



# Association of Risk Factors with At-Risk Cases of Autism

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## Abstract

A neurological condition known as autism spectrum disorder (ASD) first manifests before the age of 3. Numerous factors may have an impact on the development of autism; however, its precise causes are yet unknown. The research aims to identify certain risk factors that associate with children at a higher risk of developing autism. This study is a descriptive analysis of 80 children who were identified as being at risk for autism and meeting the requirements of the Modified Checklist for Autism in Toddlers at the community health center. A semistructured proforma was used to collect the baseline data from the mother and the child. Through the use of a thoughtfully created checklist, each child enrolled in the study had a thorough history completed, including the suspected prenatal, intranatal, neonatal, and infant risk factors with the help of their mothers. Descriptive statistics with frequency percentages were adopted for the demographic data of the participants. To find the association between possible risk factors and at-risk cases of ASD, an independent *t*-test was used. Fisher's exact test and Pearson's chi-squared test ( $p = 0.05$ , confidence interval = 95%) were used to find how the risks (odds ratios) of the factors studied affect the incidence of ASD. It was discovered that prenatal risk factors, such as pregnancy-related infections and medication use, were statistically significantly linked to an increased risk for autism. Significant intranatal risk factors for autism risk included a breech presentation, cesarean section, forced labor, and resuscitation at birth. Similar to this, the neonatal risk factors included maternal hemorrhage, Rh or ABO incompatibility, birth injuries, and feeding problems. Poor socioeconomic status and seizures were the baby risk variables, both of which were statistically significant and linked to an increased chance of autism. The results of the study support an array of perinatal, intranatal, neonatal, and infant risk factors linked to the likelihood of developing autism.

## Keywords

- ▶ autism
- ▶ perinatal
- ▶ intranatal
- ▶ neonatal
- ▶ infant
- ▶ risk factors

## Introduction

Autism spectrum disorder (ASD) is a neurobehavioral condition that is characterized by abnormal and fixed interests, repetitive behavior, and enduring deficits in social and communication interaction, as well as deficits in developing, understanding, and maintaining relationships, according to

the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. ASD is one of the most prevalent chronic childhood illnesses, having a significant negative impact on the individuals affected, their families, and society. An estimated 1 to 2% of the world's population is thought to be impacted by ASDs, which have become more prevalent

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globally. According to the Centers for Disease Control and Prevention, 1 in 59 children are said to have an ASD on average.<sup>1</sup>

The prevalence of autism has risen during the past few decades. About 26 million children are thought to be born in India each year, yet 10 million (or 42%) of those are not registered.<sup>2</sup> One in 150 to one in 500 children in India is estimated to have ASD, one of the most prevalent neurodevelopmental disorders.<sup>3</sup> Over the past few years, the prevalence of autism has increased in an alarming way.<sup>4</sup> According to studies conducted in Asian nations, India is thought to have between 1.7 and 2 million ASD sufferers.<sup>5</sup> Given these high estimates, it is imperative to investigate the potential risk factors for ASD in the Indian community.

At their 18- and 24-month well-child visits, the American Academy of Pediatrics advises that all children be tested for ASD. According to research, many autistic children's outcomes can be improved by starting an intervention program as soon as feasible.<sup>6</sup> The traditional belief that autism was uncommon is no longer supported as a problem because it is becoming an increasingly significant issue in developing nations like India. Due to the severity of the effects on the affected people and their families, the financial burden it imposes, the lack of scientific knowledge about the condition, and other factors, it presents a far more serious and significant challenge.

Regression in development (loss of previously acquired skills) happens around the time of diagnosis in 25% of affected children and may be the first sign of a disorder.

ASD often appears in infancy and toddlerhood and causes difficulties for the individual, the family, and the community. It has no known cause in particular. Regardless of race or nationality, the issue affects all children. Many causes could be involved. Certain factors, however, increase a child's risk. Finding ASD risk factors to identify children who are at risk should be encouraged because doing so can help them have a much better outlook for receiving early behavioral and diagnostic intervention for ASD. Although genetic variables are associated with ASD, epidemiological data suggest that maternal and neonatal influences may also have significant effects.

The risk factors for ASD have been the subject of several studies across the globe, yet the findings are inconclusive. Understanding the effects of prenatal, intranatal, perinatal, and neonatal risk factors for ASD is crucial. This study sought to investigate the relationship between prenatal, intranatal, neonatal, and infant risk factors and children at risk for ASD. It comprised children aged between 1 and 3 years who were at risk for developing autism. This will enable us to identify children who are at high risk, offer early intervention, and prevent autism through quality prenatal, perinatal, and postnatal care.

## Materials and Methods

### Screening with MCHAT-R

The descriptive study was conducted in the child development outpatient departments of a community health center.

All toddlers attending the outpatient department either for the consultation or the well-baby clinic accompanied by their mothers were screened for ASD using a Modified Checklist for Autism in Toddlers-Revised (MCHAT-R). The MCHAT-R is a 20-item checklist that was used to determine which children were at risk for ASD. M-CHAT screening for ASD has the benefit of quickly finding young children who are at high risk. The mothers either completed the questionnaire themselves or had it completed by the researchers on their behalf. Its total scores range between 0 and 20. The risk cases were categorized according to the child's score to mild risk (0–3), moderate risk (4–7), and high risk ( $\geq 8$ ).<sup>7</sup>

Out of 850 children screened, 80 were at risk of autism and were included in the actual study along with their mothers as the participants. The sample size was computed based on the prevalence of at-risk cases and the previous literature. A purposive sampling technique was adopted using inclusion criteria such as children of both sexes aged from 1.5 to 3 years, at-risk for autism according to MCHAT-R criteria, and who had a live biological mother. Parents who declined to participate in the study, neurologic syndromes linked to autistic behavior, other pervasive developmental problems, children with visual and auditory impairments, and suffering from chronic illnesses were among the exclusion criteria.

### Assessment of Risk Factors

The researcher interacted with the mothers face-to-face, thoroughly explained the study, secured their informed consent, and then began data collection. Anonymity and confidentiality of the data were ensured. Approval of the institutional ethics committee has been obtained. The consent to publish the research study has been received from all the participants.

The questionnaire concerned demographic information about the parents, the mothers in particular, and their children, as well as prenatal, intranatal, neonatal, and infant risk factors that may be related to autism. These risk factors were selected based on the predisposing factors proposed in earlier studies.<sup>8–11</sup> *p*-Values less than 0.05 were regarded as statistically significant.

## Results

R 4.2.1 2022 was used to analyze the data. To simultaneously examine the combined effects of several factors, the odds ratios and 95% confidence intervals were computed at  $\alpha = 5\%$ . The frequency of occurrence of risk factors determines the style of analysis used. Unadjusted analyses were first conducted on all pertinent risk factors to ascertain which risk factors were significantly associated with autism. It was done using descriptive statistics like frequency and percentage. To find the association of possible risk factors with the at-risk cases of ASD, an independent *t*-test was used. Levine's test for equality of variances was computed. To determine the association between the risk factors and the risk cases for autism, bivariate analysis was used. Fisher's exact test, and Pearson's chi-squared test ( $p = 0.05$ , confidence interval = 95%) to find how the risks (odds ratios) of the factors studied affect the

**Table 1** Demographic characteristics of mothers and children,  $n = 80$ 

	Frequency	Percentage
<b>Age in years</b>		
20–24	30	37.5
25–29	28	35
30–34	10	12.5
> 35	12	15
<b>Religion</b>		
Hindu	35	43.8
Christian	20	25
Muslim	25	31.2
<b>Area of domicile</b>		
Rural	53	66.2
Semi-Urban	27	33.8
<b>Educational status</b>		
PUC	9	11.2
High school	9	11.2
Middle school	21	26.3
Primary	30	37.5
No formal education	11	13.8
<b>Occupation</b>		
Skilled worker	5	6.2
Semi-skilled worker	22	27.5
Unemployed	53	66.3
<b>Monthly family income</b>		
Rs.50,000–Rs.74,000	3	3.8
Rs.30,000–Rs.49,000	15	18.7
< Rs.30,000	62	77.5
<b>Parity</b>		
One	39	48.8
Two	37	46.2
Three and above	4	5
<b>Consanguinity</b>		
Yes	34	42.5
No	46	57.5
<b>Age of the child in years</b>		
1–2	55	68.8
2–3	25	31.2
<b>Sex of the child</b>		
Male	55	68.8
Female	25	31.2
<b>Birth order of the child</b>		
One	41	51.2
Two	24	30

**Table 1** (Continued)

	Frequency	Percentage
Three	15	18.8
<b>Gestational age at birth</b>		
Preterm	11	13.8
Full term	69	86.2
<b>APGAR score</b>		
7–10	22	27.5
4–6	55	68.7
0–3	3	3.8
<b>History of major childhood illness</b>		
Yes	31	38.8
No	49	49
<b>History of hospitalization</b>		
Yes	33	41.2
No	47	58.8

incidence of ASD. The most significant risk factors associated with the occurrence of ASD were identified using logistic regression analysis.

### Description of the Characteristics of the Mother and Children

The mean age of the mothers was 27.2 years. About 12.5% of them were over 35 years old. The majority (43.8%) were Hindus, and most (66.2%) lived in rural areas. As far as the education level of the mothers is concerned, 37.5% of them had a primary level of education. The majority (66.3%) of the mothers were unemployed. The monthly family income of most (77.5%) of the mothers was less than Rs. 30,000. The parity of the mothers showed that almost half (48.8%) of the mothers were primiparous, and 42.5% had a history of consanguinity. The mean age of the children was 2.023 years, whereas the majority (68.8%) of them were between 1 and 2 years old, and no of males (68.8%) were significantly more than females. The birth order of 51.2% of the children was first, and most of them (86.2%) were full-term. The APGAR score at the birth of the majority (68.8%) of the children was between 4 and 6. About 38.8% of them had major childhood illnesses like lower respiratory tract disorders, anemia, and worm infestations. About 33% of them had a history of previous hospitalization with minor ailments (► **Table 1**).

### The Level of Autism Risk in Children as per the MCHAT-R Score

It was found that 65% of the children had a high risk for autism, with a score ranging from 8 to 20, while 35% of them had a moderate risk, with an MCHAT score of 4 to 7.

### Association of Possible Risk Factors with At-Risk Cases of Autism

The risk factors were classified as prenatal, intranatal, neonatal, and infant.

**Table 2** Prenatal factors possibly associated with at-risk cases of autism,  $n = 80$ 

Risk factor	Frequency	Range	Mean $\pm$ SD	Median IQR	p-Value
<b>Mothers age &gt;35 years</b>					
Yes	12	6,10	8.92 $\pm$ 1.24	9 (7–11)	0.56
No	68	3,14	8.62 $\pm$ 2.97	9 (9–10)	
<b>Fathers age &gt;35 years</b>					
Yes	14	6,14	9.07 $\pm$ 1.98	9 (9–10)	0.55
No	66	3,13	8.58 $\pm$ 2.93	9 (7–11)	
<b>Gestational diabetes mellitus</b>					
Yes	42	5,14	8.52 $\pm$ 1.52	9 (7–9)	0.65
No	38	3,13	8.82 $\pm$ 3.73	11 (4.25–12.5)	
<b>Obese mother</b>					
Yes	37	4,11	9.11 $\pm$ 1.7	9 (9–11)	0.17
No	43	3,14	8.28 $\pm$ 3.42	7 (5.5–11.5)	
<b>Infections during pregnancy</b>					
Yes	33	4,13	10 $\pm$ 2.57	11 (7–13)	<0.001 <sup>a</sup>
No	47	3,14	7.72 $\pm$ 2.54	9 (5.5–9)	
<b>Birth spacing &lt;12 months and &gt; 60 months</b>					
Yes	11	4,9	8.55 $\pm$ 1.51	9 (9–9)	0.82
No	69	3,14	8.68 $\pm$ 2.94	9 (7–11)	
<b>Medication use</b>					
Yes	19	4,14	7.53 $\pm$ 2	9 (5–9)	0.044 <sup>a</sup>
No	61	3,13	9.02 $\pm$ 2.74	9 (7–11)	
<b>History of threatened abortion</b>					
Yes	37	4,13	10.08 $\pm$ 2.42	11 (9–11)	<0.001 <sup>a</sup>
No	43	3,14	7.44 $\pm$ 2.49	7 (6–9)	
<b>History of prematurity</b>					
Yes	10	3,13	9.2 $\pm$ 2.49	9.5 (9–10)	0.52
No	70	4,14	8.59 $\pm$ 2.83	9 (7–11)	
<b>History of consanguinity</b>					
Yes	34	4,13	8.82 $\pm$ 1.59	9 (9–9)	0.63
No	46	3,14	8.54 $\pm$ 3.42	7 (6–11)	

Abbreviations: IQR, interquartile range; SD, standard deviation.

<sup>a</sup>Significant at 0.05 level.

**Prenatal risk factors:** The mean autism risk score for mothers above the age of 35 at the time of childbirth was 8.92  $\pm$  1.24, whereas, for fathers of that age, it was 9.07  $\pm$  1.98. The obtained  $p$ -Value was not significant at the 0.05 level of significance and inferred that the high parental age in the present study at the time of childbirth does not influence the risk of autism among children. Similarly, factors such as infection during pregnancy (10  $\pm$  2.57) and medication use (7.53  $\pm$  2) were found to be statistically significantly associated with an increased risk for autism. Though the frequency of gestational diabetes mellitus (42) was also found to be more in autism-risk cases, it was not statistically significant. Similarly, the mean

scores for gestational diabetes mellitus (8.52  $\pm$  1.52), obesity in mothers (9.11  $\pm$  1.7), birth spacing less than 12 months and more than 60 months (8.55  $\pm$  1.51), history of prematurity (9.2  $\pm$  2.49), and consanguinity (8.82  $\pm$  1.59) showed insignificant results (**► Table 2**).

**Intranatal and neonatal risk factors:** The mean scores for breech presentation (7.51  $\pm$  1.57), cesarean section (6  $\pm$  3.95), induced labor (10.5  $\pm$  2), and resuscitation at birth were highly significant irrespective of their frequencies being less. The results also showed an insignificant relationship between fetal distress (9  $\pm$  2.55) and low birth weight less than 1.5 kg (9  $\pm$  2). The neonatal risk factors such as maternal hemorrhage (10.29  $\pm$  2.34), Rh or

**Table 3** Intranatal and neonatal factors possibly associated with at-risk cases of autism,  $n = 80$ 

Variables	Frequency	Range	Mean $\pm$ SD	Mean IQR	p-Value
<b>Breech presentation</b>					
Yes	20	3,9	7.5 $\pm$ 1.57	7(7-9)	0 <sup>a</sup>
No	60	4,14	9.05 $\pm$ 2.99	9(6.75-11)	
<b>Caesarean section</b>					
Yes	6	4,14	6 $\pm$ 3.95	4.5(4-5)	0.01 <sup>a</sup>
No	74	3,13	8.88 $\pm$ 2.58	9(7-11)	
<b>Fetal distress</b>					
Yes	28	4,14	9 $\pm$ 2.55	9(9-11)	0.43
No	52	3,13	8.48 $\pm$ 2.9	9(7-10)	
<b>Induced labor</b>					
Yes	34	4,13	10.5 $\pm$ 2	11(9-12.5)	<0.001 <sup>a</sup>
No	46	3,14	7.3 $\pm$ 2.48	7(5.25-9)	
<b>Low birth weight &lt;1.5Kg</b>					
Yes	13	6,13	9 $\pm$ 2	9(9-10)	0.64
No	67	3,14	8.6 $\pm$ 2.91	9(7-11)	
<b>Resuscitation at birth</b>					
Yes	28	7,13	10.5 $\pm$ 1.9	9.5(9-13)	<0.001 <sup>a</sup>
No	52	3,14	7.67 $\pm$ 2.65	7(5.75-9)	
<b>Small for gestational age</b>					
Yes	23	5,13	8.74 $\pm$ 1.74	9(9-9.5)	0.85
No	57	3,14	8.63 $\pm$ 3.11	9(7-11)	
<b>Hyperbilirubinemia</b>					
Yes	23	5,14	8.91 $\pm$ 2.07	9(9-9.5)	0.61
No	57	3,13	8.56 $\pm$ 3.03	9(7-11)	
<b>Maternal hemorrhage</b>					
Yes	34	4,13	10.29 $\pm$ 2.34	-5.209	<0.001 <sup>a</sup>
No	46	3,14	7.46 $\pm$ 2.46	7(6-9)	
<b>Rh/ABO incompatibility</b>					
Yes	2	4,5	4.5 $\pm$ 0.71	4.5(4.25-4.75)	0.03 <sup>a</sup>
No	78	3,14	8.77 $\pm$ 2.73	9(7-11)	
<b>Birth injury</b>					
Yes	2	4,4	4 $\pm$ 0	4(4-4)	<0.001 <sup>a</sup>
No	78	3,14	8.78 $\pm$ 2.71	9(7-11)	
<b>Feeding difficulty</b>					
Yes	34	5,13	9.76 $\pm$ 2.51	9(9-13)	0 <sup>a</sup>
No	46	3,14	7.85 $\pm$ 2.71	9(6.25-9)	

Abbreviations: IQR, interquartile range; SD, standard deviation.

<sup>a</sup>Significant at 0.05 level.

ABO incompatibility (4.5  $\pm$  0.71), birth injury (4  $\pm$  0), and feeding difficulties (9.76  $\pm$  2.51) were statistically highly significant, though the frequencies are relatively less. The small for gestational age (8.74  $\pm$  1.74) and hyperbilirubinemia (8.91  $\pm$  2.07) were found to be insignificant (**► Table 3**).

**Infant risk factors:** The factors of poor socioeconomic status (9.22  $\pm$  2.31) and seizures (10.31  $\pm$  2.19) were statistically significant at the 0.05 level. Though the frequency of the infants was not exclusively breastfed with the mean MCHAT score being 5.67  $\pm$  1.15, this factor was not statistically significant (**► Table 4**).

**Table 4** Infant factors possibly associated with at-risk cases of autism,  $n = 80$ 

Risk factors	Frequency	Range	Mean $\pm$ SD	Mean IQR	$p$ -Value
<b>Exclusive breastfeeding</b>					
Yes	3	5,7	5.67 $\pm$ 1.15	5(5–6)	0.06
No	77	3,14	8.78 $\pm$ 2.76	9(7–11)	
<b>Poor socioeconomic status</b>					
Yes	69	4,13	9.22 $\pm$ 2.31	9(7–11)	<0.001 <sup>a</sup>
No	11	3,14	5.18 $\pm$ 3.03	4(4–5)	
<b>Seizures</b>					
Yes	29	5,13	10.31 $\pm$ 2.19	9(9–13)	<0.001 <sup>a</sup>
No	51	3,14	7.73 $\pm$ 2.65	7(6–9)	

Abbreviations: IQR, interquartile range; SD, standard deviation.

<sup>a</sup>Significant at 0.05 level.

### Relationship between the Risk Factors and the Risk of Autism (MCHAT Score Categories)

The odds ratios for the association between parents' age and high risk for autism are 3.10 and 2.24. However, these were not significant as the  $p$ -value was more than 0.05. The odds ratio for high risk for autism with obesity is 7.36, which indicates that the odds ratio for high risk for autism is almost 7 times greater for children of obese mothers than children of non-obese mothers. This is significant since the  $p$ -value is 0.001. Similarly, the odds ratio of birth spacing less than 12 months and more than 60 months is 6.43, which indicates that the odds ratio of high risk for autism is approximately six times higher than that of children with normal birth spacing but is statistically insignificant. The odds ratio of high risk for autism is almost 10 times higher for children of mothers with a history of threatened abortion compared with those without a history of threatened abortion, and this is significant as the  $p$ -value is 0.001. Also, the odds ratio of high risk for autism is six times higher for children born with an abnormal presentation compared with those born with a normal presentation, as the  $p$ -value is 0.001. The odds ratio of high risk for autism is 46 times higher for children with induced labor, and this is significant as the  $p$ -value is 0.001. The odds ratio of high risk for autism is 12 times higher for maternal hemorrhage during the postnatal period compared with that of children's normal mothers, and this is significant with a  $p$ -value of 0.001. The odds ratio of high risk for autism is 29 times higher among the children who required resuscitation than that of children who did not, where the statistically significant result shows 0.001. The odds ratio of high risk for autism is 28 times higher in children with poor socioeconomic status compared with those with affluent status, and this is statistically significant as the  $p$ -value is 0.001 ( $\rightarrow$  Table 5).

### Discussion

In this study, 66.3% of the children were males. Similarities were identified in the other studies where male children

were more compared with female children at risk of developing ASD.<sup>12,13</sup> The monthly family income was found to be more than Rs.30, 000/- This is in line with the Indian study that most families of autistic children were from the middle class.<sup>14</sup>

The first birth order in the family is occupied by over half of the children. The results of a study investigation showed that most of the children rank third or higher among their brothers and sisters.<sup>15</sup> Similar results were found in the study that among siblings of four or more, an autistic child was more likely to be born in the fourth and higher birth ranks than in the first to third ranks.<sup>16</sup>

About 42.5% of the parents of the children at risk for autism had a history of consanguinity, but the studies found that consanguinity is significantly more common in autistic children and raises the risk for autism as it increases the possibility of increasingly inherited genetic risk factors for autism.<sup>15,17</sup> Also, it was discovered that consanguineous parents' offspring typically has worse cognitive and social skills, both of which are significant factors in autism.

It was found that 65% of the children had a high risk for autism, while 35% of them had a moderate risk on the MCHAT. These findings are contradictory to a study that reported that 0.28% of children were classified as moderate risk and only 9.42% were high risk for ASD on the MCHAT score. The mean age of screened children was 24 months. Similar findings are reported in the other study.<sup>12</sup>

The mothers' ages during pregnancy were not substantially linked to cases of autism that were at risk. This study's findings are consistent with another study that also did not significantly correlate with the prevalence of ASD.<sup>18</sup> However, a pregnant woman's age of 18 is considered to be a high-risk gestational age. This result also deviates from the study, which claimed that children screened positively for ASD had advanced paternal age at the time of birthing.<sup>12</sup> A correlation between rising parental age and the likelihood of their children developing autism was also noted.<sup>19,20</sup> The other authors who examined the relationship between parental age and ASD discovered that an advanced maternal age of

**Table 5** Relationship between the risk factors and the risk of autism (MCHAT score categories),  $n = 80$ 

Characteristics	Moderate risk, $n = 28^a$	High risk, $n = 52^a$	Odds ratio <sup>b</sup>	95% CI	$p$ -Value
<b>Mothers age &gt;35</b>					
Yes	2 (17%)	10 (83%)	3.10	15.25	0.199
No	26 (38%)	42 (62%)		0.63	
<b>Fathers age &gt;35</b>					
Yes	3(21%)	11(79%)	2.24	8.80	0.357
No	25(38%)	41(62%)		0.57	
<b>Obese mother</b>					
Yes	5(14%)	32(86%)	7.36	22.49	0.000
No	23(53%)	20(47%)		2.41	
<b>Birth spacing &lt;12 months and &gt;60 months</b>					
Yes	1 (9.1%)	10 (91%)	6.43	53.12	0.086
No	27 (39%)	42 (61%)		0.78	
<b>History of threatened abortion</b>					
Yes	4(11%)	33(89%)	10.42	34.58	0.000
No	24(56%)	19(44%)		3.14	
<b>Abnormal presentation</b>					
Yes	10(20%)	41 (80%)	6.71	2.42	0.000
No	18 (62%)	11 (38%)		18.61	
<b>Induced labor</b>					
Yes	1(2.9%)	33(97%)	46.89	373.20	0.000
No	27 (2.9%)	19 (41%)		5.89	
<b>Maternal hemorrhage</b>					
Yes	3(8.8%)	31 (91%)	12.30	46.03	0.000
No	25(54%)	21(46%)		3.29	
<b>NICU stay &gt;12 hour</b>					
Yes	4 (11%)	32 (89%)	9.60	31.77	0.000
No	24 (55%)	20 (45%)		2.90	
<b>Resuscitation at birth</b>					
Yes	1(3.6%)	27(96%)	29.16	230.80	0.000
No	27(52%)	25(48%)		3.68	
<b>Poor socioeconomic status</b>					
Yes	18 (26%)	51 74%)	28.33	237.16	0.000
No	10 (91%)	1 99.1%		3.38	
<b>Seizures</b>					
Yes	2 (6.9%)	27(39%)	14.04	65.34	0.000
No	26 (51%)	25 (49%)		3.02	

Abbreviations: CI, confidence interval; MCHAT, Modified Checklist for Autism in Toddlers; NICU, neonatal intensive care unit.

<sup>a</sup> $n$  (%).

<sup>b</sup>Fisher's exact test for count data; Pearson's chi-squared test.

30 years and above was significantly related to ASD.<sup>17</sup> It has been observed that advanced parental age, particularly paternal age, is one of the most important risk factors for autism.<sup>21</sup>

According to the study's findings, the likelihood of ASD and the history of threatened abortion, pregnancy-related infections, and drug usage were significantly correlated. The

contradicting findings of a study led to the conclusion that prenatal hemorrhage is not a risk factor for ASD in children.<sup>22</sup> Additionally, it was revealed that maternal hemorrhage during pregnancy is linked to an 81% increased incidence of autism. Autism risk in the fetus can be elevated by 46% in mothers who take prenatal medications.<sup>23,24</sup>

This study's results showed no significant relationship between pregnancy intervals and the incidence of ASD. The result of this study is in line with the research which stated that there was no significant relationship between pregnancy interval and ASD events.<sup>25</sup> The interval between pregnancies that are too close can endanger the baby.

Low birth weight and preterm birth are two new-born characteristics that are thought to be indicators of an unfavorable perinatal environment.<sup>26</sup> Low birth weight has been linked to psychological illnesses like attention-deficit hyperactivity disorder and anxiety symptoms, among others.<sup>22</sup> However, the findings of this study did not reveal any significant relationship between low birth weight and the risk for ASD.

The history of prematurity was significantly related to the incidence of ASD. The results of another study also showed that insufficient months of birth had a risk of experiencing ASD. Prematurity can cause neurodevelopmental issues like behavioral abnormalities, difficulty learning and understanding language, attention or concentration problems, hyperactive disorders, inhibition in cognitive development, communication difficulties, and difficulties interacting with others.<sup>27</sup>

ASD risk factors included a breech presentation, cesarean section, induced labor, and resuscitation at delivery remained significant predictors of ASD at-risk cases after controlling for confounding variables. According to certain studies, many of these risk factors have been linked to a higher likelihood of having ASD, either individually or in combination.<sup>28,29</sup>

The study findings revealed a significant relationship between poor socioeconomic status and the risk for ASD. Autistic children and their families are primarily in a poor state when it comes to the economic, social, educational, and psychological aspects of family life. Basically, these families invariably experience unhealthy, inappropriate sociality, and unrehabilitated life conditions because of financial difficulties, occupational demands, and psychological stresses.<sup>30</sup>

Despite the use of a structured questionnaire, mothers' recollection bias was still a possibility.

Future national screenings and outreach programs can benefit from the study's findings. The study highlighted the potential for early detection of children at risk who can avail the interventions.

## Conclusion

The results of the research confirmed the relationships between ASD and numerous antenatal, intranatal, neonatal, and infant factors. Many of the findings agree with earlier accounts. Even though this research provides thorough information about the Indian population, it is constrained by issues like its reliance on maternal memory for data collection. The prenatal, perinatal, and neonatal environments do, however, appear to play a significant role in the neurodevelopment and etiology of ASD, according to many of our findings, which are consistent with other reports. Since there is no long-term treatment for ASD, early detection

helps prevent its related pathologic behaviors from getting worse and becoming a child's normative behavior. Early interventions that are evidence-based create a proactive learning foundation to support the highest quality of life that is possible.

### Ethical Approval

The study has been approved by Institutional Review Board.

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### Conflict of Interest

None declared.

## References

- 1 American Psychiatric Association. Diagnostic and Manual of Mental Statistical Disorders,. Fifth Edition (DSM-5). Washington, DC: American Psychiatric Publishing; 2013:9–50
- 2 UNICEF India – Child protection – Why is birth registration important? 2006 [Internet]. [cited 2023 Jan 3]. [http://www.unicef.org/india/child\\_protection\\_1650.htm](http://www.unicef.org/india/child_protection_1650.htm)
- 3 Usha N, Gautam S, Avasti A, Malhotra S. Practice parameters of Childhood Autism. In: Child and Adolescent Psychiatry, Clinical Practice Guidelines for Psychiatrists in India. Indian Psychiatric Society: Haryana, India; 2008:210–2372
- 4 Karimi P, Kamali E, Mousavi SM, Karahmadi M. Environmental factors influencing the risk of autism. *J Res Med Sci* 2017;22:27
- 5 Krishnamurthy V. A clinical experience of autism in India. *J Dev Behav Pediatr* 2008;29(04):331–333
- 6 Turner K. Well-child visits for infants and young children. *Am Fam Physician* 2018;98(06):347–353
- 7 Robins D, Fein D, Barton M. Modified Checklist for Autism in Toddlers, Revised with Follow-Up (M-CHAT-R/F) TM. 2009:1–25. <http://www.mchatscreen.com>
- 8 Uno Y, Uchiyama T, Kurosawa M, Aleksic B, Ozaki N. The combined measles, mumps, and rubella vaccines and the total number of vaccines are not associated with development of autism spectrum disorder: the first case-control study in Asia. *Vaccine* 2012;30(28):4292–4298
- 9 Atladóttir HO, Henriksen TB, Schendel DE, Parner ET. Autism after infection, febrile episodes, and antibiotic use during pregnancy: an exploratory study. *Pediatrics* 2012;130(06):e1447–e1454
- 10 Surén P, Bakken IJ, Aase H, et al. Autism spectrum disorder, ADHD, epilepsy, and cerebral palsy in Norwegian children. *Pediatrics* 2012;130(01):e152–e158
- 11 Newschaffer CJ, Croen LA, Fallin MD, et al. Infant siblings and the investigation of autism risk factors. *J Neurodev Disord* 2012;4(01):7
- 12 Ravi S, Chandrasekaran V, Kattimani S, Subramanian M. Maternal and birth risk factors for children screening positive for autism spectrum disorders on M-CHAT-R. *Asian J Psychiatr* 2016;22(08):17–21
- 13 Nath S, Roy R, Mukherjee S. Perinatal complications associated with autism—a case control study in a neurodevelopment and early intervention clinic. *J Indian Med Assoc* 2012;110(08):526–529
- 14 Juneja M, Mukherjee SB, Sharma S. A descriptive hospital based study of children with autism. *Indian Pediatr* 2005;42(05):453–458
- 15 Styles M, Alsharshani D, Samara M, et al. Risk factors, diagnosis, prognosis and treatment of autism. *Front Biosci (Landmark Ed)* 2020;25(09):1682–1717



- 16 Tsai LY, Beisler JM. The development of sex differences in infantile autism. *Br J Psychiatry* 1983;142(04):373–378
- 17 Mamidala MP, Polinedi A, P T v PK, et al. Prenatal, perinatal and neonatal risk factors of autism spectrum disorder: a comprehensive epidemiological assessment from India. *Res Dev Disabil* 2013;34(09):3004–3013
- 18 Hultman CM, Sandin S, Levine SZ, Lichtenstein P, Reichenberg A. Advancing paternal age and risk of autism: new evidence from a population-based study and a meta-analysis of epidemiological studies. *Mol Psychiatry* 2011;16(12):1203–1212
- 19 Budi LPR, Sitaresmi MN, Windiyani IGAT. Paternal and maternal age at pregnancy and autism spectrum disorders in offspring. *Paediatrica Indonesiana* 2015;55(05):345–351
- 20 Parner ET, Baron-Cohen S, Lauritsen MB, et al. Parental age and autism spectrum disorders. *Ann Epidemiol* 2012;22(03):143–150
- 21 Zahra RNF. Faktor Risiko terjadinya Autism Spectrum Disorder [Bachelor Scription]. Surabaya: Universitas Airlangga; 2014
- 22 Coo H, Ouellette-Kuntz H, Lam YM, Brownell M, Flavin MP, Roos LL. The association between the interpregnancy interval and autism spectrum disorder in a Canadian cohort. *Can J Public Health* 2015;106(02):e36–e42
- 23 Hernawan AD, Diningrum A, Jati SN, Nasip M. Risk factors of autism spectrum disorder (ASD). *Unnes J Public Health* 2018;7(02):104–112
- 24 Berliana SM. Factors influencing preterm birth in Indonesia: Riskesdas data analysis 2013. *E-Journal Widya Health and Environment* 2016;1(02):109–115
- 25 Goldin R. Premature Birth as a Factor in Autism Spectrum Disorder [Master Thesis]. Baton Rouge Louisiana: The Department of Psychology – Louisiana State University; 2015
- 26 Gardener H, Spiegelman D, Buka SL. Prenatal risk factors for autism: comprehensive meta-analysis. *Br J Psychiatry* 2009;195(01):7–14
- 27 Krakowiak P, Walker CK, Bremer AA, et al. Maternal metabolic conditions and risk for autism and other neurodevelopmental disorders. *Pediatrics* 2012;129(05):e1121–e1128
- 28 Kaur J, Kaur K. Conditions behind fetal distress. *Ann Biologic Res* 2012;3(10):4845–4851
- 29 Maimburg RD, Vaeth M. Perinatal risk factors and infantile autism. *Acta Psychiatr Scand* 2006;114(04):257–264
- 30 Zhang X, Lv CC, Tian J, et al. Prenatal and perinatal risk factors for autism in China. *J Autism Dev Disord* 2010;40(11):1311–1321