

Growth monitoring of small for gestational age in a Algerian cohort

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Abstract-Objectives. The aim of the study was to describe post-natal growth during a 2-year follow-up in a cohort of infants born at term but small for gestational age (SGA). **Methods.** This was a prospective study in infants with gestational age between 37 and 42 weeks amenorrhea with a birth weight below the 10th percentile. Height, weight and head perimeter were measured from birth to two years. **Results:** The prevalence of term SGA infants was 3.9% during the enrollment period (from 1 December 2012 to 31 March 2014). Of these 457 infants, 446 (97.6%) were followed up to 2 years of age. Children with height, weight and head perimeter measurements at 24 months ≥ -2 standard deviation score (SDS) were 87.9%, 96.4% and 97.1%, respectively. (i.e., 12.1% had persistent growth retardation for at least one parameter). In a multivariate analysis, the independent predictors of catch-up growth at 24 months were associated with maternal height, target height and its difference with birth height, history of SGA, breast feeding duration, ponderal index and height gain at 6 months. **Conclusion:** This study provides data concerning the epidemiology of SGA births in Algeria and the factors associated with post-natal growth. These results are in favor of setting up a national program, integrating obstetricians and pediatricians for a joint action for the ante- and postnatal follow-up of SGA infants.

Index terms: Small for gestational age; Intra-uterine growth retardation; Postnatal growth; Catch-up growth; Short stature.

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I. INTRODUCTION

Children born small for gestational age (SGA) are defined as having a birth weight and/or length standard deviation score (SDS) of < -2 , based on data from an appropriate reference population [1].

SGA is an heterogeneous group due to the varied nature of the cause including nutritional, hormonal, vascular, and genetic factors.

Parameters at birth are important predictors of infant and adult health [2]. Increased birth height and weight and decreased neonatal mortality are frequently associated with improved health and economic status. Among newborns with low birth weight, those born SGA have attracted particular attention because of the question of catch-up growth during childhood and adulthood. The rates of infants born at term, but small for gestational age (SGA), varies from 7% in developed countries to 41.5% in countries from South Asia [3],[4]. The study of Karlberg *et al* in 1995 reported that 85% of SGA infants, defined as a birth height < -2 standard deviation scores (SDS), achieved catch-up growth at 6 months [5]. Moreover, at one year, 13.4% of these infants still had a height < -2 SDS and at age of 18 years they were only 7.9%. In a recent systematic review of 11 studies in term SGA infants, Campisi *et al* evaluated the prevalence of catch-up growth. Despite the various definitions of SGA and catch-up growth, the authors estimated that the median prevalence of catch-up growth was 87.4% [2].

In Algeria, the statistics from the Ministry of Health are those of overall low birth weight. The rate of low birth weight (whatever gestational age) was 7.9% in 2011 in our maternity. Infants with low birth weight do not have follow-up in specialized consultations except for those hospitalized at birth. As a result, many children with no identifiable disease history are referred to our pediatric consultation at the age of 8–9 years to explore growth retardation. In Algeria, the approval of growth hormone treatment was obtained in 2011, but there is no reimbursement by social insurance for this expensive treatment, hardly accessible to the population concerned.

The purpose of this prospective study was to identify the population of SGA infants born at term using well-established and predefined criteria, to follow up their height and weight outcomes and to estimate the rate of children with no catch-up growth at the age of two years. The goal is to manage these children as soon as possible as recommended in the 2007 and 2023 European Society of Pediatric Endocrinology guidelines [1], [6].

II. MATERIALS AND METHODS

Type of study and patients

This was a prospective cohort study in a population of SGA infants born at term followed for a period of two years. The primary objective was to evaluate the rate of catch-up growth during this period. The secondary objectives were to identify predictive factors associated to catch-up growth at age of two years.

Neonates were recruited at the maternity ward of Béni Messous hospital, Algiers. Term neonates with gestational age between 37 and 42 weeks age (WA), from a single pregnancy and with a birth weight below the 10th percentile were included. Neonates were excluded in case of multiple pregnancies, malformative syndromes, neonatal asphyxia, syndromic intrauterine growth retardation, sex differentiation anomalies with undetermined sex and infants who received treatment that could modify growth.

The follow-up consultations of the patients were carried out in the maternal and child protection unit of the Pediatric department of Béni Messous hospital at 1, 3, 6, 12, 18 and 24 months after birth.

The study was conducted in accordance with the Declaration of Helsinki and was accepted by the hospital Ethics Committee as an observational, quality improvement project not requiring formal ethical approval. Participants were informed of the purpose of the study and gave their consent to participate in the study and for the use of their medical data and those of their children for research purposes. They were informed that their participation in the study was voluntary and that they could withdraw at any time without interfering with their medical care and that of their child.

Data collected:

The following data were recorded at inclusion and at follow-up visits: mother demographics (age, educational level, socio-professional category), mother's self-reported weight before pregnancy, mother's height, pregnancy (parity, medical history, obstetrical history, smoking, alcohol intake); infant characteristics: birth height, birth weight, birth head perimeter, ponderal index, etiology of SGA and height of father.

Methodology for obtaining anthropomorphic measurements:

In the newborn, anthropometric measurements of weight, length and head circumference were taken at 24 hours of life. Weight was measured to an accuracy of 10 grams using a mechanical baby scale model SECA® which was calibrated each day. Length was measured to an accuracy of 1 mm with a measuring rod in the form of a SECA® model mat, with the newborn lying supine, lower limbs extended, one person holding the head in a fixed position against the support board head, with a second person maintaining the thighs and the knees in extension. Head circumference was measured with a tape measure, taking the largest circumference through the from the frontal bosses to the occiput. In those babies who had been identified by hospital staff as SGA, their measurements were checked and verified by the lead investigator (FB).

Growth standards and calculations used:

For foetal growth standards, and in the absence of national standards for the Maghreb Countries including Algeria, we used the personalized and gender specific French Audipog intrauterine growth curves [7].

For evaluation of postnatal growth, we calculated standard deviation scores for Weight, Supine Length/Height and Head Circumference Using Both French and World Health Organization (WHO) data. French reference data were from Sempé and Pédrón [8] and were calculated using "Growth XP Lite" software (<https://www.growthxp.com/elementor>). WHO child growth standards were derived from WHO-Child-Growth-Velocity-Standards-Final.doc (<https://apps.who.int/iris/rest/bitstreams/52342/retrieve>) and calculated using "Who Anthro" software (<https://www.who.int/tools/child-growth-standards/software>) [9]. In the few cases with missing data, these were not imputed.

Catch-up growth was defined in accordance with the 2001 Consensus Statement of Lee et al as increase in height velocity (cm/year) above the mean for chronological age and sex [10].

We assessed catch-up growth in two ways: by calculating the 6-monthly change in SDS for weight, length, and head circumference up to the age of 24 months; and by calculating the SDS difference between both infant size at birth and at 24 months with mid-parental height SDS.

Definition of standards and variables used in data analysis

Perinatal: As stated above, term was defined as gestational age between 37 and 42 weeks. SGA was defined as weight and/or length < 10th percentile for the population standards used, this cut-off being chosen as the most widely accepted and used for newborn population studies [11], [12], [13]. SGA was considered severe when weight and/or height was < 3rd percentile.

Statistical analyses

Data were collected and stratified to demonstrate relative prevalence in older mothers (>34 years), short and borderline short mothers, under and overweight (BMI <18.5 and >25 kg/m²) mothers, primiparous and high parity status (>4 deliveries) mothers. Etiology of SGA, where known, was recorded.

A multivariate logistic regression analysis was performed to define the predictors of catch-up growth in term infants small for gestational age. Variables that were statistically significant in univariate analysis at a threshold ≤ 0.1 were entered into the overall logistic regression model (multivariate analysis).

Statistical analysis was performed using Stata 9.2 software (Statacorp, College Station, Texas, USA).

III. RESULTS

Baseline characteristics

During the enrollment period (from 1 December 2012 to 31 March 2014), 11,667 births were registered in the maternity of Beni Messous hospital; infants with low birth weight whatever the term were 8.3% (n=967) and term SGA infants were 3.9% (n=457).

Of the 457 infants enrolled in our study, 11 were excluded of the analysis (lost to follow-up, n=10; craniosynostosis, n=1); 446 (97.6%) newborns were followed until the end of the study.

The mean (SD) age of women at inclusion was 30.2 (5.8) years and 60.2% were primiparous (**Table 1**). Their mean height was 156.3 (3.8) cm and 5.2 % of them had a height < 150 cm. The mean pre-pregnancy BMI was 25.5 (3.8) kg/m² and was > 25 kg/m² in 54.3%. The mean father's height was 169.8 (5.0) cm.

Obstetrical history was reported in 18.7% of women and 13.1% had a history of SGA. The etiological diagnosis of the birth of an SGA infant was established in 36.5% of cases: placental causes (n=101; 22.1%), chronic diseases (n=26; 5.7%) or anemia (n=12; 2.6%) (**Table 1**).

The mean pregnancy gestation, as estimated by the Ballard score, was 38.3 weeks. Mean (SD) [range] birth weight was 2211.1 (201.8) [1300–2470] grammes, equating to -2.6 (0.5) SDS (WHO standards) and -2.5 (0.7) SDS (Sempé standards). Mean birth length was 43.2 (1.2) [39–46.5] cm, equating to -3.3 (0.6) SDS (WHO standards) and -3.2 (0.9) SDS (Sempé standards). Mean head circumference was 31.5 (1.4) [27–35] cm, equating to -1.8 (0.9) SDS (WHO standards) and -1.4 (0.9) SDS (Sempé standards). SGA was symmetrical in 43.3% of cases and asymmetrical (head circumference at the expected value) in 56.7%. Mean (SD) ponderal index was 2.7 (0.2) g/cm³ and < 3rd centile in 26.3% of infants (**Table 2**).

Table 1. Baseline characteristics of mothers with infants who were born at term and small for gestational age.

Number	N=457
Mean (SD) age (years)	30.2 (5.8)
Age stratification (%)	
18–34 yrs	349 (76.4)
> 34 yrs	108 (23.6)
Mean (SD) height (cm),	156.3 (3.8)
Height stratification (%)	
< 150 cm	24 (5.2)
150–160 cm	388 (84.9)
> 160 cm	45 (9.9)
BMI (kg/m ²) stratification (%)	
< 18.5	4 (0.9)
18.5–25	205 (44.9)
> 25	248 (54.2)
Parity, n (%)	
1	275 (60.2)
2–4	171 (37.4)
> 4	11 (2.4)
Etiology of SGA birth, n (%)	
Placental causes	101 (22.1)
Chronic disease	26 (5.7)
Anemia	12 (2.6)
Other	28 (6.1)
Idiopathic	187 (40.9)
Indeterminate	103 (22.6)

BMI, body mass index; SGA, small for gestational age

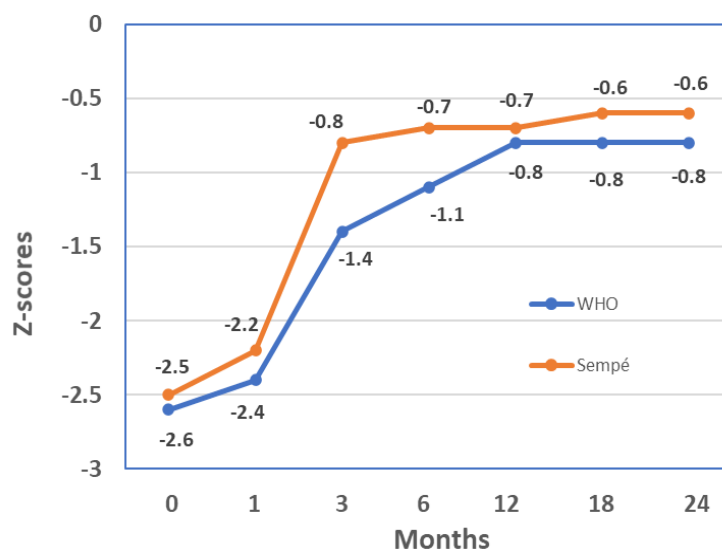
Table 2. Baseline characteristics of infants born small for gestational age at term. Mean (SD) values are shown

Characteristics	N=457
Female sex, n (%)	255 (55.8)
Birth weight (g)	2211.1 (201.8)
Birth length (cm)	43.2 (1.2)
Head circumference (cm)	31.5 (1.4)
Asymmetrical SGA, n (%)	259 (56.7)
Ponderal index, Mean (SD)	2.7 (0.2)
Stratification, n (%)	
<3rd centile	120 (26.3)
≥ 3rd centile	337 (73.7)
Weeks' gestation (Ballard score)	38.3 (1.1)

SGA, small for gestational age

Evolution of weight, height and head circumference from birth to 24 months

The mean SDS for weight at 3 months of age (n=448) was -1.4 (1) SDS (WHO standards) and -0.8 (1.1) (Sempé standards) with a ponderal gain of 1.1(1.2) SDS (WHO standards); at 24 months (n=446) weight SDS values were -0.8 (0.7) and 0.6 (0.8), respectively (**Fig. 1**). At 6 months, 91.3% of infants had weight SDS values ≥ -2 SDS. At 24 months, mean body weight was 11 (0.9) kg, with 94.8% (423 of 446; OMS standards) and 96.6% (431 of 446; Sempé standards) infants showing recovery of weight, i.e. weight ≥ -2 SDS.

**Fig. 1.** Evolution of the weight of infants from birth to 24 months (according to WHO and Sempé and Pédrón standards). Results are given as mean standard deviation scores.

The mean SDS for supine length at 6 months of age was -1.1 (1) (WHO standards) and -0.4 (1.1) (Sempé standards) with a statural gain of 2.2 SDS (WHO standards). At 24 months, the mean SDS values were -0.8 (0.7) and -0.4 (0.7) respectively (**Fig. 2**). At 24 months, the mean height was 83.2 (2.4) cm. 87.9% (392 of 446; OMS standards) and 92.2% (411 of 446; Sempé standards) of infants had height ≥ -2 SDS.

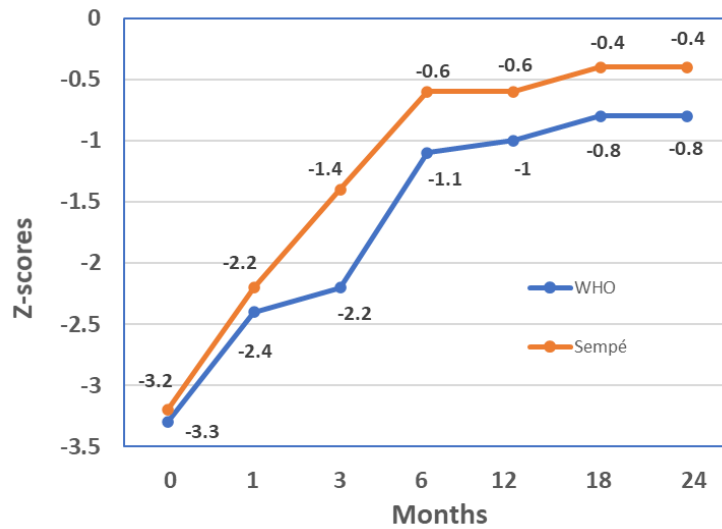


Fig.2. Evolution of the height of infants from birth to 24 months (according to WHO and Sempé and Pédrón standards). Results are given as standard deviation scores.

The mean head circumference SDS at 1 month of age was -1.5 (1.0) (WHO standards) and -1.5 (1.1) (Sempé standards); at 24 months, the mean scores were -0.6 (0.7) SDS and 0 (1) SDS, respectively (**Fig.3**). At 24 months, mean head circumference was 48.4 (1.2) cm: with 97.1% (433 of 446; OMS standards) and 96.0% (428 of 446; Sempé standards) of infants having head circumference ≥ -2 SDS.

At 24 months, 392 of 446 (87.9%) children had parameters ≥ -2 SDS (OMS standards) for all three growth parameters (height, weight and head circumference); 54 (12.1%) children failed to show full catch-up growth (i.e., one of the three growth parameters was < -2 SDS).

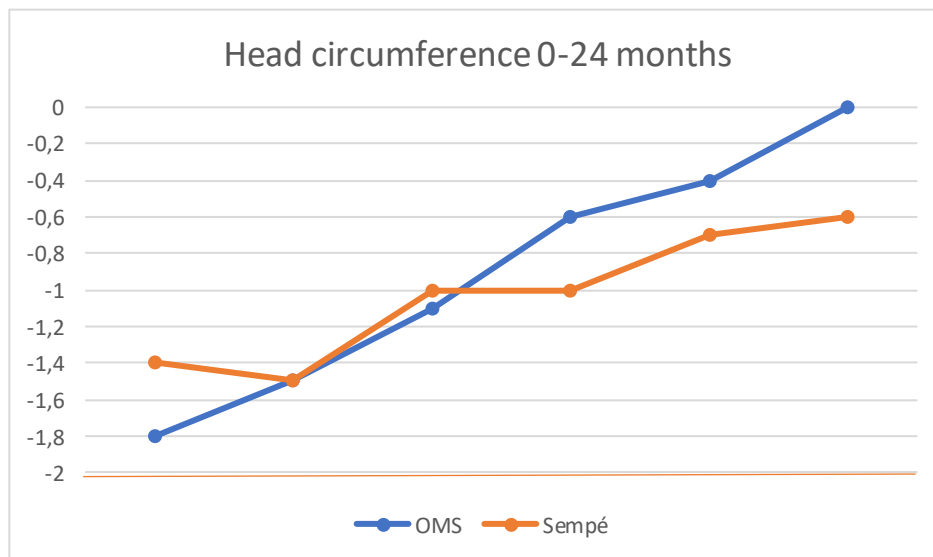


Fig.3. Evolution of the head circumference of infants from birth to 24 months (according to WHO and Sempé and Pédrón standards), given as mean standard deviation scores.

Factors associated to catch-up growth at 24 months

At 24 months, 392 of 446 (87.9%) children had parameters ≥ -2 SDS (OMS standards) for the three parameters (height, weight and head perimeter); 54 (12.1%) children did not catch-up growth (i.e., one of the three parameter was < -2 SDS).

In a univariate analysis, maternal height, history of SGA, ponderal index, severity of SGA, difference between mid-parental height and both birth length and height aged 24 months, and duration of breast-feeding were significantly associated with short stature at 24 months (**Table 3**).

In the multivariate analysis, the independent predictors associated with failure of catch-up growth at 24 months were maternal height, difference between mid-parental height SDS and birth length SDS, height at 24 months < -2 SDS below the mid-parental height, history of SGA, ponderal index $< 3^{\text{rd}}$ centile and duration of breast feeding < 3 months (**Table 4**).

IV. DISCUSSION

During the enrollment period, we recorded 967 (8.3%) low birth weight infants; 457 were born at term with SGA, representing 3.9% of births. These birth rates of SGA infants are close to that of developed countries, which range from 2.5% to 9% [14],[15]. In non-industrialized countries, the rate of births with SGA can be as high as 24.1% [4],[16],[17],[18],[19]. In the Maghreb, the prevalence of low birth weight was estimated to be 5.6% in Tunisia, of which three quarters were SGA cases, and in another study the SGA rate was estimated to be 6.1% [20],[21]. The overall incidence of low birth weight reported by UNICEF in developing countries is 14.3% [22]. Children born at term with SGA with catch-up growth at 24 months of age were compared with children with no catch-up. These comparisons allowed us to identify factors predictive of short stature at 24 months.

We observed that 89.7% of children born at term with SGA had an overall catch-up growth according to Sempé standards and 87.9% according to WHO standards with all three parameters (height, weight, head perimeter) above -2 SDS at 24 months. Therefore, according to Sempé and WHO standards, 10.3% and 12.1% of the study population showed persistent retardation, respectively. These data are comparable to those reported in the literature, with rates ranging from 8% to 13% for failure of catch up in SGA children [23],[24],[25],[26].

Our study identified independent predictive factors at birth in SGA newborns that predict failure to catch up at the age of 2 years. These parameters were maternal height, history of SGA, ponderal index and difference between mid-parental height and birth length as reported in previous studies [27]. We also identified two parameters during follow-up that predicted postnatal growth: breastfeeding for 3 months and height at 24 months less than -2 SDS below the mid-parental height SDS.

Table 3. Factors associated with catch-up growth at 24 months on univariate analysis in 457 infants who were small for gestational age at term.

Characteristics	OR (95% CI)	P-value	Significance
Mother's height, < 150 cm	9.05 (3.50-23.42)	27.10 ⁻⁷	S
≥150 cm			
Mothers BMI < 18.5	0.7(0.4-1.3)	1	NS
≥18.5			
Parity <2	0.8(0.44-1.5)	0.46	NS
≥2			
History of SGA Yes	0.28 (0.13-0.57)	763.10 ⁻⁷	S
No			
Severe SGA SGA < 3rd centile	0.4 (0.18-0.90)	0.012	S
SGA ≥ 3rd centile			
Ponderal index, < 3rd centile	4.51 (2.40-8.52)	10 ⁻⁸	S
≥ 3rd centile			
Sex Male	0.65 (0.34-1.23)	0.156	NS
Female			
Type SGA Symmetrical	1.58 (0.85-2.95)	0.117	NS
Asymmetrical			
SPC <4	1.2 (0.7-2.2)	0.90	NS
≥4			
MPH - Birth length <2.2	3.49 (1.80-6.78)	3.10 ⁻⁵	S
≥2.2			
Breastfeeding, < 3 months	2.86 (1.52-5.42)	304.10 ⁻⁶	S
≥ 3months			
MPH - Length at 24 months <-2SDS	20.40 (3.33-150.25)	35.10 ⁻⁵	S
≥- 2SDS			

BMI, body mass index; SDS, score of standard deviation; SGA, small for gestational age.

SPC, socio-professional category; MPH, mid-parental height

Table 4. Independent factors associated with catch-up growth at 24 months (multivariate analysis) in 457 infants who were small for gestational age at term.

Characteristics	B	SE	Wald	P value	OR	CI (OR: 95%)
Mother's height	2.048	0.576	12.652	0.00	7.751	2.508 23.955
History of SGA	1.448	0.456	10.076	0.002	4.255	1.740 10.402
Ponderal index	1.214	0.392	9.600	0.002	3.368	1.562 7.259
MPH -Birth length	1.295	0.412	9.899	0.02	3.652	1.630 8.183
Breastfeeding	1.046	0.402	6.785	0.09	2.847	1.296 6.256
MPH -Length 24 months	4.350	1.235	12.396	0.00	77.449	6.878 872.140

SDS, score of standard deviation; B, non-standardized coefficient, SE, standard error, OR, odds ratio, CI, confidence interval, SGA, small for gestational age; MPH, mid-parental height

In the literature, target height, birth height, sex, symmetrical or asymmetrical SGA, maternal smoking, maternal height and gestational age have been reported as predictive factors of catch-up growth [28], [29], [30], [31], [32], [33], [34], [35], [36]. Therefore, our results are comparable to those in the literature for target height, maternal height and history of SGA; however, they are discordant for birth height, which was not a predictive factor in our analysis [34],[37], [38], [39],[40]. Maternal smoking has also been identified as a predictive factor of short stature at the age of 2 years [41], [42],[43]; in our study, this factor was not found, but smoking was probably underreported. The relationship between breastfeeding duration and catch-up growth in infants with SGA is controversial [28], [31], [33], [35],[44], [45],[46]. To explain the discrepancies between our results and literature, it should be noted that the definition of SGA in these studies is heterogeneous due to a lack of consensus and different cut-offs used.

Head perimeter growth was the most rapid: 35% of children maintained a perimeter < -2 SDS at 1 month of age, whereas it was 54% for weight and 62% for height at the same age (Fig.4). A weight ≥ -2 SDS was achieved at 6 months by 78.7% of the study population and 60% for height (Fig 2,3), thus indicating slower growth for height than for weight, which is consistent with other studies [35],[47], [48],[49] .

The growth profile of the infants with SGA shows very rapid growth in the first few months of life, from 3 to 9 months, followed by a slowdown between one and two years [40],[50], [51], [52], [53], [54], [55],[56]. Thus, children who do not catch up in the first six months and the first year are likely of not catching up later [29], [47], [54],[57]. As reported in many studies, weight and height gain within the first six months is critical for postnatal growth [33], [34], [38], [39], [44], [58], [59],[60].

Studies that evaluated growth gain in SGA infants after 2 years of age are rare, but they indicate that only a small proportion achieves normal growth beyond this limit [32], [36], [58]. Currently, most authors agree that the pivotal point is 2 years of age [61]. Studies in SGA newborns have supported these findings by showing a significant influence of height at 2 years of age on adult height, with a 5- to 7-fold increase in the risk of remaining small at that age [34], [40], [60], [62].

Although our results are comparable to other studies in the world, we remain very cautious in terms of making a distinction between SGA and IUGR. Distinguishing those babies who are SGA owing to IUGR is important. Use of personalized growth curves at birth, where the newborn infant is his/her own reference, and comparison of size at 2 years with parental heights, which were available in 91% of cases in our cohort, are useful with respect to the recognition of IUGR. Continuing follow-up until the age of 4 years is also necessary in order to differentiate SGA due to constitutional small size from IUGR with no catch-up growth. This latter group of children are the population in whom growth hormone treatment may be appropriate, as per the published SGA guidelines [1],[6].

This study has some limitations. It has been performed in a unique center and there is no guarantee that the rates of prevalence of term SGA infants can be generalized to all maternity centers in Algeria. The strengths of this study are its prospective design and the systematic record of all births during 16 months in our hospital, meticulous measurement by a single observer in infants found to be SGA, and successful follow-up of the anthropological parameters of almost all enrolled infants over two years.

In conclusion, this study provides data concerning the epidemiology of SGA births in Algeria and the factors associated with post-natal growth. These results are in favor of setting up a national program, integrating obstetricians and pediatricians for a joint action for the ante- and postnatal follow-up of SGA infants, so that those children failing to show catch-up growth can be identified , and whose heights from 4 years of age continue to fall at least two or more SD below the mid-parental heights, in order to propose reserving growth hormone therapy for them.

Competing interests: The authors declare no competing interest.

Authors' contributions: Study concept: FB; Study design: FB; Data collection and processing: FB; Analysis and interpretation: FB; Literature search: FB ; Manuscript writing: FB. All authors approved the final version of the manuscript.

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