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REVIEW ARTICLE

INTRAUTERINE GROWTH RESTRICTION OUTCOMES AT THE AGE OF 2 IN RESOURCE – LIMITED SETTINGS: A SYSTEMATIC REVIEW

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ABSTRACT

Despite significant advances in neonatal and child health, morbidity related to intrauterine growth restriction (IUGR) remains concerning, particularly in developing countries where resources are limited and geographical and socioeconomic disparities persist. This study aims to describe the clinical, nutritional, and developmental outcomes of children born with IUGR at 2 years of age, as reported in previous studies. It identifies the main findings from the selected literature and proposes ways to improve monitoring. A bibliographic search was conducted using PubMed, Science Direct, and Google Scholar. A total of 15 studies were included. The systematic review was performed in accordance with the PRISMA checklist. Most studies have shown abnormalities related to the health of children born with IUGR at the age of 2 years, including height and weight retardation; cognitive, mental, language, visual, respiratory, neurological, and metabolic impairments; developmental delay in general; and affected social skills. However, two studies showed no significant differences in height and weight or in developmental and behavioral outcomes at 2 years of age. This systematic review highlights several strong and consistent trends, despite differences in methodology, health contexts, and populations studied.

Keywords: *intrauterine growth restriction (IUGR), intrauterine growth retardation, consequences of IUGR, outcome at 2 years, IUGR morbidity*

INTRODUCTION

Intrauterine growth restriction (IUGR), defined as the failure of a fetus to achieve its genetically determined growth potential, affects approximately 5-10% of all pregnancies worldwide [1, 2]. It is most commonly caused by placental insufficiency, maternal malnutrition, hypertension, or smoking, and is associated with increased risks of perinatal morbidity, mortality, and longterm developmental impairments [3, 4]. Despite significant advances in neonatal and child health, morbidity related to IUGR remains concerning, particularly in developing countries where resources are limited and geographical and socioeconomic disparities persist [5].

Infants with IUGR often present with low birth weight (< 10th percentile for gestational age), but the condition is distinct from being simply small for gestational age (SGA) because IUGR implies an active process of growth restriction with potential alterations in organ structure and function [6, 7]. While some children demonstrate spontaneous catchup growth during the first two years of life [8], others remain with persistent growth deficits, neurodevelopmental delays, and metabolic disturbances [9, 10].

The first two years of life represent a critical window for brain development, synaptogenesis,

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and motor skill acquisition. Adverse intrauterine conditions can disrupt these processes, leading to longterm consequences in cognition, language, fine motor skills, and social behavior [11, 12]. Several studies have reported that by 2 years of age, IUGR children may exhibit significant neurodevelopmental delay, including mental retardation and impaired psychomotor development [13-15]. Language delay and motor coordination impairment have also been documented at 24 months [16].

However, the literature shows notable heterogeneity in outcomes. Some cohorts show persistent delay in growth and weight gain with head circumference below -2 standard deviations (< -2 SD) [17], whereas others report no difference in body mass index (BMI) growth rate by age [8]. Metabolic abnormalities such as hyperinsulinemia and low adiponectin – have been detected as early as 2 years [8]. but not all studies have replicated these findings. Additionally, two studies have shown no significant differences in height and weight or in developmental and behavioral outcomes at 2 years of age [18, 19].These discrepancies may arise from differences in IUGR severity, gestational age at birth, postnatal nutrition, assessment tools, and sample characteristics [20].

Given the persistent gaps in knowledge and the lack of a recent synthesis focusing specifically on 2-year outcomes, this systematic review aims to describe the clinical, nutritional, and developmental outcomes of children born with IUGR at 2 years of age, as reported in previous studies. It identifies the main findings from the selected literature and proposes ways to improve monitoring and early intervention.

MATERIALS AND METHODS

Study design and PRISMA guidelines

This systematic review was conducted in accordance with the 2020 PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) statement (https://www.prisma-statement.org/) to ensure a transparent, reproducible, and unbiased selection of articles addressing our research question.

Search strategy

A literature search was conducted using three online databases: PubMed, ScienceDirect, and Google Scholar. The search strategy included the following keywords and concepts: “intrauterine growth restriction”, “intrauterine growth retardation”, “consequences of intrauterine growth restriction”, “complications of intrauterine growth restriction”, and “outcomes at 2 years”. The search was limited to articles published in English or French between 2010 and 2025.

Eligibility criteria

Studies that met the following criteria were included: (1) included the predefined keywords; and (2) assessed the health status of children born with intrauterine growth restriction (IUGR) at 24 months of age; (3) the articles must be original research (observational studies, cohort studies, systematic reviews, or meta-analyses) and (4) they must provide sufficient data on clinical, nutritional, or developmental outcomes.

Exclusion criteria: Duplicate publications, studies without full-text publications, articles that did not meet the inclusion criteria, and those lacking the information necessary for our research objective (e.g. incomplete data, poor study quality, or an inappropriate article type). Fifteen articles were selected for inclusion in this systematic review.

Data extraction and collection

The selected articles underwent a normative analysis of their content structure and classification. For each study, information was extracted on study design, sample size, definition of intrauterine growth restriction, follow-up age (24 months), and reported outcomes (growth, neurodevelopment, language, motor skills, metabolism, etc.). Data collection involved organizing and structuring the extracted information to identify converging ideas, comparing divergent viewpoints, and drawing evidence-based conclusions.

RESULTS

A total of 15 studies met the inclusion criteria and were included in this systematic review. The studies were published between 2010 and 2025 and originated from 10 countries: Spain (n = 4), France (n = 3), the Netherlands (n = 2), Italy (n = 1), Germany (n = 1), the United States (n = 1), the United Kingdom (n = 1), Austria (n = 1), Iran (n = 1), and Portugal (n = 1). Study designs included retrospective cohorts (n = 7), prospective cohorts (n = 3), observational studies (n = 2), one metaanalysis, one systematic review, and one randomized trial (DIGITAT). Sample sizes ranged from 42 to over 52,000 children. Followup assessment at 2 years (corrected age where specified) was available for all studies (Table 1).

Persistent delay in growth and weight gain was reported in several studies [7, 13, 14, 17]. Malnutrition and head circumference below < -2 SD were also noted [17]. In contrast, Crume et al. [8] found no difference in BMI growth rate at 2 years, although metabolic abnormalities were present. Gascoin & Flamant [3] reported no failure to fall in weight by 2 years.

Neurodevelopmental delay was the most frequent finding, appearing in 11 studies. Sacchi et al. [1] documented cognitive delay in a large metaanalysis.

Table 1. Summary of the results of the identified studies

First author, country, year	Study design and sample size	Age of followup	Outcomes at 2 years
González García, Spain, 2022 [31]	Retrospective/ observational (513 infants < 1500 g)	2 years (corrected)	Persistent delay in growth and weight gain; malnutrition; head circumference < -2 SD
Sacchi et al., Italy, 2020 [1]	Metaanalysis (89 samples, 52,822 children)	Up to 12 years (including 2 years)	Cognitive delay
Ferguson et al., Netherlands, 2021 [11]	Prospective cohort (5,487 mother-child dyads)	Up to 6 years	High poor prognosis; language delay
Hartkopf et al., Germany, 2018 [14]	Prospective cohort (73 newborns)	24 months	Persistent delay in growth and weight gain; visual disturbances; mental retardation; neurodevelopmental delay; Psychomotor Development Index (PDI) not affected
Bellido-González et al., Spain, 2017 [20]	Retrospective cohort (5,702 infants; 64 term IUGR)	School age (6-8 years)	Cognitive and academic deficits (especially working memory)
El Ayoubi, France, 2016 [13]	Retrospective singlecenter (463 infants)	2 years	Persistent delay in growth and weight gain; psychomotor delay (fine motor); social skills affected
Crume et al., United States, 2013 [8]	Retrospective longitudinal cohort (42 IUGR, 464 unexposed)	2 years (and preadolescence)	No difference in BMI growth rate at 2 years; metabolic problems (higher insulin, lower adiponectin)
Gascoin & Flamant, France, 2013 [3]	Systematic review	Children and adults	Poor mental development; no failure to fall in weight; respiratory problems
Torrance et al., United Kingdom, 2010 [17]	Cohort (180 fetuses)	2 years	Neurological problems
von Beckerath et al., Austria, 2013 [7]	Retrospective cohort (219 IUGR vs. 299 SGA)	Longterm including 2 years	Neurodevelopmental delay; growth retardation
Ventura et al., Spain, 2022 [16]	Observational (91 cases)	3, 9, 12, 18, 24 months	Language delay; motor coordination impairment
Mohammad Jafari et al., Iran, 2024 [21]	Retrospective cohort (80 infants)	6-12 and 24 months	Growth disorders; respiratory and orthopedic problems; neurological and motor delay
Cortez Ferreira et al., Portugal, 2023 [22]	Retrospective cohort (132 newborns)	24 months (corrected)	Developmental delay; social skills affected; language and communication delay
van Wyk et al., Netherlands, 2012 [18]	DIGITAT trial (term IUGR; 650 ASQ)	Longterm including 2 years	Mental retardation; no significant differences in developmental/ behavioral outcomes at 2 years; IUGR predictor of neurodevelopmental delay
Jarry et al., France, 2025 [23]	Retrospective-prospective cohort (57 children)	2 years	Fine motor impairment (3%); psychomotor delay; social skills affected

Hartkopf et al. [14] reported mental retardation and neurodevelopmental delay but noted that the Psychomotor Development Index (PDI) was not affected. El Ayoubi [13] described psychomotor delay (fine motor) and impaired social skills. Study of Levine et al. [24] found fine motor impairment in 3% of children. Cortez Ferreira et al. [22] reported developmental delay, social skill impairment, and language/communication delay. Von Beckerath et al. [7] confirmed neurodevelopmental delay alongside growth retardation. Torrance et al. [17] identified neurological problems.

Language delay was highlighted by Ventura et al. [16], Torrance et al. [17], and Jarry et al. [23]. Motor coordination impairment was reported by Ventura et al, [16]. Fine motor impairment was specifically noted by El Ayoubi et al. [13] and Levine et al. [24]. Metabolic problems (higher insulin, lower adiponectin) were reported by Crume et al. [8]. Respiratory problems were noted by Gascoin & Flamant [3] and Mohammad Jafari et al. [21]. The latter also described orthopedic problems and neurological/motor delay. Visual disturbances were reported by Hartkopf et al. [14]. Two studies reported no significant differences in certain outcomes at 2 years found no difference in BMI growth rate, and van Wyk et al. [18] found no significant differences in developmental or behavioral outcomes, although IUGR was identified as a predictor of neurodevelopmental delay [19].

DISCUSSION

This systematic review of 15 studies examining outcomes of intrauterine growth restriction (IUGR) at 2 years of age reveals several important findings. First, delay in growth and weight gain persists at 2 years in many IUGR infants, although some studies suggest catchup growth may occur by that age [8, 17]. Second, neurodevelopmental, language, and motor impairments are consistently reported across diverse populations and study designs [1, 13, 14]. Third, metabolic abnormalities (e.g., hyperinsulinemia, low adiponectin) can appear as early as age 2, even in the absence of overt growth failure [8].

Comparison with other studies

Our findings are broadly consistent with those of Murray et al. [25], who conducted a systematic review of early childhood neurodevelopment after IUGR and concluded that affected children are at increased risk for cognitive and motor delays by the age of 2. Similarly, study of Longo et al. [26] reported differential effects of IUGR on neurodevelopment, with language and attention being particularly vulnerable domains finding echoed in our review by Ferguson et al. [11] and Ventura et al. [16].

However, our review also highlights important discrepancies. For example, study of Figueras & Gratacos [19] found no significant differences in developmental or behavioral outcomes at 2 years, which contrasts with the majority of studies. Another study by Eixarch et al. [27] (not included in our 15) examined term IUGR infants at 2 years and also reported no significant cognitive deficits, suggesting that gestational age at birth and severity of growth restriction may modify outcomes. In contrast, study of Gutbrod et al. [28] found that IUGR fetuses with cerebral blood flow redistribution had significantly lower neurodevelopmental scores at 2 years, supporting the hypothesis that placental insufficiency severity is a key determinant.

Regarding growth, our finding that some IUGR infants achieve catchup weight but not height by age 2 is supported by Rapaport et al. [29], who reported that catchup growth is more common in weight than in stature. Another study by Jaddoe et al. [30] followed SGA infants to adulthood and noted that height catchup often occurs after 2 years, suggesting that our 2-year time point may be too early to detect full growth recovery.

Metabolic outcomes in our review were reported only by Crume et al. [8]. However, study of Barker [9] has extensively documented that IUGR programs later metabolic syndrome, with insulin resistance detectable as early as 2-3 years. A study by González García et al. [31] found that first trimester fetal growth restriction predicts higher blood pressure and adverse lipid profiles at age 6, reinforcing that metabolic monitoring should begin early.

Persistent growth delay

Approximately half of the included studies von Beckerath et al. [7], El Ayoubi et al. [13], Hartkopf et al. [14], and Torrance et al. [17] documented persistent growth delay at 2 years. This aligns with the concept that IUGR often leads to a reduced growth trajectory that may not fully normalize by the second year of life [2, 10]. However, Crume et al. [8] and Gascoin & Flamant [3] found no difference in BMI growth rate or weight failure at 2 years, suggesting that some IUGR infants achieve catchup growth in weight while remaining at risk for metabolic disturbances. The heterogeneity in findings may be explained by differences in IUGR severity, gestational age at birth, postnatal nutrition, and study definitions of growth delay [19]. Preterm IUGR infants may have poorer growth outcomes than term IUGR infants [32].

Neurodevelopmental and cognitive impairment

Neurodevelopmental delay was the most frequently reported adverse outcome, appearing in 11 of the 15 studies. The large metaanalysis by Sacchi et al. [1] provides highcertainty evidence that IUGR increases the risk of cognitive delay that persists beyond infancy. Hartkopf et al. [14] noted mental retardation and neurodevelopmental delay but found that the Psychomotor Development Index (PDI) was not affected, suggesting that motor development may be relatively preserved compared to cognitive and language domains. This dissociation merits further investigation and may reflect differential vulnerability of cortical regions [15, 32, 33].

Another study by Geva et al. [34] followed IUGR children to age 9 and found persistent deficits in attention and executive function, which were already detectable at 2 years. Similarly, Leitner et al. [35] reported that 10yearold IUGR children had lower IQ scores and more behavioral problems, emphasizing that early delays do not resolve spontaneously.

Language and motor impairment

Language delay was prominent in study of Ferguson et al. [11], Ventura et al. [16], and Cortez Ferreira et al. [22], aligning with evidence that IUGR preferentially affects cortical regions involved in language processing [36, 37]. Fine motor impairment was specifically reported by El Ayoubi [13] and Levine et al. [24] with the latter finding only 3% of children affected at 2 years a relatively low prevalence that may reflect milder IUGR or effective early intervention.

A study by Foster-Cohen et al. [38] examined language outcomes in very preterm IUGR infants at 2 years and found that receptive language was more affected than expressive language, a nuance not captured in our included studies. Future research should differentiate between language subdomains.

Metabolic and other systemic effects

Even at the age of 2, metabolic changes are detectable. Crume et al. [8] reported higher insulin and lower adiponectin levels in IUGR children compared to controls. This supports the fetal programming hypothesis, whereby undernutrition in utero leads to permanent changes in insulin sensitivity and adipose tissue function. Another study by Jensen et al. [39] found that IUGR was associated with a 2-fold increased risk of intellectual disability, independent of gestational age, suggesting that metabolic and cognitive programming share common pathways.

Respiratory problems noted by Gascoin & Flamant [3] and Cortez Ferreira at al. [22] may be related to impaired lung development or increased susceptibility to infections in growthrestricted infants [40]. Visual disturbances reported by Hartkopf at al. [14] are consistent with findings from Hellström et al. [41], who documented retinopathy of prematurity and visual impairment in IUGR preterm infants.

Divergent findings and heterogeneity

Two studies reported no significant differences in certain outcomes at 2 years: study by von Beckerath et al. [7] found no difference in BMI growth rate, and study of van Wyk [18] found no significant differences in developmental or behavioral outcomes. The latter is particularly notable because it comes from a randomized trial (DIGITAT). A possible explanation is that the DIGITAT trial included only term IUGR infants (≥ 36 weeks), whereas many other studies included preterm infants. Another study by Boers at al. [42] (same trial group) confirmed that term IUGR infants have better outcomes than preterm IUGR infants, highlighting the protective effect of gestational maturity.

Clinical implications

The high prevalence of neurodevelopmental and language delay at 2 years supports the need for routine developmental surveillance of all IUGR infants beyond the first year of life [25]. Early referral to early intervention programs (physical, occupational, and speech therapy) is warranted, even if growth appears to be normalizing [40]. Additionally, metabolic monitoring (e.g., fasting glucose, insulin, adiponectin) starting at age 2 may help identify children at risk for later metabolic syndrome, although evidence-based guidelines are lacking [9]. In low and middle income countries, where the burden of IUGR is highest [5], resources for followup are often scarce, making targeted interventions even more critical.

Limitations

Several limitations should be acknowledged. First, the included studies varied considerably in design, sample size, definition of IUGR, and outcome measurement tools, precluding a metaanalysis. Second, many studies lacked a control group of appropriate for gestational age (AGA) infants. Third, publication bias may exist, as studies reporting negative outcomes are less likely to be published. Fourth, most studies were conducted in high income European countries, limiting generalizability. Fifth, the followup period of 2 years is relatively short; long-term outcomes are needed.

Moreover, the limitation of this review is its restriction to publications in English and French between 2010 and 2025, which may have excluded relevant studies in other languages. However, adherence to PRISMA guidelines ensured methodological rigor.

CONCLUSION

This systematic review of fifteen studies demonstrates that intrauterine growth restriction (IUGR) is associated with significant and persistent adverse outcomes in children at age two. Most studies have shown abnormalities in multiple areas, including developmental delays (short stature, low weight, malnutrition, and small head circumference), neurodevelopmental disorders (cognitive delay, intellectual disability, psychomotor developmental delay, and impaired social skills), language and motor disorders (language delay, poor motor coordination, and fine motor skills difficulties), and metabolic and other disorders (hyperinsulinemia, low adenosine levels, respiratory problems, and visual impairments). However, our review reported inconsistent results: one study found no difference in the rate of growth of body mass index at age two, while another reported no statistically significant differences in developmental or behavioral outcomes, although IUGR remained a predictor of neurodevelopmental delay. The discrepancies may indicate the influence of factors such as the severity of IUGR, gestational age at birth and the quality of postnatal care. Low birth weight remains the leading indicator of adverse outcomes.

Future outlook: Further research is needed to understand the developmental trajectory of children with intrauterine growth restriction (IUGR) after age two, particularly during the first few years of life when rapid growth and development occur in all areas (height, weight, cognition, etc.). Long-term, multidisciplinary follow-up (pediatrics, nutrition, and neurodevelopmental) is essential for the early detection of disorders and improved overall prognosis. Surveys and research should evaluate the impact of current interventions and care protocols. Finally, the development of targeted guidelines including maternal awareness programs and nutritional education during the first 1,000 days of a child's life can help reduce IUGR-related illnesses.

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

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