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Original Research

Risk Factors Influencing of Autism Spectrum Disorder in Children in Kirkuk City/ Iraq: A Case-Control Study

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Abstract:

Background: Autism Spectrum Disorder (ASD) is a complex, lifelong developmental impairment that generally presents in early childhood; however, diagnosis often occurs later, particularly in cases of mild to moderate severity. Approximately one in every 100 children is affected by autism. **The aim** was to assess the risk factors associated with autism spectrum disorders (ASD) for children in Kirkuk City.

Methods: A convenience sample / case-control study was applied between November 2023 to December 2024. The study was conducted on 180 mothers (90 children diagnosed with ASDs based on the DSM-5 criteria, who were aged between 2-12 years as a case group, and 90 children were age and gender-matched control subjects. A questionnaire and interview were used as data collection tools. Descriptive and inferential statistical methods were used.

Results: The study found that most mother's education were college graduates representing (30%), with a significance of P=0.001. The majority of the mothers was housewife (70%). About 20(22.3%) of mothers had chronic hypertension and 16(17.8%) diabetes mellitus, and the study found that there was a highly significant association between family history of ASD, the interval between pregnancies, hyperemesis gravidarum and ASD at P=0.000.

Conclusion: The findings show that various risk factors are connected to autism spectrum disorder among children living in Kirkuk City. The most important of which was the Mother's Education level, the mother's Occupation and mothers with chronic Hypertension, and Family history of ASD, in addition to the father's age at conception and interval between pregnancies.

Keywords: Risk factors; autism spectrum disorder; Children.

Introduction:

Autism is a diverse and complex group of conditions with significant variation in core symptoms, language level, intellectual functioning, and co-occurring psychiatric and medical difficulties. Its onset occurs during the first years of life (10).

ASD is a severe public health concern that has a detrimental effect. The adverse effects of ASD are multifaceted and catastrophic, affecting not only the child in issue but also their siblings and parents. It significantly disrupts the daily routines of a family that is affected by it (1). The wide variety in the types and severity of symptoms seen by people

with autism spectrum disorder is a feature that defines it as a "spectrum" condition (14).

Autism prevalence estimates have consistently increased from less than 0.4% in the 1970s to the current range of 1–2%. Increased awareness and recognition of autistic traits, as well as the expansion of diagnostic criteria to encompass individuals without ID and with milder impairments, are the primary factors contributing to the increase (10).

According to previous research, the clearest clinical manifestation of autism typically manifests in children between the ages of two and three (Nofal et al., 2020). Even though the signs could be seen as early as six months of age (19). According to some past studies, the ASD prevalence in children under five years old ranged from 0.46% to 0.52% (7). Previous studies have identified a connection between autism spectrum disorder (ASD) and several developmental and mental disorders, including Tourette's syndrome, anxiety, depression, intellectual impairment (ID), language delay, and attention-deficit hyperactivity disorder (ADHD) (22)(23).

The increasing prevalence of ASD has undoubtedly been affected by a gradual evolution of the diagnostic criteria, particularly during the transition from DSM-III and DSM-IV-TR to the contemporary DSM-5, which aligned with the spectrum-based understanding of autism, this facilitated the diagnostic identification of individuals exhibiting milder autistic symptoms (8). Although the etiology of autism spectrum disorder remains unclear, various risk factors have been identified or proposed. These encompass genetic, immunological, and environmental predispositions (2).

Insufficient evidence exists regarding the risk factors for ASD in children; although ASD is primarily linked to hereditary factors, emerging epidemiological research indicates that maternal variables may also play a significant role (5). Pregnant women frequently have iron shortages, which might have negative impacts on thyroid metabolism. Maternal thyroid dysfunction during pregnancy can lead to neurodevelopmental impairments in the offspring (20). Research has focused on linkages between ASD and hypothyroidism and hyperemesis (12).

Objectives: The specific research objective of this study can be summarized as follows:

1. To identify socio-demographic characteristics among children's families in Kirkuk City.
2. To explore risk factors associated with autism spectrum disorders for children in Kirkuk City.

Methodology:

A case-control study was conducted to identify the risk factors associated with autism spectrum disorders for children in Kirkuk city/ northern Iraq, from November 2023 to December 2024. Non-probability sampling/convenience sample consists of (180) mothers, including 90 mothers of children who were referred to the autism centers after their diagnosis was confirmed by a licensed physician with expertise in ASD and were aged between 2-12 years. Children with ASD in the present study met the following criteria: (I) Diagnostic and Statistical Manual of Mental Disorders DSM-5 criteria for ASD; (II) Child Autistic Rating Scale score ≥30; and (III) The informed consent of the guardian was obtained as case group and study including all those registered with the centers in Kirkuk city. The study for the case group was conducted in five government and private centers (pediatric hospital (autism center), Raja Institute for the Disabled, Al-Tamayuz Center, Al-Erada Specialized Center, Redin Specialized Center) and compared with 90 mothers of children healthy from primary schools and kindergarten pupils had normal intelligence, normal development, and no physical and mental illnesses as confirmed by the class teachers school, conducted the study for the control group in public and private four schools and two private kindergartens in areas close to centers for special needs and learning difficulties, including autism patients (Al-Kindi Primary School (friendly child), Al-Hajar A-Aswad mixed Primary school, Al-Mustansiriya Primary School, Al-Najah Private Primary School, Baba kurkar private Kindergarten, Children of Tomorrow private kindergarten

Methods of Data Collection

A structured self-administered questionnaire written in the English language was designed after reviewing the literature. The validity and clarity of the tool used in this study were assessed by sending the questionnaire to a committee of 10 experts in different fields. A pilot test was conducted to determine the reliability of the study instrument by choosing mothers was selected with the reality of 5 children with ASD cases attending the Specialized Center of Excellence for Autism & mothers of 5 healthy children from the Al-Hajar Al-Aswad Mixed primary school respectively from the target population (they were excluded from the study sample). The results showed the pilot study 100%.

A questionnaire consists of the following 3 parts:

Section I: Socio-demographic data for families of children with some variables:

This part of the questionnaire contains 7 items including (Residence, Mother education, Father's education, Mother's occupation, Father's occupation, Marital status, and Family History of ASD).

Section II: characteristic of medical history for the mother :

This part of the questionnaire contains 5 items including a history of epilepsy disorder, History of bronchial asthma, History of thyroid, chronic hypertension, and chronic diabetes.

Section III: Characteristics associated with the prenatal factors.

This part contains 5 items including (Maternal age at conception, Father age at conception, interval between pregnancies (in months), Amniotic Fluid Around the Fetus, and Hyperemesis Gravidarum).

Statistical Analysis

The following statistical data analysis techniques were employed to analyse and evaluate the study's findings, using the Statistical Package (spss) ver. (22.0).

Result;

Section I: Distribution of Parents (SDCv.) with some variable

Table (1): Distribution of studied groups undergoing ASD children and non-ASD children according to their parents (SDCv.) with comparisons significant.

SDCv.	Groups	Study		Control		C.S. (*)
	Classes	No.	%	No.	%	P-value
Residency	Rural	19	21.1	12	13.3	CC = 0.102
	Urban	71	78.9	78	86.7	P=0.167
	Total	90	100	90	100	(NS)
Mother Education	Illiterate	7	7.8	15	16.7	CC = 0.335
	Primary School	24	26.7	14	15.6	P=0.001
	Intermediate School	2	2.2	5	5.6	(HS)
	Secondary School	18	20	4	4.4	
	Institution	9	10	15	16.7	
	College Graduated	27	30	25	27.8	
	Post Graduated	3	3.3	12	13.3	
	Total	90	100	90	100	

Father Education	**Illiterate**	**9**	**10**	**14**	**15.6**	**CC = 0.175 P=0.457 (NS)**
	Primary School	**20**	**22.2**	**12**	**13.3**	
	Intermediate School	**2**	**2.2**	**5**	**5.6**	
	Secondary School	**10**	**11.1**	**8**	**8.9**	
	Institution	**23**	**25.6**	**20**	**22.2**	
	College Graduated	**22**	**24.4**	**24**	**26.7**	
	Post Graduated	**4**	**4.4**	**7**	**7.8**	
	Total	**90**	**100**	**90**	**100**	
Mother Occupation	**Housewife**	**63**	**70**	**41**	**45.6**	**CC = 0.240 P=0.001 (HS)**
	Working	**27**	**30**	**49**	**54.4**	
	Total	**90**	**100**	**90**	**100**	
Father Occupation	**Skilled worker**	**39**	**43.3**	**50**	**55.6**	**CC = 0.121 P=0.101 (NS)**
	Unskilled worker	**51**	**56.7**	**40**	**44.4**	
	Total	**90**	**100**	**90**	**100**	
Marital Status	**Live together**	**85**	**94.4**	**86**	**95.6**	**CC = 0.134 P=0.193 (NS)**
	Separated/Divorced	**5**	**5.6**	**2**	**2.2**	
	Widowed	**0**	**0.00**	**2**	**2.2**	
	Total	**90**	**100**	**90**	**100**	
Family History of ASD	**No**	**58**	**64.4**	**88**	**97.8**	**CC = 0.392 P=0.000 (HS)**
	Yes	**32**	**35.6**	**2**	**2.20**	
	Total	**90**	**100**	**90**	**100**	

(*) HS: Highly Sig. at P<0.01; S: Sig. at P<0.05; NS: Non-Sig. at P>0.05; Testing based on a Contingency Coefficient test. Levels marked in red color indicate to the Risk Factors associated with ASD.

Table (1): Results show that more than half of the studied mothers recorded their age in the second group, either for the study sample, or controlled, with mean and standard deviations of 33.89 ± 7.15, and 32.58 ± 6.06 respectively. As for father age groups, most of the studied fathers recorded their age in the second, and third groups, either for the study sample, or controlled, with mean and standard deviations of 39.78 ± 7.69, and 37.031 ± 6.77 respectively, results show that urban residency is formed the most of the studied parent's samples, either for the study sample or controlled. They accounted for 71(78.9%), and 78(86.7%) respectively, further Mother Education shows that about one-third of the studied mother's education is formed at the low educational levels (Illiterate, and Primary School), either for the study sample or controlled. They are accounted 31(34.5%), and 29(32.3%) respectively. Results show that about one-third of the studied father's education is formed at the low educational levels (Illiterate, and Primary School), either for the study sample, or controlled, and they accounted 29(32.2%), and 26(28.9%) respectively. Regarding mother Occupation, results show that the majority of the studied mothers' education is formed at the

housewife level for the cases, they accounted for 63(70%), while 41(45.6%) at the controlled. About more than half of the studied fathers' occupations are formed at the unskilled level for the study sample, and they are account 51(56.7%), while are formed 40(44.4%) at the controlled. Meanwhile, in term of marital Status findings shows that living together are formed most of the studied parents, either for the study sample, or controlled, and they are accounted for 85(94.4%), and 86(95.6%) respectively. Results shows that a highly significant different was accounted at P<0.01 between studied samples according to family history of ASD.

Section II: Characteristics of Medical History for Mothers:

Table (2): Characteristics of the medical history of mother associated with ASD and non-ASD children with comparisons significant.

Mother's Medical History	Groups	Study		Control		C.S. (*)
	Classes	No.	%	No.	%	P-value
History of Epilepsy Disorder	No	88	97.8	90	100	CC = 0.105
	Yes	2	2.2	0	0.00	P=0.155
	Total	90	100	90	100	(NS)
History of Bronchial Asthma	No	81	90	86	95.6	CC = 0.107
	Yes	9	10	4	4.4	P=0.150
	Total	90	100	90	100	(NS)
Thyroid Problems	None	77	85.6	83	92.2	CC = 0.156
	Hypothyroidism	9	10.0	7	7.80	P=0.107
	Hyperthyroidism	4	4.4	0	0.00	(NS)
	Total	90	100	90	100	
Chronic Hypertension	None	70	77.8	87	96.7	CC = 0.272
	Hypertension	20	22.3	3	3.30	P=0.000
	Total	90	100	90	100	(HS)
Diabetes Mellitus	No	74	82.2	85	94.4	CC = 0.187
	Yes	16	17.8	5	5.6	P=0.011
	Total	90	100	90	100	(S)

(*)S: Sig. at P<0.05; NS: Non-Sig. at P>0.05Testing based on a Contingency Coefficient test. Levels marked in red color indicate to the Risk Factors associated with ASD.

Table (2): Shows characteristics of medical history for mothers associated with ASD child sample, and control, such that: "History of Epilepsy Disorder, History of Bronchial Asthma, Thyroid Problems, results show that no significant differences are accounted at P>0.05 between studied samples, exceptional of "Chronic Hypertension, and Diabetes Mellitus" which were showed significant differences in at least at P<0.05, concerning increases of ASD cases in the study sample compared with control.

Table (3): Distribution of Characteristics with the Prenatal Factors with comparisons significant.

Prenatal Factors	Groups	Study		Control		C.S. (*)
	Classes	No.	%	No.	%	P-value
Maternal Age Conception Yrs.	15 _ 19	11	12.2	11	12.2	
	20 _ 24	17	18.9	25	27.8	
	25 _ 29	23	25.6	35	38.9	CC = 0.258
	30 _ 34	24	26.7	12	13.3	P=0.025
	35 _ 39	8	8.9	6	6.7	(S)
	40 _ 50	7	7.8	1	1.1	
	Total	90	100	90	100	
Father Age at Conception	< 30 yrs.	29	32.2	48	53.3	
	30 _ 39	41	45.6	35	38.9	CC = 0.245
	40 _ 49	18	20	6	6.7	P=0.009
	> 50 yrs.	2	2.2	1	1.1	(HS)
	Total	90	100	90	100	
Interval between Pregnancies	Non-Applicable	42	46.7	19	21.1	
	< 24 m.	7	7.8	34	37.8	CC = 0.426
	24 _ 48	18	20	31	34.4	P=0.000
	> 48 m.	23	25.6	6	6.7	(HS)
	Total	90	100	90	100	
Amniotic Fluid Around the Fetus	Normal	78	86.7	79	87.8	CC = 0.080
	Poly Hydramnios	7	7.8	4	4.4	P=0.560
	Oligohydramnios	5	5.6	7	7.8	(NS)
	Total	90	100	90	100	
Hyperemesis Gravidarum	No	31	34.4	67	74.4	CC = 0.373
	Yes	59	65.6	23	25.6	P=0.000
	Total	90	100	90	100	(HS)

(*)HS: Highly Sig. at P<0.01; S: Sig. at P<0.05; NS: Non-Sig. at P>0.05Testing based on a Contingency Coefficient test. Levels marked in red color indicate to the Risk Factors associated with ASD.

Table (3): The number of maternal age of 35 yrs old and more accounted for 15(16.7%) in the ASD sample, with a significant difference at P<0.05 compared with a controlled group. Fathers aged of 40 yrs old and more are accounted for 20(22.2%) of the ASD sample, with highly significant differences at P<0.01 compared with a controlled sample. One-quarter of the observed frequencies of ASD cases regarded intervals between pregnancies of more than 48 months, they accounted for 23(25.6%). Results assigned a positive of a "Poly Hydramnios, and Oligohydramnios" disorder with

respect to the ASD sample, since they accounted for 12(13.4%), as well as similar outcomes were recorded with controlled since it accounted totally 11(12.2%). On the other hand, findings that more than a third of ASD symptoms have positive responses toward Hyperemesis Gravidarum compared with control since they account for 59(65.6%).

Discussion:

This is the first study in Kirkuk to investigate the associations between risk factors associated with autism spectrum disorder in children.

1. Discussion of Results of the Analysis of the Socio-demographic Characteristics of the Parents and with some variables.

Regarding the area of residence, the results showed that (78.9%) of the case group and (86.7%) of the control group were living in Urban areas, this indicates that the majority of the sample was living in urban areas for both groups. The findings of our study were not statistically significant at a p-value of 0.167. These findings disagree with the conclusions of the study case-control study conducted by (Arafa et al.,2022) from Egypt that mothers who lived in urban regions had a higher likelihood of having children with autism spectrum disorder (OR = 2.33)(5). In terms of the level of mother's education, the findings showed that the majority level (30%) of the case group had a bachelor's degree, and (27.8%) of the control group had a bachelor's degree, the finding of the current study shows a high significant association between mother education level and ASD for children at (P=0.001). Our findings came in line with the literature by Al-Mamari et al., 2021 from Oman the percentage of mothers of children with ASD who had a bachelor's degree was significantly higher than that of the control group (23.7%; P = 0.001)(3), however, the findings indicated that the father's education level was a majority in the category of college graduates (24.4%) for the case group and (26.7%) of the control group, indicating the current findings are not statistically significant at P=0.457. Our findings disagree with studies published by (Hrdlicka et al., 2016) that younger the age at diagnosis of ASD for children correlated with paternal education(P=0.002)(13).

In the current study, the majority of the mothers were found to be a housewife (70%) of the cases, and (54.4%) of the control group were working mothers, the study shows statistical significance between autism and the mother's occupation (P=0.001). Our findings came in line with the literature. A previous study in Bangladesh by Hamid et al, 2020 indicated a housewife mother was found to be a significant (p=0.04, and had a stronger (2.3 times) ability to predict the occurrence of autism than mothers who were working mothers with a 2.3 times higher risk compared to working mother. Thus, a higher percentage of fathers were unskilled workers (56.7%) of the study group, and (55.6%) of the control group were skilled workers the result shows no association between father job and ASD for children P=0.101 agrees with a previous study by Hamid et al, 2020 hand, it was found that the occupation of the father was a non-significant predictor of autism (9).

The results indicate that most of the parents included in the study, both in the study sample (94.4%) and the (95.6%) control group, were seen to be married and (5.6 %) of the case and (2.2%) of the control group were divorced, the finding of the current study shows statistically no significant P=0.193. Our result disagreed with the research carried out by Mkhitaryan et al. (2024) in Armenia, which revealed that a greater proportion of the sample of parents in both the study group (89.7%) and the control group (95.7%) were married also the proportion of non-married families (those that reported being single, widowed, divorced, etc.) was higher in the ASD group compared to the control group (10.24% and 4.28% respectively, $p < 0.05$)(16). Regarding family history according to the study's findings, there is a significant difference (P=0.000) in the prevalence of autism spectrum disorder (ASD) in the family history across the samples examined in contrast, with the group that performed as the control, the results of the study suggest that individuals who have a positive family history of autism spectrum disorder (ASD, are

more likely to be diagnosed with autism. These results agree with another study conducted on the Kurdish population, by Saleem and Ameen (2023) in Erbil (Iraq) this study concludes that Family History is a genetic risk factor for developing autism (20). However, our findings agree with a large Swedish study by Xie et al., in 2019, which indicated that around 6895 autistic individuals had a family history of neurological or mental disorders, which was associated with ASD (22).

2. Discussion characteristics of the medical history of mothers associated with ASD and non-ASD children with comparisons significant.

According to the findings of our study, there was no significant difference (P=0.155) in the prevalence of autism spectrum disorder for children and mothers with a history of epilepsy. Our results agree with a previous study conducted by Hegazy et al.,2022 the findings of their research show no statistically significant differences between the studied groups regarding epilepsy (11).

In terms of the History of Bronchial Asthma, the current study shows no statistically significant P=0.150, which is inconsistent with a survey done by Croen et al., in 2024 which revealed that mothers with asthma were more likely to deliver infants later diagnosed with ASD (odds ratio [OR] = 1.62) (6). Furthermore, regarding thyroid disorder in mothers, our findings showed no significant differences between cases and control at P=0.107. These current results disagree with a study conducted by Magdalena et al.,2020 which indicates that the thyroid condition in the mother had a statistically significant impact on the offspring's likelihood of developing ASD (p = 0.009 (15).

Meanwhile, the findings showed that a mother with a history of hypertension showed highly statistically significant P=0.000. The results align with the previous findings by Hegazy et al., in 2021, which indicated highly significant differences between cases and control groups regarding history of hypertension p= 0.003(11). In addition, the results of our study show mothers with diabetes mellitus are connected to ASD for children at (P=0.011). These results are consistent with a study by Arafa et al.,2022 from Egypt who found moms with a history of diabetes were statistically significantly linked to higher risks of ASD (5).

3. Discussion of results of the Characteristics Associated with the Prenatal Factors associated with the studied samples.

In this study, we found that the majority of maternal age at conception (26.7% (were aged between (30-34) years, and (25.6%) of them were (25-29) years in the case group (38.9%) was aged between (25-29) years of the control group significantly increasing the risk of ASD in offspring at P<0.05. Our study was inconsistent with the findings of a previous study by Aloufi et al., 2022 that found the majority mothers age during pregnancy of the autistic child was 20-29 years in 51% and 56% of the control group and 30-40 years in 29.4% and 21% of the control at (P>0.05) (4). Regarding father age at conception, the present results show the majority (45.6%) were aged in category (30-39) for the case group and (53.3%) were aged (< 30 yrs) of the control group at P=0.009. Our findings disagree with research conducted by Nani et al.,2020 results their study showed there was no correlation between the occurrence of autism spectrum disorders in children and the mother's and father's ages at conception onset (P > 0.05) in any of the age ranges (17).

With respect to prenatal risk factors, there were highly significant differences between the cases and controls in the intervals between pregnancies more than 48 months (P=0.000). Our results are in line with Mkhitaryan et al.,2024, finding of their study found interpregnancy intervals, showed significant differences between cases and controls (p < 0.05). Furthermore, our study results indicate that amniotic fluid around the fetus was which showed no significant differences at P>0.05 (16). Also, the investigation of this study contradicts with results of research by Chien et al.,2019 that found prenatal factors such as Polyhydramnios, oligoamnios were associated with the severity of autistic symptoms.

Regarding hyperemesis gravidarum the findings of our study were statistically significant at($p < 0.05$), Meanwhile, our findings are consistent with previous results by Getahun et al.in 2021 which showed Children exposed to HG in-utero had higher rates of ASD than those unexposed Since HG diagnosis is linked to an increased risk of ASD, it could be useful in identifying children who are at risk and who would benefit from more frequent monitoring as well as earlier diagnosis and treatment children (25).

Conclusion:

We detected several risk factors associated with ASD in children in a case-control study from Iraq. We believe that the findings of this study can help in future national screenings and educational programs. Our study showed the possibility of early identification of at-risk children who may benefit from treatments. Therefore, pregnancy complications may help identify children who could benefit from early screening and intervention for this common neurodevelopmental condition.

Recommendation:

Children with substantial risk factors such as male gender should be offered regular pediatrician visits to check for normal psychiatric development. Strict monitoring of a child for any behaviour change early intervention is associated with better outcomes. Future studies using large samples and new items (factors risk) to confirm the findings of the current study.

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