

GENDER DIFFERENCES IN CO-MORBID DISORDERS WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD)

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ABSTRACT

Objective: To assess the impact of gender on co-morbid disorders with Attention-Deficit Hyperactivity Disorder (ADHD).

Design: Cross sectional study.

Place and duration of study: We selected children and adolescents with ADHD referred to the Sheikh Hospital clinic (a subspecialty hospital for children in Mashhad, Iran) between November 2002 and March 2004.

Subjects and Methods: Two-stage ascertainment procedure was used to select the subjects. The first stage was the patient's referral to a psychiatric clinic resulting in a clinical diagnosis of ADHD by a child psychiatrist. A second stage confirmed the diagnosis of ADHD made on face-to-face structured interviews with the mother. Only patients who received a diagnosis of ADHD at all two stages were included in the final analysis. The clinical interview and the Schedule for Affective Disorders and Schizophrenia for School – Age Children Present and Lifetime version (K – SADS – PL) were used for making diagnosis according to DSM-IV.

Results: There is no meaningful statistically significant differences in the sex of probands. the proportion of male was 48.3 % (n=71) and female 51.7 % (n=76). The majority of probands were between 7-12 years old (68%). Although mood disorders (depressive disorders and bipolar), anxiety disorders and enuresis were more common in males but there were no significant differences between them. OCD and Learning disorders were more prevalent in girls but the difference was not statistically significant.

Conclusion: Our results suggest that boys and girls do not differ in the co-morbid disorders with ADHD. Although this is consistent with prior work suggesting more similarities than differences in the nature of psychiatric co-morbidity in ADHD boys and girls, we cannot make strong conclusions, thus replication studies are needed.

Key words: ADHD, Gender Differences, Co-morbid Disorders.

INTRODUCTION

Attention Deficit Hyperactivity Disorder (ADHD) is a common, heterogeneous disorder, conservatively estimated to affect 3-5% of school age children¹⁻⁴. Although ADHD is more prevalent in boys than in girls, little doubt exists that it is also an important cause of psychiatric disability in girls. While the exact prevalence of the disorder in females remain unclear, it may not be minor^{1,5,6}.

Despite the fact that a large number of girls might be suffering from attention deficit hyperactivity disorder (ADHD), the scientific literature on ADHD is almost exclusively based on boys. There is a substantial discrepancy in the male-to-female ratio between clinic-referred

(10 to 1) and community (3 to 1) samples of children with ADHD. This discrepancy shows that girls with ADHD may be under identified and under treated^{1,6,7}.

Although the reasons for the apparent under identification of girls with ADHD remain unclear, Gaub and Carlson⁷ suggested in their meta-analysis that gender differences in the phenotypic expression of the disorder may be driving referral of more boys than girls, compared with boys. Girls with ADHD tend to have greater intellectual impairments, lower levels of hyperactivity, lower rates of conduct disorder, and higher rates of mood and anxiety disorders. Because co-morbidity with conduct disorder is commonly associated with family disruption and severe behavioral disturbances, if these problems are in fact less frequent among girls with ADHD, they could explain why girls may be less likely to come to attention of health care providers^{8,9}.

The most common co-morbid conditions in ADHD are Conduct Disorder and Oppositional Defiant Disorder. These affect 40-60% of children and adolescents with ADHD^{10,11}. In addition to conduct disorder probands with ADHD were more likely to have mood and anxiety

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disorders. Co occurrence of ADHD and mood disorders is 15-75%^{10,12,13}. Association with anxiety disorders has reported in up to 25%¹⁰.

Previous studies show that ADHD girls were more likely to have mood, and anxiety disorders^{1,9,14}. The prevalence of both conduct disorder and oppositional defiant disorder found in ADHD girls was half of what has been found in boys suffering from ADHD¹³. Such co-morbid conditions have been associated not only with a more complicated course of ADHD but also with lack of therapeutic response to stimulant drugs^{1,9}.

The limitations of the previous studies of gender and ADHD that have been published stems from the lack of direct interviews with children younger than 12¹⁵. This method for assessment of psychopathology in the children may have led to under-representation of psychopathology in this group. This may be especially the case for "internalizing" disorders, such as anxiety and depression.

We aimed to assess the gender effects on co-morbid conditions in patients presenting with to ADHD, to determine whether co-morbidity of ADHD could explain discrepancy in the male-to-female ratio between clinic-referred and community samples of children with ADHD. We predicted that ADHD in girls who are referred to clinic would be characterized by lower rates of co-morbid disruptive behavior disorder, and higher rates of anxiety and depression than ADHD in boys.

SUBJECTS AND METHODS

This is a cross sectional study. We studied two groups of probands with ADHD: 76 girls with ADHD and 71 comparison boys with ADHD. All probands were between the ages of 6 and 18 years. All of the ADHD probands met the DSM-IV diagnostic criteria for ADHD at the time of the clinical referral; at the time of recruitment they all had active symptoms of the disorder. After a description of the procedures and purpose of the study Parents gave written informed consent for participation of their children, and the children and adolescents provided written assent to their participation. Informed consent (parent and children) was received before the administration of any study procedure in accordance with the ethical standards of the investigative site's institutional review board and with the Helsinki declaration of 1975, as revised in 2000¹⁶.

Potential subjects were excluded if they had been adopted, or if their nuclear family was not available for study. We excluded subjects if they had major sensorimotor handicaps (paralysis, deafness, and blindness), psychosis, autism, or a Full-Scale IQ less than 80¹⁷.

We selected participants in the study from consecutive referrals to a child and adolescent psychiatry clinic at the Sheikh Hospital clinic (a subspecialty hospital for children in Mashhad, Iran) Subjects were enrolled in the study between November 2002 and March 2004, Parents, pediatricians, and schools had referred these children for psychiatric evaluations.

Two-stage ascertainment procedure was used to select the subjects. For children with ADHD, the first stage was the patient's referral to a psychiatric clinic resulting in a clinical diagnosis of ADHD by a child psychiatrist, which was recorded in the clinic record. A second stage confirmed the diagnosis of ADHD made on face-to-face structured interviews with the mother. Only patients who received a diagnosis of ADHD at all two stages were included in the final analysis.

Psychiatric assessments of the children were made by using the Persian version* of Schedule for Affective Disorders and Schizophrenia for School-Age Children—Epidemiologic Version (K-SADS-E)^{18,19}. Diagnoses were based on independent interviews with the mothers and direct interviews with all of the children older and younger than 12 years. All assessments were made by raters who were blind to the child's diagnosis. Different interviewers met with mothers and children to maintain blindness to ADHD status and to prevent information from one informant influencing the assessment of the other.

A committee of three psychiatrists each board certified in both child and adult psychiatry, resolved all diagnostic uncertainties.

Chi-square tests were used to compare risk of ADHD in the relatives of ADHD probands between girls and boys groups. The statistical significance was set at P value less than .05.

RESULTS

There is no meaningful statistically significant differences in the sex of probands. the proportion of male was 48.3 % (n=71) and female 51.7 % (n=76). The majority of probands were between 7-12 years old (68%).

Demographic characteristics of the subjects are presented in Table 1

The profile of psychiatric co-morbidity of ADHD was broadly similar in boys and girls (Table 2). Although mood disorders (depressive disorders and bipolar), anxiety disorders and enuresis were more common in males but there were no significant differences between them. OCD and Learning disorders were more prevalent in girls but the difference was not statistically significant.

For substance use disorders there was a significant gender-by-diagnosis interaction, indicating

* Reliability and validity of the Farsi (Persian) version of (K-SADS-PL) was done in Iran. There was sufficient validity and test-retest and inter-rater reliability and good to excellent sensitivity and specificity and positive and negative predictive validity for nearly all of the disorders. Validity for ADHD, ODD, tic disorder and ...were 0.69, 0.41, 0.42; respectively. Reliabilities of ADHD, ODD, tic disorder and ...were 0.8, 0.67, 0.56. sensitivity of ADHD, ODD, tic disorder and ...were 0.77, 0.40, 0.47.

Table 1
Demographic Characteristics of Subjects with Attention Deficit Hyperactivity Disorder (ADHD)

Sex	N(%)
Male	71 (48/3)
Female	76 (51/7)
Age (years)	
4–6	22 (15)
7–12	100 (68)
13–18	24 (16.3)

that ADHD was a significantly weaker risk factor for substance use disorders in boys than it was in girls. For other disorders the gender-by-diagnosis interaction was not significant, indicating that other gender differences between boys and girls with ADHD were the same.

DISCUSSION

In this study, we assessed co-morbid disorders with ADHD in girls and boys to determine if co-morbidity of ADHD could explain discrepancy in the male-to-female ratio between clinic-referred and community samples of children with ADHD.

Our finding refutes our hypothesis that we predicted, ADHD in girls who are referred to clinic would be characterized by lower rates of co-morbid disruptive behavior disorder, and higher rates of anxiety and depression than ADHD in boys.

According prior reports¹⁵, girls with ADHD were at significant risk for substance use disorder, but current study doesn't show it. Our finding shows that the gender is a protective factor for substance use disorder in girls. This finding should be interpreted by considering the ages of our participants. The ages of onset of ADHD and substance use disorder are separated by at least a decade so the longitudinal studies are needed to confirm this finding^{20,21}.

According the previous studies, boys with ADHD had significantly higher rates of co-morbid disruptive behavior disorder than girls in both clinical and referral samples²²⁻²⁵. But current study doesn't show many differences between girls and boys, thus gender and ADHD appear to be independent risk factors for co-morbid psychopathology.

Our results must be interpreted in the context of methodological limitations. Because our sample was psychiatrically and pediatrically referred, we do not know to what degree these findings will generalize to ADHD children in the community, also this result can explain that the girls who are referred to clinic have a more behavior disruptive than community samples so there is no difference between girls and boys who are referred. Although our findings consist with some previous studies^{13,14} but it isn't consistent with our hypothesis. We predicted that higher rate of mood and anxiety co-morbid in girls may lead to the under recognition of ADHD in girls.

Methodological limitations of this study are our sample that was psychiatrically and pediatrically referred, and we can't generalize these findings to ADHD children in the community. Our results should be interpreted in the context of the statistical power to detect significant interactions between gender and the diagnosis of ADHD. Thus, replication studies are needed to

Table 2
Lifetime Prevalence of psychiatric disorder in Subjects with Attention Deficit Hyperactivity Disorder (ADHD)

Psychiatric disorders	Female Subjects		Male Subjects		Statistic P value	OR/(95% CI)
	N	(%)	N	(%)		
Depressive disorders	6	7.9	9	12.7	0.339	0.590(0.199-1.753)
Bipolar disorders	6	7.9	7	9.9	0.675	0.784(0.250-2.455)
Anxiety disorders	24	16	21	29.6	0.792	1.099(0.544-2.219)
OCD	21	27.6	14	19.7	0.260	1.555(0.719-3.360)
Tic disorders	13	17.1	13	18.3	0.848	0.921(0.394-2.149)
Substance abuse disorders	0	0	4	5.6	0.036	0.469(0.393-0.558)
ODD	16	21.1	16	22.5	0.828	0.917(0.419-2.007)
Conduct disorders	2	2.6	6	8.5	0.120	0.293(0.057-1.501)
Learning disorders	11	14.5	5	7	0.148	2.234(0.735-6.787)
Enuresis	20	26.3	23	32.4	0.418	1.259(0.272-5.834)

see if the pattern of findings we observed holds for other samples. In addition, although raters were blind to the diagnosis of probands, parents were not. Structured interviews were done with only one parent, usually the mother, and we relied on maternal reports which might have led to a bias about reporting problems in their own children.

CONCLUSION

Despite these limitations, our results show similar patterns in the co-morbid disorders in ADHD boys and girls. Thus, although ADHD is associated with the co-morbid disorders, the pattern of these conditions is not influenced by the proband's gender. These similar patterns provide further evidence for the idea that, when ADHD is diagnosed in girls, it corresponds to the same disorder diagnosed in boys. Our data support the idea that gender and ADHD are independent risk factors for co-morbid psychopathology so ADHD in girls like boys is a serious disorder associated with impairment in multiple domains of functioning and similarities in co-morbid conditions may implicate similarities in other domains like course, prognosis and responding to treatment. Thus there is no reason to assume that the treatment of girls with ADHD should be less aggressive than that of boys with ADHD.

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