Evaluation some risk factors of Libyan children with autism spectrum disorders in Tripoli

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Abstract: Autism spectrum disorders (ASDs) are a behaviorally defined group of neurodevelopmental disorders that are usually diagnosed in early childhood. With early and intensive treatment such as behavior and communication therapies with a team of specialists. Most children improve their ability to relate to others, communicate and help themselves as they grow older. In this study, we investigated some correlates with autism because we believe that the identification of causal genetic and environmental risk factors may help in the primary prevention of some cases. We investigated the association of autism with some risk factors in 82 autistic children from the Libyan Center for Special Needs, located in Salah Al-Din district in Tripoli, Libya. Diagnosis of autism of each patient was assigned by trained psychiatrists and documented in the patient′s file based on Diagnostic Statistical Manual of Mental Disorders criteria (DMS-IV-TR). The investigated risk factors were patient′s age, gender, maternal age at the birth of child and positive family history. We observed that male predominate (74%) among autistic children, however, there was no observed difference in the outcome of therapy between males and females. About 70% of patients have negative family history with autism and 38% of them were children of relative parents. Positive family history, however, lowers the outcome of therapy. Most of cases (70%) are born at mother′s age older than 30 years. We also investigated whether maternal antidepressant use during-pregnancy is associated with autism. It is found that 38% of mothers have used these drugs during pregnancy.

Introduction

Autism spectrum disorders (ASDs), also known as pervasive developmental disorders, are a behaviorally defined group of neurodevelopmental disorders that are usually diagnosed in early childhood. The phenotype of ASDs is extremely heterogeneous, with differences from person to person in a wide range of symptoms and severity as well as differences between the various subtypes of ASDs (e.g., autistic disorder, Asperger syndrome, and pervasive developmental disorder) (1). Symptoms of autism are usually noticed during the child's first three years. Parents often become concerned when their child does not seem interested in playing and does not begin to talk. Sometimes, a child with autism will start to talk at the same time as other children of the same age, then lose his language skills. With early and intensive treatment such as behavior and communication therapies

with a team of specialists most children improve their ability to relate to others, communicate, and help themselves as they grow older (2). The ultimate goal of treatment is to increase a child's ability to function, reduce symptoms and help in the child's development and learning. Children with ASD often respond well to highly structure educational programs (3).

Moreover, several diet strategies have been suggested as additional treatment for AS because many autistics have allergic or highly sensitive to foods such as that containing gluten or casein. Eliminating these compounds from diet could help in reducing gastrointestinal problems seen in autistics (4). The prevalence of ASD is increasing worldwide. The global median prevalence of ASD is estimated at 17/10,000 (5) and recent estimates from the Centers for Disease Control in the USA indicate that as many as 1/150 8 year olds in the USA may be affected (6).

In developing countries, reports on autism are mainly from neurology and psychiatric clinics and indicate a prevalence ranging from 0.7-33.6% among cases diagnosed at these clinics (7). Many causes of autism have been proposed but genetic causes predominate. Among children born in Sweden, the individual risk of ASD increased with increasing genetic relatedness and heritability of ASD was estimated to be approximately 50% (8). Although, it is uncertain which genes are responsible, these results indicate that positive family history with autism could play role in the incidence of autism (9). Additional suggested risk factor of autism in Middle Eastern populations is consanguinity (marriage between cousins) because autism is familiar recessive disorder (10) which is most common among children of parents who are relatives. It is also known that many genetic disorders are associated with maternal age. Advanced maternal age is associated with increased risk for chromosomal Down's syndrome (11), dyslexia (12) and idiopathic mental retardation (13). This makes the maternal age at the birth of child a candidate for epidemiological studies on autism. Moreover, many studies have examined the association between maternal health during pregnancy with the incidence of many genetic disorders including ASD. The incidence of autism was increased by elevated maternal temperature (14), maternal vitamin D deficiency (15), or maternal psychiatric status during pregnancy (16). On the other hand, many autistics have no known genetic etiology this could suggest that at least a fraction of these cases may be due to exposure to environmental insults.

The environmental factors implicated so far include pesticides, environmental lead, sex hormone analogs, medications such as antibiotics, plasticizers, thiomersal containing vaccines and other synthetic molecules (17, 18). Few behavioral intervention studies in ASD have been published; however, there have been a wealth of pharmacologic studies reported. The developpment of Pharmacologic treatment in ASD is complicated by many factors. These range from genetic and sex influences and include variability in the severity and presence of behavioral phenotypes such as autism like behavior and hyperactivity. In addition, the interaction between the causal biologic factors and behavioral presentation is unclear. Therefore, we aimed in this study to investigate the relationship between some risk factors of autism in Libya. It is obvious that there is poor level of awareness and

knowledge of the disorder in our community. The lack of the apeutic services such as speech and behavioral therapists, and a negative attitudinal disposition towards persons with autism necessitate more effort in research and implementation of Libyan governmental health policies that promote autism awareness and identify autistics.

Materials and methods

we investigated the association of autism with some risk factors in 82 autistic children from the Libyan Center for Special Needs, located in Salah al-Din district in Tripoli, Libya. Diagnosis of autism of each patient was assigned by psychiatrists and documented in the patient's file based on Diagnostic Statistical Manual of Mental Disorders 4th ed., text revision (DSM-IV-TR) criteria (19), The International Classification of Disease, 10th Revision (ICD-10) (20). We also administered a questionnaire to the parents. The questionnaire consisted of different questions about gender of the child, birth date, and age at diagnosis and current age. Also, we asked about maternal age at the birth of child, the maternal use of some medications and the presence of any disease during pregnancy. The family medical history was also registered.

Results

The registered number of cases diagnosed with ASD in the Libyan Center for Special Needs in Tripoli is dramatically increased from 2010 to 2015 by around 40%. Total cases registered till February 2015 is shown by the column appear at 2015 (Fig. 1).

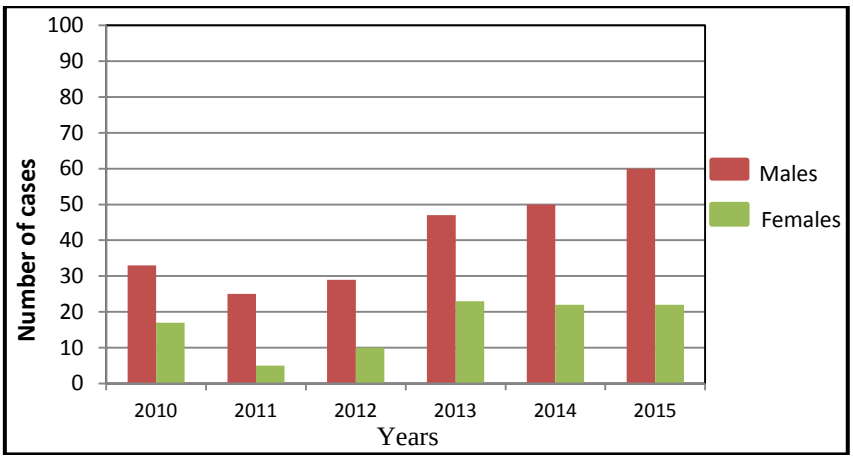

Figure 1: Evolution of Autism in Tripoli from 2010 to 2015 with relation to patient's gender. This figure presents the number of the cases diagnosed with ASD in the Center. The drop in the number between 2011-2013 might be due to the Libyan revolution events

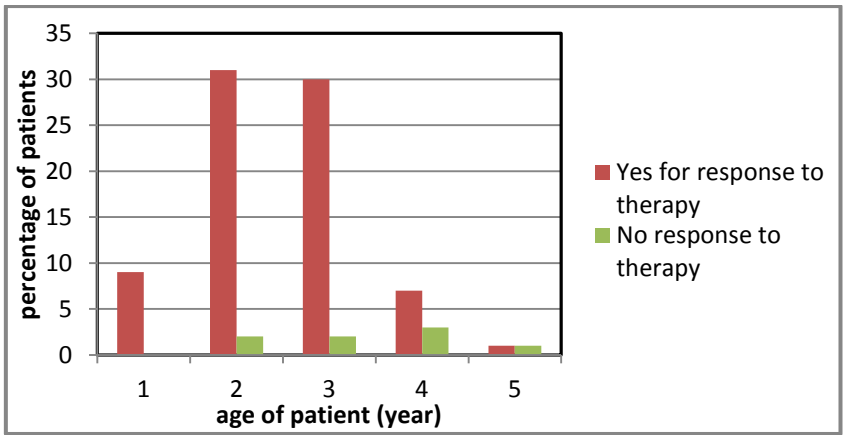

Figure 2: Patient′s age at diagnosis of Autism and its response to the therapy. Better response is observed at age younger than 4 years

Also, from this figure we can see that there is a big difference between the incidence of autism among males and females. 74% of the cases were males and 26% were females. Further, we noticed that the mean age of patients at the diagnosis was 2-3 years and a few cases were diagnosed at age of five years. Patient′s age affects the outcome of therapy measures that are employed in the center a better outcome is obtained when the patient is younger than four years (Fig. 2). Patient′s gender, however, has no relation to its response to therapy (Fig. 3).

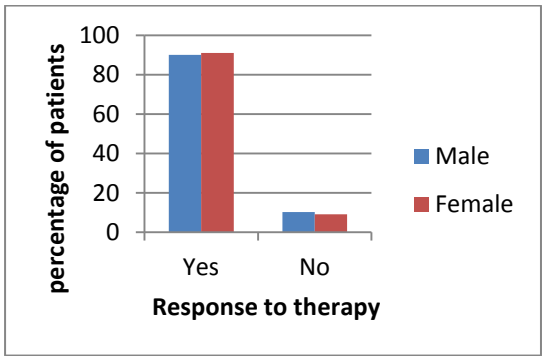

Figure 3: Patient′s gender play no role in the outcome of therapy

There is no observed difference between males and females response to therapy. It is also examined whether positive family history with autism increases the incidence of autism? We found that 68% of the cases have no other affected family member with autism; however, presence of positive family history lowers the child outcome (Fig. 4). It is claimed that consanguineous marriage could increase autism incidence, however, only 38% of the cases were children of relative parents was found but the percentage of children who respond to therapy is higher (74%) for those whom parents were non-relatives (Fig. 5).

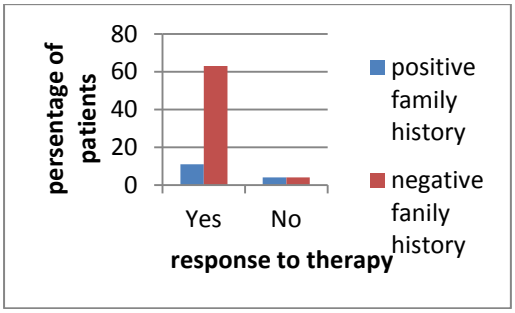

Figure 4: Positive family history with autism lowers the outcome of therapy

Positive family history means that there is another autistic member in the family. Negative family history means that there is no other autistic member in the family.

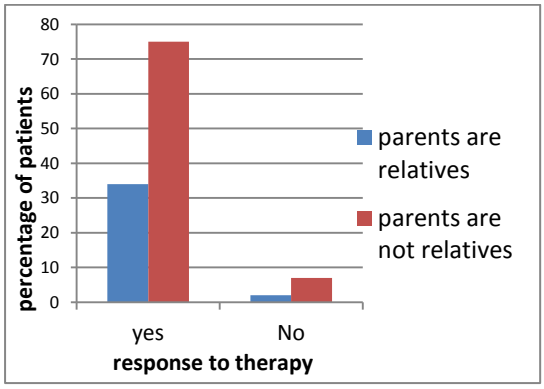

Figure 5: Autistic children of relative parents show slower response to therapy than others

Other possible risk factor of autism is the advanced maternal age, in our study most of the cases (70%) are born at mother's age older than 30 years (Fig. 6).

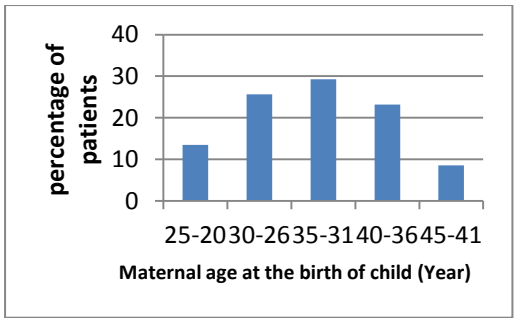

Figure 6: Autism incidence and maternal age at the birth of child.

We also investigated whether maternal antidepressant use during pregnancy is associated with autism. We found that 38% of mothers have used these drugs during pregnancy with the autistic child (Fig. 7).

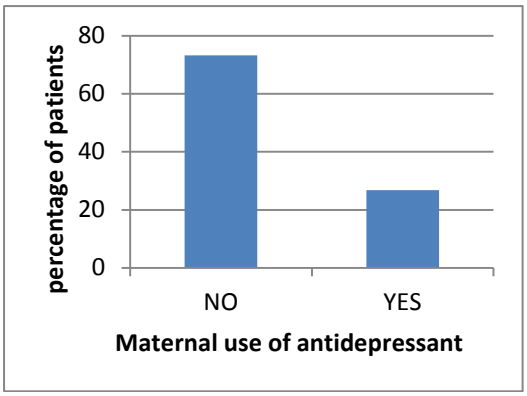

Figure 7: Autism relation to maternal use of antidepressants during pregnancy

Discussion

We noticed an increased number of diagnosed autistic kids in Tripoli in the recent years. Better awareness and more inclusive diagnostic criteria for autism spectrum disorders may explain this rising number. However, routine neuropsychological screenings of children are not yet available in Libya. A child is usually-taken to visit a doctor when parents or teachers notice unusual behavior in him/her. The age of child at the diagnosis can affect its response towards the behavior intervention. We observed that the degree of improvement is decreased when the child age is older than 3 years. It is proven that starting the treatment as soon as possible can have positive impact on the outcome of children with ASD (21) and early intervention is conditional upon early diagnosis (22). Our study also revealed that males are more affected than females, three times more common among boys. The sex ratio in ASD is one of the most consistent findings in the field (23). This could be due to the fact that the endocrine system plays a role in the etiology of ASDs.

The fetal neurodevelopment is affected by adrenal, gonadal, and thyroid hormones (24-26). With regard to maternal age, we found that high percentage of patients was born at maternal age of over 30 years. Advanced maternal and paternal ages have been associated with the risk of ASD in some, but not all, studies (27, 28). In the Chinese population, a case-control study of 190 Chinese children found that advanced maternal age (> 30 years old) was not significantly associated with the risk of autism (29). Moreover, it has been found that parental psychiatric disorders such as parental depression are associated with the risk of autism and that occurs through a genetic pathway (30, 31). When we returned to the family medical history of the affected child we noticed that depression was frequentry registered as preexisting illness during pregnancy with this child and that some mothers taken antidepressant.

Therefore, we also examined whether maternal antidepressants use during pregnancy increases the incidence of Autism or not. The most commonly prescribed antidepressants in Libya were selective serotonin reuptake inhibitors (SSRIs) and nonselective monoamine reuptake inhibitors (tricyclic antidepressants). We found that incidence of autism among children whom mothers taken antidepressant during pregnancy was lower than that of children whom mothers did not take antidepressant during pregnancy. Our finding is in contrast to that found by larger study made in Sweden where there was increased autism incidence by maternal use of antidepressant (31). This could be due to the small sample size of our study, however, we observed that antidepressants are the most encountered drugs (if any) that are used by mothers during pregnancy with the patient. Most antidepressants cross the placental barrier, and intrauterine exposure to serotonergic agents has been shown to promote persistent changes in brain circuitry, decreased serotonergic reactivity, and behavioral features analogous to autism in animal models (33).

The prevalence of consanguineous marriage in Libya is reasonable and is associated with increased manifestation of genetic disorders, however, in our study, we found that autistics of relative parents have poorer outcome than that of non-relative parents. Since relatives share a certain number of genes, consanguineous parents are much more likely to be silent carriers of the same genetic mutation.

Conclusion: Lack of appropriate treatment services and education are factors affecting the outcome of the child with autism. Early diagnosis increases the outcome of therapy. However, individual child characteristics can affect the response to therapy such as age, consanguineous marriage, positive family history, maternal age, fetus exposure to antidepressants. To explain the dramatic increase in the observed prevalence of ASD in Libya future larger studies are needed. Access to both diagnostic and treatment data at multiple stages of pregnancy may help disentangle the role of maternal depression and the individual drugs used to treat it in the risk of autism spectrum disorder.

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