ISSN - 2250-1991 | IF : 5.215 | IC Value : 79.96

Original Research Paper Pediatrics

Clinical profile of Turner's Syndrome- our experience

Dr Rahul Jahagirdar Department of Paediatrics, Bharati Vidyapeeth University Medical College, Pune, Maharashtra.

Dr Ruma Deshpande Department of Paediatrics, Bharati Vidyapeeth University Medical College, Pune, Maharashtra.

ABSTRACT

Turner syndrome (TS) refers to a condition characterized by short stature and ovarian dysgenesis in females who have a single X chromosome and absence of all or part of the second sex chromosome (X or Y). Unexplained short stature in a girl most commonly leads to evaluation during childhood and adolescence. Adult height is on average 20 cm below expected norms.
Karyotype analysis reveals that Y-chromosomal material may be present in 5% of individuals with TS, carrying a risk of developing gonadoblastoma.
Retrospective analysis over a period of 18 months, in 11 diagnosed cases of Turner's syndrome showed poor linear growth, delayed puberty and behavioral issues.
Patients benefited on start of hormonal therapy to induce pubertal changes.

KEYWORDS Turners, Linear growth, Karyotype

Introduction:
Turner syndrome (TS) refers to a condition characterized by short stature and ovarian dysgenesis in females who have a single X chromosome and absence of all or part of the second sex chromosome (X or Y). Approximately1% to 2% of all conceptuses has a 45, X chromosome constitution. The majority (99%) of these spontaneously abort, usually during the first trimester of pregnancy.

With the more frequent use of ultrasonography, it is recognized that some pregnancies with a fetal 45, X chromosome constitution progressing into the second trimester are associated with nuchal cysts, severe lymphedema, or hydropsfetalis. These pregnancies are associated with a high frequency of fetal death.

The birth prevalence of Turner syndrome has been estimated to be from 1 in 2000 to 1 in 5000 female live births in various studies.

In developed countries, unexplained short stature in a girl most commonly leads to evaluation during childhood and adolescence (82% of cases). In our country, primary amenorrhea is the commonest presentation. There is often a delay in the diagnosis of TS, averaging 5 year after patients had fallen below the 3rd percentile in height to time of diagnosis. Adult height is on average 20 cm below expected norms.

Karyotype analysis reveals that Y-chromosomal material may be present in 5% of individuals with TS, and an additional 3% of individuals may also have a marker chromosome (a chromosome fragment of X or Y origin).Risk of developing gonadoblastoma with Y material present ranges from 7-10%, thus necessitating a prophylactic gonadectomy.

Ovarian failure in TS begins by 18 weeks of gestation, after which accelerated fibrous degeneration of ovarian follicles takes place. Follicle stimulating hormone (FSH) and Luteinizing hormone (LH) levels show a rise in infancy and early childhood, gradually decline until 6 years of age, and then rise again at the normal age of puberty.

Management is mainly aimed at helping the girl achieve maximum possible linear growth and attaining pubertal development. The mainstay of management is counselling and education of the child as well as the parents/ caregivers, with stress on regular follow-up, options for fertility and psychological support.

Growth hormone (GH) therapy is advised for enhancing the linear growth. There has been extensive research suggesting that GH treatment in TS may be of benefit in areas other than linear growth. GH has been shown to improve body proportions and may contribute to lower diastolic blood pressure in TS, even after treatment is discontinued. Similar beneficial effects have been seen in relation to total cholesterol, low-density lipoprotein, and high-density lipoprotein. Therapy has to be started early as the adult height is highest in TS patients with taller stature at initiation of GH therapy, taller parental heights, younger age at initiation of treatment, longer duration of therapy, and higher GH doses.

Up to one third of girls with TS can have spontaneous pubertal development, especially those with mosaic karyotypes. Only a small percentage will have spontaneous menarche, with almost all eventually showing signs of ovarian failure. Spontaneous pregnancies are rare (2–5%).

Current recommendations to start low-dose oestrogen therapy at 12 years of age allow for normalized development of secondary sexual characteristics, as well as uterine and bone mineral development. Treatment can be started with 0.1-0.2mg/day ethinyl estradiol, given for 1-2 years, and then switched to oral contraceptive pills containing progesterone.
With this background we decided to analyse the patients with TS with the Aim and Objective to,

1) To analyse the clinical, anthropometric, biochemical & genetic profile of Turner's syndrome at diagnosis.
2) To follow-up & assess the response to treatment over a period of 6 months.

Method:
Retrospective analysis over a period of 18 months, in 11 diagnosed cases of Turner's syndrome.

They were analysed for their physical, anthropometric, biochemical, radiological & genetic features.

Their growth parameters were plotted on 2007 growth charts for affluent Indian children.
They were screened for co-morbidities like type 1 diabetes mellitus, congenital heart disease & hypothyroidism.
Treatment was initiated & cases were followed up for response.

Results:
The age of presentation varied from as low as 5 years to as high as 20.3 years, (14.2 mean).The clinical presentation was similar in all the cases. All the 11 girls (100%) presented with complaint of

poor linear growth, out of which 8 (72%) also sought medical attention for delayed puberty. 2 out of 11 girls (18%) were developmentally delayed, while only one (9%) had behavioural issues. Family history was positive for short stature for 3 cases & positive for delayed puberty for 2 of them.

Their anthropometric parameters were plotted on growth charts. All the cases studied were found to be significantly below the 3rd centile for age, with height more severely affected than the weight at the time of presentation. The mean z-score for height was -4.89, while the z-score for weight was - 3.84. **(Chart 1)**

Follicle stimulating hormone (FSH) & Luteinizing hormone (LH) levels were done for all 11 girls & were found to be significantly higher than the normal levels, suggestive of ovarian failure. The mean FSH level was 115.3mIU/ml & mean LH level was 14mIU/ml.

All the girls were screened for auto-immune diseases like thyroiditis, Type I diabetes mellitus and celiac disease. Only one was found to have hypothyroidism. They were also screened for associated cardiac anomalies by 2D-Echocardiography, which was normal in all the cases.

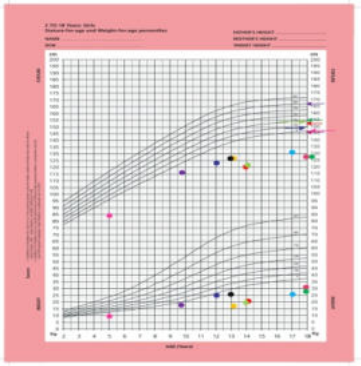
Ultrasonography was done for all the cases, to look for uterus & ovaries. They were either found to be hypoplastic for age or were not visualized at all.

Diagnosis for all the 11 girls was confirmed by karyotype. **(Table - 1).**
5 girls (45%) had the classical 45 (X, O) karyotype, whereas, the other 6 (55%) were mosaics. Y-chromosome was detected in only 1 case, for which prophylactic gonadectomy was also done.

Table -1: Patient details:

Case No.	Age at presentation (years)	Weight on presentation (kg)	Height on presentation (cm)	Mid-parental height (cm)	Karyotype
1	14.1	20	120.5	152.2	45, XO
2	17.9	32	127.2	-	45, XO
3	19.9	28	127.1	153.5	45,XO[11]/46,Xr(X)(p22.2;q28)[09]
4	17.2	26	130.2	145.5	46, XO
5	13.2	17	126	-	45, XO
6	20.3	26	135.2	155	46, XX/ 45, XO (mosaic)
7	9.6	18.3	115.5	165.5	45,XO/46,X(Yinv)(p11.31, q11.23)
8	13	27	127.3	148.5	45,XO/46 XX (mosaic)
9	14	20	120	153.2	45, X[2]/ 46,Xi (Xq)(q11-te) [12]
10	5	10	84	146	45, XO
11	12	25	123	147	46, XX/ 45, XO

Chart 1: Height and Weight parameters at time of diagnosis:



Retrospectively, we compared the growth parameters of the girls with classical karyotype with those of mosaics. We found that the mosaics were significantly taller than the classical karyotype. The mean height for mosaics was 124.6 cm, while that for classical karyotype was 117.6 cm.

For treatment, Growth Hormone (GH) therapy was offered to all the patients, but due to financial constraints, was started for only one. For hormone replacement, estradiol was started for 4 girls. All of them showed breast development on follow-up and only one had an episode of bleeding.

Discussion:
Turner syndrome is the commonest female sex chromosome anomaly, associated with a variety of karyotypes as well as phenotypes. Linear growth is almost universally poor & can be improved if GH therapy is initiated on time. Hence it is important to diagnose timely.

Karyotype is indispensable to confirm the diagnosis & to predict the linear growth, as mosaics are observed to be taller than the classical karyotype. Also, prophylactic gonadectomy can be offered in time if a Y-chromosome is detected. Therefore, it cannot be emphasized enough that any girl presenting with unexplained short stature should be tested for karyotype.

Early diagnosis also helps in counselling the child & family regarding the outcome with respect to fertility. There are associated auto-immune conditions like Type I diabetes mellitus, thyroid dysfunction which need to be diagnosed & managed without delay.

References:

1. Jordan E. Pinsker; Turner Syndrome: Updating the Paradigm of Clinical Care; J Clin Endocrinol Metab, June 2012, 97(6):E994–E1003
2. Stochholm K, Juul S, Juel K, Naeraa RW, Gravholt CH2006 Prevalence, incidence, diagnostic delay, and mortality in Turner syndrome. J Clin Endocrinol Metab 91:3897–3902
3. Bondy CA2007 Care of girls and women with Turner syndrome: a guideline of the Turner Syndrome Study Group. J ClinEndocrinolMetab 92:10–25
4. Davenport ML2010 Approach to the patient with Turner syndrome. J Clin Endocrinol Metab 95:1487–1495
5. Davenport ML, Punyasavatsut N, Stewart PW, Gunther DF, Sa¨vendahl L, Sybert VP2002 Growth failure in early life: an important manifestation of Turner syndrome. Horm Res 57:157–164
6. Nelson Textbook of Pediatrics; 20th edition, Elsevier Saulders
7. Jaime L. Frías, Marsha L. Davenport, Committee on Genetics and Section on Endocrinology. Health Supervision for Children With Turner Syndrome
8. Khadilkar VV, Khadilkar AV, Cole TJ, Cross sectional growth curves for height, weight and body mass index for affluent Indian children, 2007. Indian Pediatrics. Vol 46(6), 2009 pp 477-89