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Research Article

Implementation of Parental Stature Assessment in Girls with Turner Syndrome

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Abstract

It is common practice among paediatricians to compare the child's stature at a growth age with that of both parents.

Aim: the assessment of correlation between parental stature and that of girls with Turner Syndrome (TS).

Materials and Methods: A cohort including 186 girls with TS and their parents was evaluated since 1988. The patients, aged 4 months to 17 years, were not receiving GH therapy. The TS girls' heights and those of their parents were measured by an anthropologist. Arithmetic means and standard deviations were calculated for the entire group of subjects and their parents on the basis of anthropometric data. Mid-parental height (in cm and in SDS) was also determined in each case. For girls at the same calendar age, we have used the arithmetic means and standard deviations given in the current population standards. Parental heights were standardized by calculating the means. Standard deviations were determined by those for a population of the 18-year-olds. The correlation of mid-parental height with short stature of the daughters and their age was assessed. The difference between the mid-parental height (in SDS) and that of the daughter was calculated for each patient separately, assuming that the result should range from 0 to ±1 SDS.

Results: The mean calendar age of girls with TS was 9.46±3.90 years. In 155 girls (83.3%) the height was <-2 SDS, while in 109 patients it was <-3 SDS. The mid-parental height was higher in girls with lower height deficiency (172.1 cm in parents of 37 girls with a height of >-2 SDS *versus* 164.5 cm of parental height of 20 girls with a height of <-4 SDS). 73.7% of girls markedly differed in height from their parents (>+2 in SDS). Only the height of 9 girls (4.8%) was in the range of ±1 SDS in relation to parental height.

Conclusion: 1. The height of parents of girls with TS has features of a normal distribution in the population.

2. A considerable difference (in SDS) between the mid-parental heights and those of their daughters, found in the study, implies the necessity of including the criterion in the diagnosis of TS.

3. The girls should not be declined genetic diagnostics due to low mid-parental height.

Keywords: Girls; Turner syndrome; Parental stature

Introduction

It is common practice among paediatricians to compare the child's height at a growth age with the stature of both parents [1-6]. When both parents and at least one parent alone is of short stature the physician may be inclined to abandon diagnostic procedures and suggest a family history of short stature. Girls with TS constitute approximately 10% of all female patients with short stature seen by endocrinologists in our Department. In some girls the diagnosis is delayed and they experience difficulties in receiving appropriate health care. In the 80-ties and 90-ties of the 20th century, the diagnosis was often established at the age of 15 or later, with no apparent clinical features of puberty. In the 21st century a basic investigation which can make a diagnosis of short stature in girls (even without apparent signs of TS) considerably more straight forward is a karyotype analysis. In the present study, we measured and assessed the stature of the parents of TS girls presenting at 2 centres of paediatric endocrinology in Warsaw in 28 years. The correlation between the parental stature and that of TS girls was also analyzed.

Aim

The aim of the study was to assess the correlation between mid-parental stature and that of TS girls.

Materials and Methods

186 girls with TS aged 0.25 to 17.42 (mean age was 9.46±3.90) and their parents participated in the study conducted in Anthropology Laboratory in The Children's Memorial Health Institute and

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Table 1: Mean values of standard deviations and range of body height of the children and their parents (cm and SDS), (n=186).

Characteristics	Mean±SD	Min	Max
Mean height of children (cm)	116,99±17,92	56,5	152,3
Mean height of children (SDS)	-2.87±0.97	-6.3	-0.3
Mean height of mother (cm)	162.07±5.77	148.1	183.1
Mean height of mother (SDS)	-0.26±1.01	-2.68	2.93
Mean height of father (cm)	175.36±6.43	160	193.5
Mean height of father (SDS)	-0.27±0.99	-2.63	2.4
Parental mean height (cm)	168.72±5.03	157.75	184.8
Parental mean height (SDS)	-0.28±0.83	-2.03	2.13

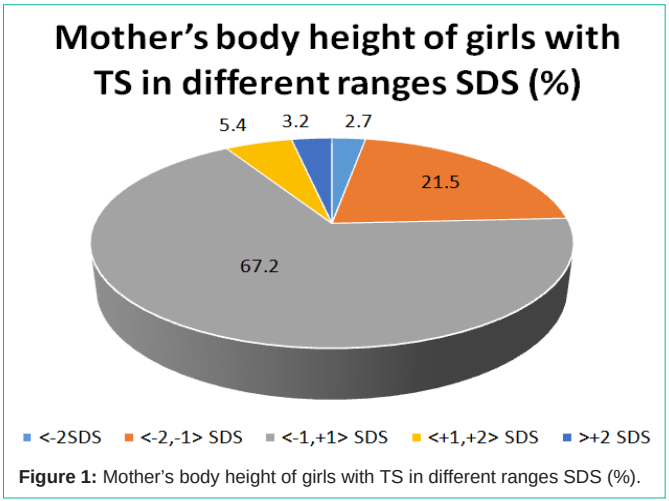

Figure 1: Mother's body height of girls with TS in different ranges SDS (%).

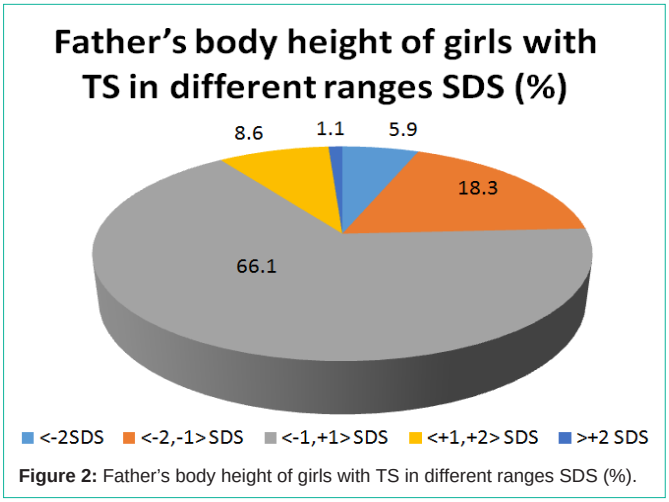

Figure 2: Father's body height of girls with TS in different ranges SDS (%).

Department of Pediatric and Endocrinology Medical University of Warsaw from 1988 to 2015. The TS diagnosis was confirmed by a cytogenetic test in each case. The patients were to be put on recombinant human Growth Hormone (rhGH) therapy and were not receiving any other hormonal growth promoting treatment. The majority of patients had a karyotype 45X. Due to prolonged collection of data and lack of access to various karyotypes, differentiation in accordance with mosaic karyotypes was omitted in prospective studies. The height measurements of the girls with TS and their parents were performed by anthropologists on a Harpenden Stadiometer in the morning hours. The patient, wearing only underwear, was put in anthropometric position, while the parents in question were wearing light clothing. The measurements of girls' heights were taken 3 times, with the arithmetic mean calculated, whereas those of the parents only once. On the basis of the anthropometric data, arithmetic mean and standard deviations for the entire cohort of girls, mothers and fathers were calculated, together with the mid-parent height (in cm). For girls at the same calendar age, we have used the arithmetic means and standard deviations given in the current population standards (IMIDZ from 1983, IMIDZ from 2001) [7,8] according to an equation: the mean height for the calendar year-the height of the child in SDS (height Standard Deviation Score). Parental heights were standardized by calculating the means. Standard deviations were determined by those for a population of the 18-year-olds according to the appropriate standards. The height calculated in SDS for each parent separately allowed to obtain the mid-parental height in SDS. The midparental-girl difference in height was then calculated in SDS assuming that the result should range from 0 to ±1 SDS.

Results

In the cohort of 186 girls with TS the mean calendar age of the patients was 9.46±3.90 years. In 155 girls (83.3%) the height was <-2 SDS, while in 109 patients it was <-3 SDS. 31 girls were at the 3 centile of height. The basic characteristics: the height of children (in cm and SDS) and those of mothers and fathers (in cm and SDS) as well as mid-parental height (in cm and SDS) are presented in table (Table 1).

The height of mothers and fathers in the entire cohort showed a distribution similar to a normal pattern. The height of 67.7% of mothers and 66.1% of fathers was within 0±1 SDS calculated for the Polish population. Only 2.7% of mothers and 5.9% of fathers had a height deficiency of <-2 SDS, while 3.2% of mothers and 1.1% of fathers were tall (>+2 SDS) (Figures 1 & 2).

Assessment of the mid-parental heights in correlation with short stature in daughters showed differences between parental height and height deficiencies in daughters with TS. A statistically significant difference ($p<0.05$) was found between the mid-parental height of mothers and fathers in relation with the height deficiencies in daughters (in SDS) (Table 2).

With the use of a linear regression method, a statistically insignificant correlation (10% maternal and 20% paternal) of parental height with that of the daughters was detected. A considerable difference, statistically ($p<0.05$), was found in test T between the mean SDS heights of girls with TS and the height of mothers and fathers as well as the mid-parental height. Studies of the entire cohort of girls revealed that the oldest girls at presentation had the largest height deficiency: the mean age of 20 girls with a height of <4 SDS was 13.08 years. Girls whose height was <-2 SDS were 9 years old on average, whereas the mean age of those with the lowest SDS was 7 when the diagnosis was made. Depending on the height deficiency of the smallest girls with TS in the group, the maternal-daughter height difference was 6.2 cm, paternal-daughter difference was 8.9 cm and the mid parental-daughter difference amounted to 7.6 cm (2.0 in SDS). Although the parental-daughter height correlation does exist, it is relatively small. However, the differences in height in girls with TS (not undergoing treatment) aggravate with age. The effect

Table 2: The mean values of mother's and father's body height (cm and SDS) depending on the deficiency of body height in girls with TS.

Height of children with TS (SDS)	N	Mean height of mother cm (SDS)	Mean height of father cm (SDS)	Mid-parental height cm (SDS)	The difference between the mid-parental height
<-4 SDS	20	158.86(-0,8)	170.22(-1,0)	164.54(-0,91)	-3.87
<-3>-4 SDS	57	160.51(-0,5)	173.54(-0,55)	167.02(-0,53)	-2.85
<-2>-3 SDS	72	162.67(-0,14)	176.29(-0,13)	169.48(-0,16)	-2.44
<-1>-2 SDS	37	165.06(0,2)	179.14(0,27)	172.1(0,22)	-1.82

Table 3: Difference between mean SDS height of girls with TS and their parents (%).

Difference between mean SDS height of girls with TS and their parents (%)		
SDS	**N**	**%**
±1 SDS	9	4.8
<1,2> SDS	41	22.0
<2,3> SDS	78	41.9
>3 SDS	58	31.2
>2 SDS	136	73.1

of age on the differences in the height of girls (in SDS) was assessed, showing the largest correlation (0.26). Similar results were obtained in a linear regression test conducted to detect whether the patient's age wasassociated with the differences in the child's height and that of the parents. The test revealed that the older the child the larger the difference with the mid-parental height (Figure 3).

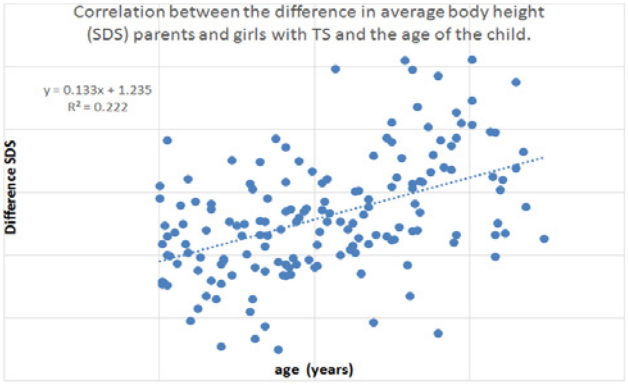

Figure 3: Correlation between the difference in average body height (SDS) parents and girls with TS and the age of the child.

Midparental-daughter height differences (in SDS) were evaluated. The height of the child (in SDS) was subtracted from the mid-parental height in SDS (Table 3).

Only 9 girls (4.8%) had a height of ±1 SDS adjusted for mid-parental height. The mean calendar age of the girls was 7.88 years with an average height of -1.69 SDS. The mean height of mothers and fathers in this group was the lowest in the study group. The height of 40 girls (21.5%) was in the range of 1 to 2 SDS from that of their parents. In case of 73.7% of girls their height in SDS differed significantly from the mid-parental height (>+2 SDS).

Discussion

Patients with TS constitute a large percentage of girls with short stature [5]. The main features of TS, making the establishing of diagnosis difficult, are a characteristic phenotype and various degrees of short stature [9]. A cytogenetic test is necessary in order to confirm or exclude TS, to diagnose short stature in girls. In the cohort participating in the study (patients presenting since 1988) all girls had karyotype-proven TS. Some girls had the test done at an age later than 15. The majority of patients had a karyotype 45X. Due to lack of access to official genetic data the differences between parental stature and a variety of mosaic karyotypes were not analyzed in the present study [10-12]. The impact of parental stature on the child's height has been investigated for decades. Guidelines for establishing diagnosis of genetic short stature in children aged 2-9 years were published by Tanner already in 1970 [1]. The principle of relating the height of a healthy child to that of the parents was emphasized by Cole who also suggested the necessity to undertake further diagnostic procedures when the child's height differed significantly from that of the parents [2]. In a study by Wright, et al. the authors recall a method of assessment of the child's height at the range of ±2 centiles of the mean mid-parental height [3]. Luo predicted the "target" adult height of a child allowing for the mid-parental height (n=2402). He concluded that, with Tanner's method, the predicted child's height was underestimated in case of mid-parental mean below 2 SDS (163 cm) since fully grown healthy children of small parents were taller than predicted from the mid-parental mean height [4]. According to Bartstow, if the expected adult height of a child is lower than the mid-parental height by 10 cm or more, pathological causes should be assumed. The height of a child is determined by many factors. Short stature, however, may be due to an underlying disease [6]. There are few reports in literature on parents of girls with TS and they are usually derived from relatively small samples or based on data from the patients' history. In a multicentre study by Ranke, et al. (1994), a positive correlation of predicted height with that of fully grown women with TS never undergoing rhGH treatment was found, confirming a significant role of mid-parental height [13]. In a Turkish study on a sample group of 842 girls with TS, conducted by Sari since 1984, it was found that mid-parental height and the child's age were the sole criteria associated with the girl's height [12]. Cohen demonstrated in a study of 75 adult females with TS (45 from Israel and 30 Italian women, with no history of GH treatment) a correlation of their final height only with that of their mothers and not the fathers' [10]. These results were consistent with those of de Lemos-Marini (n=58) [14]. On the basis of height measurements of 64 girls with TS, Salerno also concluded that the child's height was more related to maternal height than to that of the father [15]. Hagman analyzed the height of 275 mothers (from 1973 to 2005) where 83.7% of the subjects were taller than 160 cm (data derived from a questionnaire) [16]. The mid-parental height is given differently by various authors: in cm, SDS, centiles. In a study by Massa, et al. (1991) on a cohort of 100 girls with TS, the authors recommended a karyotype investigation in these girls whose height was 2 SDS lower compared with their mid-parental

height. The difference between parental height (even in small parents) and that of the daughter is a useful indication for early initial TS diagnosis [17]. Bernasconi and later Bertapelli, reported a tendency toward larger height in girls with TS, depending on the mid-parental mean [18,19]. Our earlier research, conducted on a sample group of 452 children with short stature revealed that every second girl with TS (n=22) had a height significantly smaller (in SDS) than that of the parents. A study carried out by Polish authors Wisniewski, et al., with data derived from a questionnaire [20], showed that in a group of 355 newborns with TS the occurence of short stature in parents, especially in fathers was higher than in the general population. Normal parental height, however, was noted in 70% of the subjects (-0.1 to +1 SDS). In our present study, in a group of 186 participants, girls with TS, together with their mothers and fathers, an increased, statistically significant number of girls ($p<0.05$) was shown to markedly differ in height (by more than 2 SDS) from the mid-parental mean in SDS. Girls whose height was measured in the years 1988 to 2000 were very small and were first seen at a much later age than those presenting within the last 10-15 years. This tendency is consistent with reports of other authors [16,21]. In recent years, prenatal tests have enabled growth assessment of younger patients and there were 4 participants at the age below 3 in whom the diagnosis was made *in utero*. There are many reports in literature on GH treatment of girls with TS [22-29]. The results indicate that, left untreated, the height of girls with TS often remains lower than the 3rd centile. GH treatment can improve the patients' final height [30]. Some of the girls were excluded from the growth promoting treatment, whereas some failed to attain satisfactory height in adulthood, despite undergoing treatment for several years. There is much dispute among researchers on the appropriate age to commence GH treatment, the dose of the medication and the effect of parental height on the outcomeof treatment [31-36]. Our research showed that parental height of the patients was similar in distribution to the normal population and there was no direct correlation between the height of the parents or one parent alone and the height of the daughter with TS. Conversely, a more common finding, of diagnostic importance, was a considerable difference between the daughter's height and that of the parents [5]. The eventual treatment outcome of girls with TS, their health, prospective family planning and life satisfaction have become issues frequently investigated by many researches and new results are being reported on the subject [37-39].

Conclusion

1. The height of parents of girls with TS has features of a normal distribution in the population.
2. A considerable difference (in SDS) between the mid-parental heights and those of their daughters, found in the study, implies the necessity of including the criterion in the diagnosis of TS.
3. The girls should not be declined genetic diagnostics due to low mid-parental height.

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