Psychiatric Comorbidity among Children with Autism Spectrum Disorders in Najaf Province

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الخلاصة

خلفية الدراسة: مقارنآ مع العديد من اضطرابات الطفولة المزمنة الأخرى، اضطراب طيف التوحد (ASD) هي مجموعة خطيرة ومعيقة من الاضطرابات العصبية النمائية. وقد أعطيت اهتماما قليلا نسبيا وخاصة في العالم العربي في الكشف المبكر عنها والاضطرابات النفسية المرضية المصاحبه لها.

الأهداف : الهدف الرئيسي للدراسة الحالية هو تحديد الاضطرابات النفسية المشتركة لدى الأطفال الذين يعانون من اضطرابات طيف التوحد (ASD) ومعرفة الخصائص الديموغرافية المرتبطة بهذا الاضطراب .

المنهجية : أجريت الدراسة خلال الفترة من 1 كانون الثاني 2013 إلى 30 كانون الاول 2013 .المشاركون في الدراسة هم الأطفال المراجعين الذين تتراوح أعمارهم بين 3-12 سنة (العدد الكلي = 100) في وحدة الطب النفسي لمستشفى الحكيم العام في النجف الاشرف. شملت الدراسه استبيان شبه منظم لمختلف الخصائص الديموغرافية والأكاديمية بما في ذلك العمر والجنس والتحصيل الدراسي للوالدين والمهنة الخ. استخدمت تصنيفات الطبعة الرابعة للدليل التشخيصي الإحصائي(DSM –IV) كتشخيص اولي لاضطراب طيف التوحد ، في حين تم تقييم الاضطرابات النفسية المشتركة باستخدام المقابلة التشخيصية المنظمه، المقابلة السريرية المنظمه للدليل التشخيصي الإحصائي-الطبعة الرابعة (DSM- IV ، الخاصة بالاطفال (KID – SCID) .تم إجراء التحليل الإحصائي بواسطة الحزمة الإحصائية للعلوم الاجتماعية. (SPSS)

النتائج : اظهرت الدراسه الحالية ان الغالبية العظمى من المرضى تتراوح اعمارهم مابين 5-10 سنوات. كما بينت الدراسة ان نسبة ذات دلالة إحصائية من الأطفال الذين يعانون من اضطراب طيف التوحد هم من الذكور الذين يعيشون في المدينة ، ودخل أسرهم يكفي لسد الحاجة مع حجم أسرهم صغيرة ، كما أن المستوى التعليمي للابوين جيدا ولكن والدتهم ربة منزل . تسعة وخمسون طفلا من الاطفال الذين يعانون من اضطراب طيف التوحد(59%) صنفوا على ان لديهم واحدة على الاقل من الاضطرابات النفسيه المصاحبة لاضراب طيف التوحد. ومع ذلك، كان الأطفال الذين يعانون من اضطراب طيف التوحد لديهم أكثرنسبه من الاضطرابات النفسية الاستيعابية(الداخلية) (39 ٪) مقارنة بالاضطرابات النفسية الخارجية (اضطراب المعارضة و/ أو اضطراب السلوك) (20%). وبشكل أكثر تحديدا ، كان الأطفال الذين يعانون من اضطراب طيف التوحد لديهم ارتفاع معدلات اضطرابات القلق (31 ٪) اكثر من اضطرابات المزاج.

الاستنتاجات :أكدت الدراسة الحالية ان الكثير من مرضى اضطراب طيف التوحد يعانون من اضطرابات نفسية أخرى ، لذلك لابد من الأطباء المعرفة والبحث عن الاضطرابات المشتركه ، والنظر في العلاج لمثل هذه الاضطرابات المرضية . بالإضافة إلى ذلك، هناك حاجة ماسه إلى المزيد من الأبحاث حول وبائيات ومأل الاضطرابات الطبية والنفسية المرتبطة بالتوحد.

Abstract

Background:

Compared with several other chronic childhood disorders, autism spectrum disorder (ASD) is a serious and disabling group of neurodevelopmental disorders. Relatively little attention has been given to its early identification and comorbid psychiatric disorders especially in the Arab world.

Objectives: The present study was conducted with the main aim to identify comorbid psychiatric disorders in children with autism spectrum disorders (ASD) and to find out the sociodemographic factors in relation to ASD.

Methods: The study was conducted from 1st January 2013 to 30th December 2013. Participants were clinically referred children aged 3–12 years (n = 100) at psychiatric unit of AL Hakeem General Hospital in Najaf. A semi-structured questionnaire included the various demographic and academic characteristics including age, gender, parental educational and occupational status etc. DSM-IV classifications were used

for the primary diagnosis (ASD), while comorbid psychiatric disorders were assessed using a structured diagnostic interview, the structured clinical interview for DSM-IV, childhood diagnoses (KID-SCID). Statistical analysis was performed with the Statistical Package for the Social Sciences (SPSS).

Results: The majority of the patients were aged 5–10 years. Statistically significant proportion of children diagnosed with an ASD was male who live in an urban area and had satisfactory family income with small family size, they also had well educated parents but their mother was housewife. Fifty-nine children with ASD (59%) were classified as having at least one comorbid psychiatric disorder. However, children with ASD had more comorbid internalizing disorders (39%) compared to comorbid externalizing disorders (ODD and/or CD) (20%). More specifically, children with ASD had higher rates of anxiety disorders (31%), but not mood disorders.

Conclusions: This study confirms the frequent co-occurrence of ASD with other psychiatric disorders, so it is important for clinicians to always be aware of, and screen for, comorbidity, and to consider treatment for these comorbid disorders. In addition, more research is needed on the epidemiology of autism-related medical and psychiatric disorders and outcome.

Keywords: Autism Spectrum Disorder (ASD), Structured Clinical Interview for DSM-IV, Childhood version (KID-SCID), Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), Oppositional defiant disorder (ODD), Conduct disorder (CD).

Introduction

Autism Spectrum Disorder (ASD) is a life-long developmental disability which is typically diagnosed in childhood. ASD is categorized as a "spectrum" because it encompasses a group of developmental disorders with accompanying characteristics varying in severity. ASD is shown to cause restricted and repetitive patterns of behaviors (e.g., bizarre fixation with specific parts or sensory aspects of an object), impairments in social relatedness (e.g., failure to develop appropriate peer relationships), and impairments in verbal and nonverbal communication (e.g., delay or absence of spoken language)[(1).]

The autism spectrum includes Autistic Disorder, Asperger's Disorder, Rett's Disorder, Childhood Disintegrative Disorder, and Pervasive Developmental Disorder-Not Otherwise Specified[(1).]

Patients with ASD also suffer from many comorbid features such as anxiety, depression, ADHD and behavioral problems [(2)].

Epidemiological findings reveal that ASD is the most strongly genetic developmental disorder, with a heritability factor greater than 90 percent [(3).] As stated previously, ASD is seen more commonly in boys than girls (ratio of 4:1) and biological siblings of an affected child run a higher risk of having the disorder [(1)].

As observed by Kabot, Masi and Segal [(4)], there is consensus that ASD can be classified as three different, but interdependent levels. These levels are:

1. A neurological disorder related to brain development;
2. A psychological disorder of cognitive and emotional; and
3. A relationship disorder impacting behavioral development, or in which there is a failure of normal socialization.

There is no reason to suppose that there is only one pathway or one specific risk factor; it would appear that several etiological pathways could lead to ASD.

While impairment due to the social and cognitive deficits characterizing ASD is well-demonstrated, less well-known is the

impact of co-occurring mental health disorders. Accurate reliable diagnosis of co-occurring mental health disorders is critical, due to associated problematic behaviors. When a youth's symptoms can be attributed to the mental health disorder, more targeted intervention is possible [2].

Recent studies have shown that mental health disorders are common and frequently multiple in children and adolescents with ASD [5]. Frequently, these children and adolescents are diagnosed with multiple mental health disorders. One study examined the adjusted odds of youth with ASD being diagnosed with a co-occurring mental health disorder [6]. This study found that the likelihood of a youth being diagnosed with a co-occurring psychiatric disorder rose significantly with each additional year of life and as autism severity increased. This study also revealed the likelihood of under-diagnosis of potentially treatable co-occurring disorders.

Another study investigated the rates and types of co-occurring disorders in a group of 84 children and adolescents with ASD (Moseley, Tonge, Brereton & Einfeld, 2011). This study found that 42 percent of those youth with ASD had a co-occurring mental health disorder. The disorders included mood disorders, anxiety disorders, adjustment disorders, and behavior disorders. A significant finding from this study was that the rate of co-occurring disorders was between 2 to 4 times of that found among typically developing young people [7].

Current research shows that potentially treatable co-occurring mental health disorders in youth with ASD have likely been under-diagnosed. This may be explained because no assessment instrument has the validity and reliability to deem it a "gold standard" for diagnosing present and lifetime mental health disorders in youth with ASD [2]. Accordingly, it may be prudent to incorporate an assessment for a co-occurring mental health disorders upon diagnosis of an ASD [5].

To conclude, several studies have examined psychiatric comorbid disorders by using structured diagnostic interviews in children with ASD, however examining comorbidity in clinical samples is important because they may influence the symptoms of the primary diagnosis (e.g. anxiety symptoms may exacerbate ASD-symptoms[8] and may affect treatment plans and outcomes [9].

Method participants

The study was conducted from 1st January 2013 to 30th December 2013. All children were referred to a general outpatient at psychiatric unit of AL Hakeem General Hospital in Najaf, the Iraq. In total 100 children, aged 3–12, and their parent(s) participated: all those children had a primary DSM-IV-TR classification of ASD. No standardized measures were used to confirm the primary diagnosis. However, we are confident about the reliability of the ASD classification since the agreement between a clinical DSM-IV-TR classification of ASD and an ASD classification based on the Autism Diagnostic Interview-Revised (ADI-R) [10] was excellent (97.8 %) [11].

In addition, the KID-SCID [12] was used to assess psychiatric comorbid disorders.

Instrument

A semi-structured questionnaire: The questionnaire included the various demographic and academic characteristics including age, gender, parental educational and occupational status, family size, income and residence with an assessment sheet for family history of related illness, perinatal events, and developmental factors.

The KID-SCID [13] was used to assess (comorbid) psychiatric DSM-IV disorders. The KID-SCID is based on the widely used adult SCID with the questions adapted for applicability to children (and with additional childhood disorders). The adult SCID has demonstrated acceptable reliability and validity levels [13]. In addition, several studies support the validity and reliability of the KID-SCID [14]. Kappa values for the test–retest reliability of the KID-SCID were found to range from .63 to .84 for the disruptive behavior disorders (kappa was .84, .63, and .84 for ADHD, ODD, and CD

respectively) and from .44 to 1.0 for the anxiety disorders (kappa was 1.0, .66, and .44 for social anxiety disorder, separation anxiety disorder, and post-traumatic stress disorder, respectively) [14]. In addition, kappa values for the inter-rater reliability were 1.0 for disruptive behavior disorders, .63 for anxiety disorders, and .76 for the diagnosis of a current major depressive disorder [15].

In administering the KID-SCID, a respondent is asked whether a particular DSM-IV symptom is present. The symptom is rated as: (1) absent, (2) possibly present, or (3) present. Both child and parent(s) provide answers and the interviewer combines the information of all respondents to rate a 'best' score. Next, the number of symptoms rated as 'present' is counted. If the required number of symptoms is met (i.e. the DSM-IV symptom-criterion is met), the interviewer asks about other DSM-criteria (such as 'at what age symptoms emerged' or 'whether symptoms cause interference with daily activities'). Finally, a KID-SCID diagnosis is obtained when all DSM-IV criteria are met. In the present study, information was obtained from parent(s) and child and the following sections of the KID-SCID were administered: disruptive behavior disorders (ADHD, ODD and CD), mood disorders (major depressive disorder and dysthymic disorder) and anxiety disorders (separation anxiety disorder, social anxiety disorder, specific phobia, generalized anxiety disorder, obsessive–compulsive disorder, panic disorder, agoraphobia, post-traumatic stress disorder, and anxiety disorder not otherwise specified).

Procedure

A semi-structured questionnaire: The questionnaire included the various demographic and academic characteristics including age, gender, parental educational and occupational status, family size, income and residence with an assessment sheet for family history of related illness, perinatal events, and developmental factors.

DSM-IV classification of ASD was established by psychiatrists, and was based on clinical evaluations. Clinical evaluations included for example interviews with parent(s) and child, observations of child-parent interaction, and/or psychiatric consults. Participants gave consent. The KID-SCID was administered in the outpatient psychiatric unit.

Data Analyses

In order to achieve the early stated objectives, the data of the study were analyzed through the use of statistical package of social sciences (SPSS) version 16 through descriptive and inferential statistical analyses.

Results

Table 1 Sociodemographic characteristics of reported ASD cases (Total number=100)

Variable		No.	%	df	X^2	p-value
Age(year)	Less than 5	11	11	2	25.1	<0.005
	5-10	51	51			
	10-12	38	38			
Gender	Male	80	80	1	36.0	<0.005
	Female	20	20			
Residency	Urban	84	84	1	46.24	<0.005
	Rural	16	16			
Father education	Above secondary school	65	65	1	9.0	<0.005
	≤ secondary school	35	35			

Mother education	Above secondary school	79	79	1	33.64	<0.005
	≤ secondary school	21	21			
Mother occupation	Housewife	64	64	1	7.84	<0.01
	Working outside home	36	36			
Family income	Satisfactory*	76	76	1	27.04	<0.005
	Unsatisfactory	24	24			
Family size	Less than 5 members	61	61	1	4.84	<0.05
	≥ 5 members	39	39			

***Satisfactory family income means sufficient enough to satisfy the living need of the family without being in debt.**

Table 1 shows the Sociodemographic characteristics of the enumerated cases. The majority of the patients were aged 5–10 years. Statistically significant proportion of male children diagnosed with an ASD. Most of the ASD cases were children who live in an urban area and had satisfactory family income with small family size.
Greater number of children with ASD had well educated parents but their mother was housewife.

Table 2 Family history, perinatal and developmental problems in children with ASD (Total number=100)

variable		No.	%	df	X^2	P value
Family history	Consanguinity	29	29	4	13.2	<0.005
	Autism	26	26			
	DLD*	21	21			
	MR**	9	9			
	Negative	15	15			
Perinatal problems	Yes	36	36	1	7.84	<0.05
	No	64	64			
Developmental history	Delayed Milestones	8	8	2	139.49	<0.005
	DLD	89	89			
	Negative	3	3			

DLD*: Delayed Language Development MR**: mental retardation

Table 2 showing abnormal family history was significantly more apparent represented in higher incidence of family history of consanguinity and neurodevelopmental disorders such as autism, delayed language development and mental retardation.

Perinatal problems are also more prevalent among children with ASD and this association was of statistical significance.
Moreover, reported case of children with ASD showed more delay in language development in contrary to other Developmental Milestones.

Table 3 Frequency of comorbid psychiatric disorders in children with ASD (Total number= 100)

Variable	No.	%	P value
Comorbid disorder*	59	59	**<0.01**
Internalizing disorders**	39	39	**<0.05**
Anxiety disorders	31	31	**<0.005**
• Separation anxiety disorder	7	7	
• Social anxiety disorder	2	2	
• Specific phobia	10	10	**<0.005**
• Generalized anxiety disorder	12	12	
• Obsessive–compulsive disorder	9	9	
• Panic disorder	2	2	
• Agoraphobia	1	1	
• Post-traumatic stress disorder	0	0	
• Anxiety disorder not otherwise specified	0	0	
Mood disorders	11	11	
• Major depressive disorder	2	2	**<0.005**
• Dysthymic disorder	9	9	
Externalizing disorders(or disruptive behavior) ***	20	20	**<0.005**
Oppositional defiant disorder	19	19	
Conduct disorder	1	1	**<0.005**
Attention deficit hyperactivity disorder	19	19	

*Participants met KID-SCID criteria for at least one comorbid disorder
** Participants met KID-SCID criteria for at least one anxiety disorder and/or mood disorder
*** Participants met KID-SCID criteria for ODD and/or CD

Table 3 showing that this study confirms the frequent co-occurrence of ASD with other psychiatric disorders. Fifty-nine percent of the children in our study had at least one DSM-IV Axis I psychiatric disorder in addition to ASD which considered statistically highly significant p value <0.01 which constitute of Internalizing disorders (39%) and Externalizing disorders(or disruptive behavior) (20%).

Regarding Internalizing disorders greater percentage of children with ASD stated anxiety disorders (31%), of which Generalized anxiety disorder mostly significant rather than other types of anxiety disorders.

Additionally significant percentage of children with ASD reported co-occurrence of two types of Externalizing disorders which are Oppositional defiant disorder (19%) and Attention deficit hyperactivity disorder (19%).

Discussion:

The present study examined psychiatric comorbidity in children with ASD. Autism is commonly reported in literature to have higher incidence in males than females. Fernell and colleagues reported a ratio of 5.5:1 in Sweden [16]. Others reported sex ratio of 3:1 [17] In the current study, the male to female ratio among the whole sample was 4:1 which was similar to the male to female ratio in Tripoli ,Libya study[18] but is higher than that reported in

other studies as the study on a sample of patients from Egypt, Saudi Arabia and Jordan in which the number of boys was 37 and the girls 23[19] .These results should be taken with caution as the sample in the current study is not a community representative sample neither with respect to sample size nor methodology of recruiting patients, thus cannot be granted high value for discussing sex ratio. It might only indicate that families of patients are nearly equally concerned with affected male and female offspring and not essentially with males.

Few researchers have attempted a comparative approach or explicitly addressed socio-demographic risk factors in ASD. Early descriptive studies conducted among individuals with autism found a preponderance of parents from high social class backgrounds, as defined by their occupation, education, or intellect level [20].
Recent investigations have not observed any association between higher social class and autism [21]. ASD has a clearly established neurodevelopmental etiology, various psychosocial adversities such as socioeconomic deprivation may increase the risk for associated behavior problems, and these factors have a cumulative effect [22].

Most of affected children were from urban areas comprises 84% of total sample which is in accordance to study in Cairo [23] probably because they had a better access to the psychiatry facilities. In a survey examining patterns of service use among families with at least one ASD member in Cairo found that families in urban districts were more likely to avail off residential schools, special needs resources and medical/health care, whether in addition to, or in lieu of, household care for their autistic family members[23].

The current study showed that housewives tended to more frequently report that their children displayed more autistic symptoms compared to the working mothers. It has been shown that children with ASD whose mothers were working might have more financial resources, better understanding about ASD and access to therapeutic interventions and enrolment in regular or special education schools in Egypt [23].

The higher paternal and maternal education and higher employment among parents of autistic children in the current study may explain higher concern among the parents and thus consultation for early treatment interventions. Moreover, earlier intervention may reflect easier access to services.

Abnormal family history was significantly more apparent, represented in higher incidence of family history of consanguinity and neurodevelopmental disorders such as autism, delayed language development and mental retardation (table 2). In a similar Saudi study, Al-Salehi and colleagues reported 14 autistic subjects (28.57%) with a history of consanguinity [24].
There is a well-established constant observation between higher prevalence of all genetically transmitted disorders and consanguineous marriages [25].
Perinatal problems are also more prevalent among children with ASD and this association was of statistical significance (p value <0.05) which is in accordance with Juneja and colleague's study which reported 27.5% had significant perinatal events [26].

Moreover, children with ASD showed more delayed language development (table 2) which is in accordance with Tang and colleagues who found that the most common reason for referral was language delay (39%) [27].

The current research showed that children with ASD comorbidity rate are 59% which was statistically highly significant *p value* <0.01.
The present findings suggest that children with ASD are likely to develop comorbid psychiatric disorders, although specific comorbid disorders may be more present than the other. This result is somewhat lower compared to the rates found in comparable studies (63.3–96.4 %) [2,5]. A first

explanation for the relatively low rate we found is that we included only internalizing and externalizing disorders, excluding disorders such as enuresis, encopresis, chronic tic disorder, Tourette's syndrome, and schizophrenia, which were included in several previous studies. A second explanation for the relatively low percentage of comorbidity might be related to the center to which the children of our sample were enrolled. This was a general outpatient psychiatric clinic, not particularly specialized in ASD. As such, children with a large heterogeneity in psychiatric problems were referred, and possibly the more severe or complex cases (with higher comorbidity) were referred to more specialized centers. A third explanation for the relatively low comorbidity rate is that in most other studies different standardized interviews were used (e.g. the Diagnostic Interview Schedule for Children [DISC-IV] in the study of De Bruin et al. 2007 [28]. The KID-SCID, similar to the DSM-IV, includes a criterion that the symptoms of ADHD, separation anxiety disorder, social anxiety disorder and generalized anxiety disorder may not be explained by the presence of an ASD. This criterion may have lowered the comorbidity rates of those disorders in the current study. Nonetheless, the percentage of comorbidity in children with ASD found in the current study (59%) is still much higher compared to the rates (9.5–14.5 %) commonly found in typically developing children [29].

In the present study it was found that children with ASD exhibit more anxiety disorders comprise 31% of the total sample which was statistically highly significant *p value <0.005*. This may partly be due to overlap between the core symptoms of ASD and symptoms of anxiety, particular in the case of obsessive–compulsive disorder and social anxiety disorder [8, 11].

Nevertheless, our finding that children with ASD would have more anxiety disorders is in agreement with the study of Gadow et al. [30] which found children with ASD to have more anxiety symptoms compared to children with ADHD. In addition, anxiety symptoms are usually not the core deficits in children with ASD, however, they respond favorably to treatment and extensive protocols for pharmacotherapy, and behavioral therapy for these additional anxiety symptoms in ASD is available [31].

The anxiety experienced by a child diagnosed with an ASD is frequently associated with the need for rigidity in schedules, fear of change, or in response to the child's own awareness of social expectations and becomes more pronounced with age [32].

Generalized anxiety disorder was diagnosed in 12% of our sample, which corresponds to the 13.4% observed in a previous study [5]. Seven percent of our sample was diagnosed with separation anxiety disorder, a rate which is consistent with previous studies of Leyfer et al. (2006) [2] on individuals with ASD but lower than a study done by Muris et al. 1998[33].

Furthermore, recent empirical studies have shown that these anxiety symptoms can be reduced independently from ASD symptoms with cognitive-behavior therapy (CBT), and CBT is now considered the best practice when targeting anxiety symptoms in this population [33].

In the current sample, 9% of the children with autism met DSMIV criteria for OCD. We adapted DSM-IV subjective criteria for developmentally disabled children by making the diagnosis of OCD based on signs and symptoms that could be observed by others. Only a small minority of the children would have met OCD criteria had we not allowed subjective mental experiences to be inferred from observations made by parents. The rate of OCD in individuals with autism reported by other investigators has varied from 1.5% to 81% [33, 35].

The wide variation is likely due to the different assessment methods and criteria used, including criteria for impairment.

In contrast, we did not find higher levels of mood disorders in children with

ASD. Note also that in Gadow et al. (2009)[30] symptoms instead of disorders were assessed, which may explain the disagreement. Important to add here is that our study sample consisted of school-aged children. From previous studies of Ghaziuddin et al. (2002) [36] that showed the prevalence of depression in ASD may increase with age. From the adolescent phase, and even more so for (young) adults, depression (i.e. a mood disorder) is the most common comorbid disorder in people with ASD [35]. It is therefore likely that our findings regarding comorbidity are not representative for the different stages of a life with ASD.

Of note, we also found that children with ASD and a comorbid diagnosis of ADHD (n = 19) were significantly more likely to have ODD/CD (but not internalizing disorders) compared to those children with ASD without a comorbid ADHD-diagnosis (n = 81).

It is thus important to be aware of these comorbid symptoms, because not only are they treatable (whereas the core ASD symptoms are not), not treating them may lead to extra impairments in daily life skills such as completing school work or engaging in social situations. In addition, it is commonly found that children with ASD have higher levels of anxiety compared to typically developing children [37].

The child's disability tended to produce feelings of shame and guilt among Arab societies [38]. Parental perceptions about the causes of disability have a tremendous impact on parents' behaviors in terms of seeking help or intervention for their children or the kind of help they look for, and their support of the treatment process.

Conclusions

This study confirms the frequent co-occurrence of autism with other psychiatric disorders, so it is important for clinicians to always be aware of, and screen for, comorbidity, and to consider treatment for these comorbid disorders. In addition, it is important to do more researches and to increase public awareness and integrated services for the problem of autism. Moreover, making autism care and support available, affordable and reliable should be a major health concern. It is very important therefore that all pediatricians and primary health care providers consider autism when dealing with children presenting with speech and language delay.

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