Obstetric Outcomes in Women with Turner Karyotype

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Context: Women with Turner syndrome (TS) have high risk of cardiovascular complications and hypertensive disorders. Few studies have analyzed obstetric outcome in women with TS.

Objective: This study compared obstetric outcome in women with TS karyotype with women in the general population.

Design: The Swedish Genetic Turner Register was cross-linked with the Swedish Medical Birth Register between 1973 and 2007. Obstetric outcome in singletons was compared with a reference group of 56,000 women from the general population. Obstetric outcome in twins was described separately.

Results: A total of 202 singletons and three sets of twins were born to 115 women with a TS karyotype that was unknown in 52% at time of pregnancy. At first delivery, TS women of singletons were older than controls (median 30 *vs.* 26 yr, $P < 0.0001$). Preeclampsia occurred in 6.3 *vs.* 3.0% ($P = 0.07$). Aortic dissection occurred in one woman. Compared with the general population, the gestational age was shorter in children born by TS women (-6.4 d, $P = 0.0067$), and median birth weight was lower (-208 g, $P = 0.0012$), but sp scores for weight and length at birth were similar. The cesarean section rate was 35.6% in TS women and 11.8% in controls ($P < 0.0001$). There was no difference in birth defects in children of TS women as compared with controls.

Conclusions: Obstetric outcomes in women with a TS karyotype were mostly favorable. Singletons of TS women had shorter gestational age, but similar size at birth, adjusted for gestational age and sex. Birth defects did not differ between TS and controls. (*J Clin Endocrinol Metab* **96: 3475–3482, 2011**)

Turner syndrome (TS) is the most common sex chromosome disorder and appears in about one in 2500 live-born females (1–3). The characteristic physical features of TS range from severe to mild. Some women receive their TS diagnosis late in life or not at all. Short stature, ovarian dysgenesis, webbed neck, cardiac malformations, and hypothyroidism are common (4–6).

Spontaneous pregnancies are rare and occur in about 2–8% of all TS women, (7–9). They usually occur among women with mosaic karyotypes, but pregnancies in women with a monosomy (7, 10) and in TS women with a Y fragment (11) occur as well. A high rate of pregnancy complications has also been reported with miscarriages (29%), stillbirths (7%), and birth defects (20%) (4, 7, 12). Miscarriages seem to occur particularly often in spontaneous pregnancies but might be frequent after oocyte donations as well due to uterine factors (4, 9).

Since the 1980s, *in vitro* fertilization and oocyte donation are options for women with TS (13, 14), and pregnancy and implantation rates after oocyte donation for TS women seem to be comparable with other women in need of this treatment (15–17). Studies on obstetric outcome in

Abbreviations: BMI, Body mass index; CI, confidence interval; TS, Turner syndrome.

TS oocyte donation pregnancies are sparse, but higher risks of complications, especially hypertensive disorders and preeclampsia, preterm birth, and intrauterine growth restriction have been reported (14, 18, 19). Concerns have also been raised regarding serious maternal risks and even death due to cardiovascular complications during these pregnancies (20–24). Maternal mortality owing to rupture or dissection of the aorta may be 2% (14, 25–27).

In a recent Swedish study, pregnancy outcome in women with a clinical diagnosis of TS was reported. This study was merely focused on early pregnancy outcome but did not confirm the previous findings of severe maternal risks during pregnancy (9). An extended study to further evaluate this question was therefore needed.

The aim of this retrospective population-based cohort study was to report on the maternal and neonatal outcome for women with TS karyotype giving birth in Sweden between 1973 and 2007 in comparison with the general population. We used data from the Swedish Genetic Turner Register and cross-linked it with the Swedish Medical Birth Register, the National Patient Register, the Causes of Death Register, and the Register of Congenital Malformations.

Materials and Methods

The Swedish Genetic Turner Register is a register including girls and women with a postnatal diagnosis of TS according to karyotype. It includes data on 909 women (born between 1892 and 2006, of whom 394 were born between 1950 and 1979), from 1967–2006, collected from all Swedish cytogenetic laboratories (Gothenburg, Linköping, Lund, Skövde, Stockholm, Umeå, and Uppsala) with information on date of birth, karyotype, date of diagnosis, and analyzing laboratory. In the majority of cases, the analyzed tissue and the number of analyzed cells are recorded. In almost all cases, the chromosomal analysis was performed on peripheral blood lymphocytes and in some cases also on fibroblasts and buccal cells. From 1967–1994, the TS diagnosis was based on a karyotype analyzed from 10–25 cells. Since 1995 and onward, all genetic laboratories in Sweden analyzed at least 30 cells when TS was suspected. Karyotypes were subgrouped into four groups: 1) monosomy 45,X; 2) mosaics 45,X/46,XX; 3) others, including 45,X/46XY, 45,X/47,XXX, 45,X/48,XXXX, 45,X/49XXXXX 45,X/51,XXXXXX, and 45,X/46,Xder(X) (including ring chromosomes, deletions or translocations), isochromosomes 45,X/46,X,i(X) and 46,X,i(X); and 4) mosaics 45,X/46,XX with 45,X less than 6% (low-grade mosaics). The subgroup of mosaics with less than 6% 45,X cells was chosen because they probably represent healthier TS women with few or no stigmata (28).

Via the unique personal identity number given to all citizens in Sweden, data from the Swedish Genetic Turner Register was cross-linked with the Medical Birth Register, the National Patient Register, the Causes of Death Register, and the Register of Congenital Malformations. The Swedish Medical Birth Register covers almost all deliveries in the general population in Sweden since 1973 (except for a few percent) (29). It contains informa-

tion about maternal characteristics (*i.e.* age, parity, height, and smoking habits), antenatal care, delivery and neonatal data of live births and stillbirths. In Sweden during the study period, stillbirth was defined as a fetal death after 28 completed weeks of gestation. There are no data on miscarriages or fetal death before 28 wk gestation. Data on maternal height and smoking habits were registered since 1983 in the Medical Birth Register. Data on years of infertility and infertility treatment (*in vitro* fertilization, oocyte donation, and ovulation induction) were registered since 1994, but in some cases incompletely.

The study group comprised all women with a Turner karyotype who gave birth to live-born or stillborn singletons between 1973 and 2007. The control group consisted of 500 women per TS woman randomly selected from the Medical Birth Register matched for year of birth. Maternal characteristics were age, parity, height, body mass index (BMI), and smoking habits in early pregnancy. The International Classification of Diseases (ICD) codes 8, 9, and 10 were used to study preexisting diseases such as endocrine diseases, diabetes, and essential hypertension as well as complications during pregnancy such as preeclampsia, placental abruption, placenta previa, aortic dissection, and maternal mortality. Neonatal outcomes were sex, mode of delivery, gestational week at delivery, weight and length at birth, Apgar scores, birth defects, and mortality (stillbirth and neonatal and infant mortality up to 1 yr of age). Weight and length at birth were calculated as SD from expected mean birth weight and length according to gestational age and sex in a Swedish reference cohort (30). Maternal and neonatal outcome in TS women with twins were described separately.

Statistical analysis

Data on maternal characteristics in singletons were presented for all TS karyotypes, for subgroups 1–4, and for all TS karyotypes excluding low-grade mosaics (group 4), respectively. Data on neonatal outcome was presented on singletons born to all TS women and on singletons born to all TS women excluding low-grade mosaics.

Means, SD, and medians were calculated with conventional methods.

In singletons, maternal and infant outcomes of pregnancies in all women with TS were compared with the corresponding outcomes among the reference group. Efforts were made to account for correlated outcomes within each woman. For binary outcomes, logistic regression analyses were performed, using generalized estimating equation technology to obtain robust variance estimation. For continuous outcome variables, the same technique was used to perform ANOVA with robust variance estimation. Adjustments were made for maternal age at delivery (continuous-variable, second-grade model with one linear and one quadratic term) and parity (1, 2, 3, and 4+ as class variables). Continuous maternal characteristic data were analyzed using Kruskal-Wallis test (test for heterogeneity within the TS group) and Mann-Whitney *U* test (test for difference between the TS group and the reference group), respectively. All statistical analyses were made using Gauss (Aptech Systems Inc., Maple Valley, WA; http://www.aptech.com).

Ethics

The study received approval from the Regional Ethic Committee at the University of Gothenburg.

Results

From 1973–2007, 208 children (202 singletons and three sets of twins) were born to 115 women with TS karyotype. The reference group consisted of 56,000 women from the Medical Birth Register, matched for year of birth, and their 112,330 singletons.

Maternal characteristics and outcome in singletons

Maternal characteristics are shown in Table 1. Women with a TS karyotype (n = 112) were subgrouped into 45,X monosomy (n = 10), 45,X/46,XX mosaics (n = 38), others (n = 52), and low-grade mosaics 45,X/46,XX (n = 12). Median age at TS diagnosis differed between the TS groups (P = 0.004), the monosomy group being the youngest, 16 yr (range 10–36 yr), and 45,X/46,XX mosaics the oldest at diagnosis, 35 yr (range 13–65 yr). The TS diagnosis was known in 48% of the women before the first delivery. Compared with the reference group, women with TS were older at both first and second delivery with

a median age in TS of 30 yr (range 18–41 yr) and 32 yr (range 21–43 yr) vs. 26 yr (range 13–48 yr) and 28 yr (range 16–47 yr), respectively (P < 0.0001 for both). The difference in maternal age between all TS women and the reference group for all deliveries was 2.7 yr [95% confidence interval (CI) = 1.8–3.6; P < 0.0001]. The TS woman who was diagnosed at age 65 was diagnosed in 2003. Her fourth child was born in 1973. The other children were born before 1973 and were therefore not registered in the Medical Birth Register. Her karyotype was 45X/46XX with 45X in 16% of the cells. The reason for karyotyping is unknown to us.

Women with TS had given birth to fewer children than their age-matched controls (P = 0.02). The TS groups did not differ regarding parity (P for heterogeneity between TS groups = 0.19).

As expected, the TS women were shorter than the reference group, with a median height for all TS women of 161 cm (range 140–180 cm) as compared with the refer-

TABLE 1. Maternal characteristics in women with TS karyotype giving birth in Sweden from 1973–2007

	45,X	45,X/46,XX	Others	45,X/46,XX low-grade mosaicism (<6%)	All TS women	All TS women excluding 45,X/46,XX low-grade mosaicism (<6%)	Medical Birth Register reference group[a]
n	10	38	52	12	112	100	56,000
Age at TS diagnosis (yr), median (range)	16 (10–36)	35 (13–65)	33 (8–46)	33 (8–44)	33 (8–65)	33 (8–65)	NA
TS known before first delivery [n (%)]	8 (80)	15 (39)	25 (48)	6 (50)	48 (43)	54 (54)	NA
Women's year of birth [n (%)]							
<1940	0	1 (2.6)	0	0	1 (0.9)	1 (1.0)	500 (0.9)
1940-1949	0	3 (7.9)	1 (1.9)	1 (8.3)	5 (4.5)	4 (4.0)	2,500 (4.5)
1950-1959	0	13 (34.2)	8 (15.4)	1 (8.3)	22 (19.6)	21 (21.0)	11,000 (19.6)
1960-1969	5 (50.0)	17 (44.7)	24 (46.2)	5 (41.7)	51 (45.5)	46 (46.0)	25,500 (45.5)
1970-1979	4 (40.0)	3 (7.9)	16 (30.8)	5 (41.7)	28 (25.0)	23 (23.0)	14,000 (25.0)
≥1980	1 (10.0)	1 (5.8)	3 (5.8)	0	5 (4.5)	5 (5.0)	2,500 (4.5)
Year of first delivery [n (%)]							
1973-1982	0	11 (28.9)	5 (9.6)	1 (8.3)	17 (15.2)	16 (16.0)	10,875 (19.4)
1983-1989	1 (10.0)	7 (18.4)	6 (11.5)	1 (8.3)	15 (13.4)	14 (14.0)	11,453 (20.5)
1990-1999	4 (40.0)	14 (36.8)	18 (34.6)	5 (41.7)	41 (36.6)	36 (36.0)	20,634 (36.8)
2000-2007	5 (50.0)	6 (15.8)	23 (44.2)	5 (41.7)	39 (34.8)	34 (34.0)	13,038 (23.3)
Maternal age at first delivery (yr), median (range)	28.5 (18–36)	30 (18–37)	28 (20–41)	31.5 (26.5–39)	30 (18–41)	30 (18–41)	26 (13–48)
Maternal age at second delivery (yr), median (range)	34.5 (32–37)	34 (21–42)	31.5 (22–43)	33.5 (22–38)	32 (21–43)	32 (21–43)	28 (16–47)
Parity[b] (n)							
1	8	15	24	6	53	47	17,405
2	1	14	19	4	38	34	25,509
≥3	1	9	9	2	21	19	13,086
Height[c] (cm), median (range)	157 (140–165)	162 (150–180)	161 (140–178)	166 (156–174)	161 (140–180)	160 (140–180)	166 (120[d]–190)
Smoking at first delivery[c] [n/N (%)]	2/10 (20.0)	2/26 (7.7)	6/45 (13.3)	4/11 (36.4)	14/92 (15.2)	10/81 (12.3)	8,035/42,566 (18.9)
BMI at first delivery (kg/m²), median (range)	22.4 (19.8–29.7)	25.4 (19.7–33.4)	24.4 (18.5–39.4)	25.2 (18.0–35.1)	24.5 (18.0–39.4)	24.5 (18.5–39.4)	23.0 (13.7[d]–61.3[d])

NA, Not applicable.

[a] Reference group from Medical Birth Register (500 controls per TS woman) matched on year of birth.

[b] Seven TS women had deliveries before 1973.

[c] Smoking habits and height at first antenatal visit registered since 1983 in Medical Birth Register.

[d] Extreme value as it is recorded in the Medical Birth Register.

ence cohort 166 cm (range 120–190 cm) ($P < 0.0001$) and the monosomy group being the shortest with a median height of 157 cm (range 140–165 cm).

The BMI in TS was higher at first delivery compared with the reference group ($P = 0.003$). The median BMI for all TS was 24.5 kg/m^2 (range 18.0–39.4 kg/m^2). Among TS, the monosomy women had the lowest median BMI, 22.4 kg/m^2 (range 19.8–29.7 kg/m^2).

Smoking habits did not differ between TS and controls ($P = 0.38$).

There was no maternal mortality in the TS group. The number of preexisting diseases and pregnancy complications in all pregnancies of TS women were few and did not allow for any meaningful statistical analysis (endocrine disease n = 3, diabetes n = 4, essential hypertension n = 1, and placental abruption n = 2). Miscarriages were not registered. There was a trend toward more TS women

having preeclampsia during their first pregnancy as compared with the reference group (6.3 *vs.* 3.0%, odds ratio = 1.92; 95% CI = 0.94–3.92; $P = 0.07$). One 36-yr-old woman suffered from an aortic dissection in gestational wk 32 during her second spontaneous pregnancy. She was delivered by cesarean section, and both mother and child survived. Her TS diagnosis (45,X in 46 cells and a Y mosaicism in four cells) was set 2 yr after this event and could be made in conjunction with her hypothyroidism diagnosis (11).

Neonatal outcome in singletons

Neonatal outcome is shown in Table 2.

In children of women with TS karyotype, the median gestational age after adjustment for maternal age was shorter (-6.4 d) ($P = 0.007$). Preterm deliveries were more common in the TS group ($P = 0.0003$, adjusted for ma-

TABLE 2. Neonatal characteristics in singletons born to women with TS karyotype in Sweden from 1973–2007

Outcome	All children born to women with any TS karyotype (n = 202)	All excluding children born to TS women with 45,X/46,XX low-grade mosaicism (<6%) (n = 190)	Medical Birth Register reference group[a] (n = 112, 330)	All children born to women with any TS karyotype *vs.* Medical Birth Register reference group — Difference (95% CI)[b]	OR (95% CI)[c]
Gestational age (d), median (range)	273 (168–294)	273 (168–294)	280 (154–315)	−6.4 (−11.1 to−1.8)	
≥42 wk [n (%)]	5 (2.5)	5 (2.8)	8935 (8.0)		0.3 (0.1–0.7)
32–36 wk [n (%)]	21 (10.5)	18 (10.1)	5003 (4.5)		2.4 (1.5–4.0)
<32 wk [n (%)]	4 (2.0)	4 (2.2)	814 (0.7)		3.2 (1.4–7.2)
Unknown (n)	2	2	237		
Birth weight (g), median (range)	3425 (550–5090)	3440 (550–5090)	3540 (366–9905)[d]	−208 (−333 to−82)	
<2500 g [n (%)]	17 (8.5)	15 (8.4)	3865 (3.5)		2.5 (1.4–4.4)
<1500 g [n (%)]	4 (2.5)	3 (1.7)	675 (0.6)		3.1 (1.1–8.4)
SD weight, median (range)	−0.1 (−3.8–3.0)	−0.1 (−3.8–3.0)	−0.1 (−5.0–5.0)	−0.1 (−0.3–0.1)	
SD weight <−2 [n (%)]	9 (4.5)	7 (3.9)	3110 (2.8)		1.6 (0.8–3.0)
SD weight >2 [n (%)]	7 (3.5)	6 (3.4)	3610 (3.2)		1.4 (0.7–2.8)
Unknown	3	2	397		
Birth length					
SD length, median (range)	−0.1 (−3.3–3.0)	−0.1 (−3.3–2.5)	0.1 (−4.9–4.9)	−0.1 (−0.2–0.1)	
SD length >2 [n (%)]	7 (3.6)	7 (4.0)	2896 (2.6)		1.3 (0.6–2.8)
SD length >2 [n (%)]	7 (3.6)	6 (3.4)	2453 (2.2)		1.6 (0.9–2.9)
Unknown	5	4	1716		
Male/female ratio	92/110 (0.84)	81/100 (0.81)	57,773/54,557 (1.06)		0.8 (0.6–1.1)
Mode of delivery [n (%)]					
Cesarean section	72 (35.6)	68 (37.6)	13,209 (11.8)		2.9 (1.9–4.3)
Vacuum extraction/ forceps	11 (5.4)	9 (5.0)	4,916 (4.4)		0.9 (0.5–1.7)
Apgar score <7 at 5 min [n (%)]	4 (2.1)	4 (2.3)	1,331 (1.2)		3.1 (0.8–12.5)
Unknown (n)	12	10	4,352		
Mortality[e] [n (%)]	3 (1.5)	2 (1.1)	978 (0.9)		1.8 (0.6–5.6)
Children with any birth defect [n (%)]	9 (4.5)	9 (5.0)	4,267 (3.8)		1.2 (0.6–2.3)

OR, Odds ratio.

[a] Reference group from Medical Birth Register: the children of 500 controls per TS woman. The control women were matched on year of birth.

[b] ANOVA, adjusted for maternal age, robust variance.

[c] Multiple logistic regression analyses, adjusted for maternal age and parity; robust variance.

[d] The 9905-g value is from Medical Birth Register.

[e] Stillbirth or death within 1 yr of age.

ternal age and parity). There were also fewer children of TS women born after 42 wk, $P = 0.005$, adjusted for maternal age and parity). The mean birth weight after adjustment for maternal age was 208 g lower in children of TS women ($P = 0.001$).

No difference was found in median SD for weight and length at birth or in the numbers of children with SD weight below -2 or above 2 ($P = 0.15$, $P = 0.17$) or SD length below -2 or above 2 ($P = 0.43$, $P = 0.33$).

More children of TS women were delivered by cesarean section than in the reference group ($P < 0.0001$), but no difference was found for the number of newborns with Apgar score below 7 at 5 min ($P = 0.10$). The male to female ratio was 0.84 for the children of TS women, as compared with 1.06 in the reference group ($P = 0.11$).

The total mortality rate in the children of TS women was 1.5% (three of 202, stillbirth n = 1, neonatal mortality n = 1, and infant mortality n = 1) and 0.9% in the control group ($P = 0.56$).

Birth defects/chromosomal aberrations occurred in nine children of TS women (4.5%) and in 4267 (3.8%) children of mothers in the reference group ($P = 0.60$) (Table 3). Eight of these birth defects occurred in children of women with mosaics, but the difference between the types of maternal TS regarding the risk for any birth defect in the offspring was not significant ($P = 0.16$). There was also no significant difference between the maternal TS karyotypes regarding any other investigated neonatal outcome.

Neonatal outcome in twin pregnancies

Neonatal outcome in the three twin pregnancies in the group of TS women is shown in Table 4. Two twin pregnancies occurred after oocyte donation. For the third pregnancy, no information on mode of conception was available.

Discussion

This is, to our knowledge, the largest controlled registry study of obstetric outcomes in women with a TS karyotype. A total of 115 women with TS karyotype gave birth to 208 children in Sweden between 1973 and 2007. Singletons of TS women had a shorter gestational age, but similar size at birth when adjusted for gestational age and sex. Accordingly, increased risk of intrauterine growth restriction was not confirmed in our study (7, 14). Birth defects, including chromosomal aberrations, occurred with a similar prevalence as in the reference group. A high frequency of chromosomal aberrations has been reported in offspring of TS women, but this is mainly based on case reports, reflecting uncertainty. A review by Tarani and co-workers including 94 live-born babies of 74 TS women showed that 32 babies had malformations, and 21 of them were affected by trisomy 21 or by TS (7). We reported recently that advanced maternal age (>40 yr) was a risk factor for delivering a child with TS (31). Despite the higher median age in the present mothers with a TS karyotype, no such risk was seen.

A Danish population-based study found 33 TS women who gave birth to 64 children, 25 of whom were karyotyped (8). Six of the examined children, including three siblings, had chromosomal aberrations other than trisomy 21. We have sparse information on the number of pre- or postnatal karyotypes of the children of TS women in our study. However, we suggest that prenatal diagnosis should be discussed and offered to TS women with spontaneous pregnancies until further studies have been performed.

During the study period, only live-born babies and still-births after 28 wk gestation were registered in the Swedish Medical Birth Register, and we have no information on spontaneous or induced abortions in the TS women. Still-birth occurred in one case (0.5%), which is lower than in previous reports (7, 14).

TS women are generally at higher risk during pregnancy because of their various health problems with preexisting cardiovascular, endocrine, and autoimmune diseases and overweight (27). In the present study, TS women were older at first birth and their BMI was higher than in the reference group, but few women in this study were registered as having any preexisting diseases. Hypertensive disorders during pregnancy occurred in less than 10% in both TS women and in the reference group. Pregnancy-induced hypertension has been reported more

TABLE 3. Birth defects in singletons born to women with TS karyotype in Sweden from 1973–2007

Maternal karyotype	Gender, year of birth	Birth defect
45X[3]/46XX[27]	Girl, 1986	Facial defect (nose)
45X[8]/46XX[92]	Boy, 1987	Cardiac defect
46X,der[X]t(X:3) (p26:q11)	Girl, 1992	Chromosome aberration with musculoskeletal defect
45X[3]/46XX[32]	Girl, 1993	Ventricular septal defect
45X/46XX[a]	Boy, 1999	Hip dislocation
45X[3]/46XX[22]	Boy, 2001	Urogenital defect
45X[2]/46XX[47]/ 47XXX[1]	Girl, 2003	Trisomy 21 with ventricular septal defect
45X[4]/46XX[81]	Boy, 2005	Hip dislocation
45X[5]/46XX[95]	Girl, 2006	Polydactyly

[a] Fifteen cells counted, amount of 45X unknown.

TABLE 4. Obstetric outcomes in women with TS karyotype giving birth to twins (n = 3) in Sweden from 1973–2007

Maternal karyotype	Maternal age at TS diagnosis (yr)	Maternal age at delivery (yr)	Gestational age (wk)	Birth weight (g)	Neonatal outcome
45X[6]/46XX[44]	39	41	37	2955/2950	Healthy girl and boy
45X[2]/46XX[28]	37	38	34	2235/2250	Preterm otherwise healthy boy and girl
45X[1]/46XX[26]	30	33	30	1310/1750	One preterm girl with aortic coarctation/one preterm, healthy girl

frequently after oocyte donation in general (27–31%) (32, 33) and occurs even more frequently after oocyte donation in TS women (38–70%) (14, 18, 19). We have no reliable information on the mode of conception in our study, but we assume that most of the pregnancies were spontaneously conceived because oocyte donation was not allowed in Sweden until 2003. Surprisingly, many of the mothers (52%) were not diagnosed as having TS karyotype before the first delivery. This fact also makes it most probable to believe that the majority of pregnancies between 1970 and the early 1990s were spontaneously conceived pregnancies.

Congenital cardiovascular defects are a common problem in women with TS (6, 34) and place their pregnancies at high risk independent of mode of conception. Aortic dissection can be a fatal complication during pregnancy in TS (20–23, 25, 26). Recent studies have shown that aortic dissection in TS women is related not only to aortic valve disease and coarctation but also to aortopathy similar to that in Marfan syndrome with a collagen defect or cystic medial degeneration without macrovascular defects (35–38). From a national survey and a literature review in the United States, Karnis and co-workers (25) estimated that the maternal risk of death from rupture or dissection of the aorta in pregnancy may be as high as 2% in TS. Only 50% of the TS women had had a cardiac evaluation before fertility treatment. Similar frequency of aortic dissection was seen in a recent French report on TS pregnancies (14) when the recommendations on prepregnancy cardiac screening from the Turner Syndrome Study Group were not followed (36). These recommendations were adopted by the American Society for Reproductive Medicine in 2008 and stress the importance of performing the compulsory magnetic resonance imaging and that the aortic diameter should be related to the women's height. Our study, which examined the largest number of TS pregnancies, did not find any further risk for aortic dissection as compared with previous studies (14, 24, 25). We have no information about cardiac abnormalities before or during pregnancy because the present data are based on registry information. We do know, however, that no maternal mortality occurred. One TS woman developed an aortic dissection during her second spontaneous pregnancy. She also had an aortic coarctation. Both mother and child survived. The TS diagnosis was, however, not set until 2 yr after the pregnancy at the time when she was diagnosed with hypothyroidism, which is found in one third of TS woman. She had a Y-chromosome mosaicism (11).

The main strength of this study is its size, being a nationwide study over 34 yr and including all women in Sweden who were diagnosed with a TS karyotype and a large control group from the general population. In contrast to the previous Swedish study (9), maternal and neonatal data were obtained from Swedish health registries, mainly the Medical Birth Register (29).

One limitation of this study was the sparse information about maternal phenotypes or the clinical indication for karyotype. Except for maternal height and weight, recorded in early pregnancy, no information on phenotype was available in the present registers. The higher age for pregnancy in TS women suggests that some of the women may have been karyotyped when they were investigated for infertility, recurrent miscarriages, or ovarian failure with premature menopause rather than for reasons of external TS stigmata or disease. The high age at diagnosis and few stigmata in TS mosaics is in line with previous observations (6).

Another weakness is that even though data on duration of infertility and mode of conception was registered since 1994, oocyte donation cases were not always reported as such. *In vitro* fertilization with or without oocyte donation was registered in 21 women, which is probably underreporting. Before oocyte donation was legally permitted in Sweden, some patients might have chosen oocyte donation abroad and perhaps been unwilling to have this information registered. TS women with spontaneous conception and oocyte donation may have different pregnancy outcomes. Miscarriages are reported to be more common after spontaneous pregnancies in TS women compared with pregnancies achieved after oocyte donations indicated in a parallel ongoing clinical survey of TS women in Sweden (9). The higher frequency of mis-

carriages has been explained to depend on diminished endometrial receptivity, more chromosomal aberrations in the fetuses, and more autoimmune diseases in TS women (4, 17). TS women with spontaneous pregnancies, being predominantly mosaics, may represent a healthier group of TS women with fewer maternal but more neonatal risks, *i.e.* birth defects and chromosomal aberrations. TS women with oocyte donation pregnancies entail a cumulative effect of cardiac problems associated with TS and hypertensive disorders associated with oocyte donation (18, 32, 33). Additional studies are needed with more data on pregnancies after spontaneous as well as oocyte donation pregnancies in TS women. Ideally, data should be collected prospectively and also include information on maternal cardiac screening and evaluation and fetal pre- and postnatal examination.

In conclusion, this is the largest controlled study of obstetric outcomes in women with a TS karyotype, which was favorable in most cases. In the TS study group, almost 50% had a mosaic karyotype and very few women had a monosomy. The TS diagnosis was unknown in 52% at the time of pregnancy. Singletons of TS women had shorter gestational age but similar size at birth adjusted for gestational age, and the occurrence of birth defects did not differ from the population-based reference group. Still, the one case of aortic dissection in a woman, later diagnosed as TS, underscores the need for adequate counseling, prepregnancy cardiac screening, and close surveillance before, during, and after pregnancy.

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