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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 propor- tion 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. Al- though 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 minor1,5,6.

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 ex- clusively based on boys. There is a substantial discrep- ancy in the male-to-female ratio between clinic-referred

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(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 treated1,6,7.

Although the reasons for the apparent under iden- tification 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, com- pared 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 sever 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 providers8,9.

The most common co-morbid conditions in ADHD are Conduct Disorder and Oppositional Defiant Disor- der. These affect 40-60% of children and adolescents with ADHD10,11. In addition to conduct disorder probands with ADHD were more likely to have mood and anxiety

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 disorders1,9,14. 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 drugs1,9.

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 psy- chopathology 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 be- tween clinic-referred and community samples of chil- dren 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 recruit- ment 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 pro- vided written assent to their participation. Informed con- sent (parent and children) was received before the ad- ministration of any study procedure in accordance with the ethical standards of the investigative site’s institu- tional 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 sensorimo- tor handicaps (paralysis, deafness, and blindness), psy- chosis, autism, or a Full-Scale IQ less than 8017.

We selected participants in the study from con- secutive referrals to a child and adolescent psychiatry clinic at the Sheikh Hospital clinic (a subspecialty hos- pital for children in Mashhad, Iran) Subjects were en- rolled 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 inter- viewers met with mothers and children to maintain blind- ness 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 be- tween them. OCD and Learning disorders were more prevalent in girls but the difference was not statistically significant.

For substance use disorders there was a signifi- cant 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 specifity 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 inter- action 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-fe- male ratio between clinic-referred and community samples of children with ADHD.

Our finding refutes our hypothesis that we pre- dicted, ADHD in girls who are referred to clinic would be characterized by lower rates of co-morbid disruptive be- havior disorder, and higher rates of anxiety and depres- sion 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 de- cade so the longitudinal studies are needed to confirm this finding20,21.

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 dif- ferences between girls and boys, thus gender and ADHD appear to be independent risk factors for co-morbid psy- chopathology.

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 be- havior disruptive than community samples so there is no difference between girls and boys who are referred. Although our findings consist with some previous stud- ies13,14 but it isn’t consistent with our hypothesis. We pre- dicted 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 re- ferred, and we can’t generalize these findings to ADHD children in the community. Our results should be inter- preted in the context of the statistical power to detect significant interactions between gender and the diag- nosis 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 in- terviews 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 pat- terns 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 mul- tiple domains of functioning and similarities in co-mor- bid 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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