for ADHD and other externalizing spectrum disorders in children of all alcohol dependents was high, especially with the patients of EO of dependence. Furthermore, the probability of developing alcohol dependence in children of EO patients was much more. Alcohol dependence and ADHD were significantly more represented along with a high risk of developing them in the FDR of the alcohol-dependent patients. These results were in concordance with the previous reports that the externalizing spectrum disorders are highly heritable.[16,17] A randomized placebo-controlled trial by Wilens *et al*. showed that the treatment of ADHD symptoms with atomoxetine in patients of alcohol dependence having comorbid ADHD significantly decreases alcohol craving over the long-term.[18] A previous study from our center had found that individuals with EO ADS treated with atomoxetine in addition to treatment of alcohol dependence had a longer duration of abstinence and better treatment outcome.[19] In addition, in the present study, there was a strong risk in the FDR with a history of ADHD for developing alcohol dependence. Our study extends the spectrum from the patients of EO alcoholism to their family members representing their MR for the development of alcohol-related problems and ADHD.

With further understanding of the overlap between ADHD and alcohol dependence, clinicians in India might be able to target individuals at high risk for

alcohol dependence at an early stage even before they initiate substance use. The Family history of ADHD needs to be taken into account when assessing the risk for future SUD because, should an ADHD diagnosis be established, not only the individuals with ADHD themselves but also their relatives are at risk for SUD. Involvement of family in the intervention for patients and increasing their awareness about the shared risk may decrease further morbidity. Our findings raise an avenue for research in the Indian population about this shared risk between alcohol dependence and ADHD. Maintaining a cohort of families with members having alcohol dependence may help us in pinpointing the neuronal and genetic association. This study contributes to the growing evidence of the observed overlap between ADHD and SUD and may have important clinical and public health implications in India.

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Conflicts of interest
There are no conflicts of interest.

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