

# Risk Factors of Autism Spectrum Disorders in Children

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## ABSTRACT

**Objective:** To find out demographical, medical, familial and parental risk factors of ASD in children.

**Study Design:** Case-control study.

**Place and Duration of the Study:** The department of Pediatric Neurology, The Children's Hospital & Institute of Child Health, Multan, Pakistan from November 2019 to April 2020.

**Methodology:** A total of 120 children (60 cases and 60 controls) of both genders aged up to 12 years were enrolled. Diagnosis of ASD was made as per DSM-IV-TR criteria. Demographical and medical characteristics along with familial and parental data were noted. Chi-square test was employed considering  $p < 0.05$  as significant to compare study variables between cases and controls.

**Results:** In a total of 120 children, 72 (60.0%) children were male. Overall, mean age was noted to be  $4.82 \pm 3.5$  years while 77 (64.2%) children were  $\leq 5$  years of age. In comparison to controls, lack of breastfeeding up till 2 years of age ( $p = 0.0009$ ), asthma ( $p = 0.0367$ ), hearing impairment ( $p = 0.0408$ ) and allergy to milk or wheat ( $p = 0.0475$ ) were found to be significant risk factors among children with ASD while remaining all other characteristics were not found to have any significant relationship ( $p > 0.05$ ) with ASD. It was observed that maternal education status as illiterate ( $p = 0.0267$ ) and immediate family history of ASD ( $p = 0.0475$ ) were significantly associated risk factors for ASD among cases while all remaining factors were not found to have any significant association ( $p > 0.05$ ).

**Conclusion:** Lack of breastfeeding up till 2 years of age, presence of asthma, hearing impairment and allergy to milk or wheat were found to be significant risk factors among children with ASD. Maternal education status as illiterate and immediate family history of ASD were also noted to be significantly associated risk factors for ASD.

**Keywords:** autism spectrum disorders, breastfeeding, asthma, hearing impairment, maternal education.

## INTRODUCTION

According to "Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-5)," autism spectrum disorders (ASD) are "neurodevelopmental disorders described by deficits in social communication and social interaction and the presence of restricted, repetitive behaviors".<sup>1</sup> Key attributes of ASD are described as behavioral disturbances, social abnormalities and repetitive patterns of behaviors.<sup>2</sup> ASD is considered to be complex and lifelong developmental issue generally appearing in the first few years of life but in most of the cases, diagnosis of ASD is made in the later years during mild or moderate to severe forms of ASD. Epidemiological data indicated estimated incidence of ASD to vary between 8.5-20 cases per 1,000 children.<sup>3</sup>

Children living with ASD face difficulties living life independently while parents of ASD children feel that their children cannot live on their own without any kinds of support. Studies have shown that  $< 10\%$  of ASD cases can perform basic daily routine activities like shopping, cooking, washing clothes or managing money without any additional support.<sup>4</sup> As ASD has its own influence on the social life of both the affected individual and the linked family, ASD puts increased burden on the societies as well.<sup>5</sup> Timely identification of ASD is very important for the timely interventions that can lead to major improvement in the intellectual as well as social behaviors of the children affected. Delayed diagnosis of ASD presents difficulties in the general management and introduction of interventions as late diagnosis of ASD means that brain is already more developed in the later years of life.<sup>6</sup>

Genetic risk factors seem to be the most common contributor to ASDs but it has been revealed that it's not a single gene that is involved in ASD.<sup>7</sup> Risk factors of ASD have not yet been labeled clearly. Some prenatal as well as perinatal issues are also taken as contributing factors to the development of ASD. The present study was planned to find out demographical, medical, familial and parental risk factors of ASD in children.

## METHODOLOGY

This case-control study was conducted at the department of Pediatric Neurology, The Children's Hospital & Institute of Child Health, Multan, Pakistan from November 2019 to April 2020.

Approval from "Institutional Ethical Committee" was acquired. Informed and written consents were sought from parents of all study participants.

For cases, 60 children of both genders aged up to 12 years with diagnosis of ASD were enrolled. Diagnosis of ASD was made by the institutional clinical psychologists adopting "autism diagnostic interview (ADI)". Furthermore, the diagnosis was confirmed by the treating physician as per DSM-IV-TR criteria. Same number of mentally healthy children ( $n = 60$ ) up to 12 years of age visiting institution's outpatients department of pediatric medicine due to acute gastrointestinal issues were enrolled as controls. Exclusion criteria for the study subjects was children having congenital heart disease, systemic illnesses, renal disease or those whose parents were not willing to participate. All children who were not accompanied by at least 1 of the parents (either mother or father) were also not included in this study.

After inclusion of children in the study, characteristics of children like age and gender were noted along with medical history including age up till breastfeeding was continued, mode of delivery, gestational age, any comorbid conditions like asthma, epilepsy, hearing impairment or allergy to milk/wheat. Family history of language or speech disorders were also noted. Place of residence (rural or urban) along with socio-economic status of family and mother's and father's education status were documented. A special proforma was designed to record all study data.

For data analysis, SPSS version 26.0 was employed. Quantitative data were shown as mean and standard deviation (SD) whereas frequencies and percentages were calculated for qualitative variables. Chi-square test was employed considering  $p < 0.05$  as significant to compare study variables between cases and controls.

## RESULTS

In a total of 120 children, 72 (60.0%) children were male. Overall, mean age was noted to be  $4.82 \pm 3.5$  years while 77 (64.2%) children were  $\leq 5$  years of age. Area of residence was rural in 66 (55.0%) children. Socio-economic status was low in 54 (45.0%) children. Breastfeeding up till 2 years of age was continued in 56 (46.7%) children.

Table-1 is showing comparison of demographical and medical characteristics of children in both study groups. In comparison to controls, lack of breastfeeding up till 2 years of age (p=0.0009), asthma (p=0.0367), hearing impairment (p=0.0408)

and allergy to milk or wheat (p=0.0475) were found to be significant risk factors among children with ASD while remaining all other characteristics were not found to have any significant relationship (p>0.05) with ASD.

Table-1: Comparison of Demographical and Medical Characteristics of Children among Cases and Controls

Characteristics		Cases (n=60)	Controls (n=60)	P-Value
Gender	Male	38 (63.3%)	34 (56.7%)	0.4561
	Female	22 (36.7%)	26 (43.3%)	
Age in Years	≤5	41 (68.3%)	36 (60.0%)	0.3412
	6-12	19 (31.7%)	24 (40.0%)	
Residence	Urban	25 (41.7%)	29 (48.3%)	0.4630
	Rural	35 (58.3%)	31 (51.7%)	
Socio-economic Status	Low	28 (46.7%)	26 (43.3%)	0.0656
	Medium	18 (30.0%)	28 (46.7%)	
	High	14 (23.3%)	6 (10.0%)	
Breast Feeding up till 2 years of age		19 (31.7%)	37 (61.7%)	0.0009
Asthma		10 (16.7%)	4 (38.3%)	0.0367
Epilepsy		5 (8.3%)	1 (1.7%)	0.0938
Hearing impairment		13 (21.7%)	5 (8.3%)	0.0408
Allergy to Wheat or Milk		8 (13.3%)	2 (3.3%)	0.0475
Mode of Delivery Cesarean Section		28 (46.7%)	23 (38.3%)	0.3558
Preterm Birth		10 (16.7%)	9 (15.0%)	0.8025

Table-2 is showing comparison of familial and parental risk factors between cases and controls. It was observed that maternal education status as illiterate (p=0.0267) and immediate family history of ASD (p=0.0475) were significantly associated risk factors for ASD among cases while all remaining factors were not found to have any significant association (p>0.05).

Table-2: Comparison of Family and Parental Risk Factors between Cases and Controls

Characteristics		Cases (n=60)	Controls (n=60)	P-Value
Maternal Age	≤30	31 (51.7%)	26 (43.3%)	0.3607
	>30	29 (48.3%)	34 (56.7%)	
Mother's Education	Illiterate	18 (30.0%)	8 (13.3%)	0.0267
	Literate	42 (70.0%)	52 (86.7%)	
Father's Educational Status	Illiterate	11 (18.3%)	13 (21.7%)	0.6481
	Literate	49 (81.7%)	47 (78.3%)	
Number of Siblings	≤2	38 (63.3%)	31 (51.7%)	0.1961
	>2	22 (36.7%)	29 (48.3%)	
Immediate Family History of Autism Spectrum Disorder		8 (13.3%)	2 (3.3%)	0.0475

## DISCUSSION

ASD is a complex disorder affecting the individuals and their families as well. Early identification and intervention has been known to improve the outcomes of the affected children with ASD all over the world. Recent decades have seen rising interest in identifying risk factors associated with ASD so the present research was conducted to what little is known about the demographical, medical, familial and parental risk factors of ASD.<sup>8,9</sup>

We found that lack of breastfeeding up till 2 years of age (p=0.0009) was a significantly associated risk factor with ASD as only 31.7% cases of ASD were continued breastfeeding up till 2 years of age versus 61.7% controls. Our findings are well aligned with what was found by Yousef AM et al from Egypt where only 25% children with ASD received breastfeeding versus 59.5% controls (p=0.02).<sup>10</sup> Another regional study highlighted that late initiation of breastfeeding was significantly linked with raised risk of ASD.<sup>11</sup> A systemic review also pointed out towards lack of breastfeeding to be associated with the development of ASD while breastfeeding up till 2 years of age was observed to reduce the risk of ASD in that same systemic review.<sup>12</sup>

In this study, asthma, hearing impairment and allergy to milk/wheat were significantly more existent among children with ASD. Malek A et al from Iran noted asthma, epilepsy, microcephaly, hearing or vision impairments, allergy to wheat or milk and rubella vaccination side-effect to be significantly associated risk factors among children with ASD. Some other researchers have also shown cesarean delivery and premature birth to be linked with ASD but these were not found to have any significant association with ASD in this study.<sup>14,15</sup>

Our findings revealed that maternal education status as illiterate (p=0.0267) and immediate family history of ASD

(p=0.0475) had significantly associated risk factors with ASD. Sub-optimal educational status of parents of ASD children can be a reason of inappropriate care of affected individuals. Researches in the past have shown cultural and geographical variations to be responsible for parental education status to be a known risk factor for ASD.<sup>13,16</sup> Contrary to the findings of this study, Elwardany S et al showed that 62% mothers children with ASD had university level education.<sup>17</sup>

Our study had some limitations as well. Being a single center study, our findings cannot be generalized. We were unable to assess nutritional and feeding parameters of the children. Further studies incorporating large sets of ASD children involving multiple study sites can certainly add to what is known about the risk factors of ASD in our population.

## CONCLUSION

Lack of breastfeeding up till 2 years of age, presence of asthma, hearing impairment and allergy to milk or wheat were found to be significant risk factors among children with ASD. Maternal education status as illiterate and immediate family history of ASD were also noted to be significantly associated risk factors for ASD.

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