ISSN (P) : 2589-9120 / (O) : 2589-9139
PubMed-National Library of Medicine - ID: 101773527

International Journal of Medical Science and Applied Research (IJMSAR)

Available Online at: https://www.ijmsar.com

Volume – 6, Issue – 1, February – 2023, Page No. : 29 – 37

Risk Factors of Autism Spectrum Disorders Among Non - Breast Fed Children: A Case Control Study

[1]Dr. Shaik Yeramala Dasthagiri Basha, [2]Dr. K. Nagendra Prasad

[1]Postgraduate, Department of Paediatrics, Fathima Institute of Medical Sciences, Kadapa, Andhra Pradesh, India

[2]Professor and Head, Department of Paediatrics, Fathima Institute of Medical Sciences, Kadapa, Andhra Pradesh, India

Citation of this Article: Dr. Shaik Yeramala Dasthagiri Basha, Dr. K. Nagendra Prasad, "Risk Factors of Autism Spectrum Disorders Among Non - Breast Fed Children: A Case Control Study,'' IJMSAR – February – 2023, Vol. – 6, Issue - 1, Page No. 29-37.

Corresponding Author: Dr. Shaik Yeramala Dasthagiri Basha, Postgraduate, Department of Paediatrics, Fathima Institute of Medical Sciences, Kadapa, Andhra Pradesh, India

Type of Publication: Original Research Article

Conflicts of Interest: Nil

ABSTRACT

Background

Autism spectrum disorder (ASD), or autism, is a developmental disorder defined by a deficiency in reciprocal social interaction and communication, along with repetitive and ritualistic behaviors**.** Knowing the risk factors of ASD can help clinician's better advice expecting mothers, detect risky babies and improve relevant guidelines to decrease the risk. Hence the present study was undertaken. The objective of the study is to know the risk factors for ASD among non-breast-fed children.

Methods

This is a kind of comparative case-control study done on 100 children aged 1 to 3 years who came to our tertiary care centre named Fathima Institute of Medical Sciences, Kadapa, Andhra Pradesh, India. Age, gender, mode of delivery, birth weight, intake of prenatal vitamins, prenatal exposure to stress, parent's age, education and family history were assessed and compared between groups.

Results

There are signficiant differences in gender, paternal age, paternal education, maternal education, mean birth weight, mean 1 min APGAR score, mode of delivery, admission into neonatal intensive care unit, maternal stress, maternal intake of drugs between cases (children with ASD) and controls (children without ASD).

Conclusion

Being male, increased paternal age, lack of proper parental education, poor intake of prenatal vitamins, excess maternal stress and presence of maternal illnesses are found to be risk factors for the development of ASD.

Keywords

Autism spectrum disorders, breastfeeding, speech problems, social interaction, communication

INTRODUCTION

Autism spectrum disorder (ASD), or autism, is a developmental disorder defined by a deficiency in reciprocal social interaction and communication, along with repetitive and ritualistic behaviors. ASD emerges usually before 3 years of age.[1]Certain parents may notice a regression in acquired skills among their children after the development of ASD.[2]This regression is seen in around 22% of children.[3]One study from Gulf countries reported a prevalence that ranged from 1.4 to 29 per 10,000 persons.[4]The raise in ASD incidence could be due to improved diagnostic criteria, raised awareness and actual rise in the incidence. Increased paternal age, lack of breastfeeding, and prematurity are some of the several risk factors that are associated with raised risk for ASD.[5]

Breastfeeding is the healthiest way to provide nutrition to an infant[6-8] but, many childbearing women never breastfeed. It is alive with all nutrients and various antibodies that an infant requires for the first six months of life. There is no replacement or formula feed to breast milk. It is the most appropriate way to make sure of proper child health and survival. It continues to provide up 50% of the child's nutritional requirements during 2nd half of 1st year. The Government of India, World health organization (WHO) and the United Nations Children's Fund (UNICEF) suggests for exclusive breastfeeding for 1st 6 months of life and continued feeding along with complementary food for up to two years. Breastfeeding is also important for the cognitive ability of children at risk for ASD.

Tanoue et al[9]1st reported the relationship between breastfeeding and ASD, in which most of the babies diagnosed to have ASD were weaned within 1 month of initiating breastfeeding. Certain studies identified that lack of or late initiation of breastfeeding as a risk factor for ASD.[10-12]Knowing risk factors related to ASD can help clinicians better advise expecting mothers, detect risky babies and improve relevant guidelines to decrease risk. Hence the present study was undertaken.

MATERIALS AND METHODS

Type of study and study site:

This is a kind of comparative case-control study done on 100 children who were brought by their parents to the outpatient unit of the Department of Pediatrics at Fathima Institute of Medical Sciences, Kadapa, Andhra Pradesh, India

Study duration: The study was done for 6 months from January 2022 to June 2022.

Sampling method: Convenience sampling

Sample size calculation:

As per **SK Rainaet al.**, [13] the prevalence of ASD among children in India was 0.15%

The sample size is calculated as per epi-info software 7.2.5(population proportion mode) as:

$$N=Z^2PQ/E^2$$

N-sample size

P-Prevalence

P=0.15%

Q=1-P

E-Error: 1%,

98% confidence limits

N=82

82 is the minimum sample size.

So, we included 100 children in the current study, considering a few losses to follow-up cases.

Inclusion criteria

- Children aged 1-3 years of any gender
- Children who were not exclusively breastfed for 1st 6 months of life
- Children of parents who provided informed consent

Exclusion criteria

- Children with incomplete data

Methodology

100 children were recruited after taking informed consent from parents or legally accepted representatives. They were divided into two groups. A questionnaire was given to all parents to fill, which contained questions regarding our study parameters. Children were assessed clinically to diagnose ASD. All parameters were compared between two groups of children and risk factors for ASD were identified.

Groups: The study included 2 groups of children

Cases- 50 children who were diagnosed to have ASD

Controls: 50 children who were not having ASD

Parameters assessed

- Age, Gender
- Paternal education
- Maternal education
- Paternal age
- Maternal age
- Family history of ASD.
- Prenatal intake of vitamins
- Prenatal intake of drugs (smoking, alcohol, addiction drugs)
- Illness during pregnancy
- Prenatal exposure to stress
- Admission into NICU (Neonatal-intensive care unit)
- Mode of delivery
- Birth weight
- 1 min APGAR score

Ethical considerations

Permission from the Institutional ethics committee attached to the Fathima Institute of Medical Sciences was taken before conducting the study. All parents were explained the complete process and benefits of their data for the study. After he/she accepts, an informed consent form was provided in the local language or and the person was asked to sign it or put a thumb impression.

Statistical analysis

Data analysis was done using Epi Info software version 7.2.5. The results were expressed as mean ± S.D, percentages. Comparison between the two groups were done using T-test. Percentages between two groups were compared using Z test for proportions.

P value <0.05 is considered statistically significant.

RESULTS

Age and gender: There is no significant difference in the mean age between cases and controls. There is a significant difference in gender among cases and controls. Males are more in the case group.

Table 1: Age and gender among two groups

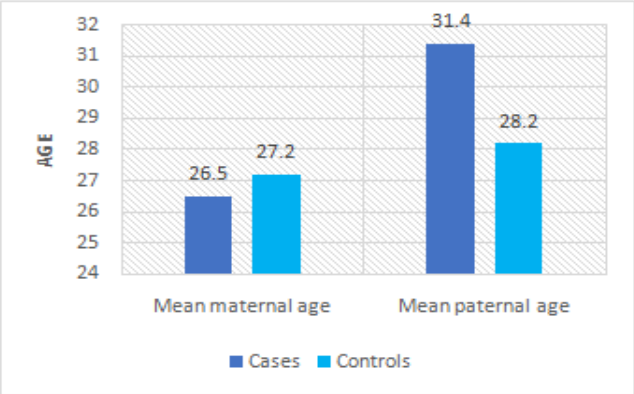
Parameter	Cases	Controls	P Value
Mean age	2.3±1.2 years	2.45±0.9 years	0.48, T=0.70
Gender	67% were males	53% were males	0.04, Z=2.02

Parental age and education: There is a significant difference in parental age and education between cases and controls as shown in table 2. Paternal age is significantly more and maternal, paternal education is significantly less in the case group.

Table 2: Paternal age and education in two groups

Parameter	Cases	Controls	P Value
Mean maternal age	26.5±4.3 years	27.2±4.7 years	0.4390, T=0.777
Mean paternal age	31.4±7.8 years	28.2±3.4 years	0.009, T=2.65
Maternal education below the university level	68%	32%	0.001, Z=5.23
Paternal education below university level	58%	24%	0.001, Z=4.88

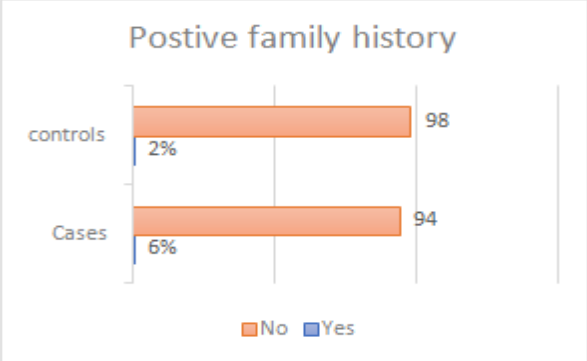
Figure 1: Mean paternal and maternal age in both groups



Family history of ASD

There is no significant difference in the incidence of a family history of ASD between cases and controls (P=0.051).

Figure 2: Family history of ASD



Maternal habits during pregnancy

Prenatal intake of vitamins is significantly less among mothers in case group. Maternal illness and maternal stress were significantly more in control group.

Table 3: Maternal habits during pregnancy in both groups

Parameter	Cases	Controls	P Value
Prenatal intake of vitamins-yes	38%	82%	0.001, Z=-6.9
Prenatal intake of drugs-Yes	6%	2%	0.149, Z=0.98
Maternal illness-yes	64%	30%	0.000, Z=4.81
Maternal stress-yes	60%	36%	0.000, Z=3.39

Neonatal factors

Mean birth weight and mean 1 min APGAR score were significantly less in cases compared to controls. Incidences of admission into NICU after birth and caesarean births are more common among cases compared to controls.

Table 4: Neonatal factors comparison between both groups

Parameter	Cases	Controls	P Value
Mean birth weight	2.65±0.9 kgs	3.2±1.2 kgs	0.011, T=2.59
Mode of delivery-caesarean section	56%	34%	0.0001, Z=3.12
Admission into NICU- Yes	42%	16%	0.0000, Z=4.05
Mean APGAR scores	8.0±1.0	5.0±1.0	0.000, T=15.0

DISCUSSION

This was acase-control studyconducted at Fathima Institute of medical sciences, a tertiary care centre with well-equipped facilities.

There is no significant difference in the mean age between cases and controls. This implied that age doesn't play a vital role in ASD, as long as all children were within 1 -3 years. There is a significant difference in gender among cases and controls. Males are more in the case group. This implies that male gender is one of the risk factors for the development of ASD. **Lama S et al.**[14] did a study on 230 children aged below 3 years. Among them, 46 were cases (children with ASD) and 184 children were controls (with no ASD) found that mean age was more among cases compared to controls and there is no significant difference in gender between cases and controls, in contrast to our study. The difference in results could be due to genetic factors as their study was done in Lebanon and they included breastfeeding children also, unlike our study. There is a significant difference in parental age and education between cases and controls. Paternal age is significantly more and maternal, paternal education is significantly less in the case group. This implies that more paternal age, less maternal and paternal education as risk factors for the development of ASD. Our findings were consistent with previous studies done by **Cheng[15], Janecka et al**.[16] regarding advanced paternal age as risk factor for the development of ASD. Basically, parents' education is one of the barriers in providing a better care to children.[17]There is no significant difference in the incidence of a family history of ASD between cases and controls. Prenatal intake of vitamins is significantly less among mothers in case group. Maternal illness and maternal stress were significantly more in control group. This implies that deficiency of

prenatal iron, calcium, folic acid increases the risk of ASD among babies. As per the study of **A Sauders,**[18] positive family history of ASD, maternal intake of antibiotics or any other drugs as risk factors for the development of ASD in children. The difference in findings regarding family history in our study could be due to less sample size and less incidence of family history in our study. Intake of alcohol, smoking or any other addiction drugs and maternal illnesses like stress, diabetes, hypertension, amniotic and placental fluid disorders may raise the risk of ASD among their babies. Mean birth weight and mean 1 min APGAR score was significantly less in cases compared to controls. Incidences of admission into NICU after birth and caesarean births are more common among cases compared to controls. Less birth weight, less APGAR score, caesarean birth and admission into NICU were also considered risk factors in the development of ASD. In previous reports also, C-section delivery was found to be a risk factor for causing autism. General anaesthesia given for C-section is suggested as main factor, as per **Glasson EJ et al** and others.[19-20]Above all, children who were not breastfed or provided formula containing docosahexaenoic acid or arachidonic acid are more likely to develop ASD, as per **Ghozy et al.** M**alek A et al.**[21-22] found that neonatal illnesses like asthma, epilepsy, microcephaly, jaundice, vision impairment, birth after 42 weeks as risk factors for ASD development. We didn't assess neonatal illnesses' association with ASD in our study, which is one of the limitations. Another limitation is our study was, it was done on small sample size and at single-center. So, the results can't be generalized completely to public.

CONCLUSION

Our study proved that being male, more paternal age, lack of proper parental education, poor intake of prenatal vitamins, excess maternal stress, less birth weight, mean APGAR score at 1 min as risk factors for ASD among non-breastfed children. So, we highly recommend taking prompt preventive measures to reduce the incidence of ASD.

ACKNOWLEDGMENTS

I would like to thank the principal and superintendent of Fathima institute of medical sciences, our institutional ethics committee and the parents of children who provided consent to the study.

REFERENCES

1. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) Washington, DC: American Psychiatric Association; 1994. [Google Scholar]
2. Lord C, Shulman C, DiLavore P. Regression and word loss in autistic spectrum disorders. J Child Psychol Psychiatry. 2004; 45:936–955. doi: 10.1111/j.1469-7610. 2004.t01-1-00287. x. [PubMed]
3. Siperstein R, Volkmar F. Brief report: parental reporting of regression in children with pervasive developmental disorders. J Autism Dev Disord. 2004; 34:731–734. doi: 10.1007/s10803-004-5294-y. [PubMed]
4. Salhia HO, Al-Nasser LA, Taher LS, Al-Khathaami AM, El-Metwally AA. Systemic review of the epidemiology of autism in Arab Gulf countries. *Neurosciences (Riyadh)* 2014;19:291–6. [PMC free article] [PubMed]
5. Ravi S, Chandrasekaran V, Kattimani S, Subramanian M. Maternal and birth risk factors for children screening positive for autism

spectrum disorders on M-CHAT-R. Asian J Psychiatr. 2016 Aug; 22:17-21. doi: 10.1016/j.ajp.2016.04.001. Epub 2016 Apr 23. PMID: 27520889.

6. Heinig MJ. Host defense benefits of breastfeeding for the infant. Effect of breastfeeding duration and exclusivity. Pediatr Clin North Am. 2001 Feb;48(1):105-23, ix. doi: 10.1016/s0031-3955(05)70288-1. PMID: 11236719.
7. Oddy WH. Breastfeeding protects against illness and infection in infants and children: a review of the evidence. Breastfeed Rev. 2001 Jul;9(2):11-8. PMID: 11550600.
8. Labbok MH. Health sequelae of breastfeeding for the mother. Clin Perinatol. 1999 Jun;26(2):491-503, viii-ix. PMID: 10394498.
9. Tanoue Y, Oda S. Weaning time of children with infantile autism. J Autism Dev Disord. 1989; 19:425–434. doi: 10.1007/ BF02212940. [PubMed]
10. Schultz ST, Klonoff-Cohen HS, Wingard DL, Akshoomoff NA, Macera CA, Ji M, Bacher C. Breastfeeding, infant formula supplementation, and Autistic Disorder: the results of a parent survey. Int Breastfeed J. 2006 Sep 15; 1:16. doi: 10.1186/1746-4358-1-16. PMID: 16978397; PMCID: PMC1578554.
11. Soke GN, Maenner M, Windham G, Moody E, Kaczaniuk J, DiGuiseppi C, Schieve LA. Association Between Breastfeeding Initiation and Duration and Autism Spectrum Disorder in Preschool Children Enrolled in the Study to Explore Early Development. Autism Res. 2019 May;12(5):816-829. doi: 10.1002/aur.2091. Epub 2019 Mar 9. PMID: 30852853; PMCID: PMC7723061.
12. Brown CM, Austin DW, Busija L. Observable essential fatty acid deficiency markers and autism spectrum disorder. Breastfeed Rev. 2014 Jul;22(2):21-6. PMID: 25109097.
13. Raina SK, Chander V, Bhardwaj AK, Kumar D, Sharma S, Kashyap V, Singh M, Bhardwaj A. Prevalence of Autism Spectrum Disorder among Rural, Urban, and Tribal Children (1-10 Years of Age). J Neurosci Rural Pract. 2017 Jul-Sep;8(3):368-374. doi: 10.4103/jnrp.jnrp_329_16. PMID: 28694615; PMCID: PMC5488556.
14. Shamsedine L, Mailhac A, Badaoui A, El Hakim R, Kibbi R, Oueidat H, et al. Breastfeeding association with autism spectrum disorders: A case-control study from Lebanon. Res Autism Spectr Disord [Internet]. 2020;78(101651): 101651. Available from: http://dx.doi.org/ 10.1016/j.rasd.2020.101651
15. Cheng J, Eskenazi B, Widjaja F, Cordero JF, Hendren RL. Improving autism perinatal risk factors: A systematic review. Med Hypotheses. 2019 Jun;127:26-33. doi: 10.1016/j.mehy. 2019.03.012. Epub 2019 Mar 23. PMID: 31088644.
16. Janecka M, Hansen SN, Modabbernia A, Browne HA, Buxbaum JD, Schendel DE, Reichenberg A, Parner ET, Grice DE. Parental Age and Differential Estimates of Risk for Neuropsychiatric Disorders: Findings From the Danish Birth Cohort. J Am Acad Child Adolesc Psychiatry. 2019 Jun;58(6):618-627. doi: 10.1016/j.jaac.2018.09.447. Epub 2019 Feb 27. PMID: 30825496.
17. Steiner AM, Koegel LK, Koegel RL, Ence WA. Issues and theoretical constructs regarding parent education for autism spectrum disorders. J Autism

Dev Disord. 2012;42(6):1218-27. doi: 10.1007/ s10803-011-1194-0. [PubMed: 21336525]. [PubMed Central: PMC3810158].

18. Saunders A, Woodland J, Gander S. A Comparison of Prenatal Exposures in Children with and without a Diagnosis of Autism Spectrum Disorder. Cureus. 2019 Jul 24;11(7):e5223. doi: 10.7759/cureus.5223. PMID: 31565625; PMCID: PMC6758968.
19. Chien LN, Lin HC, Shao YH, Chiou ST, Chiou HY. Risk of autism associated with general anesthesia during cesarean delivery: A population-based birth-cohort analysis. J Autism Dev Disord. 2015;45(4):932-42. doi: 10.1007/s10803-014-2247-y. [PubMed: 25256350].
20. Glasson EJ, Bower C, Petterson B, de Klerk N, Chaney G, Hallmayer JF. Perinatal factors and the development of autism: A population study. Arch Gen Psychiatry. 2004;61(6):618-27. doi: 10.1001/archpsyc.61.6.618. [PubMed: 15184241].
21. Ghozy S, Tran L, Naveed S, Quynh TTH, Helmy Zayan A, Waqas A, Sayed AKH, Karimzadeh S, Hirayama K, Huy NT. Association of breastfeeding status with risk of autism spectrum disorder: A systematic review, dose-response analysis and meta-analysis. Asian J Psychiatr. 2020 Feb;48:101916. doi: 10.1016/j.ajp.2019.101916. Epub 2019 Dec 27. PMID: 31923810.
22. Malek A, Farhang S, Amiri S, Abdi S, Razzaghi Rezaih A, Asadian M. Risk factors for autistic disorder: A case-control study. Iran J Pediatr [Internet]. 2019;29(3). Available from: http://dx.doi.org/10.5812/ijp.80935