Original Article

IDENTIFICATION OF RISK FACTORS ASSOCIATED IN AUTISM SPECTRUM DISORDER - A RETROSPECTIVE STUDY

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ABSTRACT

Background: The etiology of Autism Spectrum Disorder is diverse and still not fully understood. The association of various risk factors have been the prime focus of epidemiological study over the past years. **Objective**: Retrospective study for the identification of risk factors amongst patients associated with Autism Spectrum Disorders, reporting in the Department of Paediatrics, RIMS, Ranchi. **Method**: In this retrospective study, screening of 1010 toddlers was done aged between 16-30 months using the M-CHAT-R screening tool over a period of 13 months (May 2019- June 2020),out of which the medical records of 11 diagnosed cases of Autism Spectrum Disorder were reviewed. Inclusion criteria were children aged between 16-30 months, with no prior diagnosis of ASD or developmental delay. An informed consent form was duly signed by the parents of the children screened. In each such case, variables analysed were age, gender, parental age, family history, prematurity (GA <37weeks), low birth weight (<2.5kg) and perinatal asphyxia or need of resuscitation just after birth. **Result**: Among the 1010 toddlers that were screened, 11 were diagnosed with ASD. Mean maternal age was 31years and mean paternal age was 35years. Premature birth occurred in 8 (72.7%) cases, perinatal asphyxia in 6 (54.54%), and low birth weight in 7 (63.6%) cases. The prevalence of prematurity, low birth weight, and perinatal asphyxia among the children in our study was higher than the general prevalence of these conditions in the screening population of our study. **Conclusion**: Our study shows higher prevalence of prematurity, low birth weight, and perinatal asphyxia among children with ASD. Some limitations are the retrospective study design, and the small sample size. Large prospective studies are needed to clarify the possible association between perinatal complications and ASD.

KEYWORDS: Autism Spectrum Disorder, Risk factors, Prematurity, Low birth weight, Perinatal asphyxia.

INTRODUCTION

Autism spectrum disorder (ASD) is a heterogeneous neurodevelopmental disorder characterized by impairment in social communication and interaction, and by restricted and repetitive behavior, interests and activities.[1] The diagnosis of Autism depends on a range of behavioural signs, since there are no definitive biological markers for a majority of cases. ASD poses a serious developmental disadvantage to the child in the form of poor schooling, social function and adult productivity.

ASD encompasses disorders previously referred to as early infantile autism, childhood autism, Kanner autism, high functioning autism, atypical autism, Asperger disorder, childhood disintegrative disorder, and pervasive developmental disorder (NOS) [not otherwise specified]. Individuals diagnosed with one of these previous diagnoses should be given diagnosis of ASD. The diagnosis of ASD at an earlier age may lead to earlier intervention and, which typically includes behavioral, educational, and speech or language therapy.[2]

About 1 in 54 children has been identified with autism spectrum disorder (ASD) according to estimates from CDC's Autism and Developmental Disabilities

Monitoring (ADDM) Network. No data are available from India to provide an India-specific estimate of the prevalence.[3]

It is established that autism is a multifactorial condition involving both genetic and a wide range of environmental risk factors. Many recently emerging factors such as de novo gene mutation and potentially modifiable nutritional risk factors have not been studied extensively.[4]

Some of the risk factors associated with ASD are, children with a sibling with ASD, individuals with certain genetic and chromosomal conditions (Fragile X sundrome, Tuberous Sclerosis), drugs like Valproic acid and thalidomide when taken during pregnancy[2], antepartum and intrapartum conditions like gestational diabetes, preeclampsia, prematurity, perinatal asphyxia, low birth weight and children born to older parents.

Meta-analysis of various epidemiological studies conclude that the following factors – increased paternal age, increased maternal age, maternal gestational age, maternal immigration, gestational bleeding, gestational diabetes & medication use; all increase the risk of ASD.[5]

A study by Ravi et.al 2016 done in India showed that high mean paternal age at birth, need for resuscitation at birth, NICU stay > 12 hr, late initiation of breastfeeding and neonatal seizures were associated with screen positivity for ASD.[6]

Guthrie et.al 2019 suggested that maternal health problems during pregnancy and labour were found to be more significant for ASD mothers than their control. In addition, child health problems were more evident among ASD subjects as reported by their parents with significant differences from controls. The study also showed that toddlers who were born prematurely (≤37weeks) had higher chances to be screen positive.[7]

Pregnancy related exposures have been the prime focus of a significant amount of epidemiological research on possible risk factors for Autism. Some of the hypothesis suggest that obstetrical complications may increase the risk of autism. But the specific complications, the magnitude of effect and the overall conclusions of these studies are inconsistent.

The purpose of our study is to anticipate & identify the possible risk factors using M-CHAT-R amongst the screened children aged between 16-30 months on an outpatient basis in the Department of Pediatrics, RIMS, Ranchi.

MATERIALS AND METHODS

Present study was conducted in Rajendra Institute of Medical Sciences, Ranchi on 1010 toddlers who attended Pediatric OPD, from May'2019 to June'2020 and met the inclusion criteria. Informed consent was taken by the parents prior to enrolment in the study. Among 1120 subjects 90% gave consent and 10% refused consent.

The inclusion criteria were children aged 16 to 30 months, no prior diagnosis of ASD or developmental delay and parents who gave the informed consent. The exclusion criteria of our study were children who have already been diagnosed with developmental delay, communication disorders, intellectual disability and other conditions associated with autistic like behavior.

The M-CHAT-R questionnaire was used to assess the risk of Autism Spectrum Disorder, in which parents were asked to fill the questionnaire containing 20 items or were verbally questioned in 2 languages (Hindi and English) according to the convenience of the parents. The children who screened positive for M-CHAT-R were further evaluated by Diagnostic and Statistical Manual, Fifth Edition, (DSM-5) criteria and INCLEN diagnostic tool for ASD.

A total of 11 cases were diagnosed with ASD following which a detailed history including obstetrical, birth, developmental, drug and family history were taken. Semi- structured proforma was used to collect data regarding socio-demographic profile, and clinical variables like age of parents, gestational age, perinatal risk factors, history of ASD in siblings or family. Complete physical examination including neurological evaluation was done in the diagnosed cases. The association of the risk factors like prematurity, low birth weight, and perinatal asphyxia was then compared between the ASD and the non ASD group.

RESULTS

From May 2019 to June 2020, 1010 toddlers were screened in OPD in the Department of Pediatrics in Rajendra Institute of Medical Sciences, Ranchi using the M-CHAT-R, out of which 95 were screened positive for ASD.

Out of these 95 screen positive toddlers who were subjected to diagnostic evaluation of ASD, 11 were diagnosed with ASD, among which 9 were males and 2 were females. The M:F ratio was 4.5:1. The mean paternal age in the diagnosed cases was 35 years and mean maternal age was 31 years. Positive family history of ASD was seen in 27.3% of the cases.

The prevalence of low birth weight (<2.5kg) was 7 (62.6%) in ASD as compared to 319 (31.9%) among non ASD which was statistically significant with p-value as 0.025. It was also seen that the prevalence of prematurity (GA<37 weeks) was 8 (72.7%) in children with ASD and that in the non ASD group was 349 (34.9%) which was statistically significant with p-value as 0.020.

Lastly, on comparing the prevalence of perinatal asphyxia, it was seen that total of 6 (54.54%) out of 11

diagnosed cases had history of perinatal asphyxia as compared to 159 (15.9%) out of the non ASD group which was statistically significant with a p-value of 0.039.

Calculations were done using SPSS 16.0.

Table 1:

Risk factors	ASD	Non ASD	p-value
Male : Female Ratio	9:2 (4.5:1)	613:397 (1.5:1)	
Low Birth weight (LBW)	7 (63.6%)	319 (31.9%)	0.025
Prematurity (<37 weeks)	8 (72.7%)	349 (34.9%)	0.020
Perinatal asphyxia	6 (54.54%)	159 (15.9%)	0.039

Table showing the comparative data of the risk factors associated with ASD in this study with those of non ASD.

DISCUSSION

The increase in the prevalence of ASD in recent years has generated considerable concern. In developing countries such as India, accurate and reliable estimates of autism prevalence at the national level are required to enable public health professionals and government policy makers to formulate strategies to meet the needs of the growing autism community.

Early detection and timely intervention would facilitate reduction in morbidity, educational attainment, enhancement of cognitive development, reduction in lifelong disability, and overall improvement of quality of life of affected individuals. As a community-based survey, our study represents an important step in this direction.

The exact cause of autism spectrum disorder is unknown. It may be multifactorial and often thought to be associated with an interaction of genes and environmental factors.[8] Our findings showed a higher prevalence of prematurity, low birth weight, and perinatal asphyxia in individuals diagnosed with ASD, compared with the general population that were screened for ASD. Current study is in agreement with some previous studies.[8,9]

A meta‑analysis supported an association between advanced maternal age and risk of autism.[10] The relative risk of autism in mothers aged 35 years or older compared with mothers aged 25–29 years was 1.52.[11] In our sample, the mean maternal age was 31years. Therefore, one can assume that advanced maternal age was not associated with ASD in current study. Some of the studies have examined the association between prematurity and the development of ASD.[12-13] However, the etiology of this association remains unclear. In our study, the prevalence of prematurity among autistic children was higher than the general prevalence of prematurity in the study population (*72.7%, 34.9% respectively*).

Early brain insult could predispose to ASD as the association between perinatal asphyxia and ASD, suggested in many studies. Anoxia caused by birth asphyxia would excessively activate the dopaminergic system, and dopaminergic hyperactivity has been found in some autistic children.[14,15]

Perinatal asphyxia could also help to explain the male preponderance for ASD, since male infants typically suffer more neurological dysfunction due to cerebral hypoxia in comparison to females.[15] In current study, we found that there was a significant association between the history of perinatal asphyxia with the occurrence of ASD.

Limperopoulos et al.[16] found a prevalence of ASD of 26.0% in infants with low birth weight, compared with 5.7% positive screen prevalence in normal children. Lampi et al.[17], and Moore et al.[18] also showed an association between low birth weight and ASD. There was a significant association of ASD with low birth weight (<2.5kg).

Current study suggests that prematurity, perinatal asphyxia, and low birth weight may be associated with ASD, which strengthens the theory that early brain injury is involved in the pathogenesis of autism. Such conditions are modifiable risk factors, hence are of prime importance. However, the fact that this is a retrospective study and we had a convenient and a small sample size, should lead to some limitations in our conclusions. Also, confounding factors that we could not evaluate must be considered. In fact, one of the difficulties in studying perinatal features is that many of the variables are not independent from each other. Large prospective, population‑based studies may be needed to help in confirming the findings of our study, as well as to identify modifiable risk factors, to then allow early interventions, aiming at the reduction of the current increasing prevalence of ASD.

CONCLUSION

The concept of autism spectrum disorder has evolved over time. Years ago this condition was nothing more than an unrecognized developmental delay with

intellectual disabilities. The patients usually landed up in psychiatric hospitals.

Currently it is recognized as an independent neurologically based disorder of significance, a major public health issue, and more so a topic of advanced research. The etiology of ASD is multifactorial. Researchers have struggled to find a cause for the disorder without great success. Despite this difficulty research continues in cohesive manner with inter-speciality departmental coordination. Current study indicates significant association with factors like prematurity, perinatal asphyxia and low birth weight.

It is thus presumed that these findings have the potential for early identification of children who are at risk and who could benefit from further elaborate surveillance and intervention.

The risk factors identified can help in increasing the awareness among the parents and may also help to take all precautionary measures in the future pregnancies. Early intervention with behavioural and developmental therapy in children with ASD can lead to better long term cognitive and behavioural function.

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