

EVALUATION OF RISK FACTORS OF AUTISM SPECTRUM DISORDERS AMONG CHILDREN IN BABIL , 2022

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<u>Abstract</u>

Background: Autism spectrum disorders (ASD) are complex neurodevelopmental disabilities that are marked by persistent immaturity in social communication and social interaction, as well as confined and recurrent patterns of behavior, interests, or activities. These basic symptoms appear before the age of three years and continue for the rest of one's life. ASD has risen to the top of scientist's and health care provider's priority lists, as well as attracting public attention due to an increase in its prevalence.

<u>**Objective</u>**: To determine the risk factors for Autism among autistic children in Babil Province. **Type of study**: case- control study</u>

Patients and Methods: the study was conducted in four private specialized educational institutions for autistic children for cases, and controls were drawn from a kindergarten, and primary schools in Babil city. A study sample was 130 children (60 cases and 70 controls), age ranging from 2.6 to 10 years. This study conducted during the period of data collection extended from the first of February to the first of May 2022. The data were collected through a special structured validated questionnaire and analyzed by SPSS software.

Results:

Mean age of the study participants among autistic children was $(6.8\pm2\text{years})$ ranging from (2.6-10years) old. Most of the children with autism included in the study were boys (81.7%) and girls (18.3%). Both genders predominantly urban residence. More than half of fathers of the study participants were governmental employee and about half of mothers were house wife among autistic child. More than one third of mothers of autistics children had a history of psychiatric illness before pregnancy (anxiety& depression) and epilepsy. There is another statistically significant differences among cases and controls regarding the diseases of the child after delivery. *Conclusions*: There are many risk factors play an important role in the development of autism spectrum disorders, these include: gender, parent's education, parent's occupation, maternal stress, diseases during pregnancy that can affect the development of child and attributed to autism.

Key words: autism spectrum disorders, risk factors, social interaction, communication skills.

INTRODUCTION :

Autism spectrum disorder is a collection of neurodevelopmental disabilities marked by persistent immaturity in social communication and social interaction, as well as confined and recurrent patterns of behavior, interests, or activities (1). Autism Spectrum Disorder (ASD) is a term used

to describe a set of neuros-developmental diseases that includes autism, Asperger's syndrome (AS), and Pervasive developmental disorder-not otherwise specified (PDD-NOS) (2).

Kanner first discovered autism disorder in 11 children with identical characteristics such as defective speech and language, compulsive conduct, and social cognition deficiencies in 1943(3). Since Kanner, the definition of ASD has remained mostly constant. Rutter formalized these symptoms in what became the formal autism nosology, which has lasted to this day (American Psychiatric Association, 2013) with minor alterations (4). The Fifth Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) criteria requires persistent difficulties in social communication and interaction, as well as restricted patterns of behavior, interests, or activities, beginning in infancy and causing considerable functional impairment; cognitive and verbal impairment may or may not present (5). These basic symptoms appear before the age of three years and continue for the rest of one's life) (6). According to World Health Organization (WHO), about 1/100 children are diagnosed with autism spectrum disorder. Estimates of prevalence develops over time and varied significantly inside and across sociodemographic groups. These findings reflect variations in the definition of autism as well as variances in prevalence study methods and circumstances (7). Several recent studies made, one of these studies was made across 204 countries and territories in 2019, that the prevalence of ASD was rising over time, although these studies used administrative records' data rather than community-based research to support their case. The prevalence of ASD among United State (US) children aged 3 to 17 increased between 2009 and 2017 (1.1–2.5 percent), according to the National Health Interview Survey. On the other hand, India's crude prevalence of ASD dropped from 1990 to 2017 and was at 0.4%, Previous research has shown that the prevalence of ASD is substantially higher in wealthy nations than it is globally, and that rates in resource-poor nations, where it is more difficult to collect epidemiological data, are lower., It is important to note that from 1990 to 2019, the Incidence rate of ASD in various Western European nations, particularly in Germany, Italy, and Switzerland, exhibited a minor downward tendency. This trend may be related to the grave issue of aging and reduced birth rates, and more research is required (8). There are few statistics on ASD prevalence in the Middle East and North Africa (9). The pathogenesis of ASD and mechanism are unknown. However, it is thought that the process behind ASD etiology is genetic, and environmental influences may combine with genetic factors to cause the condition (6). However, a growing body of evidence suggests that genetic factors may account for only 35-40% of the causes of autism. Other environmental factors, are likely to account for the remaining 60-65 percent. Recent research has looked into how the interaction of genes and environment can cause autism (10). Genetics, prenatal factors, perinatal factors, postnatal factors, environmental variables are all thought to play a role in ASD. ASD is now widely regarded as a multifactorial condition caused by a complex combination of hereditary and non-genetic risk factors. In ten percent to twenty percent of people with ASD, genetic variables such as gene deficiencies and chromosomal abnormalities have been discovered. Prenatal, perinatal, and postnatal variables, as well as a variety of environmental causative aspects, all have a role in ASD (11). Males are four times more likely than girls to develop autism, and the reason for this disparity is unknown. Several explanations have been presented, including the function of hormonal impacts in utero and the role of the sex chromosome in the pathogenesis of ASD (12). Prenatal factors include age of parents at the time of the child birth, Parents' socioeconomic status, parental living area, occupation, mental health of mother , generalized health conditions before to and during pregnancy, and family history of autism are all considered(13). Infection, metabolic syndrome, and prenatal hemorrhage are just a few of the diseases linked to autism. Autistic children and their families are primarily of low socioeconomic class when considering economic, social, educational, and psychological elements of their lives. Because of their financial difficulties, as well as vocational and psychological strains, these families invariably endure unhealthy, improper sociality, and rehabilitated life conditions (14). Exposure to pesticide during pregnancy has been linked to neurological abnormalities in children, including autism spectrum disorder (ASD), attention deficit hyperactivity disorder (ADHD), and cognitive deficits (15).

Preeclampsia and gestational diabetes have been linked to an increased risk of ASD, according to new studies (16). In an unadjusted study, jaundice, infection (respiratory infection), epilepsy, birth hypoxia, and infant problems were all found to be related with ASD. With the exception of jaundice, which became insignificant following correction, these correlations remained. Neonatal seizure was associated with the highest risk of ASD and was linked to birth hypoxia (17). Consanguinity is thought to increase recessive gene expression and thus autosomal recessive illnesses by revealing concealed traits. A suspected genetic factor to the etiology of autism spectrum disease is autosomal recessive transmission (18). The use of digital technology has been increased rapidly increasing in the last decades, Smart devices generate radiofrequency radiation that alters children's behavior. Exposing toddlers to a lot of colored two-dimensional stimulation may be detrimental to brain development since the brain organizes during the early years of life and because humans evolved to respond to three-dimensional stimuli. The child won't be able to grasp socio-emotional relationships if they are constantly exposed to TV, have minimal parental engagement, and have fewer opportunities to play with their friends (19).

Patients and Methods:

The study is a case -control study which was conducted in Hila city, center of Babil Governorate, locate south of Baghdad, Capital of Iraq.It's area about 6,468 (km) and population estimated about 2,119,403 and include four districts(Iraq Ministery of Health. Annual Statistical Report 2020.August.2021).

This study carried out in four private specialized educational institutions for autistic children (Babil Autism institute, Al Rahma institute, Babil center for autism, and Al Atabaa center) and for the controls children including: a kindergartens, and primary schools were Omer Abid Al asis school and Al gofran school. The data collection was performed from February 2022 to the first of May 2022.

Sample size was numbered 70 for autistic children were conducted from four private specialized educational institutions for autistic children in Babil city in convince method and for controls was numbered 70 from kindergartens and primary schools in simple random sampling method.

Inclusion criteria were children with age range from 2.6 to 10 years old who were diagnosed with

autism spectrum disorder who attended the institutions and controls are also of the same age range included in the study. During the first visit, there was a total refused in participation in this study, go a second visit was done with explain the confendiality and secrecy of this study and that it is anonymous as the autism is consider as a social stigma.

Data was collected by indirect interview the parents of the child with the aid of a specially designed form that we take it from different references, corrected and translated by the Supervisor, Specialist in Internal Medicine and Specialist Psychiatrist which included the following:

Age and gender of the child, vaccination history, as well as demographic data of the family (residence of the family, education of the parents, and occupation of both parents), blood group for parents and age of both parents during pregnancy of affected & normal child & family history of Autisms spectrum disorders. The form also includes information about the mother (maternal disease before pregnancy should be diagnosed & treated like depression, anxiety, psychosis and epilepsy, drug history), information about pregnancy (pregnancy problem like anemia, infection, Rh incompatibility, gestational diabetes mellitus, preeclampsia, and prenatal & intra partum pharmacological agents use like valiproic acid &other anti-convulsion, and exposure to toxins especially pesticides during pregnancy).

Information about delivery (gestational age at birth, mode of delivery and place of birth), as well as history of child, disorders after delivery (physiological jaundice, pathological jaundice, cyanosis, premature unit admission, congenital heart diseases and congenital central nervous system), breast feeding type(exclusive till first six months of age ,bottle feeding and mixed feeding). The form also included information about immunization status of child (fully, partially and not immunized), birth order of child (first, second, and third or after) and hours number of use of smart devices by the affected child. An official agreement and facilitate letter were obtained from University of Karbala, College of Medicine to visit and collect data from autism caring centers, a , and primary a kindergartens schools of Babil Province. Information collected were treated with confidentiality during data collection and analysis, and names of the patients were replaced with identification numbers in order to protect their autonomy.







Figure-1: Distribution of fathers' occupation of the cases of the study.

Figure-2: Distribution of gender of the study.

Table	(1):	The	Association	between	the	cases	and	the	controls	regarding	the	gender,
reside	nce a	nd m	arital status	of parent	s in t	the stu	dy.					

variable	es	G	D voluo	
		Cases	Controls	I -value
	girls	11(18.3%)	27(38.6%)	
gender	boys	49(81.7%)	43(61.4%)	0.013
Rosidanca	urban	54(90%)	70(100%)	0.5
Keshuence	rural	6(10%)	0(0%)	0.5
	married	57(95%)	68(97.1)	
Marital status of	divorced	2(3.3%)	1(1.4%)	0.77
parents				
	widow	1(1.7%)	1(1.4%)	

P-value ≤ 0.05 (significant). Chi square test.

Table (2): Association between the cases and the controls regarding the father and mother educational status in the study.

	ariablas	(Groups		
v.	arradies	Cases	Controls	I -value	
	illiterate	0(0%)	1(1.4%)		
Father`s	primary	8(13.3%)	7(10%)		
education	secondary	11(18.3%)	33(47.1%)	0.002	
	college or insatiate	41(68.3%)	29(41.4%)		
Mother`s	illiterate	1(1.7%)	2(2.9%)	0.506	
education	primary	8(13.3%)	8(11.4%)	0.390	

secondary	13(21.7%)	22(31.4%)	
college or insatiate	38(63.3%)	38(54.3%)	

Table (3): Association between the cases and the controls regarding the parents occupation in the study.

vorial	Gr	P_valua			
vai iai	Cases	Controls	I -value		
	governmental	37(61.7%)	26(37.1%)		
Occupation of the father	employee			0.018	
Occupation of the father	Free work	16(26.7%)	28(40%)		
	military	7(11.7%)	16(22.9%)		
Occupation of the	Employee	28(46.7%)	38(54.3%)	0.245	
mother	Housewife	32(53.3%)	32(45.7%)	0.243	

Table (4): Association between the cases and the controls regarding the maternal diseases before and during the pregnancy in the study.

variable	a	Gi	D voluo	
variables	Cases	Controls	- r-value	
	Psychiatric	19(31.7%)	3(4.3%)	
Diseases before	illness			<0.001
pregnancy	Epilepsy	3(5%)	1(1.4%)	-0.001
	None	38(63.3%)	66(94.3%)	
	anemia	22(36.7%)	4(5.7%)	
	gestation DM	1(1.7%)	1(1.4%)	
Pregnancy diseases	infection	9(15.0%)	3(4.3%)	<0.001
	none	24(40.0%)	53(75.6%)	
	other	0(0.0%)	7(10.0%)	
	preeclampsia	4(6.6%)	2(2.9%)	

Von	ablas		Group		
vari	ables	Case	Control	r-value	
Drug use	No	54(90.0%)	68(97.1%)	0.14	
	Yes	6(10.0%)	2(2.9%)		
Exposure to toxin	No	58(96.7%)	70(100.0%)	0.21	
	Yes	2(3.3%)	0(0%)	0.21	
Gestational age	post term	6(10.0%)	1(1.4%)	0.027	

	preterm	2(3.3%)	0(0%)	
	term	52(86.7%)	69(98.6%)	
Type of delivery	Cesarean section	25(41.7%)	29(41.4%)	0.5
	Vaginal delivery	35(58.3%)	41(58.6%)	0.5
Place of delivery	hospital	53(88.3%)	66(94.3%)	0.224
	house	7(11.7%)	4(5.7%)	

Table(5): Association between the cases and the controls regarding (the drug use by mothers, exposure to toxin, gestational age, type and place of the delivery)in the study.

Table (6): Association between the cases and the controls regarding the child diseases after the delivery, feeding type, family history of autism, immunization status and birth order in the study.

	Gro	Р-			
		Case	Control	value	
	Prematurity	11(18.3%)	6(8.6%)		
	Physiological jaundice	8(13.3%)	8(11.4%)		
,	Acute respiratory distress	5(8.3%)	1(1.4%)		
History of child	syndrome			0.004	
Diseases after delivery	Pathological jaundice	4(6.7%)	1(1.4%)	0.004	
·	Congenital nervous sys. disease	3(5%)	0(0%)		
·	Congenital heart disease				
	None	27(45%)	54(77.1%)		
	bottle feeding	16(26.7%)	9(12.9%)		
Feeding type	breast feeding	24(40%)	32(45.7%)	0.13	
	mixed feeding	20(33.3%)	29(41.4%)		
Family history of	No	51(85.0%)	69(98.6%)		
autism	Yes	9(15.0%)	1(1.4%)	0.006	
	complete	51(85.0%)	65(92.9%)		
Immunization of the	9(15%)	5(7.1)	0.17		
child					
	first	18(30.0%)	28(40.0%)		
Birth order	second	19(31.7%)	22(31.4%)	0.4	
	third or after	23(38.3%)	20(28.6%)	1	

Variables	group	Mean±SD	P-value
Age of child	cases	5.8±2.01	0.006
	controls	6.8±2	
Age of mother during pregnancy	cases	28.5±5.2	0.35
	controls	27.7±5.3	
Age of father during pregnancy	cases	34.2±6.3	0.07
	controls	32.2±6.1	
Hours number of smart device	cases	3.2±2.5	0.018
use	controls	2.3±1.5	

Table (7): difference in mean of the (age of child, mother and father age at the time pregnancy with affected child, hours number of use smart devices by affected child) according to the cases and the controls in the study.

Discussion:

In the current study, the mean age of children with autism among cases was found to be 5.8 ± 2 years , and among controls was 6.8 ± 2 years ,female represented less than one-fifth of the total participants and most the cases were below 10 years age ,as it was observed that most of the children have to leave the centers between the age of 11-12 years to enter special schools because children at this age are not eligible to enter the schools and even if they are qualified ,many schools do not receive or accept them ,or they may be suffer from bullying problems from other children.

Analysis of the current data revealed that were a significant association between the gender and risk of autism .Among the 60 cases, the boys more affected than the girls ,there are (81%) of male and (18%) of female ,male :female ratio(4:1),which was consistent with the result of many studies were done in Tunis, Jorden and Malta (20),(21),(22).

Also ,the results of the present study showed that both Father's education and father's occupation were significantly associated with autism in children in cases from the controls. About two-thirds of the study participants had well-educated parents who were in college or institute and more than half of the fathers of the cases were governmental employees and half of the mothers were housewives .The result is supported by a study in Arabia Saudi Kingdom and other study in United State there were founded that the parents with high education and occupation ,have better access to ASD services and receive diagnosis earlier (23),(24). This may explian,that the parents of high educational status and governmental employees were spent less time with their children , or discover them by chance or may be due to sample size of this study.

The current study showed no significant association between paternal age and risk of autism among the cases and the controls. This result was different from many studies that demonstrated the higher risk for ASD were linked to either parent's advanced age (25),(26),(27). This might be explained because of variation in cultures, traditions, values and the important cause in our society is the early marriage in Iraq or due to small sample size.

It was found in this study, a significant association between risk of autism and the frequency of maternal diseases before pregnancy especially psychiatric illness (anxiety& depression) and epilepsy, were found in more than one third of the cases mothers while is about less than 6% of

controls mothers ,which agreement with many studies ,as in Australian study was Mothers of children with ASD had a higher prevalence of preexisting psychiatric conditions than other mothers(28), other study in the United State (29) and study in Baghdad had another similar finding (30).

In this study, also there was strong association between the risk of having autism and the pregnancy diseases (anemia ,gestational diabetes mellitus ,infection and preeclampsia), found that more than half among the cases mothers ,while less than one quarter among the controls mothers ,which is consistent with a study in United State that showed a positive relationship between diabetes and hypertension with the development of autism(31), also according to new study in United State found linkage between preeclampsia and risk of autism (16).

On the basis of observed datd, there is association between gestational age (preterm <37weeks and post term more than 42 weeks) and autism, which resulted highly percentage which about 13.3% in cases and about 1.4 % in controls. Supporting reports from Netherlands, Prevalence of post-term birth was more than three times higher in autistic children and adolescents compared to the general population, while prevalence of preterm birth was 1.5 times higher (11.56 in autism, 7.59 in comparison) (32).

In the current study, there was a significant association between the history of child diseases after the delivery and the risk of autism (jaundice both pathological and physiological, acute respiratory distress syndrom, congintal nervous system diseases and congenital heart diseases), which represented more than half of the study sample among cases, whereas represented one third among controls. Studies in France ,India and Denmark founded association between neonatal jaundice and autism (33),(27),(34).on the other hand in Palestine a case-control study founded relation between infant problems and autism, like respiratory infection, epilepsy and birth hypoxia with the exception of jaundice , which became insignificant(17). This differences among studies may be to sample size. In this study, there is an apparent increase in the risk of autism associated with family history of autism, which is about 15% among the cases and about 1.4% among the controls, may explain genetics role of autism , which is in agreement with Indian a populationbased case-control study that found a strong association between autism and family history of The analysis of the current data, concluded that significant association regarding autism (13). the hours of use of smart devices and the risk of autism ,child who use smart devices more .. A study in Republic of South Korea, revealed that the negative effects of smart devices on language during first three years of life of child (35), another studies in Bangladesh and United States show significant relation to developing of the autism with use of smart devices(19),(36). The American Academy of Pediatrics (AAP) advises against allowing children aged 2 and older to watch for longer than 1 to2 hours per day. Children under 2 should not watch anything at all.

Conclusions: There are a certain parental and child factors are increase risk of autism including gender boys ,father education (college or institute) and occupation of father(governmental employee) ,maternal diseases before pregnancy which include psychiatric illness (anxiety and depression) and mental disorders like epilepsy, diseases during pregnancy as anemia ,gestational diabetes mellitus ,infection ,preeclampsia, preterm and post term gestational age, child diseases

after birth like prematurity ,physiological and pathological jaundice ,respiratory distress syndrome ,congenital nervous system diseases, and congenital heart diseases ,family history of autism and use of the smart devices by the child.

Recommendations:

Efforts should concentrate on improving community awareness of Autism Spectrum Disorders to encourage early consultation and diagnosis. Mothers must avoid from occupational and mental stress since it directly affects the health of the fetus. will expose their children to a variety of learning and mental problems, such as autism, by tolerating mental strains such family issues, unpleasant living situations, financial difficulties, and loneliness. Parent must be spent more time with their children ,even share them in activities such as exercise in open air. Further studies in other governorates of Iraq are recommended in order to draw on epidemiological map of autism which will help tackle the problem by concentrating on governorate which have higher rate of autism. Governmental agenesis, especially Minstery of Education must provide special schools for children with autism because increasing the prevalence among kids.

Limitations: The parents were uncooperative because of the generally social stigma of the disease of their children . In Babil Governorate ,no recorded data about autistic people. So this study was applied on children who attended to the autistic centers lead to small sample size.

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