Prenatal Ultrasound–Detected Structural Anomalies Associated with Autism Spectrum Disorder: A Narrative Review

Структурные аномалии плода как ультразвуковые маркеры риска расстройства аутистического спектра: нарративный обзор литературы

doi: 10.17816/CP15700

Review

Nazyar Khamenehei, Lyudmila Tokarskaya
Ural Federal University named after the first President of Russia B.N. Yeltsin, Yekaterinburg, Russia

Назйар Хаменехи, Людмила Токарская
ФГАОУ ВО «Уральский федеральный университет имени первого Президента России Б.Н. Ельцина», Екатеринбург, Россия

ABSTRACT

BACKGROUND: Autism Spectrum Disorder (ASD) is a complex neurodevelopmental condition with a globally increasing prevalence. Early detection is crucial for effective intervention, yet current diagnostic methods often result in delays. Emerging research suggests that prenatal biomarkers, including structural anomalies detectable via ultrasound, may offer opportunities for earlier identification.

AIM: To synthesize current evidence on prenatal ultrasound-detectable anomalies associated with ASD and assess their potential as early predictors.

METHODS: A comprehensive literature search was conducted across PubMed, Scopus, and Google Scholar for studies published between 2007 and 2025. Keywords included “autism spectrum disorder”, “prenatal ultrasound”, “fetal anomalies”, “preeclampsia”, “neurodevelopment” and “biomarkers”. Priority was given to recent and high-quality studies, including systematic reviews and large cohort analyses. The selected articles were read in full, and their key findings were summarized in a narrative form. The synthesis focused on describing the scope of the existing evidence, the prenatal ultrasound findings reported in relation to ASD, and on highlighting recurrent patterns or notable differences between studies.

RESULTS: Several studies report associations between ASD and prenatal anomalies such as ventriculomegaly, increased biparietal diameter, hyperechogenic kidneys, and congenital heart defects. However, these findings are not specific to ASD and show inconsistent predictive performance. Sensitivity and specificity vary widely across studies, and ethical concerns about overdiagnosis and disparities in access to care persist.

CONCLUSION: Prenatal ultrasound may contribute to early ASD risk identification but lacks the accuracy required for standalone diagnosis. Integrating ultrasound findings with genetic and postnatal data, along with standardized protocols and further research, is essential to improve its predictive value and clinical application.

АННОТАЦИЯ

ВВЕДЕНИЕ: Расстройство аутистического спектра (РАС) представляет собой полиэтиологичное нарушение нейропсихического развития, распространенность которого в мире неуклонно растет. Ранняя диагностика имеет решающее значение для эффективного вмешательства, однако существующие методы часто не позволяют своевременно выявить это заболевание. Данные современных исследований свидетельствуют, что пренатальные биомаркеры, включая структурные аномалии плода, выявляемые в ходе ультразвукового исследования (УЗИ), могут стать инструментом для более ранней оценки риска развития РАС.

ЦЕЛЬ: Обобщить современные данные о пренатальных аномалиях плода, выявляемых с помощью УЗИ и ассоциированных с РАС, и оценить возможность использования данных аномалий в качестве ранних предикторов.

МЕТОДЫ: Был проведен комплексный поиск литературы в научных базах данных PubMed, Scopus и Google Scholar за 2007–2025 гг. с использованием ключевых слов «расстройство аутистического спектра (autism spectrum disorder)», «пренатальное УЗИ (prenatal ultrasound)», «аномалии плода (fetal anomalies)», «преэклампсия (preeclampsia)», «нейроразвитие (neurodevelopment)» и «биомаркеры (biomarkers)». При отборе публикаций приоритет отдавался наиболее релевантным и методологически качественным работам, включая систематические обзоры и крупные когортные исследования. Отобранные статьи были прочитаны полностью, а их основные результаты обобщены в описательной форме. Синтез информации сосредоточен на области применения существующих данных, характеристике аномалий, выявляемых при пренатальном УЗИ, их связи с РАС, а также на согласованности и противоречиях в результатах различных исследований.

РЕЗУЛЬТАТЫ: Ряд исследований демонстрирует связь между повышенным риском РАС и такими аномалиями плода, как вентрикуломегалия, увеличение бипариетального диаметра, гиперэхогенные почки и врожденные пороки сердца. Однако эти маркеры неспецифичны для РАС, а их прогностическая ценность существенно варьирует. Чувствительность и специфичность методов диагностики в разных исследованиях также заметно различаются; кроме того, сохраняются этические вопросы, связанные с гипердиагностикой и неравным доступом к медицинской помощи.

ЗАКЛЮЧЕНИЕ: Пренатальное УЗИ обладает потенциалом для раннего выявления риска развития РАС, но его точность в настоящее время недостаточна для постановки диагноза. Для повышения прогностической ценности и клинической значимости данных пренатального УЗИ необходима их интеграция с результатами генетического тестирования и постнатального наблюдения, а также стандартизация протоколов и проведение дальнейших исследований в этой области.

Keywords: *autism spectrum disorder; prenatal ultrasound; fetal anomalies; early diagnosis; neurodevelopmental disorders; biomarkers*

Ключевые слова: *расстройство аутистического спектра; пренатальное ультразвуковое исследование; аномалии плода; ранняя диагностика; расстройства нейропсихического развития; биомаркеры*

INTRODUCTION

According to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), autism spectrum disorder (ASD) is a neurobehavioral condition marked by enduring impairments in social and communication functioning, difficulties in forming, comprehending, and sustaining relationships, and atypical and persistent interests and repetitive activities [1]. ASD is one of the most prevalent neurodevelopmental conditions in children, with males being four to five times more likely to develop it than females [2, 3]. According to a recent meta-analysis, approximately 0.77% of children globally are diagnosed with ASD, with boys accounting for 1.14% of this population [4]. Based on a 2022 report from the Autism and Developmental Disabilities Monitoring Network (ADDM Network)[1], focusing on the prevalence

---

[1] Autism and Developmental Disabilities Monitoring (ADDM) Network — the United States – based public health surveillance program that tracks the prevalence and characteristics of autism spectrum disorder and other developmental disabilities in children.

and characteristics of ASD among four- and eight-year-old children whose parents or guardians resided in 16 ADDM sites in the United States, one in 31 (3.2%) children aged eight years had ASD [2, 5].

This appears to result from interactions between genetic and environmental factors [1, 6, 7]. ASD significantly impacts society through high healthcare and education costs, caregiver stress, and reduced employment opportunities [8]. The lifetime cost per individual can exceed $2 million due to specialized services and lost productivity [8]. Families often face emotional and financial strain, while individuals with ASD encounter barriers to education, employment, and social inclusion. These challenges are especially pronounced in low-resource settings, highlighting the need for improved access to care, early intervention, and supportive public policies [8].

Early detection of ASD is essential for optimizing developmental outcomes, reducing long-term societal and economic burdens, and enhancing support for individuals and families. Research highlights that interventions initiated before age three can leverage neuroplasticity, leading to improvements in communication, social skills, and behavior, as well as significant gains in Intelligence Quotient (IQ) and adaptive functioning[2]. Early diagnosis may also substantially reduce lifetime costs, estimated at $461 billion annually in the U.S., potentially saving up to $1.2 million per individual by decreasing reliance on special education and healthcare services [3, 9, 10]. In addition, families benefit from early access to resources, which helps to alleviate stress and improve coping mechanisms [11]. However, challenges persist, including diagnostic delays, despite recommendations for screening at 18–24 months, and ongoing disparities, particularly among minority groups who demonstrate higher rates of severe ASD[2].

ASD is usually diagnosed through postnatal behavioral markers such as language delay, social difficulties, and repetitive behaviors [12, 13], often assessed with tools like the Autism Diagnostic Observation Schedule (ADOS). However, reliance on these signs delays diagnosis until ages four to five, limiting early intervention [14]. Early behavioral markers — including reduced social attention, delayed joint attention, diminished response to name, and decreased positive affect — can be observed at 6–12 months using eye-tracking or the Autism Observation Scale for Infants (AOSI) [15], while neuroimaging and EEG evidence of atypical connectivity and rapid cranial growth indicate an early neurodevelopmental origin [16, 17]. Hybrid behavioral–biological models achieve up to ~80% predictive accuracy in high-risk groups, though generalizability, limited sensitivity (50–70% for eye-tracking), and ethical issues remain [18]. Additional postnatal indicators include increased head circumference, atypical sensory responses, and delayed motor milestones [19, 20]. Overall, converging evidence suggests ASD originates prenatally but manifests behaviorally in the first year, underscoring the need to integrate early postnatal and prenatal risk markers for more timely diagnosis.

While postnatal behavioral indicators such as delayed language development and repetitive behaviors are traditionally used for diagnosis [12, 13], emerging research suggests that prenatal biomarkers, including those detectable via ultrasound, may offer earlier identification opportunities.

This article presents a narrative review of current evidence on prenatal structural anomalies associated with ASD, highlighting the role of ultrasound in detecting these abnormalities during fetal development. By synthesizing findings from clinical, genetic, and imaging studies, this review aims to assess the predictive value of ultrasound-detectable anomalies and highlight key gaps for future research.

METHODS

Information sources

A broad literature search was conducted using PubMed, Scopus, and Google Scholar, covering publications from 2007 to 2025.

Search strategy

Search terms included “autism spectrum disorder”, “prenatal ultrasound”, “fetal anomalies”, “biomarkers”, “preeclampsia”, and “neurodevelopment”.

Selection process

Articles were selected based on their relevance to prenatal indicators of ASD, with priority given to systematic reviews, meta-analyses, large cohort studies, and recent original

---

[2] Centers for Disease Control and Prevention. (2025, April 15). Data and statistics on autism spectrum disorder. Available from: https://www.cdc.gov/autism/data-research/index.html

research. The focus was on articles published in the past five years; however, older articles were considered if they addressed key research questions. Studies focusing exclusively on postnatal diagnosis were included only if they provided an essential context for understanding early developmental markers.

Data analysis

The findings from each study were extracted and thematically organized by type of anomaly (e.g., brain, cardiac, renal) and other relevant prenatal risk factors. The synthesis adopted a descriptive approach, summarizing reported associations and identifying recurring patterns.

RESULTS

This section is organized into three main parts. First, we review prenatal indicators identified in the literature, including genetic, metabolic, and structural markers. Second, we examine structural anomalies detectable by prenatal ultrasound, grouped into brain, cardiac, and other organ systems. Finally, we discuss the diagnostic potential of prenatal ultrasound and its limitations.

Prenatal indicators of Autism Spectrum Disorder

Jensen et al. (2022) present a comprehensive review of modern biomarkers for ASD, emphasizing their potential to advance diagnosis and treatment [21]. The authors considered genetic biomarkers such as mutations in the SH3 and multiple ankyrin repeat domains 3 (*SHANK3*) gene, which encodes a scaffolding protein critical for synapse formation and function, and the chromodomain helicase DNA-binding protein 8 (*CHD8*) gene, which encodes a chromatin remodeler regulating gene expression during brain development. These biomarkers are implicated in up to 20% of ASD cases and offer insights into its molecular mechanisms, including altered synaptic signaling, disrupted chromatin remodeling, and dysregulated neurodevelopmental pathways. Epigenetic markers, such as DNA methylation patterns, reflect gene-environment interactions and may serve as indicators of ASD risk [21]. While these biomarkers show promise for improving early and accurate diagnosis, their clinical application is constrained by individual variability, underscoring the need for integrated, multi-omics approaches to address the heterogeneity of ASD and inform targeted interventions [21].

Regarding metabolic biomarkers, disruptions in folate and mitochondrial pathways have been associated with biochemical imbalances observed in approximately 30% of individuals with ASD [21]. Neuroimaging research has revealed structural and functional brain differences in ASD, including rapid amygdala overgrowth during the first two years of life [22, 23]. Behavioral biomarkers such as atypical eye-tracking patterns, evident as early as six months old, also capture early deviations in social attention [24, 25]. Although these signs emerge postnatally during infancy or early childhood, they may reflect neurodevelopmental alterations originating prenatally. Therefore, although they are observed after birth, their underlying causes can be linked to prenatal brain development.

Parellada et al. (2023) underscore the potential of prenatal biomarkers to identify ASD risk before birth, highlighting maternal immune activation (MIA) as one such marker due to elevated levels of pro-inflammatory cytokines such as IL-6 during pregnancy, observed in approximately 20% of mothers of children with ASD [26]. Hormonal imbalances, such as elevated prenatal testosterone levels in amniotic fluid, are also noted as potential predictors, with studies showing a correlation with later ASD traits in male offspring [26]. The authors also point to genetic biomarkers detectable prenatally, such as copy number variants (CNVs) and *de novo* mutations in genes such as *CHD8*, which may be identified through prenatal genetic testing in high-risk families. Structural brain anomalies, detectable via prenatal MRI, such as early overgrowth in regions like the amygdala, are also considered, though their specificity to ASD remains limited [26]. These prenatal biomarkers hold promise for identifying at-risk fetuses, yet the authors caution that their predictive accuracy is constrained by the complexity of the etiology of ASD, necessitating further research to refine their clinical application [26, 27].

Prenatal structural anomalies detectable by ultrasound in Autism Spectrum Disorder

Brain anomalies

Evidence from multiple studies indicates that specific prenatal brain anomalies, detectable by ultrasound or MRI, may be associated with a later ASD diagnosis, although the nature, timing, and specificity of these findings differ.

Zamłyński et al. provided a comprehensive review showing that mild-to-moderate ventriculomegaly (10–15 mm), even when isolated (not accompanied by other anomalies), is associated with increased risks of neurodevelopmental disorders, including ASD, language delays, and learning difficulties [28]. This is attributed to possible altered brain maturation or undetected genetic or metabolic abnormalities [28].

Aydin et al. examined 219 singleton pregnancies, using 2D ultrasound at 12, 20, and 26–30 weeks to measure head circumference (HC), ventricular atrium (VA), and transcerebellar diameter (TCD) [29]. Follow-up of 179 children at 18–20 months using The Quantitative Checklist for Autism in Toddlers (Q-CHAT) tool [30] revealed that larger TCD at 20 weeks and greater HC at 28 weeks were correlated with higher autistic traits. These associations persisted after adjusting for sex, maternal age, and birth weight, suggesting that atypical prenatal brain growth — especially in the cerebellum — may be linked to early ASD markers [29].

Hobbs et al. analyzed ultrasound data from children who were later diagnosed with ASD and typically developing controls [31]. The study found that while overall fetal HC did not differ significantly, children with ASD showed relatively larger biparietal diameter (BPD) and a trend toward increased HC during the second and third trimesters [31]. These findings suggest subtle prenatal brain overgrowth in ASD [31]. Decreased abdominal circumference (AC) was noted in multiplex ASD cases, and renal anomalies such as pyelectasis were more common [31]. The study concluded that atypical brain and organ development may begin prenatally in ASD, highlighting ultrasound's potential as an early screening tool [31].

When comparing Aydin et al. (2024) and Hobbs et al. (2007), both studies point to subtle prenatal brain overgrowth in ASD; however, the specific measurements and emphasis differ: Aydin et al. highlight cerebellar growth and HC increases in late gestation, while Hobbs et al. emphasize changes in BPD and co-occurring systemic anomalies [29, 31]. Differences in gestational timing of measurements, follow-up age, and diagnostic tools may account for these discrepancies.

Adding another dimension, Frye et al. synthesized neuroimaging and physiological evidence from prenatal studies, identifying structural anomalies such as deviations in cortical development, white matter organization, and cerebellar morphology through prenatal MRI [14]. These markers may reflect early neurodevelopmental disruptions and atypical connectivity patterns that persist postnatally, offering a window into the fetal origins of ASD. However, Frye et al. caution that these markers are preliminary and lack diagnostic specificity [14].

Regev et al. linked fetal structural anomalies to genetics, finding that 34.1% of children with ASD in their sample exhibited at least one prenatal anomaly [32]. These cases were significantly more likely to carry loss-of-function mutations, particularly in genes expressed across fetal tissues during organogenesis. This association underscores a possible shared basis for head, brain, and systemic anomalies [32].

Supporting earlier observations, a smaller study presented at the International Congress of the Royal College of Psychiatrists (RCPsych) in 2014 compared the head and abdominal diameters of 40 fetuses who were later diagnosed with ASD with 120 controls at 20 weeks' gestation. The ASD group had larger measurements in both parameters, echoing findings from Aydin et al. (2024) and Hobbs et al. (2007) that cranial and somatic growth patterns may diverge prenatally in ASD cases[3].

In summary, while these studies collectively suggest that certain prenatal brain anomalies, such as ventriculomegaly, enlarged BPD, increased HC, and greater TCD, are more common in fetuses who are later diagnosed with ASD, the variations in study design, measurement timing, and associated systemic findings highlight the need for standardized protocols. The convergence of structural imaging, genetic evidence, and multi-organ involvement suggests a complex developmental trajectory, but predictive accuracy for ASD remains limited.

Cardiac Anomalies

Popa et al. (2025) highlight the potential link between prenatal detection of cardiac anomalies and an increased risk of ASD through associated genetic conditions [33]. In the first trimester, 13 cases of cardiac anomalies were associated with genetic syndromes such as Down syndrome, Edwards syndrome, and Turner syndrome, all of which have

---

[3] Brauser D. Routine ultrasounds may detect autism in utero. In: International Congress of the Royal College of Psychiatrists (RCPsych). London, United Kingdom: Medscape Psychiatry; 2014. Available from: https://www.medscape.com/viewarticle/827333?form=fpf

a higher incidence of ASD [33]. Choroid plexus cysts and abnormal tricuspid valve flow were identified as potential indicators of underlying genetic conditions associated with neurodevelopmental disorders, including ASD [33]. A second-trimester diagnosis of DiGeorge syndrome, a condition strongly correlated with ASD, was observed [33]. These findings suggest that early detection of cardiac anomalies and related markers could aid in identifying pregnancies at higher risk for ASD due to the genetic syndromes involved [33]. Other common findings include increased biparietal diameter, hyperechogenic kidneys, and cardiac malformations. Congenital heart disease (CHD), in particular, has been repeatedly associated with ASD, potentially due to shared genetic and developmental pathways between the heart and brain [29, 34–39].

Other prenatal risk factors

A meta-analysis by Dachew et al. (2018) examined the association between intrauterine exposure to preeclampsia and the risk of ASD in offspring [40]. The pooled results showed a statistically significant 32% increase in relative risk (RR) of ASD among children exposed to preeclampsia prenatally (RR=1.32; 95% CI: 1.20–1.45). Sensitivity analyses confirmed the robustness of the findings, with relative risks ranging from 1.30 to 1.37. This study concluded that preeclampsia is a significant prenatal risk factor for ASD and emphasized the importance of early developmental screening in this high-risk population [40].

Zhang, Jin, and Liu (2022) presented a systematic review and meta-analysis examining the association between preeclampsia and ASD [41]. Their findings showed that exposure to preeclampsia was associated with an approximately 30% increased odds for ASD compared to women with normal pregnancies [41]. This analysis pooled the results of multiple studies and demonstrated a significant positive association, further supporting preeclampsia as a prenatal risk factor for neurodevelopmental disorders [41].

A large retrospective cohort study by Carter et al. examined 308,536 mother—child pairs and found that maternal obesity, diabetes, preeclampsia, and asthma during pregnancy were each significantly associated with increased odds of ASD in offspring, particularly when co-occurring with gastrointestinal disturbances (GIDs) [42]:

- ASD with gastrointestinal disturbances (GIDs): Offspring exposed to maternal preeclampsia during pregnancy exhibited a 63% higher likelihood of developing ASD with GIDs compared to unexposed children (OR=1.63; 95% CI: 1.36–1.95).
- ASD without GIDs: The effect was smaller and non-significant, with an 18% increased odds (OR=1.18; 95% CI: 1.00–1.38).
- GIDs without ASD: There was a 19% increased likelihood of gastrointestinal disturbances without ASD among offspring exposed to preeclampsia (OR=1.19; 95% CI: 1.14–1.24).

Importantly, when comparing ASD with GIDs to ASD without GIDs, preeclampsia exposure conferred 38% greater odds of ASD accompanied by gastrointestinal disturbances (OR=1.38; 95% CI: 1.09–1.75) [42].

Diagnostic role of prenatal ultrasound

Prenatal ultrasound has emerged as a widely accessible and non-invasive tool for monitoring fetal development, offering the possibility of detecting structural anomalies associated with increased ASD risk. However, its diagnostic value is challenged by variability in anomaly types, timing of detection, and limited specificity.

Population-level studies provide important baseline estimates of anomaly prevalence. Regev et al. (2022), in a retrospective case-sibling-control study of 659 children, reported that ultrasound-detected fetal anomalies (UFAs) were present in 29.3% of ASD cases compared with 15.9% of typically developing siblings and 9.6% of unrelated controls [43]. The most common anomalies involved the urinary system, heart, and brain [43]. Similar findings were observed by researchers at Ben–Gurion University of the Negev, where mid-gestation fetal anatomy surveys showed anomalies in approximately 30% of fetuses who later developed ASD — three times the prevalence in the general population. Both studies highlight that multi-organ anomalies, rather than single-system findings, may indicate broader developmental disruptions, though these patterns are not unique to ASD.

Cardiac anomalies have been a particular focus due to shared developmental pathways between the heart and brain. Popa et al. demonstrated that first-trimester ultrasound can detect cardiac defects, some linked to genetic syndromes (e.g., Down syndrome, Edwards syndrome, DiGeorge syndrome, Fragile X syndrome) with elevated ASD incidence [33]. Genetic syndromes such as Down syndrome (trisomy 21), Edwards syndrome (trisomy 18), DiGeorge syndrome (22q11.2 deletion), and

Fragile X syndrome (FXS) are known to carry an increased risk of ASD. For instance, congenital heart disease — frequently present in Down syndrome — has been linked to higher ASD probability [44, 45]. Approximately 30–40% of individuals with DiGeorge syndrome meet diagnostic criteria for ASD [46]. FXS, the most common inherited cause of intellectual disability, is also strongly associated with ASD, with prevalence estimates indicating that around 50% of males and 16% of females with FXS receive an ASD diagnosis or treatment history (Centers for Disease Control and Prevention, 2020), and peer-reviewed studies report even higher rates: 60–75% in males and 20–41% in females [47]. Their cohort of 8,944 pregnant women included 37 first-trimester CHD cases, with early diagnosis enabling genetic testing and timely intervention [33, 39].

Similarly, Bottelli et al. (2023) assessed 7,080 pregnancies and found major CHD detection rates of 58.3% in low-risk and 93.5% in high-risk populations [48]. Ling et al. (2023) evaluated a four-section ultrasound approach (upper abdominal, four-chamber, three-vessel–trachea, bilateral subclavian artery views) in 9,533 fetuses, achieving 67% sensitivity and 99.96% specificity for CHD [49]. Yang et al. (2025) reported similar sensitivity (70.5%) in a cohort of over 77,000 fetuses, but stressed that early detection should complement, not replace, second-trimester echocardiography [39, 50]. Across these studies, early cardiac anomaly detection is feasible, yet the low specificity of CHD for ASD limits its predictive value [50].

Brain anomalies are also well-documented. Zamłyński et al. emphasized the diagnostic role of ultrasound in isolated fetal ventriculomegaly, defined as an atrial diameter >10 mm, often detected during second-trimester scans [28]. While associated with neurodevelopmental disorders, including ASD, ventriculomegaly also occurs in other conditions, limiting specificity [28]. Fulceri et al. (2018), in a systematic review of 26 studies, found that recurrent markers such as enlarged lateral ventricles and increased nuchal translucency (>99th percentile) were associated with higher ASD risk (OR=2.48) [51], but methodological heterogeneity and small sample sizes limited definitive conclusions.

Comparative analysis of patterns suggests that the greatest strength of prenatal ultrasound lies in identifying combinations of anomalies. Isolated findings — such as ventriculomegaly, mild head size increases, or single cardiac defects — appear in many neurodevelopmental conditions and even in typically developing children, leading to high false-positive rates. In contrast, concurrent anomalies across the brain, cardiac, and renal systems [43] may point toward underlying genetic or developmental disruptions relevant to ASD. Despite advances in high-resolution imaging and extended protocols (e.g., 3D/4D ultrasound), prenatal ultrasound remains an adjunct rather than a standalone diagnostic tool for ASD. Its predictive value is constrained by low specificity, operator-dependent variability, and the absence of standardized ASD-specific screening protocols.

Future improvements may come from integrating ultrasound with genetic and biochemical markers (e.g., those described by Regev et al. [32]), as well as longitudinal studies validating anomaly combinations as early biomarkers.

Doppler ultrasound has also been investigated for its potential to detect early pregnancy complications that may indirectly increase ASD risk through adverse prenatal environments. For example, Oancea et al. (2020) evaluated first-trimester uterine artery Doppler parameters — pulsatility index (PI) and presence of a diastolic notch — between 11 and 14 weeks in 120 at-risk pregnancies. PI alone predicted later preeclampsia (PE) with moderate accuracy (sensitivity=61.5%, specificity=63.8%), and adding a bilateral notch slightly improved performance [52]. Lai et al. (2022) similarly found that uterine artery PI at 19–23 weeks detected preterm PE with 75.6% sensitivity; combining Doppler findings with angiogenic markers such as PlGF and sFlt-1 improved predictive accuracy [53]. Although these studies focused on PE rather than ASD directly, PE is a known prenatal risk factor for neurodevelopmental disorders, including ASD [40, 41, 54]. Thus, Doppler ultrasound — particularly when integrated with biochemical markers — may have value in identifying pregnancies with altered placental perfusion that could impact fetal brain development. However, current evidence is indirect, and no large-scale prospective studies have established Doppler parameters as reliable standalone predictors of ASD. In conclusion, while current evidence supports the role of prenatal ultrasound in identifying structural anomalies associated with ASD risk, clinical translation requires standardized protocols, integration with multimodal data, and clear guidelines to manage the ethical implications of probabilistic prenatal findings.

DISCUSSION

Overall, the evidence for prenatal markers of ASD combines structural abnormalities detectable by prenatal imaging and broader prenatal risk factors. In the genetic, metabolic, and epigenetic domains, several biomarkers (e.g., *SHANK3*, *CHD8*, folate and mitochondrial abnormalities, DNA methylation) have been implicated, highlighting the molecular underpinnings of prenatal origins of ASD. Prenatal ultrasound findings suggest that atypical neurodevelopment associated with ASD may begin in utero, with structural and systemic anomalies observed across multiple studies. Enlarged ventricles, accelerated cerebellar and cranial growth, altered biparietal and abdominal measurements, and co-occurring renal or cardiac abnormalities have all been reported in fetuses who were later diagnosed with ASD [28, 29, 31, 32, 44, 45]. These anomalies are frequently linked with genetic variants affecting organogenesis, reinforcing the view that ASD arises from complex prenatal interactions between genetic vulnerability and developmental trajectories. Neuroimaging evidence of altered cortical development and amygdala overgrowth further supports this interpretation [14].

The diagnostic value of ultrasound remains contested. Many of the reported anomalies — such as ventriculomegaly or increased biparietal diameter — occur not only in ASD but also in other neurodevelopmental disorders or even in typically developing fetuses, producing high false-positive rates [51]. Conversely, some individuals with ASD show no detectable anomalies on ultrasound [55]. This dual limitation restricts the role of ultrasound to surveillance rather than diagnosis. Inconsistencies across studies, influenced by variability in operator expertise, gestational timing, and technology, further reduce predictive reliability. Reported sensitivities range from ~58% in low-risk pregnancies to over 90% in high-risk groups, underscoring the uneven performance of current methods [48, 50].

Beyond methodological issues, ethical and clinical concerns must be considered. Prenatal labeling based on nonspecific anomalies risks unnecessary parental anxiety, stigmatization, or misguided decision-making. Equitable access is another challenge; advanced imaging modalities remain unavailable in many low-resource settings, potentially widening disparities in early identification and intervention.

Progress will require large, prospective cohort studies to validate markers and standardize protocols. Combining ultrasound with genetic, epigenetic, and metabolic data offers a path toward more reliable prediction models, while emerging imaging technologies such as 3D/4D ultrasound and Doppler may improve detection of subtle anomalies. Ultimately, ultrasound should not be viewed as a standalone diagnostic test for ASD but rather as one component in a multimodal framework aimed at earlier recognition and targeted intervention.

Although these findings suggest that prenatal ultrasound can detect developmental deviations potentially linked to ASD, their diagnostic specificity remains limited. Many of the identified markers — such as ventriculomegaly, increased HC, or renal anomalies — are nonspecific and may occur in fetuses without later neurodevelopmental disorders [56, 57]. This highlights the need for cautious interpretation and underscores that such features should not be considered definitive prenatal predictors of ASD. For example, ventriculomegaly is a relatively common finding with varied outcomes, ranging from normal development to intellectual disability or motor impairment [58]. Similarly, increased HC may also reflect constitutional growth patterns or benign familial macrocephaly [59]. The co-occurrence of non-CNS anomalies, such as pyelectasis or congenital heart disease, may indicate broader developmental disturbances, but these are also seen in other genetic and metabolic conditions unrelated to ASD. It is also important to note that the literature to date predominantly comprises retrospective analyses or small prospective cohorts, often limited by selection bias and variability in ultrasound protocols. While certain brain and organ anomalies were replicated across studies, methodological heterogeneity — differences in gestational age at assessment, imaging resolution, and diagnostic criteria — limits cross-study comparability. Only a few studies integrate genomic analysis alongside prenatal imaging, despite growing evidence that combined phenotypic and genotypic data could enhance early risk stratification [32, 60]. Taken together, current evidence suggests that prenatal ultrasound can provide valuable but indirect signals of ASD risk, and its greatest utility will probably emerge when used with genetic and longitudinal data rather than as a standalone predictive tool.

A key strength of this review lies in its comprehensive scope. By synthesizing findings from multiple disciplines — including obstetrics, genetics, and neurodevelopmental research — it provides a broad overview of prenatal ultrasound findings potentially linked to ASD. The search strategy covered major databases (PubMed, Scopus, Google Scholar) across an extended time frame (2007–2025), and priority was given to systematic reviews, meta-analyzes, and large cohort studies, which improves the reliability of the synthesis. Another strength is the explicit focus on structural anomalies detectable by prenatal ultrasound, addressing a clinically relevant and under-explored domain that bridges obstetric practice with early neurodevelopmental risk assessment.

However, several limitations must be acknowledged. First, as a narrative review, the study is subject to selection bias in the choice of included articles and may not capture all available evidence. Second, the review did not employ formal quality assessment tools, and therefore, its findings should be interpreted with caution due to the varying quality of the included studies. Finally, the heterogeneity across the included studies limits the generalizability of the conclusions.

Despite these limitations, this review provides an important foundation for future systematic investigations and highlights the need for integrated, multimodal approaches to improve the predictive value of prenatal ultrasound in ASD risk assessment.

Future research may need to prioritize large, multicenter prospective studies incorporating standardized imaging protocols, comprehensive postnatal follow-up, and integration with genomic, biochemical, and neurobehavioral data. Such multimodal approaches may improve the predictive accuracy of prenatal ultrasound findings for ASD while clarifying their specificity relative to other neurodevelopmental disorders. Until then, prenatal ultrasound should be considered a screening adjunct — identifying fetuses who may benefit from closer developmental monitoring — rather than a standalone diagnostic tool.

CONCLUSION

Prenatal ultrasound demonstrates the potential for detecting structural anomalies, such as ventriculomegaly, atypical brain growth patterns, and certain extracranial malformations, that may later be associated with ASD. However, these findings are not specific to ASD and may also occur in a range of other neurodevelopmental or genetic conditions, limiting the diagnostic precision of ultrasound as a standalone tool. Therefore, prenatal ultrasound should be regarded as a supportive screening method rather than a definitive diagnostic technique. To improve early detection and risk stratification, future research should focus on integrating prenatal imaging with genetic, metabolic, and other biological markers. Such a multimodal approach could enhance both the sensitivity and specificity of early ASD risk assessment, enabling more timely interventions during critical developmental windows. Large, prospective, and diverse cohort studies will be essential to validate these combined screening strategies and determine their feasibility for routine clinical practice.

Article history
Submitted: 9 Jun. 2025
Accepted: 22 Dec. 2025
Published Online: 27 Feb. 2026

Authors' contribution: Nazyar Khamenehei: theoretical analysis; data collection and interpretation; conceptualization; writing the original draft. Lyudmila Tokarskaya: supervision; revision and editing of the manuscript; research supervision.

Funding: The research was carried out without additional funding.

Conflict of interest: The authors declare no conflicts of interest.

Generative AI use statement: During the preparation of this work, the authors used Grok.AI in order to translate the text from Persian into English. After using this service, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

For citation:
Khamenehei N, Tokarskaya LV. Prenatal Ultrasound–Detected Structural Anomalies Associated with Autism Spectrum Disorder: A Narrative Review. *Consortium PSYCHIATRICUM*. 2026;7(1):CP15700. doi: 10.17816/CP15700

Information about the authors
***Nazyar Khamenehei,** PhD student (General psychology, Personality psychology, History of Psychology), Research Engineer, Ural Federal University named after the first President of Russia B.N. Yeltsin; ORCID: 0000-0003-0190-5007
E-mail: nazyarkh@gmail.com

Lyudmila Valerievna Tokarskaya, Cand. Sci (Psychology), Associate Professor, Deputy Director, Ural Federal University named after the first President of Russia B.N. Yeltsin;
ORCID: 0000-0002-2385-9227

*corresponding author

References

1. Diagnostic and statistical manual of mental disorders. 5th ed. Washington: American Psychiatric Association Publishing; 2013.
2. Maenner MJ, Shaw KA, Bakian AV, et al. Prevalence and Characteristics of Autism Spectrum Disorder Among Children Aged 8 Years — Autism and Developmental Disabilities Monitoring Network, 11 Sites, United States, 2018. MMWR Surveill Summ. 2021;70(11):1–16. doi: 10.15585/MMWR.SS7011A1
3. Zeidan J, Fombonne E, Scorah J, et al. Global prevalence of autism: A systematic review update. Autism Res. 2022;15(5):778–790. doi: 10.1002/aur.2696
4. Issac A, Halemani K, Shetty A, et al. The global prevalence of autism spectrum disorder in children: a systematic review and meta-analysis. Osong Public Health Res Perspect. 2025;16(1):3–27. doi: 10.24171/j.phrp.2024.0286
5. Shaw KA, Williams S, Patrick ME, et al. Prevalence and Early Identification of Autism Spectrum Disorder Among Children Aged 4 and 8 Years — Autism and Developmental Disabilities Monitoring Network, 16 Sites, United States, 2022. MMWR Surveill Summ. 2025;74(2):1–22. doi: 10.15585/mmwr.ss7402a1
6. Kobayashi T, Matsuyama T, Takeuchi M, Ito S. Autism spectrum disorder and prenatal exposure to selective serotonin reuptake inhibitors: A systematic review and meta-analysis. Reprod Toxicol. 2016;65:170–178. doi: 10.1016/j.reprotox.2016.07.016
7. Ohkawara T, Katsuyama T, Ida-Eto M, et al. Maternal viral infection during pregnancy impairs development of fetal serotonergic neurons. Brain Dev. 2015;37(1):88–93. doi: 10.1016/j.braindev.2014.03.007
8. Buescher AV, Cidav Z, Knapp M, Mandell DS. Costs of autism spectrum disorders in the United Kingdom and the United States. JAMA Pediatr. 2014;168(8):721–728. doi: 10.1001/jamapediatrics.2014.210
9. Talantseva OI, Romanova RS, Shurdova EM, et al. The global prevalence of autism spectrum disorder: A three-level meta-analysis. Front Psychiatry. 2023;14:1071181. doi: 10.3389/fpsyt.2023.1071181
10. Santomauro DF, Erskine HE, Mantilla Herrera AM, et al. The global epidemiology and health burden of the autism spectrum: findings from the Global Burden of Disease Study 2021. Lancet Psychiatry. 2025;12(2):111–121. doi: 10.1016/S2215-0366(24)00363-8
11. Masi A, Lampit A, DeMayo MM, et al. A comprehensive systematic review and meta-analysis of pharmacological and dietary supplement interventions in paediatric autism: Moderators of treatment response and recommendations for future research. Psychol Med. 2017;47(7):1323–1334. doi: 10.1017/S0033291716003457
12. Okoye C, Obialo-Ibeawuchi CM, Obajeun OA, et al. Early Diagnosis of Autism Spectrum Disorder: A Review and Analysis of the Risks and Benefits. Cureus. 2023;15(8):e434226. doi: 10.7759/cureus.43226
13. Abualait T, Alabbad M, Kaleem I, et al. Autism Spectrum Disorder in Children: Early Signs and Therapeutic Interventions. Children (Basel). 2024;11(11):1311. doi: 10.3390/children11111311
14. Frye RE, Vassall S, Kaur G, et al. Emerging biomarkers in autism spectrum disorder: a systematic review. Ann Transl Med. 2019;7(23):792. doi: 10.21037/atm.2019.11.53
15. Bryson SE, Zwaigenbaum L, McDermott C, et al. The Autism Observation Scale for Infants: scale development and reliability data. J Autism Dev Disord. 2008;38(4):731–738. doi: 10.1007/s10803-007-0440-y
16. Courchesne E, Gazestani VH, Lewis NE. Prenatal Origins of ASD: The When, What, and How of ASD Development. Trend Neurosci. 2020;43(5):326–342. doi: 10.1016/j.tins.2020.03.005
17. Hazlett HC, Gu H, Munsell BC, et al. Early brain development in infants at high risk for autism spectrum disorder. Nature. 2017;542(7641):348–351. doi: 10.1038/nature21369
18. Dawson G, Rieder AD, Johnson MH. Prediction of autism in infants: progress and challenges. Lancet Neurol. 2023;22(3):244–254. doi: 10.1016/S1474-4422(22)00407-0
19. Elder LM, Dawson G, Toth K, et al. Head circumference as an early predictor of autism symptoms in younger siblings of children with autism spectrum disorder. J Autism Dev Disord. 2008;38(6):1104–1111. doi: 10.1007/s10803-007-0495-9
20. Posar A, Visconti P. Sensory abnormalities in children with autism spectrum disorder. J Pediatr (Rio J). 2018;94(4):342–350. doi: 10.1016/j.jped.2017.08.008
21. Jensen AR, Lane AL, Werner BA, et al. Modern Biomarkers for Autism Spectrum Disorder: Future Directions. Mol Diagn Ther. 2022;26(5):483–495. doi: 10.1007/s40291-022-00600-7
22. Nordahl CW, Scholz R, Yang X, et al. Increased rate of amygdala growth in children aged 2 to 4 years with autism spectrum disorders: a longitudinal study. Arch Gen Psychiatry. 2012;69(1):53–61. doi: 10.1001/archgenpsychiatry.2011.145
23. Hiremath CS, Sagar KJV, Yamini BK, et al. Emerging behavioral and neuroimaging biomarkers for early and accurate characterization of autism spectrum disorders: a systematic review. Transl Psychiatry. 2021;11(1):42. doi: 10.1038/s41398-020-01178-6
24. Falck-Ytter T, Bölte S, Gredebäck G. Eye tracking in early autism research. J Neurodev Disord. 2013;5(1):28. doi: 10.1186/1866-1955-5-28
25. Nayar K, Shic F, Winston M, Losh M. A constellation of eye-tracking measures reveals social attention differences in ASD and the broad autism phenotype. Mol Autism. 2022;13(1):18. doi: 10.1186/s13229-022-00490-w
26. Parellada M, Andreu-Bernabeu Á, Burdeus M, et al. In Search of Biomarkers to Guide Interventions in Autism Spectrum Disorder: A Systematic Review. Am J Psychiatry. 2023;180(1):23–40. doi: 10.1176/APPI.AJP.21100992
27. Jin F, Wang Z. Mapping the structure of biomarkers in autism spectrum disorder: a review of the most influential studies. Front Neurosci. 2024;18:1514678. doi: 10.3389/fnins.2024.1514678

28. Zamłyński M, Zhemela O, Olejek A. Isolated Fetal Ventriculomegaly: Diagnosis and Treatment in the Prenatal Period. Children (Basel). 2024;11(8):957. doi: 10.3390/children11080957
29. Aydin E, Tsompanidis A, Chaplin D, et al. Fetal brain growth and infant autistic traits. Mol Autism. 2024;15(1):11. doi: 10.1186/s13229-024-00586-5
30. Allison C, Auyeung B, Baron-Cohen S. Toward brief "Red Flags" for autism screening: The Short Autism Spectrum Quotient and the Short Quantitative Checklist for Autism in Toddlers in 1,000 cases and 3,000 controls. J Am Acad Child Adolesc Psychiatry. 2012;51(2):202–212.e7. doi: 10.1016/j.jaac.2011.11.003
31. Hobbs K, Kennedy A, Dubray M, et al. A retrospective fetal ultrasound study of brain size in autism. Biol Psychiatry. 2007;62(9):1048–1055. doi: 10.1016/j.biopsych.2007.03.020
32. Regev O, Shil A, Bronshtein T, et al. Association between rare, genetic variants linked to autism and ultrasonography fetal anomalies in children with autism spectrum disorder. J Neurodev Disord. 2024;16(1):55. doi: 10.1186/s11689-024-09573-6
33. Popa AI, Cernea N, Marinaș MC, et al. Ultrasound Screening in the First and Second Trimester of Pregnancy for the Detection of Fetal Cardiac Anomalies in a Low-Risk Population. Diagnostics (Basel). 2025;15(6):769. doi: 10.3390/diagnostics15060769
34. Ong LT. Editor's Pick: Genetics and Pathophysiology of Co-occurrence of Congenital Heart Disease and Autism Spectrum Disorder. Eur Med J. 2024;9(2):73–83. doi: 10.33590/emj/mkpn4473
35. Jenabi E, Bashirian S, Fariba F, Naghshtabrizi B. The association between congenital heart disease and the risk of Autism spectrum disorders or attention-deficit/hyperactivity disorder among children: a meta-analysis. Eur J Psychiatry. 2022;36(2):71–76. doi: 10.1016/j.ejpsy.2021.10.001
36. Teerikorpi N, Lasser MC, Wang S, et al. Ciliary biology intersects autism and congenital heart disease. bioRxiv 602578 [Preprint]. 2024 [cited 2025 Dec 12]. Available from: https://www.biorxiv.org/content/10.1101/2024.07.30.602578v1. doi: 10.1101/2024.07.30.602578
37. Gu S, Zhang Q, Katyal A, et al. 9 Congenital Heart Disease and Autism Spectrum Disorders: Is There a Link? Paediatr Child Health. 2022;27(Suppl 3):e4. doi: 10.1093/pch/pxac100.008
38. Jing XY, Huang LY, Zhen L, et al. Prenatal diagnosis of 17q12 deletion syndrome: a retrospective case series. J Obstet Gynaecol. 2019;39(3):323–327. doi: 10.1080/01443615.2018.1519693
39. Liu Y, Huang Q, Han X, et al. Atrial Septal Defect Detection in Children Based on Ultrasound Video Using Multiple Instances Learning. J Imaging Inform Med. 2024;37(3):965–975. doi: 10.1007/s10278-024-00987-1
40. Dachew BA, Mamun A, Maravilla JC, Alati R. Pre-eclampsia and the risk of autism-spectrum disorder in offspring: meta-analysis. Br J Psychiatry. 2018;212(3):142–147. doi: 10.1192/bjp.2017.27
41. Zhang M, Jin H, Liu X. Preeclampsia is associated with an increased risk of autism spectrum disorder (ASD): A systematic review and meta-analysis. Asian J Surg. 2022;45(11):2521–2523. doi: 10.1016/j.asjsur.2022.05.133
42. Carter SA, Lin JC, Chow T, et al. Maternal obesity, diabetes, preeclampsia, and asthma during pregnancy and likelihood of autism spectrum disorder with gastrointestinal disturbances in offspring. Autism. 2023;27(4):916–926. doi: 10.1177/13623613221118430
43. Regev O, Hadar A, Meiri G, et al. Association between ultrasonography foetal anomalies and autism spectrum disorder. Brain. 2022;145(12):4519–4530. doi: 10.1093/brain/awac008
44. Nayar K, Katz L, Heinrich K, Berger N. Autism spectrum disorder and congenital heart disease: a narrative review of the literature. Cardiol Young. 2023 Jun;33(6):843–853. doi: 10.1017/S1047951123000598
45. Spinazzi NA, Santoro JD, Pawlowski K, et al. Co occurring conditions in children with Down syndrome and autism: a retrospective study. J Neurodev Dis. 2023;15(1):9. doi: 10.1186/s11689-023-09478-w
46. University of California. Study may show a way to predict whether children with a genetic disorder will develop autism or psychosis [Internet]. 2015 [cited 2025 Dec 12]. Available from: https://medicalxpress.com/news/2015-07-children-genetic-disorder-autism-psychosis.html
47. Roberts JE, Bradshaw J, Will E, et al. Emergence and rate of autism in fragile X syndrome across the first years of life. Dev Psychopathol. 2020;32(4):1335–1352. doi: 10.1017/S0954579420000942
48. Bottelli L, Franzè V, Tuo G, et al. Prenatal detection of congenital heart disease at 12–13 gestational weeks: detailed analysis of false-negative cases. Ultrasound Obstet Gynecol. 2023;61(5):577–586. doi: 10.1002/uog.26094
49. Ling W, Wu Q, Guo S, et al. Four-section approach of fetal congenital heart disease at 11–13+6 weeks. Front Cardiovasc Med. 2023;10:1206042. doi: 10.3389/fcvm.2023.1206042
50. Yang S, Qin G, He G, et al. Evaluation of first-trimester ultrasound screening strategy for fetal congenital heart disease. Ultrasound Obstet Gynecol. 2025;65(4):478–486. doi: 10.1002/uog.29186
51. Fulceri F, Guzzetta A, Athanasiadou A, et al. Antenatal ultrasound value in risk calculation for Autism Spectrum Disorder: A systematic review to support future research. Neurosci Biobehav Rev. 2018;92:83–92. doi: 10.1016/j.neubiorev.2018.05.016
52. Oancea M, Grigore M, Ciortea R, et al. Uterine artery doppler ultrasonography for first trimester prediction of preeclampsia in individuals at risk from low-resource settings. Medicina (Kaunas). 2020;56(9):428. doi: 10.3390/medicina56090428
53. Lai J, Syngelaki A, Nicolaides KH, et al. Using ultrasound and angiogenic markers from a 19- to 23-week assessment to inform the subsequent diagnosis of preeclampsia. Am J Obstet Gynecol. 2022;227(2):294.e1–294.e11. doi: 10.1016/j.ajog.2022.03.007
54. Kong L, Chen X, Liang Y, et al. Association of Preeclampsia and Perinatal Complications with Offspring Neurodevelopmental and Psychiatric Disorders. JAMA Netw Open. 2022;5(1):e2145719. doi: 10.1001/jamanetworkopen.2021.45719
55. Stoner R, Chow ML, Boyle MP, et al. Patches of disorganization in the neocortex of children with autism. N Engl J Med. 2014;370(13):1209–1219. doi: 10.1056/nejmoa1307491
56. Stochholm K, Juul S, Christiansen JS, Gravholt CH. Mortality and socioeconomic status in adults with childhood-onset

GH deficiency (GHD) is highly dependent on the primary cause of GHD. Eur J Endocrinol. 2012;167(5):663–670. doi: 10.1530/EJE-11-1084
57. Melchiorre K, Bhide A, Gika AD, et al. Counseling in isolated mild fetal ventriculomegaly. Ultrasound Obstet Gynecol. 2009;34(2):212–224. doi: 10.1002/uog.7307
58. Ouahba J, Luton D, Vuillard E, et al. Prenatal isolated mild ventriculomegaly: Outcome in 167 cases. BJOG. 2006;113(2):1072–1079. doi: 10.1111/j.1471-0528.2006.01050.x
59. Accogli A, Geraldo AF, Piccolo G, et al. Diagnostic approach to macrocephaly in children. Front in Pediatr. 2022;9:794069. doi: 10.3389/fped.2021.794069
60. Lombardo MV, Eyler L, Pramparo T, et al. Atypical genomic cortical patterning in autism with poor early language outcome. Sci Adv. 2021;7(36):eabh1663. doi: 10.1126/sciadv.abh1663