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Results of Turner Syndrome Treatment with Recombinant Human Growth Hormone in Albania

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Abstract

Background: There is no doubt that the use of rhGH in patients with TS brings satisfactory results regarding the improvement of height growth, realizing the improvement of the final adult height. This study aimed to evaluate the influence of the type/characteristic of the genetic anomaly on sex chromosome X on the outcome of treatment with rhGH among Albanian children diagnosed with TS.

Methods and Results: This analytical-observational study was conducted at the Pediatric Endocrine Unit at University Hospital Centre Mother Teresa in Tirana, the only one of its kind treating TS pediatrics in Albania. Only TS patients who had attained near-adult height (NAH) by December 2023 were included in the analysis of this study. Near-adult height was obtained for 44(72.1%) patients. The mean age of starting treatment was 12.68±3.03 years. After a treatment duration of 3.60±2.26 years, the patients recovered 0.88±0.56 in height-for-age Z-score (HAZ), resulting in HAZ at the end of treatment of -2.73±0.87. They achieved their NAH of 144.56±6.53 cm.

Conclusion: Despite starting treatment late, our patients managed to gain 17.70±12.53 cm in length. The progression of height improvement under rhGH treatment showed differences between chromosomal groups. The non-monosomy group had better results regarding NAH and HAZ at the treatment's end than the monosomy group.**(International Journal of Biomedicine. 2024;14(2):275-281.)**

Keywords: Turner syndrome • karyotype • rhGH • height-for-age Z-score • near-adult height

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Abbreviations

BA, bone age; **BAD**, BA deficit; **BMI**, body mass index; **GH**, growth hormone; **HAZ**, height-for-age Z-score; **IGF**, insulin-like growth factor; **MPH**, mid-parental height; **MG**, monosomy group; **n-MG**, non-monosomy group; **NAH**, near-adult height; **rhGH**, recombinant human growth hormone; **TS**, Turner syndrome.

Introduction

Turner syndrome (TS) is a congenital genetic disorder with a combination of characteristic phenotypic features caused by the loss of all or a critical part of one X chromosome. It occurs in phenotypically female individuals and affects approximately 1 in 2,000-2,500 live female births.[1] It can cause various medical and developmental problems, but short stature is the most frequent clinical feature in patients with TS. To date, there is no convincing evidence to support the view

that the growth disorder in TS is associated with a disorder in the growth hormone-insulin-like growth factor (GH-IGF) axis, but, instead, it is related to haploinsufficiency of the short stature homeobox-containing (*SHOX*) gene.[2] TS is one of the most common syndromes in Albania's list of diseases treated with rhGH during the last 22 years. This study is the first attempt to evaluate the results of this treatment on the near-adult height (NAH) of Albanian TS patients. In Albania, the use of GH has been increasing slowly since 2001 due to the high cost of treatment, lack of funding for patients, and lack of public awareness until recently. Furthermore, data regarding treatment response and factors influencing final height in TS children treated with rhGH have just been analyzed.

This study aimed to evaluate the influence of the type/characteristic of the genetic anomaly on sex chromosome X on the outcome of treatment with rhGH among Albanian children diagnosed with TS.

Materials and Methods

This is a register-based cohort study. The medical records of all patients diagnosed with TS from January 2001 in the Pediatric Endocrine Unit, Department of Pediatrics, University Hospital Centre "Mother Teresa," Albania, were reviewed. Only patients who had attained NAH by December 2023 were included in the analysis of this study. Patients with TS who discontinued the treatment with rhGH for any reason before attaining NAH, patients with TS who are still under treatment, patients with another syndrome, and patients with GH deficiency were excluded (Figure 1).

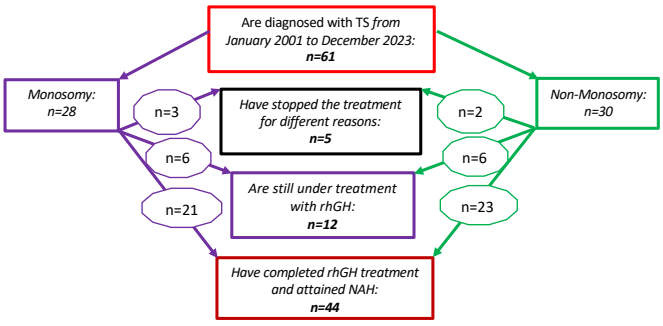

Fig. 1. *Flow chart of study methodology.*

The following data were retrieved from the patients' medical records: diagnosis, chronological age, bone age (BA) and height at starting treatment, height after the first year of treatment, age and height at onset of puberty, age of attaining NAH, duration of growth hormone (GH) treatment and mean GH dose. The height of patients was plotted using the WHO growth charts and was standardized by calculating their standard deviation (SDS) score (Z-score).[3] Administration of conjugated estrogens was initiated at 2.0 mcg/day and increased by 4.0 mcg/day every six months. At 1.5 years, estrogen replacement was given cyclically, and progesterone was added. The onset of puberty was taken to be the time when spontaneous breast development (Tanner stage B2) was first observed or the date at which estrogen replacement therapy was initiated. Bone age (BA) was calculated by reading the plain radiograph of the left hand and wrist using the Greulich and Pyle atlas [4] by a single observer. Bone age deficit (BAD) was defined as (chronological age) – (BA).

Mid-parental height (MPH) was determined by using Tanner's method for girls (cm) = (father's height + mother's height - 13)/2. Target height range = MPH ± 6.5 cm. The dosage of rhGH varied from 0.035 to 0.06 mg/kg/day (0.735-1.26 UI/kg/week). The dosage of rhGH was individualized based on the level of IGF1 and IGFBP3 and growth velocity. Thyroid function tests, biochemical panels, and complete blood counts were performed every six months. All registered subjects were visited as outpatients at the Pediatric Endocrine Unit at "Mother Teresa" University Hospital Centre in Tirana for follow-up every two months, and their height and weight were measured. Height was checked using a Harpenden stadiometer and marked to the nearest 0.1 cm. Body weight was measured with an electronic weighing scale to 0.1 kg. NAH was defined as height reached when growth velocity was less than 2 cm/year calculated over a minimum of 9 months, where the chronological age was more than 16 years or BA more than 15 years, and analysis of individual growth curves showed evidence of asymptotic proximity to final height. The height at diagnosis, NAH, MPH, and the height when puberty was started were then standardized by calculating their height SDS (Z-score) using the WHO growth charts.

Turner syndrome was diagnosed based on clinical and hormonal findings and was confirmed by cytogenetic analysis, such as classical chromosome banding, high-resolution chromosome analysis, spectral karyotype analysis (fluorescent in situ hybridization (FISH)), and array comparative genomic hybridization (aCGH), all of which allow the entire genome to be scanned for chromosome dosage abnormalities, including increases (duplications) or decreases (deletions), which may also be suggestive of an unbalanced displacement. These examinations were conducted in the Genetic Unit, Department of Paediatrics, University Hospital Centre "Mother Teresa," Albania, and other genetic laboratories outside Albania.

To simplify the data analysis, since the number of patients in the subgroups was relatively small, a regrouping of karyotype types was made in the group with monosomy (MG [Subgroup A]) and non-monosomy group (n-MG), which includes the karyotypes of Subgroups B, C, D, and E (Table 1). To eliminate the confusion between the terminology "age of diagnosis" and "age of initiation of therapy" (because for all patients, the therapy was started as soon as the genetic diagnosis was confirmed), the terminology was unified as "age of diagnosis" = "age of initiation of treatment."

Statistical analysis was performed using statistical software package SPSS version 20.0 (SPSS Inc, Armonk, NY: IBM Corp). For descriptive analysis, results are presented as mean (M) ± standard deviation (SD). Inter-group comparisons were performed using Student's t-test. Pearson correlation analysis was performed on the data to explore the relationship between various parameters with final height SDS. A P-value < 0.05 was considered statistically significant.

Table 1.

Frequency of karyotype for all TS patients and TS patients who attained NAH.

Subgroup	Karyotype	All TS patients		TS treated till NAH	
		Count (n)	Percentage (%)	Count (n)	Percentage (%)
A Monosomy	45,X	30	49.18%	21	47.73%
	Total	30	49.18%	21	47.73%
B Mosaic form with structural abnormalities of the X chromosome	45,Xt(5;16)(q11.2;q21.1)/46,XX	1	1.64%	1	2.27%
	45,X(15ps+)/46,XX	1	1.64%	1	2.27%
	45,X,/46X,der(X)	2	3,28%	0	0%
	45,X,1qh+,9qh+/46,X,i(Xq), 1qh+,9qh+	1	1.64%	1	2.27%
	45,X/47,X,i(Xq),i(Xq)/46,X,i(Xq)	1	1.64%	1	2.27%
	45,X/46,X,i(Xq)	10	16.39%	8	18.18%
	45,X/46X,der(X),t(X;X)(p;q)	1	1.64%	1	2.27%
	Total	17	27.87%	13	29.55%
C Mosaic form with numeric anomaly	45,X/46,XX	2	3.28%	1	2.27%
	45,X/47,XXX	1	1.64%	0	0%
	Total	3	4.92%	1	2.27%
D Mosaic form with presence of Y chromosome	45,X/46,XY	5	8.19%	4	9.09%
	Total	5	8.19%	4	9.09%
E Non-mosaic 46,X,der(X)	46,X,i(Xq)	5	8.19%	4	9.09%
	46,X,r(X)	1	1.64%	1	2.27%
	Total	6	9.83%	5	11.36%
Total		61	100%	44	100%

Results

Characteristics of all TS patients at baseline

During the period mentioned above, 61 patients with TS were diagnosed. Out of 61 patients, 30(49.18%) resulted in numeric anomaly with monosomy (45,X0) (Subgroup A or MG), 17(27.87%) had mosaic form with structural anomaly (Subgroup B), 3(4.92%) had mosaic form with the numeric anomaly of the X chromosome (Subgroup C), 5(8.19%) had mosaic form with the presence of Y chromosome (Subgroup D), and only 6(9.83%) had non-mosaic with X-structural abnormalities (Subgroup E) (Table 1).

The mean diagnosis age of all 61 patients with TS was 11.77±3.33 years (min. 3.52; max. 17.64 years). No statistically significant difference was identified in the age of diagnosis/ start of therapy between karyotypic groups (P=0.398). The height-for-age Z-score (HAZ) at the start of the treatment for all TS patients was -3.64±1.01 z-score (min. -6.00; max. -0.93 z-score). The most pronounced shortness at the beginning of therapy was identified in Subgroup A (-3.90±0.93 z-score), followed by Subgroup E (-3.72±0.62 z-score), Subgroup B (-3.59±0.99 z-score), and Subgroups C and D (-2.70±0.97 z-score and -2.67±1.26 z-score, respectively). Even beyond this fact, the MG (Subgroup A) was -0.518 z-score shorter than the n-MG (Subgroups B, C, D, and E), and this difference was statistically significant about the means of HAZ at the time of starting treatment between the MG and n-MG (P=0.043). BMI for age z-score at the start of the treatment was 0.20±1.19 z-score (min. -2,61; max. 3.81 z-score) for all 61 patients. No statistically significant difference was identified in BMI for age between the MG and n-MG (P=0.214).

Characteristics of patients treated to NAH

A total of 44 TS patients reached NAH. The relative frequency of the documented karyotypes for these patients is listed in Table 1. The distribution of karyotypes was not significantly different from the total group of 61 TS patients in our study. Table 2 presents the characteristics of patients at the time of starting treatment with rhGH, the dose of rhGH that was used, the age of onset/induction of puberty, the age of first menarche, the progress of growth indicators before and during puberty as well as at the end of treatment with rhGH, height changes expressed in z-score and cm, including NAH according to karyotypic groups, and, in total, including the statistical evaluation for the differences in means between the two groups.

The mean diagnosis age of all 44 TS patients who completed the rhGH therapy and achieved NAH was 12.68±3.03 years (min. 3.52; max. 14,64 years). At the time of starting the treatment, HAZ was -3.62±0.96 z-score (min. -5.49; max. -0,93 z-score), BMI for age z-score was 0.19±1.28 z-score (min. -2.61; max. 3.81 z-score), and BA for all 44 patients was 10.22±2.57 years with BAD 2.46±0.71 years. The treatment duration with rhGH was 3.60±2.26 years (min. 1.01; max. 9.88 years). All patients started puberty at 13.58±1.78 years (min. 9.65; max. 15.81 years), and at the age of 14.68±1.55 years, they experienced their first menstrual bleeding. Out of 44

patients, 6 (13.6%) had spontaneous breast development, and 4 (9.1%) had complete spontaneous pubertal development with menarche. Nine of them had pubertal arrest and subsequently received estrogen-progestin replacement. At the time before onset/induction of puberty, they had -3.11±1.04 z-score, gaining from the start of treatment to that time 0.50±0.46 z-score and over the entire period of puberty 0.38±0.56 z-score in the height. Moreover, these changes were statistically significant (P=0.000). After the entire treatment period mentioned above, all 44 patients reached NAH expressed in the HAZ at the end of treatment with -2.73±0.87 z-score, benefiting from the start of treatment, a total of HAZ gained by 0.88±0.56 in z-score, and this means change is statistically significant (Table 2). At the end of the rhGH therapy, all the patients grew by 17.70±12.53 cm, but only 6 (13.6%) patients reached the target projection for MPH.

The Pearson correlation analysis was performed between HAZ at the end of treatment and near-final height in cm with various parameters. The results showed that only six variables had a good correlation with HAZ at the end of treatment in our patients: HAZ at the start of treatment, treatment duration, HAZ before induced puberty, BMI z-score at the start of therapy, rhGH dose, and MPH; HAZ before induced puberty and HAZ at the start of treatment showed the strongest correlation with HAZ at the end of treatment (Figure 2).

Other variables, such as the age at starting treatment, BA at starting treatment, BAD, and age of induced puberty, had negative correlations with HAZ at the end of treatment, but they were not statistically significant.

On the other hand, NAH expressed in cm also correlated well with variables mentioned above: HAZ at start of treatment, treatment duration, HAZ before induced puberty, BMI z-score at start of therapy, rhGH dose, and MPH; HAZ before induced puberty and HAZ at start of treatment showed the strongest correlation with HAZ at the end of treatment (Figure 3). Other variables, such as age at starting treatment, BA at starting treatment, BAD, and age of induced puberty, had weak negative correlations with HAZ at the end of treatment.

Table 2.

The characteristics of patients at the start of treatment and the progress of growth indicators during treatment.

	Monosomy (A)	Non – monosomy (B, C, D, E)	*P*-value	Total
N	21	23		44
Age at starting treatment, years	12.62±3.26	12.74±2.88	0.899	12.68±3.03
Dose of rhGH, mg/kg/day	0.04±0.008	0.05±0.074	0.344	0.05±0.077
HAZ-score at the start of treatment	-3.87±0.88	-3.38±1.00	0.091	-3.62±0.96
BMI z-score at the start of treatment	-0.08±1.13	0.44±1.39	0.176	0.19±1.28
BA at starting treatment, years	10.15±2.84	10.29±2.37	0.858	10.22±2.57
BAD, years	2.47±0.63	2.44±0.78	0.915	2.46±0.71
MPH, cm	162.04±6.59	164.13±7.30	0.328	163.13±6.97
Age of induced puberty, years	13.35±1.80	13.78±1.78	0.426	13.58±1.78
Age of first menarche, years	14.38±1.63	15.02±1.46	0.226	14.68±1.55
Age at the end of treatment, years	15.88±1.47	16.64±1.72	0.124	16.28±1.63
Treatment duration, years	3.26±2.20	3.91±2.32	0.353	3.60±2.26
BMI z-score before puberty induced	-0.06±1.16	0.56±1.17	0.085	0.26±1.19
BMI z-score at the end of treatment	0.40±1.15	0.88±0.89	0.129	0.65±1.04
HAZ-score before puberty induced	-3.42±0.99	-2.83±1.04	0.061	-3.11±1.04
Δ-HAZ change before puberty	0.45±0.41	0.55±0.51	0.489	0.50±0.46
Δ-HAZ change during puberty	0.325±10.48	0.43±0.64	0.553	0.38±0.56
Δ-HAZ change during treatment	0.78±0.34	0.98±0.70	0.245	0.88±0.56
HAZ-score at the end of treatment	-3.10±0.73	-2.40±0.87	0.007	-2.73±0.87
Δ-cm change during treatment	17.68±13.14	17.72±12.25	0.992	17.70±12.53
NAH, cm	142.15±5.28	146.76±6.88	0.017	144.56±6.53

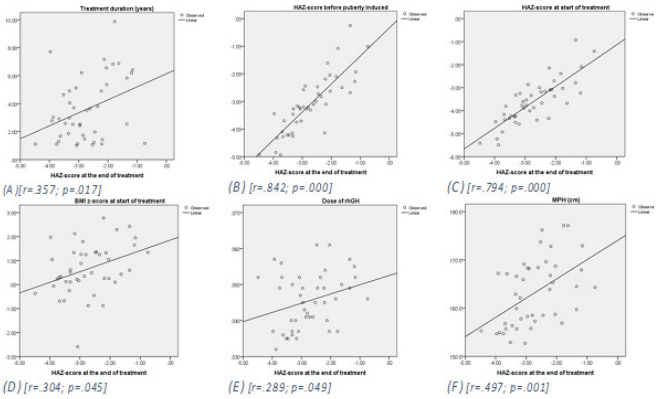

Fig. 2. *Correlations of HAZ score at the end of treatment with (A) Treatment duration, (B) HAZ score before puberty induced, (C) HAZ score at the start of treatment, (D) BMI z-score at start of treatment, (E) Mean rhGH dose and (F) MPH.*

Characteristics of patients and results of treatment under the perspective of chromosomal groups

When starting treatment, the patient age in the MG and n-MG was 12.62±3.26 and 12.74±2.88 years, respectively. No statistically significant difference was identified about the age of diagnosis/start of therapy between karyotypic groups (*P*=0.899).

At the start of the treatment, BA was 0.14 years older in the n-MG, and the BAD was 0.023 years smaller in the n-MG. However, this difference in means between the two groups for those parameters was not statistically significant (*P*=0.858 and *P*=0.915, respectively). Treatment duration with rhGH was longer in the n-MG (3.91±2.32 years), compared to the MG (3.26±2.20 years), but this difference was not statistically significant (*P*=0.353).

The most pronounced shortness at the beginning of therapy was identified in the MG (*3.87*±0.88 z-score), compared to the n-MG (*3.38*±1.00 z-score), but this difference was not statistically significant (*P*=0.091) (Figure 3A). No statistically significant difference was identified in BMI for age between the two groups (*P*=0.176). The MG started puberty slightly earlier than the n-MG (13.35±1.80 vs 13.78±1.78 years), but this difference was not statistically significant. The MG experienced their first menstrual bleeding a little earlier than the n-MG (14.38±1.63 vs 15.02±1.46), but this difference was not statistically significant. Before the onset/induction of puberty, the MG was shorter than the n-MG (-3.42±0.99 vs. -2.83± 1.04 z-score), and this difference was not statistically significant (Figure 3B); both groups gained height throughout the pubertal period with no statistically significant differences between the two groups.

The n-MG had a better total height gained than the MG in Δ-HAZ (0.98±0.70 z-score vs. 0.78±0.34 z-score) (Figure 3D) and in cm (17.72±12.25 cm vs. 17.68±13.14 cm) (Figure 3E), but these changes were not statistically significant. NAH expressed in HAZ at the end of treatment was better in the n-MG (-2.40±0.87 z-score) than in the MG (-3.10±0.73 z-score), with statistically significant differences (Figure 3C). Moreover, the NAH expressed in cm was better in the n-MG (146.76±6.88 cm) than in the MG (142.15±5.28 cm), and these changes were statistically significant (*P*=0.017) (Figure 3F).

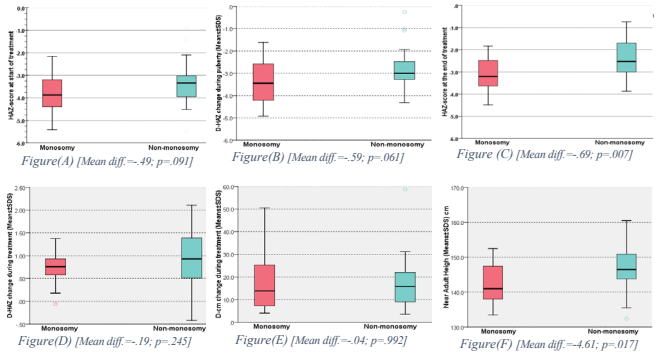

Fig. 3. *Differences in means between monosomy and non-monosomy groups for (A) HAZ score at baseline, (B) Δ-HAZ change during puberty, (C) HAZ-score at the end of the treatment, (D) Δ-HAZ change during treatment, (E) HAZ-cm change during treatment, (F) NAH.*

Analysis according to chromosomal subgroups, showed that the best result of NAH expressed in z-score was in Subgroup D ("Mosaic form with presence of Y chromosome") with -1.94 z-score followed by Subgroup C ("Mosaic form with numeric anomaly") with -2.43 z-score, Subgroup B ("Mosaic form with Structural Abnormalities of the X Chromosome") with -2.45 z-score, Subgroup E ("Non-mosaic 46, X, der(X)") with -2.70 z-score and finally Subgroup A ("Monosomy") with -3.09 z-score (Figure 4). Differences in the means of heights in z-score between chromosomal subgroups were statistically significant (*P*=0.035).

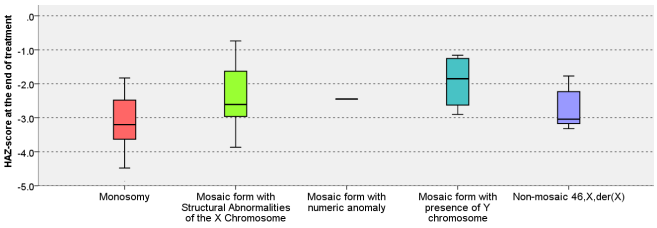

Fig. 4. *HAZ-score at the end of treatment based on chromosomal subgroups.*

Discussion

This study reflected our experiences using rhGH in TS patients. It is now well known that using rhGH effectively improves adult height in patients with TS. Our patients improved NAH by 0.88 z-score throughout treatment, or 17.7 cm in height from the start of treatment for a total duration of 3.6 years. As in the other indications for the use of rhGH, such as GH deficiency, the results depend on many different factors, such as the age at the start of the therapy, such as the duration of the treatment, the dose of the medication, the height for the age at the beginning of the treatment, the time of the onset of puberty, and MPH (which reflects the genetic

predisposition for height). From these points of view, we analyzed the results of our study.

The final height in our study showed good positive correlations with HAZ at the start of treatment, the treatment duration, HAZ before puberty was induced, BMI z-score at the beginning of treatment, rhGH dose, and MPH. Other indicators, such as the age at starting treatment, BA at starting treatment, BAD, and age of induced puberty, had a weak negative correlation with HAZ at the end of treatment.

A significant factor that could influence the therapy and its results is the age at which treatment was started. It was shown that the best response to the treatment was correlated with the age of starting treatment, whereby the girls with TS who began the therapy earlier tended to grow better.[5,6] The duration of the treatment is generally a function of the age at the start of the treatment, which means that the younger the age at the start of the treatment, the longer the treatment period. From this point of view, our patients started the treatment relatively late, compared to other studies. A study by Rosenfeld et al.[7] showed that long-term treatment with doses higher than the replacement doses applied in treating GH deficiency could increase height during childhood and final adult height in TS. In that study, with two groups of patients with TS separated into those who used only GH and the group that used GH and oxandrolone, the age at the start of GH therapy was 9.1 years and 9.9 years, respectively; the duration of treatment was 7.6 years and 6.1 years, and final height was 150.4 cm and 152.1 cm, respectively. Compared to that study, the age of our patients was 12.6 years, older than the ten years of the Rosenfeld et al. study. Our patients continued the therapy for about 3.6 years, approximately half of the treatment time of the study above, and gained during the entire treatment period about 17.7 cm in height with an average annual growth of 4.9 cm/year and reaching a near-final height of 144.56 cm, significantly shorter than the patients in the study above. Another study[8] indicated that when GH therapy was initiated at nine years of age, final height improved by approximately 8 cm/year, against a height gain of approximately 6 cm/year when therapy was started at 11-13 years, therefore, recommendations for the diagnosis and management of TS state that ''initiation of GH therapy should be considered as soon as a patient with TS has dropped below the fifth percentile of the normal female growth curve."[9] Growth failure sometimes begins prenatally, and most girls with TS demonstrate growth failure within the first 3 years of life.

Other factors that could influence the therapy and its results are the height of the parents and HAZ before starting puberty. In our study, MPH showed an excellent correlating variable with NAH and HAZs at the end of treatment, which shows the genetic influence on height growth. However, only six patients (13.6%) reached the MPH target after treatment. The pubertal spurt is absent even in those girls with spontaneous pubertal development. These alterations make short stature (a 20cm deficit in the final height) one of the main features of TS.[10] Patients with TS gain more height during the prepubertal period than in the pubertal period. Even in our study, the gain in height z-score was more significant during the period before the induction of puberty (0.50±0.46 z-score), compared to that during the pubertal period (0.38±0.56 z-score).

Besides the classic karyotype 45,X, other karyotype abnormalities can occur in TS, such as duplications of the long arm (q) of the X chromosome with concurrent loss of the short arm (p) to constitute an isochromosome (isoXq); ring formation (rX); deletions of the short and long arm of the X chromosome (Xp- or Xq-); mosaicisms (45, X/46, XX); or karyotypes with the presence of the entire Y chromosome or parts of it.[11] Patients with TS and deletions at the end of the short arm of the X chromosome (Xp-), including haploinsufficiency of the *SHOX* gene, have short stature and different orthopedic abnormalities.[12] Most girls with TS inherit just one copy of the *SHOX* gene. This state of haploinsufficiency seems to be substantially responsible for the height deficit in these patients.[13,14]

In our study, we analyzed the result of the treatment from the point of view of chromosomal abnormalities. The analysis of the results showed that the outcomes of rhGH treatment were better in the non-monosomy group than in the monosomy group. In a study similar to our research carried out in Poland [15] involving 57 patients with TS, treated for three years, the authors concluded that the use of rhGH improves the length of all abnormal karyotypic groups of TS patients, but these results were more satisfactory in patients with marker chromosome or Y chromosome and patients with X-mosaicism. It should be noted that the 3.6-year therapy using rhGH improved the height of all groups of our patients with TS expressed in terms of NAH and HAZ at the end of treatment. Although there were no statistical differences in means regarding HAZ at the start of therapy, treatment dose, duration of treatment, and MPH between groups with monosomy and non-monosomy, the best outcomes were achieved in patients with mosaic form with the presence of the Y chromosome and in patients with mosaic form with structural abnormalities of the X chromosome.

TS patients with monosomy (45,X) and non-mosaic 46,X, der(X) had a shorter final height than patients with other chromosome abnormalities. Some other studies [16,17] reached the same conclusion: TS patients with the karyotype 45,X, and patients with isochromosomes of the long arm of X tend to have a shorter final height than patients with other types of chromosome abnormalities.

Conclusion

Treatment with rhGH is effective in Albanian pediatric patients with TS. Our study showed that treatment started relatively late, approximately 12.7 years, with the recommended doses (0.05 mg/kg/day) in a relatively short period, compared to studies in the literature (approximately 3.6 years), resulting in NAH for all patients, which is considered a significant improvement, compared to HAZ at the beginning of treatment. Our pediatric population with TS recovered in height of approximately 0.9 z-score or 17.7 cm for about 3.6 years of therapy with a growth velocity of 4.9 cm/year. Based on our results, we conclude that only a minority of 6 out of 44 children with TS treated with GH achieved their genetic height

potential, benefiting more in height during the prepubertal period than in the pubertal period. Better outcomes of rhGH treatment were observed in the non-monosomy group than in the monosomy group.

Moreover, the best results were obtained in the subgroups with marker or Y chromosomes and in patients with X-mosaicism within the non-monosomy group. This study highlighted the importance of early diagnosis and starting early treatment in children with TS. This is to ensure adequate duration of therapy to optimize the prepubertal growth so that the height prognosis of these children can be further improved. Of course, the treatment results depend on many other factors, including the type of karyotypic anomaly.

Competing Interests

The authors declare that they have no competing interests.

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