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Original Article

Autism spectrum disorder screening in children aged 16-30 months using the *Modified Checklist for Autism in Toddlers-Revised* (M-CHAT-R)

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Abstract

Background Autism spectrum disorder (ASD) is a complex neurodevelopmental disorder with a global prevalence of 7.6 in 1,000 children. The *Modified Checklist for Autism in Toddlers - Revised* (M-CHAT-R) is one of many screening tools for ASD. It is fast, easy to use, and has been translated and validated in the Indonesian language.

Objective To determine the prevalence of ASD in Indonesia and its risk factors.

Methods A cross-sectional study was conducted from March to October 2020. In the first protocol (March to July 2020), 219 children aged 16-30 months from 20 hospital walk-in clinics in five districts of Jakarta were included. Subjects' parents filled out the M-CHAT-R questionnaire during their visit. A series of questions were asked to provide information about probable risk factors associated with ASD: gender, family history of ASD, preterm birth, low birth weight (LBW), and history of seizures. The second protocol (August to October 2020) was completed by parents via an online form, where 746 children aged 16-30 months were enrolled. Therefore, a total of 965 subjects were eligible for statistical analysis.

Results Of 965 subjects, 56.58% were males. Subjects' mean of age was 22.59 (SD 4.15) months. The M-CHAT-R screening showed that 34 (3.52%) subjects were at high risk of developing ASD. Only male gender was significantly associated with ASD.

Conclusion We screen for ASD in healthy 16-30-month-old Indonesian children. The rate of high-risk M-CHAT-R score is 3.52%. Male gender was a significant risk factor for high-risk M-CHAT-R results. **[Paediatr Indones. 2021;61:247-52 ; DOI: 10.14238/pi61.5.2021.247-52**].

Keywords: *autism; autism screen; M-CHAT-R; Indonesia*

Autism spectrum disorder (ASD) is a complex neurodevelopmental disorder with specific diagnostic characteristics: impaired communication and social interactions, with repetitive or stereotypical behavior.[1,2] In 2020, the international prevalence of ASD reached 0.76%, or 16% of all children in the world.[3] ASD was three times higher in boys than girls.[2] The onset of ASD usually begins at the age of three, although symptoms generally become more apparent during school age.[1] A study suggested that the onset of ASD could be seen from the age of 6-18 months, with early symptoms associated with impaired social communication.[4]

The ASD tends to run in families, however, its exact cause is still unknown.[5] The risk of a child developing ASD is 2-8% if a sibling is diagnosed with ASD.[6] Teratogen exposure during pregnancy can also contribute to the development of ASD, especially at an early gestational age.[7] Drug consumption during pregnancy, such as valproic acid and beta-2 adrenergic receptor agonists, is also believed to influence the development of ASD.[8,9]

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The diagnosis of ASD is made from the criteria in the *Diagnostic Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5). The *American Academy of Pediatrics* (AAP) recommended in 2007 that all pediatricians screen children aged 18 and 24 months for ASD. If ASD is diagnosed early, immediate intensive management can be given in the hope that the child will experience significant improvements in language, adaptive behavior, academic performance, and intelligence quotient (IQ) score.[10] The *Modified Checklist for Autism in Toddlers* (M-CHAT) is an ASD screening tool that has been widely translated into various languages. The M-CHAT is considered advantageous because it is simple and inexpensive to use.[11] The sensitivity and specificity of M-CHAT were reported to be 83% and 51%, respectively.[12] This questionnaire was modified to improve its specificity, and renamed the *Modified Checklist for Autism in Toddlers - Revised* (M-CHAT-R). It is intended for use in children aged 16-30 months. The M-CHAT-R has 91% sensitivity and 95.5% specificity.[13] The Indonesian version of M-CHAT-R has 88.9% sensitivity and 94.6% specificity in predicting ASD.[14]

This study was the first to screen ASD on a large scale in children aged 16-30 months in Indonesia. We aimed to determine the prevalence of ASD in children aged 16-30 months and the risk factors contributing to ASD in Indonesia.

Methods

A cross-sectional study was carried out from March to October 2020. The study protocol was approved by the Health Research Ethics Committee of the Universitas Indonesia Medical School. The sample size estimation was calculated based on $\alpha=0.05$, $Z\alpha=1.96$, $d=1\%$ and $P=2\%$ as the proportion of children with ASD.[1] The minimum required sample size for this study was 827. The selection of participating hospitals was carried out by cluster sampling, in which ten hospitals (five private hospitals and five government/academic/military hospitals) were randomly selected for each district in Jakarta, five districts in total. We aimed to screen 20 subjects from each hospital using the M-CHAT-R questionnaire.

The *Modified Checklist for Autism in Toddlers - Revised* (M-CHAT-R) was a screening tools specific for ASD in children, designed by Robins *et al.*[11] There were 20 yes/no questions which relies on parents' observation of their children. This tool took approximately around 5 minutes to complete. From each question, a point was given if the parent says "no", with scoring for item number 2, 5, and 12 were reversed. The points were then accumulated to a total score. The total score was further classified into: 0-2 (low risk of ASD), 3-7 (moderate risk of ASD), and 8-20 (high risk of ASD), respectively.[11]

The study was conducted at the walk-in clinic of each hospital, with each visiting child who had been selected consecutively underwent screening using inclusion and exclusion criteria. Healthy children aged 16-30 months whose parents agreed to participate were included in this study. Meanwhile, we excluded congenital or neurological disorders that could affect brain and nerve functions, previously diagnosed developmental disorders, and malnutrition. When the child met the criteria, the parent/guardian was asked to sign an informed consent. The child was then examined by a pediatrician to exclude the determined conditions. After that, the parent was asked to fill out the M-CHAT-R questionnaire. This data collection took place from March to July 2020. Using this protocol, 219 samples were obtained.

On March 11, 2020, the *World Health Organization* (WHO) stated that COVID-19 had reached a pandemic status.[15] Since then, various health protocols had been announced, including in Indonesia. This complicated our study with the first protocol, because the number of children attending the hospital was limited. Therefore, we decided to change the study protocol to using an online questionnaire. We have obtained a written consent from Robins *et al.*[11] to modify the original M-CHAT-R into online form. The amendment to this study protocol was approved by the Health Research Ethics Committee of the Universitas Indonesia Medical School.

The questionnaires were then distributed from August 1, 2020 to October 10, 2020, and 1,028 samples were obtained. After age screening (some filled out a questionnaire but the age was outside the range of 16-30 months), 746 samples were involved in data analysis. The total sample (before and after the pandemic) was 965 subjects.

A demography of parental education, parental occupation, and family income were obtained. Risk

factors regarding ASD were also acquired: gender, family history of ASD, preterm birth, low birth weight (LBW), and history of seizures. Family history of ASD referred to siblings with the same biological parents. Preterm birth was present if gestational age at birth was < 37 weeks. The LBW was classified for birthweight under 2.500 g. History of seizures was asked, specifically of seizures without fever (excluding febrile convulsions).

The independent variables in this study were gender, family history of ASD, preterm birth, LBW, and history of seizures. The dependent variable was the result of the M-CHAT-R questionnaire. Chi-square and Fisher's tests were conducted to analyze for relationships between the variables in this study.

Results

Of the 965 subjects, 546 (56.58%) were male (**Table 1**). The mean age of the subjects was 22.59 (SD 4.15) months. Most fathers had attained a bachelor's degree (55.96%) and worked as private employees (48.39%). Most mothers had a bachelor's degree (57.51%) and were housewives (49.12%). Most families had incomes above IDR 10,000,000/month (44.97%). A total of 183 of 965 subjects (18.96%) had possible risk factors for ASD (**Table 2**). Fifty-four of them had more than one (maximum three) risk factors present. The most common risk factor was LBW (97 subjects; 0.10%).

There were 811 subjects (84.04%) with a low risk of developing ASD, 120 subjects (12.44%) at moderate risk, and 34 subjects (3.52%) at high risk for ASD. Chi-square analysis showed that male gender was a

Table 1. Characteristics of study subjects

Characteristics	Offline (n=219)	Online (n=746)	Total (N = 965)
Gender, n (%)			
Male	117 (53.42)	429 (57.51)	546 (56.58)
Female	102 (46.58)	317 (42.49)	419 (43.42)
Paternal education			
Primary	8 (3.65)	1 (0.13)	9 (0.93)
Junior high	11 (5.02)	2 (0.27)	13 (1.35)
Senior high	98 (44.75)	73 (9.79)	171 (17.72)
Diploma	14 (6.39)	76 (10.19)	90 (9.33)
Bachelor's	77 (35.16)	463 (62.06)	540 (55.96)
Master's	11 (5.02)	127 (17.02)	138 (14.30)
PhD	0	4 (0.54)	4 (0.41)
Paternal occupation			
Laborer	8 (3.65)	11 (1.47)	19 (1.97)
Entrepreneur	65 (29.68)	227 (30.43)	292 (30.26)
Government employee	30 (13.70)	157 (21.05)	187 (19.38)
Private employee	116 (52.97)	351 (47.05)	467 (48.39)
Maternal education			
Primary	2 (0.91)	0	2 (0.21)
Junior high	21 (9.59)	1 (0.13)	22 (2.28)
Senior high	94 (42.92)	49 (6.57)	143 (14.82)
Diploma	23 (10.50)	104 (13.94)	127 (13.16)
Bachelor's	70 (31.96)	485 (65.01)	555 (57.51)
Master's	9 (4.11)	103 (13.81)	112 (11.61)
PhD	0	4 (0.54)	4 (0.41)
Maternal occupation			
Housewife	136 (62.10)	338 (45.31)	474 (49.12)
Entrepreneur	13 (5.94)	74 (9.92)	87 (9.02)
Government employee	16 (7.30)	81 (10.86)	97 (10.05)
Private employee	54 (24.66)	253 (33.91)	307 (31.81)
Monthly family income			
< IDR 5,000,000	80 (36.53)	100 (13.40)	180 (18.65)
IDR 5,000,000 - 10,000,000	84 (38.35)	267 (35.79)	351 (36.37)
> IDR 10,000,000	55 (25.11)	379 (50.80)	434 (44.97)

Table 2. Risk factors of autism spectrum disorder

Risk factor, n (%)	Offline (n=35)	Online (n=148)	Total (n=183)
Family history of autism	5	15	20 (2.07)
Prematurity	14	67	81 (8.39)
Low birth weight	15	82	97 (10.05)
History of seizures	18	31	49 (5.08)

Note: 54 children had > 1 risk factors

Table 3. Analysis of potential risk factors and ASD

Risk factor	M-CHAT-R score			P value
	Low-risk (n=811)	Moderate-risk (n=120)	High-risk (n=34)	
Gender, n (%)				0.000258
Male	436 (53.76)	85 (70.83)	25	
Female	375 (46.24)	35 (29.17)	9	
Family history of autism, n (%)				0.872[a]
Yes	16 (1.97)	3 (2.50)	1	
No	795 (98.03)	117 (97.50)	33	
Prematurity, n (%)				0.770[b]
Yes	67 (8.26)	10 (8.33)	4	
No	744 (91.74)	110 (91.67)	30	
Low birth weight, n (%)				0.944[b]
Yes	81 (9.99)	12 (10.00)	4	
No	730 (90.01)	108 (90.00)	30	
History of seizures, n (%)				0.372[b]
Yes	42 (5.18)	7 (5.83)	0	
No	769 (94.82)	113 (94.17)	34	

[a]Did not meet the Chi-square requirements, cell merging was performed; [b]Chi-square, not statistically significant

Table 4. Relationship between family history of autism and ASD

Risk factor	M-CHAT-R score		P value
	Low-risk (n=811)	Moderate and high-risk (n=154)	
Family history of autism, n (%)			0.544[c]
Yes	16 (1.97)	4 (2.60)	
No	795 (98.03)	150 (97.40)	

[c]Fisher's test; not statistically significant

significant risk factor of ASD (P<0.001) (**Table 3**). Analysis for family history of autism did not meet the Chi-square requirements, because the expected cell count was more than 20%. Therefore, cell-merging and the subsequent alternative Fisher's test was performed (**Table 4**).

Discussion

This study was the first to examine possible risk factors for ASD in children aged 16-30 months in Indonesia. Of 965 subjects, 154 subjects (15.96%) were at moderate or high risk of developing ASD by M-CHAT-R screening. The high-risk group alone was comprised of 3.52% of the subjects. Although M-CHAT-R scores only portrays risk of having ASD, as we could not made any confirmed diagnosis with DSM V and direct assessment due to challenges during the pandemic, but this finding was still consistent with a 2% prevalence in an American study.[10] A previous diagnostic study in Indonesia reported a rate of 9.7% for ASD.[14] This difference may have been due to different study protocols, as the previous study was not

community-based.

Male gender was the only statistically significant risk factor for ASD in this study (P<0.001). The male: female ratio with moderate-to-high risk M-CHAT-R results was 2.5:1. This finding was consistent with a global study which stated that the risk of boys having ASD was three times higher than girls.[2]

Family history of ASD, especially siblings, was found in 2.07% of subjects. To date, there has been no study on the history of ASD in families in Indonesia. American studies showed that children with autistic siblings have a 2 to 8% chance for developing ASD as well.[4,6] In our study, only 4 subjects (2.604%) with moderate and high risk of ASD, had autistic siblings (P>0.05). This finding suggests that in Indonesia, having an autistic sibling is not a risk factor for ASD in children. The role of genetics in ASD is still being investigated. A study in England and Scandinavia found that monozygotic twins had >60% chance of developing ASD, whereas that increased possibility did not seem to exist for dizygotic twins.[6] In a large cohort study in Sweden, the probability of ASD as a hereditary disease was 50%.[16]

Preterm birth and LBW rates in this study were 8.39% and 10.05%, respectively. The global preterm infant prevalence rate was 11.1%. Back in 2010, Indonesia's preterm birth rate was the fifth highest in the world (15.5%), after India, China, Nigeria, and Pakistan.[17,18] In addition, the number of LBW babies in Indonesia reached 6.2% in 2018.18 Prematurity and LBW were not significant risk factors for ASD in our subjects (P>0.05). A meta-analysis by Wang *et al.*[19] suggested that preterm birth rate and LBW were risk factors for ASD in children. However, in another meta-analysis for preterm infants, ASD was found in 7% of subjects.[20] This relatively small number implies that preterm birth did not necessarily cause ASD in children.

None of the high-risk children by M-CHAT-R had a history of seizures. We chose to evaluate seizures in reference to an epileptic syndrome, which according to several studies had been linked to ASD.[21,22] Prevalence of epilepsy in people with ASD was reportedly 11.2%, while the prevalence of ASD in people with epilepsy was 8.1%.[23] However, the relationship between ASD and epilepsy remains unclear. Genetic and environmental influences are suspected to play a role in causing both ASD and epilepsy.[24,25]

The limitation of our study was that follow-up examinations (M-CHAT-R/F) were not done by Growth and Development pediatrician consultants as was done in previous studies, due to the difficulty of executing such a protocol in the pandemic. Further study needs to be done with more thorough methods so that a true ASD prevalence can be obtained.

In conclusion, the high-risk prevalence of ASD in children aged 16-30 months in Indonesia is 3.52%. Male gender is a significant risk factor for high-risk M-CHAT-R results.

Conflict of Interest

None declared.

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