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Research Article

Association of Parental Risk Factors and Severity of Autism Spectrum Disorder Using the Autism Treatment Evaluation Checklist

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Abstract

Autistic patients experience much pathophysiological impairment involving sensory, behavioral and cognitive disorders. The Autism Treatment Evaluation Checklist (ATEC) with its four domains is an important tool that helps effectively in monitoring and diagnosing children with autism. The aim of our study is to correlate between Parents' risk factors and Severity of Autism Spectrum Disorder Using the Autism Treatment Evaluation Checklist (ATEC). Sixty autistic boys and girls aged between 2 - 8 yrs were included in the study. A questionnaire of two sections (ATEC and questions regarding the autistic child, parents, and siblings) was distributed to the parents of autistic children and the data was gathered and analyzed. There is an association between the severity of Autism spectrum disorder (ASD) with parental allergies, and chronic diseases. The severity of specific domains in ASD was also correlated with delayed diagnosis of ASD. This study investigated risk factors that affected the severity of ASD, in addition to correlation between the different domains. As ASD is still not well understood, therefore, it is important to try to understand the causes of its severity, because it will help the multi-disciplinary team to detect, diagnose and treat autism.

Keywords: *ASD; ATEC; Autism Risk Factors; Autism Pathophysiological Factors; Autistic Patients Behavior*

Introduction

Autism spectrum disorder (ASD) is a severe neurodevelopmental disorder characterized by severe communication deficits, social withdrawal, and stereo typic/repetitive behavior [1,2] which persist throughout life. Unfortunately, the precise etiology of ASD remains elusive and also debated in many cases [2,3]. However, both genetic and environmental factors have been strongly linked to ASD [4-6].

Individuals with ASD tend to have a decreased ability to communicate, such inappropriate responses in conversations, they may misread nonverbal interactions, and also display difficulty building friendships appropriate to their age. In addition, children with ASD may be overly dependent on routines, and highly sensitive to changes in their environment [7]. The term ASD actually encompasses a spectrum of disorders such as autism, childhood distinctive disorder, and Asperger syndrome [6,8] which vary in severity [3].

ASD is a usually clinically diagnosed disorder by psychiatrists using the DSMV-V criteria. These criteria permit psychiatrists to discover the disorders between the ages of 1 - 3 years. However, diagnosis is commonly delayed until the age of 3 years as parents usually fail to

pick up the early signs, but become more conscious when their child does not speak around the time other children are communicating using language [5].

The Autism Treatment Evaluation Checklist (ATEC) was developed by Bernard Rimland and Stephen M. Edelson of the Autism Research Institute [9]. The checklist is a page long document usually completed by parents, teachers or caretakers of the autistic child. It consists of four different domains: I. Speech/Language Communication (14 items); II. Sociability (20 items); III. Sensory/ Cognitive Awareness (18 items); and IV. Health/Physical/Behavior (25 items) [9]. Use of the ATEC scale is an effective way for individual's interacting closely with ASD children to monitor whether the syndrome is progressing or regressing.

The Autism Research Institute evaluated the reliability of ATEC by assessing its internal consistency in approximately 1,300 completed ATECs. The study showed a high internal consistency reliability (r = –.94 for the total score) [10]. In support of this, many studies have shown the ATEC effective in measuring effects and progress of treatment over time [10-13]. Moreover, the ATEC has been found to correlate with physical symptoms [14] and biomarkers in ASD [15]. However, ATEC validity and reliability studies remain limited still [10].

It has been described previously that the characteristics of children with autism at the Autism Treatment Center, KSA [16]. Here, the aim of this study is to examine the correlation between parents' risk factors and severity of autism spectrum disorder using the ATEC scale.

Material and Methods

This study was conducted at Prince Nasser Bin Abdulaziz Autism Center, which is situated in Riyadh Saudi Arabia. The study focused on autistic children in the center from both genders who their ages ranged from 2 - 8 years. All children included were not on any medications. The study was approved by Prince Nasser Bin Abdulaziz Autism Center, and King Abdullah Bin Abdulaziz International Medical Research Center (KAIMRC).

Inclusion Criteria

- Male and Female children aged 2-8 years (in early intervention stage).
- The study was specifically conducted on children who are enrolled in Prince Nasser Bin Abdulaziz Autism Center.
- A psychiatrist or an expert from the Prince Nasser Bin Abdulaziz Autism center must have diagnosed each child prior to their entry to the study.

Participants

- Table 1 demonstrates the characteristics of the children included in the study.

Study protocol

- Approval of parents/guardians of the children involved in the study was obtained, the consent that was signed included the objectives of the study and a detailed explanation of the questionnaire.
- The Autism Evaluation Checklist (ATEC) was translated to the parent/guardian's native language Arabic. The translation was approved by an expert. Back translation to English was performed by a separately approved expert to eliminate any discrepancies in translation.
- Parents/guardians filled out the Arabic version of ATEC.

- Principal investigators visited the center to assess the environment and additionally to personally engage with the participants to evaluate their overall health.

The questionnaire

The questionnaire that was distributed to parent/guardian's of the children in Prince Nasser Bin Abdulaziz Autism Center is divided into two main sections. The first section is focused on general information about the autistic child, parents, and siblings. Questions include age of the child, and age of diagnosis. In addition, information regarding the parent's age, region of origin, chronic diseases, difficulties during pregnancy, use of medications, allergies, and whether or not any of their siblings had ASD was also gathered. The aim of asking these particular questions was to evaluate and determine correlations, if any, between the severity of the child's disease and any environmental or genetic factors of parents. The second section included the Autism Treatment Checklist (ATEC). The ATEC scale is subdivided into four main domains and is used to evaluate how a child is affected by ASD. The four subsets include I. Speech/Language Communication); II. Sociability; III. Sensory/ Cognitive Awareness); and IV. Health/Physical/Behavior. Higher scores on the ATEC scale indicate increased severity.

Data Analysis

Qualitative ordinal data was compiled graphically with reference to the parental filled questionnaire (Autism Treatment Evaluation Checklist). Each graph displayed symptoms of the specific category which were demonstrated as percentages.

According to the results, Autism was categorized into mild, moderate, and severe. Statistical Package for the Social Sciences (SPSS) version 22 was used for data analysis. All statistical tests were conducted at significance level of 0.05.

Results

Delayed diagnosis decreases sensory / cognitive awareness and communications abilities in autistic children

Analysis of results reveal that delayed diagnosis significantly decreases sensory, cognitive, and communication abilities such as speech and language in the cohort of autistic children in our study (Table 1). The majority of the children in the center were diagnosed at or after the age 2.5 years.

Parents' chronic diseases affect healthiness and physical activity of autistic children

In order to determine whether chronic diseases in parents of the children had an impact on any of the four domains of ATEC, one section of the questionnaire was dedicated to information regarding both parents, and siblings of the child involved in the study. Analysis of the results revealed some imperative findings.

The data showed that children who had parents with positive history of chronic disease such as diabetes and hypertension had more severe health and physical problem ($P = 0.02$) than those children with healthy parents (see table 1).

Allergies in parents affect the sociability of autistic children

Children with parents who had allergies of any kind e.g drug allergies or allergies to strong chemical substances, were observed to display severe significant ($P = 0.03$. see Table 1) deficits in all socialable functions mentioned in ATEC.

Communications abilities have been observed between autistic siblings

Communications skills such as speech and language capabilities were significantly impaired ($P = 0.01$: Table 1) in autistic siblings. An example of impairment includes, the ability of the autistic child to express himself or explain what he desires. These incompetency's in

communication coincide with the results in table 1 which show decreased cognitive awareness and ability among autistic children resulting in impairment of communication with the individuals around them.

		Communications (out of 28)	Sociability (out of 40)	Sensory (out of 36)	Health (out of 75)
Gender	Male	19.7 ± 6.2	20.3 ± 8.1	19.8 ± 6.9	44.7 ± 13.3
	Female	20.2 ± 6.0	19.5 ± 6.8	18.7 ± 7.6	41.4 ± 10.3
	P-value	0.790	0.727	0.610	0.359
Age at diagnosis	30 Months or less	17.4 ± 7.7	21.5 ± 7.1	16.7 ± 5.3	44.2 ± 13.6
	more than 30	21 ± 4.7	19.4 ± 8.1	20.8 ± 7.6	43.1 ± 11.9
	P-value	0.027	0.317	0.018	0.749
Are the parents related?	No relation	19.4 ± 5.5	19.4 ± 7.1	19.2 ± 6.3	43.3 ± 12.9
	Relative	20.3 ± 6.8	20.7 ± 8.4	19.7 ± 7.9	44.4 ± 12.4
	P-value	0.538	0.512	0.769	0.733
Does any of the parents have a psychiatric Illness	No	20.1 ± 6.2	19.6 ± 7.9	19.4 ± 7.0	44.1 ± 12.4
	Yes	18.7 ± 6.2	21.8 ± 7.1	19.7 ± 7.7	42.5 ± 13.4
	P-value	0.454	0.365	0.895	0.686
Does any of the parents have a chronic disease such as diabetes or hypertension or both	No	19.7 ± 6.3	19.8 ± 7.9	19.4 ± 7.1	44.6 ± 12.9
	Yes	20.8 ± 4.3	22.2 ± 6.0	20.0 ± 7.0	36.7 ± 6.3
	P-value	0.679	0.481	0.846	0.028
Do any of the parents have Allergies	No	19.8 ± 6.4	19.8 ± 8	19.6 ± 7.3	44.5 ± 12.6
	Yes	20.2 ± 1.9	22.8 ± 1.8	18.4 ± 4.2	35.8 ± 9.7
	P-value	0.748	0.033	0.730	0.138
Does any of the parents smoke	No	19.3 ± 6.7	19.8 ± 8.3	19.4 ± 6.9	44.8 ± 12.9
	Yes	20.2 ± 5.8	20.2 ± 7.4	19.5 ± 7.3	43 ± 12.4
	P-value	0.567	0.821	0.973	0.580
Where any drugs taken during pregnancy	No	20 ± 6.3	20 ± 8	19.6 ± 7.4	43.4 ± 11.5
	Yes	19.5 ± 6.0	20 ± 7.4	19.2 ± 6.5	44.6 ± 14.7
	P-value	0.776	0.991	0.832	0.716
Was the mother diagnosed with depression during pregnancy	No	19.3 ± 6.6	19.6 ± 8.2	19.6 ± 7.4	42.6 ± 11.8
	Yes	21.9 ± 3.8	21.8 ± 5.8	19 ± 6.1	48.3 ± 14.6
	P-value	0.169	0.365	0.795	0.146
Was any of the siblings diagnosed with Autism Spectrum Disorder (ASD)	No	20.7 ± 5.8	19.6 ± 8.1	19.9 ± 6.9	44.7 ± 13.2
	Yes	15.7 ± 6.4	22.1 ± 5.8	17.4 ± 8	39.8 ± 8.2
	P-value	0.013	0.333	0.282	0.248

Table 1: *Shows the risk factors that where studied in the questionnaire. We used the P value due to its probability of obtaining the observed effect under specific circumstances and assumptions. We used the 5% level of significance as it is widely used in scientific and medical research evaluation. The table showed 5 questions that resulted in a p-value less than 5%, which indicated that their null hypothesis, is rejected and data is statistically proven and hypothesis is significantly proven.*

Positive correlation between sensory or cognitive awareness and communications abilities in autistic children

A moderate correlation between sensory/ cognitive awareness and communications abilities in autistic children was observed (R = 0.456; Figure 1). This relationship between the sensory/cognitive awareness was highly significant (P = < 0.001; table 2) suggesting that children exhibiting a better cognitive awareness with intact sensory domains, suffered less communications deficits (see Figure 1).

	Communications	Sociability	Sensory
Sociability	-0.238		
Sensory	0.456**	-0.202	
Health	0.083	-0.547**	0.245

Table 2: *The correlation analysis produced a number of significant relationships between domains that are affected in ASD. Firstly, Sociability has negative correlation with all 3 domains of autism disorders namely Communications (-0.238), Sensory (-0.202) and Health (-0.547). This suggests that children with communication defects may not have other symptoms of poor social interaction, sensory or auditory dysfunction and health/physical behavioral issues. Secondly, children with poor social interaction have very little chances to have health issues since their correlation is (- 0.547) that is between -0.5 and -1.*

On the contrast, there is positive correlation between Sensory and communication (0.456), in addition to Sensory and Health (0.245) which suggests that children with sensory or auditory dysfunction have chances of having communication disorders and health issues. Furthermore, children with sensory dysfunction have high chances of having communication issues.

The correlation between Health and Communications is 0.083, which is very near to zero. This suggests that there is no relationship between the two domains and there is equal chance of a child with communications disorder to have or not have health issues. This proves the variability between the two domains.

*** Correlation is significant at the 0.01 level.*

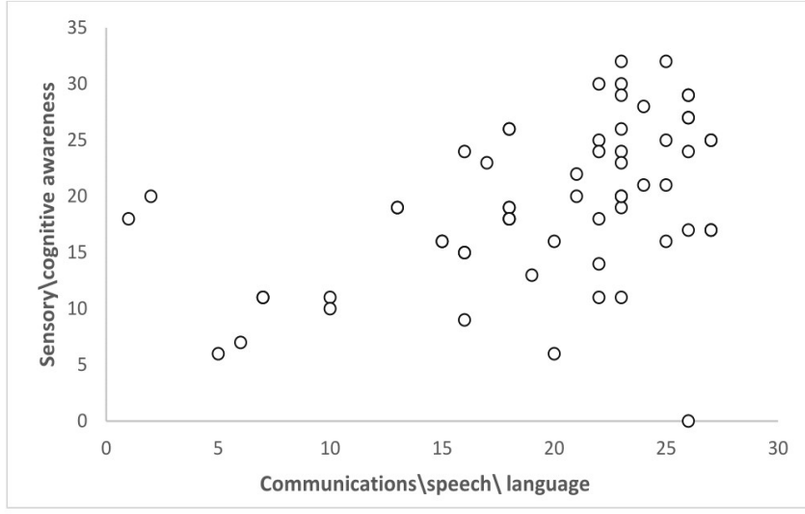

Figure 1: *Demonstrates the scatterplot chart that uses the regression analysis, and summarizes the average effect of the communication domain on the sensory domain in children diagnosed with autism spectrum disorder. In the graph, it is clear that there is a line of "best fit" which is rising upwards. This reveals that when the children diagnosed with autism start to have increased communication, speech or language issues, they tend to also face sensory, cognitive or awareness problems. Since the data in the scatterplot somewhat follow the linear path, it can be concluded that there is very moderate linear correlation between the communication, speech and language domains with the sensory, cognitive and awareness domains.*

Negative correlation between health/ physical/ behavior and sociability of autistic children

To determine if there was a relationship between the physical health and behavior of ASD children and their social skills, regression analysis was performed. A negative correlation between health/ physical/ behavior and social abilities in autistic children at the center were observed (Spearmans Rho = 0.3; P = 0.018; Figure 2). These results suggest that healthier autistic children tend to score less on the sociability domains on the ATEC scale.

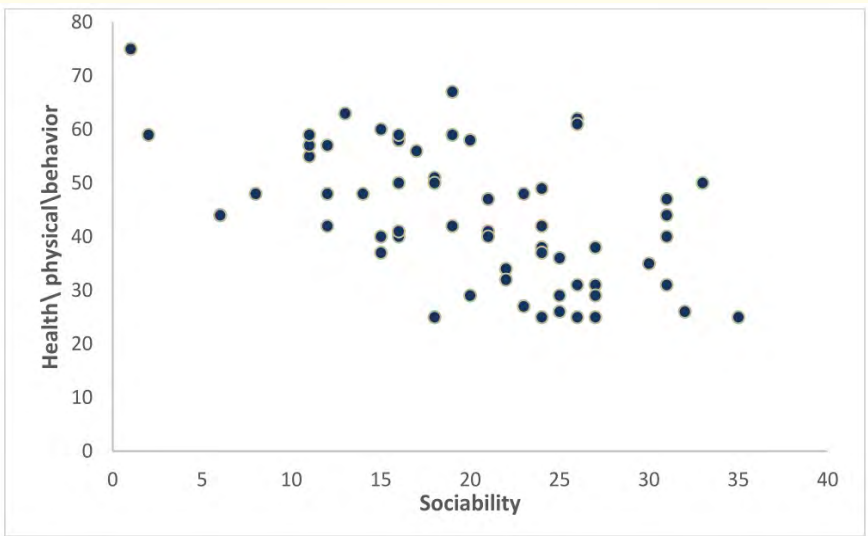

Figure 2: *Shows the scatterplot chart, which uses the regression analysis and summarizes the average effect of the social dysfunctions on the health, and physical symptoms in autistic children included in the study. The graph demonstrates a clear line of "best fit" which is moving downwards, and plots in the graph are scattered on both sides of the diagram.*

In addition, there is moderate negative linear relationship that can be found between the two domains. This suggests that the children diagnosed with autism who have health and physical behavior issues are less likely to develop social dysfunctions.

The severity of the communications, sociability and sensory/ cognitive awareness impairments observed in the autistic children

A boxplot analysis of the ATEC scores to determine the severity of ATEC domains was performed and exposed that 3 out of the 4 ATEC domains displayed increased severity in this cohort of ASD children, (Figure 3). The autistic children exhibited higher percentages of communication problems, cognitive awareness impairments, and sociability dysfunctions (80%, 55% and 52% respectively) in comparison to heath/physical/behavioral issues (28%).

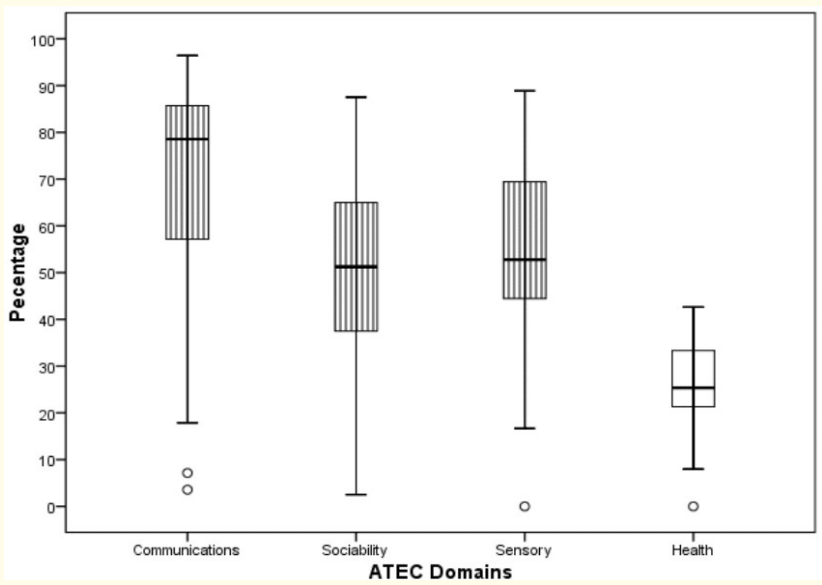

Figure 3: *Shows the boxplot chart shows the interquartile range (IQR) for all four domains namely communication, sociability, sensory and health. It revealed that children with ASD mostly face problems in three domains, which include: communications, sociability and Sensory dysfunctions; with communication being the most common problem faced by these children (above 50%). However, it was clear the physical and health problems fell below the 50%, which means that it is less common and children faced lesser difficulties in this specific problem.*

Discussion

The present study investigated the association of the severity of ASD with parental allergies, and chronic diseases. Using both the autism treatment evaluation checklist (ATEC) and specific questions answered by the parents of the children, the severity of specific domains in ASD were also correlated with delayed diagnosis of ASD.

The results of this study importantly revealed that early detection of autism results in a reduction of both the sensory and cognitive domains of ATEC, and additionally communication abilities in autistic children. Early detection and diagnosis can have a significant impact in understanding the disorder and has the potential to enhance the autism center's ability to minimize the severity of the disease by improving the autistic children communication, sociability, sensory, and health dysfunctions by intervention. The average age of diagnosis in our study was approximately 3 years, however studies have reported that ASD in children can be detected and diagnosed as early as 1.5 - 2 years [17,18].

Early detection and screening for ASD are essential for optimizing lifetime outcomes for individuals affected by the disorder. Establishing an earlier diagnosis will allow children and families to benefit from early support and intervention which will in turn lead to improved positive outcomes [19-21]. Despite converging lines of evidence which reinforce the view that early intervention leads to better prognosis, the age of diagnosis for ASD remains on average approximately 4 years, and is even later in developing countries and lagging further so by a year in lower income and rural families [22,23] .

Early interventions potentially improve the social and communicational functioning of children with ASD and may be more effective during infancy due to presence of higher neural plasticity early in life. In the realm however, the point at which children are diagnosed is still late relative to the important window of neuroplasticity present prominently in the first two years of life [22].

This study also showed a positive correlation between sensory and cognitive awareness and communication in autistic children included in the study. This association demonstrates clearly that children exhibiting a higher degree of impairment in communication, speech and language have a tendency to display more sensory, cognitive and awareness deficit's. Its seems plausible to suggest that early intervention efforts with ASD children to facilitate language development may vary the cognitive outcome in these children.

Therefore, it is paramount to increase awareness of the early signs of social and communication withdrawal during infancy to allow potential positive effects on later development.

The etiology of the majority of ASD cases have been attributed to genetic susceptibility. Studies from several thousands of studies have established that genetic factors play a predominant role of in the causation of most autistic syndromes [24]. However, during the last decade or so a diversity of potential causes have been established. Specific interest has been warranted to the role of environmental risk factors [25,26] and maternal immune disorders and infections in ASD [27,28] over the last few years. Although the neurobiology of the disease remains elusive, recent studies have advanced in showing functional brain abnormalities in autistic children. These distinct brain abnormalities suggest that period of etiological relevance for the pathogenesis of ASD may be in utero or early infancy [29]. Subsequently, maternal exposure to environmental toxins and fetal exposure to maternal complications have largely been the focus of recent research.

Several studies have also shown a link between chronic diseases in parents and the concomitant risk of ASD offspring. A study by Mouridsen and colleagues demonstrated a higher incidence of Type 1 diabetes in fathers and ulcerative colitis in mothers of children with ASD [30] supporting the theory that parental diseases have may a relevant role in contributing to development of ASD in their offspring.

In addition, this study revealed that those children whose parents had chronic diseases such as asthma, diabetes, and hypertension had a significant tendency to exhibit severe health and physical problems when compared to those with healthy parents. This finding accords with Robins., *et al*. [20] results of a case-control study conducted within a cohort of infants born between January 1995 and June 1999. The study clearly demonstrated more than a 2-fold frequency of ASD in children whose mothers were diagnosed with asthma during the first and second trimesters of pregnancy.

Additionally, the study revealed that allergic diseases were also significantly more often reported for mothers of ASD –affected children compared with controls. Again, this is consistent with our findings, which show that ASD-affected children whose parents had allergies of

any kind such as medicinal allergies or allergies to strong chemicals suffered from significantly more of the social dysfunctions described in the sociability domain of ATEC. Independent studies have also indicated a link between parental autoimmune disease and increased risk of ASD, suggesting children with autism have a greater familial history of autoimmune disease in comparison to healthy controls [31]. The role of the immune system in ASD has also been confirmed by studies which show multiple maternal infections; particularly bacterial infections during pregnancy are associated with a higher risk of ASD in the infants born to these mothers [32].

The mechanisms by which maternal infections or autoimmunity cause neurodevelopmental disorders such as ASD are still emerging. Altered circulating levels of cytokines in mothers with autoimmune disease or immune dysfunction/infection are speculated to have a direct impact on fetal brain, and there is firm evidence of the inflammatory cytokine 6 (IL-6) crossing the placenta into the fetal circulation [27]. Furthermore, animal studies have also demonstrated that injection of the cytokine IL-6 into pregnant mice resulted in behavioral and gene-expression changes in the offspring of pregnant mice [33]. IL-6 is also produced in increasing amounts during acute allergic reactions and during aggravated asthma, potentially contributing to brain dysregulation. Animal studies also show that activation of the maternal immune system with an allergy/asthma insult results in deficits in social behavior in their young [34]. This supports finding in this study that the children with ASD in our study whose parents suffered from allergic conditions had poor social activity.

A different study has shown that Infants with older siblings with Autism Spectrum Disorders (ASD-sibs) are at risk for socioemotional difficulties [13], which was also positive in our findings. Another correlation in our study was that children with intact cognitive and sensory domains had less communication difficulties. This issue can be theorized in many different ways. However, I believe that the underlying reason is that children with these intact domains are more responsive to treatment.

Conclusion

This study investigated risk factors that affected the severity of ASD, in addition to correlation between the different domains. Due to the fact that ASD is still not understood. Therefore, I believe it is important to try to understand the causes of its severity, because it will help the multi-disciplinary team to screen, and manage ASD children.

Conflicts of Interest

The author declares that there are no conflicts of interest.

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