

Presentation and clinical profile of Turner syndrome: experience at a tertiary care hospital in Bangladesh

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ABSTRACT

Background: Turner syndrome (TS) is a chromosomal disorder caused by complete or partial X chromosome monosomy that manifests various clinical features depending on the genetic background of affected girls. This study was designed to describe the presentation and clinical spectrum of patients with Turner Syndrome to create awareness for early referral.

Methods: Our study included karyotype-proven TS patients aged 0-18 years who attended the Paediatric Endocrinology & metabolism outpatient department of BIRDEM Women and Children Hospital during the years 2018-2022. Retrospective data on the initial presentation, clinical spectrum and chromosomal abnormalities of patients diagnosed with Turner syndrome were extracted from the departmental database.

Results: A total number of sixty patients were diagnosed as Turner Syndrome during the study period. The mean age was 10.6±4.0 year. The majority (63.4%) were diagnosed between 11-18 years, between 5 to 10 years of age 21.7% and 15 % were diagnosed before the age of 5 years. The common presentation complaints were short stature (75%), delayed puberty (50%) and among patients diagnosed before age one year pedal edema (8%). Common dysmorphic features were wide spaced nipple (41.6%), webbing of neck (35%), low hair line (25%), short neck (21.7%), increased carrying angle (20%) & hyperconvex nail (20%). Most of the patients presented with the karyotyping 45,XO (61.7%) followed by 46,XX/45,XO (217%). Among the associated comorbidities cardiac defects was the most common, occurring in 23.4 % of the TS cases. This was followed by dyslipidemias (10%), autoimmune hypothyroidism (8.3%), obesity (6.6%) and Type 1 DM (1.6%). Behavioral problem was found in 8.3% of patients with TS. Other manifestations included speech delay (5%), hearing problem (3.3%) and repeated otitis media (1.6%). Hypoplastic uterus with streaky ovaries were found in 91.6% cases & renal anomalies were found in 8.3% patient (horse shoe kidney 5%, hydronephrosis 1.6% & ectopic kidney in 1.6% case). Luteinizing hormone and follicular stimulating hormone was raised in 90% case with TS.

Conclusions: The majority were diagnosed and referred to Paediatric Endocrinologists after 5 years of age. A high degree of clinical suspicion can help us diagnose these children earlier. If TS is diagnosed earlier, growth can be achieved up to their maximum potential and also identification and address of comorbidities will provide better life.

Key words: turner syndrome, short stature

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INTRODUCTION

Turner Syndrome (TS) is a genetic disorder characterized by total or partial absence of one sex chromosome.¹ It is one of the most common chromosomal disorder with an incidence of 1:2500 female live births.^{2, 3} The most prevalent karyotype is 45,XO followed by mosaic patterns. TS is associated with several comorbidities that increase with age. Although TS causes several multisystem disorders, the most common presentation is usually due to short stature and primary gonadal deficiency.

Turner girls may clinically present with lymphedema, shield chest, short stature, webbing of neck, short 4th

metacarpal or metatarsal and wide carrying angle. They may also have associated comorbidities such as cardiac and renal defects. They may also develop diabetes, hypothyroidism, hypertension, hearing loss, osteoporosis and bone fractures.^{4, 5} During early infancy, cases with TS show no psychological developmental differences from infants with a normal karyotype. As they grow older, their appearance, intelligence and psychological development are seen to diverge from their peers who develop normally.⁶

Timely diagnosis and proper management of associated problems may reduce substantial morbidity and mortality and improve the quality of life of patients with TS. The present study describes the characteristics of diagnosed Turner patients in a tertiary care Paediatric Endocrinology center during the past five years. The study aims to emphasize presentation and clinical spectrum to create awareness and prevent potential delays in referral to Endocrinology services.

METHODS

This cross-sectional study was conducted at the Paediatric Endocrinology and Metabolism Outpatient department at BIRBEM Women and Children Hospital, a tertiary care hospital, Dhaka, the capital city of Bangladesh from 2018 to 2022.

This was a cross-sectional study conducted from 2018-2022.

All children below 18 years attending at our OPD with karyotype proven Turner Syndrome were included in the study. Patient who did not have adequate information regarding history and investigation reports was excluded.

Retrospective data on the initial presentation, clinical spectrum and chromosomal abnormalities of patients diagnosed with Turner syndrome was extracted from the departmental database.

Clinical examination was performed by a pediatric endocrinologist and the following data were noted: (1) age at diagnosis of TS, (2) presenting clinical features, (3) growth parameters, (4) phenotypic features, (5) pubertal staging (7) karyotype result, (8) investigations (thyroid profile, gonadotropins and estradiol levels, liver function test, lipid profile, fasting blood sugar, ultrasound abdomen and pelvis, echocardiography, audiometric evaluation, ophthalmological examination),

and (9) treatment details. The data collected were tabulated and analyzed.

Height was measured in centimeters by standard technique using a stadiometer and weight in kilograms using a digital scale.

Puberty was assessed in by rating the breast development, pubic and axillary hair development according to Tanner's staging.⁷

Parents were asked for any available previous record.

Data were entered in SPSS version (19.0). Descriptive statistics were applied. Mean and standard deviation for age were computed.

RESULTS

A total number of sixty patients were diagnosed as Turner Syndrome during the study period. The mean age was 10.6 ± 4.0 year. Majority (63.4%) were diagnosed between 11-18 years, 21.7% between 5 to 10 years of age and 15 % were diagnosed before the age of 5 years. (Figure 1)

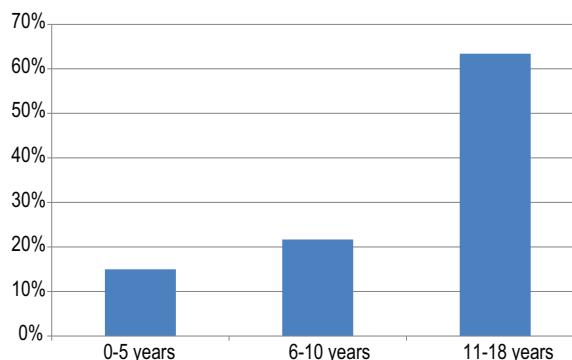


Figure 1: Distribution of the patients with Turner Syndrome according to age at presentation

The most common presenting complaints were short stature, delayed puberty and among patients diagnosed before age one year, pedal edema (Table I).

Table I. Presenting complaints

Presenting complaints	n(60)	%
Not growing well	45	75%
Delayed puberty	30	50%
Pedal edema	5	8%

Most common dysmorphic features were wide spaced nipple (41.6%), webbing of neck (35%), low hair line (25%), short neck (21.7%), hyperconvex nail (20%), increased carrying angle (20%), shield chest (16.7%), & hypoplastic nipple were (16.7%). Other features were scoliosis, downward slanting of eyes and wart (Table II).

Table II. Frequency of clinical feature in patients with Turner Syndrome

Clinical features	N (60)	%
Shield chest	10	16.7%
Hyper convex nail	12	20%
Webbing of neck	21	35%
Short neck	13	21.7%
Low hair line	15	25%
Increased carrying angle	12	20%
Hypoplastic nipple	10	16.7%
Scoliosis	1	1.6%
Downward slanting of eyes	3	5%
Wart	1	1.6%
Wide spaced nipple	25	41.6%

Among the associated comorbidities cardiac defects were the most common, occurring in 23.4 % of the TS cases. This was followed by dyslipidemia (10%), autoimmune hypothyroidism (8.3%) and obesity 6.6%. Behavioral problem was found in 8.3% of patients with TS. Other manifestations included speech delay (5%), hearing problem (3.3%) and repeated otitis media (1.6%) (Table III).

Table III. Distributions of co-morbidities in Turner Syndrome

Comorbidities	N(60)	%
Hearing problem	2	3.3%
Repeated ASOM	1	1.6%
Speech delay	3	5%
Behavioral problem/cognitive delay	5	8.3%
Dyslipidemia	6	10%
Hypothyroidism	5	8.3%
Type 1 Diabetes mellitus	1	1.6%
Obesity	4	6.6%
Cardiac problem	14	23.4%

Among the cardiac problems most common disease was coarctation of aorta (28.6%) followed by bicuspid aortic valve (21.4%), then atrial septal defect (14.3%), ventricular septal defect (14.3%) and others. (Table IV)

Table IV. Frequency of different Cardiac problems in Turner Syndrome

Cardiac problem	Number (14)	%
Coarctation of aorta	4	28.6%
Bicuspid aortic valve	3	21.4%
Atrial septal defect	2	14.3%
Ventricular septal defect with sever pulmonary hypertension	2	14.3%
Mild Tricuspid regurgitation	1	7.1%
Idiopathic dilatation of pulmonary arteries	1	7.1%
Double aortic valve with Ventricular septal defect	1	7.1%
Small Patent foramen ovale	1	7.1%
Small Patent ductus arteriosus	1	7.1%

Most of the patients presented with the karyotyping 45,XO (61.7%) followed by 46,XX/45,XO(21.7%), 46,Xisoxq (6.6%).(Table V)

Table V. Distribution of Turner Syndrome Patients by Karyotype

Karyotyping	N(60)	%
45,XO	37	61.7%
45,XO/46XX	13	21.7%
46,Xisoxq	4	6.6%
45,XO+extra genetic material	1	1.6%
46,X,i(X)[18]/45X[12]	1	1.6%
45,XO+extra genetic material	1	1.6%
46,X(delXp)	1	1.6%
45,X/46,X del X ant	1	1.6%
45,XO/46,Xiso(Xq)	1	1.6%

Hypoplastic uterus and ovaries were found in 91.6% cases & renal anomalies were found in 8.3% patient (horse shoe kidney 5%, hydronephrosis in 1.6% & ectopic kidney in 1.6% case)

Luteinizing hormone (LH) and follicular stimulating hormone (FSH) was raised in 90% case with TS. This was followed by dyslipidemia (10%), autoimmune hypothyroidism (8.3%) and abnormal liver function (3.3%).

Bone age corresponded with chronological age in most of the Turner girls (93.3%). (Table VI).

Table VI. Investigation profile of Turner Syndrome

Investigations	N (60)	%
USG of whole abdomen		
Smaller ovaries and uterus	55	91.6%
Horse shoe kidney	3	5%
Hydronephrosis	1	1.6%
Ectopic kidney	1	1.6%
High Blood glucose	1	1.6%
Abnormal thyroid function	5	8.3%
High TG	6	10%
Abnormal liver function test	2	3.3%
High LH & FSH	54	90%
Bone age		
Corresponds to chronological age	56	93.3%
Delayed	4	6.6%

DISCUSSION

This cross-sectional study was conducted to describe the presentation and clinical spectrum Turner Syndrome in children and adolescents who attended the Pediatric Endocrinology and Metabolism OPD in BIRDEM Women and Children Hospital in the year 2018-2022.

A total number of sixty patients were diagnosed as Turner Syndrome during the study period.

In our study, the mean age was 10.6±4.0 year. The majority (63.4%) were diagnosed between 11-18 years, 21.7% between 5 to 10 years of age and 15 % were diagnosed before the age of 5 years.

The diagnosis of TS is usually delayed. In up to 10% of patients, diagnosis may be delayed until adulthood.¹ However; the mean age at diagnosis in the present study is slightly higher than Belgian (6.6 years) and UK data (5.89 years).^{8,9}

In our study most common complaint at the first presentation is short stature (75%) and followed by a

complaint of delay in puberty (50%) and were in line with the literatures.^{2,4}

In our study 8% of the patients presented with lymphedema of hands and feet at birth. Congenital lymphedema of the hands, feet and neck region is a key diagnostic indicator (present in more than 60% of TS), most commonly seen in infants but can occur and recur at any age.^{10,11}

Common dysmorphic features found in our study were wide spaced nipple (41.6%), webbing of neck (35%), short neck (21.7%), hyper convex nail (20%), increased carrying angle (20%), shield chest (16.7%) & hypoplastic nipple (16%). These observations were in line with what had previously been described in other studies.^{12,13}

In our study, the frequency of 45,X monosomy was 61.7% and mosaicism was 38.3%. The most frequent mosaic patterns were 45,X/46,XX (21.7%) and 46,Xisoxq (6.6%). Studies revealed TS patients mostly present with X chromosome monosomy, followed by mosaic pattern. The most common forms of mosaicism are reported as 45,X/46,XX and 45,X/46,X,i(Xq) and the most commonly reported X chromosome structural abnormality is isochromosome Xq.^{1,2,3}

TS is associated with a wide range of abnormalities affecting nearly every organ system. Congenital cardiovascular defects constitute the most important life-threatening pathology in these patients. It has been reported in approximately 50% of patients with TS and left-sided obstructive defects predominate, especially bicuspid aortic valve (BAV) and coarctation of the aorta (CoA).^{10,14}

In our study cardiac defects were found in 23.3% of the TS cases among them most common was CoA (28.6%) followed by BAV (21.4%) then ASD (14.3%), VSD (14.3%) and others.

In the present study 10% patients with TS had dyslipidemia, 8.3% had autoimmune hypothyroidism, 6.6% had obesity, 1.6% had Type 1 DM.

Other studies also revealed that young adult women with TS are susceptible to a wide range of medical problems, including autoimmune disorders^{15,16}, overweight and obesity¹⁷, an increased risk for metabolic disorders such as glucose intolerance or dyslipidemia^{18,19}.

TS patients have an increased risk of thyroid diseases (thyroiditis, hypothyroidism, etc.)⁴. Patients with TS

have a 2-10 fold increased risk of developing inflammatory bowel disease (3%) and a 11 fold increased risk of developing (2.2-8.1%) celiac disease as compared to the normal population.^{2,20-22}

In our study two patient (3.3%) with TS had elevated liver enzyme.

Elevated liver enzymes and increased risk of cirrhosis have been reported in patients with TS.²³

In our study we found hearing problem (3.3%) and repeated otitis media (1.6%) in TS patients.

Craniofacial malformations that cause Eustachian tubes dysfunction may result in recurrent otitis media and consequent hearing problems in children with TS. Hearing problems may be seen up to 30% in childhood and up to 90% in adulthood in patients with TS.^{24, 25} Conductive type hearing loss is mostly prevalent in early ages, while sensorineural hearing loss generally develops in late childhood or early adulthood and shows an increase with age.^{26, 27}

Ophthalmologic anomalies can be observed in about 63% of patients with TS.¹ Strabismus, ptosis, amblyopia and color blindness are seen in decreasing order. In one review, strabismus was found to be as frequent as 33% and ptosis as 16%. Some studies reported that myopia can be associated with TS.^{2, 28} In our study we did not get any eye problem.

In our study behavioral problem was found in 8.3% & 5% had speech delay. Patients with speech delay presented before five years of age.

TS patients generally have normal intelligence except for mosaic karyotype with ring X chromosome who clearly has an increased risk of mental retardation. However, patients with TS have impaired non-verbal skills and low arithmetic skills. Some of these deficits may be improved by hormonal therapy at the time of puberty. A higher-than-expected rate of attention deficit disorder diagnoses (24%) is reported in school-age girls.²⁹

In this study Hypoplastic uterus and streaky ovaries were found in 91.6% cases & Luteinizing hormone and follicular stimulating hormone were raised in 90% case with TS.

TS is usually accompanied by gonadal dysgenesis, leading to hypergonadotropic hypogonadism and primary or secondary amenorrhea.³⁰

Uterine development is altered in girls with Turner syndrome. Even though with time uterus may increase in size, these measurements were significantly lower than those from the normal women as reported in other studies.³¹

In our study renal anomalies were found in 8.3% patient. Horse shoe kidney 5%, hydronephrosis 1.6% & ectopic kidney in 1.6% cases.

Other studies also found that congenital malformations of the urinary system are present in 30–40% of patients with TS. Most frequently found ultrasound abnormalities were collecting-system malformations (20%), followed by horseshoe kidneys (10%), malrotation, and other positional abnormalities (5%).³²

Conclusion

The majority of the patients with TS were diagnosed after 5 years of age. A high degree of clinical suspicion can help us diagnose these children earlier. If TS is diagnosed earlier in these girls, achieving growth up to their maximum potential will be possible with Growth hormone therapy. Girls with TS presented with a wide range of comorbidities. This indicates the need to establish an integrated treatment in order to prevent, detect and appropriately treat these comorbid conditions as well as to avoid complications. Early diagnosis, with appropriate management and follow-up will help us provide multidisciplinary care and hence prevent complications. We should ensure their smooth transition into adult care to reduce morbidity, ensuring continued care during adulthood.

Authors' contribution: SJ: Concept and designed the study, analyzed data and drafted the manuscript. FM: Helped in data collection, data analysis and review of the whole process. All authors read and approved the final manuscript.

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Conflict of interest: Nothing to declare.

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