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Environmental risk factors for Autism

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Abstract
Background: Autism spectrum disorder (ASD) is a lifetime development infirmity currently affects communication, societal interaction and how a person recognize the world around him. the expansion of the diagnostic principles, were triggered the wide pervasiveness of autism over the last years.
Objectives: To investigate various social and environmental factors associated with Autism among children.
Method: A case-control study was conducted on children aged between 3 to 12 years, using A self-administered questionnaire directed at parents of eighty cases of autism, and 140 controls.
Results: The study revealed that autism was triple times more among the only child in the family (OR 3.5, p= 0.005). Family history; of autism and other psychiatric diseases were significantly associated with autism (p=0.0001, p=0.006 respectively). Incessant viewing of various screens more than 3 hours/day, has practiced 7 folds more among autistic child than control (OR 6.97, p= 0.048). Febrile convulsion during early years of life and fathers age > 40 years were significantly associated with autism (p= 0.0001, 0.0001). Certain drugs consumption, the misery of the pregnant mother, and cesarean section were significantly higher in ASD children than controls (p= 0.0001, p= 0.009, p=0.0005). While crying at birth and breast feeding appear to act as protective factors against ASD. The study concluded that; various factors might associate with autism as being the only baby, family history, incessant viewing screens, febrile convulsion, fathers' age, pregnant mother's misery, drugs and Cesarean section. Additional more comprehensive longitudinal studies are recommended to precisely identify these factors and others.

Keywords: Autism spectrum disorder, autism, ASD, social risk factors, environmental factors

Introduction

Autism spectrum disorder (ASD) is a lifetime development infirmity currently affects communication, societal interaction and how a person recognize the world around him [1]. In a way that critically complicate the aptitude to empathize and hampers the development of self, with varying abilities [2]. Around 17% of children of the age 3 to 17 years old will be identified with developmental disorders like autism, ADHD, and cerebral palsy, according to the CDC statement [3]. Indeed, augmented communal awareness about ASD, in addition, to the expansion of the diagnostic principles, were triggered the wide pervasiveness of autism over the last years. CDC declared that about 1 in 100 of the overall world's population (over 75,000,000 people) has autism and the global Autism prevalence has increased 178% since year 2000 [4]. Autism spectrum disorder prevalence oscillates greatly across studies. In 2023, it was reported in United States, that around 1 in 36 children is diagnosed with ASD. Qatar has one of the highest rates of autism in the world, while France has the lowest rates [3]. Whereas in many low- and middle-income countries the prevalence is unknown [1].

Iraq, is one of the countries that has suffered from all kinds of violence over the past decades, that could lead to a sort of escalation of ASD occurrence. And despite the lack of official and organized statistics, it has been estimated that there are approximately 200,000 persons with ASD among Iraqi population of closely 40 million, which is not insignificant [5]. The substantial growth of the body of researches has resulted in an expansion of potential risk factors of ASD [6, 7]. Even though, the knowledge about specific causes of ASD is little, but the cause in some cases is known and unknown in others, and still certain persons are at advanced risk than others [8].

Consequently, this research was chosen to draw attention to the social risk factors behind this increment of autism in our locality, as well as to investigate various environmental factors that may be in the mind of our families as underlying causes of the disease in our society.

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Methods

A case-control study was designed to achieve objective of this study. The study conducted from the beginning of January through the end of February 2024. A special self-administered questionnaire directed at parents of the included children to be filled at home for all cases, and to be filled directly at PHCs for all controls. The form covered the topics of social and environmental characteristics. Eighty cases of ASD were collected from 2 institutions including Al-Noor and Al-Dhuha Institutes for Autism and slow learning in each side of Baghdad city. The control group was composed of 140 healthy children collected from children attending 2 Primary Health Centers Al-Khadhraa and Al-Adhamia in Al-Khark and Al-Rusafa sides of Baghdad City. All study participants ranged in age between 3 to 12 years, altogether were selected conveniently. The information was tabulated using simple descriptive measurement including absolute frequencies, Odds ratio (OR) with its 95% CI and X^2 test were used to look for the presence or absence of an association, p-value was statistically significant at a level ≤ 0.05.

Results

Table 1 shows that ASD is predominant in male more than female by a ratio of male to female is 2.6:1. More than two-third of the ASD patients diagnosed at the age of two years and thereafter.

Table 1: Characteristics of ASD cases among the sampled children.

	Autism cases (n=80)	%
Gender		:
Male	58	72.5
Female	22	27.5
Age when the child diagnosed as autism (n=80)		
< 1 year	1	1.2
1---	9	11.2
2---	25	31.3
$\geq$3 years	45	56.3

A child living with his/ her parent was a kind of protection against ASD onset (OR= 0.4, CI= 0.09- 1.91). And being the only child in the family had a significant positive association with ASD than control group (OR= 3.5, CI= 1.4 -8.7, p-value= 0.005). While fully or partially vaccination doesn't affect ASD development (Table 2).

Table 2: Characteristics of the sampled children

	Autism Cases (n= 80)	%	Control (n=140)	%	OR	95% CI	p-value
Child lives with:							
Father or mother	1	1.2	3	2.1			
Father and mother	76	95.0	137	97.9	0.42	0.09- 1.91	0.245
With relatives	3	3.8	00	00			
Sequence of the child in the family:							
1st child	25	31.3	46	32.9			
2nd or more	50	62.5	94	67.1	0.82	0. 46- 1.45	0.486
twins	5	6.2	00	00			
The only child in the family:							
Yes	14	17.5	8	5.7	3.50	1.40- 8.76	0.005*
$\geq$2 years spacing							
Yes	36	45.0	67	47.9	0.89	0.51- 1.55	0.683
Vaccination status							
Fully vaccinated	62	77.5	111	79.3	0.90	0.46- 1.75	0.756
Partially vaccinated	10	12.5	18	12.9			
unvaccinated	8	10.0	11	7.8			

Table 3 depicts among children with that family history of autism and Family history of other mental health diseases as schizophrenia and Down syndrome were significantly 7 folds and 11 folds higher in ASD children than another group (OR 7.2, p=0.0001, OR 11.2, p= 0.006 respectively). While consanguineous Marriage had more than one-fold more in ASD children with no significance.

Table 3: Family history of the sampled children

	Autism Cases (n= 80)	%	Control (n=140)	%	OR	95% CI	P- value
Consanguineous Marriage							
Yes	38	47.5	48	34.3	1.73	0.98-3.04	0.053
Family history of autism							
Yes	17	21.2	5	4.5	7.29	2.57-20.63	0.0001*
Family history of mental health diseases:							
Yes	6	7.5	1	0.7	11.27	1.33- 95.39	0.006*

Table 4 shows that history of starting watching T.V. before one year of age was 8 times higher among autistic children than healthy (OR 8.25) but not to a level of significance. While incessantly watching screens of T.V. and other smart devices for more than 3 hours per day have significantly associated with about 7 folds higher risk of autism than those viewing these devices for a shorter time or non-watcher (OR= 6.97, p= 0.048). Though the beginning of staring at these screens before or during the first year of life was many times higher within the category of autistic children, but not to a level of significance (Table 4).

Table 4: Watching screens of TV and smart devices practices by the sampled children

	Autism cases (n=80)	%	Control (n=140)	%	OR	95% CI	P- value
The age of child when began watching TV:							
<1 year	33	41.3	8	5.7	8.25	0.66-102.7	0.060
1---	26	32.5	34	24.4	1.53	0.13-17.80	0.733
2---	12	15.0	45	31.1	0.53	0.05-6.39	0.615
≥3 years	8	10.0	51	36.4	0.31	0.03-3.87	0.343
Not watched	1	1.2	2	1.4			
Number of hours of TV watching							
3hrs or less	33	41.3	102	72.9	1.61	0.18-14.35	0.663
More than 3hrs	46	57.5	33	23.6	6.97	0.78- 62.47	0.048*
Not watched	1	1.2	5	3.5			

Table 5: Condition of the sampled children at birth and in the first 2 years of life

	Autism Cases (n= 80)	%	Control (n=140)	%	OR	95% CI	P- value
Cry at birth:							
Yes	59	73.7	131	93.6	0.19	0.08-0.45	0.0001*
No	21	29	9	6.3			
Type of feeding:							
Breast	40	50.0	110	78.6	0.32	0.16-0.63	0.0008*
Formula	24	30.0	21	15.0			
Mixed	16	20.0	9	6.4	1.56	0.57-4.25	0.388
febrile convulsion during 1ˢᵗ and 2ⁿᵈ year:							
Yes	21	26.3	4	2.9	12.1	3.98-36.80	0.0001*
No	59	76.8	136	97.2			
Diseases during 1ˢᵗ year:							
Yes	14	17.5	20	14.3	1.27	0.60-2.68	0.526
No	66	79.7	120	85.9			

Table 5 demonstrates, that crying at birth and breast feeding were significantly more likely to act as a protective against ASD (OR 0.19, p= 0.0001) and (OR 0.32, p= 0.0008) respectively. However, children with history of febrile convulsion during the first two years of life, had raised significantly among ASD children by more than 12 folds than those without history of febrile convulsion (OR 12.1, p= 0.0001).

Mother's age seems to be of no influence on autism among their offspring (OR 0.46, C.I.= 0.19-1.13). In contrary, table 6 illustrates that, fathers aged > 40 years had a significantly three folds more to be found in the history of autistic offspring than those born to > 40 years old fathers (OR 3.6, p= 0.0001). Mother's job and parental education appear to be not effective in ASD development (table 6)

Table 6: Parental characteristics of the sampled children

	Autism Cases (n= 80)	%	Control (n= 140)	%	OR	95% CI	P- value
Mother's age:							
≤30 years	34	42.5	87	62.1	0.46	0.19-1.13	0.086
30-39	35	43.7	40	28.6	1.03	0.41-2.60	0.943
≥40years	11	13.8	13	9.3			
Father's age							
< 40	25	31.2	87	62.1			
> 40	55	68.8	53	37.9	3.6	0.16-0.50	0.0001*
Mother's job :							
Gov. employee	26	32.5	45	32.1	0.97	0.53-1.79	0.927
Private work	10	12.5	21	15.0	0.80	0.35-1.86	0.604
House wife	44	55.0	74	52.9			
Mother's education:							
Illiterate	4	5.0	10	7.1	1.00	0.24-4.14	0.999
Primary	5	6.3	10	7.1	1.25	0.32-4.53	0.746
Intermediate	30	37.5	57	40.7	1.32	0.52-3.34	0.563
Secondary	33	41.2	43	30.7	1.92	0.75-4.90	0.169
College & HE	8	10	20	14.4			
Father's education ;							
Illiterate	4	5.0	6	4.3	1.08	0.28-4.14	0.907
Primary	8	10.0	12	8.6	1.08	0.40-2.94	0.875
Intermediate	11	13.8	21	15.0	0.85	0.36-2.00	0.711
Secondary	25	31.2	49	35.0	0.83	0.43-1.59	0.573
College & HE	32	40.0	52	37.1			

Table 7 shows, that autistic group had significantly more than four folds history of mothers' consumptions of certain drugs, during their pregnancy as; Anti-depressant and anti-hypertensive, antiacids, and general anesthesia, than children of the women with no such history (OR 4.4, p= 0.0001). Additionally, table 7 also displays that, pregnant women engaged more in the family problems gave birth to children with autism, significantly more than those who were not (OR 2.58, p= 0.009). at the same time, table 7 demonstrates that, Cesarean Section deliveries were more

than 3 times significantly common among autistic children than control who delivered via vaginal delivery (OR 3.17, p= 0.0005)

Table 7: Maternal condition during pregnancy.

	Autism Cases (n= 80)	%	Control (n= 140)	%	OR	95% CI	P- value
During pregnancy:							
Take drugs during pregnancy	26	32.5	14	10.0	4.40	2.41 -9.08	0.0001*
Maternal diseases	38	47.5	62	44.3	1.14	0.66-1.98	0.645
Family problems during pregnancy	20	25.0	16	11.4	2.58	1.25-5.34	0.009*
Smoker mothers	9	11.3	13	9.3	1.24	0.05-3.04	0.640
Age of pregnancy							
Term	59	73.8	117	83.6			
Preterm	7	8.7	10	7.1	1.39	0.50-3.83	0.525
Post term	14	17.5	13	9.3	2.14	0.94-4.84	0.065
Type of delivery							
Normal delivery	43	53.8	107	76.4			
Complicated del	9	11.3	11	7.9	2.04	0.79-5.26	0.137
CS	28	35.0	22	15.7	3.17	1.64-6.13	0.0005*

Discussion

The study was aimed to investigate various social and environmental factors related to autism. It suggested that autism is a male predominance disorder with a male-to-female ratio of 2.6:1, this is in consistence with a study done in Salah-addin / Iraq, where 81% of the autistic sample were male [9]. The same was reported by Ratto AB *et al*., who declared that there is really a higher frequency of ASD among males, with a ratio about 3:1, This figure had attributed to the familial patterns and genetic links that made it "protective" in girls. That is beside the hormonal effects (like fetal testosterone levels) attributed to sex differences. [10]. Other Recent research suggested that ASD may looks quite unlike in female, and misdiagnosis is often common in autistic females [11]. It is possible that females often show fewer ASD traits, or better to hide their characters than boys [12].

It has been noticed that, the majority of our ASD cases diagnosis was after 2 and 3 years of age. Which was reliable with that seen in Australia, where a study conducted on a larger sample of autistic cases, the average age of diagnosis was 28 months [13]. Another study done recently in 2022, in which 61% of children with autism were diagnosed between (3-6) years of age [9].

Family history of autism or other mental health disorders, appeared in this study, to be significantly associated with autism risk p= 0.0001 & p= 0.006 respectively. The same was observed in salah-addin province/Iraq in 2022 [9]. This might explain the genetic responsibility for autism, as declared in South Carolina Project for autism, where anomalies of chromosome 15 have arisen [14].

Current study revealed that early starting gazing at screens of TV and other smart devices during infancy and before two years of age was many folds more common among autistic children than non-watchers, but not to a level of significance. At the same time Continual viewing of these screens more than 3 hours/ day had significantly associated with a high risk to develop autism than control group (OR= 6.97, p= 0.048). this figure was in consistence with the findings detected recently by Japanese researchers in Yamanashi university, who declared that boys of one year of age with screen time watching of two-four hours/day were 3.48 times more probable to be identified as autistic case at age of three years. Also, this risk was amplified, the more time used up watching at screens [15].

Crying at birth noted in this study, to be significantly protective against autism. It is well known that, cries at birth generally, been allied with brain health wellbeing. Babies with Down syndrome often make weaker [16]. No earlier comparable study been found to approve or disapprove this result. Nevertheless, it might be explained by that, the cry of newborn at birth tells that their lungs and tissues origination are healthy, as the first cry can help to expand neonatal lungs and oust mucus or fluids. In the same context, this study found that breast feeding act significantly as a protective factor against autism (OR 0.32, p= 0.0008). similar result was shown in Tawfeeq W F *et al* study, this could be explained by the fact that, breast feeding often provides an enormous expanse of psychological communication and positive emotions that might guard the baby from autism [17].

In this study, febrile convulsion during first years of infant's life, appaired significantly to increase the risk of ASD during childhood. This result was supported by another study conducted in Sweden, which declared that there is a significant association between earlier age of ASD and febrile seizers which might confer some brain or neurologic vagaries [18].

This research has instituted a link between increasing father's age and growing risk of autism in their offspring, regardless of the age of the mother. The same was detected by Tawfeeq W F *et al*. in 2016, and in U.S. at 2010 [18, 19]. This might be owing to the collective contact and interaction to countless environmental factors throughout their life, that may be accountable for certain germ line alterations and modifications in these elder fathers [19].

The study also demonstrated that, mothers of autistic children had a history of consumption of certain medications four folds than the mothers of control group (Anti-depressant and anti-hypertensive, General anesthesia). Another study has confirmed such effect, and this influence has attributed to a drug itself or to the underlying pathophysiology of the disease on mother or fetal development failure [20]. As epidemiological study about hypertension (HT) during pregnancy in 2019, conveyed that there was 40% surge in odds of ASD among offspring of hypertensive mothers; whether maternal chronic HT or gestational HT. Although, the detailed mechanism on how HT distresses fetal brain growth resulting in ASD still not so obvious [21]. On the other hand, another case-control study in 2011, declared a double-fold upsurge in the risk of autistic children for mothers with drug history of anti-depressant during gestation, principally in the first trimester [22].

History of Mother's engagement in the family problems during pregnancy were observed in this study, to surge the risk of ASD more than double folds, compared to the control group. Similar inferences were found in China [23], and in Iraq [17]. This explained by the fact that emotional

disturbances, weak social ties and repeated stressors with associated surge in adrenalin hormone of the pregnant mothers might disturbed brain and neurological development, or cerebral blood flow of fetus such influences can aid in ASD development [24].

There is a significant statistical relationship between history of birth by CS and the manifestation of autism in children than those delivered by vaginal delivery, which was revealed in this study (p= 0.0005). Similar finding was seen in a meta-analysis study, which described that there was a 23% more autistic risk among children delivered by CS than vaginal delivery [25]. This might explain the eruption in ASD incidence rate in Iraq with the steady increase in birth by CS. The conceivable elucidation for such results is that, planned CS is customarily arranged few weeks earlier to full term, in order to circumvent impulsive delivery. Consequently, the labor weeks pre full term might affect a comprehensive brain growth [26]. As well as the neonatal neurotoxicity linked to acquaintance to anesthesia might be another contributive factor [27]. In addition to depriving fetus from the advantageous effect of vaginal delivery in improving the immune system [28, 29]. Cognizance of all these influences can aid in deep considerate of the environmental and social risks of ASD.

Conclusion
There are various risk appear to be associated with development of autism like; being the only baby, family history, incessant viewing devices screens, febrile convulsion, parental age, misery of the pregnant mothers, drugs and Cesarean section.

Recommendation
Additional more comprehensive longitudinal studies need for precise identification of these risks and another additional factors, with the aim of plummeting the emergence of new autism cases.

Conflict of Interest
Not available

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Not available
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