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Original Article

Sociodemographic and Perinatal Risk Factors for Autism Spectrum Disorder: A Case-control Study

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Abstract:

Autism spectrum disorders included impaired communication and social interaction with restricted and repetitive interests and behaviors. The rising prevalence, coupled with the severe emotional and financial impact on the families, underscores the need for a particular emphasis on the prevention of autism spectrum disorder. However, risk factors for autism have not been well studied in Bangladesh. To describe the sociodemographic and perinatal aspects of a group of Bangladeshi autistic children in order to determine its possible risk factors.This case-control study was conducted at two specialized centers at Chattogram, Bangladesh, from January 2017 to December 2017. We selected 100 autistic children aged more than three years as cases and 100 age, sex-matched children without autism as control for the study. Sociodemographic and perinatal data were collected by direct interviewing of the parents of the children and reviewing the available records. We found higher maternal education and higher maternal age (≥35 years) at birth among autistic children in comparison to the controls (18% and 17% vs. 3% and 6% respectively). Higher paternal age (≥35 years) at birth and monthly family income ≥40000 Taka were found in 26% and 42% of autistic children than 23% and 7% in the control group. Perinatal asphyxia , preterm delivery, low birth weight, and gestational diabetes mellitus were associated with an increased risk of autism. Monthly family income, prematurity, and perinatal asphyxia were independent predictive factors as derived by logistic regression analysis. Higher socioeconomic status, prematurity, and perinatal asphyxia were found to be posing a significant risk to the development of autism.

Key words: Autism, Risk factors, Sociodemographic, Perinatal.

Introduction:

Autism spectrum disorder (ASD) is a complex neurodevelopment disorder of largely unknown causes[1,2]. ASD is characterized by impaired social interaction, communication development, and restricted, repetitive behaviors, and interests[3]. Globally an estimated 1-3% of children and adolescents are suffering from ASD[2,4]. In recent years, however, epidemiological studies show an increase in the prevalence of ASD partially due to increased awareness amongst the parents and changed diagnostic standards[1,5,6]. Centers for Disease Control and Prevention (CDC)'s Autism and Developmental Disabilities Monitoring (ADDM)

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Network identified that the prevalence of ASD among children aged 8 years is approximately one in 54[5]. In South Asia, the prevalence ranges from 0.09% in India to 1.07% in Sri Lanka[7]. In a recent study, the prevalence of the ASD in the rural community of Bangladesh was found 0.75/1000 children[6].

ASD is considered one of the most common childhood chronic diseases which extracts an enormous emotional, mental and financial toll on the families as well as to the society in terms of compromised quality of life and lifelong disability[8,9]. In Bangladesh, like in many other developing countries, autism and other neurodevelopmental disabilities are seen through the lens of misinformation and stigma. Hence, early detection and early intervention are the keys to reducing the burden associated with ASD.

Although significant progress has been made in identifying some of the neurological and genetic risk factors, the full range of etiologies causing ASD is still unknown[4,10]. Studies on twin and sibling pairs show a clear genetic predisposition to autism with concordance rates of 60-92%[10,11]. In many cases, autism is apparent in the first and second years of life, which indicates the involvement of environmental factors[10,12]. So, the etiology is most likely polygenic and potentially epistatic, and environmental factors may interact with genetic factors to increase the risk[13–16]. Although the distinctive neuropathology remains elusive, studies have shown macroscopic, microscopic, and functional brain abnormalities, which suggest that the relevant etiology may begin during the prenatal period[13,17,18]. Pregnancy-related exposures and possible risk factors for autism have been the focus of a significant amount of epidemiologic research. While many studies support the hypothesis that obstetrical complications may increase the risk of autism[19], the specific complications, the magnitude of the effect, and overall conclusions of these studies are inconsistent and prenatal, perinatal, neonatal, and other risk factors of autism, the causal nature of these associations is still unclear[2,8]. At the same time, a significant amount of studies have found relationship with sociodemographic status to the development of ASD.

However, studies are scarce in this field in Bangladesh. So, we aimed to find out the association between perinatal (focusing on birth weight, prematurity, and perinatal asphyxia) risk factors and autism in a group of Bangladeshi autistic children in order to better understand the possible sociodemographic and prenatal risk factors of autism. As there is no cure for this neurodevelopmental disorder, maximum effort should be given in prevention by addressing the risk factors[2]. Understanding the sociodemographic and prenatal risk factors and their association could provide clues to reveal the underlying causes of ASD, and better preventive measures would be available based on these understanding to tackle the burden of ASD.

Materials and Methods:

This case-control study was done at the 'Shishu Bikash Kendra' of Chattogram Medical College Hospital and Special Child Schools of Autism in Chattogram, Bangladesh from January 2017 to December 2017.

A total of 100 autistic children aged >3 years who met the ICD-10 criteria[20] attending these centers during the study period were included as the case. Age, sex, and demographically matched 100 children without ASD were included as control from the pediatrics outpatient department of the same Medical College Hospital.

Prior ethical clearance was taken from the ethical review committee (ERC) of Chattogram Medical College and informed written consent was taken from the parents of the selected children.

Children with developmental disorders such as Down syndrome, cerebral palsy, or with known neurogenetic conditions such as tuberous sclerosis, and neurofibromatosis were excluded from the study. The control group shared the same exclusion criteria.

In-depth interviews both from the case and control groups were taken including the sociodemographic variables such as age, gender, monthly family income, maternal and paternal education, occupation and age at childbirth. Other maternal factors such as antenatal check-up, gestational diabetes mellitus, mode of delivery, associated gestational events and perinatal factors such as birth weight of the baby, gestational age of the child at birth, perinatal asphyxia, and other perinatal events were recorded in a pre-designed data collection form.

Data were analyzed by IBM SPSS (Statistical Package for Social Science) Version 23 (SPSS Inc., Chicago, IL USA). Continuous data were described in terms of median and range, as they were not normally distributed. Qualitative or categorical data were described as frequencies and proportions. Proportions were compared using chi-square or Fisher's exact test, whichever was applicable. The odds ratio (OR) was

measured. Binary log regression analysis was performed by taking dependent as children with or without ASD and other variables such as sex, age, prematurity, birth weight as independent variables. Statistical significance was defined as $p = < 0.05$, and confidence interval set at a 95% level.

Results:

A total of 100 autistic children were included as case and 100 children without ASD were included as control. Table I shows the socio-demographics of the case and control groups. We have found that 18% of mothers of autistic children were university graduates in comparison to only 2% of the control group. Both maternal and paternal education was statistically significant. Twenty five percent (25%) of mothers of autistic children were professionals versus 10% of mothers were professionals in the control group, and this was also statistically significant. Sixty six percent (66%) of autistic children came from a family with monthly income ≥30000 Taka, and the corresponding value in the control group was only 13%.

Table-I: Sociodemographic factors of the study groups

Variables	Study groups		χ^2 &
	Case (n=100) %	Control (n=100) %	p value
Maternal education			
Primary	2	21	53.78
SSC	23	53	<0.001
HSC & Graduate	57	24	
Masters & above	18	2	
Paternal education			
Primary	2	24	58.58
SSC	13	38	<0.001
HSC & Graduate	53	35	
Masters & above	32	3	
Maternal job			
Working	25	10	7.79
House maker	75	90	0.005
Paternal job			
Business	42	36	4.22
Service	28	26	0.121
Others*	30	48	
Monthly family income			
<20000	19	67	57.86
20000-30000	21	20	<0.001
30000-40000	18	6	
≥40000	42	7	

*Others include Judge, working abroad, expired.

Table II shows the age distribution of the parents of the study population at the time of delivery. In the autistic group, 17% of the mothers' age was ≥35 years at the time of delivery of the child, and the corresponding value in the control group was only 5%, and the difference was statistically significant. A similar pattern of age at delivery was also observed among fathers.

Table-II: Distribution of the study population by the age of their parents at the time of delivery

Age at the time of delivery (years)	Study groups		χ^2 &
	Case (n=100) %	Control (n=100) %	p value
Maternal			
P≤19	1	16	30.68
20-24	25	44	<0.001
25-29	41	24	
30-34	16	11	
35-39	11	4	
≥40	6	1	
Paternal			
W≤24	2	10	13.37
25-29	38	47	0.01
30-34	34	20	
35-39	19	11	
≥40	7	12	

The number of mothers with gestational diabetes mellitus (GDM) and child who were delivered by caesarian section was significantly higher in the case group (11% and 55% respectively). However, the number of mothers who took antenatal care (ANC) >5 times during their pregnancy period was higher in the case than the control group (Table III).

Table-III: Maternal characteristics during pregnancy and mode of delivery

Variables	Study groups		χ^2 &
	Case (n=100) %	Control (n=100) %	p value
Number of ANC			
P≤5	66	90	16.78
>5	34	10	<0.001
GDM			
No	89	98	6.64
Yes	11	2	0.01
Other gestational events*			
No	78	86	2.17
Yes	22	14	0.14
Mode of delivery			
Vaginal delivery	45	71	13.87
Cesarean section	55	29	<0.001

*Others include antepartum hemorrhage, threatened abortion, hypertensive disease of pregnancy, thyroid disorder, fever, and bronchial asthma.

Table IV shows that mother of the 20% cases versus 2% of the control had a preterm delivery, and 21% of cases had low birth weight compared to 5% of control, and the differences were statistically significant. Likewise, perinatal asphyxia and other perinatal events were also significantly higher among cases than control.

Table-IV: Perinatal characteristics among the study population

Variables	Study groups		χ^2 &
	Case (n=100) %	Control (n=100) %	p value
Gestational age			
<37 weeks	20	2	16.55
≥37 weeks	80	98	<0.001
Birth weight			
<2500 gram	21	5	11.32
≥2500 gram	79	95	<0.001
Perinatal asphyxia			
No	77	98	20.16
Yes	23	2	<0.0
Other perinatal events*			
No	72	97	23.86
Yes	28	3	<0.00
Neonatal jaundice			
No	91	95	1.23
Yes	9	5	0.268

*Others include convulsion, neonatal septicemia, phototherapy, hospitalization.

By using logistic regression model and adjusting each variable for all of the other variables, perinatal asphyxia, prematurity, and monthly family income was found to be associated with a statistically significantly increased risk of autism (Table V).

Table-V: Adjusted odds ratio and 95% confidence intervals for risk factors of autism using the logistic regression model

Variables	Adjusted odds ratio	95% confidence interval	p value
Monthly family income	1	1	<0.001
Gestational DM	2.92	0.42-20.46	0.279
Delivery by CS	1.84	0.86-3.90	0.113
Perinatal asphyxia	22.56	4.54-112.07	<0.001
Prematurity	1.45	1.03-31.04	0.043
Low birth weight	3.19	0.93-11.03	0.066
Neonatal jaundice	2.21	0.56-9.29	0.278

Of the studied risk factors, 55% of the autistic children were free from prematurity, low birth weight, and perinatal asphyxia. For only 2 percent of the cases, all three risk factors were present (Figure I).

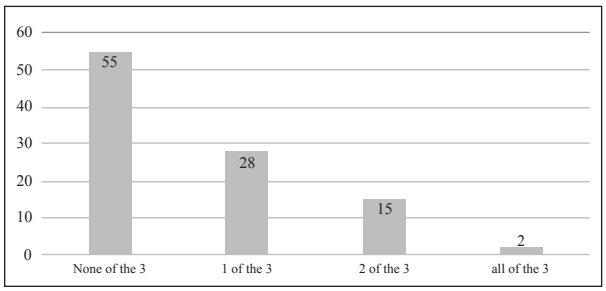

Figure I: Clustering of prematurity, low birth weight, and perinatal asphyxia among autistic children (n=100).

Discussion:

Bangladesh, like many other developing countries, needs extensive multidisciplinary action to assist and promote adequate measures for families with autism. However, adequate screening for autism, culturally and linguistically appropriate interventions are still some of the significant challenges for Bangladesh. The etiology of autism is unknown, but it has distinct risk factors that often co-occur. Adequate studies in this issue are still unavailable in Bangladesh. To fill this gap, we assessed some perinatal and sociodemographic risk factors for autism among 100 children with ASD and compared them with 100 children without ASD.

The relationship between socioeconomic status and the prevalence of autism had studied extensively. However, there was controversy in this association when this status was assessed in terms of parental education, occupation, and parental wealth[21]. We tried to assess this association in terms of the monthly family income of the subjects. In the unadjusted analyses, the risk of autism was higher for those with more monthly family income (>40000 Taka) than those with less (<20000 Taka) monthly family income; however, after we adjusted for other variables, socioeconomic status measured by monthly family income did not have a significant effect. Our result is in agreement with the finding of Larsson et al[22]. Our study also showed that parents were highly educated in autism group than in the control group. Association between parental education and job status with autism was studied by King and Bearman[23] and their results showed that higher levels of parental education and parental economic resources were consistently associated with an increase in the likelihood of diagnosis. In our study, there was a statistically significant difference between mothers of autistic children and the control group concerning university

graduation (18% and 2% respectively). Moreover, as regards mother's work, 25% of mothers of autistic children were professionals and 75% were housewives versus 10% and 90% of the control group respectively. However, it is essential to mention that all of the children in our control group were selected from the outpatient department of Chittagong Medical College Hospital, and usually low-income families seek services from the OPD of this sort of hospitals in Bangladesh.

To evaluate the maternal risk factors associated with autistic children, Riya et al. conducted a study in Dhaka Shishu Hospital and Specialized Pediatric Neurology Clinic in Dhaka in 2002-2004[24]. Their findings were also similar to ours. In a study by Khanom et al., researchers found that maternal higher education and maternal advanced age at pregnancy were related. Maternal higher education influences the family income. Therefore, these two factors were related with socioeconomic status of the family and indirectly related with the risk of ASD[25]. This finding was consistent with a study by Durkin and colleagues who used an area-based measures of socioeconomic status and found that higher educational level of mothers lead to advanced age at childbirth and the prevalence of autism increased with socioeconomic status[26].

Our study showed that high parental age (mother ≥35 years, father, ≥35 years) at birth was found in 17% and 26% of autistic children in comparison to 5% and 23% of the control group. Reichenberg et al. showed that the offspring of men aged 40 years or more had more than 5 times higher risk of ASD than offspring of men younger than 30 years[27]. In agreement with these results, Kolevzon et al. found that the parenteral characteristic associated with an increased risk of autism and autism spectrum disorders include advanced maternal age and paternal age[19]. Another study by Marissa et al. concluded that advanced maternal age, rather than paternal age, may pose a higher risk for autism[28]. Mutations, increased risk of chromosomal abnormalities and pregnancy complications which increase with advancing age could be possible explanations for such findings[29].

In our study, GDM was reported in 11% of cases versus 2% of controls ($p = <0.05$). There was a statistical association between GDM and the risk of ASD. Like our study, Alsuliamani et al. also found that gestational diabetes mellitus was more prevalent among autistic children group[30]. An association between general developmental impairments and maternal diabetes has been previously observed. Moreover, a population-based study in young children provided evidence that maternal metabolic conditions are risk factors for autism, developmental delay without autistic symptoms, and impairments in several domains of development[31]. Besides GDM, other prenatal maternal factors in our study were APH, threatened abortion, PET, and fever. These events were also significantly more in the group of autistic children.

Regarding natal and post-natal factors, a recent study noted that pregnant women who had their labor started or sped up artificially are slightly more likely to have autistic children[32]. Concerning our result, 55% of cases compared to 29% of controls were delivered by cesarean section with a statistically significant difference. Concerning birth weight and autism, 21% of cases compared to 5% of controls had low birth weight, and the difference was statistically significant. The proportion of children with the history of preterm delivery was 20% and 2% in our case and control group, respectively. These findings are consistent with results of a population-based case-control study conducted in Finland in 2013 which concluded that low birth weight is strongly related to childhood autism[33].

Conclusions:

Monthly family income, prematurity, and perinatal asphyxia have been found as independent predictive factors of ASD. However large, prospective, population-based studies to elucidate the modifiable risk factors, particularly those during the prenatal period are needed in our country perspective.

Conflict of interest: None.

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