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Journal homepage: <https://tropicalhealthandmedicalresearch.com>**Another Reason for Vaccine Hesitancy in Turkey in Siblings of Children with Autism Spectrum Disorders*****Semra Bayturan^{1,a}, Nesrin Şen Celasin^{2,a}**

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ABSTRACT: Despite studies showing no link between the measles-mumps-rubella vaccine and autism spectrum disorder (ASD), the belief that the vaccine causes autism can still affect parents' attitudes towards vaccines. This study aimed to investigate the vaccination status, vaccine information source, and the factors related to vaccine hesitancy diagnosed with ASD and their younger siblings based on interviews and questionnaires. A questionnaire was performed on 37 ASD groups (parents of children with ASD and their younger siblings) and 65 control groups (families with healthy children and healthy younger siblings). The research was conducted between 1st January 2019 and 31st December 2019. Incomplete vaccination was found higher in both children with ASD (n=37) and their younger siblings compared to the healthy control group (n=65) (p=0.045; p=0.016). The four children (10.8%) diagnosed with ASD had five siblings with incomplete or missing vaccinations. Families with children with ASD stated that their knowledge of vaccines was sufficient compared to the control group (p=0.021). All parents stated the autism vaccination relationship as the reason for incomplete vaccination. Parents of children with ASD may delay or reject vaccination for their children and their younger siblings.

Keywords: Autism spectrum disorder; vaccination; measles-mumps-rubella vaccine; younger siblings.

INTRODUCTION

The World Health Organization reported vaccine hesitation as one of the top ten threats to global health. No confidence in vaccine safety and concerns about adverse events cause vaccination refusal¹. Vaccine-preventable diseases, complications, and deaths can be prevented by maintaining confidence in vaccination². Healthcare professionals are critical in vaccine decisions, especially in primary care³.

One of the reasons for vaccination hesitation is misinformation established between autism spectrum disorders (ASD) and vaccination in the last two decades⁴⁻⁶. Autism spectrum disorder is a neurodevelopmental and genetic disorder that occurs similarly to the measles mumps rubella vaccine (MMR). No relationship with MMR was found in children or their young siblings diagnosed with ASD⁴. However, recent studies have reported that MMR vaccination was lower in siblings of children with ASD⁴⁻⁷. Low rates of MMR vaccination are associated with measles outbreaks. Therefore, studies examining the factors affecting vaccinating children with ASD and their siblings are essential².

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There are few studies to clarify the factors that can contribute to vaccine hesitation in the families of children with ASD. However, studies about the vaccination of children diagnosed with ASD and their siblings are based on patient records. Studies on this subject are rare in our country. This study aimed to investigate the vaccination status, vaccine information source, and the factors related to vaccine hesitancy diagnosed with ASD and their younger siblings based on interviews and questionnaires.

MATERIALS AND METHODS

Study Population

This prospective case-control study included parents who have autistic children with younger siblings admitted to Manisa Celal Bayar University outpatient clinic between 1st January 2019 and 31st December 2019. Our hospital is a tertiary-level care clinic.

Two groups were included in the study: ASD and the control group. The research sample consisted of 37 parents of children with ASD and 65 parents of healthy children with healthy siblings. The parents had accepted to participate in the research and completed written informed consent forms. The ASD group included parents (mother, father, or mother and father) with children diagnosed with ASD and younger siblings than the sick child. All children with ASD were diagnosed and followed up according to the Diagnostic and Statistical Manual of Mental Disorders V (DSM V) criteria in our Child Psychiatry Clinic⁸.

Parents of healthy children with healthy siblings were included in the control group. Control children had no known relatives with an ASD diagnosis. Parents of children who did not consent and had genetic, neurological, or neurodevelopmental disorders were excluded from the study. The control group and ASD group were matched according to the families' age, education level, health insurance, and income-expenditure status.

We used a standard questionnaire to evaluate vaccination status in children. We used a sociodemographic data form to assess descriptive features of the families (age of parents, education, working status, income and expense status, health insurance, and several siblings). All parents were asked about vaccination information (Have they sufficient information (yes/no/not sure) about the vaccines? What are the sources of information about the vaccines? In which health institutions are informed about vaccines? Where are the children vaccinated?).

Data were collected using a parents identification form, which the authors developed. All participants were questioned in detail about the vaccination status (participants were asked if they had the vaccination schedule or optional vaccines in our country?) of the children and their siblings. Data were collected regarding immunization up to the age of 15 years for all the children. Vaccinations of children and their siblings were noted according to the patient's declaration and medical records. Incomplete vaccinations of the children and their siblings were recorded. In the case of incomplete vaccination, we asked the reasons. In families with multiple children born after a child was diagnosed with ASD, we included data from the first younger sibling in our study.

Vaccination Schedule in Our Country

According to the immunization program updated in 2019 in our country, all children are vaccinated free of charge at nonprofit family health care centers from birth. Childhood vaccines are applied in family primary health care centers, public hospitals, private clinics, and private hospitals in Turkey. This program includes the following

vaccines: Hepatitis B (0, 1, 6 months), Bacille Calmette-Guerin (BCG) (2 months), DaBT- IPA-Hib: Diphtheria, acellular Pertussis, Tetanus, Inactive Polio, Hemophilus Influenza Type B (DaBT-IPA-Hib) (2nd, 4th and 6th month; booster at 18th month), Conjugate Pneumococcal Vaccine (CPV) (2 and 4th month, booster at 12th-month), Measles-Mumps-Rubella Vaccine (MMR) (12th month and six years old), Diphtheria, acellular Pertussis, Tetanus, Inactive Polio (DaBT-IPA) (6 years old booster), Oral Polio Vaccine (OPV) (6th and 18th month), Adult-type Diphtheria -Tetanus Vaccine (Td) (10 years old), Hepatitis A (18th and 24th month) and chickenpox (VZV) (12th month). Some vaccines are not included in the extended immunization program. Optional vaccines licensed in our country are HPV, rotavirus, meningococcus (A, C, Y, W-135, B), and Influenza vaccine.

Approval was received from the local ethics committee of the one university (Reference date and number: 22.05.2019 / 20.478.486-050.04.04). The analysis of the data obtained from the research was performed using the Statistical Package for Social Science (SPSS) 15.0 program. The descriptive data distribution containing the parents' demographic characteristics was given in numbers and percentages. The χ^2 test or Fisher's exact tests were performed for categorical variables, and the Mann-Whitney U test was used for nonparametric variables. P values <0.05 were considered statistically significant.

RESULTS AND DISCUSSION

Demographic Analysis

The study group included 37 parents of children with ASD and their younger siblings, and 65 control group families participated. There was no statistically significant difference between the ASD and the control group of mothers and fathers regarding age, education, and health security. Also, the mean age of the children with ASD and the control group was $6,71 \pm 4,06$ years and $8,59 \pm 4,94$ years, respectively (p 0.155). Children with ASD diagnoses were at most the family's first child (n= 27, 72.97%). All of the children with ASD lived in the city center. The ASD group had a median of 1 (min-max: 1-4) sibling after the autistic child. In the ASD group, 89.18% of children were diagnosed above two. A median of 1 (min-max: 1-4) sibling was reported after the diagnosis of ASD. The sociodemographic characteristics of the groups are shown in Table 1.

Vaccination Status

Vaccinations in both groups were done at most in primary health care centers (83.8%). Incomplete vaccination was statistically significantly higher in children and their young siblings diagnosed with ASD (p 0.045; p 0.016). All three patients (8.1%) with ASD were found to have incomplete vaccinations (DaBT-IPA-Hib, OPV, Hepatitis A, DaBT-IPA, and second dose of MMR(n=1); DaBT-IPA and second dose of MMR (n=1); the second dose of MMR (n=1)). Of the four children (10.8%) diagnosed with ASD, three of the five siblings had incomplete vaccinations (no vaccines after MMR and after), and two were never vaccinated (Table 2, Table 3).

The ASD diagnosis was made above two years of age in 2 of 3 children with ASD and incomplete vaccinations. In three of 5 incomplete vaccinated siblings, ASD was diagnosed in their older siblings over two years of age. The ratio of optional vaccinations in the ASD group was 21.6% (n=8), and in the control group, 12.3% (n=8). All parents of incomplete or not vaccinated children stated a causal relationship between vaccines and ASD.

Table 1. Sociodemographic Characteristics of The Parents in Autism Spectrum Disorder and Control Group

	Autism spectrum disorder group (n=37)	Control group (n=65)	p
Mothers Age (years) mean \pm SD	36,40 \pm 5,15	36,12 \pm 6,46	0,986
Fathers Age (years) mean \pm SD	40,56 \pm 6,20	39,63 \pm 6,51	0,391
Total sibling number median (min-max)	2 (2-6)	2(1-7)	0,019
Working/Non-working mother (n)	33/4	50/15	0,126
Working/Non-working father (n)	36/1	63/2	0,917
Maternal educational level (n)			
Primary school	14	34	0,166
Middle school	4	10	
High school/University	19	21	
Paternal educational level (n)			
Primary school	12	27	0,519
Middle school	3	7	
High school/University	22	31	
Income and expense status (n)	27/10	56/9	0,100
Adequate/Inadequate			
Health insurance yes/no	35/2	57/8	0,321
Consanguineous marriage (n)	8	6	0,080

P values <0.05 were considered statistically significant—Mann-Whitney U, χ^2 , and Fisher's exact test.

Table 2. Characteristics and Vaccination Status of The Autism Spectrum Disorder Group and Control Group

	Autism disorder group (n=37)	Control group (n=65)	p
First Siblings Age mean \pm SD (years)	6,71 \pm 4,06	8,59 \pm 4,94	0,155
Gender (Female/Male)	21/16	34/31	0,723
Incomplete vaccination of the autism spectrum disorder patient (n)	3	0	0,045
Incomplete vaccination of siblings (n)	4*	0	0,016
Vaccine information statement (sufficient / inadequate) (n)	19/18	47/18	0,021

*There are incomplete vaccinations in five siblings of four children; three have incomplete vaccination (MMR, DaBT-IPA-Hib, OPV, Hepatitis A, Td, DaBT-IPA); two siblings have not been vaccinated with any vaccine.

P values <0.05 were considered statistically significant.

Vaccine Information

Sixty-seven (65.68%) of the participants stated that they are sufficient vaccine information, and 35 (34.31%) of the participants were not sufficient. The sufficiency of vaccine information in the control group was significantly higher than in the ASD group (48 vs. 19, $p = 0.022$). Families with adequate information were informed by family physicians and nurses than those without ($(n=35$ vs. $11)$ $p = 0.046$; $(n=46$ vs. $15)$ $p = 0.012$) (Table 4). The nurses did not inform any of the participants in the incomplete vaccinated group. In children with incomplete vaccination, four of the five mothers and all of the fathers were all High School/University graduates.

Table 3. Demographics of Not Vaccinated Siblings in The Autism Spectrum Disorder Group

No	Age (years)	Gender (F/M)	Vaccination Status	Sibling Number after The Autistic Child
1	6	F	Incomplete	1
2	2	M	Not vaccinated	1
3	7	M	Incomplete	1
4	3	M	Not vaccinated	2
5	3	F	Incomplete	1

Numbers 3 and 4 are siblings.

Table 4. Source of Vaccine Information in Autism Spectrum Disorder and Control Group

Source of Vaccine Information	Autism Spectrum Disorder Group	Control Group	p
Doctor	13	33	0,127
Nurse	15	46	0,003
Psychology	2	1	0,297
Books	0	0	-
Internet	3	5	0,940
Family with an autistic child	2	0	0,129

P values <0.05 were statistically significant— χ^2 and Fisher's exact tests.

Despite studies showing no link between the MMR vaccine and ASD, the belief that the vaccine causes ASD can affect parents' attitudes towards vaccines. Few studies clarify the factors that can contribute to vaccine hesitation in the families of children with ASD⁴⁻⁶. Our study showed that vaccination of children with ASD and their younger siblings was impaired. All parents with incomplete vaccinated children believed that the vaccine causes ASD. Most vaccines were administered in primary health care centers, and most parents of vaccinated children received vaccine-related information from nurses (Table 4). To the best of our knowledge, this is the first report on the vaccine-related information sources of autistic children and their younger siblings based on interviews of parents in Turkey.

According to an annual report by the Turkish Health Ministry, the MMR vaccination rate was 96% in 2017. We would expect our country's children with ASD to be unaffected due to the higher vaccination rates. However, ASD and their younger siblings were found to have decreased vaccination rates than healthy participants, consistent with our results^{7,9-10}.

In the internet survey of Rosenberg et al.¹¹, which 486 parents attended, 18.9% of ASD patients received no vaccination, and 26.4% had delayed or partial uptake. Also, Bazzano et al.¹² showed that half of the parents discontinued or changed the vaccination practices of their autistic children. Belief in the vaccine-autism linkage was the primary factor associated with delaying or neglecting one or more vaccines¹². Zerbo et al.⁷ stated that siblings of ASD patients were less vaccinated due to the belief of higher ASD risk in younger children. In comparison, parents vaccinated their other children were less likely to believe that vaccines caused ASD, more likely to change their vaccine practices, and less likely to discontinue vaccines. A child diagnosed with ASD at less than 36 months and a female child were also associated with changing or discontinuing vaccine schedules. Insurance type and parental education were not associated with changing or discontinuing vaccination¹².

Similarly, ASD participants and their younger siblings had incomplete vaccination (Table 2) due to the vaccination-autism linkage belief in our study. Our rates of incomplete vaccination were higher than that of the literature⁷. All these results emphasize the importance of parent's beliefs in vaccination. In particular, parents of children with ASD might be more likely to change vaccination practices than other families. Given the high prevalence of ASD, understanding the concerns and vaccination practices of parents of children with ASD is necessary to address those concerns and maintain immunization coverage¹².

Increased mothers' education level was reported to be related to a decreased rate of vaccination of younger siblings¹¹. The parents of the unvaccinated children and siblings in our study were High school/University graduates. Most of our participants visited primary health care centers for vaccination. This result points to the need for an intellectual, professional information approach, especially for families with higher education levels in primary health care. Primary health care providers and public health professionals may consider family graduation school perspectives when educating and counseling families about vaccines¹¹. Communication problems and disinformation of patients may be the reason for incomplete vaccination decisions of parents with autistic children. Multidisciplinary teams and further studies in the information process of these patients may be necessary¹³.

The ASD diagnosis was made above two years of age in 2 of 3 children with incomplete vaccinations. In three of 5 missing vaccinated young siblings, ASD was diagnosed in their older siblings over two years of age. Our findings were consistent with previous studies and showed that diagnosis delays might affect families' vaccination behavior. Parents who perceived a more significant delay in diagnosis tended to have less confidence in their physician¹⁴.

Healthcare professionals, the Internet, and relatives were reported to be the three primary sources of vaccine information. The vaccination and acceptance of parents informed by healthcare professionals were higher than parents who received information from the Internet or their relatives¹⁵. In our study, vaccination rates were higher in children diagnosed with ASD and their siblings among children informed by health professionals, especially nurses (Table 4).

Optional vaccines are also higher in the ASD group, suggesting that families are open to information. Health care providers positively influence parents to vaccinate their children, including parents who believe vaccinations are unsafe¹⁶. For all vaccines, the attitude of the physician, nurses, and other health care professionals is mentioned as being very influential in the decision to vaccinate a child, mainly when parents express concerns about vaccine safety or have misconceptions about the benefits and risks of vaccinations^{16,17} almost all nurses working in primary care

experience vaccine hesitancy. Nurses are reported to consider the childhood vaccines recommended by the CDC as necessary for public health¹⁸. Nurses are often in the unique position of providing advice regarding vaccines in their formal practice areas and daily lives. Many consider nurses to be experts in all areas of health care, leading neighbors, patients, and others to ask for and value their opinions. Nurses participate in this crucial aspect of preventing diseases and, therefore, should have a thorough and complete understanding of the issues, concerns, and facts related to vaccines¹⁹. The scores of the nurses regarding the MMR vaccine were higher than the medical assistants²⁰. Developing guidelines and training studies for healthcare providers on vaccinating children and siblings with ASD may reduce vaccine hesitancy²¹.

The limitation in this study are some of the patients invited to the study stated that they did not want to be included in a vaccine study because of the causal relationship between the MMR vaccine and ASD. Our rates could be detected higher. Families without ASD and siblings could not be included in the study, but they also expressed vaccine insecurity. The number of participants was also limited in terms of this study.

CONCLUSION

Parents who already have one child with autism spectrum disorder may delay or decline immunization for their children and younger siblings due to the belief of the vaccination-ASD linkage, potentially placing them at increased risk of preventable infectious diseases. Nurses and family physicians informed fully vaccinated children. Primary health care providers have an essential role in informing parents about vaccines and preventing vaccine hesitancy.

CONFLICT OF INTEREST

The author has declared no conflict of interest.

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