



## SYSTEMATIC REVIEW

# Head Circumference and Cognitive Outcome in IUGR: A Systematic Review and Meta-Analysis

## Circunferencia craneal y resultados cognitivos en el RCIU: Una revisión sistemática y metaanálisis

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### ABSTRACT

**Introduction:** in intrauterine growth restriction (IUGR), variation of head circumference (HC) and impaired cognitive function have been reported.

**Objective:** to analyze HC and cognitive scores of IUGR vs. normal growth fetus (NGF).

**Method:** a systematic review and meta-analysis were conducted based on the published articles in PubMed, Scopus, Web of Sciences, and ProQuest (2003/1/1-2023/12/31) using PRISMA guidelines and RevMan 5.4. The quality assessment of each article was conducted using the Newcastle-Ottawa Quality Assessment Scale (NOS). The study protocol was registered with the CRD42024547189 number in PROSPERO.

**Results:** the final articles included are 4 (155 IUGR, 375 NGF). Pooled results from the random-effects model showed that there was a significant difference in head circumference in IUGR (n = 155) vs. NGF (n = 375) of term + preterm [SMD= -0,42, 95 % CI= -0,62 to -0,21, P < 0,0001; I<sup>2</sup> = 0 %, P = 0,79]; and IUGR (n = 128) vs. NGF (n = 326) of preterm newborns only [SMD= - 0,44, 95 % CI= -0,67 to -0,21, P<0,0001; I<sup>2</sup> = 0 %, P = 0,67]. The Bayley-III cognitive scales between IUGR (n = 94) vs. NGF (n = 292) [SMD = - 0,30, 95 % CI = - 0,66 to 0,07, P = 0,11; I<sup>2</sup> = 28 %, P = 0,24].

**Conclusions:** although there was a significant difference in the head circumference between IUGR and NGF, there were no considerable differences in cognitive achievement. These might be due to a successful effort during the catch-up period, when malnutrition and other factors are addressed.

**Keywords:** Head Circumference; Fetal Growth Restriction; Cognitive Impairment; Intellectual Disability; Learning Disabilities.

### RESUMEN

**Introducción:** en el retraso del crecimiento intrauterino (RCIU) se han descrito variaciones del perímetro cefálico (PC) y alteraciones de la función cognitiva.

**Objetivo:** analizar la HC y las puntuaciones cognitivas de los fetos con RCIU frente a los fetos con crecimiento normal (NGF).

**Método:** se realizó una revisión sistemática y un metaanálisis basados en los artículos publicados en PubMed, Scopus, Web of Sciences y ProQuest (2003/1/1-2023/12/31) utilizando las directrices PRISMA y RevMan 5.4. La evaluación de la calidad de cada artículo se realizó mediante la escala de evaluación de la calidad de Newcastle-Ottawa (NOS). El protocolo del estudio se registró con el número CRD42024547189 en PROSPERO.

**Resultados:** los artículos finales incluidos son 4 (155 RCIU, 375 NGF). Los resultados agrupados del modelo de efectos aleatorios mostraron que había una diferencia significativa en el perímetro cefálico en RCIU (n = 155)

frente a NGF (n = 375) de término + pretérmino [DME= -0,42, IC 95 % = -0,62 a -0,21, P < 0,0001; I<sup>2</sup> = 0 %, P = 0,79]; y RCIU (n = 128) frente a NGF (n = 326) de recién nacidos prematuros solamente [DME= - 0,44, IC 95 % = -0,67 a -0,21, P<0,0001; I<sup>2</sup> = 0 %, P = 0,67]. Las escalas cognitivas Bayley-III entre RCIU (n = 94) frente a NGF (n = 292) [DME = - 0,30; IC del 95 % = - 0,66 a 0,07; P = 0,11; I<sup>2</sup> = 28 %; P = 0,24].

**Conclusiones:** aunque existía una diferencia significativa en el perímetro cefálico entre RCIU y NGF, no había diferencias considerables en el rendimiento cognitivo. Esto podría deberse a un esfuerzo satisfactorio durante el período de recuperación, cuando se abordan la malnutrición y otros factores.

**Palabras clave:** Circunferencia Craneal; Restricción del Crecimiento Fetal; Deterioro Cognitivo; Discapacidad Intelectual; Dificultades de Aprendizaje.

## INTRODUCTION

Intrauterine growth restriction (IUGR) is a condition in which neonates fail to reach the appropriate growth potential due to genetic or environmental factors. It is characterized by birth weight below the 10th percentile for gestational age.<sup>(1,2,3)</sup> IUGR refers to the condition when the fetus fails to achieve the potential biological growth during pregnancy, adjusted to the age, sex, and race.<sup>(1,4,5)</sup>

The prevalence of IUGR is approximately 24 % worldwide, which is about 30 million babies per year.<sup>(6)</sup> IUGR is a significant cause of perinatal morbidity and mortality in about 5-10 % of pregnancies, with even higher rates reported in developing countries (21 %).<sup>(7)</sup>

Infants with IUGR have been reported to face various neuropathological risks, including a higher likelihood of learning difficulties and cognitive impairment. Studies by Hartkopf J. et al. (2018) and Vollmer B. et al. (2019) found lower cognitive scores in children with restricted fetal growth compared to those with normal development, assessed using tools like the Bayley-III cognitive and Wechsler Intelligence Scale.<sup>(10,11)</sup> However, some studies showed no significant link between restricted growth and later cognitive achievement.<sup>(10,11,12)</sup> In the symmetric form of growth restriction, head circumference was significantly smaller than in normally grown infants, though the brain-sparing phenomenon was observed in the asymmetric type.<sup>(13)</sup> An updated report on head circumference and cognitive function in growth-restricted infants is needed to highlight these parameters' importance in predicting morbidity. To the best of our knowledge, limited reviews on both parameters have been published recently.

We conducted a systematic review/meta-analysis based on published articles since 2003 in four major databases. This study aimed to analyze the difference in head circumference and cognitive outcome in IUGR vs. NGF using PRISMA guidelines and RevMan 5.4.<sup>(14,15)</sup>

## METHOD

We present a systematic review following the criteria of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.<sup>(16)</sup> The meta-analysis was conducted to seek differences of the head circumferences and the cognitive score between IUGR vs. NGF using Revman 5.4.<sup>(15)</sup> The study protocol was registered with the CRD42024547189 number in the International Prospective Register of Systematic Reviews (PROSPERO).

### Eligibility criteria

The inclusion criteria include an original research report, case report, and clinical trials investigating the head circumferences and cognitive outcomes among IUGR and NGF infants published in the English language, in PubMed, Scopus, Web of Sciences, and ProQuest (2003/1/1-2023/12/31). The exclusion criteria include reviews and meta-analysis-type articles.

### Research strategies

A systematic review was performed using combinations of the following keywords and terms: normal fetal growth OR normal growth fetuses OR NGF OR appropriate for gestation OR AFG AND intrauterine growth retardation OR intrauterine growth restriction OR IUGR OR fetal growth retardation AND head circumference OR HC AND cognitive.

### Data synthesis

The data extraction was processed using Mendeley Desktop software version 1.19.8, developed by Mendeley Ltd in collaboration with Elsevier in Germany.<sup>(17)</sup> Duplicate entries were eliminated, and two independent evaluators independently evaluated the full text of these articles in the next stage.<sup>(18)</sup>

### Quality assessment and risk of bias in individual studies

The studies included were assessed using the Newcastle-Ottawa Quality Assessment Scale (NOS), as

recommended by the Cochrane Collaboration.<sup>(19)</sup> This instrument has three domains: selection, comparability, and outcomes. The selection domain consists of four elements, with one element being comparability and three elements being outcomes. The article can be rated with a maximum of four stars based on each item, with selection receiving a maximum of four stars, comparability receiving one or two stars, and results obtaining three stars. An article was eliminated due to a significant risk of bias, which was determined when some domains did not obtain a star.<sup>(19)</sup>

### Statistical analysis

The heterogeneity of the studies was assessed using Cochran's Q-test and the I<sup>2</sup> index.<sup>(20)</sup> The Fisher z-transformation's findings were obtained using either a fixed effect model (I<sup>2</sup> < 50 %) or a random effect model (I<sup>2</sup> > 50 %).<sup>(21)</sup> In addition, statistical analysis was conducted using RevMan 5.4. The mean differences were calculated and shown for continuous data, while risk ratios were generated for dichotomous data. For continuous outcomes, when the unit of measurement remained the same throughout all trials, the results were reported as the weighted mean difference along with 95 % confidence intervals. A 95 % confidence interval (CI) was employed to quantify the level of uncertainty regarding the effects. The random-effects model was utilized for the calculations, and the statistical approach employed was inverse variance. Statistical significance was attributed to values of  $p < 0,05$ .<sup>(14)</sup>

For the descriptive results, we computed weighted estimated averages in each article using random effects (table 1). A t-test was conducted to verify the statistical disparities between the two groups (IUGR vs. NGF or AGA-appropriate of gestational age) based on head circumference (we conducted two types analysis: 1. From all 4 final included articles<sup>(22,23,24,25)</sup> regardless they were term or preterm newborns; 2. Only from 3 included articles<sup>(22,24,25)</sup> i.e. Morsing et al., Brembilla et al., Sacchi et al., which the newborns were all preterm, both in IUGR and AGA groups). and cognitive results. The aim was to identify statistically significant differences ( $p < 0,05$ ) and ensure the study's reliability.<sup>(14)</sup>

## RESULTS

### Study selection

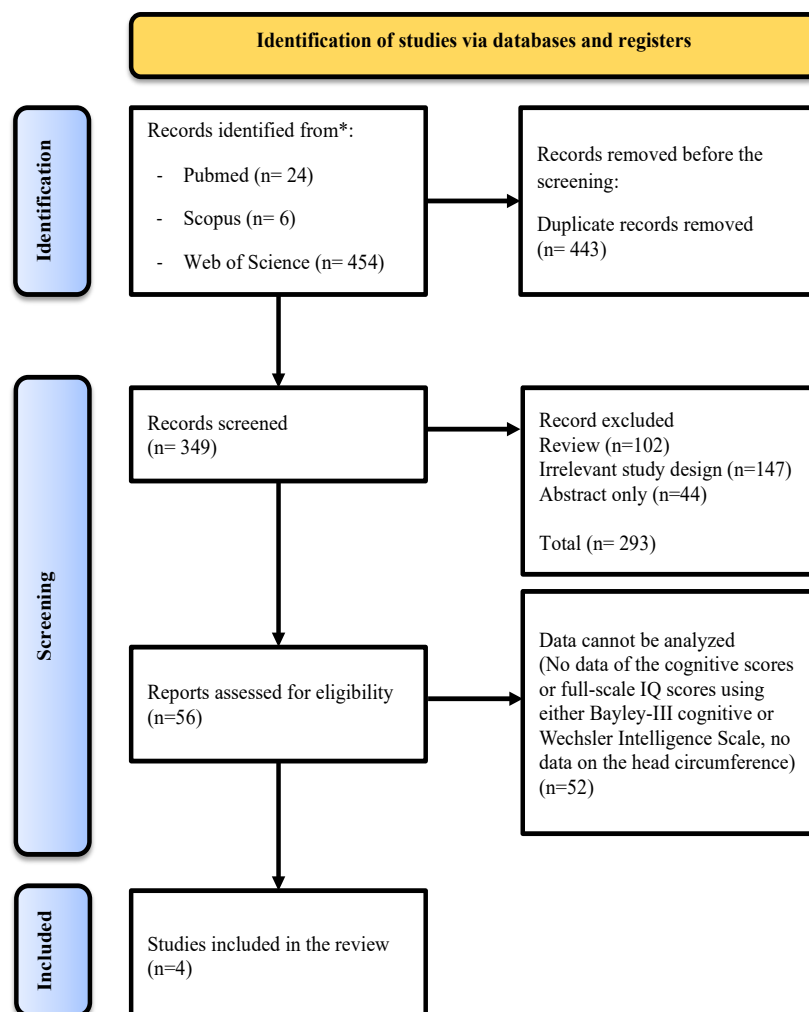


Figure 1. PRISMA flowchart of this systematic review and meta-analysis

There were 792 articles found in the initial database search. After eliminating duplicates, 349 articles met our inclusion criteria; 293 were disqualified based on a review of their abstracts and titles, leaving 56 articles eligible for a full-text analysis. For the qualitative and quantitative synthesis (meta-analysis), four studies were chosen from the remaining articles due to the availability of tested variables as indicated in the aim of this paper (i.e., IUGR is defined as newborns with birthweight lower than 10th percentile; NGF is defined as newborns with birthweight between 10th-90th percentile; cognitive outcome of the infants were measured using either Bayley-III cognitive or Wechsler Intelligence Scale Data on Children). The PRISMA flowchart was used to illustrate the basis for exclusion following full-text reading as well as the details of the approach. The PRISMA flowchart is shown in figure 1.<sup>(14)</sup>

### Study characteristics

The four studies included were published between 2003 and 2023, and all participants were children and adolescents (0-18 years old).<sup>(22,23,24,25)</sup> The sample size averaged 132,5 participants (standard deviation [SD]:  $\pm 121,04$ ; range: 68-314). The mean head circumference of IUGR participants was 34,7 cm (SD:  $\pm 11,17$ ; range: 25,8-50,6 cm). The mean head circumference of normal fetal growth participants (control group) was 35,6 cm (SD:  $\pm 11,08$ ; range: 26,9-51,5 cm). Children and adolescents between the ages of 22 and 216 months underwent cognitive assessments. A total of two of the four articles included a control group composed of children. Table 1 presents the specific information on each study.<sup>(14)</sup>

**Table 1.** Characteristics of the studies included in this systematic review

Author	Year of publication	n	Head circumference of IUGR (cm)	Head circumference of NGF (cm)	Cognitive outcomes
Morsing et al. <sup>(22)</sup>	2011	68	50,6	51,5	Full-scale IQ scores
Jensen et al. <sup>(23)</sup>	2015	76	34,5	34,9	Full-scale IQ scores
Brembilla et al. <sup>(24)</sup>	2021	72	25,8	26,9	Cognitive scores
Sacchi et al. <sup>(25)</sup>	2021	314	28,19	29,29	Cognitive scores
Mean ( $\pm$ standard deviation)			34,7 ( $\pm 11,17$ )	35,6 ( $\pm 11,08$ )	
p < 0,0001					

### Head circumference and cognitive outcomes of IUGR and NGF

Of the included articles, 3 (75 %) were observational studies,<sup>(22,23,24)</sup> and 1 (25 %) were a randomized controlled trial study.<sup>(25)</sup> All studies had a control group. All studies evaluated head circumference and cognitive outcomes.<sup>(22,23,24,25)</sup>

The instruments used were the Bayley-III cognitive scales in 2 (50 %) studies,<sup>(24,25)</sup> Wechsler Intelligence Scale for Children-III/Wechsler Preschool and Primary Scale of Intelligence-III in 1 (25 %) study,<sup>(22)</sup> and Wechsler Adult Intelligence Scale in 1 (25 %) study.<sup>(23)</sup> An overview of the study's predictors of head circumference and cognitive outcome is demonstrated in table 2.

### Quality and risk of bias assessment in studies

Our observational and randomized controlled studies assessment was performed with the Newcastle-Ottawa quality assessment scale (on the study and outcome level, e.g., risk of bias).<sup>(19)</sup> The quality scores of the studies can be found in table 2. The studies of Morsing et al. (2011), Jensen et al. (2015) received eight points, and Brembilla et al. (2021) and Sacchi et al. (2021) showed good quality with seven points. All of the four studies were observational studies in three studies: Morsing et al. (2011), Jensen et al. (2015), Brembilla et al. (2021), and randomized controlled in one study: Sacchi et al. (2021). According to the NOS assessment, all four studies were considered adequate for the meta-analysis (score >5 points).<sup>(19)</sup>

### Assessment of head circumference

We conducted the RevMan 5.4 calculation of the analysis based on the data. The results indicated that IUGR newborns had significantly smaller head circumference size compared to the control group with insignificant heterogeneity among the studies. When only the preterm newborns were calculated, Standard Mean Difference IV, Random, 95 % CI (SMD= - 0,44, 95 % CI= -0,67 to -0,21) and heterogeneity from the analysis of head circumference are  $P = 0,67$ ,  $I^2 = 0 \%$  and the overall effect  $Z = 3,80$  ( $P = 0,0001$ ). The results indicated that preterm IUGR newborn had significantly smaller head circumference size compared to the control group with insignificant heterogeneity among the studies. The details of this analysis can be seen in figure 2, 3 y 4.

Table 2. Head circumference and cognitive outcomes of IUGR and NGF

No.	Author	Year of publication	Study Design	Participant characteristic	Head circumference of IUGR in cm (Mean ± SD)	Head circumference of NGF in cm (Mean ± SD)	Cognitive outcome	Conclusion	NOS Score <sup>(19)</sup>
1.	Morsing et al. <sup>(22)</sup>	2011	Observational study	68 preterm newborns IUGR vs. AGA, (24-27 gestational weeks): 34 Preterm Intrauterine Growth Restriction (PT-IUGR). The type of IUGR was not clearly stated, however they had lower birth weight and length as usually shown in symmetric IUGR. Although, when compared preterm AGA, the head circumference of preterm IUGR was not significantly different. 34 Preterm Appropriate for Gestational Age (AGA). IUGR cases included in this study were suffered from ARED (Absent or Reversed End Diastolic) blood flow; some of these babies had cerebral palsy (12 %), severe brain damage (9 %), and most of them developed chronic lung disease (71 %).	50,6 ± 2,0 (n= 34)	51,5 ± 1,7 (n= 34)	Full-scale IQ (FSIQ) scores (e Wechsler Intelligence Scale for Children-III Intelligence Scale for Children-III/Wechsler Preschool and Primary Scale of Intelligence-III). Evaluated at 5 to 8 years of age: Preterm Intrauterine Growth Restriction (IUGR) 78,9 ± 16,6 (n= 34). Preterm Appropriate for Gestational Age (AGA) 90,1 ± 14,2 (n= 34).	The conclusion drawn from the study is that very preterm infants with intrauterine growth restriction (IUGR) and abnormal umbilical artery blood flow are at an increased risk for cognitive impairment at early school age when compared to very preterm infants born appropriate for gestational age (AGA). According to the study, neonates with PT-IUGR had smaller birth head circumferences (HC) than those with PT-AGA, indicating that very preterm infants with IUGR typically have smaller heads at delivery.	8
2.	Jensen et al. <sup>(23)</sup>	2015	Observational study	76 term newborns: 27 Appropriate for Gestational Age (AGA) + Intrauterine Growth Restriction (IUGR). The type of IUGR was not clearly stated, however there was significant difference in the head circumference between AGA vs. IUGR, indicated symmetric cases. 49 Appropriate for Gestational Age (AGA). The included IUGR cases in this study were babies of mothers with one or more risk factors i.e. previous pre-eclampsia, smoking in pregnancy, and previous birth of children with small for gestational age.	34,5 ± 1,44 (n= 27)	34,9 ± 1,19 (n= 49)	Full-scale IQ (FSIQ) scores (Wechsler Adult Intelligence Scale). Evaluated at 16 to 18 years of age (adolescence): Appropriate for Gestational Age (AGA) + Intrauterine Growth Restriction (IUGR) 85,4 ± 9,9 (n= 27). Appropriate for Gestational Age (AGA) 86,5 ± 9,5 (n= 49).	The study's findings suggest that being born Appropriate for Gestational Age (AGA), with or without intrauterine growth restriction (IUGR), does not necessarily impact cognitive ability in late adolescence. The study found that newborns with AGA + IUGR have smaller heads at delivery because they had smaller birth head circumferences (HC) than those with AGA.	8

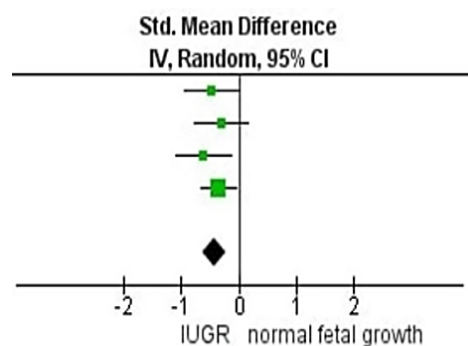
3.	Brembilla et al. <sup>(24)</sup>	2021	Observational study	72 preterm newborns FGR vs. AGA (26-32 gestational weeks): 45 Fetal Growth Restricted (FGR). The type of IUGR was not clearly stated, however there was significant difference in the head circumference and weights between FGR vs. AGA, indicated symmetric cases. 27 Appropriate for Gestational Age (AGA). IUGR cases included in this study were suffered from ARED (Absent or Reversed End Diastolic) blood flow and complicated preeclampsia.	25,8 ± 1,8 (n= 45)	26,9 ± 1,7 (n= 27)	Cognitive scores (the Griffiths and Bayley-III cognitive scales). Evaluated at a median age of 2 years:  Fetal Growth Restricted (FGR) 106,1 ± 8,6 (n= 33). Appropriate for Gestational Age (AGA) 106,3 ± 13,9 (n= 17).	A significant correlation between cerebral parenchyma area and cognitive scores in FGR infants at two years of age suggests that smaller brain parenchyma areas in FGR infants may be associated with lower cognitive outcomes. The study found that neonates with FGR had significantly lower birth weights and head circumferences (HC) than those with AGA, indicating that FGR infants tend to have smaller head sizes at birth. The study found no significant differences in cognitive scores between the FGR and AGA groups when evaluated at a median age of 2 years.	7
4.	Sacchi et al. <sup>(25)</sup>	2021	Randomized controlled trial	314 preterm newborns IUGR vs. AGA (< 33 gestational weeks): 49 Intrauterine Growth Restriction (IUGR) very preterm. The type of IUGR was not clearly stated, however there was significant difference in the head circumference between IUGR very preterm vs. AGA very preterm, indicated symmetric cases. 265 Appropriate for Gestational Age (AGA) very preterm. IUGR cases included in this study were suffered from babies born preterm.	28,19 ± 3,00 (n= 49)	29,29 ± 3,06 (n= 265)	Cognitive scores (Bayley-III cognitive scales). Evaluated at 22 months of age: Intrauterine Growth Restriction (IUGR) very preterm 88,78 ± 10,88 (n= 45). Appropriate for Gestational Age (AGA) very preterm 94,25 ± 13,31 (n= 239).	The cognitive outcomes of the study indicated that very preterm infants with IUGR are at a higher risk for cognitive impairments at 22 months of age and that brain volume alterations at term-equivalent age are associated with these outcomes. The study revealed that neonates with IUGR very preterm exhibited reduced birth head circumferences (HC) in comparison to those who were AGA, suggesting that IUGR very preterm newborns generally have smaller head sizes at birth. The study found a link between poorer cognitive scores at 22 months and larger sizes of the frontal and occipital regions of the brain at the corresponding age of a full-term baby. This suggests that changes in brain growth, which indicate brain-sparing mechanisms, could be linked to lower cognitive performance.	7



**Table 3.** Forest plot for the meta-analysis of head circumference from term and preterm IUGR vs. NFG newborns

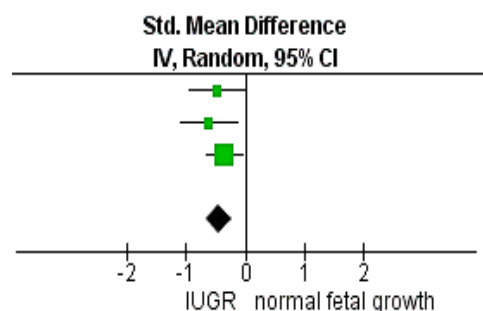
Study	IUGR			normal fetal growth			Std. Mean Difference IV, Random, 95 % CI	Weight
	Mean	SD	Total	Mean	SD	Total		
Morsing et al.	50,6	2	34	51,5	1,7	34	-0,48 [-0,96, 0,00]	18,2 %
Jensen et al.	34,5	1,44	27	34,9	1,19	49	-0,31 [-0,78, 0,16]	18,9 %
Brembilla et al.	25,8	1,8	45	26,9	1,7	27	-0,62 [-1,11, -0,13]	17,7 %
Sacchi et al.	28,19	3	49	29,29	3,06	265	-0,36 [-0,67, -0,05]	45,1 %
Total (95 % CI)			155			375	-0,42 [-0,62, -0,21]	100,0 %

Heterogeneity:  $\tau^2 = 0,00$ ;  $\chi^2 = 1,05$ ,  $df = 3$  ( $P = 0,79$ );  $I^2 = 0$  %  
 Test for overall effect:  $Z = 3,98$  ( $P < 0,0001$ )

**Figure 2.** Forest plot for the meta-analysis of head circumference from term and preterm IUGR vs. NFG newborns**Table 4.** Forest plot for the meta-analysis of head circumference from only the preterm IUGR vs. NFG newborns

Study	IUGR			normal fetal growth			Std. Mean Difference IV, Random, 95 % CI	Weight
	Mean	SD	Total	Mean	SD	Total		
Morsing et al.	50,6	2	34	51,5	1,7	34	-0,48 [-0,96, 0,00]	22,4 %
Brembilla et al.	25,8	1,8	45	26,9	1,7	27	-0,62 [-1,11, -0,13]	21,9 %
Sacchi et al.	28,19	3	49	29,29	3,06	265	-0,36 [-0,67, -0,05]	55,7 %
Total (95 % CI)			128			326	-0,44 [-0,67, -0,21]	100,0 %

Heterogeneity:  $\tau^2 = 0,00$ ;  $\chi^2 = 0,79$ ,  $df = 2$  ( $P = 0,67$ );  $I^2 = 0$  %  
 Test for overall effect:  $Z = 3,80$  ( $P = 0,0001$ )

**Figure 3.** Forest plot for the meta-analysis of head circumference from only the preterm IUGR vs. NFG newborns

## Assessment of cognitive outcomes

Table 5. Forest plot for the meta-analysis of cognitive score based on Bayley-III cognitive scale								
Study	IUGR			normal fetal growth			Std. Mean Difference IV, Random, 95 % CI	Weight
	Mean	SD	Total	Mean	SD	Total		
Brembilla et al.	106,1	8,6	33	106,3	13,9	17	-0,02 [-0,60, -0,57]	30,7 %
Sacchi et al.	88,78	10,88	45	94,25	13,31	239	-0,42 [-0,74, -0,10]	69,3 %
Total (95 % CI)			78			256	-0,30 [-0,66, -0,07]	100,0 %
Heterogeneity: $\tau^2 = 0,02$ ; $\chi^2 = 1,40$ , $df = 1$ ( $P = 0,24$ ); $I^2 = 28$ %								
Test for overall effect: $Z = 1,60$ ( $P = 0,11$ )								

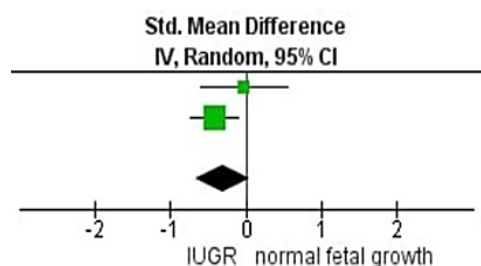


Figure 4. Forest plot for the meta-analysis of cognitive score based on Bayley-III cognitive scale

## DISCUSSION

From these 4 included articles, the head circumference in IUGR were significantly smaller compared to NGF. On the other hand, the cognitive function in IUGR vs. NGF was lower compared to NGF, although not statistically significant. (22,23,24,25)

IUGR can manifest as symmetrical or asymmetrical in children born less than 10th percentile for its gestational age. The circumstances arise during organogenesis in the first until second trimester of pregnancy. About 20-25 % of all instances fall into the first category (symmetrical IUGR). In this type, the IUGR is characterized by a permanent loss in growth potential and a decrease in all fetal body parameters, including internal organs and anthropometric dimensions. Asymmetrical IUGR, on the other hand, accounts for 75-80 % of cases; their weight is low, but their body length, head size, and chest circumference are normal.<sup>(6)</sup> It has been shown in several studies that an abnormal ratio between head circumference (HC) and abdominal circumference (AC) is a better way to determine asymmetric vs. symmetrical IUGR. In cases of symmetrical IUGR, the light-head circumference and length will all fall below the 10th percentile. In cases of asymmetrical IUGR, however, only the height will be below the 10th percentile, while the other measurements will align with the gestational age.<sup>(1)</sup> If growth limitation occurs during the early stages of pregnancy or there is no protective mechanism to support the fetal growth, the restriction may be symmetrical. It could lead to asymmetric growth restriction if it happens later, or is accompanied by adaptive processes.<sup>(13)</sup>

Several factors that could influence the postnatal growth are nutrition, the parents' socioeconomic standing, and the social environment in which they are raised. Infants with symmetrical IUGR are underdeveloped postnatally and usually stay small throughout their lives due to their reduced cell counts at birth. Individuals with asymmetrical IUGR, on the other hand, have a better outlook and healthier growth after birth because arguably they had normal cell counts at birth.<sup>(1)</sup> Asymmetrical IUGR occurs when the fetus receives inadequate nutrition or oxygen delivery, mostly in the third trimester of pregnancy, resulting in reduced body size while maintaining normal or nearly normal brain size. Neonates with symmetrical IUGR exhibit a decrease in the number of neurons in the hippocampus and cerebrum. These reductions are possibly to be responsible for the cognitive impairment reported in symmetrical IUGR cases. Nevertheless, the precise processes responsible for cognitive impairments in symmetrical IUGR still controversial.<sup>(26)</sup>

In the four included studies, the IUGR might due to several factors i.e. ARED (Absent or Reversed End Diastolic), preeclampsia, smoking in pregnancy, and previous birth of children with small for gestational age; which correlated with impaired neurocognitive outcomes.



The Bayley scales have been a valuable instrument for identifying early developmental delays in clinical and research settings for several decades. The Bayley scale is also use eligibility for early detection and intervention programs for high-risk newborns.<sup>(27,28)</sup> The Bayley Scales of Infant and Toddler Development, the third edition (Bayley III), was released in 2006 and is widely recognized as a reliable assessment instrument for measuring the development of children aged 1 to 42 months.<sup>(29)</sup> Toddlers who were born very preterm with intrauterine growth retardation or intrauterine growth restriction (IUGR) had significantly lower cognitive scores on the Bayley-III compared to those who were normal fetal growth (NGF)/appropriate for gestational age (AGA), indicating that IUGR may lead to changes in cognitive development.<sup>(25)</sup>

The Wechsler Intelligence Scale is a psychological instrument to assess an individual's cognitive abilities and problem-solving aptitude. It may be likened to a complete assortment of riddles and inquiries that assess an individual's cognitive abilities in problem-solving, memory retention, and verbal and numerical proficiency. This scale provides three primary scores: one for the verbal intelligence quotient (the proficiency in using words), one for the performance intelligence quotient (the ability to solve puzzles without relying on words), and one total score that integrates these two.<sup>(11)</sup> The study revealed that boys were born premature and with IUGR exhibited worse cognitive outcomes in comparison to those with AGA.<sup>(22,23)</sup> The examination comprises 15 subtests, out of which 10 are fundamental subtests that contribute to four index scores: Verbal Comprehension (VC), Perceptual Reasoning (PR), Working Memory (WM), and Processing Speed (PS). The Full-Scale Intelligence Quotient (FSIQ) is a comprehensive assessment of general intelligence determined based on several subtests' results.<sup>(31,32)</sup> FSIQ is standardized using a mean of 100 and a standard deviation of 15, guaranteeing its reliability and validity.<sup>(31)</sup> The WISC is commonly employed by educational and clinical psychologists worldwide, with modifications to accommodate various languages and cultures.<sup>(32)</sup>

## CONCLUSIONS

In conclusion, we observed that the head circumference in IUGR was significantly smaller than in NGF (either in term and preterm, or in preterm only); however, the cognitive scales of both groups were comparable. Although discretion must be taken when interpreting the results of this analysis, our study provides more insight about the anatomy and cognitive parameters in the IUGR compared to NGF children.

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