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ASSOCIATION BETWEEN AUTISM SPECTRUM DISORDER AND MULTIPLE FACTORS INCLUDING CONSANGUINEOUS MARRIAGE, A STUDY DONE IN AL MADINA, SAUDI ARABIA

Abdulhadi Almazroea[1], Abdulrahman Sulaiman Alhazmi [2], Mansour Nasser Alqahtani [2], Yasser Salman AlMohammedi [2], Abdullah Mohammed almohammadi [2], Meyasser Mohammed Olfat [2], Osama Awadh Alharbi [2], Omar sami aljohani [2], Yasser Abdulsalam Alquliti [2], Anas yousef Alharbi [2], Maged Abdullah aljabri [2], Mohammed khaled almolhis [2].

[1]Consultant and Associate Professor,General Pediatric,Medical College,Taibah University.,
[2]Bachelor of Medicine, Bachelor of Surgery ,Taibah University , Madina, Saudi Arabia.

Abstract:

Background: *Autism is a disease that results in abnormal biologically determined and emotional contact with others. Social abnormalities and limited interest characterize autism. Autism prevalence varies in different regions in the world. There are several risk factors for autism including pregnancy complications and parental preconception.*

Aim: *To investigate the prevalence, associated factors and risk factors of autism.*

Method: *This study is a case-control study that was conducted during the period from December 2017 to March 2018 in Hospitals and medical centers in Al-Madinah, Saudi Arabia. The data were collected using a questionnaire during face to face interview.*

Results: *Autism prevalence was 50%, factors associated with autism prevalence included nationality (P-value=0.000), children age (P-value=0.000), children gender (P-value=0.000), Rank of children (P-value=0.033), mothers' age (P-value=0.007) and fathers' age (P-value=0.001). Family history of autism was significant associated risk factor (P-value=0.001).*

Conclusion: *There was high prevalence of autism among children and there were associated factors related to parents and children. The family history for autism was the only risk factor.*

Keywords: *Autism, Risk factors, Autism prevalence, Saudi Arabia.*

Corresponding author:

Abdulrahman Sulaiman Alhazmi,
E-mail: as.alhazmi@hotmail.com,
Bachelor of Medicine, Bachelor of Surgery,
Taibah University, Madina, Saudi Arabia.

QR code

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INTRODUCTION:

Autism is an innate disability to make normal biologically determined and emotional contact with others [1]. Autism is a chronic disease, its onset is before three years of age and it is characterized by language abnormalities, common abnormalities, limited interest, persistence on sameness and stereotyped repetitive behavior patterns [2,3]. Autism prevalence varies in different regions in the world [4]. The prevalence of autism is increasing as it was noted during the past four decades [5], with more prevalence among male than female with a ratio of 4.3:1 [6]. The prevalence ranges from 0.07% to 1.8% [7,8]. In 2010, autism prevalence was estimated by Autism and Developmental Disabilities Monitoring (ADDM) to be 14.7/1000children among 8 year old children [9]. In 2013 in Saudi Arabia, the prevalence was 0.035% among primary school students of age 7 to 12 years [10]. Another study from Saudi Arabia showed that the prevalence was 1250/10000 persons as stated by Saab et al [4]. Children who suffer autism, have higher rate of co-morbidities such as anxiety, depression, epilepsy, gastrointestinal problems, allergies towards food and skin as well as skin allergies [11,12]. Diagnosis is performed by physical and neurological examination as well as complete patient history [13]. Several studies showed associations between autism and prenatal or intrapartum use of medications, obstetric complications and parental preconception chemical exposures [14,15], and another study showed that level of education and age were associated with autism risk [16]. Also, the genetic basis for autism is accepted [17,18] and autism estimated hereditary reaches 90% [10]. A study from India showed that consanguinity increased the risk of autism [19]. Other risk factors for autism mentioned included infections during pregnancy, complications of delivery and pregnancy [4]. The present study aimed to investigate the prevalence and risk factors for autism as well as associated characteristics.

SUBJECTS AND METHODS:

Subjects and study design:

This study is a case-control study that was conducted in Hospitals and medical centers in Al-Madinah. The study surveyed 181 cases and 181 controls randomly selected participants between the periods December 2017 to March 2018. Inclusion criteria were patients confirmed diagnosed with autism and their age under 15 years and healthy children aged under15 years old. Exclusion criterion was complicated cases of autism. The data were collected using a questionnaire during face to face interview. Informed consent was obtained from participants before data collection, and informed consent was obtained from authorities before viewing the subjects‘file.

Statistical analysis:

Data were analyzed using SPSS software version 16, simple descriptive analysis in the form of numbers and percent for qualitative variables and median and range for quantitative variables. The significance of relationship between the selected demographic variables scores was analyzed by using chi-square test, significant level of less than 0.05 was considered.

RESULTS:

The present study included 181 participants, 173(95.6%) of them were Saudi, whereas 8(4.4%) were non-Saudi. There were 91(50.3%) confirmed blood relation between parents and 83(91.2%) stated the relationship is being cousin. Majority of participants 151(83.4%) reported having male child, whereas 30(16.6%) reported having female child, the vast majority of participants 177(97.8%) reported that specialist doctor diagnosed their children, 162(89.5%) reported having one child having autism and 55(30.4%) reported that the child diagnosed was the first one, while 46(25.4%) said the second one. There were 97(53.6%) of children were in the age of 3-4 years when diagnosed by a doctor, and the most common symptom reported was a child doesn’t respond to calls 112(61.9%). There were 120(66.3%) of participants reported that the child complain of attention deficit hyperactivity. Father co-morbidity was more dominant 42(23.2%) than mother co-morbidity 24(13.3%). There were 85(47%) smoker parents. Only 35(19.3%) of mothers complained during pregnancy, 42(23.3%) reported administration of medication during pregnancy and 14(7.7%) reported living in polluted environment. There were 45(24.9%) reported having autism cases in the extended, and most of the 28(62.2%) reported having one case, table1 summarizes the characteristics of parents, children and risk factors of autism.

Table1: Characteristics of parents and children as well as risk factors of autism

Variables	N(%)
Characteristics of parents	
Nationality	
Saudi	173(95.6%)
Non-Saudi	8(4.4%)
Is there blood relation between parents	
Yes	91(50.3%)
No	90(49.7%)
If yes	
Cousin	83(91.2%)
Others	8(8.8%)
Characteristics of children	
Child gender	
Male	151(83.4%)
Female	30(16.6%)
Was your child diagnosed by a specialist doctor	
Yes	177(97.8%)
No	4(2.2%)
Age when a doctor diagnosed	
<1 year	12(6.6%)
1-2 years	41(22.7%)
3-4years	97(53.6%)
>4 years	31(17.1%)
Range of child	
First	55(30.4%)
Second	46(25.4%)
Third	32(17.7%)
Fourth	10(5.5%)
Fifth	38(21%)
First symptoms	
The child do not receive a response to calls	112(61.9%)
Hand fluttering	30(16.6%)
Repetition of the speech	7(3.9%)
Strong concentration	5(2.8%)
Resisting the change	5(2.8%)
Closing ears when hearing someone talking	4(2.2%)
Others	18(9.9%)
Does he complain of attention deficit hyperactivity	
Yes	120(66.3%)
No	61(33.7%)
How many of your children have autism	
1	162(89.5%)
2	17(9.4%)
3	2(1.1%)
Autism risk factors	
Father co-morbidity	
Yes	42(23.2%)
No	139(76.8%)
Mother co-morbidity	
Yes	24(13.3%)
No	157(86.7%)

Is one of the parents a smoker or was a smoker Yes No	 85(47%) 96(53%)
Did the mother complain during her pregnancy from(folic acid deficiency, measles, rubella or any other diseases) Yes No	 35(19.3%) 146(80.7%)
Did the mother live in a polluted environment or was exposed to chemicals or radiation? Yes No	 14(7.7%) 167(92.3%)
Did the mother take any medication during pregnancy Yes No	 42(23.2%) 139(76.8%)
Is there any autism cases in the extended family(cousins and other close relatives) Yes No	 45(24.9%) 136(75.1%)
if yes no of autism cases in family 1 2 3 4 7	 28(62.2%) 13(28.9%) 2(4.4%) 1(2.2) 1(2.2)

The prevalence of autism represents 50% of children of parents participated in this study, figure1.

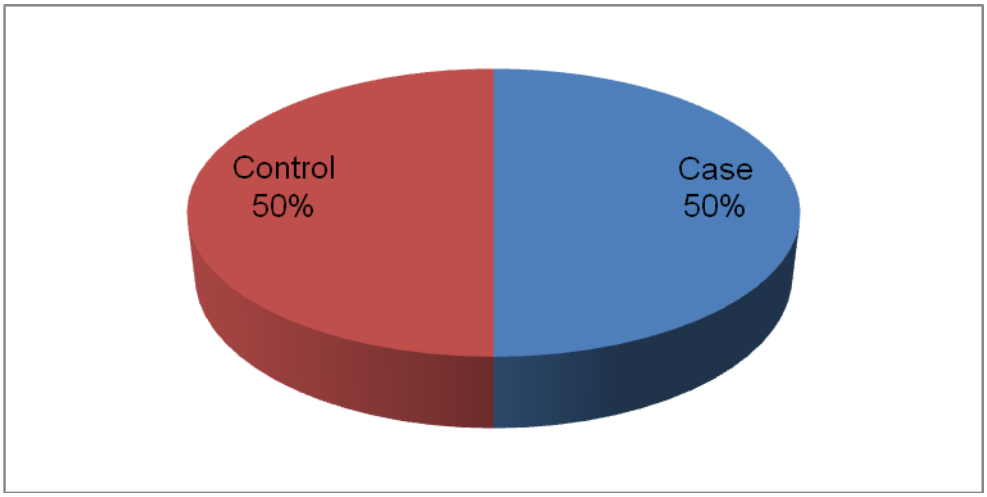

Fig1: Prevalence of autism

Regarding factors associated with autism prevalence, nationality, age of children, child gender, the rank of a child, the age of mother and father significantly associated with autism prevalence, table2. Autism was significantly more prevalent among Saudi (P-value=0.000), children with mean age of 8.93 years old (P-value=0.000), male child (P-value=0.000), first child (P-value=0.033), older mother (39.6 ±7.24 years old) and older father (44.17 ±8.97 years old) (P-value=0.007, 0.001 respectively).

Table2: Prevalence of autism regarding different characteristics

Characteristics	Case (181)		Control (181)		P-value	OR
	No	%	No	%		
Nationality of Child						
Saudi	173	**95.6**	153	**89.5**	**0.000**	**1.3(1.5-3)**
Non-Saudi	8	**4.4**	28	**16.4**		
Age of Child*						
Mean±SD	8.93±3.89		7.32±4.18		**0.000**	**1.6(1.8-3.5)**
Min/Max	1.5/20		.5/23			
Is there blood relation between parent						
Yes	91	**50.3**	85	**47.0**	**0.528**	**1.2(0.3-8)**
No	90	**49.7**	96	**53.0**		
If, yes : Relation						
Cousin	83	**91.2**	69	**81.2**	**0.053**	**2(1.2-1.8)**
Others	8	**8.8**	16	**18.8**		
Child gender						
Male	151	**83.4**	115	**63.5**	**0.000**	**1.8(2-2.5)**
Female	30	**16.6**	66	**36.5**		
Rank of Child						
First	55	**30.4**	74	**40.9**	**0.033**	**0.8(0.4-0.6)**
Second	46	**25.4**	27	**14.9**		
Third	32	**17.7**	28	**15.5**		
Fourth	10	**5.5**	18	**9.9**		
Fifth +	38	**21.0**	34	**18.8**		
Age of Mother						
Mean±SD	37.60±7.24		35.51±7.46		**0.007**	**0.9(0.4-0.8)**
Min/Max	16/55		21/56			
Age of Father						
Mean±SD	44.17±8.97		41.06±9.14		**0.001**	**1.4(1.5-1.8)**
Min/Max	26/70		23/70			

The risk factors of autism as investigated are shown in table3, there were 4 risk factors were significantly associated with autism including, mother complaining during her pregnancy from a definite disease (P-value=0.002), mother living in polluted environment (P-value=0.006), mother administered medication during pregnancy (P-value=0.004) and presence of autism cases in the extended family (P-value=0.001).

Table3: Risk factors associated with autism

Characteristics	Case (181)		Control (181)		P-value	OR
	No	**%**	**No**	**%**		
Father Co-morbidity						
Yes	42	**23.2**	32	**17.7**	**0.192**	**3(0.8-5)**
NO	139	**76.8**	149	**82.3**		
Mother Co-morbidity						
Yes	24	**13.3**	21	**11.6**	**0.633**	**2(0.7-3)**
NO	157	**86.7**	160	**88.4**		
Is one of the parents a smoker or was a smoker						
Yes	85	**47.0**	80	**44.2**	**0.598**	**1.5(0.4-0.8)**
NO	96	**53.0**	101	**55.8**		
Did the mother complain during her pregnancy from(folic acid deficiency, measles, rubella or any other diseases)						
Yes	35	**19.3**	15	**8.3**	**0.002**	**1.6(1.5-1.9)**
NO	146	**80.7**	166	**91.7**		
Did the mother live in a polluted environment or was exposed to chemicals or radiation?						
Yes	14	**7.7**	3	**1.7**	**0.006**	**2(3.2-6)**
NO	167	**92.3**	178	**98.3**		
Did the mother take any medication during pregnancy						
Yes	42	**23.2**	21	**11.6**	**0.004**	**2.2(2.6-2.8)**
NO	139	**76.8**	160	**88.4**		
Yes	45	**24.9**	20	**11.0**	**0.001**	**1.8(2.1-2.9)**
NO	136	**75.1**	161	**89.0**		
Is there any autism cases in the extended family(cousins and other close relatives)						
No of autism cases in family						
One	28	**62.2**	12	**60.0**	**0.098**	**3(0.9-4)**
Two	13	**28.9**	6	**30.0**		
Three & above	4	**8.9**	2	**10.0**		

By multiple regression, only presence of autism cases in the extended family was a significant risk factor for autism (P-value=0.003).

DISCUSSION: Characteristics of children and parents were

investigated in this study regarding autism, the vast majority of parents (97.8%) reported that their children were diagnosed by specialist doctors and common age at which they were diagnosed was at 3-4 years old, and the most affected child was the first child. Several symptoms were reported, and the most common symptom was a child does not respond to calls, and the least common symptom was closing ears when hearing someone talking. In the present study the prevalence of autism was 50%, the prevalence of autism was significantly associated with several factors including being Saudi (P-value=0.000), children age of 8.93 years, male gender for child (P-value=0.000), being first child (P-value=0.033) and older age of mother (P-value=0.007) and father (P-value=0.001). Consanguinity in this study had no significant effect on the prevalence of autism. However previous studies [20,21] showed that most of parents of autistic children were non-consanguineous, whereas in a previous Saudi study [5] it was found that 55% of children with autism had consanguineous parents. Regarding higher prevalence of autism in males than females, our study showed that 83.4% of males and 16.6% of females had autism, this was in agreement with several previous studies, including Saudi study [5] which showed that there were 76.7% of males had autism, whereas 23.3% of females suffered autism. Also, El Bas et al. [20] showed similar findings, while Shu et al [22] reported that prevalence of autism was more than twice in males than in females, this may return to the genetic variations between males and females. It was reported that the median age of autism diagnosis was 5.7 years [23], and in Saudi study [5] it was reported that the age was 2.8 years, however in our study we investigated the mean age not the medium and it was 8.93 years. This variation in age of identification may return to the wide variation in the age at which children presented for diagnosis. In our study, we found that autistic children had parents of older age and this was of considerable interest [24]. In Saudi study [5] it was found that the age of mothers didn't differ among case and control group, whereas the age of fathers was higher for children with autism, another study [25] also showed that the prevalence of autism is dependent on fathers'age but not the age of the mothers. It was suggested that the increase in autism prevalence might return to the change in environmental factors instead of genetic-environmental factors that contribute to autism or its symptoms [26,27]. In the current study, several risk factors for autism were reported. However, only four factors showed significant results. Complaining of the mother during pregnancy, an environment where mothers live, medication administration during pregnancy and presence of autism cases in the extended family were the significant factors. However, the only presence of autism cases in the extended family was associated with the presence of autism. It was reported in the Saudi study that 39% of children suffering autism had a family history of psychiatric disorders and 36.9% of autistic children vs. 11.7% of control had a family history of autism [5]. Another study [20] showed that 16% of autism children had a family history of autism compared to 1% of control.

CONCLUSION:

There was a high prevalence of autism among children, and associated factors included nationality, children age, gender, and rank as well as the age of both parents. The only risk factor for autism was the family history for autism.

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