Methods We characterized subgroups of patients using sociodemographic and clinical EHR data, and genetic data from previously collected cohorts, for 416 individuals with SLE. Single nucleotide polymorphisms (SNPs) were genotyped on the ImmunoChip. In our analysis, we included 95 variants previously associated with SLE risk. Variables extracted from the EHR included age, sex, race, ethnicity, and disease-associated laboratory results: complement C3 and C4, SSA, SSB, RNP, anti-Smith, and anti-dsDNA. We first determined subtypes by clustering variables using multi-trait finite mixture of regressions (MFMR), a new clustering method designed for large, multi-trait genome-wide datasets that appropriately accounts for the complex structure of our multi-ethnic dataset. We then used regression analyses to examine whether clinical and genetic variables had differential effects across clusters.

Results Approximately 90% of patients were female; 52% were white, 13% African-American, 13% Asian, and 22% other/mixed race. Results demonstrated three distinct clusters (Figure). Cluster 1 (n=165) was characterized as predominately white, non-Hispanic/Latino patients with higher age of onset. Cluster 2 (n=121) had a higher percentage of other/mixed race individuals with mild disease. Cluster 3 (n=130) was categorized by more severe disease, including individuals with a higher percentage of abnormal laboratory values (C3 and C4 levels,+RNP,+anti dsDNA,+SSA,+SSB) and lower age of onset. Eleven SNPs demonstrated significant genotype-cluster interaction with various phenotypes after correction for multiple testing.

Conclusions We identified three distinct subgroups of SLE via unsupervised clustering of sociodemographic and clinical variables derived from EHR and genetic data. Future work will further define these genotype-phenotype clusters and perform validation studies in additional cohorts. Our findings may assist in identifying disease treatments for SLE using a more personalized approach.

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59 WHEN STANDARD THERAPY IN PREGNANCY IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND ANTIPHOSHOLIPID ANTIBODIES IS NOT ENOUGH: THE GLOBAL ANTIPHOSPHOLIPID SYNDROME SCORE

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Background Current standard of care (SoC) in pregnancy for patients with Systemic lupus erythematosus (SLE) and/or aPL positivity includes treatment with low dose aspirin (75100 mg/day) and low molecular heparin or unfractionated heparin. However, up to 30% of women continue to have pregnancy complications despite SoC(1).

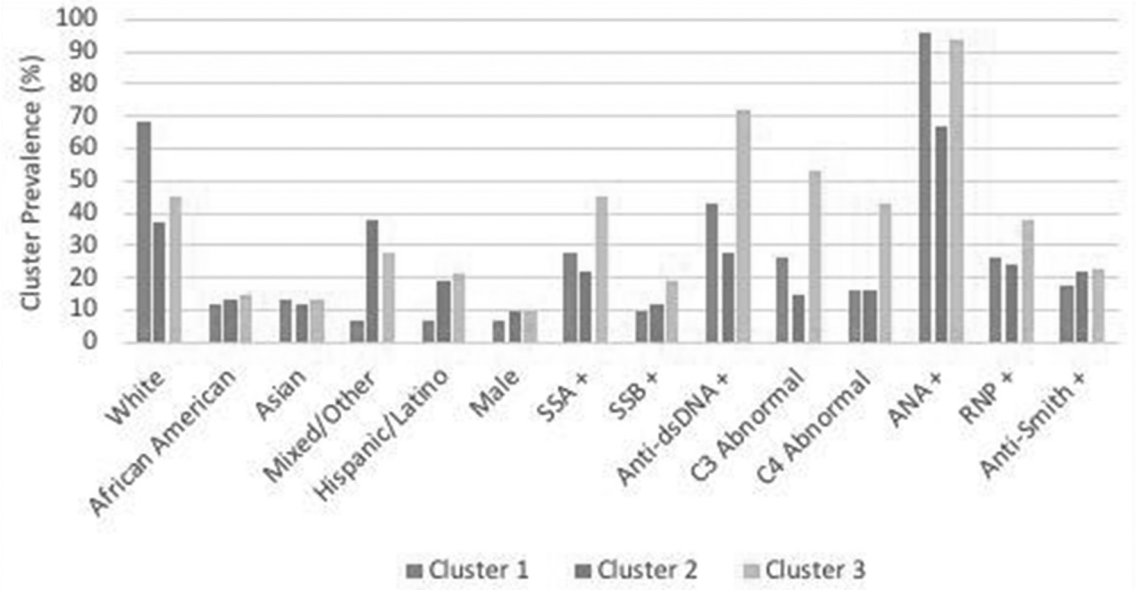
We aimed to assess the validity of the global antiphospholipid syndrome score(GAPSS)(2) in predicting pregnancy morbidity(PM) in patients treated with SoC.

Methods 143 women ever pregnant treated with SoC therapy with SLE and/or aPL positivity were included. Data on cardiovascular risk factors and aPL positivity were retrospectively collected. The individual GAPSS was calculated for each patient by calculating the sum of each risk factor score, as follows: 3 for hyperlipidaemia, 1 for arterial hypertension, 5 for anticardiolipin IgG/IgM, 4 for anti-2glycoprotein I IgG/IgM, 3 for anti-phosphatidylserine/prothrombin antibodies IgG/IgM and 4 for lupus anticoagulant. The patients GAPSS was then grouped according to the patients GAPSS into low risk (<6), medium risk (6-11) and high risk (12).

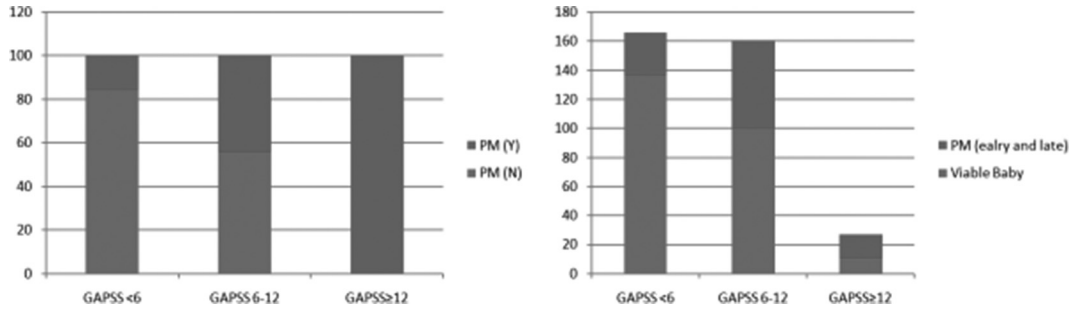
Results The analysis included 143 patients (mean age 30.8 ±6.4) with SLE (122;85.3%) and/or aPL positivity, for a total of 352 pregnancies.

Overall, we observed a live birth rate of 70.5%, with a total of live birth of 248 out of the 352 pregnancies. Forty-five patients (31%) experienced at least one event of PM, defined as early or late.

Patients were stratified according to GAPSS values, in order to identify a low risk group (GAPSS <6, n=72), a medium



Abstract 58 Figure 1 Prevalence of demographic and disease characteristics by cluster



Abstract 59 Figure 1 Pregnancy morbidity and live births divided in the three groups

risk group (GAPSS 6–11, n=66) and a high risk group (GAPSS12, n=5).

When considering patients who ever experienced PM while treated with SoC, all patients in the high risk group experienced PM, while patients in the medium group had a significant higher rate of PM when compared to the low risk group [29 (43.9%) patients V.s. 11 (15.3%), respectively; p<0.001]. When analysing the number of pregnancies in the three groups, patients in the high risk group had significantly lower live birth rates, when compared to the other groups [11 (40.7%) life births V.s. 100 (62.1%) and 137 (82.5%), respectively; p<0.05]. Furthermore, patients with medium risk group also had significantly lower live birth rates, when compared to the lower risk group (p<0.001).

Figure 1 resumes the results of PM and live births divided in the three groups.

Conclusions GAPSS might be a valuable tool in identifying patients at higher risk of developing any event of PM who might need additional therapeutic approach other than SoC.

Funding Source(s): N/A

60 ASSOCIATION OF SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) GENETIC SUSCEPTIBILITY LOCI WITH LUPUS NEPHRITIS IN CHILDHOOD-ONSET AND ADULT-ONSET WITH SLE

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Background Lupus nephritis (LN) is one of the most common and severe manifestations of systemic lupus erythematosus (SLE). We tested the association of SLE-risk loci with LN risk in childhood- (cSLE) and adult-onset SLE (aSLE).

Methods Two Toronto-based tertiary care SLE cohorts included cSLE (diagnosed <18 y) and aSLE patients (diagnosed 18y). Patients met ACR and/or SLICC SLE criteria and were genotyped on the Illumina MEGA or Omni1 arrays. Ungenotyped SNPs were imputed (1000 Genomes Project). HLA alleles were imputed in the Europeans only (SNP2HLA). Ancestry was inferred using principal components. We identified those with and without biopsy confirmed LN. HLA and non-HLA additive SLE risk-weighted genetic risk scores (GRSs) were tested for association with LN risk in logistic models, stratified by cSLE/aSLE and ancestry. Stratified effect estimates were meta-analyzed.

Results Of 1237 participants, 572 had cSLE (41% with LN) and 665 had aSLE (30% with LN). Increasing non-HLA GRS was significantly associated with increased LN risk (OR=1.26; 95% CI: 1.09, 1.46, p=0.0006) as was increasing HLA GRS in Europeans (OR=1.55; 95% CI: 1.07, 2.25; p=0.03). There was a trend for stronger associations between both GRSs and LN risk in Europeans with cSLE compared with aSLE.

Conclusions We observed an association between known SLE-risk loci and LN risk in children and adults with SLE, with the strongest effect observed among Europeans with cSLE. Future directions will include incorporating SLE-risk SNPs specific to non-European ancestral groups and validating findings in an independent cohort.

Funding Source(s): Dr. Hiraki: Canadian Institute of Health Research (CIHR) Project Scheme grant

61 DIFFERENCES IN ORGAN SYSTEM INVOLVEMENT ACROSS RACIAL/ETHNIC GROUPS: RESULTS FROM THE CALIFORNIA LUPUS EPIDEMIOLOGY STUDY

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Background SLE is a chronic disease that affects many organ systems and can cause permanent damage. We sought to determine if there are differences in patterns of SLE organ system damage among racial/ethnic groups.

Methods Data derive from the baseline visit of the California Lupus Epidemiology Study (CLUES), an ongoing cohort of patients in the San Francisco Bay Area with confirmed SLE diagnoses. Participants provided access to medical records and had a visit with a study rheumatologist. Race/ethnicity (White, African American, Hispanic of any race, and Asian) was determined by patient report. Due to the small sample size, patients from other racial groups were excluded from this analysis (n=5). Disease damage was measured using the SLICC/ACR Damage Index (SDI), calculated at the study visit. We examined damage at the organ system level, using items from the SDI, and defined glucocorticoid-related damage as avascular necrosis, diabetes, cataracts, and osteoporosis. Logistic regression was used to estimate the prevalence of damage in each organ system and the prevalence of glucocorticoid-related damage by race/ethnicity controlling for current age. We ranked the prevalence of damage in each organ system that comprises the SDI for each racial/ethnic group.