

INTRODUCTION

Preterm birth (PTB) is a major global contributor to neonatal morbidity and is associated with long-term adverse health outcomes of the children, such as learning disabilities [1]. Women with systemic lupus erythematosus (SLE) have a substantially increased risk of preterm delivery compared with the general population [2]. SLE-related risk factors for PTB reported in a recent meta-analysis include high disease activity, antiphospholipid antibodies, lupus nephritis, and hypertension [3]. However, the included studies are based on heterogeneous populations (e.g. varying levels of disease activity and planned vs. unplanned pregnancies).

AIM

To explore **risk factors for PTB** and to develop a **prediction model** for this outcome **in women with SLE** using the nationwide, multicentre, longitudinal German pregnancy register Rhekiss.

METHOD

- Women with SLE and a singleton pregnancy reported between 2015 and 2023.
- Description of maternal and disease-related characteristics, overall and stratified according to PTB.
- For regression models, two methods were applied:
 - (1) a multivariable logistic regression model including risk factors a priori selected based on literature [3]
 - (2) a prediction model which was developed using bootstrap resampling (1,000 iterations) with backward variable selection based on the Bayesian information criterion within each of the 30 imputed data sets.

Model performance was internally validated using the Brier score. The final model was defined as the model with the best average predictive performance across all 30,000 bootstrap iterations.

RESULTS

Table 1: Descriptive characteristics, first trimester		Total (n=274)	Preterm birth (n=42)	Full-term birth (n=232)
Demo-graphics	Maternal age ^{#1} , years	32±4.2	31.5±3.6	31.5±4.3
	Body Mass Index ^{#1} , kg/m ²	23.4±4.5	22.9±3.9	23.5±4.6
	Ever smoker ^{#2} , yes	70 (31%)	6 (19%)	64 (33%)
Disease activity	SLE-duration ^{#1} , years	8.3±5.4	9.4±5.8	8.1±5.8
	SLEDAI ^{#1}	1.8±2.8	2.2±3.3	1.8±2.7
	Disease activity (physician-reported, NRS 0-10) ^{#1}	1.5±1.4	1.6±1.4	1.5±1.4
	Disease activity (patient-reported, NRS 0-10) ^{#1}	2.1±1.9	2.4±1.7	2.0±1.9
Disease severity	Moderate SLE (compared to other SLE-patients) ^{#2#3}	72 (33%)	11 (36%)	61 (33%)
	Severe SLE (compared to other SLE-patients) ^{#2#3}	37 (17%)	9 (29%)	28 (15%)
	Antiphospholipid syndrome/antibodies ^{#2} , yes	79 (30%)	14 (33%)	65 (29%)
Comorbidities	Glomerulonephritis/chronic renal disease/creatinine > 1 mg/dl ^{#2} , yes	45 (16%)	10 (24%)	35 (15%)
	Chronic/gestational hypertension ^{#2*} , yes	42 (15%)	16 (38%)	26 (11%)
	Chronic/gestational diabetes ^{#2*} , yes	15 (6%)	2 (5%)	13 (6%)
Laboratory values	Low C3 ^{#2} , yes	41 (21%)	7 (25%)	34 (21%)
	Low C4 ^{#2} , yes	30 (16%)	4 (14%)	26 (16%)
	Platelet count ^{#1} , x 1000 /µl	237.1±64.8	213.9±69.8	241.2±63.2
	Leukocyte count ^{#1} , x 1000 /µl	7.3±2.3	6.7±1.9	7.4±2.3
	Hemoglobin ^{#1} , g/dl	12.5±1.1	12.2±1.2	12.5±1.1
	C-reactive protein ^{#1} , mg/l	4.5±6.8	4.9±6.5	4.4±6.9
Antibodies	Proteinuria/hematuria ^{#1} , yes	41 (19%)	10 (31%)	31 (17%)
	Anti-dsDNA ^{#2} , yes	157 (64%)	25 (68%)	132 (63%)
	Anti-SSA (Ro) antibodies ^{#2} , yes	94 (40%)	13 (36%)	81 (41%)
	Anti-SSB (La) antibodies ^{#2} , yes	48 (21%)	2 (6%)	46 (23%)
	Anti-U1-ribonucleoprotein antibodies ^{#2} , yes	33 (15%)	9 (27%)	24 (13%)

^{*}History of comorbidity prior to conception or during pregnancy; ^{#1} mean±SD; ^{#2} n (%); ^{#3} assessed by physician

Descriptive statistics

Of the total of 274 pregnancies available for analysis, 42 (15%) resulted in PTB.

- Women with PTB tended to have a longer duration of SLE compared to those with full-term birth as well as higher disease activity, and the SLE disease was reported as severe in a higher proportion of women with PTB. However, the absolute disease activity (SLEDAI) was low in this cohort (Table 1).
- Antiphospholipid syndrome or antibodies, indicators of renal involvement, and particularly hypertension were more prevalent among the PTB group.
- Laboratory parameters showed lower mean platelet counts, leukocyte counts, and haemoglobin levels in women with PTB, alongside modestly higher C-reactive protein levels. Immunological parameters were largely similar between the two groups, although anti-U1-RNP antibodies were more common in the PTB group.

Regression models

- In model (1), hypertension was the only factor associated with PTB (Table 2).
- In the prediction model (2), hypertension was selected as a robust predictor of PTB, alongside patient-reported disease activity (NRS) and smoking status as further predictors.

Table 2	Model (1)*	Model (2)**
	Odds Ratio (95% CI)	Odds Ratio (95% CI)
Chronic/gestational hypertension, yes	5.11 (2.12-12.29)	4.98 (2.22-11.14)
SLEDAI, per 1 unit increase	1.06 (0.94-1.20)	
Antiphospholipid syndrome/antibodies, yes	1.16 (0.55-2.46)	
Glomerulonephritis/chronic renal disease/creatinine > 1 mg/dl, yes	0.73 (0.27-1.97)	
Maternal age, per year	0.99 (0.91-1.07)	
Disease activity (patient-reported, NRS 0-10), per 1 unit increase		1.18 (0.94-1.48)
Ever smoker, yes		0.39 (0.14-1.11)

^{*}Based on literature review. ^{**}Based on backward selection with Bayesian information criterion.

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CONCLUSIONS

Overall, **hypertension was the most robust and consistent predictor of PTB** in this cohort of women with mostly mild to moderate SLE at start of the pregnancy. The counterintuitive association between smoking and PTB is likely explained by epidemiological bias as previously reported for preeclampsia and smoking [4], and requires further investigation.