Low aspirin use and high prevalence of pre-eclampsia risk factors among pregnant women in a multinational SLE inception cohort

Women with systemic lupus erythematosus (SLE) carry a substantially higher risk for pre-eclampsia compared with the general population.[1] Aspirin reduces the risk of pre-eclampsia in high-risk pregnancies by more than half[2] and thus is recommended in SLE.[3–5] The European League Against Rheumatism recommends aspirin in SLE pregnancies, particularly in those with nephritis or positive antiphospholipid antibodies (aPL).[5] Despite this, little is known about current practice. Therefore, we assessed the prevalence of aspirin use in SLE pregnancies within the Systemic Lupus International Collaborating Clinics inception cohort, which has been described elsewhere.[6]

SLE women aged 18–45 with a pregnancy documented at one or more annual study visits (spanning 2000–2017) were included. For each pregnant visit, aspirin use, traditional pre-eclampsia risk factors (hypertension, chronic kidney disease, diabetes, nulliparity, body mass index ≥35, age >40), aPL and active lupus nephritis were assessed (see variable definitions in online supplementary material). Aspirin use was compared among those with and without each/any risk factor, and over time.

We identified 475 pregnancies among 300 women. Mean SLE duration at the time of pregnancy was 5.6 years (SD 3.1). Half (51%) of pregnancies had ≥1 traditional pre-eclampsia risk factor, 34/104 (33%) had positive aPL and 53/475 (11%) had nephritis (table 1). Aspirin was used in 121 (25%) pregnancies. While a third of pregnancies in Caucasians (71/209, 34%, 95% CI 28% to 41%) and Hispanics (20/62, 32%, 95% CI 22% to 45%) were aspirin exposed, only 9/88 (10%, 95% CI 5% to 18%) and 7/66 (11%, 95% CI 5% to 20%) of pregnancies in Black and Asian subjects were respectively aspirin exposed. Aspirin use did not differ among pregnancies with or without ≥1 traditional risk factor (58/234, 25% (95% CI 20% to 31%) vs 63/241, 26% (95% CI 21% to 32%)), any traditional risk factor individually, or nephritis (see online supplementary table 1). There was a potential trend for increased aspirin use among pregnancies with positive aPL (13/34, 38%, 95% CI 24% to 55%) compared with those without aPL (16/70, 23%, 95% CI 15% to 34%), although CI overlapped. Sensitivity analyses excluding multiple pregnancies within the same women yielded similar results. Aspirin use did not increase from 2000 to 2017 (χ^2 test for trend in proportions, p=0.13).

Our study is the first to assess aspirin use in SLE pregnancies according to the presence of pre-eclampsia risk factors. Among the 475 SLE pregnancies in this prospective, multinational inception cohort, additional pre-eclampsia risk factors were present in half, while aspirin was taken in only one-quarter and did not differ from background aspirin use among the same women at non-pregnant visits (see online supplementary material). Even without considering SLE itself as a major risk factor, aspirin use was no more prevalent among those with other traditional indications for aspirin in pregnancy, and the majority of those with aPL and nephritis were not taking aspirin. The low aspirin use among Black SLE subjects is noteworthy given the worse reproductive outcomes observed in this population.[7]

Table 1 Characteristics of SLE pregnancies overall and according to aspirin use

Characteristic	All pregnant visits (n=475)*	Pregnant visits with aspirin (n=121)	Pregnant visits without aspirin (n=354)
Patient characteristic			
Age, mean (SD)	31.0 (4.9)	30.5 (4.6)	31.2 (5.0)
Ethnicity, n (%)			
Asian	66 (14)	7/66 (11)	59/66 (89)
Native North American	3 (1)	2/3 (67)	1/3 (33)
Black	88 (19)	9/88 (10)	79/88 (90)
Caucasian	209 (44)	71/209 (34)	138/209 (66)
Hispanic	62 (13)	20/62 (32)	42/62 (68)
Indian subcontinent	25 (5)	8/25 (32)	17/25 (68)
Other	22 (5)	4/22 (18)	18/22 (82)
Country, n (%)			
Canada	121 (25)	27/121 (22)	94/121 (78)
USA	105 (22)	20/105 (19)	85/105 (81)
Mexico	52 (11)	19/52 (37)	33/52 (63)
Europe	146 (31)	49/146 (34)	97/146 (66)
South Korea	51 (11)	6/51 (12)	45/51 (88)
Any postsecondary education, n (%)	310/452 (69)	69/310 (22)	241/310 (78)
BMI, mean (SD)	25.8 (5.9)	26.3 (5.2)	25.6 (6.1)
Obstetrical history			
Parity, mean (SD)	1.1 (1.0)	1.1 (1.0)	1.2 (1.0)
Nulliparous, n (%)	134/461 (29)	37/134 (28)	97/134 (72)
Previous fetal loss <24 weeks, n (%)	84/456 (18)	22/84 (26)	62/84 (74)
SLE characteristics			
Disease duration (years), mean (SD)	5.6 (3.3)	5.6 (3.3)	5.6 (3.3)
SLEDAI, mean (SD)	3.3 (3.8)	3.0 (3.6)	3.4 (3.9)
SLICC damage score, mean (SD)	0.5 (1.0)	0.6 (1.0)	0.5 (1.0)
Any positive aPL, n (%)	34/104 (33)	13/34 (38)	21/34 (62)
LAC, n (%)	19/104 (18)	6/19 (32)	13/19 (68)
ACL, n (%)	12/104 (12)	3/12 (25)	9/12 (75)
GP1 IgG, n (%)	18/104 (17)	9/18 (50)	9/18 (50)
Nephritis, n (%)	53(11)	11/53(21)	42/53 (79)
Comorbidities			
Any renal disease†, n (%)	83 (17)	17/83 (20)	66/83 (80)
CKD (eGFR≤90 mL/min/1.73 m²), n (%)	43/459 (9)	6/43 (14)	37/43 (86)
CKD stage ≤3 (eGFR≤60 mL/min/1.73 m²), n (%)	11/459 (2)	5/11 (45)	6/11 (55)
Hypertension, n (%)	79 (17)	24/79 (30)	55/79 (70)
Taking anticoagulation, n (%)	28 (6)	12/28 (43)	15/28 (54)
Year of pregnancy visit			
2000– 2004, n (%)	39 (8)	11/39 (28)	28 (72)
2005– 2009, n (%)	157 (33)	46/157 (29)	111/157 (71)
2010– 2014, n (%)	218 (46)	52/218 (24)	166/218 (76)
2015– 2017, n (%)	61 (13)	12/61 (20)	49/61 (80)

*Denominator=475 unless otherwise stated.
†Includes chronic kidney disease, active nephritis and/or nephrotic syndrome within the last year.
ACL, anticardiolipin antibody; aPL, antiphospholipid antibody; BMI, body mass index; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; GP1, anti-B2-glycoprotein-1; LAC, lupus anticoagulant; SLE, systemic lupus erythematosus; SLEDAI, Systemic Lupus Erythematosus Disease Activity Index; SLICC, Systemic Lupus International Collaborating Clinics.

Study limitations include lack of data on gestational age and pregnancy outcomes. In addition, aspirin could have been introduced at/or following the study visit when the pregnancy was documented, highlighting the importance of the rheumatologist in reviewing aspirin use and initiating it, if not already

done, in pregnant SLE women. However, assuming either a somewhat normal or a left-skewed distribution of gestational ages at the pregnant visits, a substantial proportion of visits would have taken place after 12–16 weeks' gestation, by which time aspirin should have been initiated.[2 3]

In conclusion, we have potentially identified an important gap between practices and current recommendations for the care of pregnant SLE women, and call for further studies of factors contributing to aspirin use in lupus pregnancies.

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