

Risk factors for autism in Baghdad city

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ABSTRACT

Background: Autism is a complex developmental disability that typically appears during the first three years of life. Autism affects the normal development of the brain in the areas of social interaction and communication skills.

Objectives: To identify risk factors for Autism among a sample of autistic children in Baghdad city.

Type of the study: this is a case - control, study.

Methods: This study was conducted during the period of data collection extended from first of November 2010 until the first of April 2011, The total number of children involved was 100 children with diagnosis of autism. Hundred children who are free from autism were taken as the control sample.

Results: there was a significant association between paternal age and the risk for autism, fathers older than 40 years had 11 times increased risk of having an offspring with autism, ($p=0.043$). Psychological problems, showed a statistically increased risk of autism associated with maternal history of (maternal unhappy emotional state), the odds ratio of this risk factor was

seven ($p=0.01$). Post term (14% in cases vs. 2% in controls) ($P=0.005$, OR 8.80) and neonatal jaundice (30% in cases and 11% in controls) ($P=0.001$, OR 3.71) were significantly associated with autism. Bottle-feeding showed the highest significant associations with risk of autism ($p=0.004$, OR=2.84).

Conclusion: Autism has many associated risk factors like paternal age (fathers older than 40 years), psychological problems (maternal unhappy emotional state), post term, neonatal jaundice and bottle-feeding

Key words: Autism, Risk factors, developmental disability, social interaction, communication skills, Post term.

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Autistic disorder (AD) is a chronic neurodevelopmental disorder. Some parents report regression in their children or a loss of previously acquired skills with the subsequent development of AD [1, 2, 3, and 4]. In most cases, the cause of AD is unknown. Awareness of autism has increased in recent years because of increased media coverage and a rapidly expanding body of knowledge. The incidence of diagnosed autism in the United States has reached staggering proportions. According to the Centers for Disease Control (2006), autism prevalence is 1:91 live births [5, 6, and 7]. Etiologic hypotheses in autism suggest a strong genetic component, as well as possible environmental risks linked to early fetal development [8]. Many factors have been identified to be associated with increased risk for autism like: paternal and maternal smoking, higher and lower maternal education, threatened abortion before 20 weeks, bleeding during pregnancy, pregnancy-induced hypertension; The mean number of autoimmune disorders was greater in families with autism; [9]

Advanced maternal and paternal ages are independently associated with AD risk [10]. People with autism, have a strong family history of schizophrenia and bipolar disorder [7].

The objectives of the study are to identify risk factors for AD among a sample of autistic children in Baghdad city.

Patients and Methods

This is a case - control study, which was conducted. The period of data collection extended from the 1st of November 2010 till the 1st of April 2011. The study was carried out in three private Specialized Educational Institutions for Autistic children (Rami, Al-Rahman and Al-Nehal) and two outpatient clinics in child central teaching hospital, and Ibn Rushd in Baghdad. The total

number of children involved was 100 children with diagnosis of autism. Age ranging from 3-15 years old. 100 children who are free from autism as the control sample, was drawn from the primary health care center (Al-dhubat) near Ibn Rushd teaching hospital and from the vaccination unit and dental unit of the outpatient clinic of child central teaching hospital. Data collection was made by a questionnaire and information's were collected from parent, (SPSS 18) used for data analysis. The Ministry Of Health in Iraq approved the study protocol.

Results

Among the 100 cases, there are (77%) males and (23%) females in cases group, male: female ratio (3.3:1).

Table (1) demonstrates a significant association between paternal age and the risk for autism, fathers older than 40 years had 11 times increased risk of having an offspring with autism, was statistically significant ($p=0.043$)

There was no association between maternal age and risk of autism ($p=0.99$)

Consanguineous marriage, history of infertility, spacing between children and twin pregnancy were not significant predictors of autism risk.

History of assisted pregnancy for both mother and father was significantly associated with autism (OR = 3.07, $P=0.039$).

Table (2) summarizes the findings of maternal conditions during gestation, the strongest of these was psychological problems, showed a statistically increased risk of autism associated with maternal history of (maternal unhappy emotional state), the odds ratio of this risk factor was 7 ($p=0.01$), while no statistically significant association was found between autism and hypertension, diabetes, bleeding, fever, Rh incompatibility and x-Ray exposure.

Table (3) shows that abnormal gestational age including preterm (12% in cases vs. 5% in controls) (P=0.047, OR3.02) and postterm (14% in cases vs. 2% in controls) (P=0.005, OR 8.80) and neonatal jaundice (30% in cases and 11% in controls) (P=0.001, OR 3.71) were significantly associated with autism. When we restricted the analysis to children born at term (cases and associated controls), the risk of autism remained higher for children who were postterm delivery. No statistically significant associations were found between autism and mode of delivery, place of birth and some problems after birth (cyanosis, phototherapy). Table (4) shows that second born of birth was 2.77 time more likely to develop autism. No significant associations were found for intrauterine exposure to cigarette smoking and marital status.

There were no findings of increased risk of autism regarding immunization status, (88.0%) case-children and control children had similar exposures to vaccine. Bottle-feeding showed the most number of significant associations with risk of autism (p=0.004, OR=2.84). There was an increase in risk of autism with both paternal age and maternal education, an increased risk of autism for children whose mothers (diploma or higher 58%) had more years of education than mothers of children in the control group (12%). Unemployment among mothers looks to be protective against autism (p=0.000, OR: 0.18). Table (5) demonstrates autistic children with family history of autism and other diseases. This study found that Significant association between family history of diabetes and autism (6%, p=0.02, OR=0.32).

Table (1): Distribution of factors associated with pregnancy

Variables	Autism	Control		OR[95%CI]
	100.0%	100.0%	P	
Maternal Age (year)				
< 20	0.0	11.0	---	---
20-24	12.0	24.0	0.999	----
25-29	28.0	37.0	0.999	-----
30-34	20.0	18.0	0.999	----
35-39	27.0	10.0	0.999	----
40 -	13.0	0.0	0.998	----
Paternal Age (year)				
< 20	1.0	3.0	---	---
20-24	0.0	10.0	0.999	---
25-29	7.0	31.0	0.751	0.68 [0.06,7.52]
30-34	13.0	22.0	0.635	1.77 [0.17,18.87]
35-39	30.0	21.0	0.221	4.29[0.42,44.09]
40 -	49.0	13.0	0.043	11.31[1.08,117.90]
Parents Consanguinity	39.0	51.0	0.089	1.63[0.93,2.85]
Assisted Pregnancy				
None	92.0	84.0	---	---
Mother	5.0	14.0	0.999	0.33[0.11, 0.94]
Father	2.0	0.0	0.800	1.40[0.10,19.01]
Both Parents	1.0	2.0	0.039	3.07[1.06,8.88]
Spacing < 2 years	0.3	0.3	0.274	1.41[0.76,2.62]
Twin Pregnancy	3.0	0.0	0.999	-----

Table (2): Distribution of maternal problems occurred during pregnancy.

Pregnancy Problems	Autism		Control		P	OR[95%CI]
	100.0%		100.0%			
None	61.0		74.0		---	---
Hypertension	1.0		3.0		0.438	0.40[0.04,3.99]
Diabetes	2.0		1.0		0.474	2.43[0.21,27.40]
Bleeding	5.0		8.0		0.642	0.76[0.24,2.44]
Fever	2.0		1.0		0.474	2.43[0.21,27.40]
Incident	1.0		0.0		1.000	*** [***, ***]
Anemia	8.0		6.0		0.396	1.62[0.53,4.92]
maternal unhappy emotional state	12.0		2.0		0.011	7.28[1.57,33.78]
Rh Incompatibility	3.0		2.0		0.519	1.82[0.29,11.24]

Table (3): Distribution of factors associated with birth and after birth

Variables	Autism		Control		P	OR[95%CI]
	100.0%		100.0%			
Gestational Age						
Term	74.0		93.0		---	---
Preterm	12.0		5.0		0.047	3.02[1.02,8.94]
Post-term	14.0		2.0		0.005	8.80[1.94,39.93]
Mode of Delivery						
Normal Vaginal	55.0		67.0		---	---
Caesarian	41.0		33.0		0.162	1.51[0.85,2.71]
Assisted Vaginal	4.0		0.0		0.999	---
Place of Birth						
Hospital	85.0		77.0		---	---
Home	15.0		23.0		0.152	0.59[0.29,1.21]
Problems After Birth						
None	58.0		79.0		---	---
Jaundice	30.0		11.0		0.001	3.71[1.72,8.02]
Cyanosis	5.0		0.0		0.999	
Phototherapy	0.0		1.0		1.000	

Table (4): Distribution of social and environmental factors

Variables	Autism	Control		
	100.0%	100.0%	P	OR[95%CI]
Birth Order				
First	14.0%	26.0%	---	---
<i>Second</i>	67.0%	45.0%	0.008	2.77[1.30,5.86]
Third or After	19.0%	29.0%	0.658	1.22[0.51,2.90]
Intrauterine exposure to cigarette smoke				
None	52.0%	47.0%	---	---
Maternal & Passive	0.0%	1.0%	1.000	
Maternal	1.0%	3.0%	1.000	0.30[0.03, 3.00]
Passive	47.0%	49.0%	1.000	0.87[0.49, 1.52]
Feeding Type after birth				
Breast Feeding	28.0%	46.0%	---	---
<i>Bottle Feeding</i>	38.0%	22.0%	0.004	2.84[1.40,5.74]
Mixed	34.0%	32.0%	0.105	1.75[0.89,3.42]
Immunization Status				
Fully Immunized	88.0%	88.0%	---	---
Partially Immunized	9.0%	10.0%	0.828	0.90[0.35,2.32]
Not Immunized	3.0%	2.0%	0.661	1.50[0.24,9.29]

Table 4: continue....

Marital Status				
Live Together	92.0%	88.0%	---	---
Separated/Divorced	4.0%	5.0%	0.697	0.77[0.21,2.94]
Death of a Parent	4.0%	7.0%	0.348	0.55[0.15,1.93]
Maternal Education				
<i>Diploma or Higher</i>	<i>58.0%</i>	<i>12.0%</i>	---	---
Secondary	31.0%	20.0%	0.008	0.32[0.14,0.74]
Intermediate	6.0%	34.0%	0.000	0.04[0.01,0.11]
Primary	5.0%	25.0%	0.000	0.04[0.01,0.13]
Read & Write	.0%	5.0%	0.999	----
Illiterate	.0%	4.0%	0.999	----
Paternal Education				
Diploma or Higher	62.0%	27.0%	---	---
Secondary	29.0%	16.0%	0.541	0.79[0.37,1.69]
Intermediate	5.0%	28.0%	0.000	0.08[0.03,0.22]
Primary	3.0%	18.0%	0.000	0.7[0.02,0.27]
Read & Write	1.0%	7.0%	0.011	0.00[0.00, **]
Illiterate	0.0%	4.0%	0.999	----
Unemployment				
<i>Maternal</i>	<i>53.0%</i>	<i>86.0%</i>	<i>0.000</i>	<i>0.18[0.09,0.37]</i>
Paternal	7.0%	4.0%	0.358	1.81[0.51,6.38]

Table (5) : Distribution of positive family history of medical problems

Variables	Autism	Control		
	100.0%	100.0%	P	OR[95%CI]
Type of Family History				
None	70.0	74.0	---	---
Autism	8.0	0.0	0.999	
Diabetes	6.0	20.0	0.020	0.32[0.12,0.84]
Hypothyroid	3.0	2.0	0.619	1.59[0.26,9.78]
Rh Incompatibility	3.0	2.0	0.619	1.59[0.26,9.78]
Systemic Lupus Erythematosus	1.0	0.0	1.000	---
Asthma	0.0	1.0	1.000	---
Hypertension	1.0	0.0	1.000	---

DISCUSSION

Sasanfare *et al* (2010)^[11] found a significant association between higher paternal age, but not maternal age, and an increasing risk of autism this was approved by this study too.

This may be explained by germ line mutations responsible, at least in part, for this association. It is possible that the accumulated exposure to various environmental toxins over the life-course could result in germline alterations in older men, given that several environmental toxins have been shown in mice to induce germline mutations, DNA damage, and global hyper methylation Lundstro S. *et al* (2010)^[12] it is highly plausible that such changes could increase with age via cumulative exposure and thus be more prevalent in older fathers:

In contrast in Western Australia, children of mothers aged 30-34 years or 35 years or more were found to have an elevated risk for autism compared with children of mothers aged 25-29 years; older paternal age was not a significant risk factor in this population Glasson EJ, *et al* (2004)^[13]. The number of sample was limited in this study, so the researcher was unable to consider maternal age related to the risk of autism compared to previous studies.

In this study, it was found that autism is 3.07 times likely to be associated with assisted pregnancy (both parents) than control.

Greater risk of infertility and exposure to assisted reproductive technologies, could increase the risk of atypical fetal brain development.

Grether J K, *et al* (2009)^[14] Kinney *et al* (2008)^[15] found associations between these technologies and adverse pregnancy outcomes, including those due to epigenetic effects.

The current study found that maternal unhappy emotional state during pregnancy, have a higher rates of obstetric and neonatal complications that influence early brain development, resulting in abnormal neurologic development and increased risk of autistic disorders. It has been reported that prenatal stress or exposure to environmental or social stressors including family problems is associated with increased autism risk Kinney *et al* (2008)^[15]; O'Donnell *et al* (2009)^[16]. Previous research in China revealed that more than 44% of mothers of autistic children experienced emotional nervousness, anxiety, or depression during pregnancy, Xucqet *et al* (2005)^[17]. (Wallace *et al* 2008)^[18] also found maternal depression to be associated with autism. The researcher hypothesize maternal unhappy mood during pregnancy may increase the level of hormones such as adrenalin in a mother's body, causing placental vasoconstriction which may affect fetal cerebral blood flow, or directly affect fetal hormone levels, with a negative impact on fetal development. The present investigations provide clues for further study in this area Postava K C, *et al* (2011)^[19].

Both gestational age preterm (less than 37 weeks) and posterm (more than 42 weeks) were considered as abnormal, and have a significant association with risk for autism. Supporting reports from Sweden, including, associations between intrauterine disturbances and autism, it is unknown whether the disturbances may

directly compromise the fetus and result in autism or whether they reflect the effects of a fetus compromised by other factors recorded by Larsson *et al* (2005)^[20]. Other investigations have suggested that the association may be due to either a genetic vulnerability to both autism and adverse pregnancy outcome. Hultman *et al* (2002)^[21] showed that postterm delivery was a risk factor for autism.

The current study also indicated that jaundice in the neonatal period could increase the risk of autistic disorders. There are a number of neonatal complications in preterm infants that may affect brain development and the risk of autistic disorders Eichenwald EC, *et al* (2008)^[22].

In this study, bottle-feeding showed the highest number of significant association with risk of autism. We did not find a previous study agree with or disagree with the result of this study.

So we can say an intense interaction needed between child and mother or autism is caused, mainly, by deficiencies in the psychological interaction with the newborn during the breast-feeding.

In this study, apparent increase in autism risk associated with higher levels of maternal education, which is in agreement with Durkin M S. *et al* (2008)^[23], the tendency to have higher levels of educational achievement and resources than other parents could further contribute to increased awareness and an expansion of the diagnosis of autism.

The same result explained by Sasanfar *et al* (2010)^[11]. they found that, the more highly educated parents may have been more aware to their affected children. Bolton PF, *et al* (1997)^[24] found those with lower education may have been less aware to their affected children.

Unemployment among mothers looks to be protective against autism, we did not find a previous study agree with or disagree with the result of this study. This may be explained by that the maternal workplace may be an important source of exposures to both illnesses and toxins like pesticides, and asbestos in many facilities.

This study found that (8%) of autistic children had family history of autism, and (5%) of patients had family history of psychological problem this, may explain genetic role for autism. Many other studies done by each of Gillberg C. *et al* (1998)^[25], Schroer RJ, *et al* (1998)^[26] and Cook EH, *et al* (1998)^[27] suggest that autism have strong genetic base.

Significant association between family history of diabetes and autism (6%, $p=0.02$, $OR=0.32$) has been found in the present study. A previous finding study confirmed increased risk of autism for children with a family history of diabetes Mouridsen SE *et al* (2007)^[28], suggesting a common genetic factor.

Conclusions:

Autism has many associated risk factors that has been studied thoroughly in many parts of the world and some of them exist in Iraq samples and has similar picture. Paternal age and birth order were associated with autism.

Psychological problems (maternal unhappy emotional state) during gestation, a postterm and jaundiced infants that may affect brain development and the risk of autism. Bottle-feeding had significant association with risk of autism.

Apparent increase in autism risk associated with higher levels of maternal education. Concerning increased risk of autism for children with a family history of psychological problem and diabetes.

Recommendations:

- 1-Increase awareness of the Iraqi families through the media about the symptoms and risk factors for autism.
- 2- family physicians should be looking for autism early in infancy, and screening during pediatric well-child visits.
- 3- Parents with strong family history of autism or psychological problems should be counseled about the risk of autism.
- 4-recommend for continuing breastfeeding each visit to the primary health care center.
- 5-Further studies should conduct on risk factors for autism in Iraq.

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