Original Article

Prevalence and Early Signs of Autism Spectrum Disorder (ASD) among 18-36 Month Old Children in Tianjin of China*

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Abstract

Objective The aim of this study is to estimate the prevalence of autism spectrum disorder (ASD) among 18-36 month old children in the Tianjin Municipality of China, and to identify early signs of autistic children and the predictability of each individual symptom.

Methods A total of 8 000 children were screened to do a questionnaire based on CHAT modified to include more early signs of autism at the age of 18-36 months. Then the at-risk children were reexamined 1.5 years later and ASD children were identified based on DSM-IV. Early signs of autism were analyzed retrospectively by using discriminant function analysis performed among ASD children, children not followed up and children followed up but failing to meet ASD criteria.

Results Three hundred and sixty seven children were screened as being at-risk to ASD, and 22 of them were identified as having ASD in the subsequent diagnosis. The prevalence of ASD was 27.5 per 10 000 in Tianjin of China with a male to female ratio of 4:1. Items addressing social interactions and communications had higher predictability than other items to distinguish autistic children from non-autistic ones. Pretend play, functional play, showing and reading parents' facial expressions distinguished autistic children from those not followed up, nevertheless those followed up but failing to meet ASD criteria were not included.

Conclusion The prevalence of ASD found in our study was lower than that reported in some studies by western researchers. Autism has its specific symptoms, such as deficits in social awareness, social relatedness, and social referencing.

Key words: Autism spectrum disorder; Prevalence; Early signs; Discriminant function analysis

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INTRODUCTION

Autism Spectrum Disorder (ASD) is referred to as a constellation of symptoms involving impairments in social interactions and communications, and restricted repetitive behaviors and interests[1]. It includes autistic disorder, Asperger disorder and pervasive developmental disorder-not otherwise specified (PDD-NOS)[2]. There is a worldwide trend of an increasing prevalence of ASD[3-4]. In some recent studies, the rate of ASD exceeds 1%[5-6]. According to

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the latest report made by the US CDC, ASD is diagnosed in approximately 1 out of 88 children[7]. All studies have indicated a higher male incidence rate, with an average male to female ratio of 4:1[5,8]. The etiology of autism is unclear, but research indicates that it is a multi-factorial disorder with both a strong genetic basis and major contributions from multiple environmental factors[9]. Autism is a lifelong chronic disorder with disruptive symptoms which causes a restricted range of social activities and interests[1]. Most people with autism require intensive parental, school and social support[10-11]. Early diagnosis of autism provides the best opportunity for early intervention, which serves to maximize positive developmental outcomes for affected children and their families[12-15]. The earlier a diagnosis is made, the sooner family stress can be reduced[16-17]. With proper intervention, about 3%-25% of children who fit the diagnostic criteria for ASD at the age of 2-3 subsequently begin to talk and communicate, and by age 6-7, they are able to blend to varying degrees into the regular school population[18-19]. There has also been exciting progress in establishing effective methods of intervention for autistic toddlers as young as 18 months[20]. However, several studies have found that the average age of autism diagnosis is 3-4[21-22]. Early identification largely depends on people's knowledge about early signs of ASD. Several groups have reported the early signs of ASD[23-27]. Consistent with retrospective videotape studies, parental reports and prospective studies all demonstrated that social behaviors were the best indicator of differential diagnosis between children with ASD and those without ASD[12,27-28]. Werner[29] found that children with ASD were reported to have higher levels of social problems than typically developing children and children with developmental delay by the age of 12-15 months. Wetherby[30] examined social communication profiles among 18-24 month old children and reported that, compared with children of the same age and developmental level who had developmental disorder, children with ASD performed significantly lower on five social communication measures: gaze shifts, gaze/point follow, rate of communicating, acts for joint attention and inventory of conventional gestures. In China, diagnosis of autism is mainly based on DSM-IV and medical professionals' clinical experience. To date, there have been few studies on the early signs of autism in the mainland of China. In this study, we try to estimate the prevalence of ASD among 18-36 month old children in Tianjin of China, and try to find out how many items will be failed by autistic children and how predictive each item will be for autism. Our goal is to know more about psychological and behavioral development in autistic children and to pave the way for early identification and early intervention.

METHODS

Study Population

Tianjin, the third largest metropolis in China, is located in the east of China about 120 miles from Beijing, Capital of China. Tianjin covers an area of about 119 000 km^2 with a total population of approximately 12.9 million in 2010[31]. In 2009, we conducted a cross-sectional study among 18-36 month old children in Tianjin by multi-stage stratified cluster sampling method. There are six districts (Heping, Hebei, Hexi, Hedong, Nankai, Hongqiao) in central city, three districts (Tanggu, Hangu, Dagang) in economic development area and six districts (Dongli, Xiqing, Beichen, Jinnan, Wuqing, Baodi) in suburban area. In Tianjin, there are 1.27 million children aged 0-14 and about 40%, 20%, and 40% of the population are in central city, economic development area and suburban area respectively. In this study, we included all six districts in the central city and randomly sampled Tanggu in the developed area. Due to the consideration of financial resources and field operation, we chose Dongli and Jinnan, which are in the mid-range of social and economic development levels among the suburban area. The percentage of population in Tanggu, Dongli, and Jinnan district are 10%, 5%, and 6% of Tianjin's total population respectively. According to the number of children in each district and the number of children registered in community hospitals, we randomly sampled a certain number of community hospitals proportional to the population of that district. This investigation is part of the early screening held by the Tianjin Municipal Maternal and Child Health Care Centre. There is also one Maternal and Child Health Care Center in each district which is under the control of the Municipal Maternal and Child Health Care Centre and supervises the work of community hospitals. All children must register in their community hospitals, so community hospitals have records of all children born in the area. The overall number of 18-36 month old children in the community hospitals chosen in

our study was 10 015, and among them, 8 428 responded, yielding a response rate of 84.2%. Among the missing cases, we couldn't get in touch with 656 children and the other 931 children did not attend the investigation either because of parental choice or change of family location. Excluding invalid questionnaires (those with more than 50% of the information missing, *n*=428), we included eight thousand 18-36 month old children in the analysis.

Instruments and Identification of Children with Autistic Disorder

We attempted to identify children with ASD by using a two-stage investigation. In 2009, we screened all participants to do a questionnaire based on the Checklist for Autism in Toddlers (CHAT)[16] modified to include early signs of autism. CHAT is a simple screening tool used for identification of autistic children at the age of 18 months in the United Kingdom[16]. Section A of the CHAT is a self-administered questionnaire for parents. Section B of the CHAT consists of five items recorded with observation of the children by general practitioners. We included all the questions of section A of CHAT (rough and tumble play, interest in peers, climbing, social play, pretend play, protoimperative pointing (pointing with finger to ask for something), protodeclarative pointing (pointing with finger to indicate interest in something), functional play, and showing and added more questions concerning social interaction (age of first smile, ≤6 month, >6 month), reading others' facial expression, imitation, communication (age to call daddy or mummy, ≤12 month, >12 month), response to their names, obedience to simple instructions, expressing needs with words, emotions (being irritable, poor sleep at night), sensation (slow to feel pain, dislike of being cuddled) and restricted behaviors or interests (special love for spinning things, playing with hands, special love for monotonic games, resistance to new circumstances). In the observation part, we included four questions of CHAT section B addressing the child's eye contact, ability to follow a point, pretend play and producing a point (the question 'making a tower' was excluded because it tests the intelligence level of children). We added questions, including response to their names, seeking sound sources, facial expressions and spoken language (normal/no language or abnormal language). All the questions were yes/no questions unless otherwise specified. At the end of the test, we asked the assessors, 'What is your impression of this child?' Normal, abnormal or possibly abnormal were the choices. The assessors were physicians or graduate students majoring in child and adolescent health. They were trained to measure the observational section by experienced pediatric psychologists. Some normal and autistic children, who were not part of the study, were videotaped, with parental consent. These videos were then viewed by the assessors to test their diagnostic accuracy. The correlation for scoring the observational section between assessor and experienced pediatric psychologists was 0.95. The further screening and diagnosis were conducted 1.5 years later. Following the pattern of the previous research[16,25,32], follow-up exams were given to those who failed in any of the following: (1) those who failed in the items of protodeclarative pointing in the parental questionnaire and producing a point in the observational section according to Baron-Cohen's CHAT based criteria[16] (*n*=19); (2) those who failed in two or more of the six items (social interest, joint attention, pretend play, protodeclarative pointing, response to their name and showing) in the parental questionnaire based on Robins's criteria[25] (*n*=382); (3) those who failed in two or more of the four items (producing a point, eye contact, ability to follow a point and pretending) in the observation section according to Wong's research[32] (*n*=180); (4) those who were thought to be abnormal or possibly abnormal by judgment of the assessors (*n*=70). Altogether, 396 children were identified for further diagnosis. Parents of 367 (92.7%) children agreed to have their child further checked. Every child was given a test by the experienced pediatric psychologists in Tianjin Children's Hospital. Based on DSM-IV criteria[33], and 22 of them were confirmed to have autism spectrum disorders.

Statistical Analysis

We first estimated the prevalence of ASD among 18-36 month old children. Chi-squared tests were used to determine the association between two categorical variables. A *P* value of <0.05 was regarded as statistically significant. Then, we used discriminant function analysis[34] to determine the order of items that were useful in differentiating autistic children from non-autistic children. Discriminant function analysis is a relatively stable and useful statistical analysis to predict a categorical dependent variable by one or more continuous or binary independent variables[34]. Children with ASD were compared to children not followed up and children followed up but failing to meet ASD criteria

respectively to determine the order of the items that were useful in differentiating between autistic and non-autistic children. We applied discriminant function analysis to the items in the parental questionnaire and the observations made by physicians respectively. We used a stepwise method to eliminate correlation among items and the probability of F value to entry and removal were 0.05 and 0.10 respectively. We also calculated the percentage of failure in each item by children with ASD and non-autistic children. The analysis was conducted by using SPSS 18.0 (SPSS Incorporation, Chicago, USA). In the parental questionnaire, each question was missed by a range of between 8 to 80 people. In the observation section, the item 'producing a point', had 39 missing, while all other items had less than 20 missing. In the discriminant function analysis, subjects with any missing data were excluded from the analysis.

RESULTS

The distribution of gender and age among the participants is shown in Table 1. Among the participants, 51.8% were male and 76.4% were under 30 months of age. Altogether, 22 were diagnosed as ASD, including 18 males and 4 females. The prevalence rate was 27.5 per 1 000, with a 95% confidence interval (CI) of 16.0-39.0. The prevalence in males (43.4 per 10 000) was significantly higher than that in females (10.8 per 10 000), with a male to female ratio of 4:1. The prevalence of autism spectrum disorder was not significantly different among different age groups.

Table 1. Distribution of Gender and Age in the Studied Population and in the Children with Autistic Spectrum Disorder (ASD)

Variables	Total Population	ASD (*n*, per 10 000)
Gender		
Male	4 142 (51.8%)	18 (43.4)**
Female	3 858 (48.2%)	4 (10.8)
Months of age		
18-23.9	2 926 (36.6%)	7 (23.9)
24-29.9	3 167 (39.6%)	11 (34.7)
30-36	1 907 (23.8%)	4 (21.6)
Total	8 000 (100.0%)	22 (0.3%)

Note. **Males had statistically higher prevalence of autistic disorders than females (Fisher's exact P=0.005).

To find out the early signs of autistic children, we divided children in our study into three groups: (a) children requiring no follow-up (n=7 604), (b) children followed up, but failing to meet the autistic criteria (n=345), (c) children followed up and diagnosed as autism spectrum disorder (ASD) (n=22). Children with ASD were compared with the other two groups mentioned above respectively. Tables 2 to 5 list the respective results of discriminant function analysis performed for items in the parental questionnaire and items in the observation made by physicians. Excluding subjects with missing data, 7 091, 7 455, 338, and 354 children completed the assessment and were used in Tables 2-5 respectively. All the items in each part were included as independent variables for separate equations. There was no multi-collinearity among the items in both parts. For insurance, we also used a stepwise method to eliminate correlation among items.

As seen from Table 2, items that were useful in differentiating children with ASD from children not followed up in the parental questionnaire included protoimperative pointing, age of first smile, protodeclarative pointing, interest in peers, pretend play, response to their names, obedience to simple instructions, age to call daddy or mummy, reading parents' facial expressions, functional play and showing. The percentages of children with ASD and children not followed up who failed each item are also shown in Table 2. Protodeclarative pointing, pretend play and functional play were failed by a relatively high percentage of children with ASD. However, protoimperative pointing (pointing with finger to ask for something) had the highest ability to differentiate children from one another.

Items that differentiate children with ASD from children not followed up by the observation of physicians are shown in Table 3 in descending order, along with the percentage of children in both groups who failed each item. As shown in Table 3, gaze monitoring, eye contact, producing a point, spoken language and pretend play were important items in differentiating autistic children from children not followed up. Response to their names, facial expressions and seeking sound sources had little differentiation between the groups.

The items that were useful in differentiating children with ASD from children followed up but failing to meet autistic criteria in the parental questionnaire are shown in descending order in Table 4. Protodeclarative pointing, age of first smile, obedience to simple instructions, age to call daddy

or mummy, response to their names, sensitive to pain, and interest in peers were important items. Percentage of failure to call daddy or mummy before 12 months of age was high in both groups (54.5% *vs*. 15.8%), as was the percentage of failure of interest in peers (42.9% *vs*. 29.1%).

Table 5 shows the items that differentiate children with ASD and children followed up on but not meeting ASD criteria by the observation of physicians in descending order. Eye contact, spoken language and gaze monitoring statistically differentiated children between the two groups.

Table 2. Standardized Canonical Discriminant Function Coefficient and Percentage of Failing Each Item by Children with ASD and Children not Followed up in the Parental Questionnaire

Items	Discriminant Function Coefficient	Failed by Children with ASD(%)	Failed by Children not Followed up (%)
Protoimperative pointing	0.700	8 (36.4)	11 (0.1)
Age of first smile (≤6 months)	0.338	4 (18.2)	17 (0.2)
Protodeclarative pointing	0.320	16 (72.7)	345 (4.6)
Interest in peers	0.212	9 (42.9)	383 (5.0)
Pretend play	0.180	14 (63.6)	488 (6.4)
Response to their names	0.162	4 (18.2)	24 (0.3)
Obedience to simple instructions	0.148	3 (13.6)	64 (0.8)
Age to call daddy or mummy (≤12 months)	0.138	12 (54.5)	646 (8.5)
Reading parents' facial expression	0.111	3 (13.6)	83 (1.1)
Functional play	0.105	13 (59.1)	1 399 (18.5)
Showing	0.101	7 (31.8)	256 (3.4)
Rough and tumble play	-0.089	4 (18.2)	1 890 (24.9)
Enjoy playing hide-and-seek	-0.074	2 (9.1)	314 (4.1)
Climbing	0.072	9 (40.9)	2 797 (36.9)
Like of being cuddled	-0.053	3 (13.6)	419 (5.5)

Table 3. Standardized Canonical Discriminant Function Coeffecient and Percentage of Failing Each Item by Children with Autism Spectrum Disorder (ASD) and Children not Followed up Observed by Professionals

Items	Discriminant Function Coefficient	Failed by Children with ASD (%)	Failed by Children not Followed up (%)
Ability to follow a point	0.691	7 (31.8)	10 (0.1)
Eye contact	0.461	13 (59.1)	86 (1.1)
Producing a point	0.277	16 (72.7)	355 (4.7)
Spoken language	0.245	16 (72.7)	369 (4.9)
Pretend play	0.181	12 (54.5)	476 (6.2)
Response to their names	0.078	3 (13.6)	19 (0.2)
Facial expressions	0.071	4 (18.2)	58 (0.8)
Seeking sound sources	0.070	4(18.2)	91 (1.2)

Table 4. Standardized Canonical Discriminant Function Coefficient and Percentage of Failing Each Item by Children with ASD and Those Followed up but not Meeting ASD Criteria in the Parental Questionnaire

Items	Discriminant Function Coefficient	Failed by Children with ASD (%)	Failed by Children Followed up but not Meeting ASD Criteria (%)
Protoimparative pointing	0.509	8 (36.4)	14 (4.1)
Age of first smile (≤6 months)	0.485	4 (18.2)	5 (1.5)
Obedience to simple instructions	0.420	3 (13.6)	8 (2.3)
Age to call daddy or mummy (≤12 months)	0.379	12 (54.5)	9 (15.8)
Response to their names	0.256	4 (18.2)	16 (4.6)
Sensitive to pain	-0.252	4 (18.2)	22 (6.4)
Interest in peers	0.234	9 (42.9)	100 (29.1)

Table 5. Standardized Canonical Discriminant Function Coefficient and Percentage of Failing Each Item by Children with ASD and Those Followed up but not Meeting ASD criteria in the Observation Section

Items	Discriminant Function Coefficient	Failed by Children with ASD (%)	Failed by Children Followed up but not Meeting ASD Criteria (%)
Eye contact	0.725	13 (59.1)	15 (4.4)
Spoken language	0.458	16 (72.7)	53 (15.6)
Ability to follow a point	0.354	7 (31.8)	13 (3.8)

DISCUSSION

The possibility of identifying children with autism before age 3, coupled with the fact that early intervention exerts a profound impact on children with ASD, has led researchers to search for early signs of autistic children. We conducted a large scale study in Tianjin, China to document prevalence and early signs of autism among 18-36 month old children. The prevalence of ASD among the children in our study was 27.5 per 10 000, with a 4:1 male to female ratio. Items addressing social interaction and communication, e.g. pointing with finger, gaze monitoring, eye contact, age of first smile, interest in peers, obedience to simple instructions, spoken language had better predictability to distinguish autistic children from both children who were not followed up and children who were followed up but did not meet autistic criteria. Autistic children showed significant differences from children who were not followed up, but no such differences were found from children who were followed up but did not meet autistic criteria on protodeclarative pointing, pretend play, functional play, showing and reading parents' facial expressions. There was no statistical difference between autistic children and other children on certain behaviors, like perseveration and restricted behaviors.

The prevalence (27.5 per 10 000) of ASD found in our study was lower than the results found in some Western studies; in the latter the prevalence of ASD was 60-70 per 10 000[1,3-4,35-36]. However, the prevalence of ASD in our study was higher than the prevalence of ASD in Beijing from the most recently published study, which reported a rate of 15 per 10 000[37]. These discrepancies may be due to differences in the survey methodology. We used a self-designed questionnaire based on CHAT as a screening tool. In our attempt to collect all of the autistic children, we followed up a greater number of children. Besides the at-risk children according to CHAT[38], we also followed up the children failing in the parental questionnaire according to Robins's study[25], whose sensitivity and specificity were 0.95 and 0.99 respectively, and children failing any 2 of 4 items (producing a point, eye contact, ability to follow a point and pretending) by the observation of physicians according to Wong's study had the sensitivity and specificity of 0.736 and 0.912 respectively[32]. Moreover, we followed up those thought to be abnormal by the physicians. Altogether, we followed up a total of 367 children in our study, which was time intensive. We also should admit that even though we studied a broad range of children, the possibility of missing cases might exist. Also, there were 29 children who satisfied the follow up criteria, but did not receive further examination. We analyzed the characteristics of these children. There was no statistical significance among all the items involved in our study between them and children who were followed up but did not meet autistic criteria. There were statistical differences in some important items concerning social interaction and communication between them and the ASD children. It is reasonable to say that the prevalence of ASD in our study can represent the prevalence of ASD in Tianjin, China. The male to female ratio in our study (4:1) was consistent with Western studies[1,3-5,7,39].

The prevalence of autism found in our study (27.5 per 10 000) was higher than that in a previous study (11.0 per 10 000 children) conducted among 2 to 6 years old children in Tianjin 7 years ago[40]. It may possibly indicate an increase in the prevalence of autistic children in Tianjin. Considering the fact that the previous study differs from the current survey in terms of diagnosis and the age range of the investigated children, more research is needed to confirm this conclusion.

CHAT is a two stage screening tool including a self-administered questionnaire for parents and items recorded with observation by health professionals. Research revealed that a two-stage screening program for autism can offer a cost-effective method for detection of autism at an

early age[32,41]. Ozonoff's study revealed that autism was associated with steadily increasing parental concerns[42]. Health care providers also play a pivotal role to detect communication problems earlier in young children[32]. Our study aimed at finding more items that were specific among autistic children before age 3. We included more items in both parts of CHAT according to the clinical symptoms of autism and symptoms reported in literature.

Consistent with former reports[12,16,25-30,32,41,43-48], we also found that impairment in social behavior was a common issue at an early age for autistic children. These 'red flags' include a lack of the following: eye contact, social smiles, pointing with their fingers, response to name call, interest and pleasure in others and joint attention[25-26,28-30,32,41,44,46-48]. In our study, items concerning social interaction, e.g. gaze monitoring, eye contact, interest in peers and age of first smile had higher ability than other items in the parental questionnaire and observation made by health professionals to distinguish autistic children from others. This evidence strongly supports previous ideas that social communication deficit is a unique and core feature of autism[29-30,44,49-52]. It also supports ideas from Volkmar et al.[53] that autistic children have fundamental difficulties in the earliest social processes, which, in turn, impacts on many other areas of development.

Autistic children showed significant differences from children not followed up in five additional 'red flags': protoimperative pointing, pretend play, functional play, showing and reading other's facial expression, but showed no such differences in comparison with those who were followed up on but did not meet autistic criteria. Among children who were followed up but did not meet autistic criteria there are likely many children with other development disorders. The results tell us that some social deficits are shared by autistic children and children with other developmental disorders, while others are unique to autism. Therefore, it is sometimes challenging to distinguish autistic children from children with developmental delay at a young age[30].

In children diagnosed as ASD, lack of language and limitations in communication were commonly reported[49,53-56]. Results in our study coincided with these reports. Even compared with children followed up but not meeting autistic criteria, age to call daddy or mummy, obedience to simple instructions and spoken language are still distinguishable items. Lack of language was the primary reason for parents to take their children to health care professionals[41,56]. Parents usually became alert and nervous when their children had no language upon reaching 2 years of age. However, abnormality in some prelinguistic predictors of language, including use of gestures, pointing with a finger, understanding and expressing also deserves attention.

Certain behaviors, like restricted behaviors or resistance to change showed no difference between autistic children and other children. These findings coincided with findings of previous studies[25,43,50,56]. Children under the age of 3 may lack the cognitive ability necessary to play repetitively[43]. Some researchers have named such a phenomenon secondary behaviors, resulting from adaption to the outside world[56]. These abnormalities are not accurate in identifying children with autism at an early age.

There were still some other behaviors reported in previous studies as early signs of autism, like no imitation and dislike of being held[25,32,56-57]. However, we did not find any difference in these behaviors between autistic and non-autistic children in our study. This does not mean they are not early signs of autistic children. Rather, it may be due to the sample size and variation of symptoms of children of different cultures and ages.

LIMITATIONS

Due to the fact that we studied a higher proportion of urban than suburban children, the study was over representative of urban children. Also, we could not collect certain measures of developmental delay. Among children followed up but not meeting autistic criteria, many were typically developing children. As a result, any conclusions about differences between autistic children and children followed up but not meeting autistic criteria might be inaccurate.

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