Original Article

Comparative study of the relationship between pregnancy and childbirth factors and autism in healthy children and children with autism

Razieh Shams Mourkani[1], Shahnaz Kohan[2], Zahra Mohebbi-Dehnavi[3], Fatemeh Shaghaghi[4], Maryam Najiabhary[5], Mahboobe Gholami[6]

[1]M.Sc. of Midwifery, Student Research Committee, School of Nursing and Midwifery, Isfahan University of Medical Sciences, Isfahan, Iran, [2]Department of Midwifery and Reproductive Health, School of Nursing and Midwifery, Nursing and Midwifery Care Research Center, Isfahan University of Medical Sciences, Isfahan, Iran, [3]PhD Candidate in Reproductive Health, Department of Midwifery and Reproductive Health, School of Nursing and Midwifery, Isfahan University of Medical Sciences, Isfahan, Iran, [4]Phd Candidate of Sexual and Reproductive Health, Department of Reproductive Health and Midwifery, School of Nursing and Midwifery, Tehran University of Medical Sciences, Tehran, Iran, [5]MSc of Counseling in Midwifery, Department of Midwifery, School of Nursing and Midwifery, Mashhad University of Medical Sciences, Mashhad, Iran, [6]Assistant Professor, Department of Midwifery, Neyshabur University of Medical Sciences, Neyshabur, Iran

Address for correspondence:
Dr. Mahboobe Gholami, Assistant Professor, Department of Midwifery, Neyshabur University of Medical Sciences, Neyshabur, Iran.
E-mail: gholamim1@nums.ac.ir

Abstract:

BACKGROUND: Autism is a group of developmental disorders of the nervous system, the main manifestations of which are defects in social interactions and communication, as well as repetitive behaviors and limited interests. The etiology of autism is not limited to a single factor. Therefore, the aim of this study was to compare the relationship between pregnancy and childbirth factors and autism in healthy children and children with autism.

MATERIALS AND METHODS: The present study was a cross-sectional study that was performed on 200 children in Isfahan in 2021. The instrument in this study was a researcher-made questionnaire. The collected data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 22 software.

RESULTS: The results of data analysis between the two groups with Mann–Whitney U test showed that there was a significant relationship between maternal age at delivery, father's age at delivery, gestational age at delivery, interval between pregnancies, and the length of hospital stay ($P \le 0.05$). Also, the results of data analysis with Chi-squared test showed that there is a significant relationship between the two groups in terms of economic status, place of residence, multiple pregnancies, neonatal sex, and disease in infancy ($P \le 0.05$).

CONCLUSION: The results of this study showed that economic status, place of residence, multiple pregnancies, sex of the baby, and disease in infancy can be effective factors for this disease. According to the results of the study, by considering the factors related to autism, many cases can be adjusted and corrected as much as possible before attempting to conceive.

Keywords:

Autism, children, children's health, developmental neurological disorders

Introduction

Autism spectrum disorder (ASD) is a group of developmental disorders of the nervous system, the main manifestations of which are defects in social interactions and communication, as well as the presence of repetitive behaviors and limited interests.[1] Autistic children also have delayed motor skills. Delays in motor abilities in autistic children are varied and include delays in sitting, crawling, and walking, as well as abnormal gait, poor posture control, and inability to plan movement.[2] The main manifestations of social deficits in autism include poor eye communication, lack of emotion or social interaction, deficits in the use of non-verbal behaviors, and lack of age-appropriate communication.[3] Its diagnostic criteria are based on the Fifth Diagnostic and Statistical Manual of Mental Disorders

as a persistent lack of communication and social interactions in different situations and patterns of limited interests, behaviors, and repetitive activities in the present or past and early development.[4–6] The exact pathophysiology of ASD is unclear due to the frequency and dispersion of the mechanisms involved.[7,8] The results show that the etiology of ASD is not only due to a single factor, but is also due to environmental, genetic, or a combination of both risk factors in the etiology of ASD.[9–11] The long course of this disorder and their multiple needs provide a great economic burden for families and society, most of which is spent on special education and treatment.[12] This has posed many challenges in terms of care and management.[11,12] A wide range of demographic causes and factors, including factors of pregnancy, psychological, social, hereditary, and environmental factors are involved in its occurrence.[13] According to studies, mothers under the age of 20 and mothers over the age of 35 are more likely than women between the ages of 20 and 29 to give birth to underweight babies, which is directly related to developmental disorders and, of course, autism. Short intervals between births increase the likelihood of preterm delivery. Premature infants are more prone to developmental delays in their early childhood and school years. The incidence of preterm labor has increased significantly in recent decades.[14] Birth weight is an important indicator of pediatric disability and infant mortality, and this incomplete weight gain itself can be a cause of short pregnancy intervals. The rate of these disabilities is higher in boys than in girls. Progression towards developmental disorders in infants weighing less than 2 kg is 30 times that of normal weight infants.[15] According to the World Health Organization (WHO) standards, a short interval between deliveries refers to a pregnancy of less than 18 months and a long interval to more than 60 months.[16] Lack of awareness of mothers about the consequences of not observing the appropriate distance between births endangers the health and efficiency of women in society and with the birth of children who may have developmental problems, the health of the next generation is also threatened.[17] Studies have shown a strong association between a reduction in gestational age of less than 18 months and an increase in gestational age of more than 60 months with a child with autism as well as other developmental disorders.[18-21] Children with developmental neurological disorders pose a great psychological and economic burden on the family and ultimately society. In the long run, due to their cognitive weakness, they have a negative effect on the growth of culture, art and science of a country. Therefore, the aim of this study was to compare the relationship between pregnancy and childbirth factors and autism in healthy children and children with autism.

Materials and Method

Study design and setting
The present study is a correlational study that was conducted on households covered by Isfahan Autism Center and Farvardin Center that have at least two children, one of whom has autism by convenience sampling method.

Study participants and sampling
The sample size was 200 based on the following formula (100 children with autism and 100 healthy children).

$$n = z (1-\alpha/2) 2 \times p (1-p)/d^2$$

Inclusion criteria were the following: those who gave written consent to participate in the study; those who were Iranian; parents being of reproductive age (mother 18–35 years and father 18–55 years); parents who did not have a child with a disease other than autism, those who did not have children from previous marriages of each couple, those who did not adopt children; absence of medical illness of parents in the period immediately before pregnancy and during pregnancy; children who were not born prematurely and whose weight was not too high or too low; couples who were non-smoking and not addicted to alcohol, drugs, and psychotropics; households with at least two children, eventually 8 years old. In the first group, all children were healthy and in the second group, at least one child had ASD.

Data collection tool and technique
This study was conducted in primary schools for healthy children and autism education centers (Ordibehesht, Hazrat Zahra, Hazrat Zeinab) in Isfahan province. This research was conducted after obtaining the necessary permits and obtaining parental consent and explaining the working method to parents.

The instrument in this study was a researcher-made questionnaire that had three parts (the first and second part of the researcher-made questionnaire, the third part of the autism diagnostic interview-revised (ADI-R) International Questionnaire for families with autistic children). The first part consisted of demographic information of the research units (6 questions). The second part consisted of information about pregnancy, delivery, and delivery intervals (11 questions). To confirm the validity of the first and second parts of the questionnaire, face and content validity were used. The third part of the questionnaire was taken from the ADI-R International Questionnaire. This questionnaire was completed in the form of an interview and assessed the child's skills based on the three sections of communication and language skills of the child, social

interactions of the child, and repetitive behaviors or other different behaviors. The validity and reliability of this questionnaire have been confirmed in a study by Gorji *et al.*[20] In this study, the reliability of the retest and alpha test was confirmed to be 0.79.

After completing the questionnaires, the data were coded and entered into the Statistical Package for the Social Sciences (SPSS) version 22 software and analyzed.

Ethical considerations

This study was conducted after the approval of the plan in the Student Research Committee of Isfahan University of Medical Sciences and receiving the code of ethics from the Vice Chancellor for Research of Isfahan University of Medical Sciences. Written consent was obtained from all participants. All study participants were assured that their information would be kept confidential.

Results

In the non-autism group, mean maternal age was 30.80 ± 5.07 years, mean paternal age was 36.12 ± 5.76 years, gestational age at delivery was 37.60 ± 1.76 weeks, gestational age was 1.85 ± 4.18 years, and hospital stay was 3.52 ± 1.23 days. In the autism group, mean mothers' age was 28.28 ± 5.07 years, mean fathers' age was 32.48 ± 5.56 years, gestational age at delivery was 38.60 ± 1.73 weeks, gestational age was 2.53 ± 3.44 years, and hospital stay was 2.84 ± 10.34 days.

The results of data analysis between the two groups using Mann–Whitney U test showed that there was a significant relationship between mother's age at delivery, father's age at delivery, gestational age at delivery, interval between pregnancies, and length of hospital stay ($P \leq 0.05$) [Table 1].

Also, the results of data analysis with Chi-squared test showed that there was a significant relationship between the two groups in terms of economic status, place of residence, multiple pregnancies, neonatal sex, and disease in infancy ($P \leq 0.05$) [Table 2].

Discussion

The results show that there was a significant difference between the variables of mother's age at delivery, father's

age at delivery, gestational age at delivery, interval between pregnancies, and length of hospital stay. The results also showed that there was a significant difference between the two groups in terms of economic status, place of residence, multiple pregnancies, neonatal sex, and disease in infancy. In this regard, the results of the study by Toomaroglu *et al.*[14] showed that family history, the child's gender, parental age, stressful pregnancy, and maternal exposure to high-risk substances are among the factors associated with autism. The study by Fernandez Carrocera *et al.*[15] showed that developmental disorders were significantly associated with days of artificial respiration and days of hospitalization in the neonatal intensive care unit (NICU) and gestational age. The results of a study by Laura Schieve *et al.*[22] showed that ASD increased in the second and subsequent children who became pregnant less than 18 months or 60 months or more after the mother's previous birth. Also, the results of the study by Soleimani *et al.*[23] showed that high-risk infants and children and those who were born earlier need special attention in order to have a favorable and appropriate development. These children are more likely than other children to have developmental or developmental delays, including motor, cognitive, speech, hearing, and visual impairments. To prevent this, it is necessary to prevent delays or developmental disorders by detecting their problems early using appropriate assessment tools and timely interventions. The results of a study by Carlsson *et al.*[24] showed that low birth weight, birth defects, and congenital hypoxia and respiratory stress with autism spectrum disorder (ASD) and gestational age and family income were associated with attention-deficit/hyperactivity disorder (ADHD). The results of a study by Chen *et al.*[25] showed that variability in the rate of mental retardation, ADHD, and autism among children in Taiwan depends on age, year of birth, period, and socioeconomic status. The relationship between age and the first diagnosis of mental retardation varies at different levels of urbanization and socioeconomic status. The results of the study by Namazzi *et al.*[26] showed that low birth weight and immediate and exclusive breastfeeding were not significantly associated with developmental neurological disorders. The results of the study by Nawaz *et al.*[27] showed that high birth weight and preterm delivery were significantly associated with developmental and neurological disorders. According to the results, it can be said that since the studies have been performed on

Table 1: Comparison of quantitative variables in two groups of children with autism and non-autism

Variables	Levine test	Significance level	*t*	df	*P*
Mother's age at delivery	0.003	0.959	−2.482	98	0.015
Father's age at delivery	0.015	0.902	−3.211	98	0.002
Gestational age at delivery	0.038	0.845	2.396	98	0.018
The interval between pregnancies	4.497	0.036	−1.665	98	0.099
Duration of hospitalization	2.355	0.492	1.845	98	0.001

Table 2: Evaluation and comparison of qualitative variables in two groups of children with autism and non-autism

Variable	Autism	Non-autism	Chi-squared test	P
Mother's education				
Primary school	2	1	1.961	0.580
High school	4	7		
Diploma	21	24		
University	23	18		
Father's education				
Primary school	5	8	2.102	0.452
High school	10	15		
Diploma	20	16		
University	13	11		
Mother's job				
Housewife	40	29	1.279	0.734
Official	7	8		
Free	1	0		
Other	2	3		
Father's job				
Official	10	12	2.441	0.295
Free	10	18		
Manual worker	17	7		
Unemployed	13	13		
Economic situation				
Good	8	8	5.974	0.05
Medium	29	38		
Bad	13	4		
Place of living				
Personal	17	30	6.784	0.009
Rent	33	20		
How many pregnancies				
1	10	2	12.829	0.012
2	31	29		
3	9	12		
4	0	5		
5	0	2		
Gender of the baby				
Boy	35	21	7.955	0.005
Girl	15	29		
Method of childbirth				
Natural childbirth	19	21	0.167	0.683
Cesarean section	21	29		
Disease in pregnancy				
Diabetes	2	3	3.420	0.331
Blood pressure	5	4		
Hyperthyroidism - hypothyroidism	0	3		
No disease	43	40		
Supplementation during pregnancy				
Yes	44	47	1.099	0.295
No	6	3		
Infantile disease				
Yes	17	7	1.084	0.001
No	33	43		

different groups of children and infants, the cultural, social, and economic level of individuals some of the factors that affect birth weight. Contradictory results can be justified. However, inconsistent with the results of the present study, a study of Soltani *et al*.[13] showed that developmental disorders in children aged 4–24 months

Variable	Autism	Non-autism	Chi-square test	P
Mother's education				
Primary school	2	1	1.961	0.580
high school	4	7		
Diploma	21	24		
University	23	18		
Father's education				
Primary school	5	8	2.102	0.452
High school	10	15		
Diploma	20	16		
University	13	11		
Mother's job				
Housewife	40	29	1.279	0.734
Official	7	8		
Free	1	0		
Other	2	3		
Father's job				
Official	10	12	2.441	0.295
Free	10	18		
Manual worker	17	7		
Unemployed	13	13		
The economic				
Good	8	8	5.974	0.05
Medium	29	38		
Bad	13	4		
Situation place of living				
Personal	17	30	6.784	0.009
Rent	33	20		
How many pregnancies				
1	10	2	12.829	0.012
2	31	29		
3	9	12		
4	0	5		
5	0	2		
Gender of the baby				
Boy	35	21	7.955	0.005
Girl	15	29		
Method of childbirth				
Natural childbirth	19	21	0.167	0.683
Cesarean section	21	29		
Disease in pregnancy				
Diabetes	2	3	3.420	0.331
Blood pressure	5	4		
Hyperthyroidism - hypothyroidism	0	3		
No disease	43	40		
Supplementation during pregnancy				
Yes	44	47	1.099	0.295
No	6	3		
Infantile disease				
Yes	17	7	1.084	0.001

were not significantly associated with mechanical ventilation, length of hospital stay, surfactant and betamethasone injections, and initial and final diagnosis of diseases. Also, there was no significant relationship with high-risk delivery and advanced resuscitation in children with developmental disorders and healthy children.

Limitation and recommendation
This study investigated the factors of pregnancy and childbirth related to autism and did not examine the cultural, social, and medical factors of the parents. Several other factors such as folic acid supplementation, folic acid levels in early pregnancy, and inflammatory diseases in pregnancy were not considered.

Conclusion

According to the results of this study, a number of demographic variables and pregnancy and childbirth were significantly different between the two groups.

References

1. Liu J, Yao L, Zhang W, Xiao Y, Liu L, Gao X. Gray matter abnormalities in pediatric autism spectrum disorder: A meta-analysis with signed differential mapping. Euro Child Adole Psych 2017;26:933-45.
2. MacDonald M, Hatfield B, Twardzik E. Child behaviors of young children with autism spectrum disorder across play settings. Adapted Physic Activ Quart 2017;34:19-32.
3. Guo X, Duan X, Long Z, Chen H, Wang Y, Zheng J. Decreased amygdala functional connectivity in adolescents with autism: A resting-state fMRI study. Psychiatry Res Neuroimaging 2016;257:47-56.
4. Charoghchian Khorasani E, Peyman N, Esmaily H. Effect of education based on the theory of self-efficacy and health literacy strategies on exclusive breastfeeding: A randomized clinical trial. Koomesh 2019;21:633-8.
5. Murphy R. SPICe Briefing: Autism Spectrum Disorder. Edinburgh: Scottish Parliament Information Centre; 2017.
6. Jiujias M, Kelley E, Hall L. Restricted, repetitive behaviors in autism spectrum disorder and obsessive–compulsive disorder: A comparative review. Child Psych Human Develop 2017;48:944-59.
7. Gross C. Defective phosphoinositide metabolism in autism. J Neuro Res 2017;95:1161-73.
8. Zhang R, Zhang HF, Han JS, Han SP. Genes related to oxytocin and arginine-vasopressin pathways: Associations with autism spectrum disorders. Neuro Bull 2017;33:238-46.
9. Ronemus M, Iossifov I, Levy D, Wigler M. The role of de novo mutations in the genetics of autism spectrum disorders. Nature Rev Gene 2014;15:133-41.
10. Olsson NC. Social Skills Group Training for Children and Adolescents with Autism Spectrum Disorder. Sweden: Karolinska Institutet; 2016.
11. Mokhtari B, Karimzadeh F. A review on the Authism with the most approach on the critical biomarkers. Razi J Med Sci 2018;24:35-46.
12. Ramshini M, Hasanzadeh S, Afroz GA, Hashemi Razini H. The effect of family-centered nature therapy on children with autism spectrum disorder. Arch Rehabil 2018;19:150-9.
13. Soltani M, Razavi Ardekani SM, Erami A, Eskandari Kootahi Z, Yazdani N. Study of factors associated with developmental delay in low birth weight infants admitted to the neonatal intensive care unit. Razi J Med Sci 2017;24:1-9.
14. Toomaroglu KH, Nobakht M. Causes and causes of autism in Ardabil. The 1st National Conference of the Future School, 2019.
15. Fernandez Carrocera LA, Jonguitud Aguilar A, Ortigosa Corona E, Barrera Reyes RH, Martinez Cruz C, Ibarra Reyes MP. Neurologic development of children at age two who had been treated at a neonatal intensive care unit. Rev Panam Salud Publica 1999;5:29-35.
16. Al-Naddawi M, Ibraheem MF, Alwan SH. Causes of global developmental delay in children welfare teaching hospital-Baghdad. Iraqi Postgrad Med J 2013;12:383-9.
17. de Moura RD, Costa JC, Santos IS, Barros DAJ, Matijasevich A, Halpern R, *et al*. Risk factors for suspected developmental delay at age 2 years in a Brazilian birth cohort. Pediatr Perinat Epidemiol 2010;24:211-21.
18. WHO_RHR_07.1_eng. pdf technical consultation on birth spacing 2005.
19. Shachar B, Liell D, Lookwood CH, Barss V. Interpregnancy interval and obstetrical complications. Up To Date. 2018.
20. Gorji R, Hassanzadeh S, Ghasemzadeh S, Qolamali Lavasani M. Sensitivity and specificity gilliam autism rating scale (GARS) in diagnosis autism spectrum disorders: Systematic review. Shefaye Khatam 2020;8:80-9.
21. Jafari A, Alami A, Charoghchian E, Delshad Noghabi A, Nejatian M. The impact of effective communication skills training on the status of marital burnout among married women. BMC Womens Health 2021;21:231.
22. Schieve LA, Tian LH, Drews-Botsch C, Windham GC, Newschaffer C, Daniels JL, *et al*. Autism spectrum disorder and birth spacing: Findings from the study to explore early development (SEED). Autism Res 2018;11:81-94.
23. Soleimani F, Sharifi N, Rasti Borujeni F, Amiri M, Khazaiyan S, Fathnezhad Kazemi A. Nourodevelopmental follow-up in high-risk infants: Review article. Tehran Univ Med J 2015;72:733-41.
24. Carlsson T, Molander F, Taylor MJ, Jonsson U, Bölte S. Early environmental risk factors for neurodevelopmental disorders-A systematic review of twin and sibling studies. Dev Psychopathol 2021;33:1448-95.
25. Chen CY, Liu CY, Su WC, Huang SL, Lin KM. Factors associated with the diagnosis of neurodevelopmental disorders: A population-based longitudinal study. Pediatrics 2007;119:e435-43.
26. Namazzi G, Hildenwall H, Mubiri P. Prevalence and associated factors of neurodevelopmental disability among infants in eastern Uganda: A population based study. *BMC Pediatr* 2019;**19**.379.
27. Nawaz FA, Sultan MA. Low birth weight prevalence in children diagnosed with neurodevelopmental disorders in Dubai. *Glob Pediatr Health* 2021. doi: 10.1177/2333794X211031782.