Original Article

Adult Height in Indian Girls with Turner Syndrome Treated with Long-Term Growth Hormone Therapy — A Western India Tertiary Centre Experience

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Abstract

Background and Objectives: Owing to paucity of data on adult height in Indian girls with Turner syndrome treated with growth hormone (GH), this study was conducted to assess improvement in height following GH therapy and adult height achieved with long-term GH therapy in Indian girls with Turner syndrome and to assess relationship between achieved and predicted height. **Methodology:** Retrospective analysis was performed on 12 girls with karyotype-proven Turner syndrome, who had attained adult height following mean duration of GH therapy of 4.8 years (range: 2.7-7.6). Adult height predictions were performed using index of responsiveness (IOR) and Ranke's prediction model. **Results:** Mean age at starting GH was 10.2 ± 1.9 years; Pubertal induction was between 11 and 15 years. Mean height gain was 29.3 ± 9.8 cm (range: 14–39.5) from onset of treatment to adult height. Significant improvement in height Z scores (IAP 2015 and Indian Turner reference data) following GH therapy (p = 0.002 and 0.012, respectively) was noted. Using Indian Turner reference data, the height Z score improved from pre-treatment 0.8 ± 0.8 to 2.0 ± 0.9 on stopping GH and adult height Z score of 1.3 ± 0.7. Using Ranke's equation for prediction of near adult height, predicted and achieved adult height showed a strong positive correlation (Spearman correlation coefficient = 0.827, significant at 0.01 level). **Conclusion:** At a dose in the lower range (40-50 mcg/kg/day) of recommendation and duration of 5 years, Indian girls with Turner syndrome can achieve adult height within the healthy Indian reference range. Dose individualization based on IOR would help in optimizing GH dosage and would turn out to be economically sustainable without compromising on height outcomes.

Keywords: Growth hormone, height, index of responsiveness, prediction, Turner syndrome

Introduction

Turner syndrome is a condition caused due to complete or partial absence of one of the X chromosomes and manifests as short stature and delayed puberty or ovarian failure in girls. Untreated girls with Turner syndrome are between 17 and 20 cm shorter than their healthy counterparts.[1,2] It has been reported that girls with Turner syndrome who receive long-term growth hormone treatment can reach a height within reference range for the population and within their mid-parental range.[3,4]

Turner syndrome is an FDA approved indication for treatment with growth hormone (GH).[5] GH not only improves height, but also has a favourable effect on body composition.[6] The response to GH is dose and duration dependent and hence a higher dose (45-68 mcg/kg/day) has been recommended.[7] The adult stature achieved with growth hormone therapy is dependent on the index of responsiveness to GH during the first year of therapy, which is defined as an individual's level of response to GH treatment.[8,9]

Though the higher dose of GH recommended for short stature in Turner syndrome has been considered safe so far, the long-term risks of exposure to supra-physiological levels

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of GH remain unknown. Also, GH therapy particularly for a longer duration may be seen as rather expensive, particularly in the middle income countries. As a result, optimization of GH dose may prove to be beneficial both physiologically and economically. Ranke *et al*.[8] have developed a regression equation for growth response prediction and optimization of GH dose in German girls with Turner syndrome. The applicability of this equation in the Indian scenario would definitely be beneficial for individualized GH therapy in girls with Turner Syndrome, so as to reduce the cost of treatment, without affecting the response in height gain.

Till date, there are no Indian studies on long-term treatment (more than 3 years) with growth hormone or adult height achieved after growth hormone therapy in Indian girls with Turner syndrome, and hence, the objectives of our study were: 1) To assess the improvement in height from the beginning to the end of GH therapy and adult height achieved with long-term GH therapy in Indian girls with Turner syndrome 2) To assess the relationship between achieved and predicted adult height based on the index of responsiveness during the first year of treatment and mean GH dose using Ranke's prediction model.

Materials and Methods

A retrospective case analysis of 12 girls with Turner syndrome was conducted at our tertiary care Paediatric Endocrinology centre (Western India). This study enrolled all karyotype proven cases of Turner syndrome diagnosed after 1 January 2000 and followed up till 31 December 2021 with euthyroid status, who had attained adult height with a mean duration of therapy of 4.8 years (range 2.7 to 7.6 years) on growth hormone. As this was a retrospective study and data were deidentified, a waiver was granted by the Institutional Ethics Committee.

The dose of GH used for the patients ranged from 40 to 50 mcg/kg/day subcutaneously at night on all days of the week.[7] Puberty was induced between 11.8 to 15 years for all patients with either valerate or ethinyl estradiol starting at a low dose of 0.25 mg or 2.5 mcg, respectively, on alternate days.[10] One patient entered puberty spontaneously at 10.9 years. IGF 1 concentrations at 1 year of treatment were recorded and are reported in seven patients.

Birth weight, chronological age, height (Seca Portable stadiometer, Hamburg, Germany up to 0.1 cm accuracy), weight (Seca 876 Flat scale, Hamburg, Germany, up to 100 g accuracy), age at pubertal onset, pubertal staging by Tanner and Marshall method,[11] bone age (Tanner-Whitehouse III method on radiographs of the left hand and wrist)[12] and mid-parental height (MPH = average of mother's and father's height—6.5 cm) were recorded at the start of GH and on stopping GH therapy and at the time of adult height achievement. Patient was considered to have achieved adult height if the height increment between two readings taken 1 year apart was less than 1 cm.[13] Height velocity during the first year of treatment, annual and cumulative height velocity throughout the treatment period were calculated (Height velocity = Change in height ÷ duration in years). Height, weight and BMI Z scores were computed based on Indian Academy of Paediatrics (IAP) 2015 growth references (devised from healthy Indian children aged 5 to 18 years) and Indian Turner syndrome reference data, using mean, standard deviation and lambda, mu and sigma (LMS) values.[1,14]

We computed the predicted adult height based on Ranke's prediction model for Turner syndrome at the end of 1st year of GH therapy.[8] The iGRO software (Pfizer, Inc, United States) was used to calculate the index of responsiveness (IOR; studentized residual for 1st year). IOR is calculated as the difference between the observed and predicted height velocity divided by the standard deviation (SD) of predicted height velocity during the first year of treatment.[9] MPH SDS based on Tanner reference data and Turner height SDS at start of GH therapy based on Ranke's Turner height reference data were calculated instead of Indian references because in the original model, Z scores, constants and IOR were based on Ranke's and Tanner's references.[2,15] The predicted adult height was calculated based on Ranke's equation: Near adult height (cm) = 142.9 + (MPH SDS * 1.37) + (height at GH start SDS * 4.11) + (studentized residual 1st year * 1.99) + (mean GH dose [mg/kg/wk] * 4.82) + (age at puberty start [years] * 0.74).[8]

Statistical methods: Data were analysed using SPSS 26.0 for Windows (IBM SPSS, Bangalore, India). Descriptive statistics were used to evaluate the demographic and anthropometric parameters (age, height, weight, BMI and their Z scores, height velocity during the first year of treatment, cumulative height velocity, increment in predicted height and bone age). The Wilcoxon signed rank non-parametric test for related samples was used to compare height Z scores (for both IAP and Indian Turner reference data) and also to compare the difference in MPH and IAP height Z scores before treatment versus at adult height achieved. The Spearman correlation coefficient was used to assess the correlation between the predicted and achieved adult height.

Ethical clearance statement

The study was approved by the institutional ethics committee named as 'Ethics Committee, Jehangir Clinical Development Center Pvt Ltd.' vide letter no NA (our ethics committee does not provide an approval number) on 19th April 2016. Written informed consent was obtained for participation in the study and use of the patient data for research and educational purposes. The procedures follow the guidelines laid down in Declaration of Helsinki 2008.

Results

Data on 12 patients with Turner syndrome were analysed. Mean age at starting growth hormone therapy was 10.2 ± 1.9 years. At the start of GH therapy, all patients were pre-pubertal and euthyroid (either normal or well-controlled on medication). 8 girls had a karyotype of 45 X, 2 had 45X/46XX, 1 patient

Table 1: Description of anthropometric parameters of 12 Turner syndrome patients at the onset and end of GH therapy

Sr. No	Karyotype	MPH Z score (IAP)	Age at onset of GH (yrs)	Bone age at onset of GH (yrs)	Height at onset of GH (cm)	Height Z score (IAP)	Height Z score (Indian Turner)	Age at stopping GH (yrs)	Height at stopping GH (cm)	Height Z score (IAP)	Height Z score (Indian Turner)	Duration of GH treatment (yrs)
1	46 X, i (Xq)	0.4	8.3	7.0	110.9	-2.4	0.3	14.9	148.0	-1.2	2.6	6.6
2	45 X	-0.5	10.5	10.1	126.8	-1.9	1.7	15	147.0	-1.4	1.9	4.5
3	45 X/46 XX	1.3	11.7	11.0	133.5	-1.8	2.2	15	154.2	-0.3	3.1	3.3
4	45 X	-0.1	12.4	10.5	118.0	-4.3	-1.1	17.2	141.0	-2.9	0.3	4.8
5	45 X	0.9	12.4	11.8	131.0	-2.6	1.0	15.3	142.0	-2.3	1.2	2.9
6	45 X	-0.1	6.8	6.0	104.0	-2.4	0.8	14.4	148.3	-1.0	2.7	7.6
7	45 X/46 XX	-0.2	12.7	10.2	125.8	-3.5	0.2	15.4	138.0	-2.9	0.5	2.7
8	45 X	0.5	9.6	9.9	118.5	-2.3	0.9	15.1	153.5	-0.4	3.0	5.5
9	45 X	-0.1	11.7	10.3	121.5	-3.4	0.1	15.1	144.0	-1.9	1.5	3.4
10	45 X	-0.5	9.2	8.0	117.2	-2.2	0.7	14.1	146.5	-1.2	2.4	4.9
11	45 X	1.0	10.0	9.7	122.0	-2.1	0.8	15.1	149.9	-0.9	2.4	5.1
12	46 X, i (Xq)/46 XX	-0.2	7.9	7.2	112.5	-1.8	1.5	14.5	148.0	-1.14	2.6	6.6
	Mean	0.2	10.2±1.9	9.3±1.8	120.1±8.5	-2.6±0.8	0.8±0.8	15.0±0.7	146.7±4.8	-1.5±0.8	2.0±0.9	4.8±1.5

GH—Growth Hormone, MPH—Midparental height, IAP—Indian Academy of Paediatrics

each had a karyotype of 46X, i(Xq) and 46X, i(Xq)/46 XX. The mean bone age at initiation of GH was 9.3 ± 1.8 years. Mean parameters at the start of growth hormone treatment are illustrated in Tables 1,2 and Figure 1. The age of pubertal induction was between 11 and 15 years for all girls, except one, who entered puberty spontaneously at 10.9 years. The mean duration of GH therapy was 4.8 ± 1.5 years. The mean height velocity during the 1st year of treatment was 6.9 ± 2.1 cm/year (range: 3.6–10) and mean cumulative height velocity was 5.4 ± 0.8 cm/year (range: 3.8–6.6). Parameters on stopping GH and adult height parameters are described in Tables 1-3 and Figure 1. Mean height gain of 29.3 ± 9.8 cm (median: 28; range: 14 - 39.5) was observed from the onset of GH therapy to adult height achievement. There was a significant improvement in the height Z scores (using both, IAP and Indian Turner data) following GH therapy [Table 2 and Figure 2] (p = 0.002 and 0.012, respectively). Using Indian Turner syndrome reference growth data, the mean pre-treatment height Z score was 0.8 ± 0.8, increasing to 2.0 ± 0.9 at the time of stopping GH and the mean adult height Z score was 1.3 ± 0.7. The mean difference in MPH and pre-treatment IAP height Z score was 2.8 ± 0.8 which decreased to 1.7 ± 0.8 at the achievement of final height (p = 0.002). Except for four patients, all others reached an adult height within the reference range for healthy Indian girls (IAP 2015 growth curves) [Table 3, Figure 1]. These four patients received GH late, i.e., after 11.7 years of age, and two among these were hypothyroid but well controlled on medication. No major adverse events were noted except in one girl, who developed headaches for the first two months and therapy had to be discontinued for a few weeks and then restarted at half the dose for four weeks and then increased to 50 mcg/kg/day.[10] IGF 1 concentrations were available for 7 children at one

Figure 1: Comparison of heights of patients with Turner syndrome (measured at the start and end of GH therapy, and final adult height) plotted on IAP (dotted lines) versus Indian Turner (solid lines) growth curves

year of therapy and remained below the safety range (+ 2SD) except in patient number 12 where it was between +2 and +3 SD.

Ranke's regression equation for prediction of near adult height was used for 10 of our patients, wherein the predicted and achieved adult height showed a strong positive correlation with a Spearman correlation coefficient of 0.827 (significant at the 0.01 level). [Table 4].

Table 2: Comparison of mean anthropometric parameters at the onset and end of GH therapy

Parameters	At the onset of GH	At stopping GH	*P*
Mean Height Z score (IAP)*	-2.6±0.8	-1.5±0.8	0.002
Mean Height Z score (Indian Turner)*	0.8±0.8	2.0±0.9	0.012
Mean Weight (kg)	24.9±5.2	44.4±7.8	-
Mean Weight Z score (IAP)*	-1.3±0.7	-0.5±0.9	0.002
Mean Weight Z score (Indian Turner)*	0.6±0.7	1.5±1.2	0.008
Mean BMI (kg/m2)	17.0±2.1	20.5±2.6	-
Mean BMI Z score (IAP)	0.0±0.7	0.1±0.7	0.583
Mean BMI Z score (Indian Turner)	0.2±0.7	0.4±0.8	0.136

* Indicates significant difference between the two groups

Discussion

Satisfactory response to growth hormone therapy in the short term (1 to 2 years) in Indian Turner syndrome girls is reported in a few published studies.[16,17] While papers from Western and Japanese literature on adult height in Turner syndrome treated with long-term growth hormone therapy are published from the 1990s, no study till date from India has been published on long-term GH therapy and adult height on girls with Turner syndrome.[3,18]

In our retrospective study, we report a mean height gain of 29.3 cm from the onset of GH therapy in girls with Turner syndrome. The mean height Z score (based on Indian Turner data) improved significantly from to 0.8 ± 0.8 pre-treatment, to 2.0 ± 0.9 on stopping GH and 1.3 ± 0.7 at adult height following GH therapy. The gap between MPH Z score

Table 3: Height velocities, adult height and Z scores in 12 Turner syndrome patients who had received GH therapy

Sr. No	Height velocity during 1st year of GH (cm/year)	Cumulative height velocity (cm/year)	Adult height (cm)	Height Z score (IAP)	Height Z score (Indian Turner)
1	6.7	5.6	149.5	-1.5	1.4
2	5.5	4.5	149.0	-1.5	1.3
3	6.5	6.3	158.0	0.0	2.6
4	5.6	4.8	143.0	-2.7	0.4
5	3.6	3.8	145.0	-2.3	0.6
6	10.0	5.8	151.0	-1.2	1.6
7	4.2	4.5	143.6	-2.6	0.4
8	9.2	6.4	155.5	-0.4	2.3
9	8.6	6.6	145.0	-2.3	0.6
10	7.6	6.0	149.0	-1.5	1.3
11	9.1	5.5	153.0	-0.8	1.9
12	6.4	5.4	152.0	-1.0	1.7
Mean	6.9±2.1	5.4±0.8	149.4±4.7	-1.5±0.8	1.3±0.7

Table 4: Adult height prediction based on the first year of GH therapy

Sr. No	MPH SDS (Tanner)	Birth weight (kg)	Studentized residual in the first year on GH (Index of responsiveness)	Mean GH dose in mg/kg/week	Age at puberty (years)	Turner Height SDS (Ranke)	Predicted adult height (cm)	Achieved adult height (cm)
1	-0.2	3.2	- 0.44	0.26	13.3	-0.5	150.8	149.5
2	-1.5	-	-	0.36	13.5	1.3	-	149.0
3	1.1	2.5	- 0.15	0.31	13.0	1.3	160.6	158.0
4	-0.9	2.2	- 0.61	0.34	14.4	-2	144.5	143.0
5	0.5	2.3	- 3.92	0.29	13.6	0.3	148.4	145.0
6	-0.9	2.4	0.67	0.34	13.9	-0.3	153.6	151.0
7	-1.1	1.9	-1.56	0.31	15.4	-0.9	147.5	143.6
8	-0.1	1.1	0.69	0.29	13.1	-0.2	154.4	155.5
9	-0.8	2.7	1.60	0.29	13.1	-0.9	152.3	145.0
10	-1.4	2.5	0.49	0.29	11.8	0.5	154.1	149.0
11	0.6	-	-	0.29	15.1	0.3	-	153.0
12	-0.9	2.4	- 0.57	0.31	10.9	0.2	151.2	152.0

– Indicates could not be calculated as the birth weights of these patients were not known

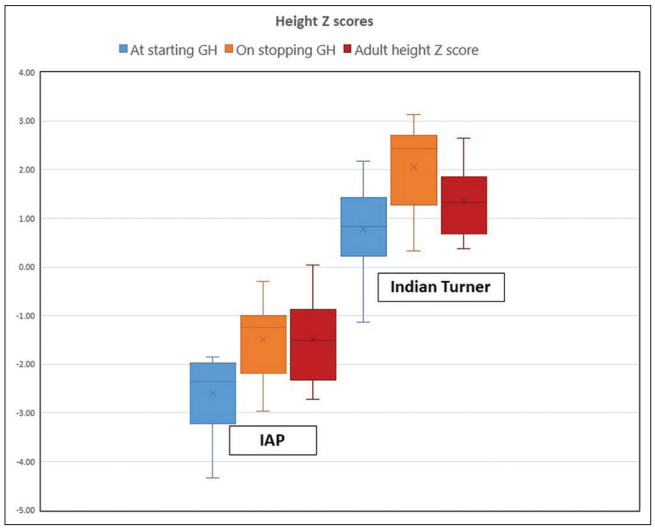

Figure 2: Box and whisker plot comparing Height Z scores (as per IAP and Indian Turner growth curves) at the start and end of GH therapy and adult height in patients with Turner syndrome

and child's pre-treatment height Z score (IAP) decreased significantly ($p = 0.002$) from 2.8 ± 0.8 to 1.7 ± 0.8 following therapy. The adult height achieved was within 2 SD score of healthy Indian girls' population mean after about 5 years of therapy, except in four patients who received GH late.

Our study reports an earlier age at initiation of GH therapy as compared to other Indian studies by Kochar *et al.*[16] and Reddy Danda *et al.*[17] (12.1, 12.7 years, respectively) whereas studies from few other countries have initiated GH therapy at a much younger age.[19] Later age of initiation of therapy in Indian girls could be due to older age at first presentation, more commonly for delayed puberty than for short stature (karyotype is often not performed in an otherwise normal looking girl and watchful waiting for height gain at puberty in a short girl still prevails, thus missing Turner syndrome at a younger age).[20]

In a similar cohort of 16 Indian Turner girls treated with GH for a year, the author's group has earlier reported short term growth velocity at 1 year of treatment to be 6.8 ± 1.4 cm/year, which was similar to the current study.[21] Ranke *et al.* (2012)[22] reported a marginally higher growth velocity of 7.7 cm/year at 1 year of therapy in German girls with Turner syndrome. Kochar *et al.*[16] studied growth parameters in 20 girls with Turner syndrome with a mean age of 12.1 years at GH initiation who received GH for a mean duration of 13 months, and observed a growth velocity of 5.4 cm/year.

In the study conducted by the author's group in 2006, the average increase in predicted height was 2.4 cm, with an improvement of 0.6 SDS in the height Z score at the end of one year of therapy.[21] Ranke *et al.*[23] evaluated longitudinal data on 188 German girls with Turner syndrome on long-term GH and observed a 1.1 SDS overall gain in height. Kochar *et al.*[16] used Ranke's data for height Z score calculations and found a difference of 0.6 between the pre- and post-treatment Z scores. In a Dutch study conducted by Sas *et al.* in 1999,[3] height increment between 12.5 and 16 cm was observed following 7 years of GH use. Using Lyon's data, a gain of 0.99 SDS was observed by Reddy Danda *et al.*[17] following GH administration for a mean duration of 25 months. Since Indian Turner syndrome specific growth reference curves are now available (2020), we assessed gain in height using the same, and found a significant improvement (1.2 SD) in height Z scores at the beginning versus end of GH therapy.[1]

Various studies from the West, China and Japan have observed an adult height of 139 to 147 cm in untreated girls with Turner syndrome; Indian data report an average height of 140.1 cm.[1,2,24,25] Sas *et al.*[3] observed an adult height between 158.8 and 162.3 cm depending on the dose of GH used, while Ranke *et al.*[22] have reported an adult height of 153.5 cm following mean GH treatment for 6.3 years. Takano *et al.*[18] evaluated 115 Japanese girls with Turner syndrome on GH for more than six years and observed an adult height of 142.2 cm with a dose of 0.5 IU/kg/week and 144.3 cm with 1 IU/kg/week. Following GH therapy for a mean duration of about 5 years, we report mean adult height of 149.4 cm, which is only 8.4 cm lesser than the mean Indian adult woman's height, whereas, the difference between untreated girls with Turner syndrome and average adult Indian women is 17.7 cm.[14] Moreover, following GH therapy, the adult height was within the target range for healthy Indian women (as observed from adult height IAP Z scores being within ± 2 SDS of the healthy Indian population norms) except for four patients who received GH late and two among these were hypothyroid but well controlled on medication. This emphasizes the importance of the effect of timely initiation of GH therapy on the normalisation of adult height.

Few models have been developed to predict growth response in Turner syndrome while on GH therapy, thereby enabling dose optimization. One such tool is iGRO (individualised growth response) by Pfizer, which uses growth prediction models derived from KIGS (Pfizer International Growth Database) for various conditions requiring GH, including Turner syndrome. It provides the index of responsiveness, which is analogous to SD wherein a positive value suggests better response and a negative value suggests reduced response in comparison to the reference cohort used for prediction model development.[9] Ranke *et al.*[8] have observed that the GH dose and the index of responsiveness during the first year of treatment are strong predictors of near adult height in girls with Turner syndrome and have developed regression equations to predict near adult height and gain in height, based on mid-parental height SDS, height SDS and age at starting GH, IOR, mean GH dose, age at onset of puberty and birth weight. Using Ranke's equation for adult height prediction, we observed a strong positive correlation between the predicted height and the achieved adult height, thereby demonstrating that the prediction equation holds good in Indian girls with Turner syndrome. This observation could help to optimize growth hormone doses in Indian girls with Turner syndrome based on their IOR during the first year on GH.

To the best of our knowledge, no other study from India has evaluated either long-term use of GH and adult height in girls with Turner syndrome, or used Ranke's prediction equation and correlated the predicted and achieved adult height. Our study is limited by the fact that this was a retrospective study and the sample size being relatively small, karyotype-wise subgroup analysis could not be done. Also, this is a single centre study, further, IGF concentrations were available only on seven girls. Larger prospective studies are thus required to further explore adult height following long-term growth hormone therapy in Indian girls with Turner syndrome and more so in those started on GH at a younger age.

In a resource-limited country like India, where a large proportion of patients cannot afford growth hormone, we conclude that at a GH dose in the lower range (40 to 50 mcg per kg per day) of recommendations (45 to 68 mcg per kg per day), with a mean duration of about 5 years, Indian girls with Turner syndrome can achieve an adult height within the healthy Indian reference range. Dose individualization based on the IOR during the first year of GH therapy would help in optimizing GH dosage and would turn out to be a more economic option without compromising on height outcomes.

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Conflicts of interest

There are no conflicts of interest.

References

1. Khadilkar VV, Karguppikar MB, Ekbote VH, Khadilkar AV. Turner syndrome growth charts: A Western India experience. Indian J Endocrinol Metab 2020;24:333-7.
2. Ranke MB, Stubbe P, Majewski F, Bierich JR. Spontaneous growth in Turner's syndrome. Acta Paediatr Scand Suppl 1988;343:22-30.
3. Sas TC, De Muinck Keizer-Schrama SM, Stijnen T, Jansen M, Otten BJ, Hoorweg-Nijman JJ, *et al*. Normalization of height in girls with Turner syndrome after long-term growth hormone treatment: Results of a randomized dose-response trial. J Clin Endocrinol Metab 1999;84:4607–12.
4. Rosenfeld RG, Attie KM, Frane J, Brasel JA, Burstein S, Cara JF, *et al*. Growth hormone therapy of Turner's syndrome: Beneficial effect on adult height. J Pediatr 1998;132:319-24.
5. Richmond E, Rogol AD. Current indications for growth hormone therapy for children and adolescents. Endocr Dev 2010;18:92-108.
6. Gravholt CH, Naeraa RW, Brixen K, Kastrup KW, Mosekilde L, Jørgensen JO, *et al*. Short-term growth hormone treatment in girls with Turner syndrome decreases fat mass and insulin sensitivity: A randomized, double-blind, placebo-controlled, crossover study. Pediatrics 2002;110:889-96.
7. Gravholt CH, Andersen NH, Conway GS, Dekkers OM, Geffner ME, Klein KO, *et al*. Clinical practice guidelines for the care of girls and women with Turner syndrome: Proceedings from the 2016 Cincinnati International Turner Syndrome Meeting. Eur J Endocrinol 2017;177:G1–70.
8. Ranke MB, Lindberg A, Ferrández Longás A, Darendeliler F, Albertsson-Wikland K, Dunger D, *et al*. Major determinants of height development in Turner syndrome (TS) patients treated with GH: Analysis of 987 patients from KIGS. Pediatr Res 2007;61:105–10.
9. Loftus J, Lindberg A, Aydin F, Gomez R, Maghnie M, Rooman R, *et al*. Individualised growth response optimisation (iGRO) tool : An accessible and easy-to-use growth prediction system to enable treatment optimisation for children treated with growth hormone. J Pediatr Endocrinol Metab 2017;30:1019–26.
10. Shah NS. Turner syndrome. In: Khadilkar VV, Bajpai A, Prasad H, editors. IAP Textbook on Pediatric Endocrinology. 1st ed. Haryana: Jaypee Brothers; 2019. p. 138–44.
11. Marshall WA, Tanner JM. Variations in pattern of pubertal changes in girls. Arch Dis Child 1969;44:291-303.
12. Tanner JM, Healy MJ, Goldstein H, Cameron N. Assessment of skeletal maturity and prediction of adult height (TW 3 method). 3rd ed. London: WB Saunder; 2001.
13. Tanner JM, Whitehouse RH, Marshall WA, Carter BS. Prediction of adult height from height, bone age, and occurrence of menarche, at ages 4 to 16 with allowance for midparent height. Arch Dis Child 1975;50:14-26.
14. Khadilkar VV, Khadilkar AV. Revised Indian Academy of Pediatrics 2015 growth charts for height, weight and body mass index for 5-18-year-old Indian children. Indian J Endocrinol Metab 2015;19:470-6.
15. Tanner JM, Whitehouse RH, Takaishi M. Standards from birth to maturity for height, weight, height velocity, and weight velocity: British children, 1965. II. Arch Dis Child 1966;41:613-35.
16. Kochar IS, Ramachandran S, Sethi A. Recombinant Growth hormone response in Indian girls with Turner syndrome. Int J Clin Endocrinol Metab 2018;4:1-3.
17. Reddy Danda VS, Sreedevi P, Arun G, Rao PS. Growth hormone treatment in Turner's syndrome: A real world experience. Indian J Endocrinol Metab 2017;21:378–81.
18. Takano K, Ogawa M, Tanaka T, Tachibana K, Fujita K, Hizuka N. Clinical trials of GH treatment in patients with Turner's syndrome in Japan--a consideration of final height. The Committee for the Treatment of Turner's Syndrome. Eur J Endocrinol 1997;137:138-45.
19. Quigley CA, Fechner PY, Geffner ME, Eugster EA, Ross JL, Habiby RL, *et al*. Prevention of growth failure in Turner syndrome: Long-term results of early growth hormone treatment in the "Toddler Turner" cohort. Horm Res Paediatr 2021;94:18–35.
20. Lee MC, Conway GS. Turner's syndrome: Challenges of late diagnosis. Lancet Diabetes Endocrinol 2014;2:333–8.
21. Khadilkar VV, Khadilkar AV, Nandy M, Maskati GB. Growth hormone in turner syndrome. Indian Pediatr 2006;43:236-40.
22. Ranke MB, Schweizer R, Martin DD, Ehehalt S, Schwarze CP, Serra F, *et al*. Analyses from a centre of short- and long-term growth in Turner's syndrome on standard growth hormone doses confirm growth prediction algorithms and show normal IGF-I levels. Horm Res Paediatr 2012;77:214–21.
23. Ranke MB, Partsch CJ, Lindberg A, Dorr HG, Bettendorf M, Hauffa BP, *et al*. Adult height after GH therapy in 188 Ullrich-Turner syndrome patients: Results of the German IGLU follow-up study 2001. Eur J Endocrinol 2002;147:625–33.
24. Low LC, Sham C, Kwan E, Karlberg J, Tang G, Cheung PT, *et al*. Spontaneous growth in Chinese patients with Turner's syndrome and influence of karyotype. Acta Paediatr 1997;86:18-21.
25. Isojima T, Yokoya S. Development of disease-specific growth charts in Turner syndrome and Noonan syndrome. Ann Pediatr Endocrinol Metab 2017;22:240–6.