Outcome of Pregnancy in Italian Patients with Primary Sjögren Syndrome

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ABSTRACT. ***Objective.*** To investigate pregnancy and fetal outcomes in patients with primary Sjögren syndrome (pSS).

Methods. An obstetric history of 36 women with established diagnosis of pSS at pregnancy was obtained from a multicenter cohort of 1075 patients. In a subgroup case-control analysis, 12 deliveries in patients with pSS were compared with 96 control deliveries.

Results. Thirty-six women (31 with anti-SSA/Ro and/or anti-SSB/La antibodies) with an established diagnosis of pSS had 45 pregnancies with the delivery of 40 newborns. Two miscarriages, 2 fetal deaths, and 1 induced abortion were recorded. Mean age at the first pregnancy was 33.9 years; mean number of pregnancies was 1.25; 18/40 (45%) cesarean births were delivered; mean pregnancy length was 38.5 weeks (range 32–43), with 6 preterm deliveries. The mean Apgar score at 5 min was 8.9, mean birthweight was 2920 g (range 826–4060 g). Congenital heart block (CHB) occurred in 2/40 (5%) newborns. The reported rate of breastfeeding for at least 1 month was 60.5%. In 4/40 pregnancies (10%) a flare of disease activity was observed within a year from delivery. In the case-control subgroup analysis, 12 deliveries were compared with 96 controls and no significant differences were found.

Conclusion. Patients with pSS can have successful pregnancies, which might be followed by a mild relapse. CHB was the only cause of death for offspring of mothers with pSS. (First Release June 1 2013; J Rheumatol 2013;40:1143–7; doi:10.3899/jrheum.121518)

Key Indexing Terms:
SJÖGREN SYNDROME PREGNANCY NEONATAL LUPUS
ABORTION ANTI-RO/LA ANTIBODIES

Primary Sjögren syndrome (pSS) usually starts after the fifth decade[1], but it can occur in all age groups. Women with pSS may become pregnant and frequently raise questions about the risks of pregnancy for themselves and for the fetus. Data regarding the influence of the disease on pregnancy and vice versa are scarce. The primary aim of our study was to describe pregnancy and fetal outcome in Italian patients with an established diagnosis of pSS. Second, in a case-control subgroup analysis, a comparison was made with the general population.

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MATERIALS AND METHODS

The clinical charts of 1075 white women with pSS (966 classified according to the American-European criteria[2] and 109 classified according to the European criteria[3]) from 4 rheumatology referral centers were evaluated. When a pregnancy had occurred in a patient with an established diagnosis of pSS, data prospectively collected from clinical records were reviewed; as well, the patient was interviewed to obtain more detailed information regarding obstetric history, and obstetric clinical charts were reviewed. Data were collected on the clinical and serologic phenotype of disease, the number and outcome of pregnancies, and age and disease duration at the time of first pregnancy after diagnosis; a disease flare was defined as the appearance and/or worsening of clinical manifestations leading to a change in treatment strategy. The following information was recorded: type of conception (natural or artificial), time of delivery or fetal loss, delivery method, and obstetrical complications. Complications were defined as follows: miscarriage (spontaneous pregnancy loss before 10 weeks); fetal death (spontaneous loss at 10 weeks or after); induced abortion (induced termination of pregnancy, voluntary or therapeutic); preterm delivery (delivery before 37 weeks); and very preterm delivery (before 34 weeks). Data regarding fetal outcome included sex, weight at

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birth (low birthweight: < 2500 g; and very low birthweight: < 1500 g), Apgar score at 5 min, congenital malformations, and breastfeeding. Congenital heart block (CHB) was defined as CHB detected *in utero* or within 28 days from birth. In a subgroup case-control analysis from a single center (Rome), each delivery in patients with an established diagnosis of pSS was compared with the first 8 consecutive deliveries that occurred during the same month in the local referral university hospital (n = 96 controls). Data were obtained from hospital registry and clinical charts. Moreover, obstetrical histories (mean number of pregnancies/patients, abortions, fetal deaths) were compared among 3 groups from the same center (Rome): patients with pSS (diagnosis according to American-European criteria[2]) with delivery before diagnosis (138 women) or after diagnosis (12 women) and the 96 controls.

Chi-square and Mann-Whitney tests were used for statistical analysis with SPSS, release 15.

RESULTS

Patients' mean age was 59 years (range 17–89), mean age at diagnosis 51.4 years; 139/1074 (12.9%) were diagnosed before age 35 years. Thirty-six women (31 with anti-SSA/Ro and/or anti-SSB/La antibodies), all with an established diagnosis of pSS according to the American-European criteria[2], had natural conception resulting in 45 pregnancies that ended with delivery of 40 newborns (Table 1). Among them, 19/36 (52.7%) had mainly sicca symptoms, 17/36 (47.2%) also had extraglandular manifestations, and 1 had a concomitant antiphospholipid antibody (aPL) syndrome. The prevalence of aPL (anticardiolipin antibodies and/or anti-β_2-glycoprotein I and/or lupus anticoagulant) was 5.5% (2/36). Two miscarriages (1 in the woman with aPL syndrome), 2 fetal deaths, and 1 induced abortion were recorded. Thirty-four of 40 babies were born between 2000 and 2011, 6 were born between 1989 and 1999. Fetal echocardiography was performed during the pregnancies of all the 31 women with anti-SSA and/or SSB antibodies and electrocardiography was performed in their newborns at birth. CHB occurred in 2/40 (5%) newborns, in both cases detected *in utero* and with fatal outcome. As well, 2 infants had cardiac incontinence and a mild interatrial defect, respectively, not requiring surgery. The reported rate of breastfeeding for at least 1 month was 60.5% (23/38 newborns; range 1–21 months), 44.7% (17/38) at 3 months, 31.5% (12/38) at 6 months, 15.7% (6/38) at 9 months, 7.8% (3/38) at 12 months, and 7.8% (3/38) of babies were breastfed for more than 12 months, even if not exclusively. During pregnancy, 1 patient presented with thrombocytopenia and 1 with palpable purpura. A flare of disease activity was observed in 4/40 (10%) pregnancies (arthralgia/arthritis and central nervous system involvement) within a year from delivery. Among patients, 52.7% (19/36) did not receive any treatment during pregnancy, while low-dose corticosteroid was used in 15%, low molecular weight heparin in 11%, hydroxychloroquine in 11%, low-dose aspirin in 13%, and intravenous immunoglobulins in 2.7%. No differences in pregnancy and fetal outcome were observed between the treated and untreated women.

Table 1. Baseline features of 36 patients with primary Sjögren syndrome (pSS) who had pregnancy after disease diagnosis and their pregnancy and fetal outcomes.

Characteristic	
Total pregnancies, n	45
Mean age at first pregnancy, yrs (range)	33.9 (27–44)
Mean no. pregnancies/patient (range)	1.25 (1–3)
Disease duration at first pregnancy, mo (range)	53.5 (12–144)
Live births, n (%)	40/45 (88.8)
Miscarriages[a], n (%)	2/45 (4.4)
Induced abortions[b], n (%)	1/45 (2.2)
Fetal deaths[c], n (%)	2/45 (4.4)
Total deliveries, n	40
Mean length of pregnancy, wks (range)	38.5 (32–43)
Preterm deliveries < 37 wks[d], n (%)	6/40 (15)
Preterm deliveries 34–37 wks, n (%)	2/40 (5)
Very preterm deliveries < 34 wks[e], n (%)	4/40 (10)
Cesarean births, n (%)	18/40 (45%)
Mean APGAR score[f], (range)	8, 9 (5–10)
Mean birthweight, g (range)	2920 (826–4060)
Congenital heart block[g], n (%)	2/40 (5)
Deaths in the first week of life, n (%)	2/40 (5)
Congenital malformations not requiring surgery, n (%)	2/40 (5)
Low birth weight (< 2500 g), n (%)	4/40 (10)
Very low birth weight (< 1500 g), n (%)	2/40 (5)

[a] Spontaneous pregnancy loss before 10 weeks; [b] induced termination of pregnancy (voluntary or therapeutic); [c] fetal death: spontaneous loss at 10 weeks or after; [d] delivery before 37 weeks; [e] delivery before 34 weeks; [f] determined at 5 min; [g] detected *in utero* or within 28 days from birth.

Pregnancy and fetal outcomes for the subgroup case-control analysis are reported in Table 2. No significant differences were found regarding age at delivery, pregnancy duration, method of delivery, or baby's sex. More very preterm deliveries were observed among cases, and the neonates of mothers with primary SS tended to have a lower weight and a lower Apgar score, but the differences compared to controls were not significant. No differences regarding obstetric history were found between pSS patients who had pregnancies before or after the diagnosis and controls (Table 3).

DISCUSSION

Facing the problems of pregnancy and autoimmune disease, 2 questions arise: what is the influence of pregnancy on the disease, and what is the effect of the disease on pregnancy? A variety of hormonal and immunological alterations are induced by pregnancy to protect the fetus from rejection, and these may influence the activity of autoimmune diseases. Pregnancy polarizes the immune response toward a Th2 response; during pregnancy, women with a Th1-dependent autoimmune disease such as rheumatoid arthritis, multiple sclerosis, or thyroiditis are highly likely to experience a marked improvement of symptoms, which generally return within 1 year after delivery. This provides

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Table 2. Subgroup case-control analysis: pregnancy and fetal outcomes in women with established diagnosis of primary Sjögren syndrome (pSS) and healthy controls.

	Deliveries in Women with pSS, n = 12	Deliveries in Controls, n = 96	p
Pregnancy length, mean wks (range)	38.5 (33–43)	38.2 (30–41)	0.8637
Preterm deliveries[a], n (%)	2/12 (16.6)	19/96 (19.7)	1
Very preterm deliveries[b], n (%)	1/12 (8.3)	5/96 (5.21)	0.5248
Neonatal deaths[c], n (%)	1/12 (8.3)	0 (0)	0.1193
Age at delivery, mean wks (range)	32 (29–34)	34 (21–50)	0.9689
Delivery, vaginal/cesarean, n (%)	3/9 (25/75)	32/64 (33.3/66.6)	0.8166
Apgar score[d], mean (range)	8.5 (5–10)	9.3 (7–10)	0.8636
Baby weight, mean g, (range)	2809 (1500–3600)	3099 (1340–4670)	0.0785
Baby sex, female/male	8/4	52/48	0.8042

[a] Before 37 weeks; [b] before 34 weeks; [c] from birth until 28 days after delivery; [d] determined at 5 min.

Table 3. Subgroup analysis: obstetric history in patients with primary Sjögren syndrome (pSS) who had pregnancies before or after the diagnosis and controls.

	Women (n =11) with Established Diagnosis of SS During Pregnancy (no. pregnancies = 14)	Women (n = 138) with Pregnancies Before Established Diagnosis of SS (no. pregnancies = 277)	Controls (n = 96) (no. pregnancies =193)
No. pregnancies per patient, mean (range)	**1.27** (1-3)	p = 0.41; p = 0.27; **2.00** (0-7)	p = 0.93; **2.01** (1-5)
Spontaneous abortions, n (%)	**1/14** (7.14%)	p = 0.67; p = 0.69; **42/277** (15.16%)	p = 0.64; **30/193** (15.54%)
Induced abortions, n (%)	**1/14** (7.14%)	p = 0.58; p = 1; **17/277** (6.13%)	p = 0.28; **15/193** (7.77%)
Fetal death, n (%)	**0** (0%)	p = 1; p = 1; **0/277** (0%)	p = 0.39; **1/193** (0.51%)

Spontaneous abortion: spontaneous pregnancy loss before 10 weeks; induced abortion: induced termination of pregnancy (voluntary or therapeutic); fetal death: spontaneous loss at 10 weeks or after.

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evidence that pregnancy-related hormones have antiinflammatory properties[4]. In contrast, other conditions such as systemic lupus erythematosus (SLE) or systemic sclerosis (SSc) may be negatively influenced by pregnancy[5,6,7,8]. Data regarding pSS are scarce and this probably reflects the frequent observation that disease onset generally occurs in the postmenopausal age. Our results overlap with those of the largest study from Spain, which reported that among more than 900 women with pSS, the diagnosis was made before age 35 years in only 14% of cases[1]. Currently, however, at least in Western countries, the age of pregnancy may be delayed, and this issue has gained importance in pSS: there are increasing numbers of affected patients asking about the risks of pregnancy for themselves and for the fetus.

Only small numbers of pregnancies in patients with established pSS are reported, with a few isolated case reports describing onset or flare of disease during pregnancy[9,10,11,12]. Clearly these case reports are biased toward patients with more severe disease and negative outcomes. A specific scoring system for disease activity in pSS has been established only recently, and it has not been validated for women in pregnancy[13]. To our knowledge no other study apart from ours has specifically addressed the problem of pSS disease activity during pregnancy and after delivery. In our experience, fewer than half of patients with established pSS were treated for their disease while pregnant, and only 2 of them presented new clinical manifestations leading to a change in treatment strategy during pregnancy; whereas a mild flare of disease was observed within the first year after delivery in 10% of the cases. Women with connective tissue diseases have a significantly increased relative risk of having a newborn that is small for gestational age, as well as higher rates of preeclampsia, premature delivery, and cesarean birth[14]. Moreover, pregnancy-related complications, spontaneous abortions, and stillbirths, as well as infertility, seem to be more common in patients with SLE and SSc than in age-matched controls[14,15]. To date, very few studies have addressed pSS. It appears that the disease does not affect the ability of these women to carry and deliver healthy babies, because fertility and parity are similar in patients and control women[16,17]. However, evaluation of the reproductive history of patients with pSS revealed a higher incidence of spontaneous abortions, independent from the presence of aCL or antibodies to SSA/Ro or SSB/La[18,19]. A recent report from Sweden[20] described pregnancy and fetal outcome of 16 pregnancies in 14 patients with pSS, observing normal fertility and parity in comparison to a control population, normal pregnancy duration, and no increase in abortions and stillbirths, but with lower birthweight in the offspring of patients with pSS and an increased frequency of delivery complications. CHB was detected in 1 newborn (6%). However, only 10 pregnancies had occurred after diagnosis. It is noteworthy that the majority of the other studies on this topic refer to the outcomes of pregnancies that occurred before the diagnosis of pSS, and all suggest that pSS has no effect on pregnancy outcome before disease onset[16,17,18,21]. In a previous report[22], we could not demonstrate any differences regarding the number of spontaneous abortions and stillbirths between 140 patients with pSS and 109 controls, while the total number of pregnancies was higher among patients. This observation suggested that fertility and pregnancy outcome was not compromised even before an established diagnosis of pSS. In the present study, the subgroup case-control analysis revealed no differences in obstetric history (mean number of pregnancies/patient, number of abortions, fetal deaths) between pSS patients in which pregnancies occurred before and those after the diagnosis and healthy controls (Table 3).

One prospective study evaluated the risk of CHB in 100 consecutive women with anti-SSA/Ro antibodies: CHB was detected in 1 out of 25 women with pSS but no information was given regarding other features of the newborns or the outcome of all pregnancies[23]. In our cohort of patients with pSS, CHB had occurred in 5.5% of 36 pregnancies in mothers with anti-SSA/SSB antibodies, the same percentage reported in the Swedish study[20]. Neonatal mortality (during the first 4 weeks of life) in newborns from mothers with pSS is higher than that reported in the general Italian population [5% vs 0.36%–0.25% in 1999-2009, the years the majority of babies from pSS mothers were born (data from the Italian National Institute of Statistics; Website: www.istat.it)] and it was exclusively linked to CHB, which therefore remains the most challenging complication in pSS women with anti-SSA and/or SSB antibodies.

Our study evaluated pregnancy and fetal outcomes in, to our knowledge, the largest cohort of women with an established diagnosis of pSS. The average number of pregnancies in this group was not reduced in comparison to the fertility rate in Italy, which is estimated at 1.32 for 1991 and 1.42 for 2010 (data from the Italian National Institute of Statistics). The rate of fetal loss (miscarriages plus fetal deaths, 10%) was not higher than that reported for the general population; indeed, it is estimated that between 10% and 20% of all clinically recognized pregnancies result in spontaneous abortion[24]. Preterm delivery was recorded in 15% of cases, a rate higher than that reported in the Italian general population, 6% to 7%[25]; this difference was not relevant in the case-control study, although a higher prevalence of preterm delivery was observed. Corticosteroid use did not seem to affect length of pregnancy; women with preterm deliveries did not have a higher rate of corticosteroid use than women who gave birth at term (7.5% vs 7.5%). The number of cesarean births was rather high in patients with pSS, but in the last 10 years, the frequency of cesarean births in Italy has increased substantially, with a peak of 52%, although it varies from region to region[26]. We observed a

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slightly higher percentage of low birthweight newborns from mothers with pSS in comparison to the general population (10% vs 6.7%)[25], but again, in the case-control subgroup analysis this difference did not appear significant. The reported rate of any breastfeeding was similar in pSS mothers to that described for the general Italian population (45% vs 42%–64% at 3 months, 30% vs 20%–35% at 6 months, 7.5% vs 5% at 12 months)[27,28], while it was lower at 1 month (57.5% in the pSS group vs 86% in the cohort described by Quintero Romero, *et al*[28]). The reasons for this difference are not clear and such analysis was beyond the scope of our study.

Our findings suggest that women with pSS can have successful pregnancies, even though, as described for other autoimmune diseases[29], we observed a tendency to have very preterm delivery and low birthweight babies.

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REFERENCES

1. Ramos-Casals M, Solans R, Rosas J, Camps MT, Gil A, Del Pino-Montes J, et al. Primary Sjögren syndrome in Spain: Clinical and immunologic expression in 1010 patients. GEMESS Study Group. Medicine 2008;87:210-9.
2. Vitali C, Bombardieri S, Jonsson R, Moutsopoulos HM, Alexander EL, Carsons SE, et al. European Study Group on Classification Criteria for Sjögren's Syndrome. Classification criteria for Sjögren's syndrome: A revised version of the European criteria proposed by the American-European Consensus Group. Ann Rheum Dis 2002;61:554-8.
3. Vitali C, Bombardieri S, Moutsopoulos HM, Balestrieri G, Bencivelli W, Bernstein RM, et al. Preliminary criteria for the classification of Sjögren's syndrome. Results of a prospective concerted action supported by the European Community. Arthritis Rheum 1993;36:340-7.
4. Kaaja RJ, Greer IA. Manifestations of chronic disease during pregnancy. JAMA 2005;294:2751-7.
5. Mintz G, Nitz J, Gutierrez G, Karchmer S. Prospective study of pregnancy in systemic lupus erythematosus: results of a multi-disciplinary approach. J Rheumatol 1986;13:732–9.
6. Lockshin MD, Reinitz E, Druzin ML, Murrman M, Estes D. Lupus pregnancy: case-control prospective study demonstrating absence of lupus exacerbation during or after pregnancy. Am J Med 1984;77:893–8.
7. Urowitz MB, Gladman DD, Farewell VT, Stewart J, McDonald J. Lupus and pregnancy studies. Arthritis Rheum 1993;36:1392–7.
8. Østensen M. Scleroderma pregnancy: can the price be too high to pay? Clin Exp Rheumatol 2008;26:979-81.
9. Aslan E, Tarim E, Kilicdag E, Simsek E. Sjögren's syndrome diagnosed in pregnancy: a case report. J Reprod Med 2005; 50:67-70.
10. Adam FU, Torun D, Bolat F, Zumrutdal A, Sezer S, Ozdemir FN. Acute renal failure due to mesangial proliferative glomerulonephritis in a pregnant woman with primary Sjogren's syndrome. Clin Rheumatol 2005;25:75–9.
11. Mutsukura K, Nakamura H, Iwanaga N, Ida H, Kawakami A, Origuchi T, et al. Successful treatment of a patient with primary Sjögren's syndrome complicated with pericarditis during pregnancy. Intern Med 2007;46:1146-7.
12. Kikuchi A, Okai T, Taketani Y. Pulmonary embolism associated with Sjögren's syndrome in pregnancy. J Obstet Gynaecol Res 1996;22:421-3.
13. Seror R, Ravaud P, Bowman SJ, Baron G, Tzioufas A, Theander E, et al. EULAR Sjogren's syndrome disease activity index (ESSDAI): development of a consensus systemic disease activity index in primary Sjogren's syndrome. Ann Rheum Dis 2010;69:1103-9.
14. Petri M. Prospective study of systemic lupus erythematosus pregnancies. Lupus 2004;13:688–9.
15. Artlett CM, Rasheed M, Russo-Stieglitz KE, Sawaya HH, Jimenez SA. Influence of prior pregnancies on disease course and cause of death in systemic sclerosis. Ann Rheum Dis 2002;61:346–50.
16. Skopouli FN, Papanikolaou S, Malamou-Mitsi V, Papanikolaou N, Moutsopoulos HM. Obstetric and gynaecological profile in patients with primary Sjogren's syndrome. Ann Rheum Dis 1994;53:569-73.
17. Haga HJ, Gjesdal CG, Irgens LM, Ostensen M. Reproduction and gynaecological manifestations in women with primary Sjögren's syndrome: a case-control study. Scand J Rheumatol 2005;34:45-8.
18. Siamopoulou-Mavridou A, Manoussakis MN, Mavridis AK, Moutsopoulos HM. Outcome of pregnancy in patients with autoimmune rheumatic disease before the disease onset. Ann Rheum Dis 1988;47:982-7.
19. Julkunen H, Kaaja R, Kurki P, Palosuo T, Friman C. Fetal outcome in women with primary Sjögren's syndrome. A retrospective case-control study. Clin Exp Rheumatol 1995;13:65-71.
20. Hussein SZ, Jacobsson LT, Lindquist PG, Theander E. Pregnancy and fetal outcome in women with primary Sjogren's syndrome compared to women in the general population: a nested case-control study. Rheumatology 2011;50:1612-7.
21. Haga HJ, Gjesdal CG, Koksvik HS, Skomsvoll JF, Irgens LM, Ostensen M. Pregnancy outcome in patients with primary Sjögren's syndrome. A case-control study. J Rheumatol 2005;32:1734-6.
22. Priori R, Medda E, Conti F, Cassarà EA, Sabbadini MG, Antonioli CM, et al. Risk factors for Sjögren's syndrome: A case-control study. Clin Exp Rheumatol 2007;25:378-84.
23. Brucato A, Frassi M, Franceschini F, Cimaz R, Faden D, Pisoni MP, et al. Risk of congenital complete heart block in newborns of mothers with anti-Ro/SSA antibodies detected by counterimmunoelectrophoresis: a prospective study of 100 women. Arthritis Rheum 2001;44:1832–5.
24. Osborn J, Spinelli A, Cattaruzza MS. Risk of spontaneous abortion in Italy, 1978-1995 and the effect of maternal age, marital status and education. Am J Epidemiol 2000;151:98-105.
25. European Perinatal Health Report. 1. Euro-Peristat project in collaboration with SCPE, Eurocat and Euroneosta. [Internet. Accessed April 17, 2013.] Available from: www.europeristat.com
26. Arsieri R, Formisano V, Pugliese A, Saporito M, Triassi M. Prevalence of cesarean section and its relation to type of delivery facility, Campania. Bollettino Epidemiologico Nazionale 2002;15. [Internet. Accessed April 19, 2013.] Available from: www.ben.iss.it/pre_2002/giugno02/2eng.htm
27. Giovannini M, Banderali G, Agostoni C, Silano M, Radaelli G, Riva E. Epidemiology of breastfeeding in Italy. Acta Paediatr Suppl 1999;88:19-22.
28. Quintero Romero S, Bernal R, Barbiero C, Passamonte R, Cattaneo A. A rapid ethnographic study of breastfeeding in the North and South of Italy. Int Breastfeed J 2006;1:14.
29. Taraborelli M, Ramoni V, Brucato A, Airò P, Bajocchi G, Bellisai F, et al. Brief report: Successful pregnancies but a higher risk of preterm births in patients with systemic sclerosis: an Italian multicenter study. Arthritis Rheum 2012;64:1970-7.

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