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Original Article

Rural-Urban Differences in Age at Autism Diagnosis: A Multiple Model Analysis

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Abstract

Objective: Early recognition of autism is important, but diagnosis age varies among children. Recent studies have aimed to identify factors affecting age of diagnosis and several studies have attempted to explore geographic variation in age at diagnosis of autism. However, there is a lack of research examining geographic variations with multiple models to find whether geographic differences can be explained by risk factors such as socioeconomic status and differences in child characteristics. This study aimed to address this gap of knowledge by comparing age at diagnosis of autism between the group of people living in the center of the province and the group of people living in the rest of the province, considering potential medical and socioeconomic confounders.
Method: The study population consisted of 50 autistic children born in East Azerbaijan Province between 2004 and 2016. Initially, univariate testing by ANOVA was performed to identify family and individual factors contributing to differences in age at autism diagnosis. Following this, the association between living in the center of the province and age at diagnosis in univariate and multivariate analyses was examined.
Results: Results from the initial univariate analysis indicate a significant association between living in the center of province and early diagnosis. However, inclusion of possible confounders in multiple model illustrates that these geographical disparities in age at diagnosis can be explained by differences in socioeconomic and medical status.
Conclusion: Although geographic variation in age at diagnosis of autism was observed, analyses show that differences in individual and family-level factors may contribute to geographic differences. In this study, most of the observed variation was accounted for by family-level factors rather than geographic policies. Findings prove that multiple strategies are required to identify targeted interventions and strategies.

Key words: *Autism Spectrum Disorder; Early Diagnosis; Health Services Accessibility; Health Status Disparities; Multivariate Analysis; Symptom Assessment; Socioeconomic Factors*

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Autism is a complex disabling continuum disorder that affects humans differently with varying degrees of impairment in social interaction, communicational skills, and repetitive behavioral patterns (1-3). It appears that the prevalence of autism is greater than previously thought. An estimation of the global incidence of autism spectrum disorders was 6 to 7 per 1000 on review of epidemiological studies (4, 5). This high rate of prevalence places Autism spectrum disorders among the most common developmental disorders in the world (5). Although autism mainly disables the child, the impact of autism on the family system is hard to ignore (6). Raising an autistic child could be an overwhelming experience for parents and families (7). Although there is no known prevention or cure, the impact of early diagnosis and early intervention to improve the functioning of autistics is well-known (8-10). Growing evidence emphasizes the importance of early detection and intervention, which can significantly affect a child's well-being and reduce family and community burden (11-13). Significant differences have been observed in age at diagnosis of autism between different socioeconomic and geographic classes. In a review of 42 studies published between 1990 and 2012, the mean age at diagnosis ranged from 38 to 120 months (14). Many studies have examined factors affecting age at diagnosis of autism including child, family, and geographical characteristics. Factors such as ethnicity, socioeconomic status, and geographical location have been found to be associated with age at diagnosis (15-17). Children in rural areas are believed to be more likely to receive a delayed diagnosis of autism. This belief is rooted in the hypothesis that many psychologists and health experts in undeveloped areas do not have sufficient knowledge and experience in diagnosis of autism. Moreover, geographic disparities in access to healthcare services seem to make parents experience a lengthier diagnosis process. To date, several studies have examined the association between residential location and age at diagnosis of autism (18-20). However, there is a lack of research that examines geographic variation in age at diagnosis with multiple models to find whether or not geographic differences can be explained by risk factors such as socioeconomic status and child characteristics. This study attempted to address this gap. In this regard, we examined whether the differences in age at diagnosis of autism between the group of people living in the center of the East Azerbaijan province and the ones living in the rest of the East Azerbaijan province, after adjusting for confounders, are statistically significant or not.

Materials and Methods

Research Location

This study was conducted in East Azerbaijan province, located in the northwestern part of Iran. East Azerbaijan province is the sixth most populous province in Iran with about four million people, most of whom have an Azeri ethnic background. Tabriz is the center of East Azerbaijan province, with a population of about 1.8 million, which is about half of the population of East Azerbaijan.

Participants

Our study participants were 50 autistic children born between 2004 and 2016 in East Azerbaijan province. These cases were contacted under supervision and in collaboration with the state welfare organization of Iran and the research plan and questionnaires were approved by the Research Ethics Committee. Participants were informed of the purpose of the study, their voluntary participation, and their right to withdraw before filling out the written consent. All the cases in our study were diagnosed to have typical autism. Pediatricians, experienced psychiatrists, and health professionals made the diagnoses. Moreover, the diagnosis was validated by census among the psychiatrists in the state welfare organization of East Azerbaijan province. The Diagnostic and Statistical Manual of Mental Disorders-IV-Text Revision (DSM-IV- TR) criteria was set as the basis for diagnosis. Children were excluded from the study if their residential location had changed between the date of entry and diagnosis ($n = 7$); we also excluded children if their parents refused to participate in our study ($n = 6$), leaving a total of 50 participants.

Measures

Participants' covariates were collected from the parent questionnaire. The survey questions were designed in three main parts:

1) Child covariates included the child's gender, date of birth, date of diagnosis, birth order, and physical disorder, whether or not the child's acquired skills have been lost in the first two years of life, and whether or not the child has experienced a seizure in his or her first two years.
2) Parental covariates at the date of diagnosis included age, education (lower than high school, high school degree, and college degree), employment, and migration.
3) Residential location included questions about the residence address and whether or not the residential location had changed between the date of entry and the date of diagnosis.

Statistical analysis

The assumption of normality needs to be checked before using linear regression. As age at diagnosis was not normally distributed, this dependent variable was log-transformed. After normalizing distribution for age of diagnosis, two statistical analyses were implemented. First, the statistically significant level of association between independent variables and log-transformed age at diagnosis was calculated by univariate testing by ANOVA. Second, after identifying those variables with P-value < 0.1, the random effect multiple linear regression adjusted for age was used to examine if living in the province's center was associated with earlier age at diagnosis when individual and family factors are controlled. Using multiple regression, the significance of prior independent variables has also been examined. Additional to this, the path analysis model has been implemented as a confirmatory method to identify the impact of residential location before and after adjustment for age and other confounders. The analysis was performed using Stata v15.

Results

Table 1 describes the overall population of autistic children recruited by the state welfare organization of East Azerbaijan province, diagnosed between 2007 and 2018, ranging from 3 to 15 years of age, with a median of 7 months.

The average age at diagnosis varies with age. Among those < 6 years old, this average was 29 months (± 10.22), age at diagnosis for children between 7 and 10 years old was 47.21 months (± 16.16), and among cases > 11 years old was 52 months (± 26.47). As seen in Table1, the results of univariate log-transformed mean age at diagnosis of autism indicate that Log-transformed mean age at diagnosis of autism was significantly lower for cases with employed and insured parents. Likewise, medical problems including physical disorders and loss of acquired skills were associated with earlier diagnosis. On the other hand, paternal education, parental age, parental migration, sex, birth order, and seizure disorders did not affect the age at which children received a diagnosis.

Table 2 shows the variation of log-transformed age at diagnosis of autism in multiple linear regression, adjusted by age with the inclusion of prior significant factors, with $P \leq 0.1$, including physical disorder, loss of acquired skills, maternal and paternal employment, family insurance status, and residential location. After the inclusion of independent factors in multiple regression, living in the center of the province was not found to be associated with earlier diagnosis. Other factors like gender, insurance status, and maternal occupation played more significant roles in the age at diagnosis. Results indicate that being a girl, living in an insured family, and having an occupied mother significantly increase the chance of early diagnosis. The amounts of R and R-square for this model are 0.797 and 0.635 respectively.

In addition to multiple analysis, a path analysis model was implemented as a confirmatory analysis. In order to assess the overall fit of the path model, a number of indicators were used. All of the generated fit indexes support the suitability of the model. The very epitome of this suitability can be seen in Goodness-of-Fit Index (GFI), Trucker-Lewis Index (TLI), and Comparative Fit Index (CFI) values that are greater than the minimum value required (0.9), demonstrating the model’s fitness (21). As well as this, the Root Mean Square Error of Approximation (RMSEA) value, which should be lower than 0.08 (21) was 0.001 in our model. The summary of fit indicators is available in Table 3. While Figure 1 shows a significant association between residential location and age at diagnosis of autism, the age-adjusted path analysis model demonstrates that sex, maternal employment, and family insurance status fully mediate the association. The results are shown in Figure 2.

Table 1. Comparison of Mean Age at Diagnosis by Characteristics Using Univariate ANOVA Test

	Characteristics	N	Age of diagnosis (months)			ANOVA test for log-transformed age at diagnosis			
						Within groups			P
			Means	SD	Median	SS	MS	F	
Child characteristics	Overall	50	42.2	20.0	37.0				
	Sex					1.89	0.04	2.74	0.104
	Female	8 (16%)	33.00	18.30	25.0				
	Male	42 (84%)	43.86	20.10	38.0				
	Current age					1.48	0.03	8.18	0.001
	3-6	18 (36%)	29.33	10.22	25.50				
	7-10	19 (38%)	47.12	16.16	48.00				
	11-15	13 (26%)	52.38	26.47	48.00				
	Birth order					1.99	0.04	0.01	0.698
	First child	27 (54%)	42.33	18.91	38.00				
	Second or more	23 (46%)	41.87	21.73	36.00				

	Physical disorder					1.81	0.04	4.94	0.031*
	Yes	7 (14%)	58.29	25.46	48.00				
	No	43 (86%)	39.49	18.04	36.00				
	Loss of acquired skill in first two years					1.82	0.04	4.82	0.033*
	Yes	13 (26%)	32.15	12.53	26.00				
	No	37 (74%)	45.62	21.12	38.00				
	Seizure in first two years					1.90	0.04	2.42	0.126
	Yes	5 (10%)	29.80	12.13	24.00				
	No	45 (90%)	43.49	20.37	38.00				
Parental characteristics	Maternal age at birth					1.81	0.04	1.17	0.336
	< 25	10 (20%)	46.70	19.05	48.00				
	25-28	10 (20%)	31.80	14.94	30.00				
	28-30	7 (14%)	43.43	16.18	42.00				
	30-35	15 (20%)	45.20	23.00	38.00				
	> 35	8 (16%)	42.38	23.91	34.00				
	Paternal age at birth					1.78	0.04	1.35	0.267
	< 25	4 (8%)	42.00	12.00	48.00				
	25-28	6 (12%)	60.17	26.08	56.50				
	28-30	4 (8%)	46.25	22.54	48.00				
	30-35	13 (26%)	36.85	12.87	36.00				
	> 35	23 (46%)	39.70	21.13	32.00				
	Maternal education					1.86	0.04	1.69	0.194
	< High school	15 (30%)	42.93	16.07	48.00				
	High school	27 (54%)	45.15	23.17	38.00				
	Collage degree	8 (16%)	30.38	10.36	31.00				
	Paternal education					1.81	0.04	2.48	0.094
	< High school	14 (28%)	52.21	22.93	48.00				
	High school	30 (60%)	37.50	16.78	36.00				
	Collage degree	6 (12%)	41.67	22.85	36.00				
	Maternal employment					1.82	0.04	4.72	0.035*
	Employed	11 (22%)	31.64	15.10	26.00				
	Unemployed	39 (78%)	45.08	20.43	42.00				
	Paternal employment					1.84	0.04	4.23	0.045*
	Employed	48 (96%)	40.88	19.47	36.00				
	Unemployed	2 (4%)	72.00	0.00	70.00				
	Maternal migration					2.00	0.04	0.01	0.956
	Migrated	15 (30%)	40.40	14.41	38.00				
	Not-migrated	35 (70%)	42.86	22.17	36.00				
	Paternal migration					2.00	0.04	0.003	0.959

Residential characters	Migrated	13 (26%)	39.77	11.74	38.00				
	Not-migrated	37 (74%)	42.95	22.32	36.00				
	Family insurance status					1.79	0.04	5.46	0.024*
	Insured	28 (56%)	36.14	15.73	36.00				
	Uninsured	22 (44%)	49.73	22.61	48.00				
	Residential location					2.00	0.04	4.31	0.043*
	Center of the province	32 (64%)	38.18	17.92	36.00				
	Rest of the province	18 (36%)	51.90	24.18	48.00				

SS = Sum of Squares, MS = Mean of squares, F = variation between sample means / variation within the samples; * = P < 0.05

Table 2. Multiple Linear Regression Model by Random-Effect of Log-Transformed Age at Diagnosis of Autism Adjusted by Age

	Parameter	Raw coefficient	Average difference in age at autism diagnosis compared with the reference group	95% confidence interval		P
Child characteristics	sex					
	Female	Ref				
	Male	0.148	0.148	0.024	0.271	0.019*
	Birth order					
	First child	Ref				
	Second or more	-0.046	-0.046	-0.141	0.049	0.346
	Physical disorder					
	Yes	Ref				
	No	-0.066	-0.066	-0.215	0.082	0.383
	Loss of acquired skill in first two years					
	Yes	Ref				
	No	0.005	0.005	-0.089	0.100	0.913
	Seizure in first two years					
	Yes	Ref				
	No	0.104	0.104	-0.053	0.261	0.196
Parental characteristics	Maternal age at birth					
	< 25	Ref				
	25-28	-0.185	-0.185	-0.325	-0.046	0.009
	28-30	-0.050	-0.050	-0.204	0.103	0.521
	30-35	-0.033	-0.033	-0.160	0.094	0.610
	> 35	-0.077	-0.077	-0.225	0.071	0.308
	Paternal age at birth					
	< 25	Ref				
	25-28	0.155	0.147	-0.055	0.349	0.155
	28-30	0.397	0.097	-0.128	0.323	0.397
	30-35	0.606	-0.047	-0.227	0.132	0.606
	> 35	0.969	-0.003	-0.175	0.168	0.969
	Maternal education					
	< High school	Ref				
	High school	0.002	0.002	-0.105	0.109	0.967

	Collage degree	-0.073	-0.072	-0.222	0.077	0.341
	Paternal education					
	< High school	Ref				
	High school	-0.101	-0.101	-0.208	0.005	0.063
	Collage degree	-0.101	-0.101	-0.259	0.057	0.211
	Maternal employment					
	Employed	Ref				
	Unemployed	0.118	0.118	0.014	0.223	0.026*
	Paternal employment					
	Employed	Ref				
	Unemployed	0.231	0.231	-0.004	0.467	0.054
	Maternal migration					
	Migrated	Ref				
	Not-migrated	-0.024	-0.024	-0.128	0.080	0.063
	Paternal migration					
	Migrated	Ref				
	Not-Migrated	0.003	0.013	-0.080	0.107	0.772
	Family insurance status					
	Insured	Ref				
	Uninsured	0.129	0.129	0.041	0.218	0.004*
Residential character	Residential location					
	Center of the province	Ref				
	Rest of the province	0.051	0.05	-0.056	0.156	0.158

Multiple Analysis has used Maximum likelihood test & 95% CI; * = P < 0.05.

Table 3. Summary of Fit Index for Path Analysis Model

x^2/df	p-Value	RMSEA	SRMR	GFI	TLI	CFI	PCLOSE
0.912	0.434	0.001	0.055	0.985	1.02	1.00	0.489

Key:

RMSEA : Root Mean Square Error of Approximation — GFI : Goodness-of-Fit Index

SRMR : Standardized Root Mean squared Residual — TLI : Trucker-Lewis Index

PCLOSE: Probability RMSEA <= 0.05 — CFI : Comparative Fit Index

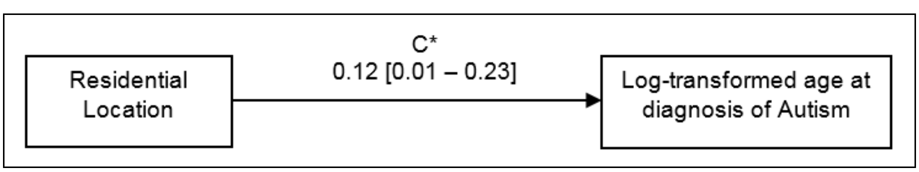

Figure 1. Association between Residential Location and Age at Diagnosis in Simple Path Model 95% CI; * P < 0.05

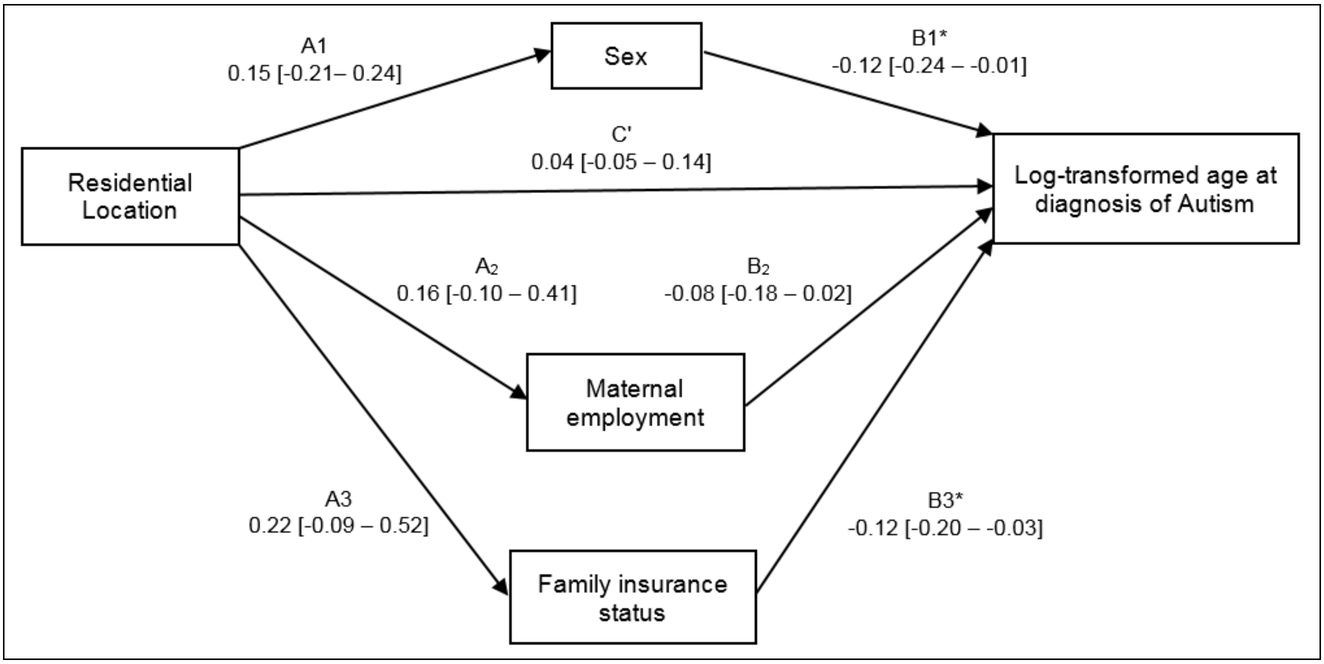

Figure 2. Age Adjusted Path Analysis Model with 95% CI and Maximum Likelihood Test, [Residential Location (Tabriz = 1, Rest of the province = 0), Sex (Boy = 0, Girl = 1), Maternal Employment (Unemployed = 0, Employed = 1), Family Insurance Status (Insured = 1, Uninsured = 0)]; * = P < 0.05

Discussion

Recent studies provide evidence on statistically significant differences in age at diagnosis of autism by residential location (8, 14, 18, 22). This diversity has been observed especially in areas with more socioeconomic diversity. This study examined geographic differences in age at diagnosis of autism before and after adjustment for risk factors in 50 autistic children of East Azerbaijan province to understand the impact of potential confounders on geographic differences in age at diagnosis. In our study, the result of univariate analysis suggests that living in the center of the province is associated with earlier diagnosis; however, evidence indicates that the role of individual characteristics is hard to ignore. For instance, diversity of insurance status, which is an important risk factor for early recognition of autism, may have accounted for geographic differences in age at autism diagnosis. In order to consider the impact of possible confounders, age-adjusted multiple models with inclusion of demographic and socioeconomic factors were implemented. A path analysis model has also been implemented as a confirmatory analysis.

The results of multiple analyses and path analysis are consistent and indicate that the geographic variation in age at autism diagnosis mainly results from differences in individual factors. Diversity in medical history and socioeconomic status affect the variation in age at diagnosis to the extent that these individual characteristics can explain geographic differences in age at diagnosis. Our study found that early diagnoses notably correlated with being a girl, living in an insured family, and having an occupied mother.

Our finding, which indicates earlier age at diagnosis for girls (1.8 months), is inconsistent with the results of some studies that observed no association between gender and age at diagnosis (23, 24), but agrees with Wiggings et al.'s study which was conducted in the state of Georgia in USA (25). In this population-based study, the comparison of mean age at diagnosis of autism between 49 males and 38 females indicated that the mean age at autism diagnosis is eight months lower for females than males, at the age of 54 and 62 months respectively. Earlier diagnosis of autism in girls can be explained by the fact that autism in females is mostly associated with a higher degree of disabilities (26) and parents are more likely to recognize early signs of atypical development in girls than boys (27). Our study found a marked relation between lack of insurance and later diagnosis of autism. The results indicate that children living in uninsured families are highly likely to receive diagnosis with more than 1.5 months of delay. Similar associations between insurance and early diagnosis have been observed previously (28). Moreover, a better health situation was associated with insurance coverage in several studies (29-31). Results from a systematic review with inclusion of 9710 studies indicate that insurance would raise medical care usage to improve overall health (32). On the other hand, according to previous studies, the health conditions of uninsured people are generally poor (30, 33). Children from uninsured families have a 70 percent lower chance of receiving medical care for their common diseases (33). Likewise, uninsured children are highly likely to be reported as having unmet needs for mental health services (34). Although all uninsured individuals may be harmed by lack of insurance, low incomes are more vulnerable. Despite the importance of insurance, more than 40 percent of our cases did not have any kind of insurance at the time of diagnosis. This low rate of insurance would be an obstacle for receiving early diagnosis and interventional services. To identify the impact of the family's economic situation and income on age at diagnosis, we asked about the amount of family's overall revenues in the interview; however, parents were unwilling to provide information about their source of income and amount of revenues. So, to identify their financial situation, some questions were asked about the occupational status of parents at the time of diagnosis. Our study found that children of employed mothers receive diagnosis 1.6 months earlier than the reference group. Likewise, paternal occupation was associated with earlier diagnosis; however, this relation was not statistically significant (P = 0.54). Our findings surrounding the association between parental occupational status and earlier diagnosis of autism are aligned with the results of previous studies that have found an earlier diagnosis of autism to be associated with higher family income (8, 35). Our results regarding the higher impact of maternal occupation on age at diagnosis in combination with the fact that mothers are generally more active in inquiring about autism (36) provide evidence on the possible impact of maternal financial independence on early diagnosis of autism, which should be included in future studies.

Our results showed an association between child's medical situation and age at diagnosis of autism; however, these associations were not statistically significant. Our results indicate that seizure experience contributes to marginally (not statistically significant) earlier diagnosis, for 1.2 months. Based on the evidence, seizures are more common in children with lower IQ (37). Moreover, seizures are mostly associated with greater signs and deficits in a child's development (38, 39). Another fact that can explain the impact of seizure on earlier diagnosis is that seizure is a typical alarm to the potentiality of autism (40). Regarding the impact of physical disorder on age at diagnosis, our study found physical disorder to be accompanied by a slightly later diagnosis, for three weeks. However, a more significant association has been observed in other studies (8, 41). In the study by Mandel et al., the average age at diagnosis of children with co-occurring hearing impairment was ten months later than the rest (8). These impairments seem to make diagnosis more difficult. Our study also found that being first-born was associated with marginally later diagnosis of autism, for two weeks. Based on previous studies, fewer children in the house would cause a higher amount of parental attention and, as a result, an earlier diagnosis of autism (42). However, having siblings would bring the possibility of comparison. Based on the study of Herlihy et al., the age at which parents become concerned about their child's development was 16 months for first-born children and 14 months for children who have an older sibling (43).

Limitation

Our study has some strengths and limitations. The noteworthy strengths of this study are in terms of data and the statistical method. The wide diversity in the medical and socioeconomic status of our cases, which increased the robustness and reliability of the results, was one strength of the data. However, the principal strength of our study was the statistical analysis that was used. Previous studies examined the impact of residential location on age at diagnosis by comparing the mean age at diagnosis between different political areas, while we implemented multiple age-adjusted models to consider the role of medical and family characteristics on age at diagnosis. On the other hand, our study had limitations in terms of sample size restriction. Accessing to a larger sample size was impossible as there is no registration for autism in Iran. Our database included cases that used governmental screening and interventional services.

Conclusion

In summary, we observed a noticeable geographic variation in age at autism diagnosis among 50 autistic children of East Azerbaijan province born between 2004 and 2016. The possible impact of individual medical history and socioeconomic status on age at diagnosis was examined in the initial analysis. Results of this univariate analysis indicate that physical disorder, experience of loss of acquired skills, paternal occupation, insurance status, and living in the center of the province contribute to the age at which diagnosis occurs. However, results from further analysis provide evidence for a more significant impact of socioeconomic status and individual medical characteristics on age at diagnosis compared to residential location. Findings from this multiple analysis adjusted for age demonstrate that early diagnosis is associated with being a girl, living in an insured family, and having an occupied mother. These factors can explain geographic diversity in age at diagnosis. This study provides evidence that a number of factors affect the age at diagnosis, and multiple regression models are more appropriate for identifying differences.

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Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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