

ORIGINAL ARTICLES

Prevalence of autism spectrum disorders and their relation to selected factors among children aged 18-30 months in Hoa Binh province, 2017

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ABSTRACT

Background: Autism spectrum disorder (ASD) is a developmental disorder among children, which is increasing worldwide and in Vietnam. This study reports the prevalence of autism spectrum disorders and examines their relation to selected factors (individual and familial factors) among children aged 18-30 months in Hoa Binh province, 2017.

Methods: This was a cross-sectional study among 5,893 children aged 18-30 months in three districts/city in Hoa Binh province, using M-CHAT to screen children with high risks of ASD in the community. All of M-CHAT positive cases (101 cases) and about 2.5% of negative cases (155 cases) were invited for ASD diagnosis, in which 97 positive and 149 negative cases were diagnosed by pediatric psychiatrists from Vietnam National Children's Hospital with criteria in the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV). Epidata 3.1 and SPSS 20 were used for the data entry and analysis.

Results: The overall prevalence of ASD among children aged 18-30 months in the study sites was 7.3%. The odds of having ASD were significantly higher among those who were boys, living in urban area, having relatives with psychiatric disorders, birth defects and mothers with miscarriage, and induced abortion history.

Conclusion: Our study revealed that the prevalence of ASD among children seems to be increasing. ASD was significantly correlated with individual and familial factors. Further and large-scale studies are needed to investigate the ASD prevalence and its related factors.

Keywords: Autism spectrum disorder, prevalence, children, 18-30 months, Hoa Binh.

BACKGROUND

Autism spectrum disorders (ASD) refer to a range of conditions characterized by some degree of impaired social behavior, communication and language, and a narrow range of interests and activities that are both unique to the individual and carried out

repetitively. ASD often cause a number of developmental challenges to the children with the disorder, and impose significant burden on their families and the community (1).

ASD prevalence appeared to be increasing over the past decades. Victor Lotter's first epidemiological study of autism in



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the 1960s posited a rate of 4.5/10,000 (0.45‰) among children aged 8-10 years. According to estimates from CDC's Autism and Developmental Disabilities Monitoring (ADDM) Network, the prevalence of ASD in the US was 1/150 (6,6‰) in 2002, increased to 1/68 (14,6‰) in 2012 and 1/59 (16,8‰) in 2014 (2).

In Vietnam, autism has emerged as a health concern drawing attention of the health officials and the community in recent times. The prevalence of ASD in the nationwide scale is so far unknown. A number of studies conducted in northern provinces of Vietnam have identified children with ASD with an average prevalence of between 4‰ and 5‰ (3-5).

Currently, identifying the prevalence of ASD in low- and middle-income countries remains a clear gap, especially for mountainous and remote areas. Thus, this study was conducted to investigate the prevalence of ASD and examine its relation to selected individual and familial factors among children aged 18 - 30 months in Hoa Binh province in 2017.

METHODS

Design

This was a cross-sectional study covering an urban area (Hoa Binh city) and two rural districts (Luong Son, Kim Boi) in Hoa Binh province in 2017.

Study participants

All children aged 18 and 30 months who were living with their parents or caregivers in the study sites at the time of research.

Sample size and sampling

The sample size (the total number of children aged 18-30 months selected into the study) was estimated using the following formula:

$$n = Z_{(1-\alpha/2)}^2 \frac{(1-p)}{\varepsilon^2 p}$$

In which, n was sample size; $Z_{(1-\alpha/2)}$ was equal to 1.96 (confidence level of 95%); ε was relative precision (35%); p was anticipated population proportion of children with ASD (0.46% (3)); and the estimated refusal rate of 15%. The total sample size was 5,918 children.

A complete list of all children aged 18-30 months in the selected districts, which was compiled with the assistance of the District Health Center and Center of Population and Family Planning, included 6,152 children. All of them were then selected into the study.

Study variables

The dependent variable was ASD, as initially identified by screening and subsequently diagnosed by pediatric psychiatrists, among the study participants. Independent variables included age, gender and living area of the child, parents' age, education and occupation, the family's economic status, familial history (including the child's relatives) of psychiatric disorders or birth defects, and mothers with miscarriage, stillbirth and induced abortion history.

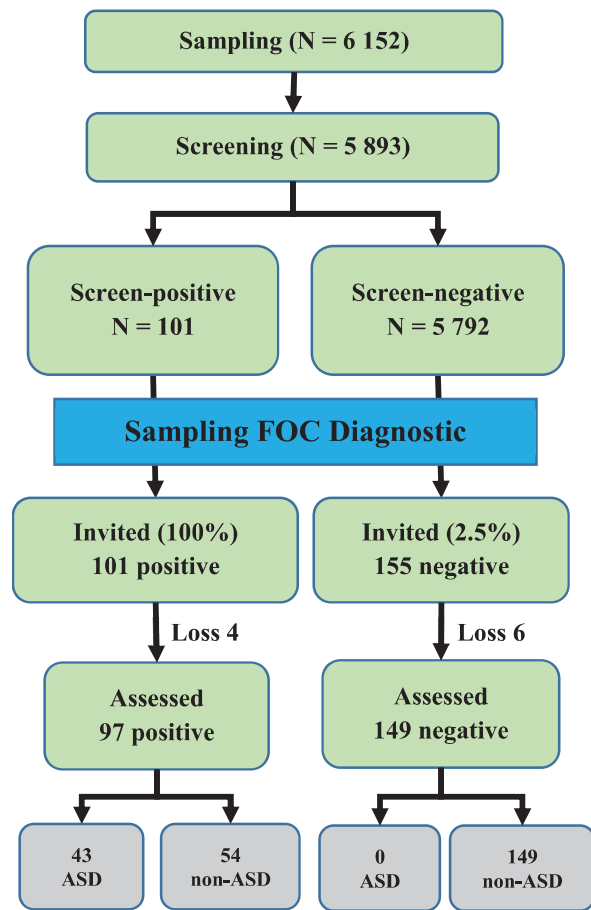
Data collection

Phase 1: *Screening with M-CHAT and epidemiological survey*: Local health workers (either medical doctor or nurse, midwives) were recruited and trained by researchers from the Hanoi University of Public Health (HUPH) at district health centers. The data collectors then performed face-to-face interviews with parents or caregivers of all children in the study sample at the household. The HUPH’s researchers as supervisors provided supportive supervision to the collectors during the beginning of data collection period and re-examined 5% of the completed questionnaires for data quality assurance. As many as 5,893 out of 6,152 children’s parents/caregivers consented to participate in the study and completed the M-CHAT interviews (the response rate was 95.8%).

Phase 2: *Diagnostic Confirmation with DSM-IV*: All children of screen-positive group (101 children) and 2.5% children of screen-negative group (155 children) were invited to diagnostic confirmation assessment at district health centers by 8 professionals (pediatric psychiatrists and psychologists) from the Vietnam National Children’s Hospital using DSM- IV criteria. Each child would get the assessment from 02 professionals, 01 pediatric psychiatrists and 01 psychologist, currently working at Department of Psychiatry, Vietnam National Children’s Hospital. Children’s families were given the child assessment results and advice from professionals about early intervention and family’s role in the child’s development.

Data analysis

Descriptive and analytical statistics were performed, with the child’s ASD result as



dependent variable (binary variable), and independent variables including individual and familial factors. Descriptive statistics were used to calculate frequencies and percentages, and analytical statistics were performed through hypothesis testing and 95% CI estimates. An alpha level of 0.05 was used to determine statistical significance in all analyses. Data were analyzed using EPI Info 3.54 and Stata 14 software.

Ethics approval and consent to participate

Ethical permission for this study was obtained in Decision No. 319/2016/YTCC-HD3 of the Hanoi University of Public Health Ethics Committee dated November 16, 2016. As participants of the study were children aged between 18–30 months, written informed consent was obtained from each of the parents or caregivers to provide information about their children.

RESULTS

Table 1 presents general characteristics of the study sample. Most of the study children (75.8%) lived in rural areas. More

than half of the children were boys (53.1%) and aged 24-30 months (58.5%); 46.6% of the children were second-born and 19.3% of the households were classified as poor/near poor.

Table 1. General characteristics of the study participants

Characteristics	Frequency (n)	Percentage (%)
Gender		
Boy	3127	53.1
Girl	2766	46.9
Living area		
Urban	1425	24.2
Rural	4468	75.8
Child's age		
18 - 23 months	2444	41.5
24 - 30 months	3449	58.5
Birth order		
First-born	2673	45.4
Second-born	2747	46.6
Third-born and over	473	8.0
Household economic status		
Non-poor	4758	80.7
Poor/Near poor	1135	19.3
Total	5.893	100.0

Table 2 demonstrates selected socio-demographic characteristics of the children's parents in the study. The majority of the children's mothers (66.5%) were aged 20 - 29 years at delivery. Most of the mothers (39.6%) had high school education and

68.1% worked as farmers or had unstable employment. Among the fathers, 62.1% were 25 - 34 years of age at delivery. Most of the fathers had high school education (41.2%), and 75.3% worked as farmers or with unstable job.

Table 2. Characteristics of the study participants' parents

Maternal characteristics	Frequency (n)	Percentage (%)	Paternal characteristics	Frequency (n)	Percentage (%)
Maternal age			Paternal age		
Less than 20 years	633	10.7	Less than 25 years	1349	23.3
20 - 29 years	3921	66.5	25 - 34 years	3595	62.1
30 - 34 years	1020	17.3	35 - 44 years	753	13.0
35 years and over	319	5.5	44 years and over	89	1.6
Maternal education			Paternal education		
Primary/Secondary school	1883	32.0	Primary/Secondary school	1918	33.1
High school	2332	39.6	High school	2384	41.2
Vocational education	942	16.0	Vocational education	686	11.9
Tertiary education	736	12.4	Tertiary education	798	13.8
Maternal occupation			Paternal occupation		
Farmer/Unstable job	4013	68.1	Farmer/Unstable job	4357	75.3
Private sector staff	1009	17.1	Private sector staff	651	11.3
Public sector staff	871	14.8	Public sector staff	778	13.4
Total	5.893	100.0	Total	5.786	100.0

The overall prevalence of ASD among children aged 18 and 30 months in Hoa Binh province was 7.3‰ (43 diagnosed with ASD out of 5,893 screened children). Univariate logistic regression analyses of child's demographic variables for association with ASD are presented in Table 3. The odds of having ASD were significantly higher

among boys as compared to girls (OR=4.59, 95% CI: 2.04-10.33), and children living in urban than in rural areas (OR=3.32, 95% CI: 1.82-6.06). There were no statistically significant differences in the prevalence of ASD by other child's socio-demographic variables, including child's age, birth order and household economic status.

Table 3. Univariate logistic regression analyses of child's socio-demographic variables for association with ASD in children aged 18-30 months

Socio-demographic variables	ASD		Odds ratio (OR)	95% CI	
	Frequency (n)	Percentage (‰)		Lower level	Upper level
Gender					
Boy	36	11.5	4.59	2.04	10.33
Girl	7	2.5	1		
Living area					
Urban	22	15.4	3.32	1.82	6.06
Rural	21	4.7	1		
Child's age					
18 - 23 months	14	5.7	0.68	0.36	1.29
24 - 30 months	29	8.4	1		
Birth order					
First-born	19	7.1	1.12	0.33	3.81
Second-born	21	7.6	1.21	0.36	4.06
Third-born and over	3	6.3	1		
Household economic status					
Non-poor	40	8.4	3.20	1.00	10.36
Poor/Near poor	3	2.6	1		

The prevalence of ASD among children of parents aged 35 years and over at delivery was higher than that in the other age groups. The rate of ASD was 12.5‰ among mothers aged 35 years and over, and 12.0‰ among fathers aged 35-44 years. As compared to other groups, the higher rate of ASD came from the children

with mothers who had vocational education (12.7‰), fathers who had tertiary education (12.5‰) and parents who were private sector staff (12.9‰ to mothers and 10.8‰ to fathers). However, there were no statistically significant differences in the prevalence of ASD by the selected parental variables.

Table 4. Univariate logistic regression analyses of parental variables for association with ASD in children aged 18-30 months

Parental variables	ASD		Odds ratio (OR)	95% CI	
	Frequency (n)	Percentage (%)		Lower level	Upper level
Maternal age					
Less than 20 years	3	4.7	0.62	0.19	2.03
20 - 29 years	30	7.7	1		
30 - 34 years	6	5.9	0.77	0.32	1.85
35 years and over	4	12.5	1.65	0.58	4.70
Paternal age					
Less than 25 years	5	3.7	0.47	0.18	1.23
25 - 34 years	28	7.8	1		
35 - 44 years	9	12	1.54	0.72	3.28
44 years and over	1	11.2	1.45	0.19	10.76
Maternal education					
Primary/Secondary school	8	4.2	0.62	0.20	1.91
High school	18	7.7	1.14	0.42	3.07
Vocational education	12	12.7	1.89	0.66	5.38
Tertiary education	5	6.8	1		
Paternal education					
Primary/Secondary school	11	5.7	0.45	0.19	1.07
High school	16	6.7	0.53	0.24	1.18
Vocational education	6	8.7	0.70	0.25	1.92
Tertiary education	10	12.5	1		
Maternal occupation					
Farmer/Unstable job	23	5.7	0.71	0.30	1.66
Private sector staff	13	12.9	1.61	0.64	4.06
Public sector staff	7	8.0	1		
Paternal occupation					
Farmer/Unstable job	28	6.4	0.62	0.28	1.37
Private sector staff	7	10.8	1.05	0.38	2.90
Public sector staff	8	10.3	1		

The rate of ASD among children who had relatives with psychiatric disorders was 19.0% and with birth defects was 52.1%. The children with familial psychiatric disorders had 2.95 times higher odds of having ASD (OR=2.95, 95% CI: 1.30 – 6.68), and with familial birth defects had 8.32 times higher odds of having ASD (OR=8.32, 95% CI: 3.20 – 21.62) than children without these abnormalities. The intervals were so widely ranged so that further work will need to be done to determine

the association between ASD and familial psychiatric disorders/birth defects.

The odds of having ASD were significantly higher among children of mothers with previous miscarriage (OR=3.41, 95% CI: 1.50 – 7.72) and previous abortions (OR = 3.74, 95% CI: 1.72 – 8.12). There was no statistically significant difference in the prevalence of ASD by previous stillbirth (OR=1.08, 95% CI: 0.15 – 7.90).

Table 5. Univariate logistic regression analyses of familial health-related and prenatal variables for association with ASD in children aged 18-30 months

Variables	ASD		Odds ratio (OR)	95% CI	
	Frequency (n)	Percentage (%)		Lower level	Upper level
Familial psychiatric disorders					
Yes	7	19.0	2.95	1.30	6.68
No	36	6.5	1		
Familial birth defects					
Yes	5	52.1	8.32	3.20	21.62
No	38	6.6	1		
Previous miscarriage					
Yes	7	21.7	3.41	1.50	7.72
No	36	6.5	1		
Previous stillbirth					
Yes	1	7.9	1.08	0.15	7.90
No	42	7.3	1		
Previous abortions					
Yes	8	23.3	3.74	1.72	8.12
No	35	6.3	1		

DISCUSSION

Our findings show that the prevalence of ASD among children aged 18–30 months in Hoa

Binh province was 7.3% or 73 per 10,000 children. The prevalence of ASD among the children found in this study is quite similar to the average prevalence of ASD in the world

(7.6‰) (6), and lower than that of high-income countries (e.g. 24.1‰ among children and adolescents in the USA in 2014-2016 (7), 10‰ in Finland and Sweden (8), and 18‰ in children in Japan in 2008 (9)). This is higher than figures reported by previous surveys in Vietnam (i.e. 4.16 – 5.2‰ in 2012-2014) (3-5).

Odds of ASD for boys were higher than for girls, and the boy-to-girl ratio in this study was 4.59:1. This is consistent with previous findings from other countries (10-14). Biologically, genetic burden and sex-specific gene mutations may be involved in increased ASD vulnerability to males or protection to females (15, 16). The other mechanism discussed is sex hormone, particularly testosterone, which may contribute to male bias in developmental disorders. Additional work is needed to advance our understanding of the interactions between sex-differential biology and risk factors for ASD.

Our study reveals that the prevalence of ASD was higher among children living in urban environments, which is concordant with findings from other studies in the world (17, 18). Increasing degree of urbanization was associated with higher risk of ASD (19, 20). The exposure to hazardous air pollutants during pregnancy and early childhood may have potential association with increased risk for ASD (21, 22) while hazardous air pollutants usually concentrate in urban environments. Becker (2007) discussed hygiene hypothesis that hygiene practices commonly in urban areas lowered microbial exposure in pregnancy and neonatal life that affects the risk for ASD (23).

The prevalence of ASD among children whose relatives had psychiatric disorders/

birth defects was significantly different from those without the abnormalities, similar to previous findings from other countries (24, 25). Genetic epidemiological findings potentially provide evidence for genetic overlap between autism, schizophrenia and bipolar disorder (25, 26). Prenatal exposure to medications, like anti-depressants (27), anti-epileptic drugs (28) and agonists (27, 29) was also found to increase autism risk or autistic traits. Other developmental disabilities, especially cerebral palsy and intellectual disability, are strongly associated with ASD. It was found that singleton siblings of children with cerebral palsy had increased risks of autism spectrum disorders (OR=1.6, 95% CI: 1.1-2.2) (30), while intellectual disability and ASD may share common genetic causes, like single gene mutations, phenotypes and molecular processes (31).

Our findings show that the percentage of ASD was higher among children whose mothers had experienced miscarriage and abortions before, similar to previous studies (32, 33). The discussion on history of spontaneous and induced abortions also might need to be reviewed, as it is complex and is still not well investigated internationally. It may be a potential confounder of the association between interpregnancy interval (IPI) and ASD. Both short and long IPI are associated with increased risk of ASD (34) while the long IPI association was partially confounded by history of previous pregnancy loss (35).

In this study, we used the 23-item Modified Checklist for Autism in Toddlers (M-CHAT) to screen children with high risk of ASD. M-CHAT is a screening tool for ASD which has been used extensively in the community and at clinics (36, 37). M-CHAT has been

validated internationally with positive predictive value ranged from 0.57 to 0.65 in low-risk populations, providing an accessible, low-cost option for universal toddler screening (38-40). In Vietnam, M-CHAT was also used in some other previous studies (3, 5). We used DSM-IV criteria for the diagnostic confirmation phase, which was also used widely in Vietnam (3) and worldwide (41). In 2013, DSM-V was introduced and changed ASD diagnostic criteria, particularly eliminating diagnosis of a number of subtypes, so DSM-V was shown to be likely to decrease the number of individuals diagnosed with ASD (42). The use of DSM-IV in this study may provide us the consistency of diagnostic criteria with previous ASD studies in Vietnam.

This study is one of few population-based studies of prevalence of ASD in children in Vietnam, especially in Hoa Binh - a northern mountainous province where the ASD prevalence is still a clear gap. Because autism is an uncommon childhood disorder, a possible limitation of the study is that a larger sample size may be required to determine with greater confidence the prevalence of autism in very young children.

CONCLUSION AND RECOMMENDATIONS

This study found a prevalence of ASD among very young children that is higher than reported from previous studies in Vietnam. The significant correlates of ASD among the children were male gender, urban setting, familial psychiatric disorders/birth defects and mothers' history of previous pregnancy loss (miscarriage and induced abortion).

There is a need of further studies with larger sample size to determine the prevalence of ASD with greater confidence and provide insights into ASD determinants.

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