

# Reproductive Anamnesis of Women's Cohort with Turner Syndrome from Lviv Region (West Ukraine)

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## Abstract

All women carrying the diagnosis of Turner syndrome are at risk during pregnancy, and there is no distinction between those with 45, X karyotypes and those with partial X chromosome deletions or mosaic karyotypes.

**Methods:** 68 women with Turner syndrome aged 18-44 from Lviv region (Ukraine) who had problems with the start, the duration of menstruation or infertility were obtained by face-to-face interview or assessment of hospital medical records (1997-2018).

**Results:** In this cohort prevailed amenorrhea or irregular menses, short and broad neck, absence of hair growth on the body, cubitus valgus, delayed puberty, pectus excavatum, mitral valve prolapse, hypertension, thyroid dysfunction (hypothyroidism). These patients had short stature with a median adult height at 153 cm (126-167) and primary amenorrhoea in the majority of cases. Among 68 adolescent patients only 20 (29.4%) had spontaneous menarche.

**Conclusion:** Among these women only two (2.9%) women with Turner syndrome from this cohort have been observed for reproductive history due to pregnant. The five infants were non-dysmorphic and without chromosomal anomalies.

**Keywords:** Turner syndrome; X chromosome; Phenotype; Pregnancy; Female infertility

## Introduction

All women carrying the diagnosis of Turner syndrome are at risk during pregnancy, and there is no distinction between those with 45, X karyotypes and those with partial X chromosome deletions or mosaic karyotypes [1-3]. Consultation with specialists in cardiovascular disease, endocrinology, and high-risk obstetrics is required to ensure the best chance for a successful pregnancy and delivery of a healthy infant [4-6].

Pregnancies in women of Turner syndrome are more likely to be complicated by thyroid dysfunction, obesity, diabetes and hypertensive disorders, including pre-eclampsia (up to 40%). Low birth weight, intrauterine growth restriction, preterm labor and preterm delivery are also more likely in pregnancies in women with TS [7-10].

The prevalence of spontaneous pregnancies in this French cohort was 5.6%. There were 18 patients (3.8%) who had at least one live born child [11].

## Materials and Methods

Women were obtained by face-to-face interview or assessment of hospital medical records. All patients were assessed with physical examination and underwent a set of diagnostic tests including general clinical tests, abdominal ultrasonography. We considered the following data for each patient: Age at diagnosis of TS, age at the time of the

study, height and weight for review time, medical history and karyotype. Clinical history was recorded.

Reproductive history was collected; Occurrence and age of spontaneous menarche, age at pregnancy, outcome of spontaneous pregnancies including maternal and fetal complications.

## Results

In Lviv region (Ukraine) according to the statistical office on January, 2017 population [20] was 2,534,000 persons, including 1,323,300 women (52.2%). Every year in the Lviv region 5-11 girls (rare women) of different ages are found to have Turner syndrome confirmed by karyotyping in the laboratory of Medical Genetics Centrum of Institute of Hereditary Pathology, National Academy of Medical Sciences of Ukraine, Lviv, Ukraine. We studied the cohort of patients came from 20 districts of Lviv region and Lviv town (January 1997-May 2018) [12].

Our cohort included 68 women with Turner syndrome aged 18-44 who had problems with the start, the duration of menstruation or infertility. In this cohort prevailed amenorrhea or non-regular menses, short and broad neck, absence of hair growth on the body, cubitus valgus, delayed puberty, pectus excavatum, mitral valve prolapse, hypertension, thyroid dysfunction (hypothyroidism). These patients had short stature with a median adult height at 153 cm (126-167) and primary amenorrhoea in the majority of cases. Among 68 adolescent patients only 20 (29.4%) had spontaneous menarche.

Seven women (10.3%) with Turner syndrome from this cohort have been observed for reproductive history of Medical Genetics Centrum of Institute of Hereditary Pathology during several years. Phenotypic characteristic these patients demonstrated in Table 1. Patient's height was within the range 134-164 cm (median of  $146 \pm 11.4$  cm), weight-

41-60 kg (median of  $48.9 \pm 5.8$  kg). Age of diagnosis was different from 11 years (the main reason for the genetic consultation-low height) till 41 years (the main reason for the genetic consultation-infertility), median of  $24 \pm 12.6$  years. The median age at the time of the study was  $11.9 \pm 6.9$  years (from 1 till 24 years).

No	Cases	Cytogenetic characteristics	Age of diagnosis	Follow up (years)	Phenotypic characteristic	Height, cm	Weight, kg	Cardio-vascular system	Endocrine system	Urinary system	Gastro-intestinal system
1	Case A	46, XX [27] /45, X [3]	41	1	Normal	164	50	hypertension disease	-	-	-
2	Case B	46, XX [25] /45, X [5]	27	24	Short neck, small breast, absence of hair growth on the body	163	53	rheumatism	goiter	Pyelo-nephritis	chronic colitis
3	Case C	45, X [47] /46,X, I (X) (q10) [3]	16	6	Low height, small breast, kifoscoliosis	140	41	-	-	-	-
4	Case D	45, X	15	13	Low height, small breast	141	60	-	-	-	cholecystitis
5	Case E	45, X	11	17	Low height, short neck, small breast	142	46	mitral volve prolapse	-	-	-
6	Case F	45, X [23] /47, XXX [17]	44	14	Low height, small breast	134	44	-	goiter	-	-
7	Case G	45, X	14	8	Low height, short neck, small breast	137	48	-	-	-	-

**Table 1:** Clinical characteristics of women with turner syndrome.

Only one patient C. did not have concomitant somatic pathology in medical history. Woman B. diagnosed Turner syndrome (46, XX [25] /45, X [5] ) at aged 27 had pathology of cardio-vascular (rheumatism), endocrine (goiter), urinary (pyelo-nephritis) and gastrointestinal (chronic colitis) systems. Patient F. diagnosed Turner syndrome (45, X [23] /47, XXX [17] ) at aged 44 had goiter. Woman A. with Turner syndrome (46, XX [27] /45, X [3]) had hypertension disease grade I. during last three years. In one case E. observed mitral valve prolapse since 11-years-old simultaneously with Turner syndrome.

Menarche is infrequent in girls with Turner syndrome. Four of these patients (57.1%) had spontaneous menarche, three women with Turner

syndrome having primary amenorrhea (Table 2). One patient developed secondary amenorrhea 5 years after the onset of menarche, and 2 patients developed oligo-menorrhea. Girls with mosaic karyotypes of Turner syndrome had regular menarche (cases A and F) in comparison with women 45, X (cases D and G). Spontaneous menarche was more common in patients with mosaicism than in those with 45, X karyotypes, leading to conclude that the additional X chromosome likely has a significant influence on the progression of puberty. Concerning cytological characteristics of the patients in our cohort, the karyotypes were in good agreement with reproductive anamnesis.

No	Cases	Cytogenetic characteristic	Ultrasonography characteristic	Menarche	Age of menarche	Treatment	Fertility	Age of first pregnancy	Number of pregnancy
1	Case A	46, XX [27] /45,X [3]	Normal	Regular, oligomenorrhea	14	-	primary infertility 1 year	-	-
2	Case B	46, XX [25] /45, X [5]	Hypoplasia of uterus gr.I	Nonregular, Amenorrhea secondary	16	-	3 children	32	3
3	Case C	45, X [47] /46, X, I (X) (q10) [3]	Hypoplasia of uterus gr.II-III	Amenorrhea primary	-	growth hormone in 14 years	primary infertility 2 years	-	-

4	Case D	45, X	Hypoplasia of uterus gr.I	Amenorrhea primary	-	estradiol	primary infertility 2 years	-	-
5	Case E	45, X	Hypoplasia of uterus and ovarian gr.II	Nonregular	14	substitution hormone therapy in 18 years estradiol	primary infertility 1 year	-	-
6	Case F	45, X [23] /47, XXX [17]	Normal	Regular, oligomenorrhea	13	-	2 children	23	2
7	Case G	45, X	Hypoplasia of uterus gr.I	Amenorrhea primary	-	substitution hormone therapy	primary infertility 1 year	-	-

**Table 2:** Reproductive characteristic women of turner syndrome.

Women (cases B and F) did not receive hormone therapy. As the majority of patients with Turner syndrome do not undergo spontaneous puberty or menarche, estrogen therapy is typically required to initiate pubertal development (cases C,D, E and G). The age at which estrogen is initiated varies but is generally around age 14 years.

Estrogen was initiated in very low doses, generally 1/10 to 1/8 the adult dose, and slowly increased to full replacement doses over a period of two years to promote normal breast and uterine growth. After two years of treatment or once breakthrough bleeding occurs, a progestin was typically added to allow for regular menstrual cycles. With the assistance of hormone therapy, girls with Turner syndrome may have regular monthly menses throughout life until hormone therapy was discontinued at the typical time of menopause.

Spontaneous pregnancy can be seen in a small percentage of individuals with Turner syndrome and generally is more likely in women with mosaicism and those who report spontaneous puberty and regular menses. Among 7 (10.3%) women in our cohort, two became pregnant and gave birth to healthy children (Table 2). There no miscarriage and perinatal mortality in our cases. Uterine development is altered in girls with Turner syndrome. Five women approached for a medical consultation on infertility by the 1-2 years of marital life.

In rare incidences, individuals with Turner syndrome are able to conceive spontaneously and deliver. Women with mosaicism are more likely to conceive spontaneously (cases B and F), women with monosomy may also be fertile (cases D, E and G). For the vast majority of women with Turner syndrome, however, infertility is inevitable. Three women are referred to the *in vitro* fertilization.

Maternal complications occurred in 2 of those 5 pregnancies (40%), with pregnancy-induced hypertensive disorders in one cases (20%) and aggravation of chronic colitis. Neither aortic dissection nor cardiac complication was observed in pregnant women B. during three pregnancies or post-partum. For two out of the 5 pregnancies, no cardiac evaluation was performed before or during pregnancies, as the diagnosis of Turner syndrome occurred after the spontaneous pregnancies.

In selected cases women with Turner syndrome are able to become pregnant successfully and deliver healthy infants at full term (cases B and F). Women gave birth naturally, the caesarean section was not conducted. In the 5 live births (one boy and four girls) we were not

found to have complications or birth defects. The infants were non-dysmorphic and without chromosomal anomalies. We did not observe the low weight of newborns from women with Turner syndrome. The birth weight of the girls was 3000-3100 g. of the boy-3600 g. Two newborn girls were diagnosed with 46, XX. Furthermore, karyotypes had not been systematically performed in all newborns, as they had not been performed in boy.

Thyroid dysfunction is common in women with Turner syndrome. Two women who gave birth to children had problems in the endocrine system-goiter, which was observed in the endocrinologist after delivery.

As children with Turner syndrome transition into adulthood it is important for practitioners to be familiar with screening guidelines and health concerns, particularly in regards to fertility and pregnancy.

Due to the pregnancy risks specific to women with Turner syndrome, all women of reproductive age who have been diagnosed with Turner syndrome should be provided with comprehensive pre-pregnancy counseling. Although uncommon, women with Turner syndrome have been reported to spontaneously conceive. Therefore, all women should be provided with adequate information regarding the importance of contraception [13-15].

## Conclusion

We evaluated 68 female patients with Turner syndrome aged 18-44 years from Lviv region (West Ukraine) who were diagnosed and followed-up at the underwent.

Among these women only two (2.9%) women with Turner syndrome from this cohort have been observed for reproductive history due to pregnant. The five infants were non-dysmorphic and without chromosomal anomalies.

The majority of women with mosaic karyotype had spontaneous pregnancy. Women with TS are at extremely high risk for infertility.

Patient with Turner syndrome transition into adulthood it is important for practitioners to be familiar with screening guidelines and health concerns, consultation with specialists to ensure the best chance for a successful pregnancy and delivery of a healthy infant.

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