Screening of Group of Iraqi Patients with Turner's Syndrome in Relation to Karyotype-Phenotype Variation

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Abstract

Background: There is variation in karyotype that can be related with the phenotype difference in patients with Turner syndrome (TS).

Objective: Asses the relationship between karyotype and phenotype of confirmed Turner Syndrome patients and Screening them for related congenital and immunological conditions.

Methods: Eighty-five cases of TS were comprised. Patients were indicated mainly for evaluation of short stature and (or) delayed puberty; Standard karyotyping was analyzed on the basis of routine G-banding technique. Turner's syndrome is divided into traditional and non-traditional with further categorization with respect to Karyotype. After full examination, screening tests comprising thyroid function tests, celiac screen, Echocardiography, Renal and pelvic ultrasonography was achieved.

Results: Webbed neck and Dysmorphic facial characteristics were more found during clinical examination in traditional TS versus Non-traditional Turner's syndrome with p-value of 0.01 and0.027, respectively. Abnormal thyroid function tests were more common in traditional TS than Non-traditional, p-value 0.02. Abnormal findings (mainly streak ovary) on pelvic ultrasound (US) was also more common in traditional TS than Non-traditional, p-value 0.01.

Conclusion: Screening of patients with Turner's syndrome with respect to phenotype -karyotype difference can provide opportunities for enhancement of our knowledge, diagnosis and further management.

Key Words: *Turner's syndrome, Karyotype, Phenotype, Mosaicism.*

Introduction

Turner's syndrome (TS) is the most frequent genetic disorder in females with prevalence of 1:2500 that is around 3% live births of females delivered, and approximately 15% of miscarriages. [1,2]. This syndrome considered by the absence of portion of or the whole X chromosome in a female, with perfect dysmorphic attributes such as short stature, primary amenorrhea, estrogen insufficiency, cardiovascular malformations, morphological features and skeletal abnormalities. There are different karyotypes and phenotypes exist [3,4]. Teenagers with the Turner's syndrome are famous for their short stature and ovarian dysfunction [5,6].

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The Objective of this Study

To determine the relationship between karyotype and phenotype of confirmed Turner Syndrome (TS)Iraqi

patients and screening them for related congenital and immunological disorders in relationship to karyotype and phenotype variation.

Patients and Method: The cases were reported in the Department of Endocrinology and Diabetes, children welfare hospital and department of gynecology, medical city complex, Baghdad, Iraq during the period (January 2009) to (January 2019). Eighty-five cases of TS were comprised, after full history and physical examination, diagnosis was made on the basis of clinical phenotype and confirmed by karyotypic analysis of a peripheral blood lymphocytes utilizing routine G-banding method with resolution of 400 band per haplotype by comprising counting of 20 metaphases, and five of them were fully analyzed. According to their karyotype, the patients were classified into two groups: the first group **A** (NO=51) include: traditional monosomy 45, X; while the second group **B** (NO=34) include: Non-traditional miscellaneous karyotypes.

Screening for related disorders was done with respect to the present recommendations [7,8]; Serum follicle-stimulating hormone and luteinizing hormone were done in patients who were ten-year of age and up. Thyroid function tests were done for patients four-year age and older. Ultrasound examination of genitourinary system, two-dimensional echocardiography was done at time of diagnosis. For screening, celiac disease that the patients will be chosen for stomach biopsy on the basis of positive antigliadin antibodies (AGA) IgA, anti-endomysia antibodies (EMA)and Anti tissue antibody (TTGA), for patient four-year age and older.

X-ray radiography of the non-dominant wrist and hand for assessment of bone age before initiation of progress hormone treatment and will fully argued in different article. Written Informed consents were occupied and high confidentially of data was maintained. If the participant was under the age of 18 years, both the participant and the parents employed the informed consent. Ethical approval was found as suitable in our country.

The Results

A total of 85patients with Turner's syndrome were comprised in the study. Turner's syndrome is then divided into traditional and non-traditional with additional categorization with respect to Karyotype. The incidence of patients in each classification are displayed in **Table (1).**

Table (1). Kind of Turner's syndrome with respect to karyotype.

Category	Karyotype categorization	N	%
Group A (traditional)	Standard Monosomy45x	51	60.0
Group B (Non-traditional)	Mosaic turner 45, x0/46, xx	14	16.5
	Isochromosome long arm46, x,i(xq)	17	20.0
	Mosaic with different45, x0/46, xiso(xq)	3	3.5
Total		85	100.0

Traditional Turner's syndrome is most frequent in age group 5.1 to 10 and non-traditional Turner's syndrome is least obtained in age group 1.1 to 5 year, however there is no significant related, p-value 0.18. Both delay puberty and short stature were the most frequent causes of transfer in both groups of Turner's syndrome , P value 0.56. Webbed neck and Dysmorphic facial appearances were more obtained in examination in traditional TS versus Non-traditional Turner's syndrome with p-values of (0.01, 0.027) (significant). The rest of result in clinical examination are scheduled in **Table (2).**

Table (2) patients with positive Dysmorphic Features on examination with respect to type of Turner's syndrome.

Dysmorphic Attributes	Non-Traditional TS n(%)	Traditional TS n(%)	p-value
Cubitus valgus	18(52.9%)	26(51.0%)	0.85
Webbed neck	8(23.5%)	26(51.0%)	0.01
Short neck	15 (44.1%)	22 (43.1%)	0.92
Shield chest	0 (.0%)	5 (9.8%)	0.06
Low hair line	15 (44.1%)	30 (58.8%)	0.18
Short 4th and 5th metacarpal bone	3 (8.8%)	5 (9.8%)	0.78
Dysmorphic facial appearances	11 (32.4%)	29 (56.9%)	0.027
Wide space nipple	20 (58.8%)	27 (52.9%)	0.59

Cardiac abnormalities were: in Non-traditional kind comprise: Coractation of aorta in 2 patients , Bicuspid aortic valve in 2 patients , Aortic stenosis in 1 patient and in traditional kind: Coractation of aorta in 2 patients , Patent Ductus arteriosus in 2 patients, Bicuspid aortic valve in 1 patient ,Pulmonary stenosis in 1 patient , Aortic stenosis in 1 patient ,P- value 0.51(non-significant).

Renal malformations were in traditional kind: horseshoe kidney, while in Non-traditional kind comprise: horseshoe kidney and renal duplication in 1 patient, respectively p- value 0.33 (non-significant). The rest of positive screening findings was illustrated in table **(3)**.

Table (3) Patients with positive screening tests with respect to kind of Turner's syndrome.

Screening test		Non-Traditional TS n (%)	Traditional TS n (%)	p-value
laboratory	Abnormal thyroid function tests	1 /28 (3.5 %)	11 /38 (28.9%)	0.02
	Raised LH and FSH tests.	21/26 (80.7%)	29/34 (85.3%)	0.92
	Positive celiac disease screen (positive jujenal biopsy).	2 /28 (7.1 %)	6/38 (15.78%)	0.49
imaging	Abnormal results on echocardiography.	5 (14.7%)	7 (13.7%)	0.51
	Abnormal findings on renal ultrasound	2 (5.9%)	1 (2.0%)	0.33
	Abnormal findings on pelvic ultrasound.	14 (41.2%)	41 (80.4%)	0.01

Statistical Analysis

An expert statistical advice was sought for Statistical analyses were done using Statistical Package for Social Sciences (SPSS) version 21 computer software. Discrete variables were introduced as number (%). Fisher exact test when suitable via using chi-square test to check the significant value of related of discrete variables where p-value of < 0.05 were regarded significant.

Discussion

The current study may concise with other Prior studies suggested that peak age at diagnosis is lower in patients with traditional kind (monosomy 45, X) compared to other karyotypes, probably due to more typical Turner stigmata in the traditional group [9-10]. Where patients with TS displayed distinctive attributes that take a strong relation with their chromosomal make-up. [11].

The whole females with TS show growth failure and achieved a final height, which is smaller than average. While children can primarily show regular growth, typically for beginning few years of lifecycle. Nonetheless, the growth rate ultimately converts slower than regular and affected children do not experience typical growth spurts [12]. Though the physical abnormalities are recognized, however a varied range of phenotypic variability was obtained in TS patients that essentially is based on the genetic constitution that can represent the karyotype-phenotype variation [13].

Gonadal dysfunction is part of the phenotype in TS and leads to absence of spontaneous puberty, estrogen deficiency, and infertility. Ovarian failure and decreased ovarian feedback result in significant elevation of FSH and LH levels during early childhood period and adolescence (Bi-phasic pattern), whereas gonadotrophins levels were not significantly raised at age 5–10 years compared with other healthy persons, for this reason gonadotropin concentration found between ages 5-9 years cannot be used to asses ovarian function [14].This study showed that approximately in most traditional TS patients, ovaries were absent or small, A subsequent reports found that 76% of those with X mosaicism and only 26% of those with 45,X karyotypes had detectable ovaries during ultrasound examination[7,15].

Congenital heart abnormalities appear in up to 50% of individuals with TS, affecting mainly the left side of the heart and comprising bicuspid aortic valve (BAV), coarctation of the aorta, and thoracic aortic aneurysm. Mortality rates are 3-fold higher in women with TS compared with the general population, with the most frequent cause of death being cardiovascular disease [16]. Patients with severe dysmorphic signs showed a significant higher relative risk of cardiac malformations and x linked factors may be complicated in determining cardiac defects in turner's syndrome [17].

This study were registered the related renal abnormalities is lower as compared to the other studies and the structural malformations appears more repeatedly with non-mosaic 45, X TS [18].

An increased incidence of autoimmunity has been largely documented in TS. Patients with traditional kind are more prone to develop thyroid autoimmunity. An early assay of autoantibodies and monitoring thyroid hormones is fundamental for detecting hypothyroidism precociously and start adequate replacement therapy [19].

The screening for Celiac disease (CD) in TS patients is based on the determination of CD-associated antibodies, this is followed by intestinal biopsy in positive patients. It is famous that both TS and CD are related with different autoimmune disorders [20].

Conclusion: The traditional kind (monosomy 45, X) considered by earlier age at presentation however with more severe dysmorphic attributes as compared to the other non-traditional kinds of turner syndrome, this may give us more opportunity for earlier diagnosis and treatment. Screening patients with turner's syndrome for the associated thyroid, cardiac, renal and celiac diseases are a significant issue because it may affect survival of those patients and may be x-linked that represent karyotype- phenotype variation.

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