PREVALENCE OF ATTENTION-DEFICIENT/HYPERACTIVITY DISORDER CO-MORBIDITIES IN CHILDREN OF SOUTH JORDAN

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Abstract

The treatment success of attention-deficient/hyperactivity disorder (ADHD) is limited by misdiagnosis or underestimated co-existing conditions, including epilepsy, mental retardation, and autism spectrum disorder. The aim of this study was to document the prevalence of these three ADHD co-morbidities in a single patient population. A total of 107 children (3-12 years) evaluated for ADHD in our neurology clinic (clinical sample) were initially considered for this study. The existence of co-morbidities was determined using parent interview, family history, medical history, developmental history, and neurological evaluation. Results showed that 82 patients (M:F; 60:22) fulfilled the criteria for ADHD diagnosis. The patient population was composed of combined ADHD (51%), hyperactive/impulsive (28%). and inattentive (21%), Boys were about three times more likely to present with combined or hyperactive/impulsive ADHD compared to girls. Among all ADHD children, 70% presented co-morbidity: epilepsy ((29.3%), mental retardation (28%) or autistic spectrum disorder (12.2%). Such common occurrence suggests that the current protocols used to diagnose ADHD should be refined to identify these co-morbidities for the development of a new approach to ADHD. Our findings add relevant clinical information on ADHD from a world region where few clinical studies on this disorder have thus far been conducted.

Keywords: ADHD, mental retardation, childhood epilepsy, autistic spectrum disorder, co- morbidities, Jordan, children

Introduction

Attention-deficient/hyperactivity disorder (ADHD) is a syndrome characterized by three types of symptoms; inattention, hyperactivity, and impulsivity (Reiff et al. 1993; Barkley 1996). It is a common

neurobehavioral disorder affecting school-aged children (Shooshtary et al. 2010). The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria define three subtypes of ADHD: inattentive, hyperactive-impulsive, and combined type (APA-1994).

ADHD symptoms present during childhood but often continue into adolescence (Biederman et al. 1996). As a result, children with ADHD may experience significant functional problems, such as difficulty in school and academic underachievement (Zentall 1993), troublesome interpersonal relationships with family members and peers (Schachar 1987; Almond et al. 1999), and low self-esteem. Individuals with ADHD present in childhood continue to show symptoms of mental disorders such as oppositional defiant conduct, depression, and anxiety in adolescence. It is also associated with many developmental and neurocognitive disorders that share common manifestations (August 1996).

ADHD and epilepsy are both common childhood disorders (Reilly CJ 2011). DSM-5 includes no exclusion criteria for people with autism spectrum disorder, since symptoms of both disorders co-occur. Because they share symptoms with ADHD, these co-morbidities may seriously interfere with the design of effective treatments. Children with epilepsy may manifest symptoms of ADHD, whereas children with ADHD may develop epilepsy. Some antiepileptic drugs such as phenobarbitone, gabapentin, topiramate, and levetiracetam, may not be helpful in controlling behavioral symptoms of ADHD. Stimulants are the main stay of pharmacotherapy for ADHD but there is a risk of decreasing seizure threshold in children with co-morbid epilepsy especially when their epilepsy is not well controlled. Existing evidence is not in favor of screening children with ADHD for an EEG abnormality before starting stimulant therapy (Kattimani S. 2011).

Recent studies suggest that ADHD is a common co-morbid condition in childhood epilepsy (Cohen R, et al.).ADHD is significantly more prevalent in new onset epilepsy than healthy controls (31% VS 6%) (Hermann B 2007). To our knowledge, no study has documented the prevalence of ADHD, epilepsy, mental disorders, and autistic spectrum disorder (ASD) in a single population. This is the first study to document the prevalence of all 3 major types of ADHD co-morbidity: epilepsy, mental retardation, and autism spectrum disorder in the same patient population. Findings of this study may lead to the development of new intervention approaches to this disorder.

Therefore, the aim of this study was to compare the prevalence of epilepsy, mental retardation, and ASD in children diagnosed with ADHD and to assess ADHD manifestations in children suffering with these three neurological conditions, as well as to increase awareness of clinicians to consider these co-morbidities in the evaluation of children having ADHD.

This study comes from a world region where little clinical research on this disorder has been conducted.

Study Design and Methods

A total of 107 children visiting any of the two pediatric neurology clinics in Al karak city of South Jordan during the period of October 2009 to 2011 for consultation regarding manifestations of ADHD were recruited in this study. Inclusion criteria for each child was to have one or combination of hyperactivity, inattention, or impulsivity. The DSM-IV diagnosis of ADHD requires the presence of six of nine items or features that must have been present for at least six months and to have had an onset before 7 years of age (Tan M. 2005). All children were accompanied by their parents. During their visit, complete details on developmental (antenatal, natal, and post-natal), medical, and family history were recorded. General and neurological examinations were performed for all children, and investigations such as brain CT or EEG were conducted when indicated. A SWAN rating scale for ADHD validated by James Swanson (Swanson 2012) including all DSM-IV criteria were completed by the mothers of all participants for the diagnosis of ADHD. An informed consent was obtained from all the parents before the questionnaire was administered.

Epilepsy was diagnosed clinically and by conducting electroencephalography [EEG] and neuroimaging examination when indicated.

Statistical analysis

Frequency, valid percentage, mean, and SD were reported for all the variables appropriately. Chi square test was performed for comparing non-categorical variables among the groups. A p value of <0.05 was considered statistically significant.

Results

Of the 107 subjects manifesting symptoms of ADHD and examined at the clinic, only 82 (76.6 %) met the criteria for ADHD. Among these patients, 60 (73.2 %) were male and 22 (26.8%) were female

Male to female ratio was found to be significantly different for hyperactive impulsive type ($p = 0.003$) compared to other groups. For the combined subtype, the male to female ratio was significantly different ($p = 0.008$). The total male to female ratio for all children (60:22) also differed significantly ($p = 0.00004$). There was no statistically significant difference observed in the male and female ratio for the inattentive subtypes ($p = 0.4$) (Table

Table 1: ADHD subtypes, male /female distribution, and ratios using Chi square test.

Sub type	Number of Cases	%	Male	%	Female	%	Ratio	Chi square	P value
Inattentive	17	20.7	10	58.8	7	41.2	1.43:1	0.53	0.4
H.I	23	28	18	78.2	5	21.7	3.6:1	7.35	0.003
Combined	42	51.2	32	76.3	10	23.8	3.2:1	6.76	0.008
Total	82		60		22		2.9:1	12.6	0.00004

Among patients who met the criteria, the combined subtype was the most common, representing (51.2%) of all cases. The hyperactive-impulsive and inattentive subtypes were diagnosed in 28 and 27.2% of patients, respectively. More than 29% of the patients in this study had both epilepsy and ADHD. Prevalence of mental retardation was 28% among patients in this study. Ten patients (12.2%) had ASD and prominent features of ADHD. On comparing gender against morbidity, it was found that only the association of ASD to male gender was significantly different ($p = 0.014$) (Table 2).

Table 2: Co-morbidities versus gender

Co morbidity	Total	Male	Female	Chi square	p value
Epilepsy	24	15	9	1.5	0.2
M.R	23	14	9	1.15	0.3
ASD	10	9	1	6.4	0.14

Regarding co-morbidities versus subtype, we found that there was an association between co-morbidities and all subtypes of ADHD; however, it was significant only with the combined subtype ($p = 0.012$) for epilepsy and mental retardation ($p = 0.008$) for ASD (Table 3).

Table 3: Co-morbidities and their correlation to subtypes

	Total	Inattentive	Hyperactive impulsive	Combined	Chi square	P value
Epilepsy	24	3	8	13	6.25	0.012
M.R.	23	6	5	12	6.25	0.012
ASD	10	0	3	7	7.56	0.008

Discussion

The rate of ADHD diagnosis among children has increased over time (Getahun D 2013). However, we now face the troubling reality that ADHD may be complicated by additional complications with common symptoms. The present study was designed to test the prevalence of epilepsy, mental retardation (MR) and autistic spectrum disorder (ASD) in a patient population presenting with ADHD manifestations.

Male to female ratios were similar to the figures commonly reported for this syndrome [overall prevalence of current DSM-IV-like ADHD was 9.2% with a male:female ratio of 2.28:1] (Ramtekkar et al. 2010). The

number of males was almost three times as great as the number of females (2.9:1) in our study population. The male to female ratios for the hyperactive-impulsive (3.6:1) and combined (3.2:1) subtypes were also similar to ratios reported in the literature. Although there was also a larger number of males with the inattentive subtype, the male to female ratio (1.43:1) was lower than that observed for the other subtypes.

The predominance of Combined ADHD has been reported in other countries (Wang et al. 2011; Chiang et al. 2010). Furthermore, boys were three times more likely to develop ADHD, especially in the Combined or hyperactive/impulsive subtypes. These data are consistent with the male predominance (70%) reported for 88 hyperactive/ impulsive ADHD patients in the US (Miller et al. 2010). In Greece, the estimated prevalence of ADHD was 8% for boys and 3.8% for girls (Skounti et al. 2010). Overall, these data demonstrate that the patient population included in the present study is representative of the global situation, with a predominance of boys diagnosed with Combined ADHD.

Over twenty-three percent of children that reported to the neurological clinic with ADHD manifestations failed to fulfill the criteria for the disorder, as established by the DSM-IV. This discrepancy can be explained by several factors. First, some children had ADHD manifestations but fulfilled only 5 of 9 behavioral criteria. Overprotection by the mothers likely contributed to this.

ADHD and epilepsy

Epilepsy and attention-deficit hyperactivity disorder (ADHD) were reported to co-occur at rates higher than expected for coincidental findings ***(***Cohen R, 2013). Population studies suggest that the prevalence of ADHD in patients with childhood epilepsy is between 12 and 17%. Several factors may account for this positive association. These include common genetic propensity, noradrenergic system dysregulation, subclinical epileptiform discharges, seizures, antiepileptic drug effects and psychosocial factors (Reilly 2011).

Population studies support the common occurrence of ADHD and epilepsy co-morbidity. A review of literature between 1990–2010 reported 20–40% ADHD children to be epileptic (Kattimani & Mahadevan 2011). These data are consistent with the present study reporting 29% of ADHD children to be epileptic. Furthermore, we documented the incidence of epilepsy morbidity in the three types of ADHD. As commonly reported for ADHD patients, more than 50% of the patients with co-morbidity belonged to the combined ADHD group. In contrast, epilepsy co-morbidity was very low in Inattentive ADHD patients. Epileptic children may manifest symptoms of ADHD due to a lifetime depression and anxiety, as well as

from seizure and brain damage (Titlic 2009). Further, children with ADHD are predisposed to epileptic seizure (Hesdorffer et al. 2004).

In addition, a strong trend towards a higher prevalence of epilepsy among children with ADHD is observed compared to those without ADHD. Epilepsy in children with ADHD appears to be more severe than those without ADHD (Davis et al. 2010). This co-condition raises issues regarding diagnostics and medications. Stimulants are the mainstay of pharmacotherapy in ADHD. But there is low risk of promoting seizures in children with co morbid epilepsy.

ADHD and mental retardation

Children with milder forms of mental retardation may escape detection until their school years, when parents or teachers begin to recognize symptoms or learning disabilities and bring them to a pediatrician for evaluation. Until recently, physicians did not believe that ADHD occurred in children with mental retardation, but assumed that these children's hyperactive or other ADHD-type behavior was simply a manifestation of mental retardation. As a result, stimulant medications were rarely prescribed, and ADHD was left untreated. A study by Das JP et al reported 33% of junior and senior high school students with mild MR had ADHD (Das & Melnyk 1989). Population studies suggest that mental retardation may be 5-10 times as common in ADHD as in children without ADHD [Kadesjo B. Gillberg C (2001), Pliszka SR (2000)]

In our study, mental retardation was determined based on the Stanford Binet intelligence test in those children who had been removed from mainstream classrooms, or with parents considering that the child was unfit for school. Based on these criteria, the incidence of mental retardation (28%) among patients in this study falls near the lower end of this range. We also observed a higher incidence in males, which is likely explained by the higher prevalence of this syndrome within this sex, and over half (52.5%) of the MR cases occurred in patients with the combined subtype.

ADHD and ASD

In a recent review, Kolevzon (Kolevzon 2007) noted that symptoms of attention deficit, impulsiveness, and hyperactivity are relatively common among individuals with ASD. Similar findings were acknowledged by Kanner et al in his original description of the symptomatology associated with autism. In a recent survey of 487 children and adolescents with ASD, more than 50% had moderate-to-severe symptoms of inattention and hyperactivity (Lecavalier 2006). In another sample of 101 children with ASD, 95% exhibited attention deficit, 50% demonstrated impulsive behavior, and 75% had symptoms consistent with ADHD (Reiersen et al. 2007). Overall, it is estimated that ADHD occurs in the range of 14–80% of patients with ASD. While ADHD is not a core symptom, the manifestations

of ADHD can be even more debilitating for patients with both disorders (Goldstein & Schwebach 2004). DSM-5 includes no exclusion criteria for people with autism spectrum disorder, since symptoms of both disorders co-occur.

In the present study, symptoms of attention deficit, impulsivity, and hyperactivity were common among individuals diagnosed with ASD. Ten patients (12.2%) had ASD and prominent features of ADHD. Of these, nine of them were males. The ratio of males to females with both disorders is much higher than the usual 4:1. Regarding subtypes, 70% of cases occurred in individuals with the combined subtype, and the remaining 30% were observed in individuals with the hyperactive-impulsive subtype.

The relationship between ADHD and childhood epilepsy, mental retardation and autistic spectrum disorder is complex. Numerous factors contribute to variation in estimates of prevalence and obscure relationships between these disorders. This study demonstrates the high prevalence of ADHD co-morbidities in Jordanian children.

Limitations in this study include the fact that these children were transferred to a pediatric neurology clinic due to ADHD manifestations, school failure, learning difficulties, behavioral disorders (ASD) and epilepsy. In other words, it is not a true group of ADHD patients (population study) but it is rather a clinical sample with a variety of neurological conditions having in common ADHD manifestations.

Conclusions

This is the first study to document the prevalence of all 3 major types of ADHD co-morbidity in the same patient population. Among all ADHD children, 70% presented co-morbidity as follows: epilepsy (29.3%), mental retardation (28%) or autistic spectrum disorder (12.2%). The present study demonstrates the common occurrence of co-morbidities in all three subtypes of ADHD, namely epilepsy, mental retardation, and autism spectrum disorder and their significant association with the combined subtypes. Since these conditions are associated with the diagnostic and treatment strategies of ADHD, it is adamant that clinicians routinely consider the possibility of co-morbidities in their diagnosis of ADHD, especially in the combined subtypes. This study is particularly important to our understanding of this condition because is originates from a world region where little clinical research on this disorder have been conducted.

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References:

Almond BW Jr, Tanner JL, Goffman HF (1999) The Family Is the Patient: Using Family Interviews in Children's Medical Care. 2nd Ed. Baltimore, MD: Williams & Wilkins

August GJ, Realmuto GM, MacDonald AW III, Nugent SM, Crosby R (1996) Prevalence of ADHD and comorbid disorders among elementary school children screened for disruptive behavior. J Abnormal Child Psychol 24:571–595

Barkley, R.A (1996) Attention Deficit Hyperactivity Disorder: A Handbook for Diagnosis and Treatment. 2nd Ed. New York: Guilford Press

Biederman J, Faraone SV, Milberger S, Curtis S, Chen L, Marrs A, Quellette C, Spencer T (1996) Predictors of persistence and remissions of ADHD into adolescence: results from a four-year prospective follow-up study. J Am Acad Child Adolesc Psychiatry 35:343–351

Chiang HL, Gau SS, Ni HC, Chiu YN, Shang CY, Wu YY, Lin LY, Tai YM, Soong WT (2010) Association between symptoms and subtypes of attention-deficit hyperactivity disorder and sleep problems /disorder. J. Sleep Res 19:535–554

Cohen R, Senecky Y, Shuper A, Inbar D, Chodick G, Shalev V, Raz R (2013) Prevalence of epilepsy and attention-deficit hyperactivity (ADHD) disorder: a population-based study. J Child Neurol. 28: 120-3. doi: 10.1177/0883073812440327. Epub 2012 May 1.

Das JP, Melnyk L (1989) Attention checklist a rating scale for mildly mentally handicapped adolescents. Psych Rep 64:1267–1274

Davis SM, Katusic SK, Barbaresi WJ, Killian J, Weaver AL, Ottman R, Elaine WC (2010) Epilepsy in children with attention-deficit/hyperactivity disorder. Pediatr Neurol 42:325–30

Diagnostic and Statistical Manual for Primary Care (DSM-PC) (1996) Child and Adolescent Version. Elk Grove Village, IL: American Academy of Pediatrics

Getahun D, Jacobsen SJ, Fassett MJ, Chen W, Demissie K, Rhoads GG (2013) Recent trends in childhood attention-deficit/hyperactivity disorder. JAMA Pediatr. 167: 282-8 doi: 10.1001/2013.jamapediatrics.401.

Goldstein S, Schwebach AJ (2004) The comorbidity of pervasive developmental disorder and attention deficit hyperactivity disorder: results of a retrospective chart review. J Autism Dev Disord 34:329–339

Hermann B, Jones J, Dabbs K, Allen CA, Sheth R, Fine J, McMillan A, Seidenberg M (2007) The Frequency, Complications and Aetiology of ADHD in New Onset Paediatric Epilepsy. Brain 130: 3135-3148

Hesdorferr DC, Hauser WA, Ludvigsson P, Olafsson E, Kjartansson O (2004) ADHD as a risk factor for incident unprovoked seizures and epilepsy in children. Arch Gen Psychiatry 61:731–36

Kadesj¸ B, Gillberg C (2001) The comorbidity of ADHD in the general population of Swedish school-age children. J Child Psychol Psychiatry 42:487–492

Kattimani S, Mahadevan S (2011) Treating children with attention-deficit/hyperactivity disorder and comorbid epilepsy. Ann Indian Acad Neurol 14:9–11

Kolevzon A (2007) Helping the hyperactive child: when autism looks like ADHD. Medscape Learning Activity

Lecavalier L (2006) Behavioral and emotional problems in young people with pervasive developmental disorders. J Autism Develop Disord 36:1101–1114

Mahadevan S (2011) Treating children with attention-deficit/hyperactivity disorder and comorbid epilepsy. Ann Indian Acad Neurol 14:9–11 (http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3098523/)

Miller DJ, Derefinko KJ, Lynam DR, Milich R, Fillmore MT (2010) Impulsivity and Attention Deficit-Hyperactivity Disorder: Subtype Classification Using the UPPS Impulsive Behavior Scale. J Psychopathol Behav Assess 32:323–32

Pliszka SR (2000) Patterns of psychiatric co morbidity with attention deficit hyperactivity disorder. Child Adolesc Psychiatry Clin North Am 9:525–540

Ramtekkar UP, Reiersen AM, Todorov AA, Todd RD (2010) Sex and age differences in attention-deficit/hyperactivity disorder symptoms and diagnoses: implications for DSM-1V and ICD-11. J Am Acad Child Adolesc Psychiatry 49:217–228

Reiersen A, Constantino J, Volk H, Todd R (2007) Autistic traits in a population-based ADHD twin sample. J Child Psych Psych 48:464–472

Reiff MI, Banez GA, Culbert TP (1993) Children who have attentional disorders: diagnosis and evaluation. Pediatr Rev 14:455–465

Reilly CJ (2011) Attention deficit hyperactivity disorder (ADHD) in childhood epilepsy. Res Dev Disabil 32:883–893

Schachar R, Taylor E, Wieselberg MB, Ghorley G, Rutter M (1987) Changes in family functioning and relationships in children who respond to methylphenidate. J Am Acad Child Adolesc Psychiatry 26:728–32

Shooshtary M, Chimeh N, Najafi M. Mohamadi M, Nouraie R, Mvaghar A (2010) The prevalence of Attention Deficit Hyperactivity Disorder in Iran: A systematic review. Iran J Psychiatry 5:88–92

Skounti M, Giannoukas S, Dimitriou E, Nikolopoulou S, Linardakis E, Philalithis A (2010) Prevalence of attention deficit hyperactivity disorder in schoolchildren in Athens, Greece. Association of ADHD subtypes with social and academic impairment. Atten Defic Hyperact Disord 2:127–32

Swanson (2012) Internet URL: http://www.ibx.com/pdfs/providers/ resources/worksheets/prevhealth_swan.pdf. Accessed on 13 May 21013
Tan M, Appleton R (2005) Attention deficit and hyperactivity disorder, methylphenidate, and epilepsy. Arch Dis Child. 90: 57-9
Teacher and Parent Rating Scale by James Swanson, PhD [home page on the internet]. Attention deficit disorder resources[cited on 2012 Nov 28]. Available from: http://www.addresources.org
Titlic M (2009). Comorbidity psychiatric disorders in epilepsy: a review of literature. Bratisl Lek Listy 110:105–109
Wang LJ, Huang YS, Chiang YL, Hsiao CC, Shang ZY, Chen CK (2011) Clinical symptoms and performance on the continuous performance test in children with attention deficit hyperactivity disorder between subtypes: a natural follow-up study for 6 months. BMC Psychiatry 11:65
Zentall SS (1993) Research on the educational implications of attention deficit hyperactivity disorder. Exceptional Child 60:143–153