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Autism spectrum disorder in relation to associated factors of children in salah-addin province: Iraq

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Abstract
Background: Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by deficits in social communication and the presence of restricted interests and repetitive behaviors.
Rising prevalence of autism spectrum disorders (ASD) in the last decades has led research to focus on the diagnosis and identification of factors associated with ASD. This paper sought for possible factors that put children at risk for ASD. In this study, we investigated the association between ASD and child factors in Iraqi people.
Aim of the study: To assess the relationship and estimate the effect of child risk factors with the development of autism spectrum disorders among Iraqi children in Salah-addin city.
Methods: An observational case-control study involving 180 children (90 autistic children and 90 healthy children), was conducted in salah-addin city through the period (from 15 Nov. 2021 to 20 march 2022), using Arabic language interviewer administered questionnaire through direct interview and the collected data was measured using chi-square and represented by a suitable tables and figures.
Results: The study shows that among 90 autistic child 81% (73) children were male in gender and 61% (55) children were diagnosed between (3-6) years of age. The study found that 68.2% (62) children have a positive family history for development of ASD.
Conclusions: Most of affected children are male and two third of them diagnosed at ages between (3-6) years. Family history of autism was common among the autistic children.

Keywords: Autism, disorder, child factors

Introduction
Autism spectrum disorder (ASD) is a lifelong condition that is being viewed increasingly as an example of neurological and cognitive variation among people. It is clinically very heterogeneous. It is associated with disabilities and everyday challenges, but may also be associated with cognitive strengths and talents [1].
Children and adults with ASD have social communication and interaction difficulties and show restricted, repetitive, and stereotyped patterns of behaviors, interests or activities. [2]
Social communication impairments and ASD behaviors are present during early childhood, but May only become manifest later.
ASD is a genetic disorder of brain development, but non-genetic factors are also likely to contribute to the phenotype and its heterogeneity [2].
Between the ages of 6 and 12 months, children with ASD may experience an expansion of cortical surface area, followed by exaggerated global overgrowth between the ages of 12 and 24 months, compared with their non-affected peers. Brain volume remains larger on average, compared with peers, until the age of 4; in particular, the amygdala, frontal cortex, and temporal cortex. However by school age, brain growth slows down in most children with ASD and by around 10 to 15 years, brain volume becomes similar to that of children without ASD [3, 4].
Regarding to child factors most of studies found that the mean age of diagnosis is 2-3 years of age when the child start to react with the surrounding environment [5, 26].
Boys are more frequently affected than girls (4:1) [6]. However, the extent to which this difference in reported prevalence is due to relative under-diagnosis in girls and women is unclear.

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For 2016, across all 11 sites, ASD prevalence was 18.5 per 1,000 (one in 54) children aged 8 years, and ASD was 4.3 times as prevalent among boys as among girls.

Among children with ASD for whom data on intellectual or cognitive functioning were available, 33% were classified as having intellectual disability (intelligence quotient [IQ] ≤70); this percentage was higher among girls than boys (40% versus 32%).

ASD in girls and women is consistently under-reported relative to male

Although the evidence base on sex-based differences is still in its early stages, the following has been suggested:

- Females may have more of a desire for social contact, friendships, and peer group acceptance than males.
- Girls with ASD may be more able to mask social play deficits by imitating non-affected peers [7, 27].
- Girls' interests may be in more socially typical domains than male interests (e.g., literature or music).
- Females may show less impairment in theory of mind tasks than males.
- Females may be more likely to present with eating disorders than males.

Birth order/parity and ASD has been studied since early 1980s. Tsai and Stewart (1983) reported significant relationship between the risk of developing autism and parity, high risk in firstborn in smaller sib ship and high risk in fourth-or-later born in large sib ship. A meta-analysis done in 2009, showed significant relationship between birth order/parity and risk of autism; 61% increase in risk of ASD among the first-born children compared with children born third or later [8, 28, 29].

Family studies found that ASD aggregates in families and early twin studies estimated the proportion of the phenotype variance due to genetic factors (the heritability), to be about 90% 2-6, making it the most heritable of all developmental disorders. As a consequence, etiological research in ASD, focus predominantly on genetic factors 7. While recent twin studies support high heritability 5, 6 a large twin study 7 indicated substantial role for shared environmental influences. Results of family studies also raise questions about the relative influence of genetic factors 8 and contribute to uncertainty regarding the etiology of ASD [9].

Clarifying etiologic factors is crucial for guiding future research. Twin studies have the potential to inform the relative contributions of genetic and environment factors to ASD etiology (Ronald and Hoekstra 2011). Early twin studies supported a strong genetic etiology to ASD. More recent diagnostic concordance studies have confirmed high monozygotic concordance for ASD (>88%), but also higher than previously appreciated dizygotic (>30%) and sibling (>15%) concordance rates. Observations of high dizygotic concordance have raised the prospect of non-trivial environmental contributions to ASD. A recent study by Hallmayer and colleagues, using a large, carefully ascertained ASD-affected twin sample, identified a substantial environmental contribution to ASD diagnosis (~58%), although other studies have found minimal shared environmental effects [10, 30].

Subjects and Methods

The current study is an observation a quantitative case-control study (autism spectrum disorder in relation to associated factors of children) which is conducted in Salah-addin regions of Iraq in both rural and urban areas. The first mission of the study started on 15/Nov/2021 until the project has finished on 20/march/2022.

A convenient sample which has been used to enroll 180 (90 autistic child and 90 healthy child) of similar demographic and socioeconomic status.

The data was collected by interviewer administered questionnaire.

The questionnaire contained closed-ended questions and was include:

Child factors: age, gender, birth order, family history.

Data analysis done by manual statistical methods. All results will have been represented by a suitable tables, charts and figures.

The descriptive analysis focused on frequencies and percentages while chi-square was utilized to determine the differences between variables. A P-value of less than 0.05 was considered statistically significant. Odd ratio was used for assessment of risk.

Ethical approval

Ethical approval for the study protocol, questions and consent statement was granted by the Ethics Committee at the University of TIKRIT.

Pilot study

Approximately the same questionnaire had tested on small sample size. Therefore, we knew that the main study is feasible with close monitoring to neglecting weak responses.

Budget

Our study is very low cost due to its case control type.

Results
The frequency of autistic and healthy children according to age group

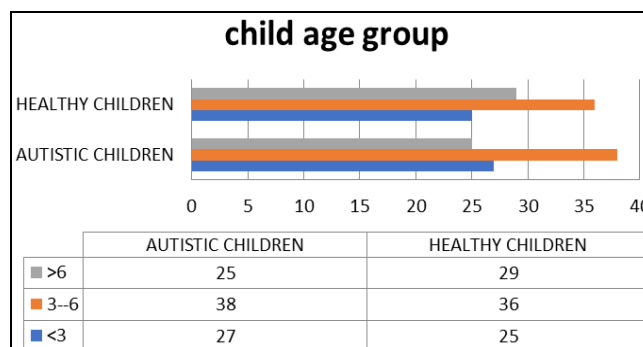|	AUTISTIC CHILDREN	HEALTHY CHILDREN
>6	25	29
3--6	38	36
<3	27	25

Fig 1: The frequency of autistic and healthy children according to age group

Showing that the study include (25 autistic child and 29 healthy child under 3 years of age, 38 autistic and 36 healthy children between 3 to 6 years of age, 27 autistic and 25 healthy children above 6 years of age

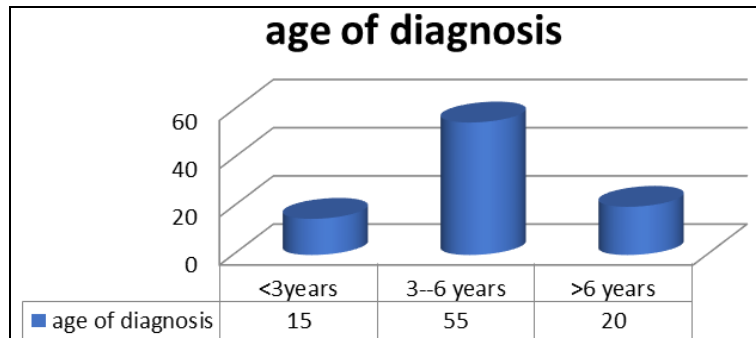**Assessment of relationship between the frequency of autism and child age**

Fig 2: The frequency of autistic children according to the age of diagnosis. Showing that 16% (15) of autistic child were diagnosed at age under 3 years, 61% (55) between 3 and 6 years of age, 23% (20) at age above 6 years

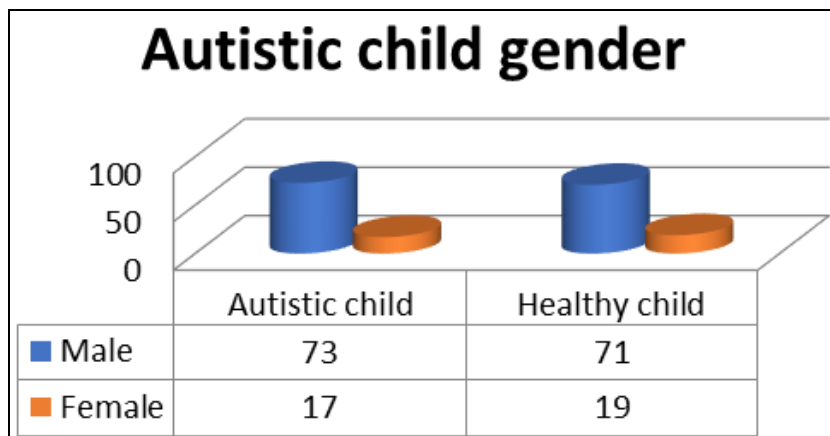**Assessment of relationship between the frequency of autism and child group**

Fig 3: The frequency of autistic child according to the gender

It was found that 73 (81%) of autistic children were male while only 17 (19%) were females, similar gender proportions were taken for control groups.

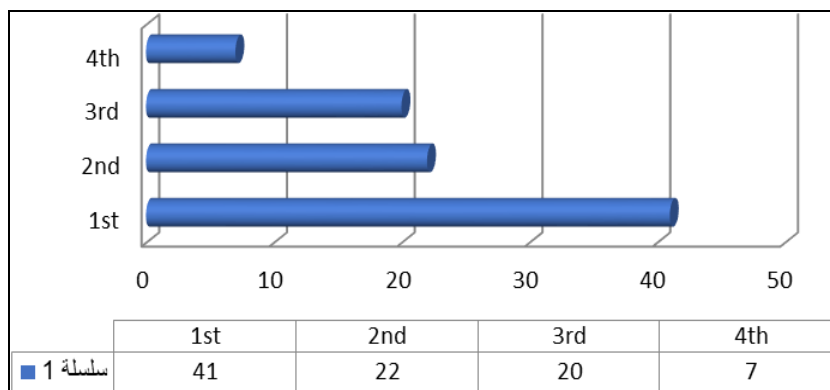**Assessment of relationship between the frequency of autism and child sequence**

Fig 4: The frequency of autistic child in relation to child sequence

Showing that 45% (41) of autistic children were the first in order, 24.4% (22) of second order, 22.2% (20) third order and the remaining 8% of fourth order or more.

Assessment of relationship between the frequency of autism and child family history

Table 1: The frequency of autism in relation to child family history

Family history	Health status	Autistic child	Healthy child	Total
Positive family history	1st degree	14 (15%)	2 (2.2%)	98
	2nd Degree	15 (16.6%)	10 (11.1%)	
	3rd Degree	33 (36.6%)	24 (26.6%)	
Negative family history		28 (31.8%)	54 (60.1%)	82
Total		90	90	180

Showing that 62 (68.2%) of autistic children were with positive family history at different degrees while 36(29.9%) of healthy children have a positive family history. The chi-square is 15.1419, the P value is 0.0001. The result is significant at p value < 0.05.odd ratio 3.32

Discussion
The current study is a case-control study was conducted among 180 children, 90 of them are autistic children opposite to 90 healthy children as a control group from TIKRIT city in Iraq in order to assess the relationship between children risk factors with the development of autism spectrum disorder. Therefore the study take several child factor such as age of diagnosis, gender, family history and child sequence as aspects of discussion.

In order to estimate the average age of diagnosis, both autistic children (cases) and healthy children (control) were divided into similar age groups, first group including those with age of less than 3 years (including 13 autistic children and 20 healthy children, the second and third groups were of 3-6 years (46 autistic children and 41 healthy children) and more than 6 years old (31 autistic children and 29 healthy children) respectively. The present study found that the largest portion of autistic children represented by 61% (55) children were diagnosed at ages between 3 to 6 years old, a smaller portion of 16% (15) children diagnosed under age of 3 years while 23% (20) children after 6 years of age.

This appears to be partially due to the high percent of children who take in age groups of 3-6 years old in comparison to only a small portion (13) below age of 3 years and at another hand most of child behavioral changes that take parents attention will be more obvious at these ages, matter who make parent visit a clinic to assess the child health to end finally with the diagnosis of ASD in this child.

By comparison with another study done in Pennsylvania among 969 children, it was found that the average age of diagnosis is 3.1 years [11-14].

This study also found that early diagnosis of autism spectrum disorders (ASD) is critical for a number of reasons, perhaps most important because interventions to improve the functioning of children with ASD may be more effective with younger children. 3–6 Evidence suggests that early treatment optimizes long-term prognosis [41] and treatment yields diminishing returns as children get older. 8 Several studies have estimated that the gains in functioning associated with early treatment will result in considerable cost savings to both families of children with ASD and the systems in which they are served [15-17].

Regarding to child gender, the result was highly significant as the present study found that 81% (73) of the affected children were male while the remaining 19% (17) were female, a similar gender proportions were taken for control group.

Other studies results pointed to the higher risk of autism in males than females with ratio of 5:1. This finding was consistent with that reported by several studies carried out in Iraq and other Arab Gulf Countries showing male predilection and there is no evidence to date that explains this finding [14, 15]. One possible reason is that female children are more able to mask their behavioral difficulties than males. Moreover, culture in developing countries may be a contributing factor, as some families may pay more attention to the development of male children compared with females. As the burden of reporting cases falls on parents; there could be a lack of detection or lack of willingness to report certain behavior exhibited by a female child [18-21].

To evaluate the relationship between the child sequence and the development of autism, the study found that the highest percentage was for the first child with 45% (41) children, this probably due to the early age of gestation in most of mothers which is in general associated with more complication of pregnancy and poor outcomes. Second order children represent 24.4% (22) children, 22.2% (20) children for third order while only 8% (7) children of 4th order or more. This result indicate that the higher the parity the lowest chance to have an autistic child another study suggest that the factor that was most commonly associated with the risk of autism in the literature was birth order. Nine studies reported a significant relationship between birth order/parity and autism [22-25].

Factors that may affect the development of many diseases, in order to estimate its effect in the development of autism the present study found that 68.2% (62) of the autistic children have a family history of autism in comparison with only 29.9% (36) of healthy children have a family history of autism. Surprisingly, the study found that the third degree relative with history of autism take the highest percentage with 36.6%, 16.6% for second degree while only 15% for first degree relatives. This results actually need for further studying and explanation to evaluate the family history effect in more detailed method.

Limitations of the study
Type of the study (case-control) make it a more complex and the work team have to work hardly collect a control group of healthy children of similar age groups and socioeconomic status. Other problems including difficulty to collect the samples through direct interview and poor response from families as many of them find it as a social stigma to have an autistic child.

Conclusions
1. The study found that most of the affected children were male gender, 61% of them diagnosed at age between 3-6 years and 41% had a 1st sequence.
2. The study found that about two third of the affected

children has a positive family history for autism, at different degrees and the third degree relation was more significant.

Recommendations

1. To family

- Children with substantial risk factors such as male gender should be offered for regular pediatrician visits to check for normal psychiatric development.
- Strict monitoring of her child for abnormal behavioral change early in life such as repetitive crying, repetitive words or actions and introvert behaviors early diagnosis associated with better outcome.

2. To gynecologist and pediatricians

- Monitoring for mother factors at risk pregnancy such as abnormal placenta implantation, early age pregnancy and gestational disease (diabetes and hypertension.

3. For researcher

- To more detailed and wider studying of the effect of maternal diabetes family history - at different degrees - on the development of ASD.

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