# PREGNANCY OUTCOMES IN TURNER SYNDROME

## *RESULTADOS DA GRAVIDEZ NA SÍNDROME DE TURNER*

Maria de Fátima Borges, Alessandra Bernadete Trovó de Marqui

Universidade Federal do Triângulo Mineiro. alessandra.marqui@uftm.edu.br

**ABSTRACT**

Turner Syndrome (TS) is a genetic condition characterized by partial or complete deletion of the X sexual chromosome and it can be present as a monosomy (45,X), mosaicism with two or three different cellular lines (45,X/46,XX; 45,X/47,XXX; 45,X/46,XX/47,XXX) or structural abnormality [46,X,i(Xq); 46,X,r(X); 46,X,del(X)]. TS is tightly associated with hypergonadotropic hypogonadism and ovarian dysgenesis, typically resulting in infertility in the great majority of patient. This manuscript addresses the fertility, pregnancy and motherhood in women with TS. In general, TS patients experience adverse pregnancy associated outcomes and this last is considered high risk. This way, the management of pregnancy in TS with a multidisciplinary team, composed mainly by maternal–fetal medicine specialists and cardiologists, should be implemented in order to reduce complications for mothers and infants.

**KEYWORD**: Monosomy; Fertility; Karyotype.

**RESUMO**

A Síndrome de Turner (ST) é uma condição genética caracterizada pela deleção parcial ou completa do cromossomo sexual X e pode se apresentar como monossomia (45,X), mosaicismo com duas ou três linhagens celulares diferentes (45,X/46,XX; 45,X/47,XXX; 45,X/46,XX/47,XXX) ou anormalidade estrutural [46,X,i(Xq); 46,X,r(X); 46,X,del(X)]. A ST está intimamente associada ao hipogonadismo hipergonadotrófico e à disgenesia ovariana, resultando tipicamente em infertilidade na grande maioria das pacientes. Este manuscrito aborda a fertilidade, a gravidez e a maternidade em mulheres com ST. Em geral, as pacientes com ST apresentam desfechos adversos associados à gravidez e essa última é considerada de alto risco. Dessa forma, o manejo da gravidez na ST com uma equipe multidisciplinar, composta principalmente por especialistas em medicina materno-fetal e cardiologistas, deve ser implementado a fim de reduzir complicações para mães e bebês.

**PALAVRAS-CHAVE**: Monossomia; Fertilidade; Cariótipo.

## NOTE

Turner Syndrome (TS) is a genetic condition characterized by partial or complete deletion of the X sexual chromosome and the average age at diagnosis is around 15 years of age. It can be present as a monosomy (45,X), mosaicism with

two or three different cellular lines (45,X/46,XX; 45,X/47,XXX; 45,X/46,XX/47,XXX) or structural abnormality [46,X,i(Xq); 46,X,r(X); 46,X,del(X)] and is crucial determine the karyotype in other biological samples, in addition to peripheral blood, as well as analyzing a greater number of cells, because hidden mosaicism may exist. TS is tightly associated with hypergonadotropic hypogonadism and ovarian dysgenesis, typically resulting in infertility in the great majority of patients[1].

A scoping review showed that prevalence of natural conception ranged from 15% to 48% in women with 45,X/46,XX, 1% to 3% in patients with 45,X, and 4% to 9% in other TS karyotypes. Only one in ten girls with TS received specialized fertility counselling including options for fertility preservation, pregnancy risks, and alternatives, such as adoption, raising the necessity to create a practical guideline for healthcare professionals and patients. The pregnancy risk with own oocytes include miscarriage (23-67%), chromosomal abnormality (0-18%), aortic dilatation (1-3%) and aortic dissection (0-1%)[2]. Altalib et al. described the case of a patient with mosaic TS (45,X/46,XX) who spontaneously conceived nine times. Only two of the pregnancies were successful, and the rest resulted in miscarriages, intrauterine fetal demise and infant death[3].

A narrative review examined reproductive health outcomes in women with TS and how best to manage them to reduce health risks and improve maternal and neonatal outcomes. In addition aortic dissection, the risks in pregnancy include preeclampsia, gestational diabetes and fetal growth restriction. The authors conclude that pregnancy is a high risk in women with TS, especially when associated with congenital heart disease, therefore, prepregnancy screening, counselling and comorbidity optimisation are imperative[4].

Cauldwell and collaborators conducted a multicentre study to determine the characteristics and outcomes of pregnancy in 81 women with TS. Of the 127 pregnancies there were 17 miscarriages, three terminations of pregnancy, two stillbirths and 105 live births. Ten of 106 (9.4%) births with gestational age data were preterm and 22/96 (22.9%) singleton infants with birthweight/gestational age

data weighed less than the tenth centile. The caesarean section rate was 72/107 (67.3%)[5].

Pregnant patients with TS of the United States were more likely to have a diagnosis of pregestational hypertension (4.8% vs. 2.8%; aOR 1.65; 95% CI 1.26–2.15), uterine anomaly (1.6% vs. 0.4%; aOR, 3.01; 95% CI 1.93–4.69) and prior pregnancy losses (1.6% vs. 0.3%; aOR 4.70; 95% CI 3.01–7.32) compared with those without TS. For the obstetric characteristics, TS was associated with an increased risk of intrauterine fetal demise (10.9% vs. 0.7%; aOR 8.40; 95% CI 5.30–13.30), intrauterine growth restriction (8.5% vs. 3.5%; aOR 2.11; 95% CI 1.48–2.99) and placenta accreta spectrum (aOR 3.63; 95% CI 1.20–10.97). For delivery outcome, pregnant patients with TS were more likely to undergo cesarean delivery (41.6% vs. 32.3%; aOR 1.53; 95% CI 1.26–1.87)[6].

Another search examined the pregnancy outcomes in women with TS undergoing oocyte donation treatment or spontaneous pregnancy and main results are showed in Table 1. The authors conclude that pregnancy in women with TS, whether oocyte donation or spontaneously conceived, carries obstetric risks, and therefore, women with TS, considering pregnancy, should receive comprehensive pre-pregnancy counselling and optimal obstetric care[7].

Table 1. Pregnancy outcomes in women with TS undergoing oocyte donation or spontaneous pregnancy, adapted from Burt et al[7].

| | TS oocyte donation | TS spontaneous |
|---|---|---|
| Women (n) | 65 | 31 |
| Pregnancies (n) | 105 | 71 |
| Number of children born | 70 | 45 |
| Live birth rate | 61/105 (58.1%) | 43/71 (60.6%) |
| Miscarriage rate | 42/105 (40%) | 23/71 (32.4%) |
| Termination of pregnancy | 0 | 5/71 (7%) |
| Intrauterine death | 0 | 0 |
| Hypertension | 8/48 (16.7%) | 5/40 (12.5%) |
| Gestational diabetes mellitus | 4/51 (7.8%) | 6/40 (15%) |
| Lower segment caesarean section | 44/53 (83%) | 21/39 (51.2%) |
| Preterm birth | 9/51 (17.6%) | 2/38 (5.3%) |
| Small for gestational age | 17/48 (35.4%) | 6/38 (15.8%) |

In addition, two recently published studies analyzed the opinions of women with TS about motherhood[8] and fertility based counseling[9]. The first was based on the web-survey and the main results were: 72/152 of the participants had not discussed motherhood options with their physicians; 85/152 expressed a desire to have children; 5/152 had biological children from spontaneous pregnancies; 5/152 had biological children through oocyte donation; 1/152 through embryo donation and 12/152 had adopted children[8]. These authors highlight that is crucial to prioritize TS patients' perspectives in fertility preservation discussions and decisions[8]. In this context, other research showed that thirty patients (27.78%) received fertility and/or fertility preservation counseling, of which six (5.56%) pursued autologous assisted reproduction technology. A multidisciplinary group of providers offered counseling[9].

In summary, TS experience adverse pregnancy associated outcomes and is considered high risk. This way, the management of pregnancy in TS with a multidisciplinary team, composed mainly by maternal–fetal medicine specialists and cardiologists, should be implemented in order to reduce complications for mothers and infants.

## CONFLICT(S) OF INTEREST

The authors declare that there are no conflicts of interest.

## AUTHORS' CONTRIBUTIONS

**MFB:** Investigation, Writing – review & editing. **ABTM**: Conceptualization, Investigation, Writing – original draft, Writing – review & editing.

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