Al Ameen J Med Sci 2012; 5(4): 394-397 ● US National Library of Medicine enlisted journal ● ISSN 0974-1143

ORIGINAL ARTICLE CODEN: AAJMBG

Three decades of turner`s syndrome–An experience from a South Indian genetic center

Abdul Mateen Athar*, Jyothi Idiculla, Seby John, Preetha Tilak and Rahul Kapur

Department of Medicine, St. Johns Medical College, Bangalore, Karnataka, India

Abstract: *Background:* Turner's syndrome (TS) arising from partial or complete X chromosomal monosomy is the most common genetic disorder in females. In South Asian countries like India diagnosis and care of patients with TS is still in the developing stage. Hence this study was undertaken to review details of patients with TS, diagnosed in the Division of Human Genetics (DHG) of our centre. *Objectives:* To study the clinical features and karyotype of patients with turners syndrome. *Method:* It is a retrospective study of patients with turners syndrome who were karyotyped over 30yrs (1978-2008) in DHG in over hospital. *Result:* In this retrospective audit, details of 89 patients with Turner's syndrome were analysed. The most common age group of presentation was 11-15 years and the most frequently observed genetic defect was 45, X followed by 46XX/45 X. Some patients were diagnosed after the age of 20 years. *Conclusion:* This study brings to light the lack of efficacy in diagnosing and referring patients with TS at a younger age, when therapies for short stature and sexual infantilism are available. In addition systemic and metabolic abnormalities can be detected and treated at the earliest. It is important to increase the awareness of this condition among pediatricians and general practitioners

Keywords: Turners syndrome

Introduction

Turner's syndrome (TS) arising from partial or complete X chromosomal monosomy is the most common genetic disorder in females [1]. There have been observations of the phenotypical features of TS from 18th century. However it is nomenclatured after Henry Hubert Turner, a 20th century Okhalahoman endocrinologist who was the pioneer of oestrogen therapy for this condition [2]. In the Western world, there have been advancements in the genetics still in and in South Asian countries like India diagnosis and care of patients with TS therapeutics of this condition. However, is the developing stage. Hence this study was undertaken to review details of patients with TS, diagnosed in the Division of Human Genetics (DHG) of our centre.

Material and Methods

This study is an audit of patients with TS who were karyotyped over 30 years (1978-2008) in the DHG. The age at referral, the reason for referral, clinical features, family history and karyotype of each patient were retrospectively reviewed.

Results

The total number of patients in this audit was 89. Of these, 20 children were born out of consanguineous marriages. Seventy eight (87.6%) were referred after the age of 10 years. The numbers of patients referred in various age groups and their chief complaints are summarised in Table-1. None of these patients were diagnosed pre-natally. The most common reason for requesting genetic analysis was amenorrhoea. The chief complaints of children aged 5 or less were delayed milestones, short statue, mental retardation, lymphedema and dysmorphism.

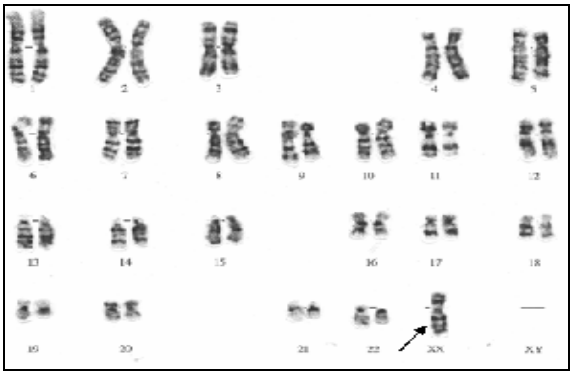
In the age group of 6-10 years, short stature was the main reason for referral, while in the 11-20 years' age group the main complaints were short stature, primary amenorrhoea and sexual infantilism. Beyond 21 years, amenorrhoea, primary infertility and bad obstetric history prompted evaluation

Table-1: Age and chief complaints at the time of referral		
Age group	**Number Total (89)**	**Chief complaints**
0-5 years	8	Dysmorphism, short stature, delayed milestones, oedema of hands and feet, webbing of neck, mental retardation
6-10 years	3	Short stature
11-15 years	28	Short stature, primary amenorrhoea, secondary amenorrhoea, hypogonadism, sexual infantalism
16-20 years	27	Short stature, primary amenorrhoea, secondary amenorrhoea, bad obstetric history, sexual infantilism
21-25 years	14	Bad obstetric history, primary amenorrhoea, secondary amenorrhoea
26 years and above	9	Primary infertility, primary amenorrhoea, secondary amenorrhoea

Table-2: Distribution of karyotypes (total=89)	
Karyotype	**number**
45,X[a]	30
46,X,i(Xq)[a](isochromosome)	4
46,X,Xq-[a] (q arm deletion)	1
46,XX/45X[b]	25
45X/46,X,i(Xq)[b]	9
47,XXX/45XX	1
47XXX/46XX/45X[b]	4
Others[a&b] (including fragments, derivatves, markers)	15
a-Single cell lines b- Mosaic cell lines	

Table 2 classifies the karyotypes of patients included in this study. The most common karyotype observed was 45, X (33%). Among the mosaics, 45X/46 XX was the commonest (28% of the total).

Photograph-1: 45, X



Photograph-2: 46,X,i(Xq)

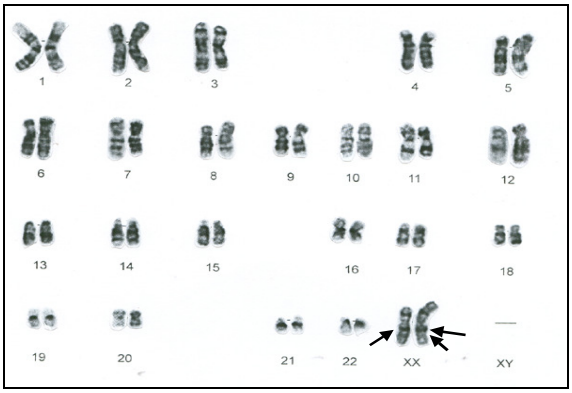


Table 3 gives a list of main phenotypical features of the karyotypes at the time of referral.The maximum number of abnormalities including cardiac are seen in patients with 45, X karyotype.

Table-3: Phenotypical features of various karyotypes						
Karyotype (number)	**Lymphoedema**	**Widely spaced nipples**	**Low hairline**	**Cubitus valgus**	**Coractation aorta**	**Short stature**
45,X (30)	6	12	9	15	2	11
46,X,i(Xq) (4)	0	0	0	1	0	1
46,XX, 45,X (25)	1	7	3	12	0	4
45X,46X,Xi(Xq) (9)	0	4	0	5	0	5
47,XXX/46XX/45X (4)	0	0	0	0	0	0
Others (15)	2	4	6	3	0	3

Discussion

Despite being the commonest chromosomal abnormality in females, only about 1% of embryos with this genetic defect survive to be born due to high rate of foetal loss [3]. Apart from obvious clinical stigmata, short stature and hypogonadism, this condition is associated with dysfunctions and disorders of various systems. These include cardiovascular diseases (coarctation of aorta, aortic dissection, valvular heart diseases and hypertension), skeletal deformities, hypothyroidism, osteoporosis, dylipidaemia, insulin resistance, renal disease, malignancies dermatological diseases and eating disorders [1, 4]. Though most patients with TS have normal intelligence, approximately 70% have deficits in specific areas of intellectual and cognitive abilities [1, 4-5].

In the Western World, one-fifth to one third are referred in the newborn period and one third in early childhood [1]. In the newborn children, puffy hands and redundant nuchal skin lead to referrals and in mid childhood short stature is the most common reason for evaluation [1,4]. Adult referrals for diagnosing Turner's syndrome account for about 10% of the total. In contrast to this in our group only 9% were referred in early childhood and a 3% in late child hood. The majority were diagnosed between the ages of 11 and 20. It is striking that 25% of patients in our series were diagnosed after the age of 20 years. These results reveal inadequacy of our system in diagnosing this condition in the younger age groups. It is worthwhile remembering here that hormonal therapies are available for short stature and sexual infantilism. A final height of more than 150 centimeters may be achieved by early initiation and continuation of growth hormone therapy [1,6]. Screening for various disorders is also important to diagnose and treat them at the appropriate time as it is now known heart diseases and diabetes shorten the life expectancy [7]. And, cognitive and behavioural therapies have been of significant help to women with TS, some of whom are able to pursue university degrees and various occupations [1].

It is of note that 20 of the children were born out of consanguineous marriages. This practice despite inbreeding of pathogenic genes continues in some communities. However, the role of consanguinity in the development of TS is yet to be elucidated. On listing phenotypical features, 45,X karyotype is associated with maximum abnormalities, which is in concordance with known literature [1]. The numbers in the rarer types in our group are small to derive conclusions. Molecular analysis has begun to pinpoint specific genes involved in the Turner phenotype. For example haploinsuffuciency of SHOX gene in the pseudoautosomal region of the short arm (Xp) has now been known to result in short stature [8]. The main drawback of this audit is that being retrospective in nature clinical data could not be clarified or verified. However, the results draw attention to the inadequacy of referrals at the appropriate time. A high index of suspicion from the treating GP/paediatrician is the key to early referrals. Educating doctors to pick up physical features and also delay in growth or slowing of growth velocity would improve referral rates. The aim of projecting our data is to increase the awareness of this condition among doctors and also general public. There are genetic centres situated in various Indian states offering genetic analysis and counseling. Diagnosis of this condition can even be made in the antenatal period based on foetal oedema on ultrasound scanning and maternal triple screeing [5]. Most of these centres also have facilities for endocinological and medical evaluation and management and all these should be made available to every affected child. While molecular research on various aspects of TS continues, medical community should strive to ensure current benefits of therapy to every affected child. It is also important to maintain a registry of Indian patients with Turner's syndrome in order to obtain data on the heights attained, quality of life achieved and also on the morbidity and mortality conferred by this condition.

References

1 Elsheikh M, Dunger DB, Conway GS, Wass GAH. Turner's syndrome in adulthood. *Endocrine Reviews* 2002; 23: 120-140.

2 Turner HH. A syndrome of infantilism congenital webbed neck and cubitus valgus. *Endocrinology* 1938; 23: 566-574.

3 Stratakis CA, Rennert OM. Turner syndrome: molecular and cytogenetics, dysmorphology, endocrine and other clinical manifestations and their management. *Endocrinologist* 1994; 4: 442-453.

4 Sybert VP, McCauley E. Turner's syndrome. *New Engl J Med* 2004; 351: 1227-38.

5 Ross JL, Stefanatos G, Roeltgen D, Kushner H, Cutler GB Jr. Ullrich- Turner syndrome: neuro-developmental changes from childhood through adolescence. *Am J Med Genet. Jul* 1995; 31;58(1): 74-82.

6 Rosenfeld RG, Attie KM, Frane J et al. Growth hormone treatment of Turner syndrome: beneficial effect on adult height. *J Paediatr* 1998; 132: 319-324.

7 Gravholt CH, Jule S, Naera RW, Hansen J. Morbidity in Turner's syndrome. *J Clin Epidemiol* 1998; 51: 147-158.

8 Rao E, Weiss B, Fukami M et al. Pseudoautosomal deletions encompassing a novel homeobox gene cause growth failure in short stature and Turner Syndrome Nat Genet 1997; 16: 54-63.

*All correspondences to: Dr. Abdul Mateen Athar, Department of Medicine, St. Johns Medical College, Sarjapur road, Kormangala, Bangalore-34 Karnataka, India. E-mail: mateenathar@yahoo.co.in