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Indonesian Modified Checklist for Autism in Toddler, Revised with Follow-Up (M-CHAT-R/F) for autism screening in children at Sanglah General Hospital, Bali-Indonesia

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ABSTRACT

Background: Autism Spectrum Disorder (ASD) is a developmental disorder characterized by impaired reciprocal social interaction and communication, and by a restricted, repetitive or stereotyped behavior. Early detection of autism is recommended on all toddlers from the ages of 9 months because of increasing in prevalence. The Modified Checklist for Autism (M-CHAT) in Toddlers, a Revised with Follow-Up (M-CHAT-R/F) is a 2-stage parent-report screening tool to assess a risk for ASD and it demonstrates an improvement compared to the original M-CHAT. It is translated to Indonesian language by Soetjiningsih and colleagues, and it needs to be validated.

Methods: This is a diagnostic accuracy study conducted at Sanglah Hospital, Bali, conducted from March 2015 to December 2016. We included children 18-48 months in this study. The parents of the outpatient children in the growth and development clinic of Sanglah Hospital were asked to fill out the Indonesian M-CHAT-R/F form. In the same visit, the Autism Spectrum Disorder (ASD) assessment according to the DSM-5 as a gold standard was done by the researchers, without knowing the M-CHAT-R/F result. The assessment comparison based on M-CHAT-R/F and DSM-5 was analyzed to obtain the AUC intersection on ROC curve that gives the best sensitivity and specificity.

Results: We found 10.71% of our outpatient was diagnosed with autism according to DSM 5, when they are 18-24 months old. The Indonesian version of M-CHAT-R/F as an ASD screening tool has 88.9% in sensitivity and 94.6% in specificity.

Conclusion: Our results suggest that the Indonesian translation of the M-CHAT-R/F is an effective screening instrument for ASD, particularly when a two-step screening process is used.

Keywords: M-CHAT-R/F, Modified Checklist for Autism, Autism Spectrum Disorder, Validity Test

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INTRODUCTION

Autism spectrum disorder (ASD) is a syndrome with a wide clinical phenotype, characterized by impairments in social interaction and reciprocal communication, and by patterns of stereotyped behaviours. The term ASD is used here to define a broad concept of autism, manifested as a spectrum of behavioural, cognitive, and linguistic problems that include autistic disorder, Asperger syndrome, and pervasive developmental disorder not otherwise specified (PDDNOS). ASD is a chronic and severe neurodevelopmental disorder with a significant social impact.[1]

Recent epidemiologic studies have confirmed that ASD is more common than previously thought, with a rate of approximately 6 to 7 per 1,000 children.[1-3] The most recent estimation in the United States in children of 8 years old was as high as 6.5 per 1,000 in 2002, to 10.2 per 1,000 in 2006 and 13.0 per 1,000 in 2008.[4] Autism in aged 18-48-month old constitutes 9.7% of all Sanglah Hospital pediatric outpatient.[5] An early detection is essential for children with ASD. Clinical studies that have shown that an early intervention subsequent to early detection can enhance their potential and lead to an optimal outcome.[4,6]

The original Modified Checklist for Autism in Toddlers (M-CHAT) is currently one of the most widely used ASD screening instruments both in the United States and internationally, providing an accessible and a low-cost option for universal toddler screening.[6,7] A paper by Robins in 2014, reported the first published data for a revised version of the M-CHAT screening instrument and follow-up interview, and so called the Modified Checklist for Autism in Toddlers, a Revised with Follow-Up (M-CHAT-R/F).[8] The purpose of revising the M-CHAT was to reduce the number of cases who initially screen positive and need a follow-up, while maintaining a high sensitivity. The overall rate of detection of ASD was higher

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for the M-CHAT-R/F, which detected 67 cases per 10,000, compared with the original M-CHAT/F, which detected 45 cases per 10,000. The M-CHAT-R/F has been shown to have an adequate sensitivity and specificity, 47.5% of children screen-positive cases on the basis of the M-CHAT-R/F were diagnosed with ASD and 35.7% presented with developmental delay or concerns.[8] We have not found any research done regarding the M-CHAT-R/F use in Indonesia. The aim of this study is to update the findings regarding the use of the Indonesian version of M-CHAT-R/F as an ASD screening instrument.

METHODS

This is a diagnostic accuracy study to evaluate the validity of the Indonesian version of M-CHAT-R/F. The study was conducted at the children growth and development outpatient clinic, Sanglah General Hospital, from March 2015 to December 2015. The subjects were 110 patients who fulfilled the inclusion and exclusion criteria. We used a consecutive sampling method. The inclusion criteria are: (1) the age of the patient who visit the clinic within the study time frame is between 18 and 48 months, (2) the parents are willing to participate in the study and signed an informed consent form. The exclusion criteria are: (1) the patient was diagnosed with ASD before the visit, (2) the patient has a severe sensory and communication disability (eg. blindness or deafness) or severe motoric disability (eg. cerebral palsy or hydrochepalus) which prevents them from completing study assessment.

The gold standard of the diagnosis of ASD is The American Psychiatric Association's Diagnostic and Statistical Manual, Fifth Edition (DSM-5). The age was determined by checking the patient birth date against the date of the visit. The sex was determined based on the phenotype appearance; divided into male and female.

The M-CHAT-R/F is a 2-stage parent-report screening tool to assess the risk of ASD.[8] It is free for a clinical, a research, and an educational use, and it requires little or no training for health care professionals. The instruments were available at www.mchatscreen.com. Initially, the parents have to answer 20 yes/no questions using the M-CHAT form, which takes 5 minutes. If the child is screened positive, the parent is asked a structured follow-up questions, using the M-CHAT-R/F form, to obtain an additional information and examples of at risk behaviors. It takes approximately 5 to 10 minutes with a professional. The scoring algorithm of M CHAT-R/F.

First stage using M-CHAT-R form:
A total score of 0-2 is considered as low risk. A total score of 3-7 is considered medium risk and the evaluation proceeds to the second stage using the M-CHAT-R/F. If the M-CHAT-R/F score remains at 2 or higher, the child is positive. If the score is 0-1, child has screened negative. A total score of M-CHAT-R of 8-20 shows a need to bypass the second stage and a need torefer immediately for diagnostic evaluation and eligibility evaluation for an early intervention.

Second Stage using the M-CHAT-R/F form:
The follow-up items are selected based on which items the child failed on the M-CHAT-R. Only those items that were originally failed need to be administered for a complete interview. The interview is considered positive if the child fails any two items on the follow-up.

The reliability of the instrument is done through a process of translation of the M-CHAT-R/F into Indonesian by Soetjiningsih and colleagues, with Diana Robins permission. The original is available at www.mchatscreen.com. The reliability test was performed by calculating the coefficient of test-retest reliability. Fifteen parents of children who joined the study were asked to fill out the form two times, first in their first visit, and the next within 3 weeks to a month after the initial visit. The Bland-Altman plot was used to measure the reability of the translated M-CHAT-R/F. Pediatric residents who were stationed in the clinic helped the parents filling the M-CHAT-R form, if the parents has any question in filling out the form. In the same visit, the researchers conducted a n examination using DSM-5 criteria. The diagnosis is made based on the DSM-5 as the gold standard. The researchers did not know the M-CHAT-R/F result while conducting the examination using the DSM-5.

The data were analyzed using Stata E 15. Descriptive statistics were used to evaluate the data distribution based on the characteristics and the frequency of the disorders. An analysis was performed to calculate the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (LR+), negative likelihood ratio (LR-). The study was approved by the Ethics Committee of Udayana University School of Medicine in conjunction with Sanglah General Hospital, the university teaching hospital.

RESULTS

The Bland-Altman plot showed the limit of agreement between the first and second M-CHAT-R/F scores. The scores of M-CHAT-R/F as measured in

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different time periods has a not statistically significant mean difference, 0.067 (-0.964-0.830, 95% CI) with p=0.118.

A total of 168 children were studied from March to December 2015. Fifty-eight children were excluded due to suffering a global developmental delay. The remaining 110 children were screened with the M-CHAT-R/F (see Table 1). They are 74 males (67.27%) and 36 females (32.73%), with male: female ratio of 2.05:1. The median age was 30.6 months, SD 9.55 months, range 18-48 months. Based on their nutritional status, 23 (20.91%) were underweight, 66 (60%) were normal, 18 (16.36%) were overweight, and 3 (2.73%) were obese. Most of the respondence was the mother 93 (84.55%). Among the pediatric outpatient of the Sanglah Hospital, autism aged 18-48 months was found as much as 10.71%, and became 16.36% when the global developmental delay was excluded.

Table 1 The Subject Characteristics

Variables	Autism (DSM-5) n = 18 f (%)	Total n = 110 f (%)
Sex		
Male	15 (83.33)	74 (67.27)
Female	3 (16.67)	36 (32.73)
Age in months mean (min-max)	34.33 (20-48)	30.6 (18-48)
Nutritional Status		
Underweight	4 (22.22)	23 (20.91)
Normal	9 (50.00)	66 (60.00)
Overweight	4 (22.22)	18 (16.36)
Obese	1 (5.56)	3 (2.73)
Responden		
Mother	17 (94.44)	93 (84.55)
Father	1 (5.56)	14 (12.73)
Others	0 (0.00)	3 (2.73)
Father's Education		
Elementary School	0 (0.00)	2 (1.82)
Junior High School	2 (11.11)	17 (15.45)
Senior High School	8 (44.44)	53 (48.18)
Undergraduate	8 (44.44)	38 (34.55)
Mother's Education		
Elementary School	1 (5.56)	6 (5.45)
Junior High School	3 (16.67)	24 (21.82)
Senior High School	7 (38.89)	54 (49.09)
Undergraduate	7 (38.89)	26 (23.64)

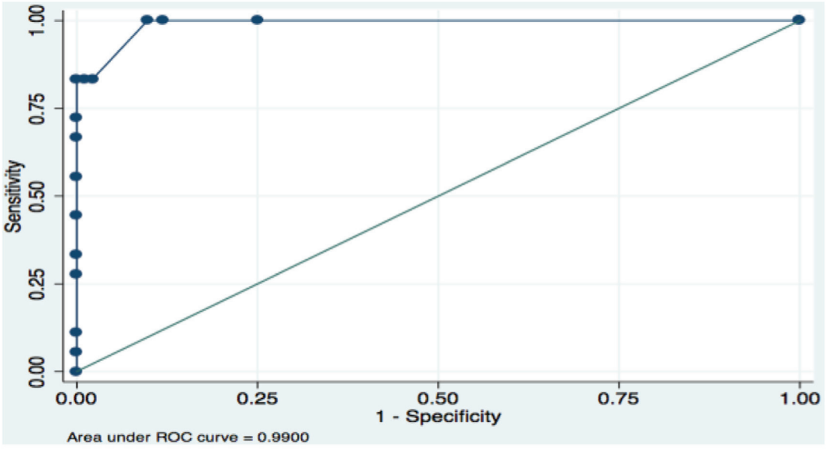

Figure 1 ROC curve for first-stage M-CHAT-R. AUC, area under the curve; ROC, receiver operating characteristic.

First-Stage M-CHAT-R Scoring

From 110 children screened with the first stage M-CHAT-R, 83 (75.45%) was negative (low risk), 15 (13.64%) was medium risk and required an additional follow-up, and 12 (10.90%) was positive (high risk) and required no additional follow-up. Area under the curve was 0.990 (Figure 1). The threshold for which both sensitivity and specificity exceeding 0.80 was 6 (Table 2).

Two-Stage M-CHAT-R/F Scoring

Fifteen children in medium risk completed the second stage M-CHAT-R/F, 9 (60%) was positive and 6 (40%) was negative. A total of 89 children was screened negative, 21 children was positive using the M-CHAT-R/F. The DSM-5 examination showed 92 children non-ASD and 18 children diagnosed with ASD. Five children who screened positive using M-CHAT-R/F was diagnosed with non-ASD using DSM-5. Two children who was screened negative using M-CHAT-R/F was diagnosed with ASD using DSM-5. The Indonesian version of M-CHAT-R/F has a sensitivity of 88.9% and specificity of 94.6%

Table 2 Sensitivity and Specificity for Each M-CHAT-R Total Score.

AUC = 0.990

Cutoff on M-CHAT-R Total Score	Sensitivity (%)	Specificity (%)
0	100	0.00
1	100	75.00
2	100	88.04
3	100	90.22
4	83.33	97.83
5	83.33	98.91
6	83.33	100
7	72.22	100
8	66.67	100
9	55.56	100
10	44.44	100
11	33.33	100
12	27.78	100
14	11.11	100
16	5.56	100
>16	0.00	100

Table 3 **Psychometric Properties of M-CHAT-R/F Scores**

M-CHAT-R/F	DSM-5		Sen (%) (95% CI)	Spe (%) (95% CI)	PPV (%) (95% CI)	NPV (%) (95% CI)	LR+	LR-
	ASD	Non-ASD						
Positive	16	5	88.9 (65.3-98.6)	94.6 (87.8-98.2)	76.2 (52.8-91.8)	97.8 (92.1–99.7)	16.4	0.117
Negative	2	87						

with PPV of 76.2% and NPV of 97.8% to predict ASD (Table 3).

DISCUSSION

Our study analyzed the validity of the Indonesian version of the M-CHAT-R/F as a screening tool for early detection of ASD. We found a proportion of autism patient aged 18-48 months was 10.71% among overall Sanglah Hospital outpatient. The previous study in the same hospital reported a lower rate of 9.7%.[5] The reported prevalence of ASD has increased in recent decades. For example, data from the Centers for Disease Control and Prevention's (CDC) National Health Interview Survey (NHIS) revealed a nearly fourfold increase in parent-reported ASD between the 1997–1999 and 2006–2008 surveillance periods.[9] The CDC's Autism and Developmental Disabilities Monitoring (ADDM) Network revealed a 78% increase in ASD prevalence between 2002 and 2008.[10] Various community-based studies showed different results about the prevalence of autism. A study in the United States reported the prevalence of autism among children age 3 to 5 years was 8.5 per 1000 children.[2] A study in 14 states in the U.S. found the prevalence of autism has increased from 6.5 per 1,000 children aged 8 years in 2002, to 10.2 per 1,000 in 2006 and 13.0 per 1,000 in 2008.[10] A community-based study in South Korea showed the autism prevalence in children aged 7-12 years was 2.64% (1.91-3.37, 95% CI).[11] Another two-stage community-based study in Spain reported a prevalence of 0.92% and 0.29% respectively.[12]

In this study, we found that the male female was 5:1 for all ASD cases. This finding is consistent with previous study in Sanglah Hospital that have demonstrated a higher proportion of male, with a ratio of 4.7:1.[5] A sex difference in the prevalence of ASDs has been well documented in epidemiologic studies since the 1960s, and boys with an ASD outnumbered the girls by a ratio of about 4 to 5.[13] A study in the U.S. showed the prevalence of ASD was significantly higher among boys than among girls, with ratios ranging from 3.6 to 5.1 ($p<0.01$).[10] The specific factors responsible for the higher male prevalence in ASD remain unclear. The extreme male brain (EMB) theory, first proposed in 1997, is an extension of the Empathizing-Systemizing (E-S) theory of typical sex differences proposes that females on average have a stronger drive to empathize while males on average have a stronger drive to systemize.[14]

The best age for autism screening is an ongoing debate, and the AAP currently recommends autism-specific screening at both 18 and 24 months of age.[10] An important findings in our study is that the average age of diagnosis was just before the third birthday, which is 1 years earlier than the median age of diagnosis.[10] This finding suggests that implementing a standardized screening and an expeditious evaluation for positive cases can greatly increase the time that children are eligible for early intervention services, and therefore improve the outcome.

The recommended algorithm classifies children into 3 ranges of risk, on the basis of the initial questionnaire. The children who score in the low-risk range (75.45% of cases) are not in need of M-CHAT-R follow-up or an additional evaluation. Children should be rescreened if they are younger than 24 months, as recommended by the American Academy of Pediatrics.[15] The children whose scores are in the medium-risk range (13.64% of cases) require administration of the follow-up, which gathers additional detail about at-risk items. The children who score in the high-risk range (10.9 % of cases) may bypass the follow-up. This result a consistency with a validation study of M-CHAT-R/F that showed 93%, 6%, and 1% of children who score low-risk range, medium-risk range, and high-risk range, respectively.[8]

The first stage result in this study indicates an optimal sensitivity and specificity, and demonstrates an area under the curve of 0.990 were achieved using the cutoff score of 6 items on the M-CHAT-R. This cutoff score was lower than the previous recommended algorithm, which use score ≥ 8 as high risk range.[8] Our study recommends children with a M-CHAT-R score of ≥ 7 can bypass the follow up, because approximately 60% of the children whose parents completed the second stage of M-CHAT-R/F continue to show ASD risk and require referrals for an evaluation and a possible early intervention.

The sensitivity and specificity of M-CHAT-R/F in this study were 88.9% (65.3%-98.6%, 95% CI) and 94.6% (87.8%-98.2%,95% CI), respectively.

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This finding is consistent with the previous study using the original English version of M-CHAT-R/F demonstrating the sensitivity of 85.4% (79%-92%, 95% CI) and specificity of 99.3% (99%-99%, 95% CI).[8] This study showed a good PPV 76.2%, which supported the purpose of revising the M-CHAT to M-CHAT-R/F: to reduce the number of cases who initially screen positive and need the follow-up, while maintaining a high sensitivity. A good diagnostic test has LR+ >10, LR- <0.1 and their positive result has a significant contribution to the diagnosis. Our Indonesian translation of M-CHAT-R/F can be classified as a good diagnostic test because the LR+ is 16.4 and LR- 0.117.

The limitation of our is the small sample size and all of the examination, the M-CHAT-R, the follow-up and the ones using DSM 5, was performed at the same visit time. In addition, this study was not done in a community setting. Thus, we should avoid over generalizing the findings of this study. Some modifications of the form may be necessary to cater the age of children, different cultural attitudes and values. Nonetheless, our Indonesian translation of the M-CHAT-R/F can be considered reliable and valid to be used as a first-level screening tool for early detection of ASD.

CONCLUSION

Our study provides an empirical support for the utility of screening for ASD by using the M-CHAT-R/F in the primary care setting. The result suggests that Indonesian translation of the M-CHAT-R/F continues to be an effective screening instrument for ASD in our hospital, particularly when the two-step screening process is used. A screening with the M-CHAT-R/F potentially reduces greatly the age at diagnosis, facilitates an early intervention, and optimizes the long-term prognosis. The simplified scoring of the M-CHAT-R/F, paired with specific algorithms based on the outcome, should simplified the implementation.

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