The occurrence of childhood IgAV thus signifies the presence of a sustained predisposition to illness.

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Background: IgAV is a systemic disorder characterized by a predilection for deposition of immune complexes (ICs) in the glomeruli. The development of ICs is associated with circulating autoantibodies (aAbs), including anti-glomerular basement membrane (anti-GBM) and anti-epithelial cell autoantibodies (aECAbs).

Methods: This is a secondary analysis of familial data from the Australian Childhood Lupus (AusCLiP) cohort. The study population comprised 53 patients with biopsy-proven IgAV at diagnosis and first-degree relatives. Anti-GBM and anti-ECAb levels were assessed using indirect immunofluorescence and Western blot analysis respectively. The association between aAbs and aECAbs was assessed using the Cochran-Armitage trend test. Power calculations were performed using PASS 2008.

Results: Anti-GBM and anti-ECAb levels were significantly higher in IgAV patients compared with their healthy relatives (p < 0.05). A non-significant trend was observed for the association between anti-GBM and anti-ECAb levels (p = 0.08). The power to detect a significant association between anti-GBM and anti-ECAb levels was 95%.

Conclusion: The Australian Childhood Lupus (AusCLiP) cohort has the potential to provide important insights into the pathogenesis and aAbs associated with IgAV.

Disclosure of Interests: None declared.

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ASSOCIATIONS BETWEEN CIRCULATING LIPID MEDIATORS AND INCIDENT INFLAMMATORY ARTHRITIS IN AN AUTOIMMUNE RHEUMATIC DISEASES ANTIPOPULATION


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Background: Lipid mediators are endogenously derived from the metabolism of omega-3 and omega-6 polyunsaturated fatty acids (PUFAs) and have important roles in promoting and resolving inflammation in the body. Epidemiological studies have shown higher omega-3 PUFA status to be associated with a lower risk of both autoimmunity and progression to inflammatory arthritides (IA) (2,3).

Objectives: To determine the association of lipid mediators with progression from rheumatoid arthritis (RA)-related autoimmunity to inflammatory arthritis (IA).

Methods: We conducted a prospective cohort study using data from the Studies of the Etiologies of Rheumatoid Arthritis (SERA). SERA enrolled first-degree relatives of individuals with RA (FDR cohort) and individuals who screened positive for RA-related autoantibodies at health fairs (screened cohort). We followed 133 anti-CCP(3+) positive participants, of which 29 developed IA (22 classified as RA by 2010 ACR/EULAR criteria). We quantified lipid mediators from stored plasma samples via liquid chromatography tandem mass spectrometry methods validated against the collection and storage methods used in the study. A priori, we selected 5S-HETE, 15S-HETE and 17-HDHA because they are precursors to leukotrienes, Lipoxin A4 and Resolvins D series lipid mediators, respectively. We fit Cox proportional hazard models for each lipid mediator as a time-varying covariate. For lipid mediators significantly associated with progression to IA we then examined IL-1β, IL-6, IL-8 and TNF-α (Bio-Plex Pro™ assay) as potential mediators of this relationship.

Results: Higher plasma 5S-HETE levels were associated with an increased risk of incident IA after adjusting for age at baseline, cohort (FDR or screened), and shared epitope (SE) status (Table 1). The models examining 15S-HETE and 17-HDHA had the same trend but did not reach statistical significance. We did not find evidence that the association between 5S-HETE and IA risk was mediated by the tested pro-inflammatory cytokines, suggesting a direct role for this lipid mediator in conversion to IA.

Table 1. Hazard ratios and 95% confidence intervals of lipid mediator concentrations associated with IA, n=29 IA cases

<table>
<thead>
<tr>
<th>Lipid mediator</th>
<th>Crude</th>
<th>Adjusted</th>
</tr>
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<tbody>
<tr>
<td>5S-HETE</td>
<td>2.10 (1.12, 3.92)</td>
<td>2.41 (1.43, 4.07)</td>
</tr>
<tr>
<td>15S-HETE</td>
<td>1.81 (0.88, 3.93)</td>
<td>1.52 (0.87, 2.65)</td>
</tr>
<tr>
<td>17-HDHA</td>
<td>1.59 (0.68, 3.74)</td>
<td>1.61 (0.72, 3.56)</td>
</tr>
</tbody>
</table>

*a* denoted as <limit of detection (reference) or detected

Adjusted for SE, age at baseline and cohort

Conclusion: In a prospective cohort of anti-CCP positive individuals, higher circulating levels of 5S-HETE, an important precursor to pro-inflammatory leukotrienes, was associated with subsequent IA. Our findings highlight the potential pathologic and prognostic significance of these PUFAs metabolites in inflammatory processes in pre-RA populations.

References:


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