

Relationship between epileptic seizures and Autism Spectrum Disorder in preschool aged children: an integrative review

Relação entre convulsões epiléticas e Transtorno do Espectro Autista em crianças pré-escolares: revisão integrativa

Relación entre convulsiones epiléticas y trastorno del espectro autista en niños en edad preescolar: revisión integrativa

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Abstract:

Objective: to investigate the clinical relationship between Autism Spectrum Disorder and epileptic seizures in preschool aged children. **Methods:** an integrative review was conducted in October 2025, using the Health Sciences Descriptors “Autism Spectrum Disorder”, “Seizures”, “Child”, and “Preschool”, through the PubMed database. **Results:** the initial search identified 114 articles. Of these, 19 were selected for full-text reading, resulting in 12 studies for analysis, four from 2024 and four from 2025. **Conclusion:** the coexistence of ASD and epilepsy in preschool aged children presents challenges in diagnosis and therapy that require an integrated and personalized clinical approach. Although genetic and neurobiological factors provide clues about the intersection of these conditions, the ideal management of these children requires a multidisciplinary approach that combines medical, psychological, and social care. The implications of this clinical relationship are broad and complex, highlighting the importance of early diagnosis, appropriate interventions, and continuous support to improve the quality of life for affected children and their families.

Keywords: Autism Spectrum Disorder; Seizures; Child; Child, Preschool; Epilepsy.

Resumo:

Objetivo: investigar a relação clínica entre o Transtorno do Espectro Autista e as crises epiléticas em crianças em idade pré-escolar. **Método:** revisão Integrativa realizada em outubro de 2025, utilizando os Descritores em Ciências da saúde Transtorno do Espectro Autista, Convulsões, Criança e Pré-Escolar, por meio do portal PubMed. **Resultados:** a busca resultou em 114 artigos inicialmente. Destes, 19 foram selecionados para leitura na íntegra que resultou em 12 estudos para a análise, sendo quatro produções em 2024 e quatro em 2025. **Conclusão:** a coexistência de TEA e epilepsia em crianças em idade pré-escolar apresenta desafios nos diagnósticos e terapêuticos que exigem uma abordagem clínica integrada e personalizada. Embora os fatores genéticos e neurobiológicos forneçam pistas sobre a interseção dessas condições, o manejo ideal dessas crianças requer uma abordagem multidisciplinar que combine cuidados médicos, psicológicos e sociais. As implicações dessa relação clínica são vastas e complexas, sublinhando a importância de diagnósticos precoces, intervenções adequadas e um suporte contínuo para melhorar a qualidade de vida das crianças afetadas e suas famílias.

Palavras-Chave: Transtorno do Espectro Autista; Convulsões; Criança; Pré-escolar; Epilepsia.

Resumen:

Objetivo: investigar la relación clínica entre el Trastorno del Espectro Autista y las crisis epiléticas en niños en edad preescolar. **Método:** revisión integradora realizada en octubre de 2025, utilizando los Descriptores en Ciencias de la Salud Trastorno del Espectro Autista, Convulsiones, Niño y Preescolar, a través del portal PubMed. **Resultados:** la búsqueda resultó en 114 artículos inicialmente. De estos, 19 fueron seleccionados para lectura a texto completo, lo que resultó en 12 estudios para el análisis, siendo cuatro producciones en 2024 y cuatro en 2025. **Conclusión:** la coexistencia de TEA y epilepsia en niños en edad preescolar presenta desafíos en el diagnóstico y en las terapéuticas que exigen un enfoque clínico integrado y personalizado. Aunque los factores genéticos y neurobiológicos proporcionan indicios sobre la intersección de estas condiciones, el manejo ideal de estos niños requiere un enfoque multidisciplinar que combine cuidados médicos, psicológicos y sociales. Las implicaciones de esta relación clínica son amplias y complejas, subrayando la importancia de diagnósticos precoces, intervenciones adecuadas y un apoyo continuo para mejorar la calidad de vida de los niños afectados y sus familias.

Palabras clave: Trastorno del Espectro Autista; Convulsiones; Niño; Preescolar; Epilepsia.

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INTRODUCTION

Autism Spectrum Disorder (ASD) and epilepsy are common neuropsychiatric conditions in childhood, and often coexist in a significant proportion of children, particularly in preschool years¹⁻³. It is estimated that the prevalence of epilepsy in children with ASD ranges from 5% to 46%, a significantly higher percentage when compared to the general child population, for which the prevalence of epilepsy is around 1%. This co-occurrence suggests a possible intersection of neurobiological and genetic factors in both conditions⁴.

ASD is classified into three levels⁵, which reflect the severity of symptoms and the level of support required. These levels indicate the degree of impairment in social interaction, communication, and the presence of restricted and repetitive behaviors⁵⁻⁶.

Level 1 corresponds to individuals with mild autism. These individuals experience difficulties in social interactions, but are able to maintain some autonomy, leading relatively independent lives. The most common complications at this level involve subtle impairments, such as communication and less evident repetitive behaviors⁵⁻⁶.

They may struggle to make friends or maintain prolonged conversations, understand social rules and nonverbal communication, and may experience stress or anxiety in social situations⁷.

Level 2 support corresponds to moderate autism, where social difficulties are more visible and restricted and repetitive behaviors have a significant impact on daily life. At this level, complications include difficulty initiating and sustaining social interactions, as well as the presence of repetitive behaviors such as echolalia (repetition of words or phrases), flapping (repetitive hand movements), or obsessive organization of objects⁵⁻⁷.

Resistance to change is a notable characteristic, requiring a rigid routine for the person to cope with daily demands. In addition, there are more noticeable communication impairments, although speech may be present in some cases; at this level, daily challenges are more pronounced than at the previous level⁵⁻⁷.

Level 3 requires very substantial support and includes the most severe cases of autism. At this level, there is great difficulty in social interactions, very limited communication, and repetitive behaviors that significantly interfere with daily life. Severe verbal and nonverbal communication impairments are common, and some individuals may be completely nonverbal. Repetitive behaviors are more intense, and the ability to cope with changes in the environment or routine is extremely compromised⁵⁻⁶. These individuals often require constant supervision and ongoing support to perform daily activities.

In addition to these specific levels, ASD can be accompanied by a number of other complications. Problems such as insomnia, gastrointestinal disorders⁸, and emotional disorders such as anxiety and depression are common, often related to difficulties in social interaction and coping with change. Sensory disorders are also common, with many individuals exhibiting hypersensitivity or hyposensitivity to stimuli such as sounds, lights, or textures⁹⁻¹¹.

Cognitive deficits, which may be associated with intellectual disability, can range from mild to severe. Epilepsy is also a condition frequently associated with ASD, with a higher prevalence of epileptic seizures compared to the general population⁸.

A significant proportion of children with ASD also struggle with epilepsy. The characteristics observed in the Electroencephalogram (EEG) of these children frequently show anomalous patterns, suggesting altered brain activity that may predispose individuals to epileptic seizures¹. This co-occurrence is frequently observed in clinical practice, suggesting an intersection of neurobiological factors that should be better understood to improve diagnosis and management.

The identification of specific patterns in EEG exams, as well as specific genetic mutations, can clarify the existing relationship between these two neuropsychiatric conditions.

On the other hand, understanding the clinical relationship between ASD and epilepsy is important for therapeutic management, early diagnosis, and interventions that improve the quality of life of affected children. Thus, this study aims to investigate the clinical relationship between Autism Spectrum Disorder (ASD) and epileptic seizures in preschool children (0-5 years).

METHODS

This is an integrative review following the guidelines of the Joanna Briggs Institute (JBI) Manual for Evidence Synthesis¹², and the guidelines of the international guide Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR)¹³ to ensure the transparency, quality, and reproducibility of the study. This review was registered on the Open Science Framework (OSF) platform under the number <https://doi.org/10.17605/OSF.IO/BKU6C>¹⁴.

The study was conducted in five stages: identification of the study question, database search, evaluation of the studies found, analysis of the results, and presentation of the data.

To guide the research question, the mnemonic strategy Population, Concept, and Context (PCC) was used (Chart 1); Therefore, the following question was formulated: "*What is the*

clinical relationship between Autism Spectrum Disorder (ASD) and epilepsy in preschool children aged 0 to 5 years?".

Chart 1. Strategy Population, Concept, and Context, Taubaté/SP, Brazil 2025.

Mnemonic	Meaning	Description
P	Population	Children between 0 and 5 years of age
C	Concept	Autism Spectrum Disorder
C	Context	Epilepsy

The articles included were studies with primary quantitative, qualitative, and mixed-method approached that discussed the clinical relationship between ASD and epilepsy in children under six years of age, available in full and free of charge, in Portuguese, English, and Spanish, published between 2014 and 2025. Studies that did not address the topic, as well as editorials, theses, dissertations, review studies, case studies, and experience reports were excluded.

The search and selection of articles was carried out in three databases – Medical Literature Analysis and Retrieval System Online (MEDLINE) – through the PubMed portal, Latin American and Caribbean Literature in Health Sciences (LILACS), and Scientific Electronic Library Online (SciELO) in October 2025, using the Health Sciences Descriptors (DeCS) and Medical Subject Headings (MeSH) as a search strategy to ensure the comprehensiveness and accuracy of the search. The descriptors used were “*Transtorno do Espectro Autista*”, “*Convulsões*”, “*Criança*” and “*Pré-Escolar*”, “Autism Spectrum Disorder”, “Seizures”, “Child”, and “Preschool”, applying the Boolean operator AND in both languages.

In the article selection process, the Rayyan^{®15} software was used. After the search, the files were exported to this platform, and subsequently, the selection was carried out. The title and abstract were read, and then, those considered relevant were selected for full-text reading, carried out independently by two researchers. Discrepancies in this process were analyzed by a third researcher.

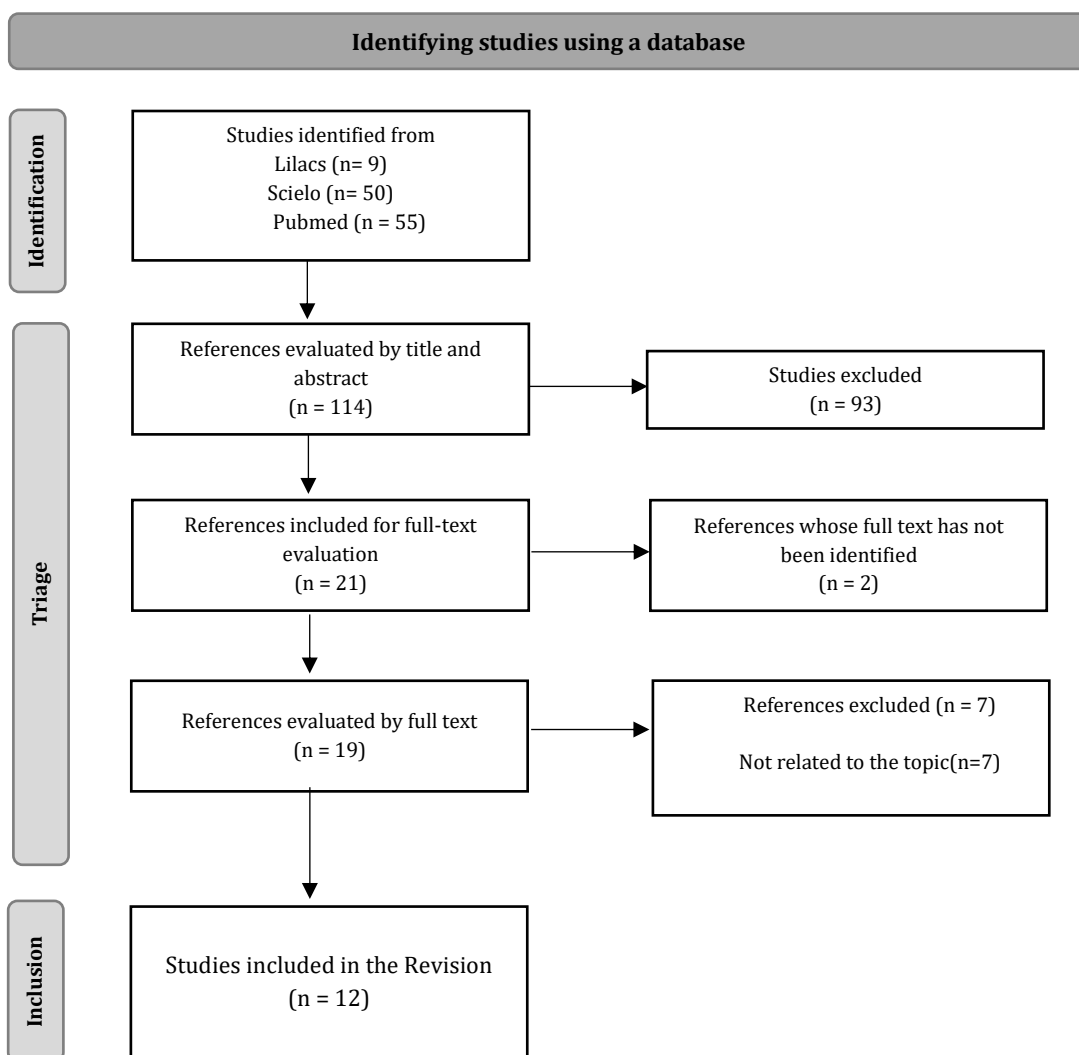
The article data were extracted using a spreadsheet created in Google[®] Sheets by the researchers, identifying year, author, title, journal name, objective, methods, result, and conclusion. The data underwent narrative analysis and were described based on the collected material and related studies.

The data collection, article selection, and screening process is demonstrated using the PRISMA 2020 flowchart, and the articles included in this research are organized using a table identifying year, author, title, journal, objective, methods, result, and conclusion.

RESULTS

The database search resulted in 114 articles (LILACS = 9; SciELO: 50; PubMed = 55); no duplicate articles were identified. Of these, 19 were selected for full-text reading, resulting in 12 studies for analysis (Figure 1).

Figure 1. Selected studies on the relationship between epileptic seizures and ASD in preschool aged children. Taubaté, SP, Brazil, 2025.



After reading, analysis, and selection of the studies, they were identified with author/year of publication, title, objective, methods, and results. The years 2023 and 2024 had four articles each; the others were published from 2021 onwards (Table 2).

Table 2. Selected articles on the Relationship between Epileptic Seizures and Autism Spectrum Disorder in Preschool aged children. Taubaté, SP, Brazil, 2025.

Author/Year	Title	Objective	Methods	Results
Santore ME <i>et al.</i> , 2023 ¹	EEG Features in Autism Spectrum Disorder: A Retrospective Analysis in a Cohort of Preschool Children	Classify and quantify EEG abnormalities recorded in a cohort of preschool children with ASD	Retrospective quantitative	High rate of EEG abnormalities in preschool aged children diagnosed with ASD. These changes relate both to the characteristics of background activity and, mainly, to the presence of PS-IEDs. These EEG abnormalities appear to be much more noticeable during sleep than when awake
Shanmuganathan H <i>et al.</i> , 2022 ³	Assessment of behavioural problems in preschool and school going children with epilepsy	Identify and assess behavioral problems in children with epilepsy	Prospective cross-sectional study	Of the 50 individuals, 72% were between 6 and 18 years old; 60% of the children had generalized seizures, 58% had epilepsy for less than 2 years, 80% had abnormal EEG; 6% of the children had behavioral problems and 4% had borderline conditions. The correlation of behavioral problems with age was statistically significant, with a p-value of 0.027. The behavioral problems identified were aggression and anxiety
Bennett S <i>et al.</i> , 2024 ⁷	Clinical effectiveness of the psychological therapy Mental Health Intervention for Children with Epilepsy in addition to usual care compared with assessment-enhanced usual care alone: a multicentre, randomised controlled clinical trial in the UK	Evaluate the clinical effectiveness of integrated mental health treatment for children and young people with epilepsy	Randomized clinical trial	MICE demonstrated significant positive results for young people with epilepsy and their caregivers, which were maintained 12 months after randomization, showing the benefits of integrated physical and mental health care
Dhawan A <i>et al.</i> , 2023 ⁸	Exploring the neurological features of individuals with germline PTEN variants: A multicenter study	Report the early life neurological characteristics, complications, and treatment of individuals with a molecular diagnosis of PHTS	Prospective and longitudinal study	ASD and epilepsy were frequent among patients with PHTS (51% and 15%, respectively), with generalized epilepsy strongly associated with ASD. Patients with epilepsy frequently required two anticonvulsant medications. Neuroimaging revealed prominent perivascular spaces and decreased peritrigonal myelination in individuals with PHTS-ASD
Giorgi S <i>et al.</i> , 2024 ¹⁰	A tool for Dravet syndrome associated neuropsychiatric comorbidities evaluation (DANCE)	Early, consistent, and systematic identification of DANC	Pilot study with focus group	Patients with DS presented a wide range of neuropsychiatric symptoms related to DS. The most commonly reported cognitive domains were attention difficulties and problems with multitasking and impulsivity, while the most common psychiatric symptoms were tantrums, mood swings, and autism spectrum disorder
Matos MB. <i>et al.</i> , 2024 ¹⁶	Risk of autism spectrum disorder in children with infantile epileptic spasms syndrome: a retrospective study in a single center in Brazil	Investigate the prevalence of ASD and correlations with clinical characteristics in patients with infantile epileptic spasm syndrome	Retrospective cross-sectional study	Children with infantile epileptic spasm syndrome have a higher risk of being diagnosed with autism spectrum disorder. Later age of onset and period of spasm occurrence may be predisposing risk factors

Author/Year	Title	Objective	Methods	Results
Reilly C <i>et al.</i> , 2023 ¹⁷	Intellectual functioning and adaptive behaviour in children with Dravet syndrome: A population based study	Identified prevalence of intellectual disability in children with Dravet syndrome	Cross-sectional, analytical	This study demonstrates a very high prevalence of intellectual disability in children with Dravet syndrome. In addition, most children with the syndrome have significant difficulties with adaptive behavior, indicating a very significant impact on daily functioning. The association between increased deficits in adaptive behavior with advancing age highlights that the need for support likely increases with age. The association with autism symptoms indicates the need to screen for autism characteristics and implement supports when necessary
Stödberg T <i>et al.</i> , 2022 ¹⁸	Outcome at age 7 of epilepsy presenting in the first 2 years of life. A population-based study	Analyze outcome at 7 years of age and potential prognostic factors in a well-characterized population cohort with onset of epilepsy during the first 2 years of life	Prospective cohort study	Eleven children (9.5%) died before the age of 7. Polytherapy was common. Surgery for epilepsy was performed on two children. At age 7, 61 of 116 children (53%) had been seizure-free for the past 2 years or more. Intellectual disability was diagnosed in 57 of 116 children (49%), autism spectrum disorder in 13 (11%), and cerebral palsy in 28 (24%). West syndrome had a similar seizure remission rate, but a worse cognitive outcome
Kaminski VL <i>et al.</i> , 2023 ¹⁹	Association between NKG2/KLR gene variants and epilepsy in Autism Spectrum Disorder	Evaluate the influence of KLRC2 gene deletion, as well as variants in the KLRK1 gene in children diagnosed with ASD and their respective biological parents	Analytical cross-sectional study	The study demonstrates a relationship between the deletion of the KLRC2 gene and the presence of epilepsy in individuals with ASD. The KLRK1 receptor is an activator of NK cells. The variants rs1049174 and rs2255336 were associated with epilepsy in individuals with ASD. The study provides further evidence that NK cell function may be altered in individuals diagnosed with ASD
Marinõ NA <i>et al.</i> , 2021 ²⁰	Relationship between autism spectrum disorder and epilepsy in a pediatric population in Quito-Ecuador	Establish the prevalence of epilepsy in patients with ASD and identify associations with other factors	Retrospective longitudinal study	81 patients with a diagnosis of ASD were identified, 15% had concomitant epilepsy. The highest prevalence was ASD in grade 3 (58.33%). The first epileptic episode occurred between 5 and 10 years of age in 42%; 25% had concomitant epilepsy. The first epileptic episode occurred between the ages of 5 and 10 (42%); 25% of patients had a previous history of epilepsy; 8% had a previous history of ASD. Most were affected by focal seizures (58%). There was a 100% improvement in autistic behavior in patients who received antiepileptic treatment; 8% presented with difficult-to-control epilepsy
Serra-Pinheiro MA <i>et al.</i> , 2021 ²¹	High prevalence of psychiatric comorbidities in children and adolescents at a tertiary epilepsy center	Investigate the frequency of different psychiatric comorbidities in children with refractory epilepsy	Observational study	The most common comorbidities in our sample were autism spectrum disorders and ADHD; antipsychotics and selective serotonin reuptake inhibitors (SSRIs) were the most commonly prescribed psychiatric medications
Lin J <i>et al.</i> , 2024 ²²	Risk factors and clinical profile of autism spectrum disorder in southern Brazil	Explore maternal risk factors and clinical characteristics of children with ASD	Retrospective cross-sectional study	Of the 321 children with ASD, 86.5% were male, and 49.3% had severe ASD. There was an association between epilepsy and severe ASD. The results demonstrate that our population shares characteristics associated with ASD worldwide, such as gastrointestinal symptoms, epilepsy, and high serotonin levels

DISCUSSION

In the selected studies, the main aspects linking ASD to epilepsy are found in neurophysiological alterations. Studies using EEG have revealed that many children with ASD exhibit abnormal brain activity patterns, even in the absence of epileptic seizures^{1,3}. The presence of epileptiform discharges in EEGs of children with ASD without evident seizures may indicate a latent susceptibility to the development of epilepsy, reinforcing the need for continuous monitoring¹. In addition, the occurrence of epileptic seizures can negatively impact the cognitive and behavioral development of these children, leading to greater difficulties in areas such as emotional regulation and social interaction^{1-3,7,17}.

The use of EEG for early detection of abnormalities in the brain activity of children with ASD supports clinical interventions and treatment, improving prognosis, as these conditions affect child development and there is still no specific treatment for ASD²³.

Genetic and neurobiological factors influence these neuropsychiatric conditions. Of the selected studies, three showed results on genetic issues^{1,8,19}. The first identified a mutation in the CUL3 gene associated with both ASD and epilepsy, suggesting that genetic mutations may be key factors in the overlap of these conditions²⁻⁸. Similarly, the work on germline PTEN variants reinforced the idea that specific genetic variants may predispose children with ASD to develop epileptic seizures⁸.

These findings are supported by another study¹⁹ that analyzed the influence of the KLRC2 gene in children diagnosed with ASD and their parents and showed a relationship between gene deletion and the presence of epilepsy in individuals with ASD, as well as that NK cell function may be altered in individuals with ASD.

Mutations in genes have frequently been associated with the co-occurrence of both conditions. The mutation in the PTEN gene is known to affect the cell signaling pathway, which may be associated with complex neurological disorders, such as ASD and epilepsy, as evidenced in multicenter studies conducted in Brazil. These findings suggest that shared genetic factors may predispose some children with ASD to the development of epilepsy^{2,8,19}.

The prevalence of ASD and its correlation with genotypes and phenotypes have been widely studied and consistently reported, demonstrating not only a relationship with epilepsy but also associations with other conditions²⁴.

Epilepsy has been associated with ASD, intellectual disability, and other symptoms such as anxiety, irritability, and behavioral and adjustment problems, which significantly impact daily life and functioning of children and their families^{3,10,17-18}.

The quality of life of these children can be influenced by their level of language, cognition, adaptation, severity of symptoms, family and community support network, and family and individual stress²⁵. Early support, diagnosis, and treatment tend to improve quality of life for these children, as well as significantly influencing the prognosis of patients with ASD. The earlier the diagnosis and the start of intervention, the better the changes in cognition, social skills, and atypical behaviors, with observable benefits in school settings²⁶.

A multidisciplinary approach to the treatment of these children, therapeutic interventions, combined with psychological care and traditional medical treatments for epilepsy, improve prognosis in children with ASD⁷.

This neurodevelopmental condition has behavioral and cognitive impacts. An investigation that evaluated behavioral problems in children with ASD and epilepsy highlighted that the co-occurrence of these conditions can aggravate cognitive and behavioral deficits. Children who presented both conditions demonstrated greater difficulties in areas such as emotional regulation and social skills¹.

Regarding clinical and therapeutic consequences, children with ASD and epilepsy tend to have poorer responses to conventional epilepsy treatments, such as anticonvulsants, which require a multidisciplinary approach involving neurologists, psychologists, and psychiatrists for adequate management of associated conditions⁵.

In Brazil, where the prevalence of ASD has increased in recent years, the management of these co-occurring conditions poses significant challenges, especially in resource-limited settings. Some research^{18,21-23} emphasizes the importance of public policies that guarantee access to early diagnostic tests, such as EEG, and specific treatments, such as cognitive-behavioral therapy for children with ASD and epilepsy.

Four articles analyzed the prevalence between epilepsy and ASD, and found that children with epileptic seizures are frequently diagnosed with ASD^{16,20-22}. The relationship between ASD and epilepsy in preschool aged children requires an integrated and personalized approach, taking into account neurobiological, genetic, and behavioral factors. Furthermore, early diagnosis, appropriate interventions, and continuous support are fundamental to improving the quality of life of affected children and their families.

CONCLUSION

The coexistence of ASD and epilepsy in preschool children presents challenges in diagnosis and therapy, requiring an integrated and personalized clinical approach. Although genetic and neurobiological factors provide clues about the intersection of these conditions, the

ideal management of these children requires a multidisciplinary approach that combines medical, psychological, and social care.

The implications of this clinical relationship are broad and complex, underscoring the importance of early diagnosis, appropriate interventions, and continuous support to improve the quality of life of affected children and their families, and may contribute to a better understanding of this relationship, encouraging further research.

The limitations of this study include the choice of three databases for searching for articles, which showed few studies on a relevant subject, suggesting that further research is needed to clarify this issue. In turn, it presents the relationship between ASD and epilepsy as an area that requires further investigation to improve management and interventions.

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