Review Article Available online www.ijsrr.org ISSN: 2279–0543

International Journal of Scientific Research and Reviews

Is Caesarean section a cause for Autism Spectrum Disorder?-Review

Jayashree S[1*] and Kalpana S[2]

Department of Epidemiology, The TN Dr.MGR Medical University, Chennai. India
Email:drjaishreehomeo95@yahoo.com

ABSTRACT

Autism Spectrum Disorder (ASD) is a chronic neurodevelopmental disorder characterized by deficits in social interaction and communication and restricted, repetitive interests and behaviors beginning in infancy and toddler years. ASD has been now increasing in India without proper epidemiological evidence or just a simple unknown cause. ASD is a condition that affects all the ethnic groups, social and geographical groups. Depending on the cultural belief and practice, the treatment varies. Based on the ICD-10 classification these are some diagnostic criteria used to diagnose childhood autism before the onset of 3 years of age. This differs from Asperger's syndrome, its said to be a milder variant of Autism while pragmatic and social interaction deficits are always present. While PDD, Pervasive Developmental Delay, have several developmental delays in learning, communication, socializing skills, where, these do not meet A as per gers and childhood autism, this always relates to developmental problems. The study and case reports about ASD in India was found from the 1960s, the number of cases in India was comparatively less when compared to western countries. Since the last two decades, there was a tremendous improvement in ASD in India in growth as well as in treatments. A recent study suggests that genetic factors account only for 35-40% of the contributing elements. The remaining 60-65% is likely due to other factors, such as prenatal, perinatal, and neonatal environmental factors. But still, the not single etiology can be counted for this. The Rest of the percentage to 100 remains unknown. It is important to understand why there may be a link between caesareans and some disorders, especially as C-section rates have risen in recent years. From the literature, we conclude that there is no proper evidence shows the only association between C-section and ASD, hence researchers should continue to investigate further the underlying causes of the observed associations between cesarean and ASD because CS deliveries are increasing as well as ASD in India.

KEYWORDS: Caesarean, Autism Spectrum Disorder, genetic factors

[*]Corresponding Author:
Jayashree S
Post Graduate Student, Department of Epidemiology, The Tamil Nadu Dr. M.G.R Medical University, 69, Anna Salai, Guindy, Chennai – 600032 India
Mobile:9940494830, Email: drjaishreehomeo95@yahoo.com

INTRODUCTION:

Autism Spectrum Disorder (ASD) is a chronic neurodevelopmental disorder characterized by deficits in social interaction and communication and restricted, repetitive interests and behaviors beginning in infancy and toddler years. Based on the 5th edition of Diagnostic Statistical Manual of Mental Disorders (DSM-5), specific diagnostic criteria for childhood autism include social skills and communication deficit associated with restrictive and repetitive behaviors, interests, or activities[1–4.]ASD has been now increasing in India without proper epidemiological evidence or just a simple unknown cause. ASD is a condition that affects all the ethnic groups,social and geographical groups. Depending on the cultural belief and practice, the treatment varies[5]. ASD presents with qualitative repetitive social interactions, repeated behavior, language, and patterns of social communication by restrictive, stereotyped, based on the ICD-10 classification these are some diagnostic criteria used to diagnose the childhood autism before the onset of 3 years of age. This differs from Asperger's syndrome, its said to be a milder variant of Autism while pragmatic and social interaction deficits are always present. While PDD, Pervasive Developmental Delay, have several developmental delays in learning, communication, socializing skills, where, these do not meet Aspergers and childhood autism, this always relates to developmental problems[6–10.] There has been 20 fold increase in ASD since the 1980s, in India, now it has been observed that there is a huge increase in ASD and ADHD cases,but the cause is still unknown or cannot be prejudiced or confined to one factor.

History of ASD:

In 1942, Dr.Leokanner, discovered or started observing the groups of children who were diagnosed previously as mental retardation was observed to have difficulty in speech and did not socially interact with people around them. The child was observed and diagnosed for doing repetitive behaviors. These people cannot be considered as a normal child. At those times, treatment for ASD was far less, the children used to live in institutions and far from society. In those times, professionals used to observe that due to refrigerator mothers, children have resulted in this. To the better statement, poor attachment or absentee of parentism leads to the signs of ASD. ASD generally observed during late life, after 3 years mostly. In those times, parents were blamed for such disorders, while most of them shamed the parents of such a child. Later, after the research in later years, studies found that it was a result of environmental and genetic factors[11]. Two groups were observed to differentiate severity in signs and symptoms of ASD Dr kanner was identifying symptoms of Autism in one group while,Dr. Hans

asperger found the symptoms in other groups, whereas, Asperger found that his group also had social interaction problems and also behavioral problems. However, it was found that this group of children did not have any problem with speech and language formation also no problem with adaptive functioning(they can feed themselves, dress themselves). Most of the children observed by Kanner did not have lowered cognitive abilities. Unfortunately, Asperger's discovery did not observe until decades late[11]. His study had a tremendous difference in the way of understanding ASD. While in India, ASD was found by Dr. Ronald who was a pediatrician in Darjeeling in 1943 overviewed these symptoms and termed them as a difficult child. He matched the symptoms with kanner. The study and case reports about ASD in India was found from the 1960s, the number of cases in India was comparatively less when compared to western countries. Since the last two decades, there was a tremendous improvement in ASD in India in growth as well as domains, in diagnosis, treatment options, parental involvement, prevocational, vocational, human resource and development and also in research[5,12,13,13–15.]

Epidemiology:

It is estimated that worldwide one in 160 children has an ASD. This estimate represents an average figure, and reported prevalence varies substantially across studies. Some well-controlled studies have, however, reported substantially higher figures. The prevalence of ASD in many low- and middle-income countries is so far unknown.Based on epidemiological studies conducted over the past 50 years, the prevalence of ASD appears to be increasing globally. There are many possible explanations for this apparent increase, including improved awareness, expansion of diagnostic criteria, better diagnostic tools, and improved reporting. (WHO). Even though, there has been a vast increase in the number of cases detected, especially, adults remain undiagnosed for ASD and they do not receive the service they need[5]. Now in India Caesarean section rates increases and now the very unprecedented increase in the CS section, the average rate of CS section is about 17.2%(According to NFHS-4 2016).

The prevalence of ASD, in western countries, 1 in 59 children are diagnosed with ASD, which is the 15% increase from 2012. Now, 1in 54 children are diagnosed with autism that is before 8 years of age(16). Global prevalence from 2000, it was 1in 150, now recently prevalence estimates are about 1 in 54. In India, there is still a lack of epidemiological studies in our country. Very few studies have been focused on epidemiological, population ASD cases in India. It is still difficult to present a definite estimate of the prevalence of ASD. A Rough estimate was done and it was found that ASD prevalence

was 15 per 10,000 in the 2000s which was nearly raising to 64 per 10,000 in the following years. Approximately it was studied as 1 in 500.

Etiology of ASD:

There is still not a single etiological cause that has been identified. It has been found that the environment and genetic play a role. To date, not even as single etiology was confined for the reason for ASD. To date, so many researches have been done to find out the reason for ASD. Prenatal, perinatal, and neonatal factors of ASD have an independent role. More risk factors by previous research were confined to Obstetric and psychological factors found to be more contributing risk factors for ASD. Many research papers have been found in its association with the Caesarean section and ASD. Most of the research papers like(Curran et al,) compared the odds of Caesarean section and Vaginal delivery and the results found were favoring the CS section.The rate of planned CS deliveries is increasing in singleton deliveries[17]. ASD and ADHD are highly heritable, there is evidence suggesting that environmental factors are important for the development of either disorder(Guinchat al 2012, polanshka et al).Recent papers suggested that the association of CS delivery with the outcome of ASD. Now, Caesarean section prevalence is increasing,it is very important to understand its modesty and its impact ON ASD. A Recent study suggests that genetic factors account only for 35-40% of the contributing elements. The remaining 60-65% is likely due to other factors, such as prenatal, perinatal, and neonatal environmental factors.But still, the not single etiology can be counted for this. The Rest of the percentage to 100 remains unknown.The main aim of this research is to identify that does Caesarean section has an impact on the outcome of neurodevelopment disorders like ASD.

METHODS:

Search strategy:

We searched in the MEDLINE database for studies reporting the association ASD with Caesarean section. The keywords selected were Association between Caesarean section AND Autism OR Obstetric complication AND Autism OR perinatal risk factors AND Autism.

The search strategies on various databases yielded that many risk factors contribute to the development of ASD. While some of the studies showed the greater and increased for mothers undergoing CS section. Many articles explained its increased odds, also with obstetric risk factors and increased rate of Caesarean section.

RESULTS:

Screening and Diagnosis of ASD:

ASD is difficult to diagnose at an early stages. Most of the ASD cases can be diagnosed only after 3 years. The most observed symptoms or the diagnosis of ASD done as follows:

1.Poor Eye contact.

2.Delayed speech

3. Do not play with other children

4.Limited display of language.

5. Repeating the actions again and again.

6. Inability to explain their needs and emotions.

7.Inability to interpret body language, facial expression, and voice.

8.May get uncomfortable with some touch or physical contact.

9.Fear of harmless objects

10. Sudden mood changes, laughing and crying without obvious reasons.

11.Difficulty in following instructions or directions.

12. Aggression or temper tantrums are observed, mostly by change and demand.

13.Very focused on unusual objects like wood, cloth, utensils, leaf, chains, Rocks

Diagnosis of ASD:

Diagnosis can be done by the following methods as

1.Neurological test-Physical and Nervous System.

2.Autism Diagnostic Interview-Revised.

3.CARS-Childhood Autism Rating Scale.

4.Pervasive Developmental disorder screening test.

5.Genetic test to check for Chromosomal abnormalities.

6. Tests on communication, language, speech, motor skills, academic performance and progress, cognition skills[18].

POSSIBLE RISK FACTORS OF ASD:

Up to date, there has been no single risk factorfound to cause ASD. The possible risk factors from previous researches said to be during prenatal,perinatal, obstetric risk factors, and postnatal and neonatal factors. During the prenatal period, events include both psychological and Environmental factors like change of place, death of closed one, financial problems, vomiting, and any chronic illness like eclampsia, pre-eclampsia, Diabetes, any injury everything before the labor is included in this prenatal period. The perinatal period(Refer table 5)events include from delivery to baby's 28th day, any complication during this period. The Neonatal period includes the period before 1 year. Postnatal are the events happening to children after 1 year which are life-threatening.

Table 1:.The below-listed factors are the Specific perinatal factorsaffecting a child's Mental health.

1.Acute fetal distress
2.Preterm labor
3.Prolonged labor
4.Obstructed labor
5.Low birth weight
6.Macrosomia.
7.Forceps delivery
8. Vacuum Delivery
9.Cord around neck
10.Pre Matured rupture of membrane(PROM)
11. Induced labor.
12. Breech Presentation of the child.
.

ASSOCIATION OF CS SECTION WITH ASD:

Table 2: The below table explains some evidence on the association of CS section and ASD.

Author and year	Type of study	Number of patients enrolled	Risk assessment of getting ASD
Dodds et al(2010)	A Database Cohort study from 1990 and 2002	29,733 patients,924 were ASD Diagnosed	RR=1.23(1.06-1.44), while in this article all the risk factors have been evaluated, including obesity, parity. As a result, some obstetric risk factors had an individual role for ASD. When compared to other modes of delivery, CS had higher impact[19].
Curran et al(2014)	A Systematic Review and Meta-analysis	Data on 1,384,278, children, 14,214 had ASD. Adjusted analysis,1,192,806 12,089 has ASD.	13 studies reported the risk assessment of CS-ASD of OR=1.23. Delivery by CS has increased odds for ASD when compared to Vaginal delivery[20].
Duan et al(2014)	Case-control	286-ASD cases 286-Healthy children	RR=2.03, perinatal care would reduce the incidence of ASD[21].
Garadner et al(2014)	Metaanalysis.	698 in Pubmed 176 in Embase 416 in Psychinfo	RR=1.26, wherein this study, induced labor, are at increased risk when compared to CS[22].
Gross et al(2016)	Population-based registers collected-Review	671,646 CS deliveries and 31,073 ASD children.	OR=1.26-1.38, increased association was found for ASD with CS. 23% increased risk in odds of getting highly diagnosed with ASD to CS[17].
Hadjkacem et al(2016)	Case-control study	N=101	Here, this study concludes that the obstetric factors are having an association with ASD. Having Prematurity has an 18% link with ASD in this study an also some of the delivery mode practices. From this, the CS section is having some odds of connection with ASD[1].
Huberman Samuel et al(2019)	Nested Case-control study	347 children with ASD, 117 with other DD 2226 age, sex, and ethnicity matched controls.	CS has significantly increased its association with aOR=1.537. The Study concludes that General anesthesia during CS has a significant association with ASD[23].
Perales-Marín(2018)	Hospital Nested-Case-Control study	N=261., %3 cases, and 198 controls.	OR=3.37. The results suggested that birth by CS predictor for ASD. Regular follow-up by a pediatrician may help in the early detection of ASD[24].
Polo-Kantola et al(2014)	Registry-based Case-control study.	N=4713	OR=1.34. Here in this study, concludes that the OR for CS is more than Normal delivery[6].
Yip et al(2016)	A Population-based cohort study.	671 646 CS deliveries and 31 073 ASD children	Logistic Regression OR=1.26, Stratified OR=1.15 It was associated with gestational age(36-42 weeks). CS consistently associated with ASD.
Mammiburg et al(2006)	A Population-based matched Case-control study	473 children, each identified with 10 controls.	OR=1.5(1.1-1.9) aOR=1.1(0.7-1.7) The study concluded that though there is a significant association with CS. Genes may be involved[10].

ROLE OF CS IN ASD:

In the present state, the planned and unplanned Caesarean sections are increasing with the complications of labor. From the early 60s till now, there have been so many risk factors are growing day by day, but still, there are many kinds of research that are going on, yet there has been not a conclusion of a single factor of ASD.Even ART procedures, obesity, Diabetes also have been shown as some significant associations. ASD has a severe impact on the child's brain activity, so many parents miss out on the early detection of ASD. The etiology of the ASD is not known and seems to be multifactorial, Genetic factor also seems to be linked. There was more link found between perinatal factors. Some of the researchers had a significant association with CS and ASD. Haglund et al found out in his research paper, that the significant association with CS by elective CS was 2.4, emergency CS 1.4. But the paper concluded that Obstetrical factors had insignificant association when compared to prematurity, low Apagar score, and macrosomia, and this study found more association with sub-Saharan Africa[25–29]. Alexander kolvezon et al on the review found that obstetric complications along with Apgar score, Cs delivery had a significant association with RR=16-1.8, they also concluded that the obstetric related hypoxia had increased significant association[30–32]. Zhang et al, conducted a case-control study in China, the result showed a significant association with CS delivery OR=1.79cesarean delivery (50.0% in cases vs. 35.8% in controls)[33–36]. Though some researches have found that association with CS and ASD. But the delivery complications also play a major role like prematurity, abnormal presentation which leads to CS delivery also had a significant association. LBW, Macrosomia also have some significant association.Some pregnancy risk factors also contribute to Caesarean delivery. Some research showed that there is CS delivery as a significant association, but more research needed to prove this hypothesis in the upcoming years of studies.

OTHER RISK FACTORS CONTRIBUTING TO ASD:

There are prenatal and neonatal factors that are also involved in ASD as follows.

Prenatal Factors:

As previous research suggests that, some environmental factors, Mental state of mother and infections during the prenatal period also, suboptimal temperature and also parental age, also individual chronic illness like diabetes, hypertension plays a major role. Hadjkacem et al, in his study, found that Parental age higher in ASD parents when compared to the control group, but this considered a separate factor as Parental factor. Researches found that prenatal factors like maternal infections had an

association with ASD[19,37]. Dam et al, in his study, found that prenatal factors like the bleeding have some association with ASD[38,39]. Environmental factors like living situation, air pollutions, insecticides have their role, but the researches are going on. Lower protein and calcium intake had some associations with ASD[40,41]. More Researches are needed to examine the facts, vitamins, endocrine-disrupting chemicals, and pesticides. The plausibility between these two to be found out on the upcoming researches[42]. Strong evidence suggests that the intake of some nutrients and folic acid supplements have less association with ASD.Along with these, a maternal psychiatric condition during that time has some degree of association.

Perinatal factors:

These factors include the modes of delivery, complications in delivery, complications after birth like birth asphyxia, low birth weight, cord around the neck, macrosomia also as we discussed above the modes of delivery like CS delivery forceps, Forceps and CS delivery had more association also LBW, macrosomia had contributed to ASD[39].

Neonatal factors:

These factors include the complication after birth preterm birth, Jaundice, Low birth weight, Birth Asphyxia, Delayed birth cry. Birth Asphyxia had a significant and strong association with birth asphyxia from Mammidala et al. The LBW, and neonatal encephalopathy, Apgar score also had an association with ASD[43]. No individual factors from above are associated with ASD. All the risk factors are interlinked. The most associated factors and more researches on psychiatric associations, nutrition, and infections, and some of the neonatal factors.

CONCLUSION:

While researchers said the links between C-sections and autism and ADHD were statistically significant, other disorders including learning disabilities, tics, obsessive-compulsive disorder, and eating disorders carried similar or higher odds of diagnosis in tandem with a cesarean section, but those odds were not statistically significant. That may have been due to a small sample of prior studies on the conditions included in the new analysis.Recent studies found close to no association between cesarean delivery and depression and affective or no affective psychotic disorders.Researchers said it's important to understand why there may be a link between caesareans and some disorders, especially as C-section rates have risen in recent years. we conclude that Researchers should continue to investigate what are

the underlying causes of the observed associations between cesarean and ASD. From all the researches analyzed previously, each research had all the above risk factors as a significant association in some articles. Not a single factor still can be found in association with ASD. Though we know in ASD there will be a change in the child's brain chemicals,but the maternal psychological stress, complications in pregnancy, and neonatal diseases have its role in causing ASD. Thus, in the upcoming years, more researches are needed in exploring the exact cause of ASD also more researches needed to identify the link between Maternal psychological stress, infections, and also Perinatal factors.

CONFLICT OF INTEREST:

There is no conflict of interest

ETHICAL CONSIDERATIONS:

This study did not require approval from the ethics of co individuals.

ACKNOWLEDGEMENTS:Nil

REFERENCES:

1. Hadjkacem I, Ayadi H, Turki M, Yaich S, Khemekhem K, Walha A, et al. Prenatal, perinatal and postnatal factors associated with autism spectrum disorder. J Pediatr (Rio J) [Internet]. 2016 Nov [cited 2020 Apr 1];92(6):595–601. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0021755716301024
2. Tchaconas A, Adesman A. Autism spectrum disorders: a pediatric overview and update. Curr Opin Pediatr. 2013 Feb;25(1):130–44.
3. Hallmayer J, Cleveland S, Torres A, Phillips J, Cohen B, Torigoe T, et al. Genetic heritability and shared environmental factors among twin pairs with autism. Arch Gen Psychiatry. 2011 Nov;68(11):1095–102.
4. Elsabbagh M, Divan G, Koh Y-J, Kim YS, Kauchali S, Marcín C, et al. Global prevalence of autism and other pervasive developmental disorders. Autism Res Off J Int Soc Autism Res. 2012 Jun;5(3):160–79.
5. Juneja M, Sairam S. Autism Spectrum Disorder - An Indian Perspective. :15.
6. Polo-Kantola P, Lampi KM, Hinkka-Yli-Salomäki S, Gissler M, Brown AS, Sourander A. Obstetric Risk Factors and Autism Spectrum Disorders in Finland. J Pediatr [Internet]. 2014 Feb

[cited 2020 Mar 31];164(2):358–65. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0022347613012158

7. Lampi KM, Lehtonen L, Tran PL, Suominen A, Lehti V, Banerjee PN, et al. Risk of Autism Spectrum Disorders in Low Birth Weight and Small for Gestational Age Infants. J Pediatr [Internet]. 2012 Nov [cited 2020 Apr 1];161(5):830–6. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0022347612004945
8. Is Older Maternal Age a Risk Factor for Preterm Birth and Fetal Growth Restriction? A SystematicReview: Health Care for Women International: Vol 26, No 9 [Internet]. [cited 2020 May 29]. Available from: https://www.tandfonline.com/doi/abs/10.1080/07399330500230912
9. Neonatal Jaundice, Autism, and Other Disorders of Psychological Development | American Academy of Pediatrics [Internet]. [cited 2020 May 29]. Available from: https://pediatrics.aappublications.org/content/126/5/872
10. Perinatal risk factors and infantile autism - Maimburg - 2006 - Acta Psychiatrica Scandinavica - Wiley Online Library [Internet]. [cited 2020 May 29]. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1600-0447.2006.00805.x
11. Historical Perspective « National Autism Center [Internet]. [cited 2020 Apr 2]. Available from: https://www.nationalautismcenter.org/autism/historical-perspective/
12. Daley TC. From symptom recognition to diagnosis: children with autism in urban India. Soc Sci Med 1982. 2004 Apr;58(7):1323–35.
13. National Consultation Meeting for Developing IAP Guidelines on Neuro Developmental Disorders under the aegis of IAP Childhood Disability Group and the Committee on Child Development and Neurodevelopmental Disorders, Dalwai S, Ahmed S, Udani V, Mundkur N, Kamath SS, et al. Consensus Statement of the Indian Academy of Pediatrics on Evaluation and Management of Autism Spectrum Disorder. Indian Pediatr. 2017 May 15;54(5):385–93.
14. Singh AS, Chandra R, Guhathakurta S, Sinha S, Chatterjee A, Ahmed S, et al. Genetic association and gene-gene interaction analyses suggest likely involvement of ITGB3 and TPH2 with autism spectrum disorder (ASD) in the Indian population. Prog Neuropsychopharmacol Biol Psychiatry. 2013 Aug 1;45:131–43.
15. Family-based Studies Indicate Association of Engrailed 2 Gene With Autism in an Indian Population - PubMed [Internet]. [cited 2020 May 29]. Available from: https://pubmed.ncbi.nlm.nih.gov/20050924/

16. CDC increases estimate of autism's prevalence by 15 percent, to 1 in 59 children [Internet]. Autism Speaks. [cited 2020 Apr 12]. Available from: https://www.autismspeaks.org/science-news/cdc-increases-estimate-autisms-prevalence-15-percent-1-59-children
17. Gross R. Is cesarean section associated with risk for autism spectrum disorder? :1.
18. Autism Spectrum Disorders: Symptoms, Signs, Causes & Treatment Method [Internet]. WhiteSwanFoundation. [cited 2020 May 25]. Available from: https://www.whiteswanfoundation.org/disorder/autism/?gclid=CjwKCAjw2a32BRBXEiwAUcugiN4gbzgGgUI0sNnucDhFNFYP_cfszdVaKJVvWY5ZZ7QRuCWiYqwPiRoC5mgQAvD_BwE
19. Dodds L, Fell DB, Shea S, Armson BA, Allen AC, Bryson S. The Role of Prenatal, Obstetric and Neonatal Factors in the Development of Autism. J Autism Dev Disord [Internet]. 2011 Jul [cited 2020 Apr 1];41(7):891–902. Available from: http://link.springer.com/10.1007/s10803-010-1114-8
20. Curran EA, O'Neill SM, Cryan JF, Kenny LC, Dinan TG, Khashan AS, et al. Research Review: Birth by caesarean section and development of autism spectrum disorder and attention-deficit/hyperactivity disorder: a systematic review and meta-analysis. J Child Psychol Psychiatry [Internet]. 2015 May [cited 2020 Mar 31];56(5):500–8. Available from: http://doi.wiley.com/10.1111/jcpp.12351
21. Duan G, Yao M, Ma Y, Zhang W. Perinatal and background risk factors for childhood autism in central China. Psychiatry Res [Internet]. 2014 Dec [cited 2020 Apr 1];220(1–2):410–7. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0165178114004788
22. Gardener H, Spiegelman D, Buka SL. Perinatal and Neonatal Risk Factors for Autism: A Comprehensive Meta-analysis. PEDIATRICS [Internet]. 2011 Aug 1 [cited 2020 Mar 31];128(2):344–55. Available from: http://pediatrics.aappublications.org/cgi/doi/10.1542/peds.2010-1036
23. Huberman Samuel M, Meiri G, Dinstein I, Flusser H, Michaelovski A, Bashiri A, et al. Exposure to General Anesthesia May Contribute to the Association between Cesarean Delivery and Autism Spectrum Disorder. J Autism Dev Disord [Internet]. 2019 Aug [cited 2020 Apr 7];49(8):3127–35. Available from: http://link.springer.com/10.1007/s10803-019-04034-9
24. Perales-Marín A, Llópis-González A, Peraita-Costa I, Cervera-Boada P, Téllez de Meneses M, Marí-Bauset S, et al. Cesarean Section as a Predictor for Autism: a Case-Control Study in Valencia (Spain). Adv Neurodev Disord [Internet]. 2018 Jun [cited 2020 Mar 31];2(2):190–8. Available from: http://link.springer.com/10.1007/s41252-018-0061-9

25. Caesarean section and risk of autism across gestational age: a multi-national cohort study of 5 million births | International Journal of Epidemiology | Oxford Academic [Internet]. [cited 2020 Jun 8]. Available from: https://academic.oup.com/ije/article/46/2/429/2739042
26. ADI^{TM}-R - Autism Diagnostic Interview^{TM}- Revised [Internet]. [cited 2020 Jun 8]. Available from: https://eprovide.mapi-trust.org/instruments/autism-diagnostic-interview-revised
27. Haglund NGS, Källén KBM. Risk factors for autism and Asperger syndrome: Perinatal factors and migration. Autism [Internet]. 2011 Mar [cited 2020 Jun 8];15(2):163–83. Available from: http://journals.sagepub.com/doi/10.1177/1362361309353614
28. Ehlers S, Gillberg C. The epidemiology of Asperger syndrome. A total population study. J Child Psychol Psychiatry. 1993 Nov;34(8):1327–50.
29. Kolevzon A, Gross R, Reichenberg A. Prenatal and perinatal risk factors for autism: a review and integration of findings. Arch Pediatr Adolesc Med. 2007 Apr;161(4):326–33.
30. Perinatal Factors and the Development of Autism: A Population Study | Autism Spectrum Disorders | JAMA Psychiatry | JAMA Network [Internet]. [cited 2020 Jun 8]. Available from: https://jamanetwork.com/journals/jamapsychiatry/fullarticle/482014/
31. The UCLA-University of Utah Epidemiologic Survey of Autism: Prenatal, Perinatal, and Postnatal Factors | American Academy of Pediatrics [Internet]. [cited 2020 Jun 8]. Available from: https://pediatrics.aappublications.org/content/86/4/514.short
32. Risk Factors for Autism: Perinatal Factors, Parental Psychiatric History, and Socioeconomic Status | American Journal of Epidemiology | Oxford Academic [Internet]. [cited 2020 Jun 8]. Available from: https://academic.oup.com/aje/article/161/10/916/104855
33. Juul-Dam N, Townsend J, Courchesne E. Prenatal, perinatal, and neonatal factors in autism, pervasive developmental disorder-not otherwise specified, and the general population. Pediatrics. 2001 Apr;107(4):E63.
34. PRE-. PERI-, AND NEONATAL FACTORS AND INFANTILE AUTISM - Finegan - 1979 - Journal of Child Psychology and Psychiatry - Wiley Online Library [Internet]. [cited 2020 Jun 8]. Available from: https://acamh.onlinelibrary.wiley.com/doi/abs/10.1111/j.1469-7610.1979.tb00492.x
35. Pregnancy, Delivery, and Neonatal Complications Among Autistic Children | JAMA Pediatrics | JAMA Network [Internet]. [cited 2020 Jun 8]. Available from: https://jamanetwork.com/journals/jamapediatrics/article-abstract/509440

36. Viral Exposure and Autism - PubMed [Internet]. [cited 2020 Jun 8]. Available from: https://pubmed.ncbi.nlm.nih.gov/222139/
37. Guinchat V, Thorsen P, Laurent C, Cans C, Bodeau N, Cohen D. Pre-, peri- and neonatal risk factors for autism. Acta Obstet Gynecol Scand [Internet]. 2012 [cited 2020 Jun 11];91(3):287–300. Available from: https://obgyn.onlinelibrary.wiley.com/doi/abs/10.1111/j.1600-0412.2011.01325.x
38. Finegan JA, Quarrington B. Pre-, peri-, and neonatal factors and infantile autism. J Child Psychol Psychiatry. 1979 Apr;20(2):119–28.
39. Deykin EY, MacMahon B. Pregnancy, delivery, and neonatal complications among autistic children. Am J Dis Child 1960. 1980 Sep;134(9):860–4.
40. The Relationship between Zinc Levels and Autism: A Systematic Review and Meta-analysis [Internet]. [cited 2020 Jun 11]. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5100031/
41. Serum concentration of 25-hydroxyvitamin D in autism spectrum disorder: a systematic review and meta-analysis | SpringerLink [Internet]. [cited 2020 Jun 11]. Available from: https://link.springer.com/article/10.1007/s00787-015-0786-1
42. Maternal Lifestyle and Environmental Risk Factors for Autism Spectrum Disorders - PubMed [Internet]. [cited 2020 Jun 11]. Available from: https://pubmed.ncbi.nlm.nih.gov/24518932/
43. Schendel D, Bhasin TK. Birth weight and gestational age characteristics of children with autism, including a comparison with other developmental disabilities. Pediatrics. 2008 Jun;121(6):1155–64.