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Relationships between Autism Spectrum Disorder, language delay and prematurity: A scoping review

Relações entre o Transtorno do Espectro do Autismo, atraso de linguagem e a prematuridade: revisão de escopo

Relaciones entre el trastorno del espectro autista, retraso del linguaje y la prematuridad: una revisión exploratoria

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Abstract

Introduction: The prevalence of prematurity and Autism Spectrum Disorder (ASD) has increased in recent years. Although the etiology of ASD may be genetic, certain groups of children, such as premature infants, are at higher risk for ASD. **Objective:** To map data reported in the literature on the association between autism spectrum disorder and prematurity. **Objective:** To map data reported in the literature on the association between autism spectrum disorder and prematurity. **Methods:** This is a literature review, in which the guiding question was used as the research strategy, followed by the selection of articles and

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BSAC: data collection, literature review, and manuscript preparation;
AGE: data analysis, literature review, and critical analysis of the text;
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compilation of results. The selection criteria were: studies with samples of children that addressed autism spectrum disorder, language development and prematurity. After reading the titles, descriptors, abstracts and reading the articles in full by independent evaluators, the data recorded for the review were: year and country of publication, type of study, sample, instruments used and main findings. **Results:** The initial search included 144 articles. Of these, 68 were excluded due to duplication, 54 through independent reading of the titles and abstracts and one because it was a case study. Of the remaining 22, after reading in full, 13 were selected because they met the established inclusion and exclusion criteria. **Conclusion:** The analysis of the selected studies allowed us to conclude that there may be an association between autism spectrum disorder and prematurity, however, there was no evidence of which prematurity factor may influence the emergence of signs of autism or the diagnosis of the disorder.

Keywords: Autism Spectrum Disorder; Autistic Disorder; Prematurity; Language Studies; Child Language; Language Development.

Resumo

Introdução: A prevalência de prematuridade e do Transtorno do Espectro do Autismo (TEA) tem aumentado nos últimos anos. Embora a etiologia do TEA possa ser genética, certos grupos de crianças, como bebês prematuros, podem apresentar maior risco de atraso de linguagem e de TEA. **Objetivo:** Mapear dados relatados na literatura acerca da associação entre transtorno do espectro do autismo, atraso de linguagem e prematuridade. **Métodos:** Trata-se de revisão da literatura, na qual se utilizou como estratégia de pesquisa a pergunta norteadora seguida da seleção de artigos e compilação dos resultados. Foram critérios de seleção: estudos com amostras de crianças que abordaram transtorno do espectro do autismo, desenvolvimento da linguagem e prematuridade. Após leitura dos títulos, descritores, resumos e leitura dos artigos na íntegra por avaliadores independentes, os dados registrados para a revisão foram: ano e país de publicação, tipo de estudo, amostra, instrumentos utilizados e principais achados. **Resultados:** A busca inicial incluiu 144 artigos. Destes, foram excluídos 68 por duplicação, 54 por meio das leituras independentes dos títulos e resumos e um por ter se tratado de estudo de caso. Dos 22 restantes, após leitura na íntegra, 13 foram selecionados por terem contemplado os critérios de inclusão e exclusão estabelecidos. **Conclusão:** A análise dos estudos selecionados permitiu concluir que pode existir uma associação entre transtorno do espectro do autismo e prematuridade, porém, não houve evidências de qual fator da prematuridade pode influenciar no surgimento dos sinais de autismo ou no diagnóstico do transtorno.

Palavras-chave: Transtorno do Espectro do Autismo; Transtorno Autístico; Prematuridade; Pesquisa sobre Linguagem; Linguagem Infantil; Desenvolvimento da Linguagem.

Resumen

Introducción: La prevalencia de la prematuridad y el trastorno del espectro autista (TEA) ha aumentado en los últimos años. Si bien la etiología del TEA puede ser genética, ciertos grupos de niños, como los prematuros, presentan un mayor riesgo de padecerlo. **Objetivo**: Mapear datos reportados en la literatura sobre la asociación entre trastorno del espectro autista y prematuridad. **Métodos:** Se trata de una revisión de la literatura, en la que se utilizó la pregunta guía como estrategia de investigación, seguida de la selección de artículos y compilación de resultados. Los criterios de selección fueron: estudios con muestras de niños que abordaran trastorno del espectro autista, desarrollo del lenguaje y prematuridad. Luego de la lectura de títulos, descriptores, resúmenes y lectura completa de los artículos por evaluadores independientes, los datos registrados para la revisión fueron: año y país de publicación, tipo de estudio, muestra, instrumentos utilizados y principales hallazgos. **Resultados**: La búsqueda inicial incluyó 144 artículos. De estos, 68 fueron excluidos por duplicación, 54 mediante lectura independiente de títulos y resúmenes y uno por ser un estudio de caso. De los 22 restantes, luego de la lectura completa, 13 fueron seleccionados por cumplir con los criterios de inclusión y exclusión establecidos. **Conclusión**: El análisis de los estudios seleccionados permitió concluir que puede existir una asociación entre el trastorno

del espectro autista y la prematuridad, sin embargo, no hubo evidencia de qué factor de la prematuridad puede influir en la aparición de signos de autismo o en el diagnóstico del trastorno.

Palabras clave: Trastorno del Espectro Autista; Trastorno Autista; Prematuridad; Estudios del Lenguaje; Lenguaje Infantil; Desarrollo del Lenguaje.

Introduction

Autism Spectrum Disorder (ASD) is characterized by deficits in social interaction and communication, along with restricted, repetitive, and stereotyped behavioral patterns, interests, and participation in activities[1]. Analysis of recent years shows a significant increase in ASD prevalence and, according to data from the Centers for Disease Control and Prevention, it is estimated that one in every 36 children is diagnosed with ASD[2]. Although its etiology is multifactorial, with emphasis on the genetic component, certain groups, such as preterm infants, present a higher risk for developing the disorder[3].

According to the Diagnostic and Statistical Manual of Mental Disorders – DSM-5-TR (APA, 2022), ASD is classified as a neurodevelopmental disorder characterized by persistent deficits in social communication and the presence of restricted and repetitive patterns of behavior. These diagnostic criteria help explain why certain populations, such as preterm infants, may present earlier and more intense signs of the disorder, since neurological alterations associated with prematurity may directly impact the domains described in the manual.

Another relevant finding is that preterm infants show a higher frequency of characteristics compatible with ASD in early childhood compared to full-term infants[4]. Additionally, mothers of preterm infants perceive these symptoms two to four months earlier than mothers of full-term infants, and symptoms tend to be more severe in preterm children[4]. It has also been demonstrated that preterm infants fail the Modified Checklist for Autism in Toddlers (M-CHAT)[5] at rates 7% to 27% higher than their full-term peers, reinforcing the need for studies involving this population to better understand the relationship between ASD and prematurity.

Moreover, there has been an increase in late preterm births, defined as those occurring between 34 and 36 weeks of gestational age[6]. Recent studies suggest that these infants present increased risk for neurological alterations compared to full-term infants.

It is also noteworthy that several physiological conditions have been associated with a higher incidence of autistic characteristics, such as low birth weight, congenital malformations, fetal distress, hypoxic-ischemic encephalopathy, congenital cytomegalovirus infection, phenylketonuria, and prematurity[7]. Recent discussions regarding ASD pathophysiology reinforce this association. Authors have proposed a comprehensive model integrating neuroanatomical and neurodevelopmental evidence, including alterations in circuits related to language, sensory processing, and brain connectivity, suggesting that perinatal factors, such as prematurity, may significantly influence mechanisms involved in the development of the disorder.

Thus, considering the increase in ASD prevalence as well as the number of preterm births, the objective of the present study was to map data reported in the literature regarding the relationship between ASD and prematurity.

Methods

This is a scoping review developed in accordance with the recommendations of the Joanna Briggs Institute (JBI)[8]. The Scoping Review technique proposes a rigorous and transparent methodology and has been widely used in the health field as a means of mapping and synthesizing evidence available in the literature on a given topic. Initially, the guiding research question was defined: "Is there an association between language delay in preterm children and ASD?"

Thus, studies addressing preterm children and their relationship with ASD were included in the search, as well as those describing criteria used to assess the risk of the disorder and delays in speech and language development in this population. The search for articles was conducted between August 2023 and April 2024.

This review followed the guidelines of the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) – extension for Scoping

Reviews[10] and was registered in the Open Science Framework (OSF).

Research strategy

To guide the search for relevant articles, the Population, Concept, and Context (PCC)[8] criteria were used, considering: a) Population: preterm children; b) Concept: prematurity and risk signs for autism, according to the assumptions of the Diagnostic and Statistical Manual of Mental Disorders (DSM-V)[1] c) Context: clinical and outpatient settings.

Selection criteria

Studies involving children born with gestational age less than 37 weeks, of both sexes, diagnosed with ASD were included, as well as articles describing criteria used to assess ASD risk in preterm children. The search also included studies that considered assessment, therapy, or monitoring of preterm children with and without an ASD diagnosis.

Articles including children with hearing loss, cognitive impairments, and/or other comorbidities were excluded. Regarding the concept, studies addressing children with comorbidities that excluded the diagnosis of ASD or children diagnosed with ASD without prematurity were excluded. In addition, case studies were excluded, since, according to JBI methodological recommendations for scoping reviews, this design has an individual descriptive character and limited generalizability, not adequately contributing to the objective of this review, which is to broadly and systematically map the available body of evidence, identify key concepts, types of studies, and gaps in the literature.

Full-text studies published between 2013 and 2023 in Portuguese, English, and Spanish were included, encompassing quantitative and qualitative articles, without restriction regarding year of publication. The Rayyan software[9] was used as a tool for selection, inclusion, and exclusion of articles from the Cochrane, Scopus, Web of Science, Embase, and MEDLINE databases via PubMed.

Chart1. Search strategy used in the databases (Population, Concept, Context – PCC).

BASE	STRATEGY
BVS	("Transtorno do Espectro do Autismo" OR "Autism Spectrum Disorder" OR "Trastorno del Espectro Autista" OR "Trouble du spectre autistique" OR "Transtorno Autístico" OR "Autistic Disorder" OR "Trastorno Autístico" OR "Trouble autistique" OR Autismo OR Autism) AND ("Nascimento Prematuro" OR "Premature Birth" OR "Nacimiento Prematuro" OR "Naissance prématurée" OR "Recém-Nascido Prematuro" OR "Infant, Premature" OR "Recien Nacido Prematuro" OR Prématuré OR Prematuridade OR "Premature Infant" OR "Neonatal Prematurity" OR Prematurity) AND ("Linguagem Infantil" OR "Child Language" OR "Lenguaje Infantil" OR "Langage de l'enfant" OR "Desenvolvimento da Linguagem" OR "Language Development" OR "Desarrollo del Lenguaje" OR "Développement du langage oral")
MEDLINE VIA PUBMED	("Autism Spectrum Disorder" OR "Autistic Disorder" OR Autism) AND ("Premature Birth" OR "Infant, Premature" OR "Premature Infant" OR "Neonatal Prematurity" OR Prematurity) AND ("Child Language" OR "Language Development")
COCHRANE	("Autism Spectrum Disorder" OR "Autistic Disorder" OR Autism) AND ("Premature Birth" OR "Infant, Premature" OR "Premature Infant" OR "Neonatal Prematurity" OR Prematurity) AND ("Child Language" OR "Language Development")
SCOPUS (Portal Capes)	("Autism Spectrum Disorder" OR "Autistic Disorder" OR Autism) AND ("Premature Birth" OR "Infant, Premature" OR "Premature Infant" OR "Neonatal Prematurity" OR Prematurity) AND ("Child Language" OR "Language Development")
WEB OF SCIENCE (Portal Capes)	("Autism Spectrum Disorder" OR "Autistic Disorder" OR Autism) AND ("Premature Birth" OR "Infant, Premature" OR "Premature Infant" OR "Neonatal Prematurity" OR Prematurity) AND ("Child Language" OR "Language Development")
EMBASE (Portal Capes)	(autism) AND (prematurity) AND ('language development')

Data analysis

The initial selection of articles was carried out independently by two of the authors through reading of titles and abstracts, with duplicate publications removed. A consensus meeting was then held with two additional authors. Subsequently, a new selection was performed by the same authors, who conducted full-text reading of the articles initially selected.

Disagreements were resolved in a new consensus meeting with the other two authors, following these definitions: when both reviewers indicated "yes," the study was included; when both indicated "no," the study was excluded. In cases where one reviewer indicated "maybe" and the other "yes," the study was included, adopting an equivalent procedure for exclusion. Final consensus was reached after discussion among the authors based on the established inclusion and exclusion criteria.

The initial search identified 144 articles, of which 68 were excluded due to duplication, 54 after independent reading of titles and abstracts, and one for being a case study. Of the remaining 22, after full-text reading, 13 were selected for meeting the established inclusion and exclusion criteria.

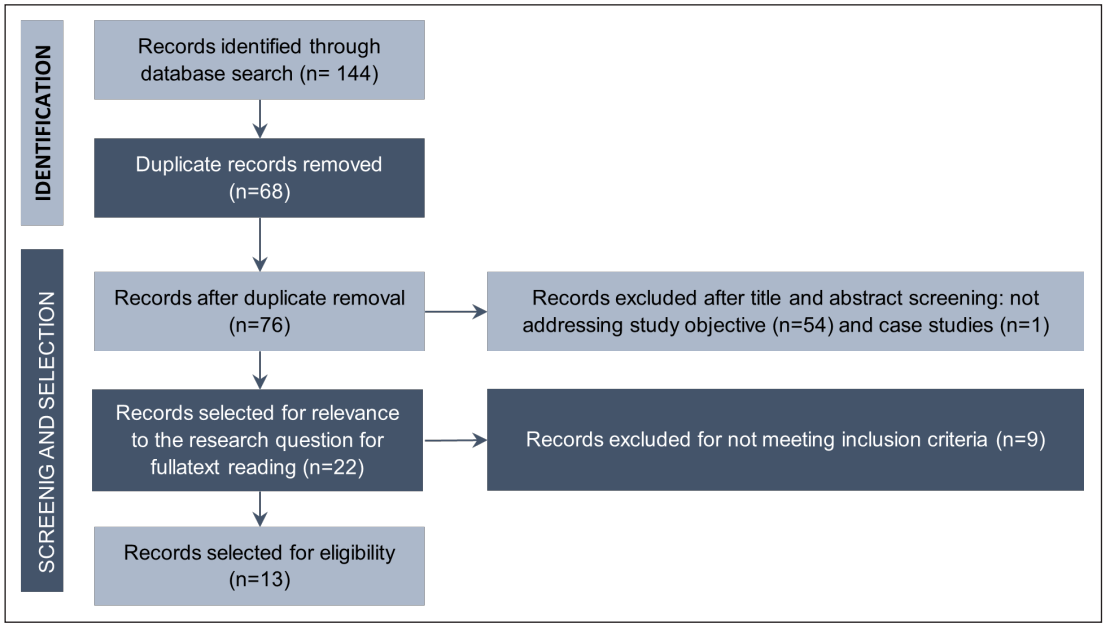

Figure 1. Flowchart of the study selection process according to PRISMA guidelines

Literature review

Results from electronic databases

Thirteen studies addressing prematurity, ASD, and language development in children were included. The selected studies were articles published in scientific journals between 2013 and 2023.

Detailed data from the studies included in the review, such as year of publication, authors, objectives, study design, sample size, participant characteristics (age, sex, groups), instruments used, results, and conclusions, are available as supplementary material to this article.

Analysis of selected studies

Regarding study design, two were literature reviews[11,12], two were experimental[11,13], and nine were observational[7,14-21]. Concerning the topic addressed, ten articles reported an association between prematurity and delay in speech and language development; one study identified an association between prematurity and ASD risk[17]; and two studies found no association between prematurity and ASD risk[7,15].

These results were heterogeneous, indicating a lack of consensus regarding the relationships

among prematurity, language development delay, and ASD risk. Furthermore, two articles addressed the application of screening protocols or questionnaires to assess language development in preterm children[19,22], contributing to understanding the tools used for early detection of possible developmental delays.

Regarding sample characteristics, two articles were literature reviews and eleven were studies involving individuals aged 0 to 18 years. Most (seven of the eleven) included children under five years of age[15-16,19-22]; three involved school-age children[18], 10-year-olds[14], and 18-year-olds[13]. One study did not report the age of participating children[7].

Chart 2. Characterization of the studies included in the scoping review (authors, year, country, design, sample, instruments, and main findings).

Authors, year and country	Main objectives	Type of study	Sample	Instruments used	Main findings
Joseph et al., 2023 USA[16]	Compare the core symptoms of ASD and associated characteristics between preterm (PT) and full-term (FT) children with ASD	Prospective multicenter observational study	1,506 infants born before 28 weeks of gestation, approximately 10 years old	Autism Diagnostic Interview-Revised (ADI-R)	Lower physical growth parameters and increased delays in developmental milestones among PT compared with FT children
Foster-Cohen et al., 2023 Israel[20]	Compare MLU and LD within and between diagnostic groups using data visualization and mixed-effects modeling	Cross-sectional analytical study	88 English-speaking children aged 2;6 to 5;6 years who received multidisciplinary intervention	New Zealand MacArthur-Bates Communicative Development Inventory (NZCDI)	Only prematurity reached significance, interacting with age, as a predictor of morpholexical scores
Brocchi & Lima, 2021 Brazil[19]	Relate two screening instruments for developmental assessment and language development in preterm children	Prospective cross-sectional study	69 preterm children aged 0–24 months of corrected age who were hospitalized in the NICU	Anamnesis, Early Language Milestone Scale (ELM), observation protocol and developmental follow-up	The protocols for assessing language acquisition were complementary, providing important data on developmental delay
Hendricks et al., 2021 India[22]	Present a structured protocol to implement caregiving intervention for preterm neonates in a NICU environment and compare neurodevelopment outcomes between experimental and control groups	Non-blinded randomized clinical trial	106 preterm newborns born between 26 and 34 weeks of gestational age	Ages and Stages Questionnaire (ASQ-3-12) and Trivandrum Language Development Screening Chart	The trial provides comprehensive data on the effectiveness of caregiving intervention on neurodevelopment, language development, and ASD risk
Srinivas, 2018 Australia[11]	Review current evidence on risks of neurodevelopmental impairment, sensory impairment, cerebral palsy, epilepsy, ASD and ADHD in preterm infants	Systematic review	16 articles	Specific form developed for literature search	Preterm infants show higher risk of sensory impairment and intellectual disability
Silva et al., 2017 Brazil	Review instruments used to assess spoken language in preschool children born preterm	Integrative literature review	11 articles	Eight instruments assessing spoken language skills in preschoolers born preterm	Expressive and receptive language deficits were greater than cognitive and motor deficits
Ribeiro et al., 2017 Brazil[17]	Compare neurodevelopment of low birth weight and very low birth weight preterm children with full-term children aged 1–3 years	Cross-sectional cohort study	150 preterm and full-term children divided according to weight and age	Anamnesis, socioeconomic classification and Denver Developmental Screening Test II (DDST-II)	Statistically significant differences in all assessed domains between preterm and full-term children
Carniel et al., 2017 Brazil[12]	Identify evidence regarding the influence of risk factors on child language development and contributions of speech-language pathology	Integrative literature review	29 articles	Studies addressing risk factors for language development	Delays or alterations observed in several domains among preterm children
Pineda et al., 2015 USA[15]	Define neonatal social characteristics related to ASD risk	Longitudinal observational study	62 preterm infants aged 2 years	Modified Checklist for Autism in Toddlers and Bayley Scales of Infant Development	No atypical social interactions were observed among children who later screened positive for ASD

Authors, year and country	Main objectives	Type of study	Sample	Instruments used	Main findings
Bowers et al., 2015 USA[13]	Characterize the phenotype of males and females with ASD born preterm versus full-term	Experimental study	1,069 individuals with ASD born preterm, older than 18 years	Specific form for anamnesis and medical record data collection	Females born preterm were more likely to be nonverbal
Gabis & Pomeroy, 2014 USA[7]	Classify children diagnosed with ASD according to etiological investigation	Retrospective study	446 children diagnosed with ASD	Institutional database records	Most perinatal factors did not contribute to the development of core ASD symptoms
Ribeiro & Lamônica, 2014 Brazil[21]	Compare communicative skills of preterm, extremely preterm and typically developing children aged 2–3 years	Case-control study	20 PT and 16 extremely PT; 20 children with language delay and 16 with typical development	Communicative Behavior Observation (CBO)	Statistical differences in communicative skills between preterm and full-term children
Mackay et al., 2013 Scotland[18]	Determine whether associations with gestational age and birth weight vary among causes of special educational needs	Retrospective cohort study	407,503 schoolchildren	Multinomial logistic regression	Gestational age and birth weight strongly associated with developmental and learning disabilities

Legend: AC = cognitive delay; AF = speech delay; AV = assessment; BP = low birth weight; DA = atypical development; DF = physical disabilities; DG = global development; DI = intellectual disability; DIN = child development; DLGG = language development; DL = lexical development; DM = motor disabilities; DMF = morphological development; DP = premature development; DS = sensory disabilities; DT = typical development; EP = early stimulation; FPN = perinatal factors; FR = risk factors; GE = experimental group; GT = control group; H = males; IC = chronological age; ICO = corrected age; LC = receptive language; LE = expressive language; LGG = language; M = females; MBP = very low birth weight; MF = fine motor; MG = gross motor; ND = neurodevelopment; NEE = special educational needs; NV = nonverbal; P = preterm; PC = cerebral palsy; PE = extremely preterm; PP = weight percentile; PS = personal-social; RA = autism risk; T = term; TDAH = attention-deficit/hyperactivity disorder; UTI = neonatal intensive care unit (NICU).

Discussion

Among the selected studies, one systematic review[11] identified only one study[14] that reported the risk of Autism Spectrum Disorder (ASD) in late preterm infants at two years of corrected age using the Modified Checklist for Autism in Toddlers (M-CHAT). According to the authors, 14.5% of late preterm infants, compared with 9.3% of infants in the full-term control group, scored above the clinical cutoff for ASD at two years of age. It is noteworthy that information regarding the occurrence of neonatal complications was not included in that study[14]. A more detailed analysis showed that late preterm infants with sensory problems, developmental delays, and speech and language difficulties were more likely to obtain higher scores on the ASD screening tests used[14].

Another study[15], which evaluated 62 preterm infants at two years of age using the Modified Checklist for Autism in Toddlers and the Bayley Scales of Infant and Toddler Development, found that approximately one fifth of the sample screened positive for ASD risk, while 28 children (45%) presented developmental delay. Among the children with positive ASD screening results, nine (69%) also showed developmental delay. The main conclusion of this study was that preterm infants at risk for ASD at two years of age exhibited alterations in early social interaction behaviors. Furthermore, infants with positive screening results were less likely to demonstrate gaze aversion and endpoint nystagmus during social interaction in the neonatal period[15].

These findings suggest that preterm infants, because they are at greater risk for developmental impairments, may present a developmental trajectory that differs from that of full-term infants at risk for ASD. Considering that an ASD diagnosis is rarely confirmed at two years of age, these results contribute to a better understanding of early signs as well as the developmental pathway leading to diagnosis[16].

Most perinatal factors and minor physical anomalies observed in the evaluated infants did not contribute to the development of the core symptoms of autism, according to one of the studies[17]. However, differences related to sex, clinical characteristics, and diagnostic features were observed when etiology was used to create ASD subtypes. Another important aspect concerns the association between low birth weight and the disorder. The authors were unable to distinguish low birth weight resulting from prematurity from that resulting from intrauterine growth restriction. Therefore, the

conclusion was that there is no association between intrauterine growth restriction and ASD[17].

One study demonstrated that children born preterm with low or very low birth weight may present developmental delays even in the absence of brain injury[22]. This finding corroborates the results of another study in which birth weight percentile was associated with several deficits, including language, motor, and intellectual development[18].

Another important factor concerns language development, since language impairment is the most frequent alteration observed in preterm children. One study[13] found that individuals born preterm were more likely to be nonverbal, with a statistically significant difference among girls but not among boys[13].

In a literature review[12], all included studies identified delays or alterations in groups of children born preterm across several assessed domains. According to the authors, factors such as birth weight, gestational age, and Apgar Scorenegatively influence language development[12].

Another study highlights that the assessment of language in preterm children, as well as monitoring their acquisition processes and providing timely intervention, are important strategies for preventing or reducing sequelae associated with preterm birth[19]. These findings are consistent with those of another study that evaluated older children, in which prematurity alone reached statistical significance as a predictor of morphological and lexical alterations in language[20].

Some authors reported an association between speech and language delay in preterm children, although without linking these findings to ASD. The analysis of the selected studies suggests that there may be an association between ASD and prematurity. However, it is not possible to specify which factors related to prematurity are associated with the emergence of autistic signs or with the diagnosis of the disorder.

As a contribution, the present study provides an updated synthesis of the literature regarding the relationship between prematurity, language development, and risk for ASD, highlighting knowledge gaps that may guide future research in the field of Speech-Language Pathology, particularly in the area of Child Language. As a limitation, the restricted number of studies simultaneously addressing autism and prematurity should be noted, especially those investigating which prematurity-related factors are associated with ASD beyond low birth weight.

A further important gap concerns the prevalence of preterm children diagnosed with ASD, as well as the proportion of children with ASD who were born preterm. This finding reinforces the need for additional studies focusing on these aspects and contributing to a better understanding of how these factors may inform new strategies for screening, monitoring, and early intervention.

Conclusion

The results of this scoping review suggest that prematurity is frequently associated with delays in speech and language development. However, evidence directly linking prematurity to Autism Spectrum Disorder remains limited and inconclusive.There is insufficient evidence to determine which prematurity-related factors may influence the emergence of autistic signs or the diagnosis of ASD.

Given the increasing prevalence of both prematurity and ASD, further studies with robust methodological designs, larger samples, and longitudinal follow-up are necessary to clarify possible mechanisms underlying this relationship.From a clinical perspective, systematic monitoring of language development in preterm children is essential, as early identification of alterations may allow timely intervention and potentially reduce long-term developmental impacts.

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