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Study of the Clinical-Metabolic Evolution of a Cohort of SGA Children from the OSI Araba

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ABSTRACT

Introduction: The term "Small for Gestational Age" (SGA) refers to infants whose birth weight and/or length is below the 10th percentile or - 2 SD for their gestational age and sex. This condition can result from multiple maternal, fetal or placental factors, reflecting the impact of social conditions on perinatal health. The long-term consequences of being born SGA include an increased risk of developing obesity, hypertension, metabolic syndrome, type 2 diabetes, hormonal disturbances such as precocious puberty, as well as neurodevelopmental and cognitive difficulties, including learning disabilities, ADHD and lower IQ. These risks are increased in cases of rapid weight regain during childhood, especially if based on caloric excess.

Hypothesis and Objectives: The hypothesis of this study proposes that being born SGA may result in a different clinical-metabolic profile compared to children born AGA. The following objectives have been established: Conduct a clinical-epidemiological description of a cohort of SGA children, followed since birth, at around 10 years of age. Determine the proportion of SGA children in our cohort who, upon reaching puberty, present weight and height appropriate for their reference population. Assess whether females have a higher likelihood of experiencing precocious puberty. Determine whether SGA children with metabolic alterations have a larger abdominal circumference and/or higher weight at 2 years of age. Examine whether there is a relationship between thyroid alterations in SGA children and their TSH values. Determine whether early catch-up growth in SGA children is associated with hormonal parameter alterations. Analyze whether being born SGA is associated with a higher risk of developing comorbidities.

Materials and Methods: 14 articles have been used as bibliographic references, obtained from different digital sources such as PubMed, WHO, Nature, SEEP and Annals of Pediatrics. In addition, this research project, under file number 2012-050, was approved by the Clinical Research Ethics Committee of the University Hospital of Araba on 25th January 2013, with a favorable opinion for its prospective use. Microsoft Excel and Statisty have been used for statistical analysis.

Conclusion: A clinical-epidemiological description has been made of the variables in the database containing information on SGA children. The proportions of SGA children in our population who, at 10 years of age, present with normal, above-average, or below-average weight and/or height compared to the reference population have been determined. It has been confirmed that 85 - 90% of SGA children achieve catch-up growth in both weight and height by the age of 2. There are statistically significant differences in the incidence of precocious puberty based on sex. No differences have been found in TGs and glucose levels with respect to abdominal circumference. No differences have been found in insulin, LDL, or HDL levels based on weight at 2 years of age. No differences have been observed in TSH levels in relation to the presence of thyroid alterations. No differences have been identified in IGF-1 and IGF-BP3 levels with respect to early catch-up in height. Comorbidities potentially associated with being born SGA have been analyzed.

Keywords: SGA; Small for Gestational Age; Growth; Obesity; Metabolic Syndrome

Introduction

The term "low birth weight infant" refers to a birth weight below 2500 grams, regardless of gestational age, sex, ethnicity, or other related clinical conditions. This group includes constitutionally small babies, preterm infants, small for gestational age (SGA) newborns, and those with intrauterine growth restriction (IUGR) [1]. Birth weight and length are key indicators throughout fetal development, as well as during the neonatal and adult stages. An increase in birth size, together with a reduction in neonatal mortality, is often seen as a marker of improved socioeconomic conditions in a country [2]. Globally, about 15–20% of all births are SGA, with rates ranging from 7% in industrialized nations to 41.5% in South Asia [2,3]. For instance, a prevalence study conducted in Guangdong province (China) found a negative correlation between the prevalence of SGA births and GDP per capita [4]. In 2010, 32.4 million infants (27% of live births) were born SGA in low- and middle-income countries, which raises concern for long-term health outcomes in these populations [2]. Additionally, SGA prevalence was 12.03% in boys and 12.57% in girls, with a statistically significant higher prevalence among girls ($p < 0.05$) [4]. A SGA newborn is defined as having a weight and/or length below the 10th percentile for their gestational age and sex or falling more than two standard deviations below the population reference mean [1,5,6]. While this condition is not always pathological, some SGA infants may experience growth patterns that reflect IUGR [1,6].

Pathophysiology

Fetal growth is a complex process involving multiple factors, primarily regulated by insulin and hormones secreted by the thyroid, adrenal, and pituitary glands [4]. Among these, insulin-like growth factor I (IGF-1) is likely the most significant. IGF-1 facilitates the transport of amino acids and glucose across the placenta and plays a vital role in fetal neurodevelopment by promoting brain growth, increasing oligodendrocyte and neuronal numbers, and enhancing axonal branching [4]. Several risk factors can disrupt the performance of these growth-regulating hormones. These include genetic conditions, congenital malformations, and diseases that limit intrinsic growth potential, as well as maternal and placental conditions that hinder normal development [5].

- **Maternal Factors:** extreme maternal age (<16 or >35 years), low maternal weight and height, malnutrition, parity (nulliparity, grand multiparity, short interpregnancy intervals), uterine malformations, history of SGA pregnancies, chronic hypertension or preeclampsia, exposure to tobacco or other toxic substances, medication intake (anticoagulants, antiepileptics, chemotherapy, folic acid antagonists), infections (TORCH, varicella, malaria, syphilis, Chagas, listeria, HIV), and chronic diseases (renal insufficiency, anemia, lung disease, cancer, cyanotic heart disease) [5].
- **Placental Factors:** placental insufficiency, infarction or abruption, vascular abnormalities, implantation defects, and inflammatory conditions [5].
- **Fetal Factors:** chromosomal abnormalities (monosomies, trisomies, deletions), genetic disorders (achondroplasia, Bloom syndrome), congenital anomalies (cardiac, renal), inborn errors of metabolism, and multiple gestations [5].

Diagnosis

Diagnosing an SGA infant requires accurate anthropometric measurements at birth and comparison with established reference charts, such as those by Carrascosa et al., as recommended by the Spanish Society of Pediatric Endocrinology [5].

Short- and Long-Term Risks and Repercussions

Postnatal Growth: Most SGA infants undergo postnatal catch-up growth, defined as an increase in growth velocity above normal statistical limits for age or maturity during a specific timeframe [2]. This typically occurs within the first 12 months of life and is nearly complete by age two, with 85–90% achieving a height above -2 SD [2,5,7]. In preterm SGA infants, catch-up growth may be delayed by up to a year. Those who are very premature or have particularly low birth length have a lower likelihood of reaching normal adult stature [5,7]. Approximately 40–50% of SGA children recover normal weight and height. Another 40% may gain excess weight due to overfeeding, leading to adipocyte hyperplasia and increased fat accumulation. Around 10% failed to achieve catch-up growth despite intervention. These children may benefit from recombinant human growth hormone (rh-GH) therapy to mitigate future health complications [8]. Anthropometric indicators such as mid-upper arm circumference, which reflect muscle and fat stores, and abdominal circumference, potentially linked to metabolic syndrome, are also useful in monitoring growth [9].

rh-GH Therapy: Recombinant human growth hormone (rh-GH) therapy has proven effective in SGA children who do not show adequate catch-up growth. In Europe, it is approved for non-syndromic SGA children who remain below −2.5 SD in height at age 4, and whose height is also below −1 SD adjusted for target height [5,7]. Early initiation, greater individual height deficit, and higher GH doses predict better treatment outcomes. Conversely, delayed initiation is associated with a poorer response. Long-term safety remains a subject of debate, with some studies linking rh-GH to increased adult mortality, particularly from bone tumors or cardiovascular diseases [5,7]. However, the FDA has concluded that current evidence does not definitively support these associations [7,10]. Spanish national data show that height gain during the first year of rh-GH therapy averages 0.7 ± 0.2 SD, increasing to 1.2 ± 0.8 SD after two years, with a total gain of 2 ± 1.9 SD after five years [11].

Adrenarche and Puberty: SGA infants are born with low subcutaneous fat. If postnatal weight recovery is rapid and excessive, lipids tend to accumulate ectopically (centrally), promoting insulin resistance, altering adipokine patterns, and increasing serum IGF-1 levels. This sequence may lead to early adrenal steroid synthesis and adrenarche, as well as gonadal steroid production and elevated gonadotropins, triggering early puberty [5,7,10]. The growth spurt occurs at an earlier pubertal stage and tends to be shorter in duration. These events can lead to premature epiphyseal closure and a shorter adult stature than expected, sometimes below target height [5,7,10]. These hormonal axis alterations are more frequent in SGA girls compared to children born appropriate for gestational age (AGA) [5,7,10]. Girls with rapid, excessive catch-up growth, particularly in weight, are more likely to experience early pubarche (as early as 8–9 years).

Studies have also reported significant differences in hormone levels and ovarian maturation between SGA and AGA girls, which may later contribute to a higher risk of developing polycystic ovary syndrome (PCOS), a common cause of infertility. Additionally, internal genitalia may be smaller and ovulatory frequency lower [5,7]. In boys, some studies have proposed a possible future increase in testicular cancer risk [5,7,10]. Prevention and treatment of early adrenarche, precocious puberty, and PCOS involve early weight control, healthy nutrition, and regular physical activity [10]. Experimental studies have shown that reducing ectopic fat and insulin resistance using metformin during the peripubertal period can normalize the endocrine-metabolic profile, delay menarche, improve final height, and prevent PCOS [5,7,10].

Cardiovascular and Metabolic Risks: An unfavorable intrauterine environment leading to low birth weight and/or length is associated with an increased risk of coronary heart disease, stroke, and insulin resistance, especially when birth weight is particularly low. These risks are heightened in children with rapid postnatal weight gain and poor lifestyle habits, making them more vulnerable to developing type 2 diabetes and metabolic syndrome in adulthood [5,7,10,12]. The incidence of metabolic syndrome is six times higher in low-birth-weight children compared to those born heavier and is linked to traditional cardiovascular risk factors such as hypertension, dyslipidemia, and insulin resistance [5,7]. Rapid catch-up growth is also associated with changes in body composition and adipose tissue function, contributing to central obesity and dyslipidemia later in life [9,10,12]. Many of these risks may be modulated by epigenetic factors, avoiding excessive weight gain during the first months and years of life has been shown to reduce these adverse outcomes [12]. Exclusive breastfeeding plays a protective role, promoting compensatory gains in length and head circumference (but not weight) [5,7,10,12,13]. In contrast, formula feeding often leads to excessive fat accumulation, altered lipid profiles, and a higher likelihood of insulin resistance and future diabetes [5,7].

Neurodevelopment, Behavior, and Learning: Placental insufficiency that causes fetal growth delay leads to nutrient deprivation and hormonal disruptions that may impair fetal brain development. SGA children often have reduced head circumference and brain volume, especially affecting the hippocampus (linked to memory), neuronal density, and myelination, all of which may contribute to cognitive impairment [5,7]. Being born SGA can also affect frontal lobe functions such as attention, language, memory, and mathematical abilities. However, visual-spatial, sensory, and motor skills are usually comparable to those of AGA children [5,7]. Thyroid hormones play a key role in growth and neurodevelopment, and SGA children have been observed to show higher TSH levels than AGA peers [14]. Cognitive deficits, including lower IQ, are among the most significant long-term effects in SGA children, with some severe cases showing intellectual disability [5,7]. Concentration difficulties, learning disorders, attention-deficit/hyperactivity disorder (ADHD), and behavioral or emotional problems are also common, often emerging in early childhood and potentially worsening with age [5,7,10]. Children who achieve catch-up growth tend to have better neurological outcomes than those who do not, although cognitive deterioration can still occur in both groups over time [5,7,10].

Hypothesis and Objectives

The hypothesis of this study proposes that being born with SGA may result in a different clinical-metabolic profile compared to children born AGA.

To address this, the following primary objectives have been established:

- Conduct a clinical-epidemiological description of a cohort of SGA children, followed since birth, at around 10 years of age.
- Determine the proportion of SGA children in our cohort who, upon reaching puberty, present weight and height appropriate for their reference population.
- Additionally, the study aims to explore the following secondary objectives:
- Assess whether females have a higher likelihood of experiencing precocious puberty.
- Determine whether SGA children with metabolic alterations have a larger abdominal circumference and/or higher weight at 2 years of age.
- Examine whether there is a relationship between thyroid alterations in SGA children and their TSH values.
- Determine whether early catch-up growth in SGA children is associated with hormonal parameter alterations.
- Analyze whether being born SGA is associated with a higher risk of developing comorbidities.

Materials and Methods

To obtain general bibliographic information on SGA and FGR infants, an advanced search was conducted in the "PubMed" section of the National Library of Medicine website (pubmed.ncbi.nlm.nih.gov). In the query box, the following terms were used: (((sga [Title]) OR (small for gestational age [Title])) OR (fetal growth restriction [Title])) OR (fgr [Title]), yielding 5777 results. Filters then applied: "last 5 years," "free full text," "systematic review," and "humans," which narrowed the search to 37 results. From these, the following articles were selected: "Early-onset fetal growth restriction: A systematic review on mortality and morbidity", "Catch-up growth in full-term small for gestational age infants: A systematic review", "Breastfeeding supports growth in small for gestational age infants: A systematic review and meta-analysis" and "Fetal growth restriction". The remaining articles were excluded for being overly specific. To gather information on the prevalence of SGA infants, a search was performed via the World Health Organization website (who.int/es) using the term "SGA". The first result, titled "Newborn Health - World Health Organization (WHO)" was selected. It refers to a Guideline Development Group Meeting on the update of WHO recommendations for the care of preterm or low birth weight infants.

To obtain global prevalence data, a search was conducted on the Nature website (nature.com). Using "Advanced search," the terms (prevalence AND world) in "that contain these terms" and (small for gestational age) in "where the title contains" were used. This search returned 344 results. Filters were applied to narrow results by "Scientific Reports" (Journal), "Medical research" (Subject), and publication date within the last 5 years, resulting in 34 articles. From these, the article "Prevalence of small for gestational age infants in 21 cities in China, 2014–2019" was selected. The remaining articles were excluded as they focused on adult diseases associated with being born SGA or on maternal pregnancy-related factors. To explore the consequences and clinical implications of being born SGA, information was retrieved from the Spanish Society of Pediatric Endocrinology (seep.es). Through the section "Publicaciones Grupos de Trabajo SEEP," the Clinical Practice Guideline for the follow-up of SGA children was accessed—this served as a primary bibliographic source for this work. Upon reviewing the references used in this guideline, it was observed that many originated from articles published in Anales de Pediatría (analesdepediatria.org). An advanced search using the term "pequeño para la edad gestacional" in the title, restricted to the last 5 years, returned three publications.

From these, the following were selected: "Recién nacido pequeño para la edad gestacional: concepto, diagnóstico y caracterización neonatal, seguimiento y recomendaciones" and "Diferencias en la función tiroidea de los pequeños para la edad gestacional y los de peso adecuado. ¿Es normal la función tiroidea de los recién nacidos pequeños para la edad gestacional?". The other article was excluded as it focused solely on prenatal evaluation. For the analysis of comorbidities in SGA children, another "PubMed" search was conducted using the query: ((sga[Title]) OR (small for gestational age [Title])) AND (comorbidities [Title]), which yielded one result. Lastly, following the recommendation of Dr. Ignacio Díez López, the following articles were consulted: "Tratamiento con hormona de crecimiento en pequeños para la edad gestacional en España" and "Pautas para el seguimiento clínico del niño pequeño para la edad gestacional". In addition, the bibliography was complemented with information provided by Dr. Díez during university lectures. With respect to bioethics, due to the limitations of being a sixth-year medical student, I was not allowed to have direct contact with patients or access their medical records. Therefore, Drs. Ignacio Díez López and Eder Arruti Onaindia provided me with an anonymized, non-traceable, and coded database. This database was created using data collected from SGA children born between June 2013 and May 2015. This research project, under file number 2012-050, was approved by the Clinical Research Ethics Committee of the University Hospital of Araba on January 25, 2013, with a favorable opinion for its prospective use.

Statistical Analysis and Interpretation

The statistical tool Statisfy was used to analyze the clinical-epidemiological status of our cohort at the age of 10. Firstly, to determine when the cohort achieved catch-up growth in height, a descriptive analysis was conducted on the relevant variables individually "Catch up T3m", "Catch up T6m", "Catch up T1a", "Catch up T1,5a" and "Catch up T2a". The same procedure was followed to assess catch-up growth in weight using the variables "Catch up P3m", "Catch up P6m", "Catch up P1a", "Catch up P1,5a" and "Catch up P2a". To evaluate the proportions of the cohort who were below, above, or within the normal height range at 10 years old, a one-sample t-test was performed using the variable "Talla groups 10a". The one-sample t-test is a statistical hypothesis test used to determine whether the mean of a single sample differs significantly from a known population mean. A p-value > 0.05 leads to acceptance of the null hypothesis, indicating that the sample mean is equal to the population mean. Conversely, a p-value < 0.05 confirms that the sample mean is significantly different from the population mean. The same process was repeated for weight at 10 years using the "Peso grupos 10a" variable.

To assess the relationship between sex and the presence of precocious pubarche, a Chi-square test was performed between the variables "Sexo" and "Pubarquia precoz". The Chi-square test is used to investigate whether there is an association between two categorical or nominal variables. The test compares observed and expected frequencies, and degrees of freedom (df) are calculated. If the Chi-square value is less than the df, no significant difference is present. Then, metabolic parameters were evaluated, considering values of glucose, insulin, LDL, HDL and TGs. To assess whether there is a relationship between the presence of metabolic syndrome and abdominal circumference at 2 years, the Pearson correlation test was applied with the variables "TG" and "PAbd 2a". The Pearson correlation test is

used to measure the relationship between two quantitative (metric) variables, yielding a coefficient between -1 and +1. A negative value indicates an inverse relationship between the variables, typically represented by a downward-sloping line. A positive value indicates a direct relationship, shown by an upward-sloping line. The same procedure was used for the variables "Glucosa" and "PAbd 2a". Similarly, insulin, LDL and HDL values were analyzed in relation to weight at 2 years, performing the Pearson correlation test three times with "Peso 2a". To determine whether there is an association between TSH levels and the presence of thyroid disorders, an independent samples Student's t-test was conducted. For this, the Levene's test for equality of variances must first be performed. If Levene's test yields a p-value < 0.05, equal variances cannot be assumed. Based on this result, the appropriate interpretation of the t-test is chosen.

- If equal variances cannot be assumed, the t-test results under this condition must be interpreted.
- If equal variances can be assumed, the corresponding row for equal variances is used.

Finally, for hormonal parameters, IGF-1 and IGF-BP3 values were analyzed. An independent samples t-test was performed between "Catch up T3m" and "IGF-1". The same process was applied for "IGF-BP3".

Results

The database includes information on 103 patients: 58 males and 45 females. Follow-up was lost in 11 cases, and 2 patients passed away. A total of 60 variables were studied using Microsoft Excel and Statisfy. 27 of them are metric variables, which are "talla 3m", "talla 6m", "talla 1a", "talla 1,5a", "talla 2a", "talla 10a", "peso 3m", "peso 6m", "peso 1a", "peso 1,5a", "peso 2a", "peso 10a", "PAbd 3m", "PAbd 1a", "PAbd 1,5a", "PAbd 2a", "PBraq 3m", "PBraq 1a", "PBraq 1,5a", "PBraq 2a", "glucemia", "insulinemia", "LDL", "TG", "HDL", "IGF-1" and "IGF-BP3". 12 are ordinal variables, which are "percentilT 3m", "percentilT 6m", "percentilT 1a", "percentilT 1,5a", "percentilT 2a", "percentilT 10a", "percentilP 3m", "percentilP 6m", "percentilP 1a", "percentilP 1,5a", "percentilP 2a" and "percentilP 10a". The remaining 20 are nominal variables, which are "sexo", "catch up T3m", "catch up T6m", "catch up T1a", "catch up T1,5a", "catch up T2a", "Talla grupos 10a", "catch up P3m", "catch up P6m", "catch up P1a", "catch up P1,5a", "catch up P2a", "Peso grupos 10a", "Problemas SiVsNo", "Problemas", "Asma", "Alt OFT", "Pubertad precoz", "Tiroides" and "TDAH".

Regarding catch-up growth in height, 38.75% of the sample had not achieved catch-up by 3 months of age; at 6 months, 35.23% had not yet achieved it; at 1 year, 30.77%; at 18 months, 25.56%; and by 2 years, only 7.61% had not achieved catch-up growth. For catch-up in weight, 35.90% had not achieved it by 3 months; 35.29% by 6 months; 30.68% by 1 year; 26.14% by 18 months; and only 4.44% remained without catch-up by 2 years of age. At 10 years old, 70.59% of the children had normal height, 14.12% had short stature, and 15.29% had above-average height. A one-sample t-test yielded a p-value < 0.001 ($p < 0.05$), indicating a statistically significant result. As for weight at 10 years of age, 62.07% had normal weight, 12.64% were underweight, and 25.29% were overweight. The one-sample t-test gave a p-value of 0.02 ($p < 0.05$), also statistically significant.

In the "Chi-square test" assessing the association between sex and the likelihood of precocious pubarche, a value of $Chi^2 = 9.49$ and $df = 1$ was obtained, with a p-value = 0.002 ($p < 0.05$), indicating a statistically significant association. In the metabolic assessment, the "Pearson correlation test" between abdominal circumference at 2 years and triglyceride (TG) levels yielded a p-value of 0.893 ($p > 0.05$), not statistically significant. Similarly, the Pearson test between abdominal circumference at 2 years and glucose levels resulted in $p = 0.191$ ($p > 0.05$), also not statistically significant. For the relationship between insulin levels and weight at 2 years, the "Pearson correlation test" gave p= 0.084 ($p > 0.05$), not statistically significant (Figure 1); however, the scatter plot shows a directly proportional relationship with an ascending straight line. The test between weight at 2 years and LDL levels gave $p = 0.498$ ($p > 0.05$), not statistically significant. Lastly, the correlation between weight at 2 years and HDL levels resulted in $p = 0.289$ ($p > 0.05$), also not statistically significant.

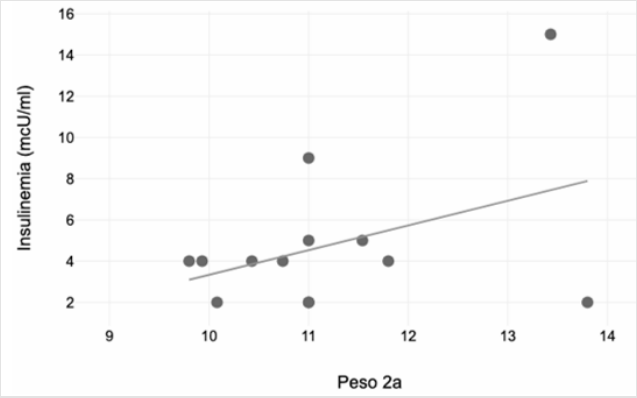

Figure 1.

Concerning thyroid alterations and TSH levels, "Levene's test for equality of variances" yielded a p-value of 0.581 ($p > 0.05$), so equal variances were assumed. The "independent samples Student's t-test" under this assumption gave a p-value of 0.076 ($p > 0.05$), indicating a non-statistically significant result (Figure 2). In the hormonal evaluation, when comparing IGF-1 levels between children who did or did not achieve catch-up growth in height at 3 months, "Levene's test" showed $p = 0.673$ ($p > 0.05$), so equal variances were assumed. The "Student's t-test" under equal variances gave $p = 0.076$ ($p > 0.05$), a non-significant result (Figure 3). Likewise, for IGF-BP3 values in relation to catch-up height at 3 months, "Levene's test" gave $p = 0.485$ ($p > 0.05$), and the "Student's t-test" under equal variances gave $p = 0.582$ ($p > 0.05$), again not statistically significant. Finally, possible comorbidities related to being born SGA were assessed. It was found that 57.61% of the cohort had at least one comorbidity. Notable findings among these include:

- 30.43% had some form of ophthalmologic alteration.
- 11.95% had ADHD.
- 8.70% were asthmatic.
- 7.61% had thyroid disorders
- 7.61% had precocious puberty.
- 4.35% had motor developmental delays.
- 3.26% had hemangiomas.
- 3.26% had celiac disease.
- 3.26% had intellectual disability.

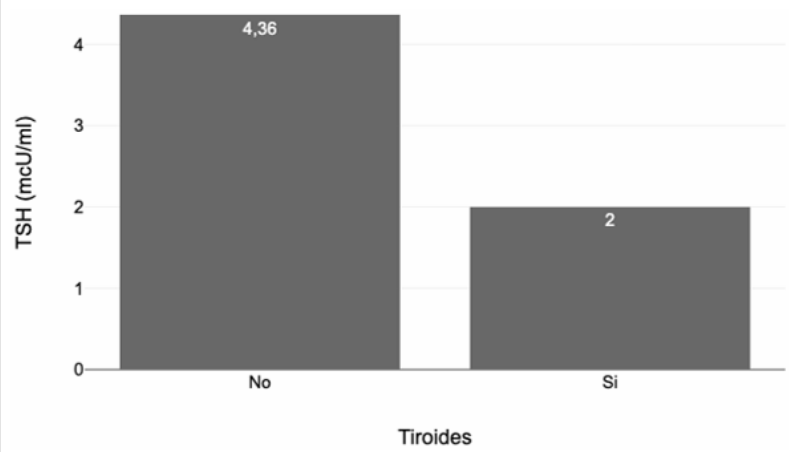

Figure 2.

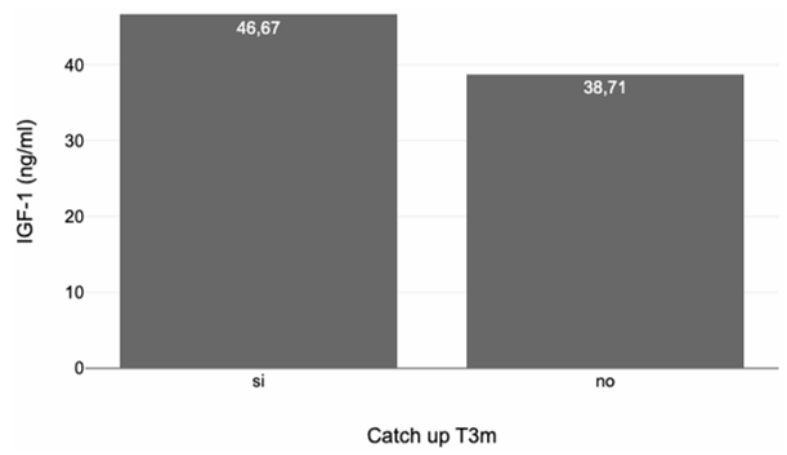

Figure 3.

Discussion

The database used for this study contains data on boys and girls born SGA, tracking their evolution up to the age of 10 in order to conduct a clinical-metabolic analysis. The results obtained from our cohort are based on statistical data derived from this database, which includes 60 variables and was used to study 103 children. Firstly, in line with both national and international literature [2,5,7], it is generally observed that 90% of SGA children achieve catch-up growth by the age of two. In our cohort, 92% achieved catch-up in height and 95% in weight by that age, suggesting that our population behaves similarly to what has previously been reported. Several authors have also highlighted that SGA girls who experience rapid catch-up growth, particularly in weight, are more likely to develop early pubarche [5,7,10]. In our cohort, we accepted the alternative hypothesis that there are significant differences between sexes, with a higher likelihood of precocious pubarche among girls. Regarding sex distribution, our population showed a higher number of male SGA births, in contrast with prevalence studies such as the one conducted in China, which found a higher prevalence among females [4]. This discrepancy may be due to selection bias in our sample; for instance, a larger number of female SGA cases may not have participated in the study.

Furthermore, while the literature indicates that by puberty, 50% of SGA children reach normal weight, 40% are overweight or obese, and 10% remain underweight [8]; our cohort showed only a 25% prevalence of overweight or obesity. This statistically significant difference supports the alternative hypothesis and may reflect better oversight by pediatric and primary care services, leading to improved weight management in our sample. With regard to metabolic status, some authors have suggested a relationship between abdominal circumference and the presence of metabolic syndrome [9]. However, in our cohort, we found no significant associations between abdominal circumference and triglyceride or glucose levels. Similarly, although literature indicates a positive relationship between weight and metabolic syndrome [5,7,10,12], our findings did not show significant differences in insulin, LDL, or HDL levels by weight, preventing us from confirming this association. These discrepancies may stem from our lower-than-expected prevalence of overweight children and the low statistical power of the study (N < 30 for some variables). In the hormonal evaluation, several studies have reported a positive association between IGF-1 levels and early catch-up growth in SGA children [5,7,10]. However, our results showed no significant differences in IGF-1 or IGF-BP3 levels between those who achieved early catch-up in height and those who did not, confirming the null hypothesis. As previously mentioned, this may be due to differences in the characteristics of our cohort or insufficient statistical power. Increasing the sample size in future studies would be advisable, as the IGF-1 trend, while not statistically significant, was nonetheless positive.

Likewise, it has been reported that SGA children tend to have higher TSH values than AGA children [14]. However, in our study, no significant differences in TSH levels were observed among SGA children with thyroid disorders. In fact, contrary to expectations, elevated TSH levels were more commonly found in SGA children without thyroid alterations. As discussed earlier, this may be due to the low statistical power of blood test-related variables (N < 30). Finally, 57% of the children in our cohort presented some type of comorbidity. Among them, ophthalmological disorders were particularly notable, affecting 30% of SGA children. However, we were unable to compare these results with existing literature, as previous studies did not examine the same variables. It would be useful to contact the authors of similar studies to determine whether comparable findings were observed. Additionally, the literature indicates a 5–7% incidence of ADHD among SGA children, compared to AGA peers [5,7,10]. This is supported by our cohort, where we found a 12% incidence. In conclusion, although our data support some of the hypotheses described in the literature, they also highlight the need to expand the sample size and standardize the variables analyzed in future research. Only then will it be possible to determine more precisely the true impact of being born SGA on future health, both from a metabolic perspective and in relation to the wide range of associated comorbidities. This study contributes to current knowledge and may serve as a foundation for future, more robust and comparable research.

Conclusion

Based on this study, the following conclusions have been drawn from the analysis of our cohort:

- A clinical-epidemiological description has been made of the variables in the database containing information on SGA children born within the OSI ARABA.
- The proportions of SGA children in our population who, at 10 years of age, present with normal, above-average, or below-average weight and/or height compared to the reference population have been determined.
- It has been confirmed that 85–90% of SGA children achieve catch-up growth in both weight and height by the age of 2.
- There are statistically significant differences in the incidence of precocious puberty based on sex.
- No differences were found in TGs and glucose levels with respect to abdominal circumference.
- No differences were found in insulin, LDL, or HDL levels based on weight at 2 years of age.
- No differences were observed in TSH levels in relation to the presence of thyroid alterations.
- No differences were identified in IGF-1 and IGF-BP3 levels with respect to early catch-up in height.
- Comorbidities potentially associated with being born SGA have been analyzed.

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