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ASSOCIATION OF LOW BIRTH WEIGHT AND AUTISM SPECTRUM DISORDER

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Abstract

Autism spectrum disorder (ASD) is a complex developmental condition resulting mainly in social and communication problems, the risk factors of which are still not substantially explored. The study aims to identify the probable association between ASD and low birth weight in the Georgian population, to promote early identification of disease in those patients.

A total of 100 patients aged 2-18 years with ASD diagnosed via ICD 10 were analyzed. Birth weight was obtained from medical records and the prevalence of low birth weight in ASD children was determined. Patients were stratified according to other possible risk factors. 11 out of 96 had low birth weight, out of which 73% were preterm, 55% were delivered with C-section, 45% had neonatal complications, and 55% had pregnancy complications. The findings showed an 11.5% prevalence of low birth weight in ASD patients that suggest a possible relationship between these two and warrant more extensive investigation.

Introduction

Autism spectrum disorder (ASD) is a complex developmental condition that involves persistent challenges in social interaction, speech and nonverbal communication, and restricted/repetitive behaviors. According to the World Health Organization [12], one in 160 children have ASD. In 2020, the CDC reported that approximately 1 in 54 children in the U.S. [4]. However, it is an estimated average, and the prevalence varies in different studies. The effects of ASD and the severity of symptoms differ in each person.

The diagnostic criteria vary in different countries [2]. The Diagnostic and Statistical Manual of Mental Disorders (DSM-5), updated in 2013, is used in the United States [2]. According to DSM-5, ASD is characterized by deficits in social interaction and restrictive, repetitive interests and patterns of behavior [1]. In 2013, the American Psychiatric Association reclassified autistic disorder, Asperger's syndrome, childhood disintegrative disorder, and pervasive developmental disorder not otherwise specified (PDD-NOS) as autism spectrum disorders. In contrast, ICD-10 classifies ASD in different subtypes: childhood autism, atypical autism, pervasive disorders and Asperger syndrome.

There has been ongoing research about the potential risk factors for the development of autism. ASD is considered to have a multifactorial origin, with both genetic and environmental factors playing a vital role in its development [5]. One potential risk factor can be the low birth weight which is categorized into3 types: low birth weight (<1500g -2499g), very low birth weight (1000g - 1499g), and extremely low birth weight (999 g. or less) [14].

Hisle-Gorman et al. tried to investigate prenatal, perinatal, and postnatal risk factors [6]. In adjusted analysis, they found a strong association between low birth weight and an autism spectrum disorder. A similar relationship was found in a case-control study conducted in Finland. According to it, there is a higher risk of ASD in an extremely low birth weight (<1000g) group with the adjusted odds ratio of3.05, 95% CI 1.4–6.5 [7]. They also found preterm birth to be an independent risk factor for ASD [7]. However, it is difficult to indicate only one risk factor for ASD [11]. It is unclear if these causes are primary or secondary risk factors for the disease and further investigation is needed [11].

While all the above-mentioned studies investigate singleton gestation, Losh et al. used a co-twin-control design to investigate low birth weight as a risk factor for ASD [9]. Although genetic effects are of major importance, a non-genetic influence associated with birth weight may contribute to the development of ASD [9]. Examining twins addressed the issue of genetic variants as a confounder [9]. Low birth weight infants were 3 times more likely to develop ASD [9]. However, as twins on average have lower birthweight than singleton births, it is controversial whether it can be generalized to every pregnancy and warrants further investigation [9].

Other possible correlations that should be taken into account are as follows: preterm birth, C-section, complications during the neonatal period, pregnancy and delivery, as well as medications used by mother during pregnancy [7]. Therefore, they should be considered as confounding factors [7]. Early screening in children with risk factors may lead to early diagnosis and intervention, which is crucial for a better outcome [8].

There have been studies determining an association between preterm birth and an autism spectrum disorder. However, the Georgian population has not been studied. This study allows us to research the situation in Georgia and have a more profound understanding of potential risk factors, in particular, low birth weight.

Methodology

This is a cross-sectional study conducted in Georgia that determines the prevalence of low birth weight (<2500g) in autistic spectrum disorder children. It also tries to determine the association of birth weight as a potential risk factor for autism spectrum disorder. Involved children were already diagnosed with ASD by ICD-10criteria (the international standard for defining and reporting diseases/health conditions which provide a diagnostic classification standard for all clinical and research purposes) or had features suggesting ASD (confirmatory test was not done yet). We gained access to the available medical records with the birth weight. A total of 96 patients aged 2-18 years with ASD were involved. We also stratified the risks to avoid confounders like neonatal complications (e.g. respiratory distress, infections, any need for neonatal intensive care) pregnancy complications (e.g. anemia, preeclampsia, amniotic fluid abnormalities), delivery method (vaginal or cesarean), delivery complications (eg. hemorrhage, asphyxia, dystocia, prolonged delivery), medication use (e.g. iron supplementations, aspirin, antihypertensive) and maternal psychiatric illness. Vaginal delivery included both physiologic and assisted methods. Inclusion criteria was children aged 2-18 diagnosed with ASD with ICD-10 criteria or having features of ASD. Exclusive criteria are neuropsychiatric developmental disorders concomitant with or without ASD, metabolic disorders like hypothyroidism or lysosomal storage diseases, congenital abnormalities, epilepsy, genetic disorders like down syndrome, or fragile X syndrome.

Results

This study investigated 96 patients aged 1.5-10 years old with confirmed or suspected ASD. Out of this 96, 11 (~11.5%) had low birth weight, 8 (~8.3%) were macrosomic, and77 (~80.2%) were born with normal weight (**Figure 1; Table 1**). Among the examined cases, 84 (87.5%) were term, 11 (~11.5%) were preterm, and 1 (~1%) was post-term (**Figure 2**). Majority (~69.8%) of them were delivered vaginally (**Figure 3**). Only 12(12.5%) patients developed neonatal complications (**Figure 4; Table 2**). 72 (75%) mothers of our cases did not have any complications during pregnancy (**Figure 5; Table 3**). The majority of deliveries (~96%) were uncomplicated (**Figure 6**).

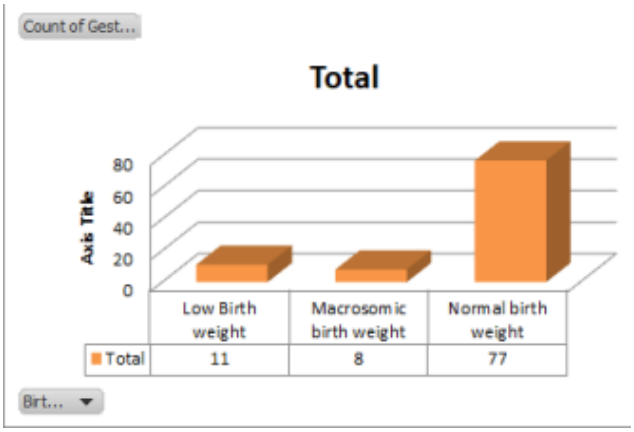

Figure 1. Distribution of birth weight among cases

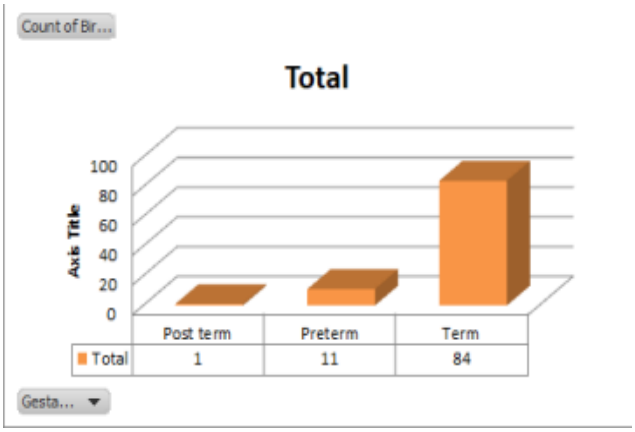

Figure 2. Distribution of gestational age among case

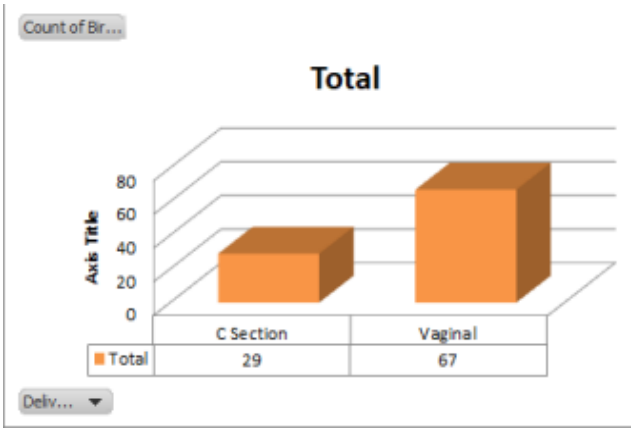

Figure 3. Distribution of delivery method among cases

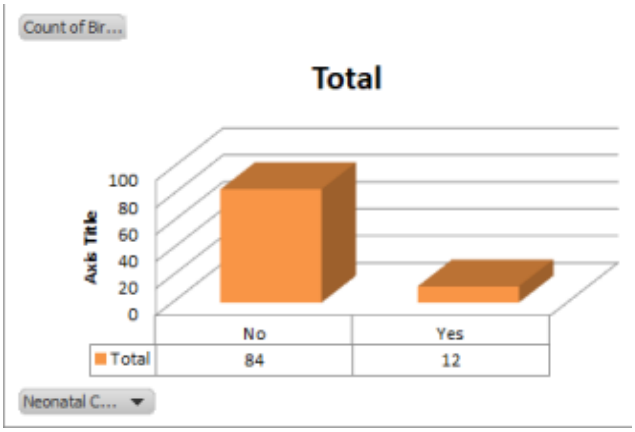

Figure 4. Neonatal Complications among cases

Table 1. Distribution of birth weight among cases

Count of Gestational age	Low Birth weight	Macrosomic birth weight	Normal birth weight	Grand Total
Post term	-	-	1	1
Preterm	8	-	3	11
Term	3	8	73	84
Grand Total	11	8	77	96

Table 2. Neonatal Complications among cases

Neonatal Complications	Low Birth weight	Macrosomic birth weight	Normal birth weight	Grand Total
No	6	8	70	84
Yes	5	-	7	12
Grand Total	11	8	77	96

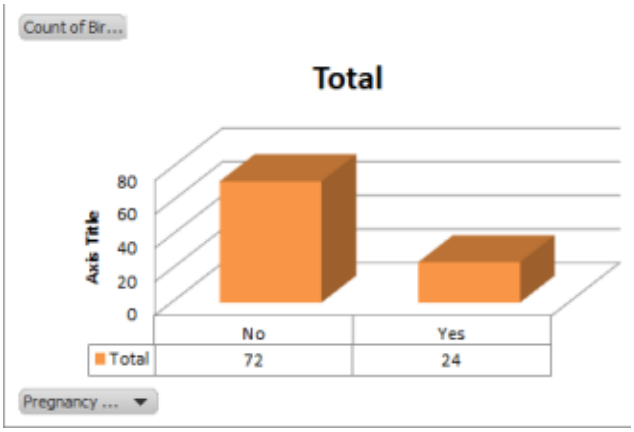

Figure 5. Pregnancy complications in cases

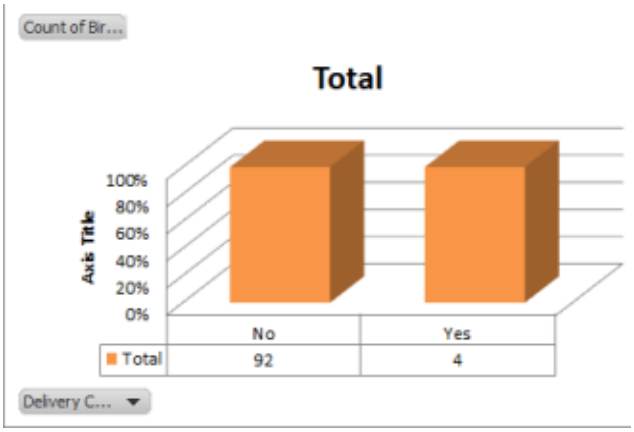

Figure 6. Delivery complication in our cases

Table 3. Pregnancy complications among cases

Pregnancy Complications	Low Birth weight	Macrosomic birth weight	Normal birth weight	Grand Total
No	5	7	60	72
Yes	6	1	17	24
Grand Total	11	8	77	96

Discussion

The study tried to find any correlation between low birth weights (as a potential risk factor). 96 children were included in the study. The results showed that the prevalence of low birth weight among ASD cases was 11.5%. According to WHO 2015 data, the prevalence of low birth weight in the Georgian population was 6.1% CI [5.6-6.6] [3]. Since our findings revealed a higher prevalence of low birth weight compared to the general population (11,5% versus 6,1% - p=0.0271) we can make an assumption that there is an association between low birth weight and ASD.

Birth weight is influenced by various maternal and pregnancy factors [7]. For example, uteroplacental insufficiency causes intrauterine growth restriction, smoking during pregnancy is also associated with low birth weight, maternal alcohol/illicit drug use likewise might be a reason for low birth weight, premature newborns have weight deficit, and etc. [7]. All of these factors by themself can be considered as risk factors for ASD [5,7].

In our study 8 (8.3%) out of 11 low birth weight infants were premature, but according to NCDC [10] overall prematurity rate is 8,7%, so almost the same, makes no difference. But our study results, revealing 11% of low birth weight more than overall low birth weight data (6,1%), raises a question: is low birth weight a confounder or is it independently associated with ASD? Answering this question is critical and requires a higher sample size, control group, and stratification of data. For example, Fezer et al. [5] conducted research that analyzed only the group of low-birth-weight infants who were not premature (18 patients) and obtained statistically significant differences compared to the general population (p=0.000).

Interestingly, there were 8 patients (~8%) with macrosomic birth weight. Several studies had inconclusive evidence about macrosomic birth weight and ASD association. Comparison of the prevalence of macrosomic birth weight in ASD patients should be compared to prevalence in the Georgian population. This will give us significant information but further emphasis should be paid to this. The purpose of this study is to question low birth weight as a possible risk factor for ASD development. As a result, more attention will be paid on low birthweight infants, including implementation of screening programs for ASD. This will aid in early diagnosis and initiation of interventions, which is crucial and has direct correlation with favorable outcomes.

Study limitations

The fact that our research had a small sample size (only 96 participants), and did not have a control group should lead to some limitations in our conclusions. The absence of a control group interferes with establishing the correlation between low birth weight and ASD and highlights the importance of having a control group in order to make a more precise interpretation.

Another potential limitation in our study is the lack of confirmatory assessment for ASD diagnosis in some patients and reliance on direct clinical assessment (evaluation of intellectual disability, deficits in social communications and interactions, presence of restricted, repetitive patterns of behavior). Individuals with only significant social communication deficits and lack of other characteristic features for ASD are usually evaluated for social (pragmatic) communication disorder. However, participants whose diagnosis was not confirmed yet had other clinical features of ASD making this diagnosis more probable.

Conclusion

Based on the results of the study there was a higher prevalence (11.5%) of low birth weight among ASD cases than in the general population of Georgia (6.1%) (p=0.0271). As low birth weight is a risk factor for development of ASD, conducting screening for ASD in lowbirth weight infants, would assist in early diagnosis and initiation of intervention leading to better outcomes. These results warrant further investigation with more extensive studies which will have a greater sample size and control group.

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References

1. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 2013
2. Augustyn, M. Autism spectrum disorder: Terminology, epidemiology, and pathogenesis. UpToDate. 2020, May 4; https://www.uptodate.com/contents/autism-spectrum-disorder-terminology epidemiology-and-pathogenesis.
3. Blencowe, H. Krasevec J, Onis M, et al. National, regional, and worldwide estimates of low birthweight in 2015, with trends from 2000: a systematic analysis. Lancet Glob Health 2019 Jul;7(7):e849-60.
4. Centers for Disease Control and Prevention.Data & statistics on autism spectrum disorder. Centers for Disease Control and Prevention. 2020, September 25; https://www.cdc.gov/ncbddd/autism/data.html.
5. Fezer GF, de Matos MB. Perinatal features of children with autism spectrum disorder. Rev Paul Pediatr 2017 Apr-Jun;35(2):130–35.
6. Hisle-Gorman E, Susi A, Stokes T, Gorman G, Erdie-Lalena C, Nylund CM. Prenatal, perinatal, and neonatal risk factors of autism spectrum disorder. Nature.2018 Aug;84(2):190-98
7. Lampi KM, Lehtonen L, Tran PL, et al. (n.d.). Risk of autism spectrum disorders in low birth weight and small for gestational age infants. J Pediatr 2012 Nov;161(5):830-36
8. Lederman1 VRG, Goulart AL, Santos AMN. Screening for ASD signs in very low birth weight preterm infants. Revista Psicologia: Teoria e Prática, 2018;20(3):86-99.
9. Losh M, Esserman D, Anckarsäter H. Lower birth weight indicates higher risk of autistic traits in discordant twin pairs. Psychol Med 2012 May;42(5):1091-102.
10. NCDC - healthcare statistical data Georgia 2020. NCDC.GE. (n.d.). 2021. https://www.ncdc.ge/#/pages/file/ebe72ea5-5087-4dc3-aaf1-c94cda232ad2.
11. Wang C, Geng H, Liu W, Zhang G. Prenatal, perinatal, and postnatal factors associated with autism: A meta-analysis. Medicine. Medicine (Baltimore). 2017 May; 96(18):e6696
12. World Health Organization. Autism spectrum disorders. World Health Organization. 2021. https://www.who.int/news-room/fact-sheets/detail/autism spectrum-disorders.
13. World Health Organization. International classification of diseases for mortality and morbidity statistics (11th Revision). 2018 https://icd.who.int/browse11/l-m/en.