Endocrine disorders and maxillary and mandibular growth in children and adolescents treated at the Pediatric Endocrinology Service at CES Clinic in Medellín Colombia.

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Abstract

Objective: To establish the influence of medicated hypothyroidism, overweight/obesity and medicated non-syndromic hypogrowth on maxillary and mandibular growth.

Materials and methods: Cross-sectional study that evaluated the relation between craniofacial anthropometric measurements with hypothyroidism (n=216), overweight/obesity (n=108) and non-syndromic hypogrowth (n=250) in patients between 1 and 19 years old and a control group of healthy patients (n=587). A subgroup analysis was performed at peak growth in groups.

Results: Patients with hypothyroidism and overweight/obesity showed increased craniofacial growth; hypogrowth patients showed differences in growth in zygomatic width and nasal base. At peak growth, there was a decrease in head circumference in females with hypothyroidism and non-syndromic hypogrowth. In patients with overweight/obesity, head circumference was increased together with other anthropometric measurements. When all ages were analyzed, overweight/obese patients or hypothyroidism showed increased zygomatic width while decreased hypogrowth. Most craniofacial anthropometric measurements in overweight/obese patients were increased when age was not discriminated. Finally, growth peak in males with hypothyroidism and males and females with non-syndromic hypogrowth was delayed compared to the control group ($P<0.05$).

Conclusions: Children and adolescents with endocrine disorders present alterations in craniofacial growth. Clinicians must be aware that the growth peak in these patients may be delayed when determining the precise timing for the initiation of maxillary and mandibular orthopedic treatment.

Key Words

Thyroid disorders, obesity, growth hormone deficiency, anthropometry.

Introduction

General somatic growth, and specifically craniofacial growth, depends on interacting processes that transform the human being from birth to adulthood (Gorstein 1994). Craniofacial growth is characterized by marked changes in speed, size, shape, and function, attributed to genetic, hormonal, and environmental factors. Hypothyroid status, obesity, and growth hormone deficiency can alter normal growth and maturation of developing children, affecting the harmonious relationship between different facial structures (Nahhas 2014).

Said alterations are highly prevalent in the Colombian population; a 2020 report by the Colombian Association of Endocrinology, Diabetes and Metabolism, indicates that hypothyroidism has a prevalence of 9.9% in Colombia. Moreover, the 2015 National Nutritional Health Survey conducted by the Colombian Ministry of Health showed that the prevalence of overweightness was 37.7% and obesity 18.7% for a total of 56.4% and the prevalence of growth hormone deficiency was 10.8% in children younger than 5, 7.4% in children between 5 and 12 and 9.7% in children between 13 and 17.

Hypothyroidism affects cardiovascular, neurological, gastrointestinal, and metabolic functions (Wassner, 2017). At the craniofacial level, delayed tooth eruption, enamel hypoplasia, micrognathism and retrognathism, as well as anterior open bite and tooth impaction, have been observed (Vuccic 2017). Overweightness and obesity at a general level increase musculoskeletal injuries, alters bone metabolism, stimulates bone growth and inhibits bone remodeling (Dimitri 2019) and at a craniofacial level, can cause prognathism (Danze 2021), increased facial height (Cuccia 2007), early tooth eruption (Saloom 2017) and periodontitis (Zhu 2017); growth hormone deficiency decreases growth velocity, leading to an immature facial appearance, short stature, hair deficiency and delayed puberty (Ogilvy-Stuart 1992), and at a craniofacial level, can lead to maxillary hypoplasia and/or mandibular retrognathism (Atanassio 2017), anterior open bite, hyper divergence (Buschang 2005), decreased anterior facial height and short mandibular ramus (Oliveira Neto 2011).

These disorders cause changes in craniofacial growth and development structures, including the maxilla and mandible, thus the importance for clinicians to be aware that they can affect peak growth. The objective of this study was therefore to establish the influence of medicated hypothyroidism, overweightness/obesity and medicated non-syndromic hypogrowth on maxillary and mandibular growth, in a group of patients treated between 2014 and 2021 at the Pediatric Endocrinology Outpatient Service at CES Clinic in Medellín, Colombia using anthropometric measurements when compared with a control group of healthy individuals.

Materials and methods

This quantitative, retrospective cross-sectional analytical study was carried out on a sample of 1508 children and adolescents, between 1 and 19 years old, distributed in 4 age groups between 1 to 4, 5 to 9, 10 to14 and 15 to 19 years old with a clinical diagnosis of hypothyroidism (n=216), overweight/obesity (n=108), or non-syndromic hypogrowth (n=250) and a control group of 587 healthy subjects. Patients with hypogrowth of syndromic origin or with syndromes that affect craniofacial morphology were not included nor were children who did not consent to participate in the study or whose relatives did not consent to do so.

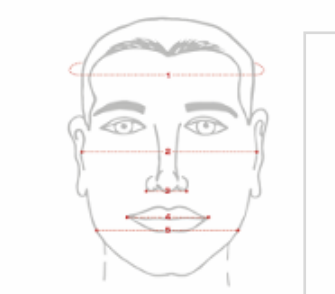
Data was collected from the medical records of the Pediatric Endocrinology Outpatient Service at CES Clinic between 2014 and 2021, prior authorization from the Institution, and assent of minors and informed consent from the families was obtained. The study was approved by the Universidad CES Institutional Ethics Review Board as stated in minute number 178 of October 28, 2021.

Patient weight was recorded in grams using a SECA 803 electronic scale and height with a wall measuring rod that complies with Colombian regulations (Resolution 2465 of 2016). Bone maturation, as an indicator of skeletal age, was calculated using the Greulich and Pyle method (Greulich 1950). Hypothyroidism was evaluated by measuring TSH and T4 hormones with a blood test with a prior 8 hour fasting period. Hypothyroidism was diagnosed when TSH > 6 mU/L or T4 < 0.8 mU/L (based on the Latin American Association of Endocrinology). Obesity was classified at two moments between birth and 5 years; weight was evaluated when height was more than 3 standard deviations (SD) above the median established for childhood growth standards based on the WHO Growth Chart tables between 5 and 19 years old, and Body Mass Index (BMI) was assessed for age and gender with more than 2 standard deviations (SD) above the established median in according to the same growth charts. Hypogrowth was diagnosed when height was 2 standard deviations (SD) below the median in the same growth chart (Mercedes 2006). Anthropometric measurements were taken with a Mitutoyo reference 530-114 caliper with an error limit of 0.05mm/m. Graph 1 shows the reference points for each of the anthropometric distances measured (Vásquez 2014).

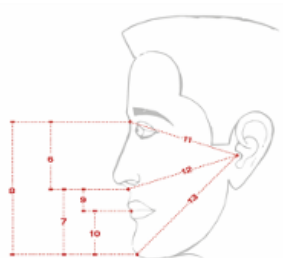
To determine the Tanner growth stage, as an indicator of pubertal development, the stages suggested by Tanner and Marshall (Marshall 1970) made through breast analysis and pubic hair growth in females, and testicle analysis and pubic hair growth in males (see graph 1) (Molina 2009).

Anthropometric measurements were taken by a single operator, who was previously standardized in the location of points with an expert endocrinologist with an average intra-observer reliability of 0.97 according to the intraclass correlation coefficient (ICC), with a minimum of 0.95. and a maximum of 0.99. Measurements were made at three different times until obtaining an ICC value >= 0.95 in every individual. Likewise, a new standarization was carried out, which was carried out each time a new group of patients was available with a pilot test of at least 20 readings.

Figure 1. Anthropometric measurement (Alfaro 2014)

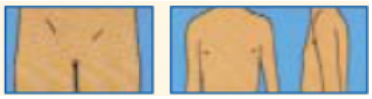
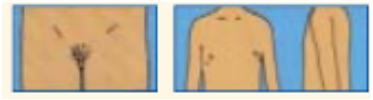
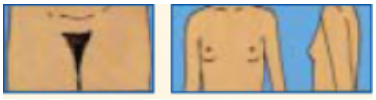


1. Head circunference
2. Zygomatic width
3. Nasal base width
4. Intercommissural distance



5. Nasion-Subnasal
6. Subnasal- Interlabial
7. Interlabial-Menton
8. Cranial base lenght
9. Maxillary lenght
10. Mandibular lenght

Figure 2 . Tanner scale according to gender (Tanner 1969)

Females	**Males**
 **Stage 1.** Infantile chest, no pubic hair.	 **Stage 1.** No pubic hair. Infantile testicles and penis.
 **Stage 2.** Breast bud, sparse non-curly pubic hair, in labia majora.	 **Stage 2.** Enlargement of the scrotum and testicles, reddened and wrinkled scrotal skin, infantile penis. Sparse pubic hair on penis pass.
 **Stage 3**. Breast and areola augmentation and elevation, curly, coarse, dark hair on the pubis.	 **Stage 3.** Enlargement and thickening of the penis. Enlargement of testicles and scrotum. Curly, coarse,

	dark pubic hair.
 **Stage 4.** Areola and nipple raised above the breast. Adult type pubic hair not on thighs.	 **Stage 4.** Enlargement of the penis and glans, enlargement of testicles, enlargement and darkening of scrotum. Adult pubic hair does not cover thighs.
 **Stage 5.** Adult breast, areola not raised. Adult medial thigh hair.	 **Stage 5.** Adult genitalia. Adult hair that extends to the medial area of the thighs.

Statistical analysis

To determine the relationship between endocrine disorders and craniofacial development in children and adolescents, a non-probabilistic sample was formed by concurrence based on the medical records of patients who consulted the Pediatric Endocrinology Service at CES Clinic in Medellín. Sagittal and vertical facial anthropometric measurements were taken of each patient using a Mitutoyo reference 530-114 instrument. Measurements and variables related to somatic growth including Tanner scores, age, height, weight and skeletal age were recorded.

A descriptive analysis was carried out in tables and graphs for the categorical variables, while quantitative variables such as summary, central tendency, dispersion, and position measures were estimated; normal distribution of said variables was assessed with the Shapiro-Wilks and Asymmetry and Kurtosis tests with statistical significance established at $p<0.05$. Given that none of the quantitative variables related to facial anthropometric measurements and somatic growth presented a normal distribution, the comparisons in the bivariate analysis were made using the Mann-Whitney U test.

Results

The total sample analyzed consisted of 1,506 patients (49.14% (n=741) male and 50.73% (n=765) female), there was no information on the gender or age of 2 participants (0.13%) who were not included in the analysis by sex and age. The age groups with the highest number of patients were 10 to 14 years old (49.4% males and 46.0% females) and 5 to 9 years old (24.2% males and 36.6% females) (see table 1).

Table 1. Description of age groups according to gender.

Age	Gender	
	Male	Female
	n (%)	
1 - 4	44 (5.9)	49 (6.4)
5 - 9	179 (24.2)	280 (36.6)
10 - 14	366 (49.4)	352 (46.0)
15 - 19	152 (20.5)	84 (11.0)
Total	741	765

n sample size.
% percentage.

According to the diagnostic classification of the patients, as shown in Table 2, there was a total of 38.9% healthy individuals (n=587), and 61% (n=921) presented some type of disorder. There were no significant differences in the proportion of healthy subjects and those with obesity between male and female patients (p=0.685 p=0.533 respectively); there was a higher proportion of girls with medicated hypothyroidism compared to boys (17.1% Vs 11.5%, p=0.002), while there was a higher proportion of boys with non-syndromic hypogrowth compared to girls (23.5% Vs 9.9%, p=0.000). The other disorders found were diabetes, dyslipidemia, thyroiditis, young pregnant girls, and hyperthyroidism, which were not considered for the analysis due to the differences observed when compared with other disorders.

Table 2. Distribution of disorders according to gender.

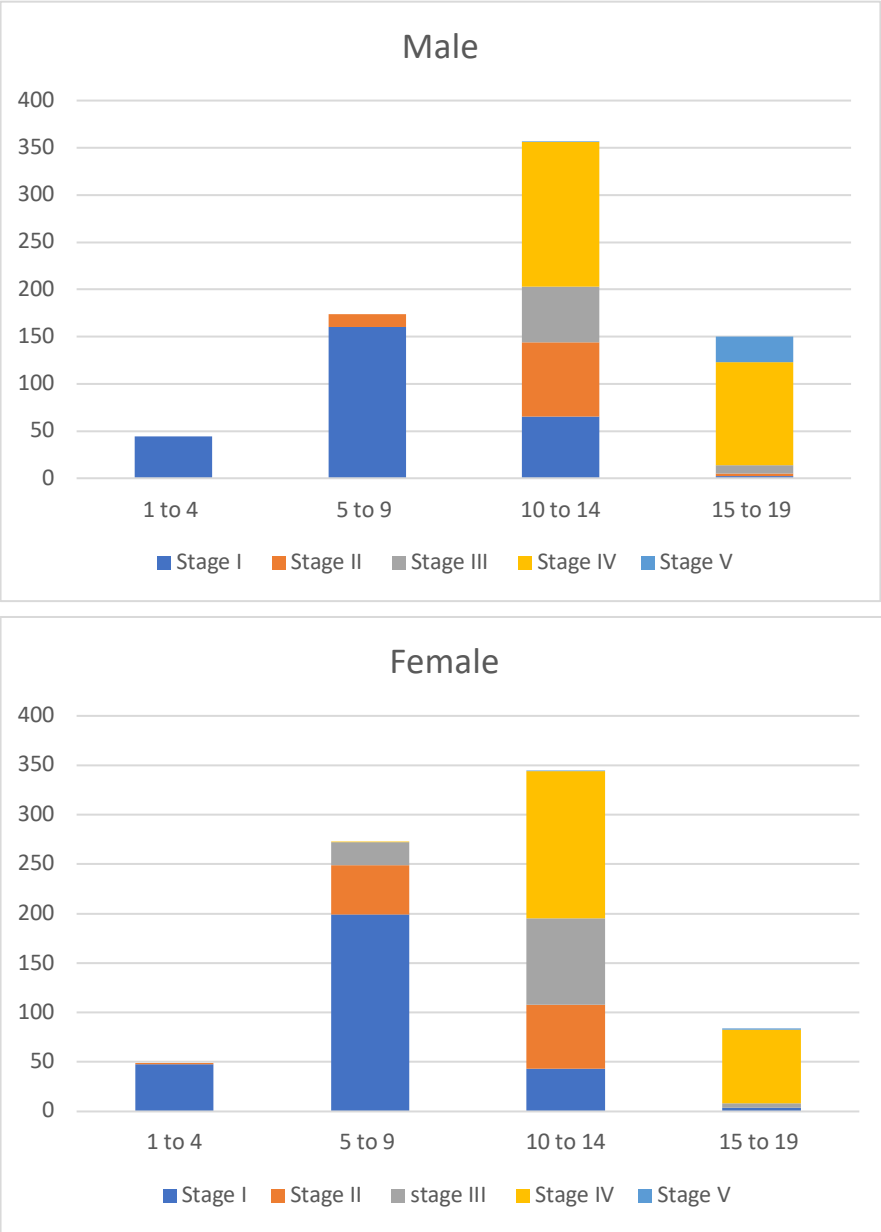
Condition	Sex		Total	p-value
	Male	Female		
	n (%)			
Healthy	285 (38.5)	302 (39.5)	587 (38.9)	0.685
Medicated hypothyroidism	85 (11.5)	131 (17.1)	216 (14.3)	0.002*
Obesity/ Overweight	50 (6.8)	58 (7.6)	108 (7.2)	0.533
Non-syndromic hypogrowth	174 (23.5)	76 (9.9)	250 (16.6)	0.000*
Other endocrine disorders	147 (19.8)	198 (25.9)	347 (23.0)	0.005*
Total	741 (100)	765 (100)	1.508 (100)	

n sample size
% percentage.
* p-value calculated with the non-parametric Mann–Whitney U test..

No significant differences were observed between boys and girls on Tanner scores in the 1–4-year-old group. In the 5 to 9 age group, most boys presented a Tanner I stage and some Tanner II, while a small proportion of girls presented Tanner I and there was an increased proportion of those in stages II, III and IV. A similar distribution was also observed in the 10-14 age group, while in the 15-19 age group, Tanner IV and V scores

represented the highest proportion in both boys and girls, with Tanner V scores representing a small proportion in girls compared with boys the same age (see table 3).

Grafic 3. Tanner scores according to chronological age and gender.



Comparison of anthropometric measurements in all age groups described in Table 4 indicates that there were some significant differences between healthy subjects and those with hypothyroidism, obesity/overweight and hypogrowth. Although the mean and standard deviation are described, the comparison between the groups was made using a Mann-Whitney U non-parametric test given that none of the measurements followed a normal distribution pattern. Children with hypothyroidism who were obese/overweight, presented head

circumference, zygomatic width, nasal base width, inter-commissure distance, cranial base length, maxillary length, and mandibular length measurements that were significantly different when compared with healthy individuals. In addition, obese/overweight children presented subnasal-interlabial and inter-labial chin measurements that were also significantly higher, indicating that except for the subnasal-nasion measurement, all other anthropometric variables were significantly altered when compared to healthy individuals in this group. With regards to children that presented hypogrowth, significant differences were only observed for zygomatic width, which was decreased, and nasal base width, which was increased when compared to healthy subjects.

Table 4. Comparative table of anthropometric measurements for each diagnosis at all ages.

	Healthy children (n:587)	Mmedicated hypothyroidism (n:216)		Obesity/ Overweight (n:108)		Non-syndromic hypogrowth (n:250)		Other disorders (n:347)	
Measurement	**Median +/- SD mm**	**Median +/- SD mm**	**p-value***	**Median +/- SD mm**	**p-value ***	**Median +/- SD mm**	**p-value***	**Median +/- SD mm**	**p-value***
Head circunference	52.9 +/- 2.5	53.5 +/- 2.2	0.0014*	54.7 +/- 2.0	0.000*	52.7 +/- 2.2	0.183	53.2 +/- 2.3	0.1237
Zygomatic width	110.9 +/- 10.2	112.9 +/- 10.9	0.011*	118.9 +/- 13.8	0.000*	107.7 +/- 10.7	0.0003*	111.7 +/- 11.6	0.229
Nasal base width	28.1 +/- 5.9	29.4 +/- 5.8	0.003*	29.9 +/- 6.9	0.009*	29.1 +/- 5.8	0.016*	29.0 +/- 6.2	0.040*
Intercommissural distance	42.9 +/- 5.1	43.8 +/- 5,3	0.0164*	43.7 +/- 6.0	0.046*	43.2 +/- 5.6	0.115	43.4 +/- 5.8	0.127
Nasion-Subnasal	55.1 +/- 5.8	55.7 +/- 6.8	0.115	55.4 +/- 6.3	0.650	54.6 +/- 6.7	0.948	54.4 +/- 6.5	0.217
Subnasal-Interlabial	19.6 +/- 2.7	19.6 +/- 2.5	0.979	20.6 +/- 4.6	0.006*	19.5 +/- 2.8	0.917	19.5 +/- 2.6	0.709
Interlabial-Menton	42.5 +/- 5.0	42.5 +/- 5.3	0.755	45.2 +/- 5.5	0.000*	41.8 +/- 5.8	0.223	42.4 +/- 5.5	0.896
Cranial base length	110.6 +/- 8.6	112.6 +/- 9.6	0.000*	115.5 +/- 10.0	0.000*	108.9 +/- 10.0	0.078	110.2 +/- 10.5	0.863
Maxillary Length	108.4 +/- 8.1	110.8 +/- 8.3	0.000*	113.6 +/- 9.1	0.000*	107.5 +/- 11.2	0.527	108.8 +/- 8.7	0.444
Mandibular Length	121.6 +/- 47.4	122.5 +/- 10.0	0.001*	127.5 +/- 12.5	0.000*	119.3 +/- 10.9	0.750	120.8 +/- 10.7	0.168

n sample size

* p-value calculated with the non-parametric Mann–Whitney U test..

The correlation between chronological and skeletal age variables, according to the Spearman correlation coefficient (rho) as shown in table 5, indicates a strong and positive correlation for the different disorders as well as in healthy children in both sexes, except for obese children, where the correlation coefficient between said variables was not significant (p=0.108)

Table 5. Correlation between chronological and skeletal age according to disorder and gender.

	Male		Female	
Disorder	rho	p-value	rho	p- value
Healthy	0.9	0.000*	0.8	0.000*
Medicated Hypothyroidism	0.8	0.000*	0.6	0.000*
Overweight/Obesity	0.6	0.108	0.8	0.000*
Non-syndromic hypogrowth	0.8	0.000*	0.8	0.000*
Others	0.8	0.000*	0.7	0.000*

Spearman rho correlation coefficient.

Overall, no significant difference in average skeletal age between males and females between 5 to 15 years of age when comparing the different groups of disorders with healthy counterparts were observed, with the exceptions of increased skeletal age in healthy males between 10 and 15 years of age when compared to hypothyroid individuals (p = 0.037), in healthy females between 5 and 9 years old compared to non-syndromic hypogrowth patients (p =0.001), and healthy males between 10 and 15 years old compared with non-syndromic hypogrowth males (p=0.001).

Table 6. Comparison of skeletal age according to chronological age group and gender.

Age Group	Gender	Healthy children	Medicated hypothyroidism		Overweight/ Obesity		Non-syndromic hypogrowth		Other disorders	
		Median +/- SD	Median +/- SD	P value	Median +/- SD	P value	Median +/- SD	p value	Median +/- SD	p value
5-9	Female (n:273)	7.4 +/- 2.0	8.1 +/- 1.9	0.29	8.1 +/- 1.5	0.559	5.8 +/- 2.2	0.001*	8.3 +/- 2.2	0.017
	Male (n:174)	6.3 +/- 1.9	6.0 +/- 1.2	0.618	8.7 +/- 1.6	0.17	6.5 +/- 2.0	0.628	7.0 +/- 2.5	0.14
10-15	Female (n:345)	10.3 +/- 2.1	10.2 +/- 1.9	0.977	10.3 +/- 1.3	0.543	9.5 +/- 2.2	0.018	10.7 +/- 1.5	0.243
	Male (n:366)	11.7 +/- 2.0	10.1 +/- 3.0	0.037*	10.6 +/- 2.2	0.246	10.4 +/- 2.5	0.001*	11.7 +/- 1.9	0.931

n sample size.

* p-value calculated with the non-parametric Mann–Whitney U test.

Considering that the Tanner II index in females and the Tanner IV index in males are related to the maximum peaks of skeletal maturation, the different anthropometric measurements were compared between healthy patients and those with different disorders. Tanner IV male hypothyroid patients did not present significant differences of any of the anthropometric measurements with respect to healthy patients, while significant differences were observed for head circumference (p=0.035) and the interlabial-chin distance (p=0.030) in Tanner II hypothyroid female patients compared to healthy ones in the same group. In the case of overweight/obese patients for both genders and in the Tanner groups specified in Table 7, it was observed that many of the anthropometric measurements were significantly higher compared to healthy non-obese patients. When comparing Tanner II healthy females with those presenting non-syndromic hypogrowth, the only anthropometric measurement that was significantly different was decreased head circumference (p=0.049) in those with the disorder; moreover, a difference in zygomatic width (p= 0.023) between Tanner IV healthy males with those that presented non-syndromic hypogrowth , which was decreased in the latter group was observed.

Table 7. Comparison of anthropometric measurements between the groups of healthy children and those with disorders according to gender and Tanner.

Gender	Tanner	Measurement (mm)	Healthy children Median +/- SD	Medicated hypothyroidism Median +/-SD	p value	Overweight/ Obesity Media +/- DE	P value	Non-syndromic hypogrowth Median +/- SD	p value	Other disorders Median +/-SD	p value
F	Tanner II (n:116)	Head circunference	52.7 +/- 1.7	51.3 +/- 2.0	0.035*	54.6 +/- 1.2	0.002*	51.5 +/- 1.5	0.049*	53.2 +/- 1.8	0.264
		Zygomatic width	109.3 +/- 7.8	108.2 +/- 8.9	0.869	119.0 +/- 7.8	0.003*	109.2 +/- 8.1	0.920	111.8 +/- 8.0	0.080
		Nasal base width	28.0 +/- 5.0	31.3 +/- 4.7	0.082	31.4 +/- 4.8	0.051	27.8 +/- 5.6	0.902	28.1 +/- 5.6	0.993
		Intercommissural distance	42.1 +/-4.3	43.0 +/- 4.7	0.634	42.9 +/- 6.3	0.233	39.2 +/- 10.2	0.484	43.6 +/- 3.9	0.071
		Nasion-Subnasal	54.3 +/- 5.3	52.7 +/- 6.0	0.289	57.5 +/- 5.9	0.130	54.4 +/- 4.4	0.984	55.8 +/- 4.1	0.335
		Subnasal-Interlabial	18.7 +/-2.2	18.7 +/-2.0	0.676	19.7 +/- 3.1	0.229	19.3 +/- 2.4	0.296	19.5 +/- 2.4	0.119
		Interlabial-Menton	41.6 +/-2.9	38.7 +/-4.0	0.030*	44.6 +/- 2.9	0.011*	40.1 +/- 4.2	0.339	41.9 +/- 4.6	0.700
		Cranial base length	108.6 +/- 7.2	109.1 +/-5.1	0.846	118.7 +/- 2.6	0.000*	103.6 +/- 11.2	0.080	108.9 +/- 10.9	0.257
		Maxillary length	107 +/-5.0	10.5 +/- 5.5	0.540	114.6 +/- 2.5	0.000*	102.9 +/- 6.8	0.051	107.3 +/- 7.1	0.426
		Mandibular length	118.5 +/-6.1	116.7 +/- 6.3	0.307	127.1 +/- 2.9	0.000*	116.2 +/- 5.7	0.258	118.4 +/- 6.1	0.731
M	Tanner IV (n:262)	Head circumference	54.5 +/- 1.8	55.0 +/- 1.5	0.108	56.0 +/- 2.0	0.006*	54.2 +/- 1.7	0.154	54.9 +/- 1.7	0.148
		Zygomatic width	115.7 +/- 8.6	118.2 +/-8.7	0.120	121.1 +/- 19.1	0.002*	112.9 +/- 8.0	0.023*	116.8 +/- 15.2	0.663
		Nasal base width	29.9 +/- 6.7	31.7 +/- 6.3	0.164	32.2 +/- 9.3	0.403	31.1 +/- 6.5	0.242	33.1 +/- 6.1	0.006*
		Intercommissural distance	47 +/- 4.2	45.7 +/- 6.1	0.669	49.0 +/- 4.4	0.168	46.9 +/- 3.4	0.908	47.4 +/- 3.9	0.564
		Nasion-Subnasal	58.5 +/-4.7	57.9 +/- 4.7	0.557	56.5 +/- 3.7	0.085	58.7 +/- 4.2	0.661	58.8 +/- 5.4	0.809
		Subnasal-Interlabial	21.1 +/-2.5	21.6 +/-2.7	0.286	23.7 +/- 9.9	0.416	21.0 +/- 2.5	0.848	20.6 +/- 2.7	0.239
		Interlabial-Menton	45.9 +/-4.6	45.8 +/- 5.2	0.735	50.3 +/- 4.7	0.001*	45.4 +/- 4.8	0.680	46.1 +/- 4.9	0.535
		Cranial base length	116.9 +/- 6.9	118.1 +/- 7.2	0.114	118.1 +/- 16.4	0.006*	115.5 +/- 8.4	0.449	117.1 +/- 9.2	0.311
		Maxillary length	116.2 +/- 5.3	117.4 +/- 5.9	0.147	118.0 +/- 16.6	0.003*	116.6 +/- 6.1	0.747	116.6 +/- 6.9	0.550
		Mandibular length	129.1 +/-7.3	130.1 +/- 7.4	0.119	134.5 +/- 21.1	0.000*	128.7 +/- 6.6	0.752	130.4 +/- 9.0	0.254

n sample size

* p-value calculated with the non-parametric Mann–Whitney U test..

Discussion

This study pretended to establish the influence of endocrine disorders evaluated have on maxillary and mandibular growth in a sample of 1,508 patients, selected by gender and divided into age groups by analyzing quantitative variables. Overall, medicated hypothyroid and obese patients in all the age groups had increased anthropometric measurements; with respect to peak growth, medicated hypothyroid and non-syndromic hypogrowth individuals exhibited decreased measurements, while in obese patients they were increased.

According to national surveys, the prevalence in Colombia of medicated hypothyroidism is 9.9%, overweight and obesity 56.4%, and non-syndromic hypogrowth varies between 7.4% and 10.8% depending on the age (Min Salud 2022). In the population studied, the disorder with the highest prevalence was non-syndromic hypogrowth with 16.6%, followed by medicated hypothyroidism with 14.3% and overweight/obesity with of 7.2%. Other studies such as Danze (2021) and Chavez (2018), showed different prevalence levels, with overweight/obesity being the highest, followed by hypothyroidism and non-syndromic hypogrowth. This can be explained by the fact that the population studied was undergoing treatment and that there is a lower

proportion of obese patients that seek treatment at the Pediatric Endocrinology Service where the sample was taken.

In relation to the influence that endocrine disorders had on craniofacial growth, it was observed that anthropometric measurements studied can present alterations which included cranial base length, maxillary length, and mandibular length in the sagittal plane; head circumference, zygomatic width, nasal base width, inter-commissure distance and bigonial width in the transverse plane, as well as nasion-subnasal, subnasal-interlabial and interlabial-chin distances in the vertical plane.

Hypothyroid patients presented increased head circumference and the zygomatic width, nasal base width, inter commissure distance, cranial base length and maxillary and mandibular length which is in accordance with the study by (Gunes 2020) who suggested hypothyroid individuals could present early changes in body composition parameters. However, results contradict those of Vucic (2017), who reported a possible relation between hypothyroidism and a decrease in maxillary and mandibular growth that could cause impaction of the teeth, and Wassner (2017), who reported delayed tooth eruption. However, it is important to note that these studies were carried out on non-treated individuals, while this study was in carried out in controlled patients.

No significant differences were found in overweight/obese patients for the same anthropometric measurements as in hypothyroid ones; in addition, subnasal-interlabial and interlabial-chin distances were greater, giving a leptoprosopic facial appearance. Some reports indicate a relationship between this disorder and the stimulation of bone growth, as shown by Dimitri (2019) and Zhu (2017). Moreover, craniofacial growth, similarities were observed between the results of this study and those of Danze (2020), where an increased sagittal position of pogonion was evidenced, leading to prognathism; Cuccia (2007) reported increased longitudinal facial measurements in overweight-obese patients, while Sánchez (2019) demonstrated an association between obesity and early eruption in both dentitions related when comparing anthropometric measurements at peak growth ages.

With regards to the non-syndromic hypogrowth disorder, zygomatic width was significantly smaller, in accordance with the findings of Attanasio (2017) and Neto (2011) who also reported decreased maxillary and mandibular size.

To identify the differences in pubertal development between healthy individuals and patients with disorders, pubertal development was evaluated using the Tanner index (Marshall 1969) according to the four age groups. In the 1 - 4-year-old group, no substantial differences were observed in both sexes; in the 5 - 9-year-old group, boys were mostly in Tanner I and Tanner II stages, while girls were distributed between Tanner I and Tanner IV stages, in the 10 - 14-year-old group, a more homogeneous distribution was observed in both sexes and finally in the 15-19-year-old group, Tanner IV and V stages predominated. An analysis to determine if skeletal age was like chronological age was carried out in the 5 - 9 and 10 -15-year-old groups,

given that at these ages peak growth occur; females presented mainly Tanner II and males Tanner IV which was related to the maximum peaks of skeletal maturation; a comparison of the anthropometric measurements of each disorder at these ages was made.

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When said measurements were analyzed at peak growth ages, in medicated hypothyroid individuals they were significantly decreased when compared to healthy children, suggesting delayed growth, in accordance with the study by Williams (2018) who reported that hypothyroidism could cause delayed skeletal development and linear delay; head circumference and inter-labial-chin circumference in females were also significantly lower, while no differences were observed in males. Regarding obesity and overweight, results showed significantly increased measurements in both boys and girls compared to those of healthy children, indicating that the growth peak in obese patients occurs earlier, in agreement with the findings of Danze (2020). Finally, non-syndromic hypogrowth females presented a significant decrease in head circumference while males presented decreased zygomatic width, that is, in facial width. Comparison of average skeletal age with chronological age, revealed significant differences in males with hypothyroidism in the 10 to 15-year-old group and in the non-syndromic hypogrowth group, as well as females between 5 and 9 and males between 10 and 15, where skeletal age was delayed compared to chronological age.

The objective of this study was to establish craniofacial growth parameters by comparing facial anthropometric measurements of healthy children with patients that presented medicated hypothyroidism, overweight-obesity or non-syndromic hypogrowth, to understand how different growth disorders can influence craniofacial growth and development, as well as identifying the timing for maxillary orthopedic intervention depending on the type any underlying disorder, based on how it may influence the onset of peak growth.

When comparing the results of this study with similar ones reported in the literature, some of the differences could be attributed to the fact that anthropometric measurements were always taken by a previously calibrated operator and made directly on the patient without the use additional diagnostic aids. Some of the limitations of the study however included the extended period for data collection due to the COVID-19 pandemic that required numerous virtual appointments, and that it was not possible to record the skeletal age of every patient given that carpal radiographs were not indicated in many cases. Therefore, it is important to emphasize that assessment based on Tanner stages was of great importance in predicting skeletal maturation.

Conclusions

Children and adolescents who present a growth disorder may also present craniofacial growth alterations, which are dependent on their age and growth stage. Hypothyroid, obese, and overweight patients presented some increased anthropometric measurements when compared to healthy individuals, while those with non-syndromic hypogrowth presented a significant decrease in measurements. More specifically, girls with hypothyroidism or non-syndromic hypogrowth exhibited decreased head circumference and inter-labial chin

distance at peak growth while overweight/obese patients of both sexes presented increased measurements. These findings are important when diagnosing and planning maxillary and mandibular orthopedic treatment given the fact that said disorders can influence treatment outcomes over time.

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