# Pregnancy Outcome in Patients with Primary Sjögren's Syndrome. A Case-Control Study

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*ABSTRACT.* ***Objective.*** To study the outcome of pregnancy in patients with primary Sjögren's syndrome (pSS).
***Methods.*** A questionnaire covering demographic data and the outcome of pregnancies was answered by 58 patients with pSS and 157 controls. For 36 patients and 93 controls, we analyzed detailed data about pregnancy, birth, and status of the newborn from the Medical Birth Registry of Norway (MFR) for birth order one, 2, and 3. Thirty-two of 36 patients registered in MFR were diagnosed with pSS after the last birth.
***Results.*** Pregnancy outcomes were not different in patients compared to controls. Two patients (3.4%) reported giving birth to a child with congenital heart block.
***Conclusion.*** PSS had no impact on pregnancy outcome before disease onset. The most important condition associated with pSS in anti-SSA positive mothers was congenital heart block in the offspring. (J Rheumatol 2005;32:1734–6)

*Key Indexing Terms:*
SJÖGREN'S SYNDROME PREGNANCY

Primary Sjögren's syndrome (pSS)[1-3] is a common disease in women, but few studies are available on pregnancy outcome. Women with connective tissue diseases in general have higher rates of preeclampsia, premature delivery, and cesarean section as well as a significantly increased relative risk of having a child small for gestational age[4]. In one study, babies born to women with pSS were not more premature or growth restricted than those of healthy women[5]. In another study, the authors concluded that neither pSS nor the presence of anti-SSA and anti-SSB antibodies influenced pregnancy outcome[6]. In contrast, a Greek study found increased frequency of spontaneous abortions before diagnosis in patients with pSS[7].

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Conflicting studies on pregnancy outcome in pSS prompted us to investigate pregnancy outcome in a case-control study.

## MATERIALS AND METHODS

*Patients*. Sixty-three women at the outpatient rheumatology clinic, Haukeland University Hospital, fulfilling the revised criteria for Sjögren's syndrome[8], were consecutively invited and 58 (91.5%) patients agreed to participate in the study.

As a reference group, 4 age-matched women living in the same county were selected for each patient. This control group was randomly selected by a computerized method from the Medical Birth Registry of Norway (MFR)[9]. For the 22 pSS-patients not registered, controls were selected from the National Population Registry. Altogether 67.7% of the 232 selected controls responded to the questionnaire. Women not registered in the MFR have either not given birth at all, or gave birth before 1967 when the registry was established. The study was approved by the regional medical ethics committee.

*Questionnaire*. A questionnaire comprising demographic data, questions about pregnancy, and pregnancy outcome was sent to the 58 pSS-patients and the 232 control subjects. Questions included age at first pregnancy, number of pregnancies, number of deliveries, age at last delivery, number of abortions (induced and spontaneous), number of stillbirths, number of living children, treatment with antimalarials, steroids, azathioprine or salicylates during pregnancy, complications during pregnancy (hypertension, proteinuria, preeclampsia, bleeding, edema, and thromboembolic events).

*Data analysis*. For the 36 patients with pSS registered in the MFR and their 93 controls, we analyzed the following data for birth order one, 2, and 3 between 1967 and 1997: maternal age, small for gestational age (< 10th percentile after 28 wks), preeclampsia (high blood pressure > 140/90 mm Hg and proteinuria > 0.3 gram protein per 24 h), hypertension (> 140/90 mm Hg), complications during delivery, instrumental delivery, birth defects, stillbirths, infant death, birth length, birth weight, duration of pregnancy (wks), and Apgar scores after 1 and 5 minutes.

*Statistical methods*. Groups were compared using chi-square testing, Wilcoxon sum-rank test, Cramers V, or independent t test; p values < 0.05 were regarded as statistically significant.

## RESULTS

*Demographic data*. Mean age of patients with pSS was 55 years (range 32-78) and mean age at diagnosis was 51.3 years (range 26-73). Four patients were diagnosed with pSS before the last pregnancy, and 58 were diagnosed after all analyzed pregnancies. Two patients and one control had never been pregnant.

During pregnancy, oral steroids were taken by one patient and one control, and 3 patients were receiving antimalarials. No patients were receiving cytotoxic drugs during or before pregnancy. Two patients with anti-SSA and anti-SSB autoantibodies (3.4%) reported that they had given birth to a child with congenital heart block.

Self-reported numbers of pregnancies and births per woman in patients and controls were 3.41 versus 3.50 pregnancies (not significant, NS) and 2.91 versus 2.92 births (NS). The proportion of patients and controls reporting spontaneous abortions was 27.3% versus 35.5% (NS); stillbirths were reported by 7.4% of patients and 5.2% of controls (NS).

Results of self-reported complications during pregnancy are shown in Table 1. Smoking during pregnancy was reported by 4/56 (7.7%) patients and 38/154 (32.8%) controls (p = 0.006).

*Pregnancy outcome*. Results of pregnancy outcome in 36 patients with pSS and 93 controls registered in the MFR are shown in Table 2 for birth order 1, 2, and 3. Only 4 patients were diagnosed with pSS before the last pregnancy. After excluding patients and controls who smoked during pregnancy, no significant difference for the variables listed in Table 2 was found.

*Table 2*. Pregnancy outcome in 36 patients with pSS and 93 controls at birth order 1, 2, and 3 as registered in the Medical Birth Registry of Norway between 1967 and 1997. The only significant difference between patients and controls (p = 0.022) was Apgar score after 1 minute in birth order 2, which is probably of no clinical significance. Results are expressed as percentages unless otherwise stated.

| Pregnancy Outcome | Patients Birth Order 1/2/3, n = 36/23/10 | Controls Birth Order 1/2/3, n = 93/62/32 |
|---|---|---|
| Maternal age, yrs, mean | 26/28/30 | 26/28/31 |
| Small for gestational age | 11/21/0 | 13/10/12 |
| Preeclampsia | 3/0/0 | 4/0/0 |
| Hypertension during pregnancy | 0/0/0 | 0/1/0 |
| Complications during delivery | 33/31/30 | 29/30/28 |
| Surgical delivery, incl. cesarean | 14/14/10 | 20/12/13 |
| Birth defects | 0/0/0 | 1/3/0 |
| Stillbirth | 6/0/0 | 1/1/0 |
| Infant death = 1 year | 0/0/0 | 1/0/3 |
| Birth length, cm, mean | 49/50/50 | 49/50/51 |
| Birth weight, g, mean | 3252/3418/3636 | 3297/3558/3730 |
| Duration of pregnancy, wks, mean | 39/39/40 | 39/40/41 |
| Apgar score after 1 min, mean | 8.8/9.0/9.0 | 8.5/8.0/8.7 |
| Apgar score after 5 min, mean | 8.9/9.1/9.1 | 9.1/8.7/9.1 |
| * Prematurity rate | 5.9/8.6/8.3 | 5.7/5.6/4.1 |
| ** Low birth weight rate | 7.8/5.4/7.7 | 6.0/6.4/1.9 |

* < 37 wks gestation. ** < 2500 g.

## DISCUSSION

Only 4 patients in our cohort had a pregnancy after the diagnosis of pSS, consistent with the small numbers of pregnancies in patients with established pSS in other studies[5-7]. A high risk of pregnancy loss and adverse advents may precede the clinical onset of connective tissue diseases[10] or indicate the presence of an underlying autoimmune disease[11]. Accordingly, 2 studies have reported that spontaneous abortions occurred significantly more frequently in patients with pSS before disease onset than in controls[5,7]. This was not confirmed by our results: both our patients with pSS and controls reported a high frequency of stillbirths and spontaneous abortions, probably due to overreporting in both groups of women.

The discrepancy between self-reported and registered data, as found for preeclampsia, may be due to the fact that delivery data for 22 patients were not registered in the MFR, probably because the births took place before 1967. In addition, recall bias increases with the interval between pregnancy and questioning as well as maternal age[12]. The only significant difference between patients and controls in the MFR, Apgar score after 1 minute in birth order 2, is probably of no clinical significance.

Maternal smoking during pregnancy is a major cause of reduced birth weight, decreased lung function, and sudden infant death syndrome[13]. Our results could therefore have been confounded by the significant difference between patients and controls regarding smoking during pregnancy.

*Table 1*. Complications during pregnancy and delivery reported by patients with pSS and controls in Hordaland county. Results are reported as proportions in each group reporting each event (%). Not all individuals answered all questions. Pre-eclampsia comprised both hypertension and proteinuria.

| Group | Hypertension | Proteinuria | Pre-eclampsia | Bleeding During Pregnancy | Premature Labor | Premature Rupture of Membranes |
|---|---|---|---|---|---|---|
| Patients N = 58 | 9/47 (19.1) | 9/47 (19.1)* | 6/45 (13.5)** | 11/46 (23.9) | 11/46 (23.9)* | 8/46 (17.4) |
| Controls N = 157 | 22/149 (14.8) | 33/148 (22.3) | 6/145 (6.2) | 20/149 (13.4) | 10/144 (6.9) | 16/144 (11.1) |

* p < 0.05. ** p < 0.01.

However, in a stratified analysis after exclusion of smokers, we still found no influence of pSS on pregnancy and delivery.

Two of our 58 patients with anti-SSA autoantibodies reported giving birth to a child with congenital heart block. A previous prospective study reported 2 congenital heart blocks in offspring of 100 women with anti-SSA autoantibodies[14]. Lack of an association between SSA or SSB autoantibodies and pregnancy outcome has been documented in several studies[5-7,14].

We reported earlier that 5.9% of patients with pSS chose not to have children due to their disease[15]. Our study shows that pSS does not influence pregnancy outcome before disease onset[6]. The most important condition associated with pSS is the development of congenital heart block in children of mothers positive for anti-SSA or anti-SSB antibodies.

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