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RELATION OF PERINATAL RISK FACTORS WITH SEVERITY OF AUTISM SPECTRUM DISORDERS IN CHILDREN ATTENDING TERTIARY CARE PSYCHIATRIC UNIT IN NORTHEAST INDIA.

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ABSTRACT Many studies have suggested the association of perinatal factors in mothers with increased risk of Autism Spectrum Disorders(ASD) in their offspring. However, few reports have addressed the question of their influence on the severity of clinical presentation of children with ASD. Hence, this study was undertaken to assess the relation between the presence of perinatal risk factors and severity of Autism Spectrum Disorder. Study was undertaken using a cross sectional study design using 50 children attending psychiatry OPD or admitted in psychiatry ward of the institute. Proforma for sociodemographic characteristics and perinatal risk factors were collected retrospectively from parents. Occurence of perinatal risk factors was highest for caesarean delivery (70%) followed by preterm birth (62%) and delayed breast feeding (60%) respectively which was much higher than in the general population. Most of the children were functioning in the moderate ASD range (66%) followed by mild (28%) and severe (6%) respectively. A significant association was found (p=0.001) between Breech presentation and severity of autistic symptoms. However, other perinatal risk factors were found to be statistically not significant. Hence, this study suggest the need of further research to verify and assess the effects of individual perinatal factors on ASD.

KEYWORDS : Autism spectrum disorder, Perinatal, Severity, Breech presentation, Caesarean delivery

INTRODUCTION:

Autism spectrum disorder (ASD) is a complex neurodevelopmental disorder, which is usually diagnosed at a young age. Autism spectrum disorder includes a range of conditions characterized by persistent deficits in social communication and social interaction and restricted, repetitive patterns of behaviour, interests or activities which must be present from early childhood and limit everyday functioning. These disorders include autism, pervasive developmental disorders not otherwise specified and Aspergers syndrome.

According to the World Health Organization (WHO), the prevalence of ASD is 1 in 160 children globally, and has continue to increase since the last two decades. Studies from Asia, Europe, and North America have reported prevalence rates for ASD in the range of 1% to 2% for ASD and studies from India report a prevalence for around 3.2%.[1] The increase in prevalence may be due to extensive screening, increased awareness, better access to health care, broadened criteria of diagnosis.

A recent study by Santino et al. suggests that genetic factors account for only 35-40% of the contributing elements.[2] The remaining 60-65% are likely due to other factor such as prenatal, perinatal and postnatal environmental factors. [3] Multiple perinatal risk factors during pregnancy appear to be associated with an elevated risk of ASD in the offspring, supporting the hypothesis that environmental influences in conjunction with genetic vulnerability contribute to the risk of developing ASD4 . Although perinatal factors have been reported to increase the risk of ASD, how these factors impact the clinical severity is largely unknown. It is interesting that children with typical autism suffered from more maternal complications during pregnancy or delivery than those with Asperger syndrome or atypical autism [5], suggesting a potential impact of these perinatal factors on clinical subtypes of ASD. Many studies have suggested the association of perinatal factors in mothers with increased risk of Autism Spectrum Disorders (ASD) in their offspring. However, few reports have addressed the question of their influence on the severity of clinical presentation of children with ASD.

Pregnancy-induced hypertension, preeclampsia, albuminuria, generalized oedema, and parental depression were shown to be associated with more severe deficits of children with ASD in communication and/or severe repetitive behaviour assessed by the ADI-R (Autism Diagnostic Interview-Revised) '[6]. Hadjkacem et al. did not show any significant association between clinical severity accessed via the CARS (Childhood Autism Rating Scale) and prenatal, perinatal, or post-natal factors for 50 children with ASD7. By contrast, Chien et al. showed preeclampsia, polyhydramnios, oligohydroamnios, inserted lower placenta, umbilical cord knots, and gestational diabetes to be significantly associated with greater stereotypical behaviour and socio-communicative impairment in children with ASD[8].

Studies related to ASD especially in Assam is very scarce, also this study would be an eye-opener to many psychiatrist as well as parents to understand the possible factors and its related outcome that are associated with ASD. Hence, this study was carried out to study the sociodemographic profile and occurence of various perinatal risk factors in children with Autism Spectrum Disorders(ASD) and to assess the relation between perinatal risk factors and severity of ASD. To the best of our knowledge, this is the first study in North-eastern part of India which focuses on various perinatal factors associated with severity of ASD.

MATERIALS AND METHODS:

The study was conducted in Gauhati Medical College and Hospital, Guwahati, Assam, India from June, 2021 to May 2022. It was a cross sectional study with a sample size of 50 children attending psychiatry OPD or admitted in psychiatry ward of the institute. The study was approved by the Institutional Ethical Committee of Gauhati Medical College and Hospital. Children with age group – 3- 18 yrs of both male and female gender and diagnosed with ASD with written informed consent (from parents) were included in the study. Those with serious neurological disorder (tuberous sclerosis, neurofibromatosis, fragile X syndrome) and those reporting head injury were excluded from the study.

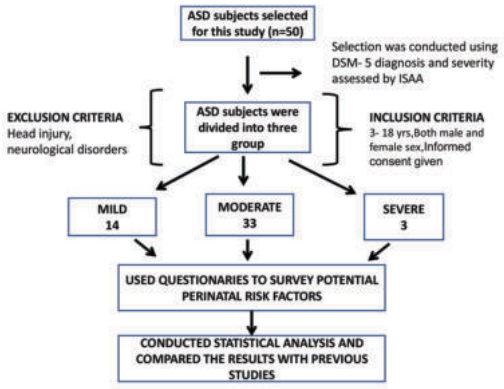
Children were diagnosed using DSM-5 criteria for ASD. Proforma for sociodemographic characteristics were used and data on perinatal risk factors were collected retrospectively from parents. The proforma was designed to acquire the information regarding the ASD affected children and as well as their paternal and maternal associated factors which was required to investigate any association between demographic, environment and perinatal risk factors among ASD children. The investigated perinatal factors were caesarean delivery, low gestational age at birth(< 37 weeks), delayed breast feeding, delayed crying, neonatal jaundice, fetal hypoxia, premature rupture of membranes, low birth weight(< 2.5kg), pre-eclampsia, me conium-stained, polyhydramnios/ oligohydramnios, getational diabetes, breech presentation, ABO and RH incompatibility, fetal nuchal cord and maternal gestational bleeding accounting for total 16 perinatal factors. The studied variables were designed according to the probable risk factors of ASD from existing literature. Modified kuppuswamy scale was used for determining the socioeconomic status of families with ASD children. Indian Scale for Assessment of Autism (ISAA) was administered to grade the severity of ASD.

STATISTICALANALYSIS :

The characteristics of the sample are described by frequencies for

qualitative variables and mean and standard deviation for quantitative variables. Distribution of each perinatal risk factors was demonstrated individually. Univariate analysis were used to examine associations between perinatal risk factors and dependent variable (severity of ASD, ISAA score) using chi square test. Association between various demographic variables which are independent variables with severity of ASD was also tested using chi square test. The level of bilateral significance was 0.05. The statistical analysis was performed using SPSS software version 26.

Figure 1 : Flowchart describing the study design.



RESULTS :

SOCIODEMOGRAPHIC PROFILE OF CHILDREN WITH ASD :

Mean age at diagnosis was 8.5 years with a male preponderance of 88%. Majority children (28%) under the study were studying in class 1-6 and 54% of all children were from upper middle socio-economic status. 70 % of children lived in nuclear family and mean maternal and paternal age were found to be 26 years and 31 years respectively. Developmental milestones were delayed in 88% of children with 82% being first born child. Most of the children were functioning in the moderate ASD range (66%) followed by mild (28%) and severe(6%) respectively which is shown in Table 1.

Table 1 : showing distribution of severity of ASD

	Frequency	Percent	Mean	SD
Mild (70 -106)	14	28.0	99.21	7.79
Moderate (107 - 153)	33	66.0	124.21	12.94
Severe (>153)	3	6.0	157.66	4.72
Total	50	100.0	119.22	18.65

OCCURENCE OF PERINATAL RISK FACTORS :

Occurence of perinatal risk factors was highest for caesarean delivery(70%) followed by preterm birth (62%) and delayed breast feeding (60%) respectively. The least common perinatal factors were ABO and RH incompatibility, fetal nuchal cord and maternal gestational bleeding.(Table 2)

Table 2: showing the occurrence of various perinatal risk factors'

Perinatal risk factors	Total	Occurence(%)
Caesarean delivery	35	70
Low gestational age at birth	31	62
Delayed Breast feeding	30	60
Delayed crying	26	52
Neonatal Jaundice	17	34
Fetal distress/Hypoxia	14	28
Premature rupture of membrane	12	24
Low Birth weight	11	22
Pre-Eclampsia	10	20
Meconium stained	5	10
Polyhydramnios/Oligohydramnios	4	8
Gestational Diabetes	2	4
Breech of presentation	6	12
ABO and RH Compatibility	1	2
Fetal nuchal cord	1	2
Maternal Gestational Bleeding	1	2

RELATION OF SOCIODEMOGRAPHIC AND PERINATAL FACTORS WITH SEVERITY OF CLINICAL PRESENTATION OF ASD:

Among demographic variables, a significant association was found between upper socio-economic status and severity of Autism Sectrum Disorder (p=.039<.05) whereas other sociodemographic variables did not show any association(Table 3). A significant association was found (p<0.05) between Breech presentation and severity of autistic symptoms. However, other perinatal risk factors were found to be statistically not significant (Table 4)

Table 3: showing the association between various sociodemographic factors and clinical presentation of ASD.

Sociodemographic variables		Severity of ASD			Total	Percentage(%)	P value
		Mild	Moderate	Severe			
Age	Early childhood(3-7yrs)	4 (15.4%)	20 (76.9%)	2 (7.7%)	26	52	0.254
	Late childhood(8-12 yrs)	6 (46.2%)	7 (53.5%)	0 (0.0%)	13	26	
	Adolescence (13-	4 (36.4%)	6 (54.5%)	1 (9.1%)	11	22	
Gender	Male	12 (27.3%)	30 (68.2%)	2 (4.5%)	44	88	0.443
	Female	2 (33.3%)	3 (50.0%)	1 (16.7%)	6	12	
Religion	Hindu	12 (27.3%)	39 (65.9%)	3 (6.8%)	44	88	0.976
	Islam	1 (33.3%)	2 (66.7%)	0 (0.0%)	3	6	
	Christian	1 (33.3%)	2 (66.7%)	0 (0.0%)	3	6	
Education	Illiterate	3 (23.1%)	9 (69.2%)	1 (7.7%)	13	26	0.555
	Special school	1 (9.1%)	9 (81.8%)	1 (9.1%)	11	22	
	Play group	1 (25.0%)	3 (75.0%)	0 (0.0%)	4	8	
	Preparator	0 (0.0%)	2 (100.0%)	0 (0.0%)	2	4	
	Class1-6	7 (50.0%)	7 (50.0%)	0 (0.0%)	14	28	
	Class 7-10	2 (33.3%)	3 (50.0%)	1 (16.7%)	6	12	
Socio economic status	Upper	1 (20.0%)	2 (40.0%)	2 (40.0%)	5	10	0.039
	Upper middle	7 (25.9%)	20 (74.1%)	0 (0.0%)	27	54	
	Lower middle	3 (30.0%)	6 (60.0%)	1 (10.0%)	10	20	
	Upper	3 (37.5%)	5 (62.5%)	0 (0.0%)	8	16	
Family type	Nuclear	9 (25.7%)	23 (65.7%)	3 (8.6%)	35	70	0.590
	Joint	5 (38.5%)	8 (6.5%)	0 (0.0%)	13	26	
	Extended nuclear	0 (0.0%)	2 (100.0%)	0 (0.0%)	2	4	
Family history	Present	1 (25.5%)	3 (75.5%)	0 (0.0%)	4	8	0.849
	Absent	13 (28.3%)	30 (65.2%)	3 (6.5%)	46	92	
Maternal age	20-25 yrs	7 (28%)	17 (68%)	1 (4%)	25	50	0.954
	26-30 yrs	4 (23.5%)	11 (64.7%)	2 (11.8%)	17	34	
	30-35 yrs	2 (33.3%)	4 (66.7%)	0 (0.0%)	6	12	
	35-40 yrs	1 (50.0%)	1 (50.0%)	0 (0.0%)	2	4	
Paternal age	25-30 yrs	3 (42.9%)	4 (57.1%)	0 (0.0%)	7	14	0.450
	30-35 yrs	1 (9.1%)	8 (72.7%)	2 (18.2%)	11	22	
	35-40 yrs	4 (22.2%)	13 (72.2%)	1 (5.6%)	18	36	
	40-45 yrs	4 (40.0%)	6 (60.0%)	0 (0.0%)	10	20	
	45-50yrs	2 (50.0%)	2 (50.0%)	0 (0.0%)	4	8	
Delayed development milestones	Delayed	11 (24.4%)	13 (68.9%)	3 (6.7%)	45	90	0.231
	Not delayed	3 (60.0%)	2 (40.0%)	0 (0.0%)	5	10	
Academic performance	Good	7 (53.3%)	6 (46.2%)	0 (0.0%)	13	26	0.171
	Poor	2 (20.0%)	7 (70.0%)	1 (10.0%)	10	20	
	Not applicable	5 (18.5%)	20 (74%)	2 (7%)	27	54	
First birth order	Yes	13 (31.7%)	25 (61.0%)	3 (7.3%)	41	82	0.266
	No	1 (11.1%)	8 (88.9%)	0 (0.0%)	9	18	

Table 4: showing the association between various perinatal risk factors and clinical presentation of ASD.

Perinatal risk factors	Severity of ASD			Frequency	Occurrence(%)	P value
	Mild	Moderate	Severe			

Pre-eclampsia	Yes	3 (30.0%)	6 (60.0%)	1 (10.0%)	10	20	
	No	11 (27.5%	27 (67.5%)	2 (5.0%)	40	80	
Gestational diabetes	Yes	0 (0.0%)	2 (100.0%)	0 (0.0%)	2	4	0.585
	No	14(29.2%)	31 (64.6%)	3 (6.3%)	48	96	
Maternal gestational bleeding	Yes	0 (0.0%)	1 (100.0%)	0 (0.0%)	1	2	0.769
	No	14 (28.6%	32 (65.3%)	3 (6.1%)	49	98	
Premature rupture of membranes	Yes	4 (33.3%)	8 (66.7%)	0 (0.0%)	12	24	0.574
	No	10 (26.3%)	25 (65.8%)	3 (7.9%)	38	76	
Polyhydramnios/oligohydramnios	Yes	0 (0.0%)	4 (100.0%)	0 (0.0%)	4	8	0.326
	No	14 (30.4%)	29 (63.0%)	3 (6.5%)	46	92	
Breech presentation	Yes	4 (66.7%)	1 (16.7%)	1 (16.7%)	6	12	0.001
	No	10 (22.7%)	32(72.7%)	2 (4.5%)	44	88	
Caesarean delivery	Yes	8 (22.9%)	26 (74.3%)	1 (2.9%)	35	70	0.120
	No	6 (40.0%)	7 (46.7%)	2 (13.3%)	15	30	
Preterm (<37 weeks)	Yes	9 (29.0%)	20 (64.5%)	2 (6.5%)	31	62	0.958
	No	5 (26.3%)	13 (68.4%)	1 (5.3%)	19	38	
Fetal nuchal cord	Yes	0 (0.0%)	1 (100.0%)	0 (0.0%)	1	2	0.769
	No	14 (28.6%)	32 (65.3%)	3 (6.1%)	49	98	
Low birth weight at delivery	Yes	4 (36.4%)	6 (54.5%)	1 (9.1%)	11	22	0.651
	No	10 (25.6%)	27 (69.2%)	2 (5.1%)	39	78	
Delayed crying	Yes	8 (30.8%)	17 (65.4%)	1 (3.8%)	26	52	0.752
	No	6 (25.0%)	16 (66.7%)	2 (8.3%)	24	48	
ABO and RH incompatibility	Yes	0 (0.0%)	1 (100.0%)	0 (0.0%)	1	2	0.769
	No	14 (28.6%)	32 (65.3%)	3 (6.1%)	49	98	
Delayed breast feeding	Yes	8 (26.7%)	21 (70.0%)	1 (3.3%)	30	60	0.572
	No	6 (30.0%)	12 (60.0%)	2 (10.0%)	20	40	
Meconium stained	Yes	1 (20.0%)	4 (80.0%)	0 (0.0%)	5	10	0.732
	No	13 (28.9%)	29 (64.4%)	3 (6.7%)	45	90	
Fetal distress/ hypoxia	Yes	5 (35.7%)	9 (64.3%)	0 (0.0%)	14	28	0.452
	No	9 (25.0%)	24 (66.7%)	3 (8.3%)	36	72	
Neonatal jaundice	Yes	5 (29.4%)	11 (64.7%)	1 (5.9%)	17	34	0.987
	No	9 (27.3%)	22 (66.7%)	2 (6.1%)	33	66	

DISCUSSION :

The average age of participants was 8.5 years when they received a confirmed diagnosis of ASD , which is comparable to a study by David S. Mandell et al. where the mean age of diagnosis of children with Aspergers syndrome was 7.2 years.[9] Most children were boys corresponding to other studies[10]. Overall 66% of children had moderate level of clinical severity similar to a study by Balachandra et al.[11]

The occurence of perinatal risk factors in our sample is in the high range as compared to that reported in the general population (6-35%). In addition, the occurrence of caesarean delivery was found to be highest in our sample(70%) as compared to that of general population12 .This could be due to increasing demand for caesarean delivery among young educated women residing in urban areas[13].

Rate of prematurity was 62% which was much higher as compared to general population 14. This was very much similar to a study by Kuzniewicz et al. 15where it was suggested that ASD was 3 times more prevalent in infants born at < 27 weeks as compared with term infants. Each week of short gestation was associated with an increased risk of ASD. Hemodynamic/ respiratory instability in preterm infants leading to high frequency ventilation, use of inotropes, long hospitalisation in ICU may be one of the reason. The extra uterine environment in which the preterm brain matures may alter gene expression and result in impaired neurodevelopment. Twin studies have shown that highly heritable autistic traits are modified by environmental factors [16,17].A significant increase in self-injurious behavior in preterm children as compared to term ASD children was seen which was consistent with a study by Movsas et al.[14]

Delayed breast feeding was seen in 60 % of ASD children which may be due to the high rate of caesarean delivery in our study. Findings from a study by Xiaoyun Qin et al. revealed that delayed initiation of breastfeeding, delayed onset of lactogenesis and the short duration of exclusive breastfeeding related to Caesarean Delivery (CD), as could be supported by many other studies. Studies have also noted that women who delivered by CD may have less intention to breastfeed or did not initiate breastfeeding compared with those who delivered vaginally (7.4 and 4.3% respectively) . The caesarean delivery might itself cause lots of postpartum pain and may delay the initiation of breastfeeding. Infants' sucking action during breastfeeding increases maternal oxytocin level. Also, oxytocin in breast milk can promote mother-infant attachment, as it is helpful for infants' social cognition and neurodevelopment. Delayed skin contact between mothers and infants occurs more frequently in CD than between mother-infant pairs in vaginal delivery, and this would also prolong the initiation of breastfeeding after Caesarean delivery .[18]

A significant association was found between breech presentation and severity of clinical presentation of ASD which was consistent with results from a metanalysis by Gardener in.19 This could be attributed to increased risk of birth trauma associated with Breech presentation such as injuries to baby's after coming head, umbilical cord prolapse, dislocated or broken bones . However in another metaanalysis by Ensiyeh Jenabi et al. , no association was found between breech presentation and clinical severity of ASD.20 They proposed in their study that the association between breech presentation and severity of ASD shared aetiology rather than a casual relationship. Risk factors for breech presentation such as advanced maternal age, low birth weight, prematurity, primiparity, polyhydramnios may act as confounders. Therefore, this association may be of no significant when some confounders variable is adjusted.[21]

Also a significant association was found between upper middle socioeconomic class and ASD severity. This reasoning could also be consequences of the sample under study which were mostly from urban areas. This is in contrast to a study by Balachandra et. al 2021 where low income or middle income group was significantly associated.11The absence of significant associations between other perinatal factors and clinical severity in children with ASD were found to be consistent with findings by Hadjkacem et al.2016 where no association was found between clinical severity of ASD and perinatal risk factors.7. The overepresentation of first born children in ASD group may be explained by parents reluctance to have more children after one children has been diagnosed with ASD.[3,11,22]

Particular strengths of this study were that the diagnosis of ASD was confirmed using DSM-5 diagnosis and that the children's clinical presentation was fully described using Indian Scale For Assessment of autism. In addition, this is one of the rare studies done to explore the association between perinatal factors and the severity of clinical presentations among children with confirmed ASD.

Our study had certain limitations also. Firstly, the data on perinatal factors were collected retrospectively, resulting in a memory bias. Secondly, the data for certain perinatal factors, such as preeclampsia, polyhydramnios, or oligo-hydramnios, breech presentation were not systematically collected in the medical records , limiting comparisons with past studies. Thirdly, because of the limited sample size , there was difficulty in generalizing the findings to the entire population. Other study limitations were lack of a comparision group and the majority of sample belonged to urban residential areas

CONCLUSION:

The results of the study highlighted the importance of systematic screening for perinatal risk factors in mothers and to ensure that they are regularly followed during their pregnancy period .Our findings suggest that a history of breech presentation is associated with more severe clinical presentation. Despite the fact that no statistically significant association were observed between other perinatal factors and severity of ASD , the prevalence of perinatal factors was higher in the ASD children compared to in the general population. Parents must

be made aware regarding prenatal screening and timely intervention of their children. Larger studies will be needed in order to clarify the underlying biologic mechanisms driving these findings.

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The authors declare no conflicts of interest.

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The study was approved by the Institutional Ethics Committee

REFERENCES:

1. Sagar, R., Dandona, R., Gururaj, G., Dhaliwal, R. S., Singh, A., Ferrari, A., Dua, T., Ganguli, A., Varghese, M., Chakma, J. K., Kumar, G. A., Shaji, K. S., Ambekar, A., Rangaswamy, T., Vijayakumar, L., Agarwal, V., Krishnankutty, R. P., Bhatia, R., Charlson, F., … Dandona, L. (2020). The burden of mental disorders across the states of India: The Global Burden of Disease Study 1990–2017. The Lancet Psychiatry, 7(2), 148–161. https://doi.org/10.1016/S2215-0366(19)30475-4
2. Autism Spectrum disorders (ASD) in South Asia: A systematic review | SpringerLink. (n.d.). Retrieved March 12, 2023, from https://link.springer.com/article/10.1186/s12888-017-1440-x
3. Froehlich-Santino, W., Londono Tobon, A., Cleveland, S., Torres, A., Phillips, J., Cohen, B., Torigoe, T., Miller, J., Fedele, A., Collins, J., Smith, K., Lotspeich, L., Croen, L. A., Ozonoff, S., Lajonchere, C., Grether, J. K., O'Hara, R., & Hallmayer, J. (2014). Prenatal and perinatal risk factors in a twin study of autism spectrum disorders. Journal of Psychiatric Research, 54, 100–108. https://doi.org/10.1016/j.jpsychires.2014.03.019
4. Pre- and Perinatal Risk Factors for Autism Spectrum Disorder in a New Jersey Cohort—Lauren A. Maramara, Wenzhuan He, Xue Ming, 2014. (n.d.). Retrieved September 30, 2022, from https://journals.sagepub.com/doi/abs/10.1177/0883073813512899
5. Glasson, E. J., Bower, C., Petterson, B., de Klerk, N., Chaney, G., & Hallmayer, J. F. (2004). Perinatal Factors and the Development of Autism: A Population Study. Archives of General Psychiatry, 61(6), 618–627. https://doi.org/10.1001/archpsyc.61.6.618
6. Wallace, A. E., Anderson, G. M., & Dubrow, R. (2008). Obstetric and Parental Psychiatric Variables as Potential Predictors of Autism Severity. Journal of Autism and Developmental Disorders, 38(8), 1542–1554. https://doi.org/10.1007/s10803-007-0536-4
7. Hadjkacem, I., Ayadi, H., Turki, M., Yaich, S., Khemekhem, K., Walha, A., Cherif, L., Moalla, Y., & Ghribi, F. (2016). Prenatal, perinatal and postnatal factors associated with autism spectrum disorder. Jornal de Pediatria, 92, 595–601. https://doi.org/10.1016/j.jped.2016.01.012
8. Chien, Y.-L., Chou, M.-C., Chou, W.-J., Wu, Y.-Y., Tsai, W.-C., Chiu, Y.-N., & Gau, S. S.-F. (2019). Prenatal and perinatal risk factors and the clinical implications on autism spectrum disorder. Autism, 23(3), 783–791. https://doi.org/10.1177/1362361318772813
9. Mandell, D. S., Novak, M. M., & Zubritsky, C. D. (2005). Factors Associated With Age of Diagnosis Among Children With Autism Spectrum Disorders. Pediatrics, 116(6), 1480–1486. https://doi.org/10.1542/peds.2005-0185
10. Werling, D. M., & Geschwind, D. H. (2013). Sex differences in autism spectrum disorders. Current Opinion in Neurology, 26(2), 146–153. https://doi.org/10.1097/WCO.0b013e32835ee548
11. Geetha, B., Sukumar, C., Dhivyadeepa, E., Reddy, J. K., & Balachandar, V. (2019). Autism in India: A case–control study to understand the association between socio-economic and environmental risk factors. Acta Neurologica Belgica, 119(3), 393–401. https://doi.org/10.1007/s13760-018-01057-4
12. Saroukhani, S., Samms-Vaughan, M., Lee, M., Bach, M. A., Bressler, J., Hessabi, M., Grove, M. L., Shakespeare-Pellington, S., Loveland, K. A., & Rahbar, M. H. (2020). Perinatal Factors Associated with Autism Spectrum Disorder in Jamaican Children. Journal of Autism and Developmental Disorders, 50(9), 3341–3357. https://doi.org/10.1007/s10803-019-04229-0
13. Lei, H., Wen, S. W., & Walker, M. (2003). Determinants of Caesarean Delivery Among Women Hospitalized for Childbirth in a Remote Population in China. Journal of Obstetrics and Gynaecology Canada, 25(11), 937–943. https://doi.org/10.1016/S1701-2163(16)30242-0
14. Movsas, T. Z., & Paneth, N. (2012). The Effect of Gestational Age on Symptom Severity in Children with Autism Spectrum Disorder. Journal of Autism and Developmental Disorders, 42(11), 2431–2439. https://doi.org/10.1007/s10803-012-1501-4
15. Kuzniewicz, M. W., Wi, S., Qian, Y., Walsh, E. M., Armstrong, M. A., & Croen, L. A. (2014). Prevalence and Neonatal Factors Associated with Autism Spectrum Disorders in Preterm Infants. The Journal of Pediatrics, 164(1), 20–25. https://doi.org/10.1016/j.jpeds.2013.09.021
16. McNamara, I. M., Borella, A. W., Bialowas, L. A., & Whitaker-Azmitia, P. M. (2008). Further studies in the developmental hyperserotonemia model (DHS) of autism: Social, behavioral and peptide changes. Brain Research, 1189, 203–214. https://doi.org/10.1016/j.brainres.2007.10.063
17. Rosenberg, R. E., Law, J. K., Yenokyan, G., McGready, J., Kaufmann, W. E., & Law, P. A. (2009). Characteristics and Concordance of Autism Spectrum Disorders Among 277 Twin Pairs. Archives of Pediatrics & Adolescent Medicine, 163(10), 907–914. https://doi.org/10.1001/archpediatrics.2009.98
18. Qin, X., Li, P., Wu, Y., Wang, X., Yan, S., Xu, Y., Zhu, P., Hao, J., Tao, F., & Huang, K. (2022). Impact of caesarean delivery on children's autism-like behaviours: The mediation of exclusive breastfeeding. International Breastfeeding Journal, 17(1), 53. https://doi.org/10.1186/s13006-022-00493-6
19. Gardener, H., Spiegelman, D., & Buka, S. L. (2011). Perinatal and Neonatal Risk Factors for Autism: A Comprehensive Meta-analysis. Pediatrics, 128(2), 344–355. https://doi.org/10.1542/peds.2010-1036
20. Jenabi. (n.d.). Is breech presentation associated with autism spectrum disorders among children: A meta-analysis. Retrieved September 30, 2022, from https://www.aihbonline.com/article.asp?issn=2321-8568;year=2019;volume=9;issue=1;spage=12;epage=15;aulast=Jenabi
21. Bilder, D., Pinborough-Zimmerman, J., Miller, J., & McMahon, W. (2009). Prenatal, Perinatal, and Neonatal Factors Associated With Autism Spectrum Disorders. Pediatrics, 123(5), 1293–1300. https://doi.org/10.1542/peds.2008-0927
22. Traver, S., Geoffray, M.-M., Mazières, L., Geneviève, D., Michelon, C., Picot, M.-C., & Baghdadli, A. (2021). Association between prenatal and perinatal factors and the severity of clinical presentation of children with ASD: Report from the ELENA COHORT. Journal of Psychiatric Research, 137, 634–642. https://doi.org/10.1016/j.jpsychires.2020.11.005