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Psychiatric Comorbidity Differences in Clinic-Referred Children and Adolescents With ADHD According to the Subtypes and Gender

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There are controversial or even opposite findings about gender and prevalence of comorbid psychiatric disorders among different subtypes of attention-deficit hyperactivity disorder (ADHD). The participants were children with attention-deficit hyperactivity disorder. Gender, subtype of attention-deficit hyperactivity disorder, and the interaction effects were evaluated by logistic regression. Of the 171 children, 73 (42.7%) were of the combined subtype, 45 (26.3%) inattentive, and 52 (31.0%) were hyperactive/impulsive. The prevalence of attention-deficit hyperactivity disorder subtypes was not different between genders. There was no

significant difference of gender by subtype interaction effects on the children's age. This study does not provide evidence supporting attention-deficit hyperactivity disorder subtypes as distinct clinical entities in terms of comorbidity. Association of attention-deficit hyperactivity disorder subtypes and psychiatric disorders in Iran is somehow different from that in some studies conducted in the Western culture. It is more similar to that of other Asian countries.

Keywords: attention-deficit hyperactivity disorder; subtypes; comorbidity; gender; Iran

Attention-deficit hyperactivity disorder (ADHD) is a common psychiatric disorder in children and adolescents. The 3 subtypes of ADHD are predominantly inattentive, predominantly hyperactive-impulsive, and the combined type.¹ Its prevalence among preschool children is reported to be about 10.3% to 14.2%. Its rate in boys is more than that in girls.² A recent study in Iran on 2000 community sample of students with the parent-completed *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)*-referenced rating scale of ADHD symptoms indicated that the rate of probable ADHD was about 10.1%. Its rate among boys and

girls was 13.6% and 6.5%, respectively. Attention-deficit hyperactivity disorder hyperactive-impulsive type was the most common type of ADHD among both genders. The least frequent type was ADHD-combined type.³ It was concluded that the rate of probable ADHD in Iran was very similar to that in other countries.³

More than 55% of the children and adolescents with ADHD meet the criteria for oppositional defiant disorder. More than one third of the children with ADHD have co-occurring anxiety disorders.⁴ This phenomenon is not due to referral biases or methodological artifacts.⁵ The prevalence of mood disorder in ADHD is very controversial. It is reported to occur in 1.3% to 75% of cases.⁶ Even some studies have suggested that ADHD and major depression represent different expressions of a common etiology.⁷

The presence of comorbid psychiatric disorders can affect the manifestation and prognosis of children with ADHD.⁸ Comparing comorbidities in different types of ADHD might help understand whether different types of ADHD represent independent diagnostic entities or whether the ADHD subtypes and comorbid disorders are coupled. However, the presence of comorbid psychiatric disorders may be related to selecting different interventions. If different ADHD subtypes and the comorbid disorders are relatively independent, then, different treatments may be needed to address them.

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Previous studies in different cultures reported that different subtypes of ADHD are differentially associated with patterns of comorbidity. A study on a clinical group of children with ADHD in the United States concluded that predominantly inattentive features are more likely to have comorbid internalizing disorders such as mood and anxiety; predominantly hyperactive-impulsive and/or combined ADHD subtypes are more frequently associated with delinquency and oppositional behavior.⁹ Another general population study conducted in United States on children aged 7 to 19 years showed that internalizing and externalizing disorders did not cluster differentially within ADHD subtypes.¹⁰ A study on the children with ADHD referred to a psychiatric clinic in United States reported that girls with ADHD were more likely to have predominantly inattentive type of ADHD than boys. Furthermore, girls with ADHD are at less risk for comorbid major depression, conduct disorder, and oppositional defiant disorder than boys with ADHD.¹¹ A similar level of anxiety among children with ADHD-combined and ADHD-inattentive types has been reported in a clinical sample in the United States.¹² Another study in the United States on nonreferred children with ADHD, diagnosed according to *Diagnostic and Statistical Manual of Mental Disorders, third edition*, revised criteria, reported that the prevalence of different comorbid psychiatric disorder in children with ADHD versus non-ADHD was similar for males and females. In other words, there is no significant interaction between gender and different types of ADHD.¹³ In addition, boys and girls were not different in the subtypes of ADHD.¹³

However, a study in a nationally representative sample of Australian children suggests that depressive disorders are more common in male children with ADHD than non-ADHD male.¹⁴ In a study, comparison of attention-deficit disorder with hyperactivity and attention-deficit disorder without hyperactivity found that children with attention-deficit disorder without hyperactivity were more likely to have anxiety or affective disorders.¹⁵

A recent review study reported that girls were more likely to be inattentive without being hyperactive or impulsive, as compared with boys. Girls and boys have similar, although not identical, comorbidity.¹⁶

Different studies in Asia also reported different findings. In a study in Taiwan, 21 girls and 21 age-matched boys with ADHD were strikingly similar on behavioral ratings.¹⁷ A study on a clinical sample of children with ADHD in China reported that there was no difference between subtypes of ADHD for comorbidity of psychiatric disorders, except for oppositional defiant disorder. It was more common in ADHD-combined type than the other types of ADHD.⁶ A study on the clinical sample of Korean children with ADHD indicated that age and gender were not related to comorbidity of psychiatric disorders.

However, ADHD-combined type was associated with oppositional defiant disorder and conduct disorder.¹⁸

There is a substantial discrepancy in the boys to girls ratio clinic-referred children with ADHD, being reported to be up to 10 to 1.¹⁹ However, it is postulated that girls referred to clinics are as impaired as boys.²⁰

The rates of the subtype's comorbidity are likely to vary with age. In general, hyperactivity-impulsivity symptoms emerge earlier in childhood, and this ADHD type is more common in preschool children. Whereas the inattentive type of ADHD is more common in adolescents.²¹

According to the above studies, there is a controversy or even some opposite findings about gender and comorbid psychiatric disorders in different ADHD subtypes, not only in different cultures but also in different studies in United States. Hence, more studies are required to survey them in children with ADHD. It is hypothesized that ADHD in girls would be characterized by lower rates of overall comorbid disorders than ADHD in boys. This is the first study from Iran on the correlation between different types of ADHD and the other comorbid psychiatric disorders, using a well-known interview.

Methods

The participants were 171 children and adolescents with ADHD referred to the outpatient Child and Adolescent Psychiatric Clinic affiliated to Shiraz University of Medical Sciences. The age of children and adolescents was from 5.5 to 18 years. All the participants were examined, including neurological examination. The participants with mental retardation or major sensorimotor problems such as paralysis, deafness, blindness, psychosis, and autism were excluded from this study. The parents and their children were interviewed by a board-certified child and adolescent psychiatrist.

Income does not have a strong relationship with educational level and job in Iran. Therefore, measures of socioeconomic status such as the Hollingshead index representing levels of profession and education cannot be used.²² Parental education level and type of occupation as measures of socioeconomic status were included. The demographic characteristics of the children and their parents were obtained by face-to-face interview with the child and the parents.

The Farsi version of Schedule for Affective Disorders and Schizophrenia for School-Age Children was performed with children and adolescents and also their parents. It is a semi-structured diagnostic interview for children and adolescents aged 6 to 18 years, based on *DSM-IV* diagnostic criteria.^{23,24} Its reliability, validity, administrative characteristics, and uses of the Schedule for Affective Disorders and Schizophrenia for School-Age Children have been reported before.²⁴ Its validity and test-retest and interrater reliability is enough. Test-retest and interrater reliability of ADHD diagnosis are 0.81 and 0.69, respectively. Tic disorder and ADHD have the highest positive predictive validities. Test-retest and interrater reliability of oppositional defiant disorder are 0.67 and 0.69, respectively.²⁴

Table 1. Mean Age of the Children With ADHD by Their ADHD Type

	ADHD-C, n = 73	ADHD-I, n = 45	ADHD-HI, n = 53	Significance
Age, year (Mean, SD)	8.7 ± 2.1	10.3 ± 2.6	8.4 ± 2.5	$F(2, 167) = 8.4, P < .001$
Preschool age (5-6 years)	5.6 ± .5	-	5.7 ± 0.46	$F(1, 20) = 0.17, P = .6$
School age (7-11 years)	8.5 ± 1.3	9.1 ± 1.5	8.5 ± 1.5	$F(2, 118) = 2.35, P = .1$
Adolescents (12-18 years)	12.7 ± 1.3	13.8 ± 1.8	12.7 ± 1.4	$F(2, 25) = 1.3, P = .2$

Note: ADHD, attention-deficit hyperactivity disorder; ADHD-C, ADHD combined type; ADHD-HI, ADHD predominantly hyperactive impulsive type; ADHD-I, ADHD predominantly inattentive type.

The children with ADHD and their parents were informed about the study and they provided informed consent for participation. It was stressed that their information would be confidential. Their participation was voluntary. The protocol for the research project conforms to the provisions of the Declaration of Helsinki. The parents gave consent and the children assent. The protocol was approved by the Institutional Review of Board.

The data were statistically analyzed using SPSS statistical software. The Pearson chi-square test was used to assess gender differences and comorbid psychiatric disorders according to the ADHD subtypes. The mean age of the girls and boys were compared with *t* test. Analysis of variance was used for comparing the variables of children's age of ADHD subtypes, their parental education level, and age between the 3 types of ADHD. The effects of independent variables including gender, subtype and the interaction between gender and subtype on children's age, parental age, and educational level were analyzed by linear regression models. Comorbid psychiatric disorders as the dependent variable were analyzed by logistic regressions. Gender and ADHD subtypes were used as the independent variables. The significance level was set at 0.05 and all the tests were 2-tailed.

Results

Of the 171 children and adolescents participating, 136 (79.5%) were boys and 35 (20.5%) were girls. The male–female ratio of the sample was about 3.89:1. The mean age of the sample was 9.0 (standard deviation = 2.5) years and that of the girls and boys was not different ($t = .12, df = 168, P = .9$). In addition, the preschool, school age, and adolescents' means of age for different types of ADHD were not different (Table 1).

Of the 171 children and adolescents, 73 (42.7%) were of the combined subtype, 45 (26.3%) inattentive, and 52 (31.0%) hyperactive. Of the 136 boys, 44.5% were from the combined type and the percentages of inattentive and hyperactive/impulsive type were 25.0% and 30.1%, respectively. However, from the 35 girls, 34.3% were combined type and the percentages of inattentive and hyperactive/impulsive type were 31.4% and 34.3%, respectively. There was no significant difference between boys and girls in terms of the prevalence of different ADHD subtypes ($\chi^2 = 1.3, df = 2, P = .5$).

Is ADHD Subtype Associated With Children's Age, Parental Age, Educational Level, and Type of Occupation?

There were no significant gender by subtype interaction effects on the children's age, parents' education level, and age (Table 2). Gender and ADHD subtypes were not associated with parental age and father's education level, but were associated with the mothers' education level. Mothers' education level of boys with ADHD-inattentive type was more than that of boys with ADHD-hyperactive/impulsive type. The fathers' and mothers' type of occupation was not related to the subtypes of the ADHD groups ($\chi^2 = 12.2, df = 12, P = .4$; $\chi^2 = 5.6, df = 8, P = .6$, respectively).

Are Subtypes of ADHD Associated With Increased Risk for Other Comorbid Disorders?

About 26% of the participants had no comorbid psychiatric disorder. In other words, more than 73% of the children with ADHD had at least 1 of the comorbid psychiatric disorders. The most common disorders were oppositional defiant disorder ($n = 93, 54.1\%$) and separation anxiety disorder ($n = 34, 19.8\%$). The rate for other disorders in the whole sample was as follows: conduct disorder 9.9%, obsessive-compulsive disorder 7.6%, tic disorder 14.0%, major depressive disorder 2.3%, and enuresis 11.7%. The frequency of different types of comorbid psychiatric disorders in various ADHD subtypes is shown in Table 3.

The prevalence of none of the psychiatric disorders as the dependent variable was more common in girls than boys (Table 3). There were no gender or subtype differences for oppositional defiant disorder, conduct disorder, separation anxiety disorder, obsessive-compulsive disorder, tic disorder, and enuresis.

Discussion

More than two thirds of the children with ADHD had at least 1 comorbid psychiatric disorder. It is in accordance with the previous studies in the West or Asia using similar

Table 2. Linear Regression Models for Children's Age, Parental Educational Level, and Age in Relation to Gender and ADHD Subtypes

Dependent Variables							Statistical Analysis					
	Boys (n = 136)			Girls (n = 35)			Independent Variables					
							Interaction Effect of Gender and Subtypes of ADHD		Gender Effect		Subtype Effect	
	Inattentive (n = 33), Mean (SD)	Combined (n = 61), Mean (SD)	Hyperactive/Impulsive (n = 44), Mean (SD)	Inattentive (n = 11), Mean (SD)	Combined (n = 12), Mean (SD)	Hyperactive/Impulsive (n = 12), Mean (SD)	t	P*	t	P*	t	P*
Age of children	10.4 (2.7)	8.7 (1.8)	8.4 (2.7)	10.0 (2.3)	8.5 (3.3)	8.5 (2.0)	0.4	.6	0.3	.7	1.6	.1
Age of father	42.4 (11.7)	38.5 (5.8)	41.5 (11.0)	40.8 (5.4)	38 (10.1)	39.2 (5.3)	0.2	.8	0.4	.6	0.08	.9
Fathers' educational level	11.3 (2.7)	9.5 (3.6)	10.3 (3.9)	11.2 (3.4)	10.1 (3.5)	12.6 (3.6)	1.2	.2	1.7	.07	1.3	.1
Age of mothers	33.0 (10.6)	30.7 (8.6)	31.4 (6.8)	34 (6.1)	39.2 (9.2)	31.9 (6.9)	0.1	.8	0.1	.8	.1	.8
Mothers' educational level	11.0 (4.3)	9.7 (3.6)	8.9 (3.8)	10.2 (4.0)	10.4 (3.0)	11.5 (3.3)	1.8	.06	2.2	.02	2.3	.02

Note: ADHD, attention-deficit hyperactivity disorder; P*, significance; t, t student.

Table 3. Logistic Regression Models for Prevalence of the Comorbid Psychiatric Disorder in the Children With ADHD in Relation to Gender and ADHD Subtypes

Dependent Variables							Statistical Analysis			
	Boys (n = 136)			Girls (n = 35)			Independent Variables			
							Gender Effect		Subtype Effect	
	Inattentive (n = 33), n (%)	Combined (n = 61), n (%)	Hyperactive/Impulsive (n = 41), n (%)	Inattentive (n = 11), n (%)	Combined (n = 12), n (%)	Hyperactive/Impulsive (n = 12), n (%)	Wald	P*	Wald	P*
Any psychiatric disorder	23 (67.6)	46 (75.4)	34 (82.)	6 (54.5)	8 (66.7)	9 (75.0)	1.3	.2	3.3	.1
Oppositional defiant disorder	14 (41.2)	33 (54.1)	27 (65.9)	5 (45.5)	7 (58.3)	7 (58.3)	.001	.9	4.6	.9
Conduct disorder	1 (2.9)	11 (18.0)	5 (12.2)	0 (0.0)	0 (0.0)	0 (0.0)	.001	.9	3.6	.1
Separation anxiety disorder	5 (14.7)	16 (26.2)	9 (22.0)	0 (0.0)	0 (0.0)	4 (33.3)	1.7	.1	2.8	.2
Obsessive compulsive disorder	3 (8.8)	6 (9.8)	3 (7.3)	0 (0.0)	0 (0.0)	1 (8.3)	1.2	.2	0.04	.9
Tic disorder	5 (14.7)	10 (16.4)	8 (19.5)	0 (0.0)	1 (8.3)	0 (0.0)	3.4	.06	0.3	.8
Enuresis	8 (23.5)	5 (8.2)	6 (14.6)	1 (9.1)	0 (0.0)	0 (0.0)	3.0	.07	5.0	.07

Note: ADHD, attention-deficit hyperactivity disorder; P*, significance.

method and instruments.^{18,25} In addition, as in the previous studies, oppositional defiant disorder was the most common comorbid disorder detected in more than 50% of the children with ADHD.¹⁸ It seems that the rate of some of the disorders such as conduct disorder, separation anxiety disorder, obsessive compulsive disorder, tic disorder, and enuresis is low in girls. It is possible that the assessment tool might not be sensitive enough for detecting these problems in girls. However, there are 2 other stronger possible explanations. First, most of the children and adolescents with ADHD in the clinic sample are referred by teachers for management of their inattentiveness and hyperactivity.²⁶ Hence, probably many of the

teachers might not be aware of some behaviors such as separation anxiety or enuresis, or the behaviors are not their priority for referring. Second, many parents would like to hide conduct or other behavioral problems of their girls. Of course, the prevalence of comorbid psychiatric disorders in a recently published study on 79 children (78% boys) with ADHD at Stockholm, Sweden, were as follows: Tourette's disorder (11 children) and obsessive-compulsive disorder (2 children). Only 2 children had either oppositional defiant disorder or conduct disorder.²⁷ These rates are lower than the current results.

Comorbidity profiles were not different between the ADHD subtypes. This is in contrast with the results of

some previous studies.^{18,28} Higher rates of “oppositional defiant disorder” and “conduct disorder” in males, and higher rates of “separation anxiety disorder” in females were reported before. They concluded that internalizing disorders were more common in females and externalizing disorders occurred more often in males. In addition, the combined subtype was most likely to have comorbidity. That study was carried out on nonclinical samples and relied on the data of mailed *DSM-IV*-based questionnaires.²⁸ Another study on ADHD in schoolchildren using a questionnaire responded by schoolteachers reported that the hyperactive-impulsive subtype was more frequently identified in girls, whereas the inattentive subtype was more prevalent among boys.²⁹ Both these studies were based on questionnaires without any clinical interviews. However, the current study was conducted on a clinical sample using face-to-face interview. Attention-deficit hyperactivity disorder case identification studies using questionnaires fail to take the criteria concerning the impairment and exclusion due to other disorders into account. In addition, in that study, the parents were the sole informants of the study, and it can be an explanation for the finding that girls were not more likely to present with inattentive type than boys.

In the study by Byun et al in Korea, a greater prevalence of the subtypes was not seen among any genders. The current results are similar to theirs. In addition, they reported that oppositional defiant disorder was more common in the ADHD-combined type.¹⁸ Neither the current study nor the Byun et al study included the severity of ADHD, although it is expected that the clinical samples are suffering from more severe forms of ADHD than the community sample of children with ADHD. There are some studies in which oppositional defiant disorder is related to socioeconomic statuses of the family. Attention-deficit hyperactivity disorder children comorbid with oppositional defiant disorder have mothers with lower socioeconomic level and lower maternal profession than ADHD children without oppositional defiant disorder.^{30,31} The current study included age and educational level of parents as possible predictors.

Another study in the United States reported that oppositional defiant disorder and conduct disorder were significantly more common in ADHD-combined type than in ADHD-inattentive type. In addition, they did not find any difference between the 2 groups in terms of internalizing disorders.⁹ Moreover, the current results are not in accordance with those of the studies in the United States, indicating that oppositional defiant disorder and conduct disorder were more common in boys than girls.¹¹ They also reported that ADHD-inattentive type was more common in girls than boys.¹¹ Meanwhile, the current results are similar to those of the 2 other studies in the United States.^{10,13} They reported that subtypes of ADHD were

not associated with gender, internalizing behavior, and externalizing behavior.^{10,13}

The current result is in accordance with that of the study reporting a similar level of anxiety among children with ADHD-combined and ADHD-inattentive types.¹² Moreover, similar to a study's finding in Korea, the most common anxiety disorder was separation anxiety disorder.¹⁸

Most of the above-mentioned studies did not include the socioeconomic status of the children as the covariant factor. A study reported that social class of inattentive type of children with ADHD was lower than that of the other types of ADHD³² while in the current study, the education level of the mothers of children with ADHD-inattentive type is more than that of the other types. Differences of socioeconomic status of different types of ADHD in the current study can be an explanation for this difference with the prior studies. In addition, some of the previous studies are not based on *DSM-IV* diagnostic criteria and it can be another possible explanation for these differences.³²

The participants were a clinical sample, and lack of some comorbidity patterns may not be real because the participants with more severe impairment of function might be referred to clinics and any inferences that these findings are applicable to ADHD comorbidity patterns in the general population are not warranted. Another concern is the reliance of the study on parents' report for differentiation of ADHD subtypes. Meanwhile, knowledge of parents of children with ADHD in Iran is relatively low and they usually refer with a significant delay.²⁶ This cultural aspect might affect the results, because they probably refer for treatment when there is a higher impairment. The sample was not so large and it might not have enough power to detect some differences. Hence, the fact that no statistically significant difference was found between the groups does not prove that the different groups are equivalent. Further studies with consideration of impairment, severity, and multiple informants are recommended.

It can be concluded that ADHD subtypes of comorbidity in Iran are somewhat different from those of some studies in the western culture. The current results are more similar to those of the other Asian countries. However, there are some differences between them.

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