Original Article

Perinatal Risk Factors among Iraqi Children with Autism Spectrum Disorder: A Case–Control Study

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Abstract

Background: Autism spectrum disorder (ASD) is a neurodevelopmental condition characterized by deficits in social communication and restricted, repetitive behaviors. Increasing evidence suggests that prenatal, perinatal, and postnatal factors contribute to ASD risk, with variations across populations. **Objectives:** To assess the prevalence of prenatal, perinatal, and postnatal risk factors among Iraqi children with ASD and to evaluate their association with ASD occurrence. **Materials and Methods:** Case–control study was conducted between April and June 2024 in Kerbala, Iraq. Children diagnosed with ASD according to DSM-5 criteria were enrolled as cases, while children without neurodevelopmental disorders served as controls. Data were collected through structured face-to-face interviews with mothers. **Results:** Eighty-two children with ASD and 164 controls were included. ASD was more frequent among males and children living in urban areas. Maternal emotional distress during pregnancy was associated with increased odds of ASD. Maternal anemia, infections, and medication use during pregnancy were associated with lower odds of ASD. Neonatal respiratory distress and neonatal feeding difficulties were significantly associated with ASD. Maternal age at conception was an independent predictor of ASD, whereas paternal age was not. **Conclusion:** Several prenatal and postnatal factors were associated with ASD in Iraqi children. Maternal stress during pregnancy, neonatal respiratory distress, and feeding difficulties increased ASD risk, while maternal age was the strongest parental predictor. These findings emphasize the importance of maternal health and early neonatal care.

Keyword: Autism spectrum disorder, Perinatal risk factors, Maternal age, Neonatal complications, Iraq.

Introduction

Autism spectrum disorder (ASD) is defined by the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), as a neuro-developmental disorder characterized by persistent deficits in social communication and interaction, along with restricted and repetitive patterns of behavior [l]. Globally, ASD affects approximately 1–2% of children, with recent estimates reporting a cumulative prevalence of around 1.5% [2,3]. ASD contributes substantially to lifelong disability, accounting for 58 disability-adjusted life years per 100,000 populations worldwide [4]. Epidemiological data on ASD in Iraq remain limited. Available estimates from the Kurdistan region suggest a prevalence of approximately 89.4 per 10,000 children [5]. The etiology of ASD is multi-factorial, involving genetic susceptibility and environmental influences. Twin and family studies have demonstrated strong genetic contributions, with concordance rates reaching 88% in monozygotic twins compared with 31% in dizygotic twins [6,7]. However, incomplete concordance among monozygotic twins indicates the role of non-genetic factors [8]. Environm-ental influences, particularly prenatal, perinatal, and postnatal factors, have been extensively

investigated. Structural and functional brain abnormalities observed in ASD have prompted interest in the intrauterine and early neonatal environment [9]. Several systematic reviews and meta-analyses have identified associations between ASD and maternal conditions, obstetric complications, and neonatal outcomes [l0,11]. Importantly, the strength and presence of these associations may vary across populations and ethnic groups [l2,13]. In the Arab region, studies from Egypt, Saudi Arabia, and the United Arab Emirates have explored local risk profiles for ASD [l4-16]. In Iraq, few studies have examined perinatal risk factors, and many potential contributors identified in international literature have not been comprehensively assessed [17,18]. Therefore, this study aimed to determine the prevalence of prenatal, perinatal, and postnatal risk factors among Iraqi children with ASD and to assess their association with ASD occurrence.

Materials and Methods

Study design and participants

A case–control study was conducted between 1 April and 1 June 2024. Children with ASD were recruited from private tertiary centers for autism treatment (Al-Subtain Academy for Autism and Al-Hussein Center for Autism). Any child diagnosed with ASD (according to DSM-5 criteria) are eligible for inclusion in the study as a convenient sample. Children with other neurodevelopmental disorders, such as cerebral palsy were excluded. Controls were children without neurodevelopmental disorders attending a private clinic or outpatient clinic of Al-Imam Al-Sadiq general Hospital.

Data collection

Data were collected using a structured questionnaire consisting of four sections: demographic characteristics, prenatal factors, perinatal factors, and postnatal factors. The questionnaire was developed based on previous systematic reviews and pretested among mothers prior to data collection where a pilot study was conducted on 20 patient (10 cases + 10 controls) and these participants were excluded from the final study sample. The questionnaire was administered by the researcher and through face-to-face interviews conducted exclusively with mothers to ensure accuracy of antenatal and perinatal data.

Statistical analysis

Statistical analysis was performed using SPSS version 28. Categorical variables were summarized using frequencies and percentages, while continuous variables were expressed as median and interquartile range. Group comparisons were conducted using Chi-square or Fisher's exact tests for categorical variables and the Mann–Whitney U test for continuous variables. Odds ratios with 95% confidence intervals were calculated. Stepwise logistic regression analysis was performed to assess the independent effects of maternal and paternal age. A p-value <0.05 was considered statistically significant.

Ethical approval

Institutional approval was obtained from Al-Imam Al-Sadiq Hospital/ Ministry of Health and Environment, Iraq. Verbal consent was obtained from all participating mothers.

Results:

Sample characteristics

Eighty two participant were included in the current study: 72 (87.8%) from Al-Subtain Academy for Autism and 10 (12.2%) from Al-Hussein Center for Autism due to the difference the total capacity of the two centers. 164 Controls were also included: 140 (85.4%) from the private clinic and 24 (14.6%) from Al-Imam Al-Sadiq Hospital.

As shown in Table 1, statistically significant differences were detected in the age groups between children in the patients and control groups (p-value = 0.026). Additionally, children with ASD were more likely to be male (86.6% vs. 50.6%, p-value <0.001) and from urban environments (73.2% vs. 53.7%, p-value = 0.003).

Table 1: Sociodemographic and clinical characteristics of the study participants.

Characteristics	Patient N = 82 (%)	Control N = 164 (%)	P-value [a]
Age (Year)			
<3	7 (8.5)	16 (9.8)	**0.026[b]**
3 – 4.9	21 (25.6)	50 (30.5)	
5 – 7.9	21 (25.6)	54 (32.9)	
≥8	33 (40.3)	44 (26.8)	
Gender			
Male	71 (86.6)	83 (50.6)	**<0.001**
Female	11 (13.4)	81 (49.4)	
Birth order			
1st	28 (34.2)	77 (47.0)	0.052
2nd	23 (28.0)	48 (29.3)	
3rd or more	31 (37.8)	39 (23.7)	
Vaccination status			
Complete	69 (84.1)	146 (89.0)	0.238
Partial	13 (15.9)	16 (9.8)	
None	0 (0.0)	2 (1.2)	
Residence			
Urban	60 (73.2)	88 (53.7)	**0.003**
Rural	22 (26.8)	76 (46.3)	
Maternal education			
No formal education	6 (7.3)	18 (11.0)	0.376
Primary school	14 (17.1)	29 (17.7)	
Secondary school	23 (28.0)	31 (18.9)	
Bachelor or above	39 (47.6)	86 (52.4)	
Maternal employment			
Yes	38 (46.3)	87 (53.0)	0.321
No	44 (53.7)	77 (47.0)	
Paternal education			
No formal education	5 (6.1)	16 (9.8)	0.350
Primary school	12 (14.6)	36 (22.0)	
Secondary school	22 (26.8)	37 (22.6)	
Bachelor or above	43 (52.4)	75 (45.7)	
Paternal employment			
Yes	60 (73.2)	98 (59.8)	0.099
Self-employment	20 (24.4)	56 (34.1)	
No	2 (2.4)	10 (6.1)	
Consanguinity			
Yes	29 (35.4)	49 (29.9)	0.383
No	53 (64.6)	115 (70.1)	
Family history of autism spectrum disorder			
Yes	24 (29.3)	28 (17.1)	**0.027**
No	58 (70.7)	136 (82.9)	

[a] Chi-square test was used for analysis with 0.05 as the cut-off point for statistical significance

[b] Man-Whitney U test was used for analysis with 0.05 as the cut-off point for statistical significance

Prenatal, perinatal, and postnatal risk factors

As demonstrated in Table 2, among the listed prenatal factors, mothers who experienced emotional distress during their pregnancy had 2.6 times higher odds of having a child with ASD (p-value = 0.002). The presence of maternal anemia and infections during pregnancy resulted in lower odds of having a child with ASD with an odd ratio of 0.35 (p-value = 0.0007) and 0.45 (p-value = 0.007), respectively. The usage of medications during pregnancy also resulted in statistically significant lower odds of having a child with ASD (OR = 0.48, p-value = 0.009). Among the listed postnatal factors, the occurrence of respiratory distress during the neonatal period resulted in 2.09 higher odds of having a child with ASD (p-value = 0.047). Additionally, mothers who had children with ASD had 5.80 times the odds of experiencing difficulties when feeding their children (p-value = 0.008).

Table 2: Association between perinatal risk factors and autism spectrum disorder

Factors	Patient N = 82 (%)[a]	Control N = 164 (%)[a]	OR (95% CI)	P-value[b]
Prenatal factors				
In-vitro fertilization	2 (2.4)	3 (1.8)	1.34 (0.22 – 8.19)	0.749
Spacing >2 years[c]	43 (79.6)	71 (81.6)	0.88 (0.37 – 2.073)	0.772
Multiple gestations[d]	3 (3.7)	5 (3.0)	1.20 (0.28 – 5.18)	1.000
Maternal conditions: Any	45 (54.9)	107 (65.2)	0.64 (0.37 – 1.11)	0.115
Maternal conditions: Gestational diabetes	8 (9.8)	8 (4.9)	2.10 (0.76 – 5.83)	0.144
Maternal conditions: Hypertensive diseases	9 (11.0)	23 (14.0)	0.75 (0.33 – 1.71)	0.503
Maternal conditions: Anemia	18 (22.0)	72 (43.9)	0.35 (0.19 – 0.65)	**0.0007**
Maternal conditions: Infections	21 (25.6)	71 (43.3)	0.45 (0.25 – 0.80)	**0.007**
Maternal conditions: Emotional distress	27 (32.9)	26 (15.9)	2.60 (1.39 – 4.85)	**0.002**
Maternal conditions: Asthma[d]	2 (2.4)	0 (0.0)	N/A	0.110
Maternal conditions: Trauma[d]	1 (1.2)	1 (0.6)	2.01 (0.12 – 32.5)	1.000
Maternal conditions: vaginal bleeding	14 (17.1)	25 (15.2)	1.14 (0.56 – 2.34)	0.714
Smoking during pregnancy: Passive	33 (40.2)	56 (34.4)	1.28 (0.745 – 2.22)	0.366
ABO or Rh incompatibility	5 (6.1)	16 (9.8)	0.60 (0.21 – 1.70)	0.333
Maternal medications during pregnancy	31 (37.8)	91 (55.5)	0.48 (0.28 – 0.83)	**0.009**
Natal factors				
Type of delivery: Cesarean section	34 (41.5)	82 (50.0)	0.70 (0.41 – 1.21)	0.206
Type of Cesarean section: Emergency	15 (44.1)	27 (32.9)	1.60 (0.70 – 3.64)	0.254
Type of presentation: Breech	0 (0.0)	0 (0.0)	N/A	N/A
Place of birth: Home	6 (7.3)	18 (11.0)	0.64 (0.24 – 1.68)	0.362
Preterm	9 (11.0)	25 (15.2)	0.68 (0.30 – 1.54)	0.360
Low birth weight (<2500 g)	7 (8.5)	20 (12.2)	0.67 (0.27 – 1.66)	0.387
Umbilical cord complications[d]	0 (0.0)	2 (1.2)	N/A	0.554
Birth injury/Trauma[d]	0 (0.0)	1 (0.6)	N/A	1.000
Congenital malformations[d]	3 (3.7)	3 (1.8)	2.03 (0.40 – 10.32)	0.403
Postnatal factors				
Neonatal conditions: Any	49 (59.8)	91 (55.5)	1.19 (0.69 – 2.04)	0.586
Neonatal conditions: Jaundice	44 (53.7)	89 (54.3)	0.97 (0.57 – 1.66)	0.928
Neonatal conditions: Respiratory distress	16 (19.5)	17 (10.4)	2.09 (0.99 – 4.40)	**0.047**
Neonatal conditions: Anemia[d]	2 (2.4)	4 (2.4)	1.00 (0.17 – 5.57)	1.000
Neonatal conditions: Seizures[d]	1 (1.2)	0 (0.0)	N/A	0.333
Neonatal conditions: heart disease[d]	0 (0)	1 (0.6)	N/A	1.000
Neonatal conditions: infections[d]	6 (7.3)	6 (3.7)	2.07 (0.64 – 6.66)	0.222
Oxygen or ventilation requirement	17 (20.7)	21 (12.8)	1.78 (0.88 – 3.59)	0.105
Neonatal feeding: Formula[e]	14 (26.9)	24 (21.6)	1.33 (0.62 – 2.86)	0.456
Neonatal feeding: Mixed feeding[e]	30 (44.1)	53 (37.9)	1.296 (0.72 – 2.33)	0.387
Neonatal feeding: Difficulties[d]	8 (9.8)	3 (1.8)	5.80 (1.49 – 22.49)	**0.008**

[a] Distribution was reported in terms of column percentages

[b] Chi-square test was used for analysis with 0.05 as the cut-off point for statistical significance

[c] Spacing of pregnancies for >2 years was not applicable for children who were 1st in birth order and for families with only one child

[d] Fisher exact test was used for analysis for these items with 0.05 as the cut-off point for statistical significance

[e] Compared against exclusively breastfeeding

As shown in Table 3, both paternal and maternal ages at conception had statistically significant associations with the presence of ASD with p-values of 0.002 and <0.001, respectively. However, when tested with stepwise multiple linear regression, only the maternal age was a significant positive predictor of the presence of ASD in the children (p-value = 0.0002).

Table 3: Association between paternal and maternal ages at conception and autism spectrum disorder.

Factors	Study groups	Median (IQR)	Mean rank	P-value[a]
Maternal age at conception (Years)	Patient	28 (24–33)	152.07	<0.001
	Control	24 (21–28)	109.22	
Paternal age at conception (Years)	Patient	31 (28–37)	143.83	0.002
	Control	28 (25–33)	113.34	

[a] Man-Whitney U test was used for analysis with 0.05 as the cut-off point for statistical significance

Table 4: Logistic multiple regression analysis for the effects of maternal and paternal age on autism spectrum disorder in children.

Model	Variables	B	S.E	P-value[a]	R^2
1	Constant	3.977	0.741	<0.001	0.091
	Maternal age	-0.124	0.027	<0.001	
2	Constant	2.581	0.670	<0.001	0.035
	Paternal age	-0.061	0.021	0.004	
3	Constant	3.880	0.785	<0.001	0.091
	Paternal age	0.011	0.029	0.714	
	Maternal age	-0.133	0.036	0.0002	

Discussion

This study identified several prenatal and postnatal factors associated with ASD among Iraqi children. The higher prevalence of ASD among males aligns with international evidence, reflecting well-established sex differences in ASD occurrence [19]. Urban residence was also associated with ASD, potentially reflecting improved access to diagnostic services and environmental exposures [20]. Recent evidence from Iraq has further emphasized the contribution of environmental and lifestyle-related factors, including excessive screen time exposure, to the clinical profile of children with ASD [21]. Maternal emotional distress during pregnancy was significantly associated with ASD, supporting evidence that prenatal stress adversely affects neurodevelopment [22]. In contrast, maternal anemia and infections were associated with lower odds of ASD, a finding that contrasts with some previous studies and may reflect differences in diagnosis timing, healthcare access, or residual confounding [23].

Neonatal respiratory distress was associated with increased ASD risk, possibly due to hypoxic effects on early brain development [24]. Feeding difficulties were also more frequent among children with ASD, consistent with sensory processing and behavioral challenges characteristic of the disorder [25]. Maternal age emerged as the strongest parental predictor of ASD. Advanced maternal age has been linked to chromosomal abnormalities, genetic mutations, and increased obstetric complications, which may contribute to ASD risk [26].

Limitation of the study

This study was conducted in 3 institutions, and this can limit the generalizability of the study. Case control design can limit the causality inference of the study.

Conclusion

Prenatal stress, neonatal respiratory distress, and feeding difficulties were associated with increased odds of ASD among Iraqi children. Maternal age at conception was the most significant parental predictor of ASD. These findings highlight the importance of maternal

mental health, prenatal care, and early neonatal management in reducing ASD risk.

Conflict of Interest Statement

The authors declare no conflicts of interest related to this manuscript.

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