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Prevalence of Prenatal, Neonatal and Postnatal Complications among Healthy Children and Children Diagnosed with ASD in Central Asia and Eastern Europe

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Abstract

The prevalence of prenatal, neonatal, and postnatal complications among 89 children diagnosed with autism spectrum disorder (ASD) and 207 healthy children living in Kazakhstan and Ukraine are compared and reported. The mothers of children later diagnosed with ASD had significantly higher rates of infections (56.2% vs. 24.6%, $p<0.001$) and placental detachment (9% vs. 3.4%, $p<0.05$) during pregnancy than mothers of healthy children. Children later diagnosed with ASD had higher rates of hypoxia (58.4% vs. 13.5%, $p<0.001$), asphyxia (23.6% vs. 3.4%, $p<0.001$), active congenital infection (15.7% vs. 1.4%, $p<0.001$), and different types of CNS damage (15.7% vs. 4.3%, $p<0.001$) at birth. Children later diagnosed with ASD were significantly more often characterized as withdrawn (59.6% vs. 13%, $p<0.001$), and having frequent episodes of health problems (18.1% vs. 3.9%, $p<0.001$) during the first three months after birth.

Keywords: *Autistic disorder; Infection; Parturition; Pregnancy*

Introduction

The American Psychiatric Association defines Autism Spectrum Disorder (ASD) as neurodevelopmental pathology with typical symptoms and signs of social interaction disruption, language impairment, and repetitive patterns of behavior, interests or activities [1]. A growing number of scientific publications indicate that ASD could be a congenital disorder. For example, in a 2010 study, one of the factors found to play a role in the prenatal origin of ASD was maternal infections and immune activation during pregnancy. Analysis of the anamneses of 96,000 children born in Denmark from 1980 to 2005 showed that the mother's admission to a hospital due to maternal viral infection in the first trimester and maternal bacterial infection in the second trimester was associated with the diagnosis of ASD in the offspring [2]. As well, in a large Swedish study published this year, in which 1,8 mln children participated, it was shown that any viral infection during pregnancy significantly increases the risk of ASD in children [3].

According to the American Psychiatric Association, ASD is usually diagnosed around ages 2 to 3; however, studies show that both behavioral and clinical signs and symptoms of ASD could be manifested in the first months of an infant's life [1,4,5]. Furthermore, some of the brain alterations commonly observed in ASD children is only initiated during prenatal brain development. For instance, ASD children have a decreased number of Purkinje cells (PCs) along with the absence of interneuron basket cells. PCs only develop in the prenatal period; consequently, this alteration had to have occurred in the prenatal period [6].

Other studies confirm the association between a mother's clinical manifestations during pregnancy and labor and an increased risk of ASD in her child. For example, mothers of children who are later diagnosed with ASD are more likely than mothers of neurotypical children to have had such complications as, vaginal bleeding, risk of miscarriage, prolonged labor, prematurity, hypoxia at birth, etc [7-11]. As was discussed by, some of these complications may be the result of infection, inflammation and maternal immune activation during pregnancy [12]. Infection may lead

to maternal immune activation resulting in placental inflammation that causes disruption of oxygen transfer and prenatal hypoxia as a result. As well, according to the authors, maternal immune activation induces some of the genes associated with hypoxia.

Despite this knowledge, the current understanding of ASD lacks the consideration of the prenatal, postnatal and infantile manifestations of the increased ASD risk, which could help in diagnosis, prevention and early treatment of this disorder.

In this paper, we present data about the pre-, neo- and postnatal complications and peculiarities as well as the pregnancy and labor complications in the mothers of 89 children diagnosed with ASD and 207 healthy children.

Materials and Methods

Participants

The participants of this descriptive study were 89 children aged 2 to 16 years old (mean age = 5.6 y.o.) diagnosed with ASD, and 207 healthy children aged 6 months to 16 years old (mean age = 5.8 y.o.). All children were residents of Ukraine and Kazakhstan. Parents of children diagnosed with autism were self-referred; the healthy children were invited to participate in the online survey via Facebook using the snowball sampling method in which the initial subjects were asked to recruit future subjects from among their acquaintances to increase the size of the study sample. All parents gave their written consent to participate in the study. The study represents all the results obtained from all the parents responding. The only inclusion criteria for the group of autistic children were a confirmed diagnosis of ASD and written consent form from their parents. The inclusion criteria for the control group were the absence of a diagnosis of ASD or other neurodevelopmental disorders and written consent form from their parents. There were no exclusion criteria for any of the two groups.

Collection of information

All parents answered the six-question Internet survey regarding pregnancy, labor, neonatal complications, and their child in its first three months of life.

Statistical analyses

Statistical analyses were performed with SPSS II for Windows (IBM SPSS). Fisher's exact test was used for the 2-by-2 table with consequent Yates correction.

Results

Complications during pregnancy

The main complications during pregnancy included active infection (including, but not limited to respiratory infection of known and unknown origin and UTI of known and unknown origin), risk of miscarriage, placental detachment, polyhydramnios, and vaginal bleeding. The prevalence of these complications in the group of mothers of ASD children and in the group of mothers of healthy children is represented in Figure 1.

There were 50 out of 89 women among mothers of children, who were later diagnosed with ASD who had had active infection during pregnancy. Active infection among mothers of healthy children was diagnosed in 51 out of 207 women. The prevalence of active infections in mothers of children diagnosed with ASD was more than double the prevalence in mothers of healthy children, indicating statistical significance between the groups ($p<0.001$).
The risk of miscarriage among mothers of ASD children was occurred in 20 women out of 89, while among mothers of healthy children it was in 33 women out of 207. This difference was not statistically significant ($p>0.05$).
Placental detachment during pregnancy was reported by 8 out of 89 mothers of children diagnosed with ASD, and by 7 out of 207 mothers of healthy children. The rate of placental detachment was higher among mothers of ASD children ($p<0.05$), but after a Yates correction, the difference was not considered statistically significant ($p>0.05$).
Polyhydramnios was reported by 4 out of 89 mothers of children diagnosed with ASD, and by 5 of 207 mothers of healthy children. This difference was not statistically significant ($p>0.05$).

Bleeding was reported by 5 out of 89 mothers of children diagnosed with ASD, and by 10 out of 207 mothers of healthy children. This difference was not statistically significant ($p>0.05$).

The absence of complications during pregnancy was reported by 29 out of 89 mothers of children diagnosed with ASD and by 124 of 207 mothers of healthy children. The mothers of ASD children had a significantly higher prevalence of pregnancy complications than mothers of healthy children ($p<0.001$).

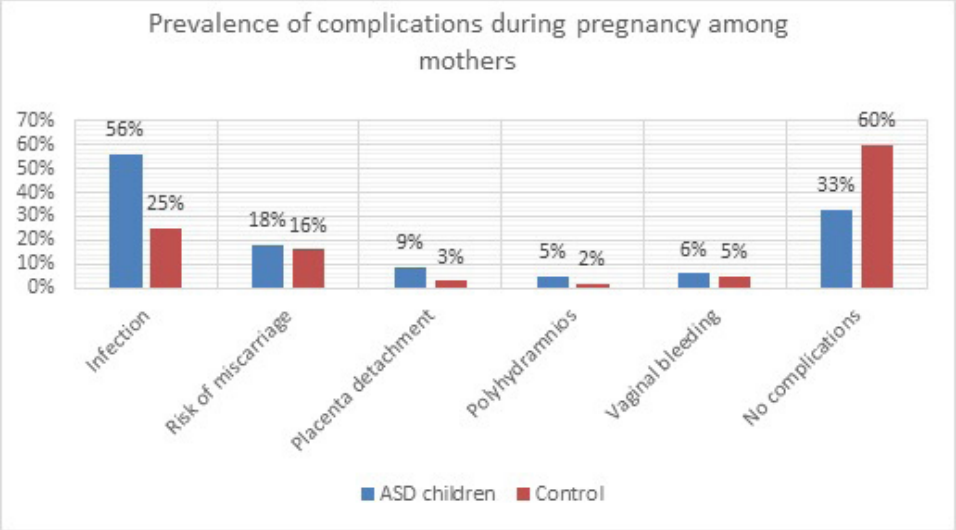

Figure 1: Prevalence of complications during pregnancy. The figure represents the rates of the most common complications among mothers of children diagnosed with ASD and mothers of healthy children. There are statistically significant differences in infection rates during pregnancy, placenta detachment, and the absence of complications.

Type of delivery

All mothers had a cesarean section, induced labor, a combination of both, or natural delivery. The prevalence of each of the types in both groups is represented in Figure 2.

In the group of mothers of ASD children, 23 out of 89 reported induced labor and 28 out of 89 reported cesarean section. Seven of the mothers had an induction but it was not sufficient for delivery, so they had cesarean sections. Slightly more than half, 45 out of 89 mothers of children diagnosed with ASD had natural delivery. In the group of mothers of healthy children, 36 out of 207 reported induced labor and 56 out of 207 reported cesarean section. None of them had both induction and cesarean section. More than half, or 115 out of 207 mothers of healthy children, had natural delivery.

The differences in the rates of cesarean section, induced labor, and natural delivery were not statistically significant ($p>0.05$).

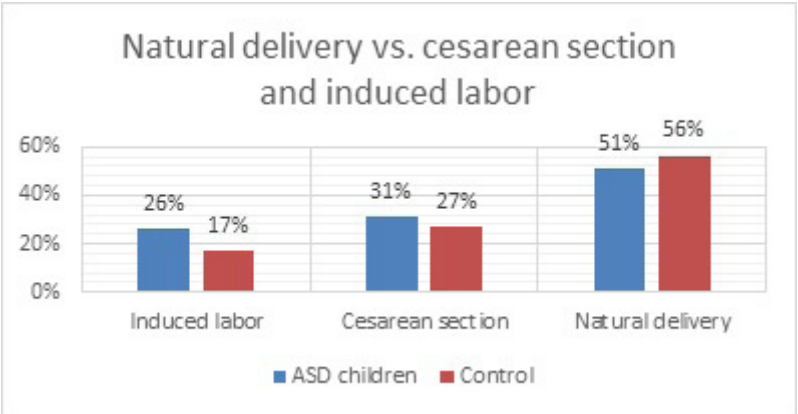

Figure 2: Prevalence of types of delivery among mothers of children diagnosed with ASD and mothers of healthy children. There is no statistically significant difference in rates of each of these types of delivery.

Complications among newborns

The most common complications among newborns included hypoxia, asphyxia, protracted anhydramnios, jaundice, preterm birth, and active congenital infection. The prevalence of each of these complications among children later diagnosed with ASD and in healthy children is presented in Figure 3.

There were 52 out of 89 children in the ASD group and 28 out of 207 children in the healthy group born with hypoxia. The prevalence of hypoxia among ASD children was significantly higher than among healthy children ($p<0.001$).

There were 21 out of 89 children in the ASD group and 7 out of 207 children in the healthy group born with asphyxia. The prevalence of asphyxia among ASD children was significantly higher than among healthy children ($p<0.001$).

There were 5 out of 89 children in the ASD group and 10 out of 207 of children in the control group who were born after a protracted anhydramnios. This difference is not statistically significant ($p>0.05$).

Jaundice was detected in 12 out of 89 children in the ASD group and in 52 out of 207 children in the healthy group. The rate of jaundice was significantly higher in healthy children ($p<0.05$).

Preterm birth was defined as a birth that occurred on the 37th week or earlier. Preterm birth was reported in 10 out of 89 ASD children and in 16 of 207 healthy children. This difference was not statistically significant ($p>0.05$).

Active congenital infection was diagnosed in 14 out of 89 children with ASD and in 3 of 207 healthy children. The rate of congenital active infection among children with ASD was significantly higher than among healthy children ($p<0.001$).

Mothers of 21 out of 89 children diagnosed with ASD and 118 out of 207 healthy children reported no complications in their newborn children. Children later diagnosed with ASD had significantly higher rates of complications than healthy children ($p<0.001$).

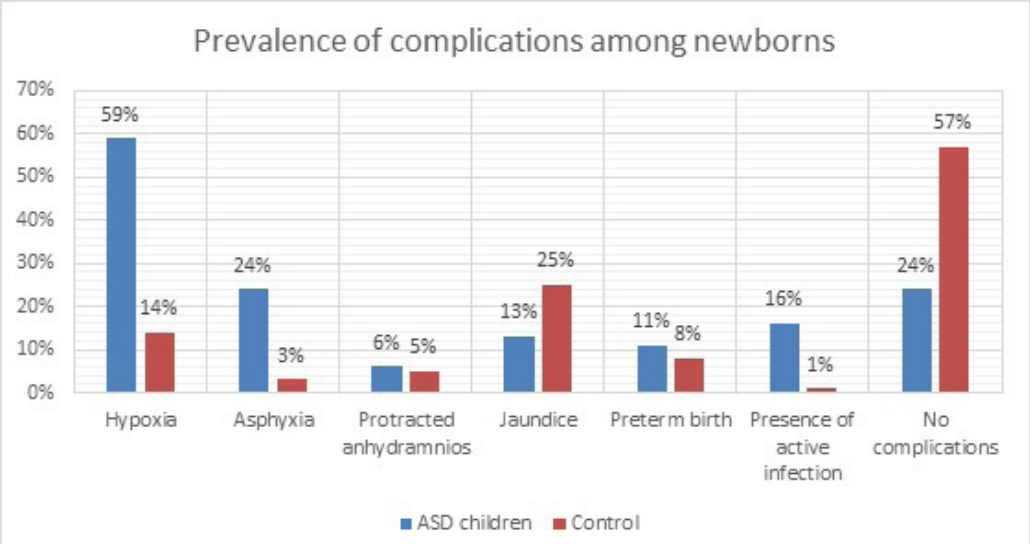

Figure 3: Prevalence of complications among newborns. The figure represents the rates of the most common complications among children later diagnosed with ASD and healthy children. There are statistically significant differences in rates of hypoxia, asphyxia, jaundice (higher in healthy children), presence of active congenital infection, and the absence of complications.

Peculiarities of the first 3 months of life

The most common peculiarities were withdrawnness, irritability, frequent episodes of illness, and CNS damage (including hydrocephaly, presence of liquid in brain tissues, and asymmetry of brain volumes). The prevalence of these peculiarities is represented in Figure 4.

Withdrawnness in the context of this study means that a child was unusually quiet and characterized by the parents as "causing no inconvenience". These children were described as having little or no social interest, decreased engagement of attention, and expressing marked passivity. Among children who were later diagnosed with ASD, 53 out of 89 were reported to be withdrawn in the first 3 months of their lives. Among healthy children, 27 out of 207 were reported to be withdrawn. Children with ASD had a significantly higher rate of this peculiarity ($p<0.001$).

Irritability in the context of this study means that a child was "very problematic", "hypersensitive", "irritable", and "suffering from sleeplessness". Among children who were later diagnosed with ASD, 25 out of 89 were reported to be irritable in the first 3 months of their lives. Among healthy children, 47 out of 207 were reported to be irritable. This difference between the two groups was not statistically significant.

Frequent episodes of illness in the first 3 months were reported in 16 children with ASD out of 89 and in 8 of 207 healthy children. Children with ASD had statistically significant higher rates of frequent illnesses than healthy controls ($p<0.001$).

CNS damage that was not mechanical (due to trauma), but rather seemed to be due to long-term birth complications was reported by 14 out of 89 children with ASD, and among healthy children, the CNS damage was in 9 cases out of 207. The higher rates of CNS damage among children later diagnosed with ASD were statistically significant ($p<0.001$, and after Yates correction $p<0.01$).

No peculiarities were reported in 7 out of 89 children later diagnosed with ASD and in 120 out of 207 healthy children. ASD children had statistically significant higher rates of the abovementioned peculiarities than healthy children ($p<0.001$).

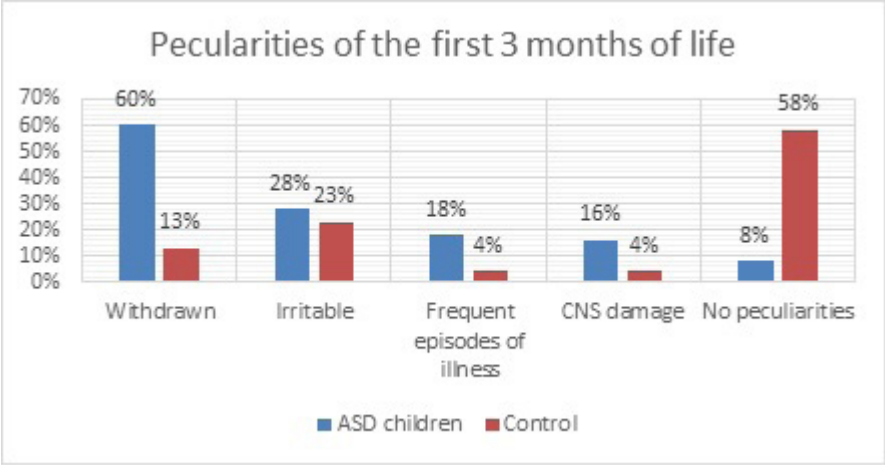

Figure 4: Peculiarities of the first 3 months of life. The figure represents the rates of the most common peculiarities among children later diagnosed with ASD and healthy children. There are statistically significant differences in rates of withdrawnness, frequent episodes of illness, CNS damage, and absence of peculiarities.

Events coinciding with regression in children with ASD

Parents of children with ASD were asked whether there were any events that occurred before the first manifestation of autistic symptoms. Out of 89 parents, three said that the first manifestation of ASD symptoms occurred after a surgical operation, four said that it occurred after the mother stopped breastfeeding, five said that ASD manifestation was after vaccination, six said after illness, and 71 said that there were no significant events prior to initial ASD symptoms. Figure 5 depicts the responses.

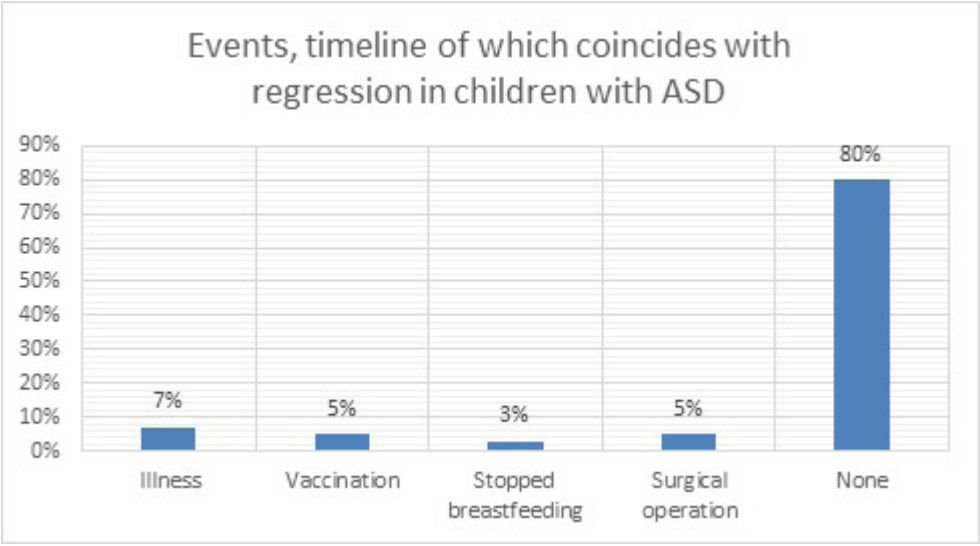

Figure 5: The events coinciding with the first manifestation of autistic symptoms in 89 children. The number of events is small and does not differ significantly from each other. Most parents stated that no event occurred prior to the first manifestation of autistic symptoms..

Discussion

In this study of children from Central Asia and Eastern Europe, it was found that several prenatal, neonatal, and postnatal complications are more likely to occur in children later diagnosed with ASD than in healthy children.

In pregnancy, the complications included infection, placental detachment, risk of miscarriage, polyhydramnios, and vaginal bleeding. Although all other types of complications were not significantly higher in children with ASD, the overall rate of infection during pregnancy was significantly higher in ASD children compared to healthy children.

Causes of placental abruption are unknown. Among the recognized risk factors are the following, trauma or injury to the abdomen, rapid loss of the amniotic fluid, infection, and inflammation [13,14].

The statistical distribution of the types of labor was not different in children diagnosed with ASD and in healthy children.

The neonatal complications of hypoxia, asphyxia, or presence of active infection were significantly higher among children with ASD. Jaundice was negatively associated with ASD in this study.

Hypoxia may be caused by maternal anemia, birth asphyxia, lack of adequate fetal monitoring, maternal smoking, traumatic brain damages, placental abruption, asphyxia, and mother-to-fetus infection [15,16].

Asphyxia may be caused by inadequate oxygen levels in the mother's blood due to heart or respiratory problems or lowered respirations caused by anesthesia, low blood pressure, inadequate relaxation of the uterus during labor that prevents oxygen circulation to the placenta, early separation of the placenta from the uterus, compression of the umbilical cord that decreases blood flow, or poor placental function that may occur with high blood pressure or in post-term pregnancies, particularly those past 42 weeks [17].

Peculiarities of the first three months of an infant's life included withdrawnness, frequent episodes of illness, and CNS damage. The overall number of peculiarities in this period was higher in children with ASD than in healthy children.

Some of the types of CNS damage such as hydrocephalus with asymmetry of the choroid plexus may be due to infection, hemorrhage, tumor, and inflammation [18,19].

The obtained data shows that the given prenatal and postnatal complications may be considered as possible etiologic and pathogenetic factors. We analyzed the prenatal, neonatal, and postnatal complications for possible causes, excluding placental detachment, and the only possible common causes of the complications were infection and inflammation. Additional studies are needed to confirm the role of infection and inflammation in these complications, but it is highly likely that infections and inflammation are the main etiologic factors leading to manifested complications in ASD. The data could contribute to the development of preventive measures and early diagnostic instruments for ASD detection.

Limitations of the study

This study included a small sample size. For more sophisticated statistical analysis of the prevalence of these complications, further study with a larger sample size is recommended. The data was collected via surveys, thus possessing a risk that not all the data is authentic, because participated mothers could forget or confuse some of the information after the years since the periods, details of which were asked. For more reliable analysis and conclusions, it is suggested to use medical supporting documents as the data source.

Conclusion

The study showed some differences in the rates of prenatal, neonatal, and postnatal complications between children diagnosed with ASD and healthy children in Kazakhstan and Ukraine. The mothers of children later diagnosed with ASD had significantly higher rates of infections (56.2% vs. 24.6%, $p<0.001$) and placental detachment (9% vs. 3.4%, $p<0.05$) during pregnancy than mothers of healthy children. Children later diagnosed with ASD had higher rates of hypoxia (58.4% vs. 13.5%, $p<0.001$), asphyxia (23.6% vs. 3.4%, $p<0.001$), and active congenital infection (15.7% vs. 1.4%, $p<0.001$), CNS damage (15.7% vs. 4.3%, $p<0.001$). Children later diagnosed with ASD were significantly more often characterized as withdrawn (59.6% vs. 13%, $p<0.001$), and having frequent episodes of illness (18.1% vs. 3.9%, $p<0.001$).

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References

1. American Psychiological Association (2016) What Is Autism Spectrum Disorder?

2. Atladóttir H, Thorsen P, Ostergaard LO, Schendel D, Lemcke S, et al. (2010) Maternal Infection Requiring Hospitalization During Pregnancy and Autism Spectrum Disorders. J Autism Dev Disord 40(12): 1423-1430.

3. Al-Haddad B, Jacobsson B, Chabra S, Modzelewska D, Olson E, et al. (2019) Long-term Risk of Neuropsychiatric Disease After Exposure to Infection In Utero. JAMA Psychiatry.

4. Dawson G, Osterling J, Meltzoff A, Kuhl P (2000) Case Study of the Development of an Infant with Autism from Birth to Two Years of Age. J Appl Dev Psychol 21(3): 299-313.

5. Steinman G (2013) Predicting autism at birth. Med Hypotheses 81(1): 21-25.

6. Fatemi SH, Aldinger KA, Ashwood P, Bauman ML, Blaha CD, et al. (2012) Consensus Paper: Pathological Role of the Cerebellum in Autism. Cerebellum 11(3): 777-807.

7. Brimacombe M, Ming X, Lamendola M (2006) Prenatal and Birth Complications in Autism. Matern Child Health J 11(1): 73-79.

8. Fassett M, Peltier M, Wing D, Xiang A, Chiu V, et al. (2017) Association of Perinatal Risk Factors with Autism Spectrum Disorder. Am J Perinatol 34(03): 295-304.

9. Glasson EJ, Bower C, Petterson B, de Klerk N, Chaney G, et al. (2004) Perinatal Factors and the Development of Autism. Arch Gen Psychiatry 61(6): 618.

10. Wang C, Geng H, Liu W, Zhang G (2017) Prenatal, perinatal, and postnatal factors associated with autism. Medicine 96(18): e6696.

11. Zwaigenbaum L, Szatmari P, Jones MB, Bryson SE, Maclean JE, et al. (2002) Pregnancy and Birth Complications in Autism and Liability to the Broader Autism Phenotype. J Am Acad Child Adolesc Psychiatry 41(5): 572-579.

12. Steinman GD (2014) The Cause of Autism: Concepts and Misconceptions. Baffin Publishing Company.

13. Mayo Clinic (2019) Placental abruption - Symptoms and causes.

14. Nath CA, Ananth CV, Smulian JC, Shen-Schwarz S, Kaminsky L (2007) Histologic evidence of inflammation and risk of placental abruption. Am J Obstet Gynecol 197(3): 319.e1-319.e6.

15. Cerebralpalsysymptoms.com (2019) Perinatal Hypoxia - Causes & Complications During Birth.

16. Kendall G, Peebles D (2005) Acute fetal hypoxia: the modulating effect of infection. Early Hum Dev 81(1): 27-34.

17. Ucsfbenioffchildrens.org (2019) Birth Asphyxia | Conditions & Treatments | UCSF Benioff Children's Hospital.

18. Karimy JK, Zhang J, Kurland DB, Theriault BC, Duran D, et al. (2017) Inflammation-dependent cerebrospinal fluid hypersecretion by the choroid plexus epithelium in posthemorrhagic hydrocephalus. Nature Med 23: 997-1003.

19. nhs.uk (2019) Causes: Hydrocephalus.