Researchers use blood serum markers to develop lupus risk index

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Researchers at the Feinstein Institute for Medical Research, USA have developed an index that identifies the risk for lupus based on the presence and amount of Immunoglobin G (IgG) and Immunoglobin M (IgM) antibodies and levels of C1q, a protein complex associated with protection from lupus, in blood serum. The findings are published in the open access journal *Molecular Medicine*.

The risk index, which needs to be validated in further studies, could be useful in following at risk individuals over time to identify those that may benefit from early interventions, and to identify diagnosed lupus patients who might be at risk of an impending flare.

Dr. Betty Diamond, the corresponding author said: "Lupus—or systematic lupus erythematosus (SLE) - is a multi-organ autoimmune disorder with disproportionally higher prevalence in individuals of West African descent. Understanding risk and why it differs between populations may enable prevention studies. Here we analyzed serum from unique populations with varying degrees of risk in order to identify serologic factors that might correlate with risk of or protection against SLE."

To compare potential biomarkers of SLE among women with different SLE risks, the authors analyzed blood serum samples from five cohorts: 40 Malian women with a history of malaria infection (MAL), 51 African American lupus patients (SLE), 80 healthy African American women (AAHC), 98 unaffected sisters of lupus patients (SIS), and 16 Caucasian

healthy controls (CHC).

The authors found that titers of IgM antibodies—which are known to protect against lupus onset—were lowest in the SLE, SIS and AAHC cohorts and higher in the MAL and CCH cohorts. Levels of IgG antibodies—the presence of which precedes lupus onset—were highest in the SLE and MAL cohorts and similar in the CHC, AAHC and SIS cohorts. The SLE cohort was also found to have the lowest C1q levels. C1q promotes immune tolerance, which includes stopping immune cells from attacking the body's own cells as is the case in autoimmune diseases such as lupus. Ninety percent of individuals with hereditary C1q deficiency also have lupus.

Dr. Diamond said: "The possibility that a risk index could help identify populations as risk for development of clinical lupus is novel and exciting. The risk index we developed was highest in SLE patients; second highest in unaffected sisters of SLE patients; third highest in healthy African-American women and lowest in healthy Caucasian women and malaria-exposed West African women. Thus, it confirms known lupus risk, as well as our hypothesis that high levels of IgG, low levels of IgM (and the resulting high IgG to IgM ratio) and low levels of C1q predispose to lupus. Our results also confirm the hypothesis that exposure to malaria results in increased levels of protective IgM antibodies and C1q which may delay onset of lupus in genetically predisposed individuals."

The authors caution that their risk index needs to be validated in future longitudinal studies which also need to determine the actual risk of developing SLE for each risk score. However, the observations made in this study may suggest new therapeutic approaches for SLE treatment and could eventually be used in early diagnosis, according to the authors.

More information: Jyotsna Bhattacharya et al, Serologic features of

cohorts with variable genetic risk for systemic lupus erythematosus, *Molecular Medicine* (2018). DOI: 10.1186/s10020-018-0019-4