Risk factors for autism spectrum disorders. A single-center observational study.

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Abstract

Introduction: Autism spectrum disorders (ASDs) are a group of neurodevelopmental disorders characterized by social and language difficulties and stereotyped behavioral patterns. The high etiological complexity of these diseases is due to their multifactorial nature.

Methods: An observational, cross-sectional, retrospective, and analytical study was conducted using a mixed data collection technique. The sample included 126 patients diagnosed with ASD treated at Francisco Icaza Bustamante Hospital between 2019 and 2022.

Results: A total of 77.0% (n= 97) of the participants were male, and 23.0% (n= 29) were female. The mean age of the sample was 9.26 years (SD: 4.08), while the mean age at diagnosis was 2.38 years (SD: 1.91). The associations between Asperger syndrome and male sex were determined by the Pearson chi-square test (P = 0.007), likelihood ratio (P = 0.002), and Fisher's exact test (P = 0.038).

Conclusions: Male sex predominated in the sample. The mean age at diagnosis complied with the recommendations of the Clinical Practice Guide for ASD. The high percentage of concomitant disabilities suggests the need for multidisciplinary interventions. Finally, a significant association was identified between Asperger syndrome and male sex.

Keywords:

Autism spectrum disorders, Autism, Risk factors, Prenatal factors, Perinatal factors, Autism spectrum disorders.

Abbreviations

ASD: autism spectrum disorder.

Additional information

No supplementary materials were declared.

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Authors' contributions

Mónica Leonor Jaramillo Castro: Conceptualization, data curation, formal analysis, funding acquisition, investigation, writing - original draft.
Alejandro Alberto Rodríguez Mero: Funding acquisition, research, methodology, resources, supervision, validation, visualization, writing – original draft, writing – review and editing.
Andrés Mauricio Ayón Genkuong: Conceptualization, data curation, formal analysis, funding acquisition, research.
All the authors read and approved the final version of the manuscript.

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Availability of data and materials

The datasets used and analyzed during the present study are available from the corresponding author upon reasonable request.

Introduction

Autism spectrum disorders (ASDs) are a group of neurodevelopmental disorders characterized by social and language difficulties and stereotyped behavioral patterns. The etiology of ASD has both genetic and environmental origins, with family factors being prominent in the latter. , maternal, prenatal, perinatal, and neonatal [1, 2].

In 2020, the World Health Organization estimated that 0.625% of children globally are diagnosed with one of the ASDs [3]. In 2023, the Centers for Disease Control and Prevention (CDC) of the United States estimated that approximately 1.5% of 8-year-old children were diagnosed with ASD based on bibliographic reviews by health experts [4]. In our country, the prevalence of ASD, according to a report by the Ministry of Public Health (MSP) for 2016, was 1,258 people [5].

Given the increase in prevalence and the multifactorial complexity linked to the etiology of this group of disorders, this research is necessary to provide updated information on the subject. Understanding the risk factors associated with ASD will contribute to the development of preventive approaches and early detection of these disorders.

The objective of this study was to evaluate the risk factors associated with autism spectrum disorder (ASD) in patients at Francisco Icaza Bustamante Hospital from 2019–2022.

Materials and methods

Study design

This cross-sectional observational study is descriptive. The source is retrospective.

Scenery

The study was conducted at Francisco Icaza Bustamante Hospital of the Ministry of Public Health of Ecuador in Guayaquil, Ecuador. It lasted from January 1, 2019, to December 31, 2022.

Participants

Records of patients with autism spectrum disorders were included. No patients were excluded or removed from the analysis.

Variables

The variables were age, autism spectrum diagnosis, concomitant disabilities, age of the mothers, prenatal factors, morbidities during pregnancy, use of drugs during pregnancy, and perinatal factors.

Data sources/measurements

The source was indirect; an electronic form was filled out from the data in the medical records. Records with the following ICD-10 codes were included:
F84.0 Childhood autism, F84.1 Atypical autism, F84.5 Asperger syndrome, F84.2 Rett syndrome, F84.3 Other childhood disintegrative disorders, F84.4 Hyperactivity disorders associated with mental retardation and stereotyped movements, F84.8 Other pervasive developmental disorders, F84.9 Pervasive developmental disorders not otherwise specified.

Biases

The application of the participant selection criteria avoided observation and selection bias. To prevent possible interviewer, information, and memory biases, the principal investigator kept the data at all times via a guide and records approved in the research protocol. Two researchers independently analyzed each record in duplicate, and the variables were recorded in the database once their concordance was verified.

Study size

The sample was probabilistic. According to INEC data, there are 4.392 million inhabitants in Guayas, with 4.33% of the population under 5 years of age, corresponding to 190,173 children in the Universe. The prevalence rate of autism spectrum disorders is 3.3%, the confidence limit is 5%, and the confidence interval is 99%. The sample size was 85 patients. The EPI info TM program (Version 7.2.5, CDC, Atlanta, USA, September 2022) was used for the sample calculation.

Quantitative variables

Descriptive statistics were used. The results are expressed as frequencies and percentages. The categorical variables were not converted into quantitative variables.

Statistical analysis

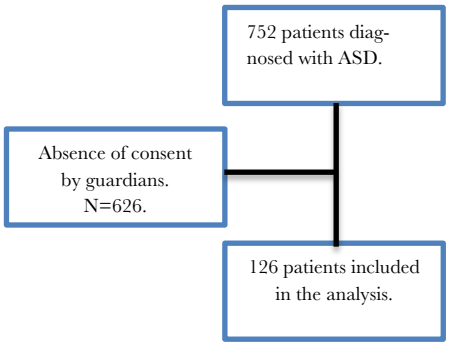
Qualitative variables are presented as frequencies and percentages. A 95% confidence interval is presented for a proportion of relevant prevalences. The statistical package used was IBM SPSS Statistics for Windows, Version 25.0, released in 2017. Armonk, NY: IBM Corp.

Results

Participants

A total of 126 records of patients with autism spectrum disorders were included (Figure 1).

Figure 1. Study participants.



Main characteristics of the study group

The sample consisted of 126 patients, 77.0% (n=97) of whom were men and 23.0% (n=29) of whom were women. The mean age of the sample was 9.26 years, while the mean age at diagnosis was 2.38 years. A total of 67.46% (n=85) of the patients were diagnosed before age three (Table 1).

According to the ICD-10, 54.0% (n=68) of the patients were classified as having childhood autism (F840), 27.0% (n=34) as having "pervasive developmental disorder not otherwise specified" (F849), and 10.3% (n=13) as having Asperger syndrome (F845). There were no cases of hyperactive disorders associated with mental retardation or stereotyped movements (Table 1).

Regarding concomitant disabilities, the majority were language, multiple, and intellectual disabilities. A total of 19.0% (n=24) had no concurrent disability (Table 1). Concerning family history, 71.4% (n=90) of the sample reported not having any ASD, whereas 28.6% (n=36) reported having at least one family member with ASD. The mean age of the mothers at the time of birth was 28.6 ±10.5 years, whereas that of the fathers was 32.2 ±11.5 years. In both groups, the predominant educational level was high school, with 59.52% (n=75) of the mothers and 50% (n=63) of the fathers.

Prenatal factors

For prenatal factors, 90.5% (n=114) of the sample had at least five prenatal check-ups, whereas 9.5% (n=12) did not. Concerning birth order, 48.9% (n=61) of the sample were firstborn. Among the remaining participants, 18.3% (n=23) had a long interbirth interval (equal to or greater than 60 months), whereas 15.9% (n=20) experienced a short interval (less than 18 months).

Concerning morbidities during pregnancy, 63.4% (n=80) reported no history of complications, 16.7% had a history of hypertension, and 14.35% had experienced infections (Table 1).

Regarding the use of drugs during pregnancy, 76.9% (n=97) denied usage, whereas 11.1% (n=14) reported using antibiotics, 5 cases (4%) involved using analgesics, and 4% (n=5) reported using psychoactive drugs.

Table 1. Demographic and clinical characteristics of the study group.

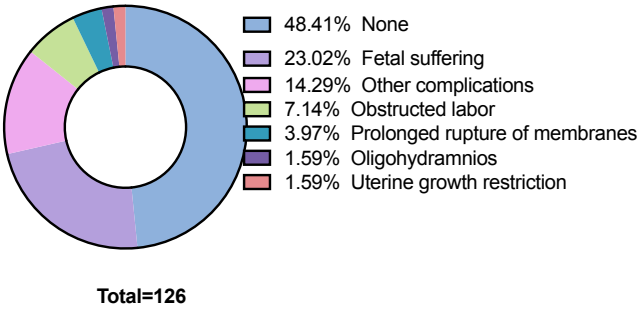
	N=126	Standard deviation/Percentage
Age		
Age (Years)	9.3	±4.1
Age at diagnosis (years)	2.4	±2.4
Autism spectrum disorders		
Autism in childhood	68	54.0%
Pervasive developmental disorder not otherwise specified	34	27.0%
Asperger Syndrome	13	10.3%
Atypical autism	6	4.8%
Other pervasive developmental disorders	3	2.4%
Rett Syndrome	2	1.6%
Concomitant disability		
Language	39	31.0%
Multiple disabilities	30	23.8%
Intellectual	24	19.0%
Does not possess	24	19.0%
Physics	5	4.0%
Auditory	3	2.4%
Visual	1	0.8%
Maternal morbidity during pregnancy		
None	80	63.4%
Hypertensive disorders	21	16.7%
Infections	18	14.3%
Thyroid disorders	5	4.0%
Hemorrhages	1	0.8%
Other disorders	1	0.8%
Diabetes mellitus	0	0%

Prenatal and neonatal factors

The most frequent type of delivery in the sample used was cesarean section, represented by 70.6% (n=89), whereas 29.4% (n=37) corresponded to vaginal delivery. With respect to obstetric complications, 48.2% (n=61) denied having any complications, with fetal distress being the most common, with 23.0% (n=29) (Figure 2). Concerning birth weight, 19.0% (n=24) were underweight, whereas 80.2% (n=101) were not underweight. Finally, regarding the type of breastfeeding, 40.5% (n=51) had mixed breastfeeding, 36.5%

(n=46) had exclusive breastfeeding, and only 23.0% (n=29) had exclusive formula feeding.

Figure 2. Obstetric complications in patients with autism.



Relational statistics

For the relationship between sex and ASD classification, a statistically significant association between Asperger syndrome and male sex was determined via Pearson chi-square tests (P = 0.007), likelihood ratios (P = 0.002), and Fisher's exact tests (P = 0.038) (Table 2). In contrast, a value close to significant was found for Rett syndrome and the female sex through the Fisher exact test (P = 0.052), which could be substantial with the increase in cases. Other classifications, such as "Autism in childhood" (P = 1.0), "Atypical autism" (P = 0.335), "Other pervasive developmental disorders" (P = 0.132), and "Pervasive developmental disorder, not otherwise specified" (P = 0.635), did not present significant associations with the sex of the child.

A significant association was found between a history of ASD and the age of diagnosis via the Pearson chi-square test (P = 0.001). No significant association was found (P = 0.471) between ASD classification and concomitant disability according to the chi-square test (Table 3). Finally, the chi-square test (P = 0.718) revealed no significant association between maternal education level and the type of breastfeeding (Table 4).

Table 2. Characteristics of autism types by sex.

	Female n=29	Male n=97	*P*
Autism in childhood	16 (55.2%)	52 (53.6%)	0.882
Pervasive developmental disorder not otherwise specified	9 (31.0%)	25 (25.8%)	0.575
Asperger Syndrome	0 (0%)	13 (13.4%)	0.038
Atypical autism	0 (0%)	6 (6.1%)	0.170
Rett Syndrome	2 (6.9%)	0 (0%)	0.0516
Other pervasive developmental disorders	2 (6.9%)	1 (1.0%)	0.69

Discussion

The clear predominance of the male sex (77%) in this work's sample agrees with previous descriptions, in which the prevalence of the male sex is approximately four times greater than that of the female sex [6]. To explain this phenomenon, genetic factors linked to the X chromosome, genetic imprinting, or levels of steroidal sex hormones have been proposed [7].

The mean age of diagnosis of the sample was 2.38 years, according to the Clinical Practice Guidelines of the Ministry of Public Health of Ecuador, which establishes a range of 12 months to 3 years of age for diagnosis [5]. Comparatively, the Centers for Disease Control and Prevention (CDC) reported a mean age of early diagnosis of ASD of 51 months in the USA (4). This suggests an efficient early detection system based on the results obtained from the sample. Additionally, a significant association was found between a history of autism spectrum disorders and the age of diagnosis, suggesting that family history may increase surveillance and early recognition of ASD.

With respect to the classification of ASD, childhood autism was the most frequently observed diagnosis in the present study, representing 54.0% (n=68) of the sample; these results are consistent with those of previously published studies [8].

Regarding the relationship between sex and ASD classification, a significant association has been described between Asperger syndrome and the male sex and between Rett syndrome and the female sex, findings that were replicated in the present study [9]. The greater prevalence of female sex in Rett syndrome patients could be associated with a mutation in the MECP2 gene of the X chromosome. Two copies of the X chromosome can compensate for the defect [9].

Table 3. Characteristics of autism type due to disability.

	Without disability n=24	Auditory n=3	Physics n=7	Intellectual n=24	Language n=39	Visual n=1	Multiple disabilities n=30	*P*
Autism in childhood	12 (50.0%)	2 (66.6%)	2 (28.57%)	14 (58.33%)	22 (56.41%)	1 (100%)	16 (53.3%)	0.471*
Atypical autism	0 (0%)	0 (0%)	0 (0%)	1 (4.17%)	2 (5.13%)	0 (0%)	3 (10%)	
Rett Syndrome	0 (0%)	0 (0%)	1 (14.29%)	1 (4.17%)	0 (0%)	0 (0%)	0 (0%)	
Asperger Syndrome	6 (25.0%)	1 (33.3%)	1 (14.29%)	2 (8.33%)	1 (2.56%)	0 (0%)	2 (6.7%)	
Other pervasive developmental disorders	1 (4.1%)	0 (0%)	2 (28.57%)	1 (4.17%)	0 (0%)	0 (0%)	1 (3.3%)	
Pervasive developmental disorder not otherwise specified	5 (20.8%	0 (0%)	1 (14.29%)	5 (20.83%)	14 (35.90%)	00 (0%)	8 (26.7%)	

Table 4. Characteristics of children with autism classified by mother's education and type of breastfeeding.

	Exclusive breastfeeding n=46	Exclusive formula feeding n=29	Mixed breastfeeding n=51	*P*
Basic education for young people and adults n=1	0 (0%)	0 (0%)	1 (2.0%)	0.477
Initial n=2	1 (2.2%)	0 (0%)	1 (2.0%)	0.735
Basic education (high school) n=2	1 (2.2%)	0 (0%)	1 (2.0%)	0.735
Basic education (elementary and secondary) n=15	7 (15.2%)	1 (3.4%)	7 (13.7%)	0.260
Higher basic education n=5	2 (4.4%)	1 (3.4%)	2 (4.0%)	0.981
High school n=75	26 (56.5%)	23 (79.3%)	26 (51.0%)	0.040
Senior technician n=9	2 (4.4%)	2 (6.8%)	5 (9.8%)	0.580
Third grade level n=14	6 (13.0%)	1 (3.4%)	7 (13.7%)	0.324
Fourth level of postgraduate studies n=3	1 (2.2%)	1 (3.4%)	1 (2.0%)	0.91

One of the most frequently described concomitant disabilities is intellectual disability. However, the studies published thus far have reported highly variable prevalence rates of intellectual disability in autism spectrum disorders, ranging from 16.7% to 84% [10, 11]. In the present study, a prevalence of 19.0% was obtained, ranking second after language disabilities (31.0%), within the described range.

This study revealed that 71.4% of the sample reported no family history of ASD. Although patients with ASD have a strong genetic component, the underlying genetic cause is unknown in at least 70% of cases. This may be associated with de novo mutations, environmental factors, or underreported family history [12].

Advanced parental age has been identified as an essential risk factor for the development of ASD, linking it to de novo mutations, impairments in epigenetic regulatory mechanisms, and obstetric complications [13]. However, in the present study, the mean age of the mothers at the time of birth was 28.6 years, whereas that of the fathers was 32.2 years. These results could be explained by a possible selection bias, given that the sample is not sufficiently representative of the general population, as it only includes patients treated by the Ministry of Public Health who share the same socioeconomic level, which can be seen in the predominant educational level, high school. Research has shown that attaining better socioeconomic status is one of the main reasons for delays in procreation [14]. This situation needs to be reflected in the sample used.

Pregnancy morbidities have been associated with a greater risk of developing ASD [15]. However, in the present study, 63.4% did not suffer from any of these factors, which could be associated with underreporting during data collection. Despite this, the most frequently observed complication, hypertensive disorders (16.7%), coincides with that described [16].

This finding highlights the high prevalence of cesarean births (70.6%) compared with that of vaginal births (29.4%). However, cesarean section corresponds to a risk factor for ASD that is currently highly debated since not all studies agree on its significance [15].

The preponderance of mixed feeding (40.5%) over exclusive breastfeeding (36.5%) in the present study could be influenced by several factors, such as hypokalemia, mastitis, maternal fatigue, and insufficient weight gain in the infant [16].

Conclusions

A significant association was found between Asperger syndrome and male sex. Male sex was predominant in the sample of patients with ASD.

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Statements

Ethics committee approval and consent to participate

The bioethics committee of the Faculty of Medical Sciences of the University of Santiago de Guayaquil approved the study.

Consent to publish

This information was unnecessary because the present study did not publish images, radiographs, or specific patient studies.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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