

ORIGINAL ARTICLE

Frequency of Different Risk Factors of Autism Spectrum Disease: A Multicentre Comparative Study

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ABSTRACT

Objective: To determine the frequency of different prenatal risk factors associated with autism spectrum disease.

Study Design: A Case-control study.

Place and Duration of Study: The Study was conducted at Rawalpindi. Cases were recruited from Autism resource centre (ARC), Step to learn (STL) Rawalpindi, Hassan academy for special children, and Army public academy for special children Rawalpindi and controls from DHQ hospital Rawalpindi from February 2014 to January 2015.

Materials and Methods: Two groups of children were included in the study, Group one were diagnosed case of autism ASD (n=101) aged between 3 to 10 years and Group two (control n=233). The data was collected and entered in a self designed structured questionnaire. Data was analyzed by SPSS (Statistical Package for the Social Sciences) Vs 20.

Results: Over 30 risk factors have been identified. 67.3% cases were males and 32.6% were females whereas 34% controls were males and 66% controls were females. The factors associated with autism were male gender, advanced father's age at child birth, severe iron deficiency anemia during pregnancy, vitamin D deficiency, maternal hypothyroidism, asthma, hypertension, diabetes mellitus and obesity, high stress during pregnancy, C-section, valporoic acid use, antidepressants and antibiotics use in mothers, infection during pregnancy, no or minimum exposure of sunlight during pregnancy, premature birth, Meconium aspiration syndrome and late cry, blood group incompatibility with mothers and Rh incompatibility between mothers and fathers.

Conclusion: Prenatal risk factors like stress, vitamin D deficiency, iron deficiency anemia, hypothyroidism, obesity, diabetes, blood group incompatibility with mothers, children born in spring and C section are the strong causes to develop autism in children.

Key Words: Autism, Neurodevelopmental Disorder, Risk Factors.

Introduction

Autism is a wide-ranging term used to illustrate an assemblage of complex neurodevelopmental disorders also known as Pervasive Developmental Disorders (PDD) or Autism Spectrum Disorders (ASD). ASDs are a collection of developmental disabilities characterized by atypical development in socialization, behavior and communication. Symptoms of ASDs are present before age 3 years and frequently are accompanied by difficulty in

learning, cognitive functioning, sensory processing and attention.¹ The phrase "spectrum disorders" is used to point out that ASDs include a variety of behaviorally concerned conditions, which are diagnosed by clinical observation of development. These conditions encompass autistic disorder (i.e., autism), and pervasive developmental disorder and Asperger disorder.² ASDs, related to other neurodevelopment disabilities, are usually not curable and chronic maintenance, preservation and management is requisite. Regardless of the fact outcomes are diverse and specific behavioral characteristics vary over time, the majority of children with ASDs remains within the spectrum like adults and, disregarding of their intellectual level, undergo to experience problems with employment, independent and self-regulating living, communal relationships, mental health and societal problem.^{3,4} The diagnostic criteria depend upon the symptoms that become evident before a child is three years old.⁵ Causative factors for autism are inadequately

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understood. Both environmental and genetic risk factors are likely to commit etiology. Although autism appears to have its roots in very early brain development, mainly identifiable signs and symptoms are likely to appear between two and three years of age. Mostly parents are the first to note and identify that their child is presenting a typical behaviors such as deteriorating to make eye contact, not answering to his or her name or playing with toys in unusual, repetitive behavior.⁶ The purpose of this study is to determine the frequency of different prenatal risk factors associated with ASD so that these new risk factors should be used to make recommendations for clinical practice and by the avoidance of these risk factors, prevalence of ASD decreases.

Materials and Methods

It was a multicentre case control study. There were total 334 children enlisted in this study in which 101 were diagnosed case of autism and 233 healthy controls were taken with no neurological, musculoskeletal or cardiopulmonary abnormalities. Non probability convenient sampling technique was used. The Case data was collected from ARC (Autism Resource Center, Rawalpindi), STL (Step to Learn), Hassan academy for special children, Rawalpindi and Islamabad branch and Army Public Academy for special children Rawalpindi. Control data was collected from DHQ Hospital, Fauji Foundation Hospital Rawalpindi, National Institute of Rehabilitation and Medicine Islamabad, Railway General Hospital Rawalpindi and Divisional Public School Rawalpindi from January 2014 to December 2014. Permission was taken from respective institutes.

Data Collection Tool and Procedure: A self designed structured questionnaire was used for data collection. The questionnaire had 33 items (Appendix A). The different risk factors causing autism included in our questionnaire were based on literature search different studies in different settings by different authors. It included Iron deficiency anemia, vitamin D deficiency in mother during pregnancy, older parents, C section, mother high stress level during pregnancy due to any reason, blood group incompatibility with mother and many more. Ethical permission was taken from Medical Superintendent of DHQ, FFH, NIRM and PRH. After

obtaining informed consent from parents, data was collected using self designed structured questionnaires. Questions were first explain and then asked from parents of study groups. Data was filled personally by the authors.

Statistical Analysis: Data was analyzed by using SPSS (statistical package for social sciences) VS 20.

Results

30.2% ASD cases and 69.7% healthy controls were taken in this study. In ASD cases 6.9% mothers were suffering from obesity and 11.8% from diabetes and 21% from hypothyroidism (Fig 1). Table I show Stress mothers taken during pregnancy, infection during pregnancy, exposure of sunlight during pregnancy, premature births, C section, episiotomy, SVD, meconium aspiration syndrome, late cry of baby at birth, Different Rh and different blood group among parents and blood group incompatibility with mothers. Controls had lesser frequency of iron deficiency anemia during pregnancy whereas ASD cases had prevalence of moderate and severe iron deficiency anemia during pregnancy increases in mothers of cases (Fig 2). 70.27% mothers of children with ASD used folic acid and vitamin D during pregnancy whereas less usage in mothers of controls. Mothers of children with ASD had history of more usage of valproic acid, antidepressant and antibiotics i.e. 6.9%, 22.7% and 14.8% respectively whereas only 2.57% mothers of controls used antidepressant and 3.0% used antibiotics and none used valproic acid.

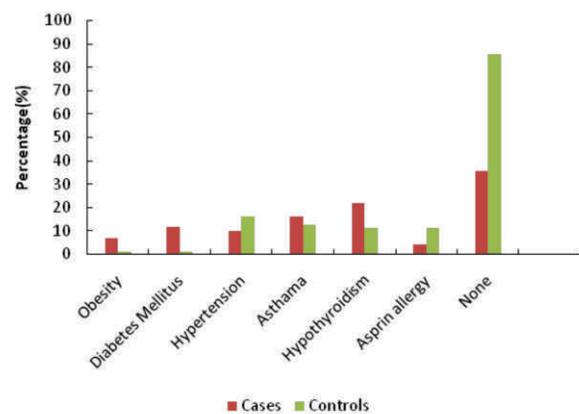


Fig 1: Comparison of Mother's medical history between cases and controls

Table I: Comparison of different conditions between cases and controls

	Cases (%)	Controls (%)	P value
Stress during pregnancy	42.5	14.5	0.032
Infection during pregnancy	13.8	1.71	0.045
Exposure of Sunlight during pregnancy	31.68	52.36	0.029
Premature birth	41.58	22.3	0.028
C-section procedure	81.18	18.82	0.030
Episiotomy	7.92	92.08	0.001
SVD	18.89	81.11	0.011
Meconium aspiration syndrome	26.7	73.3	0.029
Late cry at birth	13.8	86.2	0.015
Different Rh and different blood group among parents	55	31.7	0.034
Blood group incompatibility with mothers	73.26	13.30	0.025

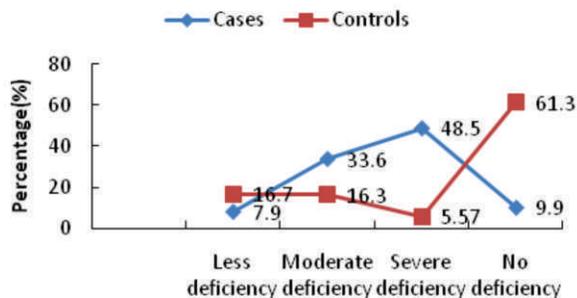


Fig 2: Comparison of Iron deficiency anemia between cases and controls

Discussion

In our study 67% cases of autism were found out to be males and only 29% were females hence supporting male gender as a risk factor of autism. Males are at higher risk for neurodevelopmental disorders, such as autism spectrum disorder (ASD), than females, but the fundamental reasons have been uncertain.⁷

Scientists have supposed a connection between iron deficiency and autism spectrum disorder. In a study maternal intake of supplemental iron and risk for autism spectrum disorders by Schmidt RJ, et al

establishes a strong relationship between iron deficiency and autism.⁸ In our study 48% severe deficiency of iron is found in cases and only 5% severe deficiency is found in controls. 9% of the cases had no iron deficiency while 61% of the controls also did not have any iron deficiency. This signifies the iron deficiency as one of the contributory risk factors for development of ASD. According to Kinney DK et al, in their study, “prenatal stress and risk for autism” stress of expectant mother is a noticeable reason for the symptoms of autism.⁹ In another study “timing of prenatal stressors and autism” by Beversd of DQ et al, it was reported that prenatal stress has a role in causing autism.¹⁰ In our study 42% cases had self-reported moderate to severe stress during their pregnancies and only 14.5% of controls also reported stress. So we can deduct the conclusion that stress is as one of the risk factor for ASD.

A prospective study of Exposure to valproic acid and risk for autism spectrum disorder indicates that valproic acid usage may be an important factor in causing autism.¹¹ In our study 6.9% cases taken valproic acid during pregnancy (anti- seizure medicine) whereas none of the control took valproic acid. This finding is in agreement with previous studies but further investigation is warranted.

Prenatal exposure to SSRIs, particularly during the first trimester, may moderately increase the risk of ASDs.¹² 22% cases in our study used antidepressant during pregnancy whereas only 2% controls were on antidepressant indicating either it's the antidepressant drugs or the depression which is hidden behind and need further investigation.

Studies showed that antibiotic use in pregnancy might cause autism.¹³ In our study 14% cases took antibiotics during pregnancy whereas only 3% controls took antibiotics during pregnancy but the need is to investigate the group of antibiotic, dose, frequency and all the minor details, so further investigation is warranted. Drugs possibly will activate the disease, earlier researchers found that use of medications during pregnancy may have an effect on the developing fetus and may cause autism.¹³ In our study 55% cases taken no drug during pregnancy emphasizing that it is not only the drugs that causes autism, there are some other factors that may in combination with the drugs causes autism.

Conclusion

Prenatal risk factors like stress, vitamin D deficiency, iron deficiency anemia, hypothyroidism, obesity, diabetes, blood group incompatibility with mothers, children born in spring and C section are the strong causes to develop autism in children. It is concluded that there is insufficient evidence to implicate any one prenatal factor in autism etiology, although there is some evidence to suggest that exposure to pregnancy complications may increase the risk.

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