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Research Article

Investigation of risk factors of autism spectrum disorders in primary care: Aydın City Center sample

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ABSTRACT

Objective: Autism Spectrum Disorder (ASD) is the second most common developmental disability after intellectual disability. The study aimed to determine the prevalence of ASD risk in children aged 18-36 months admitted to Family Health Centers (FHCs) in Aydın city center, considering the role of FHCs as the first point of contact, and to identify the factors increasing ASD risk.

Methods: Descriptive and cross-sectional study. Assuming 1% prevalence based on DSM-5 data and a sampling error of 0.05, the sampling size of the study planned with a descriptive cross-sectional design was calculated as 392 using the G*Power program. 431 participants were targeted with a 10% margin of error. The data collection form prepared through a literature review and the Modified Checklist for Autism in Toddlers (M-CHAT) scale were administered to all participants who applied to the 8 FHCs (6 urban and 2 rural) selected through cluster sampling method and agreed to participate in the study. Descriptive analyses for non-categorical variables and chi-square analyses for categorical variables were used. $p<0.05$ was considered to be statistically significant. Additionally, in order to eliminate its confounding effect, logistic regression analysis was applied to all variables considered to be associated with ASD.

Results: In the sampling with a mean age of 27.5±6.5 months, ASD risk was found to be 5.8%, and ASD diagnosis prevalence was found to be 0.92%. Sociodemographic features, such as male gender, having a low-income family, maternal use of medication during pregnancy, low birth weight, being born before 35th week of gestation and not being vaccinated in accordance with the vaccination calendar were found statistically significant associated risk factors for ASD.

Conclusion: Continuous follow-up is crucial for individuals identified as being at risk for autism spectrum disorder (ASD) but who do not yet meet the diagnostic criteria. Given the role of early diagnosis in treatment, raising awareness of ASD is a priority in the fight against autism. Furthermore, more research is needed to assess the knowledge levels of both healthcare personnel working at Family Health Centers (often the first point of contact for children aged 18-36 months) and families with children under 36 months.

Keywords: autism spectrum disorders, risk factors, primary health care

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Introduction

Autism Spectrum Disorder (ASD) is a neuro-developmental disorder characterized both by deficits in social and communicational areas and also by repetitive and restricted behaviours. The symptoms appear in the early periods of life.[1] According to the Republic of Türkiye Ministry of Health's autism guidelines, the risk of autism in our country has increased 200-fold in the last 20 years.[2] Although the exact cause is still unknown, genetic, epigenetic and environmental factors are considered to play a part in its etiology.[3]

An increase has been observed in ASD prevalence since the first epidemiological studies conducted.[4-6] In the first studies, the prevalence in United Kingdom was found to be 4.1 per 10.000.[4] In recent studies, an approximate prevalence of 1% has been observed, which was sometimes as high as 2.6%. The prevalence in males is considered to be 4-5 times higher.[5,6]

Development of strategies for early diagnosis is quite challenging because ASD has clinical diversity and varying patterns of onset.[7] Despite the challenges in its early diagnosis, application of cognitive and behavioral therapies through the early identification of ASD has a positive effect on the prognosis.[8] An increase in capabilities such as reading, working and living independently and, a decrease in conditions such as being abused and criminal acts, have been observed in cases receiving early diagnosis and education.[9] Accordingly, the American Academy of Pediatrics (AAP) recommends the screening of children at 18 and 24 months of age for autistic symptoms.[10]

"National Action Plan II for Individuals with Autism Spectrum Disorder" has been developed with the slogan "Differences are our Wealth" for the years 2023-2030 in Türkiye. This action plan was developed with the goals of increasing social acceptance and awareness, providing data-driven monitoring through statistical production, strengthening early diagnosis, monitoring and intervention programs, and empowering individuals and families through effective social service models., In addition, it had the aims of supporting scientific research and development studies, strengthening special and supportive education services, creating an open, inclusive and accessible labor market and working environments to ensure the implementation of the right to work, supporting participation in sporting, artistic and cultural activities and developing a monitoring system based on cooperation and coordination.[11] Early diagnosis and screening of ASD are very important due its increasing prevalence, chronic nature, the proven social and cognitive gains in case of early diagnosis, reduction of annual costs in case of early diagnosis and late detection by families and educators in the absence of screening.[8,12] Due to these reasons, the American Academy of Pediatrics (AAP) recommends evaluating the children at 18 and 24 months of age.[10,12] Similarly, the screening of all children at 18 and 24 months is also recommended in Türkiye.[13]

Although it has symptoms in early months, the average age of diagnosis for ASD cases has been found to be 40 months.[14] However, no definitive diagnosis method exists for the identification of ASD at an early stage. There are only certain screening methods available to assist the monitoring of development and diagnosis.[15] Modified Checklist for Autism in Toddlers (M-CHAT) is one of the tests used for screening and monitoring Autism Spectrum Disorder. The Turkish validity and reliability study of the mentioned test was conducted between June 2011 and June 2012 with children aged 18-30 months registered in 14 FHCs in Kayseri. The sensitivity of the M-CHAT test was calculated as 100%, specificity as 76%, positive predictive value as 12%, negative predictive value as 100%, and correct discrimination rate as 77%. The Cronbach's alpha value for the 23-item M-CHAT screening test was found to be 0.69,

interpreting the scale as highly reliable ($0.60 < \alpha < 0.80$). The Cronbach's alpha value for the 6 critical items was 0.67, also indicating high reliability ($0.60 < \alpha < 0.80$).[16]

The importance of ASD screening is better understood when the increasing prevalence of the disorder and the positive outcomes of early diagnosis are considered. Family Health Centers (FHCs), which are often the first first point of contact for infants and children, have a significant role in ASD screening which should not be underestimated. Based on this fact, the present study aimed to determine the prevalence of ASD risk and identify the factors increasing this risk among children aged 18-36 months who were admitted to Family Health Centers (FHCs) in the city center of Aydın.

Materials and Methods

Type of research

The objective of the descriptive and cross-sectional study was to determine the prevalence of ASD risk and the factors influencing the in children aged 18-36 months who were admitted to Family Health Centers in the Efeler district of Aydın.

Research location

The FHCs included in our study were selected through cluster sampling method. Through a 25% representation rate, it was calculated that 8 out of 32 FHCs were going to be included. In order to determine which FHCs to be included, Efeler district was divided into clusters, and one FHC was selected from each, including six urban and two rural districts (FHCs No 1, 3, 4, 9, 14, 24 and Çeştepe and Kuyulu Family Health Centers).

Research population and sampling

The research population covered 5600 children aged 18-36 months who were registered at 32 FHCs in the Efeler district of Aydın. Assuming a prevalence rate of 1% according to DSM-5 data and calculating a sampling error of 0.05, the sampling size was determined as 392 and by adding 10% to this value, it was determined as 431.

Study inclusion criteria

All adults who visited the designated FHCs with children aged 18-36 months for any reason during the study period were included.

Study exclusion criteria

Having any known physical or mental diseases, neurodevelopmental disorders or being followed-up due to any developmental disorder and having hearing loss (data was collected based on declaration).

Children taken to the interview by someone other than their primary caregivers (The answers to the M-CHAT test must be provided by the individual monitoring the child' development).

Incomplete or incorrect completion of the data collection form.

Data collection

Data were collected face-to-face by the researcher after taking written consents of the participants. In the data collection form prepared based on a review of literature and in line with the objective of our study, and included questions on the sociodemographic characteristics, perinatal story, breast-feeding situation, presence of ASD in siblings and additional diseases of the child, alcohol use-smoking, medicine, supporting treatment, infection story of the mother during pregnancy and parental consanguinity. Then, the M-CHAT scale was administered to all participants.

M-CHAT scale consists of 23 questions which are answered by the parents as "yes" or "no". For questions 11, 18, 20 and 22, "Yes" response was considered negative while "No" indicated a negative answer for all the other questions.[17]

Diagnostic strength of questions 5, 10, 17, 19 and 21 in the Turkish version of the test was found to be high – similar to that of questions 2, 7, 9, 14 and 15 in the English original. However, the diagnostic strength of question 13 was found to be lower than the original format. Based on these data, the mentioned questions were designated as "Critical Questions".[17] If the negative response was selected for least two of these questions or at least for three of the 23 questions, the child was considered to be at a high autism spectrum disorder risk and was referred to Child and Adolescent Psychiatry and Neurology Outpatient Clinics for autism evaluation.

Data analysis

Statistical analyses were performed using IBM SPSS Statistics version 21.0 (IBM Corp., Armonk, NY, USA). The distribution of continuous variables was evaluated using the Kolmogorov–Smirnov and Shapiro–Wilk tests, as well as graphical methods including histograms. Although normality tests indicated slight deviations from normal distribution, the sample size was sufficiently large (n=431). According to the Central Limit Theorem, parametric tests are considered robust to moderate deviations from normality in large samples. Therefore, parametric methods were used for the comparisons.

Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as number and percentage (%). Comparisons between categorical variables were performed using the Chi-square test or Fisher's exact test, as appropriate.

To determine independent factors associated with the dependent variable, multivariable regression analysis was performed to control for potential confounding effects. A two-tailed p-value < 0.05 was considered statistically significant.

Permissions

Ethical approval required for the study was obtained from Aydın Adnan Menderes University Faculty of Medicine Non-Interventional Researches Ethics Board (approval no:2019/124, Dated: 29.08.2019). As the study was conducted in Family Health Centers, the required administrative permission was taken from Aydın Provincial Directorate of Health.

Results

Sociodemographic characteristics of the participants

The mean age of the 431 children participating in the study was found to be 27.5±6.5 months. Among the participants, 50.8% (n=219) were female. Some of the sociodemographic characteristics of the children are presented in Table 1.

The ASD risk of the participants was evaluated using the M-CHAT scale. According to the results, 5.8% of the children (n=25) were in the high-risk group for ASD. Children in the risky group were evaluated by a child and adolescent psychiatrist, and four of them (16%) received clinical diagnosis of ASD.

The ASD risk was higher among boys (8.5%) compared to girls (3.2%), and among children from families with low economic status (12.5%) compared to those with high economic status (2.0%) (p=0.019 and p=0.014 respectively). The comparison of ASD risks of participating children based on their prenatal characteristics is presented in Table 2.

ASD risks of children were evaluated based on their prenatal characteristics. Accordingly, children whose mothers used medication during pregnancy (8.5%) had a higher risk for ASD compared to those whose mothers did not use any medication (4.2%) (p=0.047). 43.9% of

Table 1. Sociodemographic characteristics of the children

Sociodemographic Variables		**Mean±SD**	
Age (months)		27.50±6.50	
		n	**%**
Gender	Female	219	50.8
	Male	212	49.2
Mother's Education Level (years)	≤8	160	37.1
	9-12	96	22.3
	≥13	175	40.6
Father's Education Level (years)	≤8	123	28.5
	9-12	127	29.5
	≥13	181	42.0
Place of residence	Rural Area	83	19.3
	Urban Area	348	80.7
Health insurance	No	24	5.6
	Yes	407	94.4
Mother's Employment Status	Unemployed	273	63.3
	Public Sector Employee	95	22.0
	Private Sector Employee	51	11.8
	Self-employed	12	2.8
Father's Employment Status	Unemployed	28	6.5
	Public Sector Employee	126	29.2
	Private Sector Employee	163	37.8
	Self-employed	114	28.5
Economic condition	Low	48	11.1
	Medium	281	65.2
	High	102	23.7
TOTAL		431	100.0

the mothers with reported use of medication during pregnancy (n=72) stated that they used paracetamol, 17.1% (n=28) used phosphomycine and 12.8% (n=21) used levothyroxine. However, there was no statistically significant difference in ASD risk between different medication groups (p>0.05). Comparison of ASD risks of participating children based on their prenatal characteristics is presented in Table 3.

ASD risks in children were evaluated based on their postnatal characteristics. According to the results, the risk of ASD was significantly higher in children born before the 35th week of pregnancy (24.0%) compared to those born at or after the 35th week (4.7%). Likewise, children with a birth weight of less than 2500 grams (15.4%) had a higher risk compared to those weighing 2500 grams or more (4.8%). Additionally, children who were not vaccinated according to the recommended schedule (33.3%) had a significantly higher risk of ASD compared to those who were vaccinated as scheduled (5.4%) ($p = 0.002$, $p = 0.018$, and $p = 0.042$, respectively). Comparison of ASD risks of children based on their postnatal characteristics is presented in Table 4.

Logistic regression analysis

Regression analysis was performed to eliminate the confounding effect and determine the effect size. Variables that were statistically significantly

Table 2. Comparison of ASD risk based on the sociodemographic characteristics ofchildren , n=431

Sociodemographical variants		**Non-risky group**	**Risky group**	**Total**	**p-value**
Age (months), Mean±SD		27.5±6.5	27.5±7.1	27.5±6.5	p>0.05*
		n (%)	n (%)	n (%)	
Gender	Female	212 (96.8)	7 (3.2)	219 (100)	0.019**
	Male	194 (91.5)	18 (8.5)	212 (100)	
Mother's Education Level	≤8 years	149 (93.1)	11 (6.9)	160 (100)	p=0.41**
	9-12 years	89 (92.7)	7 (7.3)	96 (100)	
	≥13 years	168 (96.0)	7 (4.0)	175 (100)	
Father's Education Level	≤8 years	114 (92.7)	9 (7.3)	123 (100)	p=0.34**
	9-12 years	118 (92.9)	9 (7.1)	127 (100)	
	≥13 years	174 (96.1)	7 (3.9)	181 (100)	
Place of residence	Rural Area	78 (94.0)	5 (6.0)	83 (100)	p=0.92**
	Urban Area	328 (94.3)	20 (5.7)	348 (100)	
Health insurance	No	22 (91.7)	2 (8.3)	24 (100)	p=0.58**
	Yes	384 (94.3)	23 (5.7)	407 (100)	
Mother's Employment Status	Not working	255 (93.4)	18 (6.6)	273 (100)	p=0.44**
	Public Sector Employee	92 (96.8)	3 (3.2)	95 (100)	
	Private Sector Employee	47 (92.2)	4 (7.8)	51 (100)	
	Self-employed	12 (100)	0 (0.0)	12 (100)	
Father's Employment Status	Not working	25 (89.3)	3 (10.7)	28 (100)	p=0.50**
	Public Sector Employee	121 (96.0)	5 (4.0)	126 (100)	
	Private Sector Employee	152 (93.3)	11 (6.7)	163 (100)	
	Self-employed	108 (94.7)	6 (5.3)	114 (100)	
Economic Status	Low	42 (87.5)	6 (12.5)	48 (100)	p=0.035**
	Medium	264 (94.0)	17 (6.0)	281 (100)	
	High	100 (98.0)	2 (2.0)	102 (100)	
TOTAL		406 (94.2)	25 (5.8)	431 (100)	

Values are presented as **n (%) unless otherwise indicated**.
SD: Standard deviation.
ASD: Autism spectrum disorder.
*Student's t-test, **Chi square test, ***Fishers exact test

associated with ASD risk in the binary analyses (gender, economic condition, birth week, birth weight, mother's medication use during pregnancy, and vaccination status according to the schedule) as well as variables that were considered to be potentially related to ASD risk based on literature, but showed no relationship in the binary analyses conducted in our study (child's age, mother's pregnancy age, father's pregnancy age, parental consanguinity, and mother's smoking status) were included in the multiple logistic regression analysis. The resulting five-variable model explained 19.9% of the variance (r^2=0.199, p=0.007). Accordingly, ASD risk increased 3.0 times in boys compared to girls, 7.6 times in children from families with low economic status, 5.6 times in children born before the 35th week compared to those born after the 37th week, 2.7 times higher in children whose mothers used medication during pregnancy and 7.7 times higher in children not properly vaccinated compared to those vaccinated according to the schedule (Table 5).

Table 3. Comparison of ASD risks of the children according to their prenatal characteristics, n=431

Prenatal characteristics		Non-risky group n (%)	Risky group n (%)	Total n (%)	p-value
Maternal Age During Pregnancy (years)	<35	370 (93.9)	24 (6.1)	394 (100)	p=0.66**
	35-39	30 (96.8)	1 (3.2)	31 (100)	
	≥40	6 (100.0)	0 (0.0)	6 (100)	
Paternal Age During Pregnancy (years)	<40	384 (94.1)	24 (5.9)	408 (100)	p=0.75**
	≥40	22 (95.7)	1 (4.3)	23 (100)	
Parental Consanguinity	No	384 (94.3)	23 (5.7)	407 (100)	p=0.58**
	Yes	22 (91.7)	2 (8.3)	24 (100)	
Alcohol comsumption status of the mother during pregnancy	No	403 (94.2)	25 (5.8)	428 (100)	p=0.66***
	Yes	3 (100.0)	0 (0.0)	3 (100)	
Smoking status of the mother during pregnancy	No	349 (94.6)	20 (5.4)	369 (100)	p=0.68**
	Pre-pregnancy	31 (91.2)	3 (8.8)	34 (100)	
	Yes	26 (92.9)	2 (7.1)	28 (100)	
Medication usage status of the mother during pregnancy	No	256 (95.9)	11 (4.1)	267 (100)	p=0.047**
	Yes	150 (91.5)	14 (8.5)	164 (100)	
Taking medical assistance for pregnancy	No	388 (94.6)	22 (5.4)	410 (100)	p=0.08***
	Yes	18 (85.7)	3 (14.3)	21 (100)	
Supportive treatment using condition of the mother during pregnancy	No	25 (96.1)	1 (3.9)	26 (100)	p=0.088***
	Yes	381 (94.1)	24 (5.9)	405 (100)	
Infection condition of the mother during pregnancy	No	215 (93.1)	16 (6.9)	231 (100)	p=0.38**
	Yes	191 (95.5)	9 (4.5)	200 (100)	
TOTAL		406 (94.2)	25 (5.8)	431 (100.0)	

Values are presented as **n (%) unless otherwise indicated**.
SD: Standard deviation.
ASD: Autism spectrum disorder.
**Chi square test, ***Fishers exact test

Discussion

25 among the 431 children included in our study were identified to be at risk according to M-CHAT scale and were referred to Child and Adolescent Mental Health and Diseases polyclinics. a. Upon detailed evaluation by Child and Adolescent Mental Health and Diseases specialist 4 out of the 25 children (16%) were diagnosed with ASD.

The results of our study presented an ASD risk of 5.8% and a ASD diagnosis prevalence of 0.92% in the Efeler District of Aydın.

International studies on ASD diagnosis prevalence in the literature reported a range of prevalence at 0.07%-3%.[6,18-23] or instance, in the United States, a study conducted by the Center for Disease Control and Prevention (CDC) on ASD screening showed that the prevalence, which was 1 in 150 in 2002, increased to 1 in 110 in 2006, and 1 in 88 in 2012. 2016 report of the study showed that one in every 68 children had ASD. It is still unknown whether this increase throughout the years represents a real increase or whether it is related to the increasing of awareness of the disease, the clarification of diagnosis criteria and easier access to health services.[19]

In the study conducted by Robins et al. in 2001, the M-CHAT scale was administered to 1293 children aged 18-30 months and 132 of them (10%) were

Table 4. Comparison of ASD risks of the children compared to their postnatal characteristics, n=431

Postnatal characteristics		Non-risky group n (%)	Risky group n (%)	Total n (%)	p-value
Birth week of the child (weeks)	<35	19 (76.0)	6 (24.0)	25 (100)	p=0.002**
	≥35	387 (95.3)	19 (4.7)	406 (100)	
Birth weight of the child (grams)	<2500	33 (84.6)	6 (15.4)	39 (100)	p=0.018***
	≥2500	373 (95.2)	19 (4.8)	392 (100)	
Intensive care unit treatment condition of the child	No	352 (94.9)	19 (5.1)	371 (100)	p=0.13**
	Yes	54 (90.0)	6 (10.0)	60 (100)	
Presence of chronic disease in the child	No	381 (94.3)	23 (5.7)	404 (100)	p=0.71**
	Yes	25 (92.6)	2 (7.4)	27 (100)	
Feeding with nutrients other than breast milk during the first six months	No	279 (94.6)	16 (5.4)	295 (100)	p=0.62**
	Yes	127 (93.4)	9 (6.6)	136 (100)	
Proper vaccination condition of the child	No	4 (66.7)	2 (33.3)	6 (100)	p=0.042***
	Yes	402 (94.6)	23 (5.4)	425 (100)	
TOTAL		406 (94.2)	25 (5.8)	431 (100.0)	

Values are presented as **n (%) unless otherwise indicated**.
SD: Standard deviation.
ASD: Autism spectrum disorder.
**Chi square test, ***Fishers exact test

Table 5. Factors affecting ASD risk in binary and multiple logistic regression analyses, n=431

Dependent variable: high autism spectrum disorder risk						
Independent variables	**Binary logistic regression analysis**			**Multiple logistic regression analysis (enter*)**		
	OR*	**95% CI***	**p**	**OR**	**95% CI**	**p**
Child's Age	-	-	AD	-	-	AD
Male (Ref: Female)	2.810	1.149-6.874	0.024	3.025	1.127-8.118	0.029
Low economical condition (Ref: High economical condition)	7.143	1.385-36.837	0.019	7.624	1.204-48.259	0.031
Birth week <35 Weeks (Ref: >37 weeks)	6.372	2.254-18.009	<0.001	5.552	1.096-28.128	0.038
Birth weight <2500 gr (Ref: >2500 gr)	3.569	1.334-9.533	0.011	-	-	AD
Medicine using condition of the mother during pregnancy (Ref: Mother not using medicine during pregnancy)	-	-	AD	2.689	1.071-6.754	0.035
Proper vaccination (Ref: Improper vaccination)	8.739	1.521-50.221	0.015	7.715	1.044-56.982	0.045
Pregnancy Age of the Mother	-	-	AD	-	-	AD
Father's Age	-	-	AD	-	-	AD
Parental consanguinity	-	-	AD	-	-	AD
Maternal Smoking Condition	-	-	AD	-	-	AD

found to be at risk for ASD. Children found to be at risk at the second stage of the study were re-evaluated through phone and the number of children at risk decreased to 58 as the result of this evaluation. In the further evaluations of these children, 39 (3%) were diagnosed with ASD.[18] The

study conducted by Yama et al, using the M-CHAT scale, showed an ASD risk of 2.8% in children aged between 20 and 32 months.[24]

The validity study of M-CHAT scale was conducted in 2005 in Türkiye.[17] Despite the high false positive rate of the test, the study concluded that it is easy to administer the test, it has a high positive predictive value and can be used as a screening test for ASD.[17,25] The first large-scale study evaluating the ASD in Türkiye was conducted by Türkiye Autism Early Diagnosis and Education Foundation (TOHUM). After removing the missing data from the analysis, 41290 children were included in the evaluation. 4605 of the children included in the analysis (11.2%) were found to be at risk for ASD.[26] In national studies conducted through similar methods, the prevalence of ASD was reported to be between 0.1% and 11.2%.[16,27,28] The ASD risk found as 5.8% in our study was similar to other studies in our country and the world.

The 0.92% diagnosis prevalence found in our study was consistent with the studies in our country, but was close to the lower end of the spectrum when compared to the data of recent studies from other countries.[6,19-23,29] This condition may be due to the appliance of M-CHAT scale to a wider age range in literature, although it is especially suited for children under three years of age.[13,18,25,27] On the other hand, there are also studies showing that usage of M-CHAT scale alone may not be sufficient to diagnose ASD. As we used only M-CHAT in our study, it is an expected condition that the ASD prevalence is lower than what is reported in international studies.[27,30]

The average age of the four children diagnosed with ASD in our study was 33 months. The average diagnosis age of children with ASD was reported as 40 months in literature.[14] The lower average age of children diagnosed in our study compared to the literature can be explained by the fact that the children in our sample were between 18 and 36 months of age.

49.2% of the participants in our study were male. 8.5% of the boys and 3.2% of the girls were in the ASD risky group and this difference between genders was statistically significant. Three out of four children diagnosed with ASD were male and being male increased the ASD risk three times based on the advanced analysis conducted. ASD risk in males was reported to be 2-6 times higher in literature, which was consistent with our study.[10,19]

No statistically significant difference was detected in terms of ASD risk based on parental education conditions, place of residence, employment status or presence of health insurance. This condition is in line with the literature.[16,28,31,32] Similarly, no statistically significant relationship was found between consanguineous marriage and ASD risk. Although the literature suggests that consanguineous marriage does not constitute a direct risk for ASD, it may lead to the transfer of defective DNA.[33]

When the effect of income level on ASD risk was evaluated in our study, it was observed more in families with a low-income compared to those with a high-income and this risk was detected to be six times higher in those with low-income. Similarly, studies in literature show a significantly higher ASD risk in countries and families with low income.[34-36]

A statistically significant relationship was not detected between maternal smoking and ASD risk in our study but there are some studies reporting such a relationship in literature.[37,38] Although no statistically significant relationship was found between maternal smoking and ASD in our study, some studies reporting such as relationship in literature may be caused by the lower maternal smoking rate in our sample compared to the general population.

No relationship was found between maternal alcohol use and ASD risk in our study as supported also by data provided in literature.[39,40]

All participants reporting the use of medication during pregnancy stated a usage of medication known to be safe during pregnancy (eg. paracetamol, phosphomycine and PPI) and a statistically significant relationship was found between this medication usage and ASD risk. Similarly, literature suggests an increasing risk of ASD in case of maternal medication use during pregnancy.[41,42] Therefore, the relationship between maternal drug use and the risk of ASD is not clear and may depend on underlying diseases or similar contributing factors.

Since almost all mothers of the children participating in the study used supplements during pregnancy, this situation was not found to have a statistically significant effect on the risk of ASD. However, literature provides evidence that maternal supplementation with folic acid, iron and vitamin D support pregnancy reduces the risk of ASD.[43-45]

Contrary to the claims blaming vaccines for Autism Spectrum Risk, many studies in the literature have provided evidence that vaccination does not constitute risk for ASD.[46,47] However, our study showed that children who were not vaccinated according to the vaccination schedule had a statistically significantly higher risk of ASD. Further analyses showed that the risk of ASD was 7.7 times higher in unvaccinated children compared to the vaccinated ones. No previous study evaluated the relationship between being unvaccinated and ASD risk.

Some studies have shown an increasing ASD risk in conditions such as low birth weight, preterm birth before 37 weeks and neonatal treatment in intensive care unit.[33,48] Our study presented a statistically significant difference between low birth weight, delivery week of the child and ASD risk. However, advanced analyses showed the significance of this relationship only with birth weight variable and detected a 5.6 times increase in ASD risk in case of birth before 35th week. This condition is consistent with the literature.

A meta-analysis identified "advanced maternal and paternal age" as risk factors for ASD.[49] Our study detected no statistically significant relationship between the age of parents at the beginning of pregnancy and ASD risk. There are studies both supporting and contradicting our finding in literature.[32,50] The mentioned differences in literature may be related to the average ages of the parents across the samples.

Strengths and limitations

This is the first study investigating ASD risk in Aydın City center using M-CHAT scale. strength is that the research was conducted in a primary healthcare unit which is generally the first point of contact for healthy infant and child follow-ups and reflects a realistic reflection of disease prevalence. Also, the sampling of the study was selected to represent both the rural and urban populations in Aydın City Center. The M-CHAT test was applied face-to-face by the researcher in our study.

Cross-sectional nature of the study is one of the limitation. The fact that our study was conducted on minimum calculated sampling size due to the time constraints while investigating ASD with a low prevalence is an aspect of our study which should be strengthened. Also the use of M-CHAT scale alone can also be considered as a limitation of our study.

Ethical approval

This study has been approved by the Aydın Adnan Menderes University Faculty of Medicine Non Interventional Researches Ethics Board (approval no:2019/124, Dated: 29.08.2019).

Author contribution

The authors declare contribution to the paper as follows: Study conception and design: SAŞ, AG; data collection: MD, SAŞ; analysis and interpretation of results: MD, SAŞ, AG; draft manuscript preparation: MD, SAŞ, AG. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest to disclose.

Generative AI Statement

No generative artificial intelligence (AI) tools were used in the preparation of this manuscript.

Data Availability Statement

The datasets generated and analyzed during the current study are not publicly available due to privacy and ethical restrictions but are available from the corresponding author on reasonable request.

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