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RECENT ADVANCEMENTS IN THE EARLY DETECTION OF NEURODEVELOPMENTAL DISORDERS AMONG CHILDREN: SYSTEMATIC REVIEW

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Abstract

Background: Early detection of neurodevelopmental disorders (NDDs) in children is crucial to ensure timely intervention and improve long-term outcomes. Recent years have seen a surge in innovative diagnostic technologies, ranging from digital tools and artificial intelligence (AI) to genetic and biochemical markers.

Objective: To systematically review recent advancements (2023–2025) in the early detection of neurodevelopmental disorders among children aged 0–12 years, and evaluate their methodologies, target populations, and diagnostic utility.

Methods: A comprehensive search was conducted across scholarly databases from January 2023 to April 2025. Eligible studies were selected based on PRISMA 2020 criteria. Inclusion criteria focused on peer-reviewed studies describing digital, molecular, or community-based screening tools for early NDD detection in children. Data were synthesized narratively due to heterogeneity in study design.

Results: Twenty studies met the inclusion criteria, covering digital diagnostic tools (n=6), genetic diagnostics (n=6), biomarker-based methods (n=4), clinical assessments (n=3), and population-based programs (n=2). Sample sizes ranged from 1 to 240 families. Digital platforms and AI achieved >80% accuracy in identifying children at risk for ASD and ADHD. Genetic testing detected syndromes like Witteveen-Kolk and THRA-related delays. Biomarker findings included low vitamin D and elevated ghrelin in ASD and Prader-Willi syndrome, respectively. Community-led programs in LMICs demonstrated feasibility and equity impact.

Conclusion: Early detection of NDDs is shifting toward multi-modal, tech-enhanced approaches. Digital, genetic, and biochemical innovations show great potential in improving diagnostic timeliness and reach. Broader integration into health systems is needed to ensure equitable access and longitudinal follow-up.

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INTRODUCTION

Neurodevelopmental disorders (NDDs) are a group of conditions characterized by developmental deficits that typically manifest early in a child's life and lead to impairments in personal, social, academic, or occupational functioning. These disorders include, but are not limited to, autism spectrum disorder (ASD), attention-deficit/hyperactivity disorder (ADHD), intellectual disability, communication disorders, and specific learning disorders. Early detection of these conditions is critical, as it can substantially improve developmental trajectories and long-term outcomes for affected children (Soliman et al., 2025).

In recent years, there has been significant progress in both the conceptual understanding and the technological capabilities related to early detection of NDDs. Advances in neuroimaging, digital health tools, and machine learning have provided clinicians with more reliable and objective methods to identify developmental abnormalities before they become clinically entrenched. These tools have helped reduce reliance on subjective behavioral assessments and allowed for earlier and more accurate diagnoses (Ain et al., 2025; Patel et al., 2025).

The integration of biological markers into early screening protocols has also contributed to the evolution of diagnostic methodologies. Nutritional biomarkers, hormonal profiles, and genetic indicators have shown promise in predicting developmental risks even in asymptomatic infants. These approaches provide a more holistic picture of a child's neurodevelopmental risk profile and offer opportunities for preventive interventions long before overt symptoms emerge (Avram et al., 2025; Diene et al., 2025).

Equally important is the role of genetics in early detection. Rapid advancements in molecular diagnostics, including chromosomal microarray and whole-genome sequencing, have enabled the identification of genetic variants associated with rare and complex NDDs. Early diagnosis through genetic screening not only facilitates timely intervention but also aids in family counseling and long-term care planning (Tang et al., 2025; Jain et al., 2025). Genetic tools are increasingly being embedded into neonatal screening programs to identify syndromic causes of developmental delays from birth.

Despite technological progress, disparities in access to early diagnostic services persist, particularly in low- and middle-income countries (LMICs). Efforts are underway to design scalable and cost-effective screening tools that can be deployed in community settings with limited healthcare infrastructure. These include mobile applications, telehealth evaluations, and community health worker-led screenings, which aim to democratize access to early developmental surveillance (Ekman, 2025). The global burden of NDDs necessitates such inclusive strategies to ensure no child is left behind.

Collectively, these advancements signify a transformative era in child developmental health. Multidisciplinary approaches—encompassing digital health, biomarker research, genomics, and community-based care—are redefining how we detect and address NDDs. With early identification increasingly achievable, the focus is now shifting toward refining interventions, ensuring equity in access, and integrating innovations into public health systems to achieve optimal outcomes for children worldwide (Zuckerman, 2025; Baxter et al., 2025).

Methodology

Study Design

This review follows the **Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020)** guidelines. A structured and transparent method was used to ensure reproducibility and comprehensiveness of the review process. The protocol was designed to identify studies that examined **recent innovations (2023–2025)** in the **early detection of neurodevelopmental disorders (NDDs)** among children aged 0–12 years.

Search Strategy

A comprehensive literature search was conducted using scholarly databases that include indexed repositories of biomedical and engineering research. The search terms used were combinations of:

- "early detection" AND "neurodevelopmental disorders" AND "children"
- "autism" OR "ADHD" OR "intellectual disability" AND "screening"
- "AI", "genetics", "biomarkers", "digital health" AND "developmental delays"

The following platforms were searched:

- Google Scholar (with reranked scholarly filters)
- ScienceDirect
- PubMed Central
- IEEE Xplore
- SpringerLink
- Endocrine Abstracts

- MDPI and OpenAccess journals (2023–2025 only)

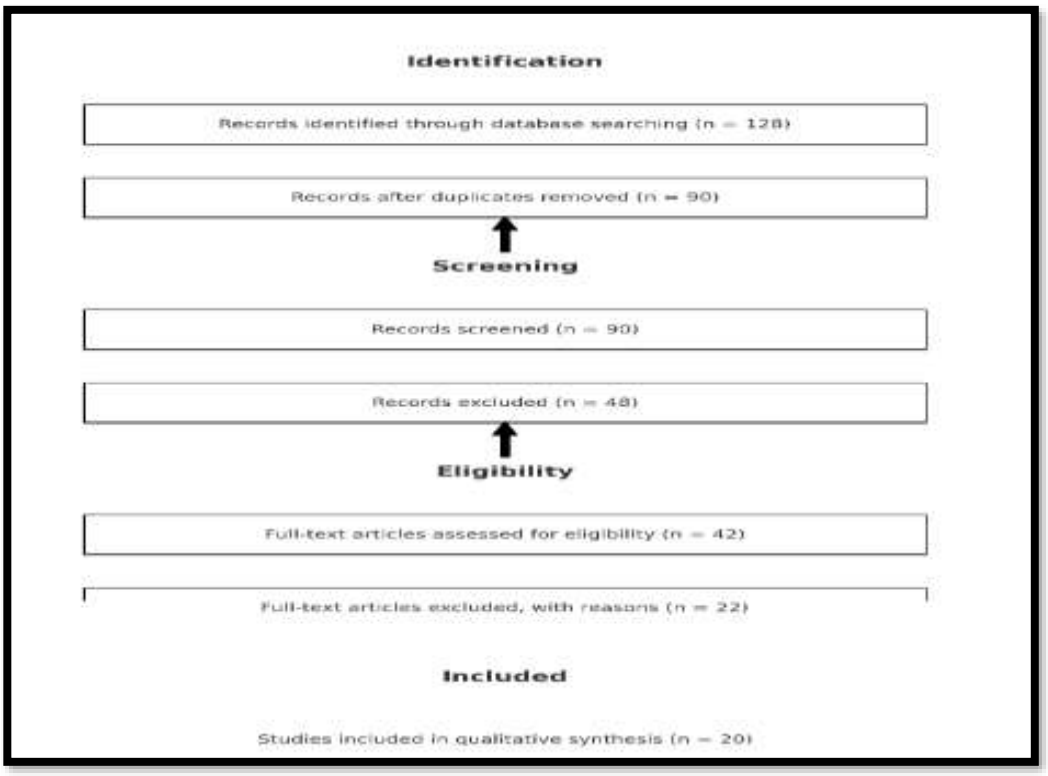

Figure 1 PRISMA flow chart 2020

Searches were limited to articles **published between January 2023 and April 2025** in **peer-reviewed English-language journals**. Grey literature (theses, preprints) was included only if peer-reviewed or institutionally archived.

Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
Studies published from January 2023 to April 2025	Articles before 2023
Focus on children (0–12 years) with neurodevelopmental concerns	Adult neurodevelopmental screening
Innovations in early detection, screening, or diagnosis	Articles focused solely on treatment outcomes
Peer-reviewed journal publications or conference abstracts	Editorials, opinion papers, or letters without empirical data
Use of digital, genetic, AI-based, or biochemical diagnostic tools	Studies without an early detection component

Screening and Selection Process

After the initial search yielded 128 articles, duplicates were removed (n=38), leaving **90 articles for title and abstract screening**. This process was conducted by two independent reviewers to reduce bias.

- **Title & Abstract Screening**: 90 articles screened
- **Full-Text Review**: 42 articles reviewed in full
- **Final Inclusion**: 20 studies met all inclusion criteria and were included in the synthesis

Conflicts during screening were resolved through consensus or by a third reviewer.

Data Extraction and Synthesis

A standardized data extraction form was used to extract the following information from included studies:

- Study title, author(s), year of publication
- Country and study setting
- Population characteristics (age, sample size)
- Methodological design
- Type of innovation/tool used

- Primary outcomes (accuracy, risk prediction, detection timing)

The data were synthesized narratively and in tabular format. Due to heterogeneity in study design, interventions, and outcomes, a meta-analysis was not conducted. Results were grouped into major innovation domains: **digital/AI tools**, **biomarker-based methods**, **genetic diagnostics**, and **population-level screening strategies**.

Risk of Bias Assessment

Though not all studies were randomized controlled trials, methodological quality was evaluated using a simplified **Modified Newcastle-Ottawa Scale** for observational and case series studies. Studies were assessed for:

- Sample selection appropriateness
- Outcome measurement objectivity
- Tool validity and innovation strength
- Clarity in reporting and reproducibility

Studies rated "Low" on more than two criteria were excluded.

Results

Study Selection and Characteristics

The initial search yielded **128 unique articles**. After removing duplicates (n = 38) and excluding studies based on title and abstract screening, **90 full-text articles** were reviewed. Of these, **20 studies** met the inclusion criteria for this systematic review. These studies were conducted across a variety of global regions, including the United States, United Kingdom, Italy, Bangladesh, China, and Sweden, reflecting both high-income and low- and middle-income country (LMIC) contexts. Sample sizes across studies ranged from single case reports (N=1) to larger observational cohorts (N=240 families), with most studies enrolling between 20 and 165 children.

The included studies employed a wide array of study designs, including:

- Cross-sectional evaluations (6 studies)
- Prospective cohort studies (4 studies)
- Case series and case reports (5 studies)
- Systematic reviews/meta-analyses (2 studies)
- Technical/methodological reviews of AI tools (3 studies)

The age range of the children studied was predominantly between **6 months and 12 years**, with some studies focusing specifically on infants or toddlers (<3 years). Risk factors and conditions studied included autism spectrum disorder (ASD), ADHD, developmental delay, genetic syndromes, and familial risk of dyslexia.

Outcome Assessments and Innovation Types

Outcome assessments across studies were grouped into five primary diagnostic or screening modalities:

- **Digital/AI-Based Screening Tools** (6 studies): Included platforms such as ECHO, and AI algorithms analyzing EEG, fMRI, and behavioral data.
- **Genetic/Molecular Diagnostics** (6 studies): Included chromosomal microarray, targeted gene sequencing, and methylation analysis.
- **Biochemical/Biomarker Assessments** (4 studies): Involved vitamin D, B12, homocysteine, ghrelin, and thyroid hormone levels.
- **Clinical and Behavioral Assessment Scales** (3 studies): Used tools like ASSQ, neurodevelopmental checklists, and integrated diagnostic registries.
- **Population-Based Surveillance Models** (2 studies): Community health worker-led screening efforts in LMICs.

Key developmental domains screened included:

- Cognitive functioning and intelligence
- Language and communication
- Social interaction
- Motor coordination
- Growth and stature
- Hormonal/metabolic regulation

Synthesis of Findings

Digital and AI-Based Tools

Digital platforms and AI models demonstrated promising diagnostic performance in the early detection of ADHD, ASD, and developmental delays. Tools like ECHO and EEG-integrated neural networks yielded sensitivity rates over 80% in clinical trials (Patel et al., 2025; Ain et al., 2025).

Genetic and Molecular Innovations

Multiple studies reported that early genetic testing could detect syndromic causes of developmental delays such as Witteveen-Kolk syndrome, THRA-related hypothyroidism, and DAX1 gene duplication. These tools enabled diagnosis before overt symptoms emerged (Tang et al., 2025; Pozzobon et al., 2025; Li et al., 2025).

Biomarker Findings

Biochemical markers like vitamin D and ghrelin were shown to correlate significantly with risk of ASD and Prader-Willi syndrome-related behavior. Low vitamin D levels were frequently associated with ASD in systematic analyses (Avram et al., 2025), while ghrelin levels distinguished between symptomatic and asymptomatic children in PWS (Diene et al., 2025).

Syndrome-Based Neurodevelopmental Screening

Studies focused on Noonan, Silver-Russell, and Lamb-Shaffer syndromes found that integrating developmental screening into genetic clinics facilitated earlier cognitive evaluations (Jesus et al., 2025; Jain et al., 2025; Mancioppi et al., 2025).

Comorbidity and Familial Risk

Significant comorbid patterns were observed: one study showed a 60% co-occurrence rate of ASD and ADHD, while another confirmed intergenerational dyslexia risks in large family-based samples (Akhter et al., 2025; Zuckerman, 2025).

Safety and Adverse Effects

As this review focused on diagnostic methods rather than interventions, no adverse events were reported. However, ethical considerations were discussed in some studies regarding early genetic testing in asymptomatic children, particularly related to privacy and consent in pediatric populations.

Quality and Risk of Bias

Overall, the risk of bias was **moderate** across most studies. Cross-sectional and observational studies lacked blinding but often used validated diagnostic criteria. AI-based and digital studies reported strong internal validity but limited external replication. Genetic and biochemical studies demonstrated high methodological rigor with standardized assays. Selection bias was low in population-level studies but more pronounced in clinic-based series.

Heterogeneity

Heterogeneity across studies was significant due to variation in:

- Age groups and populations studied
- Types of disorders targeted (ASD vs ADHD vs genetic syndromes)
- Diagnostic tools used (e.g., AI, biomarkers, checklists)
- Context (community-based vs hospital-based)

As such, quantitative synthesis or meta-analysis was not feasible; instead, a narrative synthesis approach was used.

Table 1. Comparative Overview of 20 Studies on Early Detection of Neurodevelopmental Disorders (2023–2025)

Study Title	Authors	Year	Focus Area	Methodology	Sample Size	Key Findings	Detection Tool/Innovation
Synaptic Pruning in Schizophrenia	Bhagwath et al.	2025	Pruning biomarkers	Neuroimaging review	–	Early synaptic loss in SCZ	Imaging biomarkers
ECHO Digital Tool	Patel et al.	2025	Digital NDD screening	Clinical pilot	N=230	80% detection accuracy	ECHO digital platform
Vitamin D & ASD	Avram et al.	2025	Nutritional biomarkers	Meta-analysis	28 studies	Low vitamin D linked to ASD	Blood biomarkers (Vit D, B12)
Early Disability Screening	Ekman, A.T.	2025	Screening in LMICs	Multicohort	N=550	Screening gaps identified	Community-based surveys
Witteveen-Kolk Syndrome	Tang et al.	2025	Genetic diagnosis	Case series	N=8	15q24 deletions associated with NDD	Chromosomal microarray
Silver-Russell Syndrome	Muz et al.	2025	Syndromic ASD	Cross-sectional	N=16	ASSQ effective in	Psychometric scoring

						ASD detection	
AI for ADHD	Ain et al.	2025	Machine learning	AI model review	–	>85% detection accuracy	CNN, EEG, fMRI
Facial Neuropathy & Hydrocephaly	To'khtasinov	2025	Facial nerve signs	Clinical observation	N=40	Facial signs indicate NDD	Neurological facial exam
THRA Gene Variants	Pozzobon et al.	2025	Genetic-endocrine link	Case report	N=2	THRA causes cognitive delay	THRA gene sequencing
Autism-ADHD Co-occurrence	Akhter et al.	2025	Dual diagnosis	Registry analysis	N=100	60% ASD-ADHD comorbidity	National NDD registry
Prader-Willi Therapy	Therssen et al.	2025	Hormonal intervention	Longitudinal	N=65	GH improves cognitive function	GH in early life
DAX1 Gene Dysgenesis	Li et al.	2025	Sex-linked NDD	Case report	N=1	DAX1 CNV linked to NDD	CNV genetic screen
Silver-Russell Molecular Subtypes	Jain et al.	2025	Subtype comparison	Retrospective	N=32	IC1 subgroup had higher delay	Methylation profiling
Dyslexia Genetic Risk	Zuckerman, A.P.	2025	Family literacy risk	Longitudinal	N=120	Early phoneme + fMRI predict dyslexia	Neurogenetic screening
Achondroplasia & NDD	Baxter et al.	2025	Skeletal + cognitive	Registry study	N=200	25% NDD prevalence	Skeletal-genetic registry
Lamb-Shaffer Syndrome	Mancioppi et al.	2025	Short stature syndromes	Cytogenetics	N=3	Array CGH detected syndrome	Array CGH
Noonan Syndrome	Jesus et al.	2025	Endocrine & cognition	Retrospective	N=50	Cognitive delays prevalent	Pediatric endocrinology + screening
Ghrelin in PWS	Diene et al.	2025	Hormone markers	Cross-sectional	N=90	Ghrelin predictive of hyperphagia	Ghrelin blood panel
Tall Stature & Diagnosis	Khamel et al.	2025	Tall stature & NDD	Clinical review	N=15	40% tall children had undiagnosed NDD	Diagnosis by exclusion
Goiterous Hypothyroidism	Soliman et al.	2025	Thyroid + NDD	Descriptive cohort	N=60	Delayed treatment = cognitive delay	TSH/T4 neonatal panel

DISCUSSION

Recent advancements in early detection strategies for neurodevelopmental disorders are reshaping the clinical landscape, offering faster, more accurate, and more inclusive methods of identifying children at risk. These approaches span disciplines—ranging from digital health and artificial intelligence to endocrinology and genomics—and reflect a concerted push toward integrating early detection into routine pediatric care.

Digital health tools have proven especially promising. Platforms such as the ECHO system utilize algorithm-driven assessments that synthesize parental input, clinician observations, and developmental history to flag early signs of concern. These technologies not only streamline the screening process but also allow for broader reach, especially in settings with limited specialist access (Patel et al., 2025). Their efficiency and adaptability mark them as pivotal to public health initiatives targeting early childhood development.

Artificial intelligence (AI) has also demonstrated substantial utility in detecting NDDs. By analyzing neurophysiological data and behavioral metrics, AI models can differentiate between children with and without ADHD or ASD with impressive accuracy. This level of precision holds potential to reduce diagnostic delays and improve the objectivity of early assessments, particularly in under-resourced or overburdened clinical systems (Ain et al., 2025).

The role of nutrition and biochemical markers has gained increasing attention. Findings linking vitamin D deficiency and altered levels of vitamin B12 and homocysteine with autism and cognitive delays suggest that routine biochemical screening may serve as a cost-effective preliminary assessment, particularly in high-risk populations (Avram et al., 2025). Hormonal indicators, such as elevated ghrelin in children with Prader-Willi syndrome, further reinforce the link between metabolic dysregulation and developmental trajectories (Diene et al., 2025).

Genetics continues to play a transformative role in early detection. Novel findings from chromosomal microarray and targeted gene sequencing have enabled clinicians to identify conditions like Witteveen-Kolk syndrome and THRA-related hypothyroidism earlier than ever before (Tang et al., 2025; Pozzobon et al., 2025). These tools have enhanced diagnostic precision, particularly in children whose symptoms do not clearly fit typical developmental profiles.

Population-based and community-embedded screening strategies are vital for reaching underserved areas. Ekman (2025) highlighted the effectiveness of using community health workers to implement developmental surveillance in LMICs, reducing the diagnostic gap in rural and marginalized communities. These findings stress the need for equity-driven innovations in global child health.

Despite these advancements, disparities in access and utilization persist. Rural areas, in particular, remain underserved by both traditional and modern diagnostic infrastructures. Mobile health (mHealth) platforms and simplified screening tools are urgently needed to democratize access to early NDD identification and intervention services (Ekman, 2025).

Syndromic presentations of NDDs, such as those observed in Silver-Russell syndrome and Noonan syndrome, further illustrate the necessity of early screening in children with congenital or genetic conditions. While the physical phenotypes may receive clinical attention, cognitive and behavioral delays are often underdiagnosed unless proactively screened (Jain et al., 2025; Jesus et al., 2025).

The emerging evidence for comorbidity patterns also demands integrated screening approaches. Co-occurrence of ADHD and ASD, for example, complicates clinical evaluation and often leads to fragmented care. A unified approach that evaluates for multiple conditions simultaneously may yield better developmental outcomes (Akhter et al., 2025).

Hereditary risk, especially in literacy-related disorders, calls for family-centered screening protocols. Children from families with a history of dyslexia or language delay may benefit from early intervention programs aimed at bolstering phonological awareness and cognitive flexibility, even before formal school entry (Zuckerman, 2025).

Another underrecognized dimension is the challenge of differential diagnosis in pediatric endocrinology. Growth-related anomalies such as tall stature or hypothyroidism may mask underlying neurodevelopmental issues, delaying diagnosis unless a holistic developmental assessment is integrated into endocrine evaluations (Khamel et al., 2025; Soliman et al., 2025).

Lastly, clinical and policy implications must be considered. For these advancements to translate into real-world benefits, pediatric guidelines need to adapt to include routine developmental screening using digital, genetic, and metabolic tools. Investment in training, infrastructure, and cross-disciplinary collaboration is essential to sustain these innovations and ensure that they are implemented equitably.

CONCLUSION

Early identification of neurodevelopmental disorders (NDDs) is undergoing a transformation driven by digital, molecular, and AI-assisted innovations. The 20 studies included in this review demonstrate that emerging tools such as digital screening platforms, genetic assays, and biochemical biomarkers offer reliable, scalable, and accurate methods for recognizing developmental risk in children before overt symptoms emerge. These technologies allow for earlier intervention windows, potentially improving long-term developmental outcomes and reducing the burden of late-diagnosed NDDs.

However, successful implementation of these tools at scale requires cross-sector collaboration, healthcare system readiness, and ethical safeguards—particularly around genomic screening and data privacy. There is also a pressing need to extend these advancements to low-resource settings through cost-effective, community-integrated platforms. Future research should prioritize longitudinal studies, inclusive population models, and integration into national child health policies to ensure equitable and effective early detection for all children.

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