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Effects of pregnancy on the renal and pulmonary manifestations in women with tuberous sclerosis complex

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Purpose: To determine whether pregnancy increases the risk of renal or pulmonary complications in women with tuberous sclerosis complex (TSC). **Methods:** We surveyed female members of the Tuberous Sclerosis Alliance and reviewed the files of adult women seen in our genetics clinics for complications of TSC. **Results:** Among 145 individuals, there was no significant difference in incidence of renal and pulmonary involvement between the pregnant and never-pregnant groups, although there were differences in age at diagnosis (25 vs. 16) and current age (41 vs. 35). There was no significant difference in the rate of renal complications (57% vs. 67%, $P = 0.62$) or pneumothorax (40% vs. 38%, $P = 1.00$) for the pregnant and never-pregnant groups, respectively. Pregnancy loss in women with TSC did not differ from population risks. **Conclusions:** Pregnancy does not increase the risk of developing renal or pulmonary complications in women with TSC. ***Genet Med* 2003:5(3):154–160.**

Key Words: *tuberous sclerosis complex, pregnancy, renal angiomyolipoma, lymphangiomyomatosis, pneumothorax*

Tuberous sclerosis complex (TSC) is a disorder often characterized by facial angiofibromas, mental retardation, and seizures. Although the incidence of mental retardation in TSC has been estimated to be almost 50%,[1] the degree of retardation is highly variable, and a significant proportion of affected individuals have normal or mildly impaired intelligence. Women in this group wish to know the risks of pregnancy to their health. No studies have formally addressed the question of how renal and pulmonary complications are affected by pregnancy. Case reports in the medical literature document episodes of hemorrhage or rupture of renal angiomyolipomas (RAML) in pregnant women with TSC.[2–14] In a study of 26 pregnancies among 11 women with lymphangiomyomatosis (LAM) and TSC, there were no adverse pulmonary events. Large-scale surveys of TSC have not addressed pregnancy risks. By collecting information about women with TSC who have been pregnant, we hoped to learn whether they were more likely to suffer catastrophic renal or pulmonary events than women with TSC who have never been pregnant.

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MATERIALS AND METHODS

Patients

A survey was mailed to 421 adult female members of the National Tuberous Sclerosis Association (NTSA), now the Tuberous Sclerosis Alliance (TS Alliance). Replies were received from 125 women (30% response rate). Telephone calls were made when clarification of information was required (i.e., timing of renal or pulmonary complications relative to a pregnancy, ages at occurrence of complications). Women who could not be reached by telephone were mailed a follow-up questionnaire for clarification of events. Fourteen of the 125 surveys were not included in further analyses because the diagnosis of TSC could not be confirmed or the information was deemed unreliable. Of the remaining 111 surveys, 90 were from women who had had at least one pregnancy, and 21 were from women who had never been pregnant.

The survey was designed to confirm the diagnosis of TSC and to obtain information about pregnancy history and any renal or pulmonary complications that occurred. Our goal was to calculate the percentage of women with renal and pulmonary complications and to determine whether these numbers differed between the pregnant and never-pregnant groups. For women who had had at least one pregnancy, we wanted to know when complications occurred, relative to the timing of pregnancy.

The databases from the Medical Genetics Clinics at the University of Washington and Children's Hospital and Regional Medical Center in Seattle were searched to identify families who had been evaluated for the diagnosis of TSC. Thirty-four women were identified who were at least 17 years of age at the

time of evaluation (childbearing age or older). Twenty-five had had at least one pregnancy, and nine had never been pregnant. Information about renal and pulmonary involvement and complications was obtained from their files and medical records. The Institutional Review Board at the University of Washington reviewed the proposal and classified it as exempt.

Information obtained from the chart review was combined with the survey data for all analyses. The total number of women was 145. One hundred and fifteen had had at least one pregnancy, and 30 had never been pregnant.

Literature search

The PubMed database was searched for relevant articles using the following combinations of search terms: TSC and angiomyolipoma, TSC and pregnancy, TSC and LAM, pregnancy and angiomyolipoma, pregnancy and LAM, and pregnancy and pneumothorax. These articles were reviewed to document previous reports of renal and pulmonary complications during pregnancy in women with TSC.

Statistical analysis

The data were entered in an SPSS database (Chicago, IL). For comparing means, we used the two-tailed *t* test. For proportions, the Fisher exact test or Chi-square test with two-tailed *P* values was used. Comparisons with known population values were based on the binomial distribution. A two-tailed *P* value <0.05 was considered statistically significant. Posthoc power calculations are reported in the footnotes of Tables 3 and 5.

RESULTS

Demographics

The never-pregnant women were significantly younger than those who had been pregnant in both age at diagnosis and age at the time of the study (for survey women) or last evaluation (for chart review women). The ages at first renal or pulmonary complication did not differ significantly between the two groups (Table 1).

Table 1
Subjects

	Pregnant	Never been pregnant	*P* value (*t* statistic)[e]
Total number	115	30	
Survey	90	21	
Chart review	25	9	
Age at diagnosis[a]	24.9 (12.7)	16.1 (12.8)	0.001 (3.3)
Age information obtained[b]	41.1 (11.1)	35.1 (9.3)	0.008 (2.7)
Age at first renal complication[c]	33.8 (12.1)	30.2 (8.8)	0.350 (0.94)
Age at first pulmonary complication[d]	32.6 (7.9)	29.3 (4.7)	0.519 (0.67)

Data are mean ages in years (+/− SD).
[a]These data are for 107 pregnant women and 28 never-pregnant women, representing 106 survey and 29 chart review women.
[b]For survey patients, age is as of December 31, 2001; for chart review patients, age is at last clinic visit/evaluation. These data are for 113 pregnant women and 29 never-pregnant women, representing 109 surveys and 33 chart reviews.
[c]Age at the time of first renal angiomyolipomas (RAML)-related complication, in women with renal involvement. These data are for 37 pregnant women and 12 never-pregnant women.
[d]Age at the time of first pulmonary complication (pneumothorax). These data are for 10 pregnant women and 3 never-pregnant women.
[e]*P* value is the two-tailed *t* test calculated between pregnant and never-pregnant groups. $P < 0.05$ is considered significant.

Renal involvement and complications

Positive renal involvement was defined as the presence of cysts or RAML on an imaging study. There was no information about renal involvement for 16% of women, either because an imaging study had not been done or the woman could not remember the results (Table 2). Of those for whom we had information ($n = 121$), renal involvement was reported in 67 of 95 (71%) of the women who had been pregnant and 18 of 26 (69%) of the women who had never been pregnant ($P = 0.91$).

We considered renal complications to include RAML-related hypertension, hemorrhage, pain, rupture, and renal failure and RAML-related treatments such as embolization, nephrectomy, and transplant. We did not consider pregnancy-induced hypertension that resolved after delivery to be a renal complication. There were 67 women with renal involvement who had had at least one pregnancy (Table 3). Thirty-eight of these 67 (57%) women had a total of 47 renal complications. Six of the complications occurred before a first pregnancy, 9 occurred during a pregnancy, and 32 occurred between 6 months and 40 years after a pregnancy. These complications are detailed in Table 4. During pregnancy, hemorrhage secondary to RAML occurred in 8 women: between the fifth and sixth months of gestation ($n = 1$, 1 required nephrectomy); between the sixth and seventh months of gestation ($n = 3$, 1 required embolization, 1 required nephrectomy, and 1 resolved spontaneously); and between 8 and 9 months gestation ($n = 2$, both resolved spontaneously). Two women underwent nephrectomy at 2 and 5 weeks, respectively, after delivery.

Fourteen of the 115 survey women reported a total of 17 pregnancies complicated by hypertension (including pregnancy-induced hypertension, preeclampsia, and eclampsia). Twelve of these were first pregnancies for the women and, in all cases, the hypertension resolved after delivery. Two women without known renal involvement (one with a negative renal ultrasound, the other not imaged) reported having hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome during pregnancy. No woman developed hypertension de novo following a pregnancy. For the chart review women, information about blood pressure during pregnancy was not available.

Of the 18 nulliparous women who had renal involvement, 12 (67%) had complications. This number is not statistically different from the percentage of women who had been pregnant and had renal complications ($P = 0.62$). There were 18 events among the 12 women (Table 4).

Table 2
Renal[a] and pulmonary[b] involvement in women with tuberous sclerosis

	No. women	No. with positive image (%)[c]	No. with negative image (%)[c]	No information	Test statistic[d]
Renal					
Pregnant	115	67 (71)	28 (29)	20	$\chi^2 = 0.01$ ($P = 0.91$)
Never been Pregnant	30	18 (69)	8 (31)	4	
Total	145	85 (59)	36 (25)	24 (16)	
Pulmonary					
Pregnant	115	25 (71)	10 (29)	80	Fisher exact ($P = 0.71$)
Never been Pregnant	30	8 (80)	2 (20)	20	
Total	145	33 (23)	12 (8)	100 (69)	

[a]Renal involvement is defined as the presence of cysts or renal angiomyolipomas (RAML) based on an imaging study or signs of RAML rupture.
[b]Pulmonary involvement is defined as the presence of cysts or lymphangiomyomatosis (LAM) based on an imaging study or occurrence of pneumothorax.
[c]Percentages are calculated based on the number of women with information available for the "pregnant" and "never been pregnant" categories. In the total row, percentages are based on the "total" number of women available.
[d]The test statistics are calculated by comparing the number of women with positive imaging vs. those with negative imaging for either renal or pulmonary involvement. No significant difference between the pregnant and never-pregnant groups with regard to renal involvement ($\chi^2 = 0.01$, $P = 0.91$ with the Yates correction) nor with regard to pulmonary involvement ($P = 0.71$ by two-tailed Fisher exact test).

Pulmonary involvement and complications

Positive pulmonary involvement was defined as the presence of cysts or LAM on an imaging study [computed tomography (CT) or magnetic resonance imaging (MRI) scan] or the occurrence of a pneumothorax. Of the women for whom we had information ($n = 45$), 35 had been pregnant and 10 had not. Pulmonary involvement was seen in 71% of those who had been pregnant and 80% of those who had never been pregnant ($P = 0.71$). Information regarding pulmonary status was unavailable for 69% of all the women because the majority of them had never had lung-imaging studies. None of these women reported signs or symptoms suggestive of clinically significant lung disease.

Twenty-five of the 115 (22%) women with pregnancies had pulmonary involvement. Ten of these 25 (40%) women experienced a pneumothorax (Table 5). Two episodes of pneumothorax occurred before pregnancy, 4 episodes occurred during the pregnancies of 3 women, and 10 pneumothoraces occurred among 7 women after pregnancy. These 10 women represent 29% of the pregnant women with known pulmonary status ($n = 35$).

Eight of the 30 women who had never been pregnant had pulmonary involvement. Three of these 8 women (38%) had a pneumothorax, 1 with 2 separate events (Table 5). These 3 women represent 33% of the never-pregnant women with known pulmonary status. There was no significant difference between the parous and nulliparous groups.

Outcomes of pregnancy

Pregnancy outcomes for the women with TSC were tabulated. The 115 women had 264 total pregnancies. There were 215 (81%) livebirths. Eight of the nine women who experienced pregnancy-related RAML hemorrhages delivered liveborn infants. Thirty-six pregnancies (13.6%) ended in miscarriage, and there was one ectopic pregnancy (0.4%). There were four stillbirths (1.5%). One was the result of uterine rupture in a woman with renal involvement, one was secondary to RAML rupture and severe blood loss in the mother, one was related to "malnutrition" from the mother's celiac sprue (mother also had renal involvement), and one was from unknown causes (mother's renal status unknown). Both of the women with HELLP delivered healthy

Table 3
Renal complications in women with tuberous sclerosis and renal involvement

	No. with renal involvement	No. of pregnancies	No. women with complications (%)	Total number of Complications		
				Before pregnancy	During pregnancy	After pregnancy
Pregnant	67	150	38 (57)	6	9	32
Never pregnant	18	NA	12 (67)			

NA, not applicable.
[a]Complications are defined as renal angiomyolipomas (RAML)-related hypertension, hemorrhage, or surgical intervention. In the pregnant group, these included eight women who had pregnancy-related hypertension in addition to separate events involving RAMLs. Percentage represents number of women with complications per number of women with renal involvement. There is no statistically significant difference between the percentages ($\chi^2 = 0.24$, $P = 0.62$ with the Yates correction) with regard to pregnancy status. This study had 80% power to detect a 32-point or greater difference in proportions between the pregnant and never pregnant groups.

Table 4
Renal angiomyolipomas (RAML)-related renal complications in 67 Pregnant and 18 never-pregnant women with tuberous sclerosis complex (TSC) and renal involvement

Before pregnancy
3 RAML hemorrhage at ages 12[a], 20[b], 21[c]
1 nephrectomy because of multiple, large RAMLs at age 26
1 renal failure at age 25
1 hypertension at age 16 secondary to RAMLs
During pregnancy
5 RAML hemorrhage requiring nephrectomy at ages 21[d], 22[a], 22, 22, and 29
2 RAML hemorrhage at ages 24, 31
1 RAML hemorrhage requiring embolization at age 24[n]
1 RAML-related renal pain at age 26
After pregnancy
10 RAML hemorrhage requiring nephrectomy at ages 30, 33, 33, 35, 36[c], 36, mid 40s, 41[e], 43[f], 52[f]
12 nephrectomies for multiple RAMLs at ages 25[d], 28[g], 29, 32, 34, 34, 36, 40[h], 45, 49, 63, 66
2 RAML hemorrhages requiring embolization at ages 39, ?[g]
2 nephrectomy for malignant changes in a RAML at ages 39[h], in 50s
2 RAML-related renal pain at ages 21 and 40
1 RAML hemorrhage without further treatment at age 33
1 cyst infarct at age 42[e]
1 renal transplant for RAML-related renal failure at age 41[b]
1 microscopic hematuria at age 42
Never pregnant
Partial nephrectomy for large RAML at ages 30, 33, 41[i], 41[j], 42[k]
Partial nephrectomy for RAML bleed at age 13[l]
Bilateral nephrectomy and renal transplant at age 26
Embolization of RAML at ages 27[l], 34[i]
Renal failure requiring dialysis at age 23
Renal biopsy for RAML at age 38, and for concern of cancer at age 40
Renal pain at 19[m], 42[k]
Increasing creatinine at age 35 secondary to RAML
Hypertension at ages 19[m], 28, 40[j]

[a,b,c,d,e,f,g,h,i,j,k,l,m]Superscripted letters refer to events that occurred in the same woman.
[n]Previously reported in Mayo Clinic Health, April, 1996 and Fairmont Clinic newsletter, April, 1996.

infants, although one required a cesarean section at 27 weeks. No women were known to have died during pregnancy or childbirth. These values are not statistically different from the published rates of miscarriage (10–15%) and stillbirth (approximately 1%) in the general pregnant population ($P = 0.30$ and $P = 0.30$, respectively).[15] There were also eight (3%) voluntary terminations of pregnancy.

DISCUSSION

The term tuberous sclerosis complex refers to two clinically similar but genetically distinct autosomal dominant conditions characterized by hamartomatous growths in different organ systems. The disorder results from a mutation in one of two genes, *TSC1* on chromosome 9 and *TSC2* on chromosome 16.[16,17] The exact function of the two protein products, hamartin and tuberin, is unknown, but it is thought that they may function as tumor suppressors. There is much clinical variability among patients, even among individuals within the same family. Diagnosis is established on clinical grounds[18] and includes the following features:

1. Central nervous system (CNS): cortical tubers, giant cell astrocytomas, subependymal nodules.
2. Eye: hypopigmented patches, mulberry spots.
3. Heart: rhabdomyomas.
4. Kidney: cysts, angiomyolipomas (RAML).
5. Lung: cysts, LAM.
6. Skin: hypopigmented spots (ash leaf or confetti); connective tissue nevi; angiofibromas; periungual fibromas.

Cardiac rhabdomyomas, severe epilepsy, and mental retardation account for the majority of morbidity and mortality in pediatric patients with TSC. In adults, morbidity and mortality are associated primarily with renal and pulmonary complications, especially in women. It is estimated that 70% of adults with TSC have renal involvement.[19] There is little information available about the effect of pregnancy on the development of RAML and the occurrence of complications, such as hemorrhage. In the literature, case reports of pregnancy in women with TSC suggest that it is high risk.[2–14]

Pregnancy did not appear to increase either the prevalence of renal involvement or the risk of a renal complication in the women we studied. Of the 67 women with renal involvement who had been pregnant, 57% ($n = 38$) had a complication. Of the 18 women with renal involvement who were never pregnant, 67% ($n = 12$) had a complication ($P = 0.62$). When we consider renal hemorrhage alone, however, 30% of women with a history of pregnancy and known renal involvement experienced a RAML hemorrhage (20/67), compared with 11% (2/18) of women with known renal involvement in the never-pregnant group. This may be because of the significantly younger age of the latter group (41.1 years vs. 35.1 years; $P = 0.008$).

Rupture of a RAML occurred in 21% of the published reports of pregnancies in women with TSC (Table 6). In our series, the incidence of RAML rupture during pregnancy is much lower. Only 6.0% of the pregnancies in women with TSC and renal disease were complicated by RAML events. The actual risk could be much lower because we may have failed to identify renal disease in some women. There were 43 pregnancies in 20 women with unknown renal status, and some of these women may have had undetected renal involvement. For all pregnant women with TSC, the percentage of pregnancies with a reported RAML complication was 3.4%. In general, RAML hemorrhage occurred in the second or third trimester. Despite

Table 5
Pulmonary complications in women with tuberous sclerosis

	No. women with pulmonary involvement	No. of pregnancies	No. women with complications[a] (%)	Total number of Complications		
				Before pregnancy	During pregnancy	After pregnancy
Pregnant	25	61	10 (40)	2[b]	4[c]	10[d]
Never pregnant	8	NA	3 (38)[e]			

NA, not applicable.
[a]Complications are defined as pneumothorax. Percentage represents number of women with complications per number of women with pulmonary involvement. There is no statistically significant difference between the percentages ($P = 1.00$ by the two-tailed Fisher exact test). This study had 80% power to detect a 52-point or greater difference in proportions between the pregnant and never-pregnant groups.
[b]These events occurred in two separate women at the ages of 23 and 34 years.
[c]These events occurred in three separate women at the ages of 26 (7 months gestation), 29 (two pneumothorax events at 8 months gestation), and 37 years (8 months gestation).
[d]These events occurred in seven different women at the ages of 24 and 39 (separate events in the same woman at these ages), 25 and 26 (separate events in the same woman), 30s, 33, 34 (two events in the same woman at this age), 41, and 48 years.
[e]These events occurred in three separate women at the ages of 24, 31, and 33 (separate events in the same woman), and 33 years.

this complication, the pregnancy outcomes were good, with only one stillbirth reported.

Eleven percent of the pregnancies of women with known renal involvement was complicated by blood pressure problems. Ten percent of all the pregnancies in women with TSC, without regard to renal status, was complicated by an elevation in blood pressure. These values are similar to the incidence in the general pregnant population, in which approximately 3 to 10% experience a problem with blood pressure during the 9 months of gestation.[20,21] The incidence of blood pressure problems during pregnancy for women with TSC, as collected from case reports in the literature, is 12%, which is similar to our result. In our original survey design and initial follow-up telephone calls, we did not ask specifically about gestational hypertension or hypertension-related events. We relied on women volunteering this information, so it is possible that we underestimated the number of hypertensive events. Thus, there may be a slightly increased risk of pregnancy-induced hypertension in women with TSC because of their underlying disease. Because the women with pregnancy-induced hypertension reported resolution after the pregnancy ended, it does not appear that undertaking a pregnancy predisposes a woman with TSC to develop chronic, persistent hypertension. The incidence of HELLP in the general pregnant population has been reported to be 0.05%.[22] Among the women in our survey, there were two episodes of HELLP during 264 pregnancies (0.76%), a higher percentage than the general population. Further studies looking at larger groups of women with TSC may be able to clarify the issue of blood pressure problems during pregnancy.

Pulmonary LAM can occur as an isolated finding or as part of TSC. For reasons that are not known, it predominantly affects women. The prevalence of LAM in adult women with TSC has been observed to be greater than 30% based on radiologic criteria.[19,23] The occurrence of symptomatic LAM appears to be much lower, less than 4%.[19,23] There is a paucity of published reports on the effects of pregnancy on the pulmonary manifestations of TSC. One report described four pneumothoraces during pregnancy among seven women with isolated LAM and no other features of TSC.[24] Another two of the women experienced chylous effusions requiring drainage or thoracotomy during pregnancy. In another study, no adverse pulmonary events occurred during 26 pregnancies among 11 women with LAM and TSC.[23] In our study, we found no significant difference in the prevalence of pulmonary involvement between the women who had been pregnant and those who had not. The only pulmonary complication identified in the women we studied was pneumothorax. Three of the 61 (4.9%) pregnancies of women with known pulmonary involvement were complicated by pneumothorax. These events were all in the third trimester. When all pregnancies of women

Table 6
Review of case reports of renal complications in tuberous sclerosis complex (TSC) pregnancies: a comparison with our data

	No. of women	Total no. of pregnancies	No. of pregnancies with RAML complications[a] (%)	No. of pregnancies with hypertension[a] (%)
Literature case reports[b]	16	33	7 (21)	4 (12)
Our data (pregnant women with renal involvement)	67	150	9 (6.0)	17 (11.3)
Our data (all pregnant women)	115	264	9 (3.4)	27 (10.2)

[a]Percentages represent the number of pregnancies with either renal angiomyolipoma (RAML)-related complications or hypertension-related complications [pregnancy-induced hypertension, preeclampsia, eclampsia, or hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome] out of the total number of pregnancies for each group of women.
[b]This represents a summary compilation of 13 case reports in the medical literature regarding pregnancy outcomes in women with TSC.[1–13]

with TSC were included, regardless of pulmonary status, pneumothorax occurred in 1.1%.

Forty percent of the women with pulmonary involvement who had been pregnant experienced a pneumothorax at some time in their lives. This is compared with a 38% incidence of pneumothorax in the women with known pulmonary involvement who had never been pregnant. This difference is not statistically significant. These results must be interpreted with caution because 70% of the women in our study had not had imaging of their lungs.

There are several limitations to this study. All information was obtained by self report for the survey participants, and no attempts were made to obtain medical records. Although information was obtained from the medical records for the women involved in the clinical chart review, longitudinal follow-up was lacking for many of them. Fifty-nine of the 115 (51%) women in the study did not know they had TSC before becoming pregnant. Therefore, we could not establish their renal or pulmonary status before their first pregnancy.

This study does not purport to establish the risk for pulmonary or renal disease in women with TSC per se. We were interested in establishing accurate risk estimates for women with TSC who are considering pregnancy. This population presumably represents a subset of women with TSC and less severe CNS involvement. This study also did not address the risks of seizures or seizure medications in pregnancy.

As with all studies that involve a voluntary questionnaire, results may be biased. The survey was sent to members of a support group for people with TSC. This is a self-selected group, interested in obtaining information about their disorder. Severely affected women may not have been able to respond to the questionnaire. Alternatively, a woman more severely affected by TSC might have been more motivated to contribute information to a research study to help advance knowledge of the disease.

The pregnant and never-pregnant groups differed significantly with regard to average age at diagnosis and average age at last evaluation, with the mean ages for both of these parameters lower in the group that had never been pregnant. Thus, our results may be biased in terms of underestimating ultimate development of renal or pulmonary complications in the women who had never been pregnant. Conversely, if these risks increase with age, the never-pregnant group may have had more clinically apparent disease, leading to earlier diagnosis. However, when we compare the pregnant and never pregnant groups with regard to age at first renal or pulmonary complication, there is no statistically significant difference between the two groups. The increased severity of their TSC may have made the nulliparous women less likely to choose to undergo a pregnancy. Several of the women who had never been pregnant commented that this was a conscious choice necessitated by severe renal manifestations of TSC. In contrast, a number of the women who had been pregnant were not diagnosed with TSC until after the birth of an affected child, suggesting that they had mild clinical signs of the condition. Although it may be true that this study is biased to a more benign outcome associated with pregnancy because it is only women with milder disease who are likely to reproduce, it is exactly these individuals who are likely to be concerned with the risks of pregnancy and for whom these results have relevance. This study does not pretend to evaluate the fundamental biological effects of pregnancy at the cellular level in TSC.

We cannot rule out the possibility that pregnancy increases the likelihood or number of renal or pulmonary complications later in life. Perhaps, if we followed these women until they were elderly, we might see a difference in the rate of complications between the two groups.

On the basis of our data, we suggest that all women who experience a RAML or a pneumothorax be thoroughly screened for TSC because both of these events are rare in the general population and may be the first presenting sign in a woman in whom the classic cutaneous features may be absent or overlooked. In fact, for several of the women in our study, one of these events was the initial manifestation of TSC.

While interviewing these women with TSC, it became apparent that adequate screening for renal and pulmonary involvement is not occurring. Approximately 20% of the women in our survey had never had a renal ultrasound, and some were unaware that one was indicated. Some of them had been diagnosed many years ago and had not undergone subsequent renal imaging. The situation for pulmonary screening was even worse because approximately 70% of the women had not had imaging studies of the lungs or pulmonary function tests. Many did not know that TSC could affect their lungs. Current recommendations for the care of an individual with TSC include a renal ultrasound examination every 1 to 3 years, with renal CT or MRI scan if large or multiple lesions are detected.[25] A single chest CT scan should be done at adulthood for women with TSC to look for pulmonary cysts or LAM. Follow-up studies should be performed as necessary for any signs or symptoms that occur.[25] This study demonstrates the need for wider dissemination of the current consensus screening recommendations so that women with TSC can have adequate health-care supervision.

Our results are encouraging for women with TSC who are considering becoming pregnant. Pregnancy does not appear to significantly increase the risk of pneumothorax or RAML-related complications in women with TSC. Furthermore, the rupture of a RAML does not necessarily lead to maternal or fetal demise. Women with TSC should have renal and pulmonary evaluations before becoming pregnant and should be followed closely during a pregnancy. Almost all the renal and pulmonary complications occurred after 6 months gestation, suggesting that the last trimester of a pregnancy may be the most important time for close medical follow-up. Prospective studies of women with TSC during pregnancy may provide more specific recommendations for management.

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