# BODY SIZE IN CHILDREN
# WITH CONGENITAL HYPOTHYROIDISM

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Abstract: *In 1995, the Italian Study Group for Congenital Hypothyroidism (ISGGH) undertook a multicentre survey (18 centres) involving the retrospective collection of endocrinological and growth profiles of 844 subjects (580 girls and 264 boys) with congenital hypothyroidism (CH), and born between 1957 and 1995. In this note body size and proportions at diagnosis of 111 patients (83 girls and 28 boys) detected between 2 and 36 months of age are compared with Italian norms for children up to 3 years. In children with GH, spontaneous growth of body length was found to be impaired more (-2.03±0.16 SDS, mean±standard error) than weight (-0.93±0.13 SDS) and head circumference (-0.26±0.15 SDS). This results in a disproportionate appearance which becomes more severe with increasing age: the difference between the SDS of height and head circumference was larger than 2 in 9% of babies aged under 6 months and in 80% of children aged over 18 months. Mean adult height (available for 40 subjects) was 2.9±1.9 cm above the target in children diagnosed and treated before 6 months, and -3.3±1.3 cm below the target in children diagnosed after 18 months. These findings confirm the importance of screening tests for hypothyroidism at birth and immediate thyroid hormone replacement also to correct short stature in CH.*

Keywords: *Congenital hypothyroidism, lenght, weight, head circumference.*

## Introduction

Congenital hypothyroidism (CH) is a pathology characterised by severe mental retardation, delay in skeletal and pubertal maturation, and growth impairment. Neonatal screening and early treatment with thyroid hormone replacement are known to prevent children with congenital hypothyroidism (CH) from abnormal development.

In Italy, where CH is observed in 4.1 newborn infants out of 10,000 (Giovannelli 1995), neonatal screening was introduced in 1978 and was extended to the whole country since 1992. In 1995, the Italian Study Group for Congenital Hypothyroidism (ISGCH) undertook a retrospective multicentre survey with the aim of evaluating skeletal maturation and somatic growth in CH children detected at birth by screening, and during infancy by signs and symptoms. Actually, most literature focuses on neurologic development of CH children, but relatively few are data on somatic growth, mainly as regards final height (Bucher, Prader and Illig 1985, Chiesa, Gruñeiro de Papendieck, Keselman, Heinrich and Bergada 1994; Boersman, Otten, Stoelinga and Wit 1996).

The aim of this note is to describe body size and proportions at diagnosis of CH children detected between 2 and 36 months of age, and the effects of late diagnosis and treatment on adult height.

## Subjects and methods

Data here analysed come from the retrospective collection of endocrinologic and auxo-logic profiles of 844 CH subjects (580 girls and 264 boys) born between 1957 and 1995. Among these, 111 children (83 girls and 28 boys) were detected by signs and symptoms between 2 and 36 months of age.

Supine length, body weight and head circumference at birth were compared with the Italian neonatal charts (Bossi and Milani 1986, 1987), based upon sample of 16,336 neonates. Supine length, body weight and head circumference at diagnosis were compared with the Italian longitudinal norms for children up to 3 years (Cortinovis, Bossi, Milani 1993), based upon a sample of 10,414 reference infants measured at birth, and approxi-mately at 3, 6, 9,12, 18, 24, 30 and 36 months of life. Final height was compared to final height of Tanner-Whitehouse norms (1976). Target height was defined as the midparental height decreased by 6.5 cm in girls, and increased by 6.5 cm in boys. Skeletal age at diag-nosis was assessed, in most cases, by Greulich-Pyle atlas method (1959).

Standard deviation scores (SDS) were derived from the above standards as follows:

$$SDS = \frac{child's\ size\ at\ age\ t - mean\ size\ at\ age\ t}{standard\ deviation\ at\ age\ t}$$

In children aged under 3 years, the distribution is approximately Gaussian not only for supine length and head circumference but also for body weight: therefore SDS values have Gaussian distribution for all these auxometric traits.

## Results

In our sample CH neonates are similar to normal neonates for gestation age (mean = 40.0 weeks, SD =1.3 weeks), but are slightly heavier. In CH neonates mean birthweight is 3396 g (SD = 515 g) for girls, and 3608 g (SD = 698 g) for boys; in normal at-term neonates mean birthweight values of 3319 g (girls) and 3475 g (boys) are reported (Bossi and Milani 1986). On the average, birthweight is appropriate for supine length (difference weight-SDS minus length-SDS: -0.09±0.19, mean±SE), whereas head circumference is slightly dispro-portionate (difference head circumference-SDS minus length-SDS: +0.44 ±0.22).

In untreated CH girls and boys, growth of length appears to be affected progressively with age: at 2 months most of babies are below the 50th percentile of the Italian norms, and all children aged over 18 months are below the 3rd percentile (Figure 1, top). In untreated CH girls and boys, growth of weight appears to be less impaired than growth of length, in any case most of children aged over 18 months are below the 10th percentile (Figure 1, centre). As a result, untreated CH children show too high values of weight for length. This disproportionate appearance becomes more severe with increasing age: the dif-ference between the SDS values of weight and length (W-L-SDS) is larger than 2 in 4% of babies aged under 6 months and in 37% of children aged over 18 months (Figure 2, left).
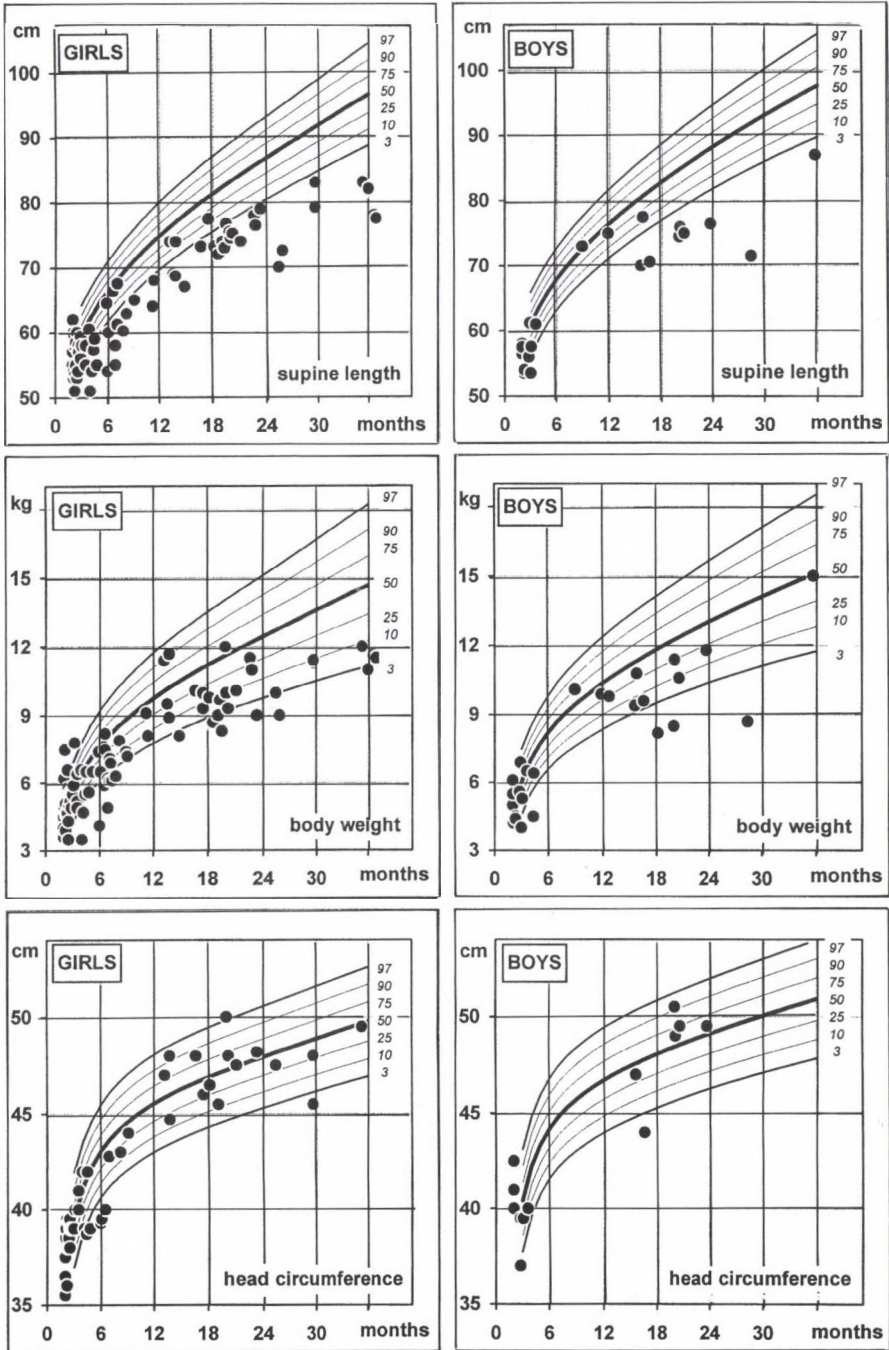
*Fig. 1:* Supine length (top), body weight (centre) and head circumference (bottom) at diagnosis in CH children (dots), compared with Italian longitudinal norms for children up to 3 years (continuous lines)

In this regard, is useful to recall that under assumption of proportionate growth, only 0.7% of children are expected to show a W-L-SDS larger than 2, the standard deviation (conditional on sex and age) of the differences W-L-SDS being equal to 0.82. Therefore the frequency of CH children with W-L-SDS larger than 2 is from 6 (under 6 months) to about 50 (over 18 months) times higher than the frequency expected in the case of proportionate growth. On the other hand, only 8% of children show negative W-L-SDS values, the expected frequency being 50%.

In untreated CH children aged up to 3 years, growth of head circumference does not seem different from that of normal children (Figure 1, bottom). For this reason, untreated CH girls and boys show too high values of head circumference for length. This disproportionate appearance becomes more severe with increasing age: the difference between the SDS of head circumference and length (H-L-SDS) is larger than 2 in 9% of babies aged under 6 months and in 80% of children aged over 18 months (Figure 2, right). Under assumption of proportionate growth, only 2.9% of children are expected to show an H-L-SDS larger than 2, the standard deviation of the differences H-L-SDS being equal to 1.06. Therefore the frequency of CH children with H-L-SDS larger than 2 is from 3 to about 30 times higher than the expected frequency. Only 9% of children show negative H-L-SDS values.
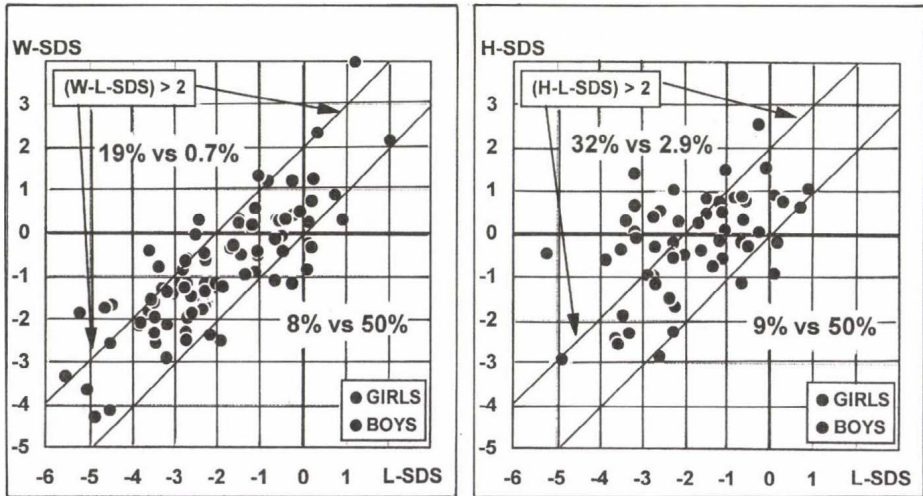


*Fig. 2:* Relationship of weight SDS (W-SDS, left) and head circumference-SDS (H-SDS, right) to supine length SDS at diagnosis in CH children
The children with W-SDS (or H-SDS) lower than L-SDS are represented by the dots below the lower oblique line. The children with W-SDS (or H-SDS) higher than L-SDS by 2 SDS are represented by the dots above the upper oblique line

Skeletal age at diagnosis, available for 27 children only, appears to be delayed by 0.94±0.14 years with respect to chronological age. In particular, in the 14 children diagnosed after the 18th month, skeletal age is delayed by 1.49±0.42 years.

Late diagnosis and therapy are related to low final height (Figure 3 and Table 1).
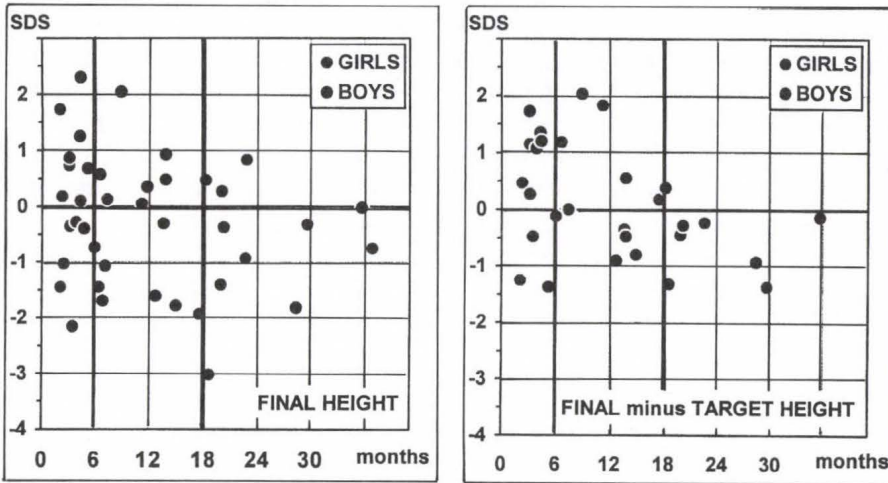


*Fig. 3:* Relationship of final height-SDS (left) and difference final height-SDS minus target height-SDS to age at diagnosis (right)

*Table 1:* Mean final height and mean difference between final height and target height (expressed as SDS) in CH children

| Age at diagnosis | Final height SDS | | Final minus target height SDS | |
|---|---|---|---|---|
| | N | mean±SE | N | mean±SE |
| under 6 months | 15 | +0.10±0.31 | 12 | +0.45±0.30 |
| 6 to 18 months | 14 | -0.38±0.33 | 10 | +0.32±0.33 |
| over 18 months | 11 | -0.64±0.34 | 8 | -0.54±0.22 |
| **all children** | **40** | **-0.27±0.19** | **30** | **+0.14±0.19** |

Out of the 29 CH subjects detected within 18 months of age, 15 have achieved a final height above the average adult height. By contrast, only 3 out of the 11 subjects diagnosed after the 18th month show final height above the average (Figure 3, left). This result does not depend on differences in target height between children diagnosed within the 18th month and those diagnosed after the 18th month. As a matter of fact, when the difference final height minus target height is taken into account, it emerges that 13 out of the 22 CH subjects detected within the 18th month show final height greater than target height, whereas only 1 girl among subjects detected after the 18th month went beyond her target.

## Comments

Neonatal data reported above indicate that CH and normal newborn infants are similar for length of gestation as well as for body size and shape, although in CH neonates head circumference tends to be slightly too large with respect to crown-heel length. This finding indicates that during intrauterine life thyroid hormones have mild effects on somatic growth, while are essential to the normal neurologic development.

During infancy, height growth of untreated CH subjects is affected more severely than weight and head circumference growth. The growth damage leads to a disproportionate shape, which becomes more and more apparent with increasing age. Of course, the age at the beginning of the treatment with thyroid hormone is not the only factor which affects somatic growth of CH children: type of diagnosis (agenesis, ectopic gland, hypothyroidism with gland in place) and its correlation with the severity of hormone deficit, concomitant congenital anomalies, type of drug administered (extract of dry thyroid gland or L-thyroxine), dosage and patient's compliance may have a not negligible role. In any case, early diagnosis and adequate treatment with thyroid hormone may prevent CH children from impairment of growth, while a belated intervention may result in a final short stature.

The results here outlined confirm the importance of screening tests for hypothyroidism at birth and immediate thyroid hormone replacement as regards not only psychological and intellectual maturation, but also somatic development

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