



Autism: Clinical impacts and late diagnosis in women - Literature review

Autismo: Impactos clínicos e diagnóstico tardio em mulheres - Revisão bibliográfica

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ABSTRACT

Autism Spectrum Disorder (ASD) is a common neurodevelopmental disorder marked by deficits in communication and social interaction and by restricted, repetitive patterns of behavior. With the expansion of information about autism and the improvement of diagnostic methods, the prevalence of the disorder has increased considerably in recent decades. However, because autism has multiple facets and different presentations, the diagnosis is still a challenge, especially in females, in which there are singularities that further impair suspicions, leading to underdiagnosis. There are multiple questions about the causes and implications of these factors in the diagnosis of autistic girls and women. Thus, the objective of this research is to verify the causal factors and clinical implications associated with the difficulty of diagnosing ASD in females. This is a narrative literature review, in which searches were carried out in established databases. In general, it is noted that the diagnosis of autism in girls and women can be impacted by genetic, developmental, psychological, social and cultural influences, involving factors such as subtlety of symptoms, capacity for social adaptability, lack of studies, failure of methodologies and diagnostic instruments, as well as stereotypes and prejudices. Understanding these elements is essential to broaden the view of girls and women with ASD, highlight their particularities, and ensure that they receive early diagnosis and treatment.

Keywords: Autism Spectrum Disorder, Women, Late diagnosis.

INTRODUCTION

Autism Spectrum Disorder (ASD) is defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) as a neurodevelopmental disorder characterized by persistent deficits in communication and social interaction and restricted and repetitive behavior patterns, and the severity of the condition is based on impairments in social communication and behavior¹.

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The diagnosis of the disorder is clinical, based on the evaluation of health professionals, with the help of instruments and questionnaires provided to parents, guardians and teachers. This analysis includes the presence of social behavior and communication patterns and investigation of the child's developmental history². Intellectual and language impairments, medical or genetic conditions, and accompanying environmental factors are also observed³.

Data from the Centers for Disease Control and Prevention (CDC)⁴ point to an increase in the prevalence of autism in recent years. In 2020, one in 36 children was autistic in the United States, with no preference for ethnicity, race, or socioeconomic class. In 2000, one in every 150 children had ASD in the country, which indicates that the prevalence of the disorder has quadrupled in 20 years. In addition, the CDC also raised another important fact: autism is four times more common in boys than in girls, which points to several doubts and research that tries to explain the factors and causal relationships of this discrepancy².

Even in the face of the increase in the prevalence of the disorder in recent decades, through the wide dissemination of information and improvement of investigative methods, the diagnosis is still a challenge, especially in females. Girls and women with ASD still have little diagnostic visibility because they encounter several singularities due to the spectrum and the involvement of genetic, developmental, psychological, social and cultural factors⁵.

In view of this, it is hypothesized that the disparity in diagnosis between sexes is related to underdiagnosis in the female population, causing many girls to take a long time to receive the correct diagnosis, to be diagnosed in adulthood or even never to reach a diagnosis.

Underdiagnosis or late diagnosis in girls can have serious consequences, as it comes up against the fact that adequate therapies are not instituted early in the lives of these children. Even with a correct diagnosis, it is common for girls to grow up and develop anxiety attacks, depression, panic disorder, social phobias, bipolar affective disorder or even become aggressive in some cases, which can become even more intense if there is no correct diagnosis and treatment⁵.

In view of the searches to carry out this research, there was a lack of studies related to the various facets of autism in females, especially in Brazil. Thus, it is essential to carry out research on this subject, which still has many gaps to be filled by the literature, in order to contribute to an early diagnosis and ensure correct treatment from an early age, avoiding underdiagnosis of girls and women.



This article consists of a narrative literature review, with the objective of verifying the causal factors and clinical implications associated with the difficulty of diagnosing ASD in females.

MATERIALS AND METHODS

This article is a qualitative research of the narrative literature review on the diagnostic difficulties of ASD in females and their clinical implications and associated causal factors.

Literature reviews aim to make direct contact with everything that has been recorded on the subject, not only as a repetition of data, but also through an analysis of the theme under another approach, with the aim of generating new conclusions⁶.

More specifically, narrative review is appropriate when one wishes to obtain a revision in order to develop or evaluate a new theory, based on a set of quantitative studies that used different methodologies or that examined different theoretical conceptualizations⁷.

The research problem was formulated based on the PICO strategy (acromion for Patient, Intervention, Comparison and Outcome), according to Evidence-Based Practice (EBP). The The PICO strategy, according to EBP, should be used to organize clinical problems that arise in care, teaching or research practice⁸. Thus, the question delimited for the present study is: "What are the causal factors involved and the clinical implications covered by the difficulty of diagnosing ASD in females?", where P is females with autism. I: does not apply to search. C: does not apply to search. O: causal factors and clinical implications involved in the difficulty of diagnosing ASD.

After defining the keywords of the study, 13 scientific studies were selected, in Portuguese and English, published in the last five years, between 2019 and 2023, on the Google Scholar, PubMed and Scielo platforms. The selection of the bibliography used was initially made by reading the title, abstract and methodology. After delimitation, a complete reading of the studies selected for the research was performed.

The search terms that gathered elements of the keywords of the research were, in Portuguese: "autism diagnosis", "late autism diagnosis", "autism women", "autism diagnosis women", "late diagnosis autism women" and, in English: "autism diagnosis", "late autism diagnosis", "autism women", "autism diagnosis women", "late diagnosis autism women".

The inclusion criteria were articles, monographs, theses, dissertations, manuals and/or published books, written in English or Portuguese, that dealt with the themes analyzed in this study, preferably in the last five years. The exclusion criteria were articles published before



2019, written in a language other than English or Portuguese, and/or that did not deal with topics associated with the research.

RESULTS AND DISCUSSION

Autism Spectrum Disorder (ASD) is a common neurodevelopmental disorder with hereditary and heterogeneous characteristics, marked by persistent deficits in communication and social interaction and by restricted and repetitive behavior patterns^{1,2}. The severity of the condition is based on impairments in social communication, which impair the individual's daily functioning, and on restricted or repetitive patterns of behavior¹.

The etiology of the disorder is not yet fully elucidated, but studies suggest that it is the result of a combination of genetic, environmental, and neurobiological factors. Its heritability was estimated to be about 80% in a study carried out in Nordic countries, with the involvement of hundreds or thousands of genes and little contribution from maternal factors. In addition, it has been shown that environmental elements influence the onset of ASD in a percentage of approximately 20%⁹.

According to statistics, the number of children with ASD has been increasing with each passing year. According to the Centers for Disease Control and Prevention (CDC), in 2020, one in 36 children was autistic in the United States, with no preference for ethnicity, race, or socioeconomic class, making it one of the most common conditions affecting childhood neurodevelopment. This figure represents a leap when compared to the year 2000, when one in every 150 children had ASD in the country⁴.

In Brazil, although there are no concrete data on the number of autistic people, mainly due to lack of research and underdiagnosis, the WHO estimates that the prevalence of people diagnosed with ASD in the country is 2 million¹⁰. When transposing the CDC survey, conducted in 2020 in the USA, to Brazil, there would be about 5.6 million autistic people living in the country⁴.

According to authors, the increase in the prevalence of autism in recent years may be related to some factors, such as: expansion of diagnostic criteria, expansion of knowledge and studies in relation to the disorder, reporting practices, and diagnostic replacement when necessary¹².

According to the Brazilian Society of Pediatrics (2019), ASD usually originates in the first years of life, however, this does not occur uniformly. In most cases, symptoms are not evident until after 12 to 24 months of the child. On the other hand, some may present traits after



birth¹³. Other children may develop well for a period of time but lose skills they have already gained, causing delays to be evident later in life.

According to the diagnostic criteria for ASD according to the APA (2023)¹, deficits must be present early, from the developmental period, and, in addition, cause significant impairments in social functioning. Nor can all these disorders be explained by intellectual disability or global developmental delay.

The diagnosis of the disorder is clinical, based on the evaluation of health professionals, with the help of instituted instruments and questionnaires provided to parents, guardians and teachers. The analysis should be based on the presence of social behavior and communication patterns, combined with the history of development². Intellectual and language disabilities, medical or genetic conditions, and accompanying environmental factors are also observed¹².

It is evident that most parents seek professional help before their children are two years old, but it takes about two to three years to have a closed diagnosis, and about five to six professionals during this period¹⁴.

The CDC also found another important piece of data on the prevalence of autism in the U.S.: autism is four times more common in boys than in girls⁴. A study conducted in southern Brazil in 2019 pointed out that, for the most part, the prevalence of ASD in girls is 0.3%, while in boys it is 1.1%, meeting well-founded diagnostic criteria^{15,16}.

In a systematic review that included 20 studies related to autism in women¹⁶, of the 3,394 people included in the study, 79.91% were male, compared to only 20.09% female. In 50% of the cases, there was an indication of underdiagnosis or underreporting of females and, in 40%, notes on late diagnosis.

In view of these findings, researchers seek to clarify the causes and impact of this discrepancy in the prevalence of ASD between both sexes. There are hypotheses that ASD has genes linked to the X chromosome, making males more vulnerable to the disorder, but there is no scientific proof for this information. There are studies that suggest that there are protective genetic factors for ASD in females, so that girls need a greater genetic load to manifest symptoms².

There are also important notes on the subtlety of symptoms and adaptability in girls; the existence of few studies in relation to ASD in this gender, the lack of methodologies and diagnostic instruments applied to girls, and the stereotypy of seeing ASD as a typically male disorder. Therefore, the diagnosis of autism in girls and women can be impacted by genetic, developmental, psychological, social, and cultural influences.



Authors of a study¹⁶ point out that autism in girls is actually performed late or never defined because of the subtlety of the symptoms and camouflage techniques. The research also suggests that there is a difference between the symptoms presented between the sexes. In 45% of the studies, there is evidence that, in boys, repetitive behaviors and stereotypies are more frequent, making the diagnoses clearer. On the other hand, in girls, the symptoms tend to be more subtle and accompanied by greater socio-communicative difficulty, which can lead to underdiagnosis, late diagnosis, or even an alternative diagnosis.

A study carried out in 2021¹⁷ pointed out that men are more prone to aggression and hyperactivity and/or attention deficits, while women, to exhibit staring, have worse recognition of emotions, greater difficulty in communication and lower level of verbal ability. However, girls tend to have less impaired behavior in play, with imaginative abilities superior to boys and observation and imitation of typical peers¹⁸.

Researchers also point out differences in interests between individuals with ASD in both sexes². Boys with ASD tend to be hyper-focused on maps, phone books, blueprints; while girls, in animals, objects, dolls and musical artists, which can make it difficult to suspect the disorder in females.

It is noteworthy that what is understood as "feminine" is defined by a set of behaviors and stereotypes that have been constructed and culturally accepted for centuries and passed on to new generations, although many standards are currently being highly challenged. Girls, for example, are expected to play with dolls, to be loving, understanding, emotional and dependent; differently from boys, in whom the still mostly patriarchal and conservative society expects independence, domination, power and assertiveness¹⁹.

In this way, characteristics that could raise the suspicion of autism, such as isolation, introspection, communication difficulties and sociability can be confused with shyness and empathy. This occurs when these characteristics are mainly found in females, since culturally this is what is expected of girls most of the time, to the detriment of boys¹⁹. Thus, the suspicion of ASD could be more easily raised in boys than in girls.

It was noted that girls, in addition to presenting more subtle symptoms, have a greater ability to use camouflage techniques to mask social difficulties and to adjust their behaviors to adapt to the people around them, which is known as *masking*^{5,17}. Thus, women tend to develop strategies to fit into social groups, which may be related to theories about the presence of a unique phenotype in girls with ASD⁵.



Camouflage can be divided into two types: 1) Active – in which the child with ASD uses strategies to disguise social difficulties, managing to maintain friendships and leading an apparently "typical" life; 2) Passive – in which the child imitates the behaviors of typical peers². The literature indicates that *masking* practiced by autistic girls and women can cause long-term mental health problems, such as depression, anxiety and emotional exhaustion, due to the effort put into strategies to appear neurotypical¹⁹.

Authors also point out another problem: the diagnostic criteria for ASD currently available were established based on male stereotypes and do not take into account the individualities in the behavior of women with autism¹⁸. In addition, these methodologies were developed according to research conducted with predominantly male samples, which hinders an efficient screening in relation to the female gender.

The diagnosis of ASD is influenced by several factors, such as symptoms presented by the child; parents' perception of their children's difficulties; understanding of these complaints by health professionals; perception of problems and guidance from education professionals. Thus, the authors suggest that family and sociocultural factors may be determinant for the diagnosis of ASD in girls².

Authors¹⁸ point out that the difficulty in diagnosing ASD, especially in women, is related to a range of factors: lack of a biomarker that confirms the diagnosis; The number of women diagnosed is still small, which makes it difficult to compare the two sexes; The criteria and diagnostic tools available were created based on the male symptom picture, not taking into account the specificities of the disorder in women; the existence of several diagnostic methodologies, which makes it difficult to compare results between studies; Interviews are predominantly conducted with parents, which carries a recall bias; ASD is accompanied by multiple comorbidities, and there may be overlapping symptoms of autism, attention deficit hyperactivity disorder (ADHD), and bipolar affective disorder (BAD).

It is suggested that the fact that autistic girls have more subtle symptoms most of the time impairs the suspicion of ASD on the part of parents or guardians and even non-specialized professionals, reducing the likelihood of referral for evaluation. In addition, it is assumed that the diagnostic criteria that currently exist may not be sensitive enough to identify the needs of both sexes¹⁷.

Social problems tend to be perceived initially in the school environment, in socialization with peers. Thus, teachers play an important role in suspecting and referring children to health



professionals. However, in the case of girls, as already highlighted, the presence of more subtle symptoms can impair this perception on the part of education professionals².

In addition, there is bias on the part of health professionals themselves, who usually dismiss the diagnosis of ASD in girls initially, even in the face of complaints and suspicions from parents, especially when other conditions are present or there are hypotheses of differential diagnoses¹⁷. Studies indicate that there is a greater chance of diagnosis when the suspicion is in a male patient, with the presence of some associated intellectual deficit and/or some degree of regression of neurological development². This data means that when girls and women do not have symptoms and gaping delays, they have a lower chance of diagnosis.

Underdiagnosis or late diagnosis in girls can have serious consequences, as it comes up against the fact that adequate therapies are not instituted early in the lives of these children. Even with a correct diagnosis, it is common for girls to grow up and develop anxiety crises, depression, panic disorder, social phobias, bipolar affective disorder or even become aggressive in some cases, which is even worse in the face of an underdiagnosis⁵.

In view of the above, in order to expand the capacity for early diagnosis in girls and women, it is important to increase public awareness about the particularities of autism in the female population, with a greater representation of female autism in the media, for example.

Also noteworthy is the relevance of training health professionals and educators, who are essential parts of this diagnostic process, which address the singularities of the female phenotype of autism, which are presented through behaviors that are often made up, as well as the chances of overlapping ASD with other psychiatric or developmental disorders, which can end up creating diagnostic doubts and confusion.

In the same sense, the instruments and questionnaires that help in the diagnosis of ASD should be reviewed and updated, incorporating data from research on autism in women, making the investigation methods less partial.

FINAL THOUGHTS

ASD has multiple facets and spectrums, which makes the diagnosis naturally complex due to the variety of presentations in each patient. However, this becomes even more visible in females. Thus, it was noted that the diagnosis, both in girls and women, can be delayed by a range of factors, whether genetic, social, cultural or psychological, including the presence of more subtle behaviors, masking techniques, lack of studies directed to the female sex, failure of investigation instruments, stereotypes and culturally instituted patterns of behavior.



Understanding these elements is essential to broaden the view of girls with ASD, highlight their particularities and ensure that they receive early diagnosis and treatment. Thus, it is essential to raise public awareness about these aspects, to review diagnostic methods, with a focus on female singularities; the promotion of training of health professionals and educators and the realization of more studies on the subject.



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