Understanding the Association of Neuropsychiatric Disease with Lupus Nephritis in Childhood-onset Systemic Lupus Erythematosus: A Retrospective Study (Research-In-Progress)

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Background

- What is childhood-onset systemic lupus erythematosus (cSLE)?
  - cSLE is a chronic autoimmune disease with a prevalence of 3.3 - 8.8 children per 100,000. It can affect multiple tissues and organs, including the kidneys and the brain (Levy et al, 2012).
- What are the symptoms of cSLE?
  - cSLE can cause inflammatory rashess anywhere on the body, pain in joints, swelling in feet, and/or extreme fatigue.
- What is lupus nephritis (LN)?
  - When cSLE attacks the kidneys, it is known as LN. LN is characterized by kidney inflammation and could result in kidney failure and death.
- Correlation between patients with LN and cSLE?
  - About 30-50% of patients that are diagnosed with cSLE will develop LN often within the first 2 years of cSLE diagnosis. According to previous studies, male cSLE patients have a higher prevalence of LN, and age does not play a significant role (Almaani et al, 2016).
- What neuropsychiatric diseases is this study focusing on?
  - The study focuses on cerebrovascular accidents: a loss of blood flow to parts of the brain, psychosis: a mental disability in which one loses the ability to recognize reality, and seizures: a burst of electrical activity in the brain (Arciniegas, 2015).
- Correlation between systemic lupus erythematosus (SLE) and neuropsychiatric diseases?
  - Studies note that patients with SLE have an incident rate of up to 20% for cerebrovascular accidents (CVA), especially within the first three years of SLE diagnosis. Patients with cSLE also have an increased risk for psychosis and seizures, at 5.3% and 7.1%, respectively (Meier et al, 2021; Amorim et al, 2017).
- Correlation between LN and patients with neuropsychiatric diseases?
  - Patients with LN have an increased risk of having neuropsychiatric diseases.

Although tremendous progress has been made regarding cSLE, there is still a lack of understanding about the association between LN and neuropsychiatric complications in children.

Aims

1. In cSLE, there is a higher prevalence of LN in non-White and patients with lower socioeconomic status (SES) compared to White patients, and patients with higher SES patients.
2. In cSLE the prevalence of neuropsychiatric manifestations higher in cSLE patients LN compared to cSLE patients without LN.

Methods

A retrospective cohort study of patients seen at Cincinnati Children’s Hospital Medical Center (CCHMC)

Study Design/Analysis

Study Population

Patients diagnosed with cSLE at CCHMC between January 2009 and 2012.

Inclusion Criteria

Individuals who meet 1997 ACR criteria for SLE and/or 2012 EULAR/SILC.

- ICD 9/ICD-10 codes corresponding to cSLE and/or CVA.
- < 18 years at time of cSLE diagnosis.
- Under the age of 25 at time of chart review (July 2023).

Exclusion Criteria

Patients with other autoimmune diseases, neonatal and drug-induced lupus.

Data Extraction

Data was manually extracted from the electronic record system into REDCap, a web-based application for clinical data to create databases and projects.

Data Analysis

We used chi-square test for analysis of categorical data and t-test for analysis of continuous data.

Results

Table 1: Socio-demographics of cSLE patients by presence of LN

<table>
<thead>
<tr>
<th>Race (n%)</th>
<th>cSLE with LN (n=34)</th>
<th>cSLE no-LN (n=130)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-White</td>
<td>18 (29%)</td>
<td>45 (71%)</td>
<td>.025</td>
</tr>
<tr>
<td>White</td>
<td>13 (14%)</td>
<td>80 (86%)</td>
<td></td>
</tr>
<tr>
<td>Sex (n %)</td>
<td>Male 5 (19%)</td>
<td>21 (81%)</td>
<td>.837</td>
</tr>
<tr>
<td>Female</td>
<td>29 (21%)</td>
<td>109 (79%)</td>
<td></td>
</tr>
<tr>
<td>Age in years (Mean (SD))</td>
<td>13.6 (2.8)</td>
<td>13.9 (3.0)</td>
<td>.610</td>
</tr>
</tbody>
</table>

Median Household Income (Mean (sd)) | $47,293.4 (17,770.7) | $55,648.8 (19,556.2) | .026 |

Table 2: Association of neuropsychiatric manifestations in LN patients with cSLE

<table>
<thead>
<tr>
<th>Patient has Lupus Nephritis?</th>
<th>Neuropsychiatric manifestations (n (%))</th>
<th>No (n (%))</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes (n=34)</td>
<td>2 (5.9%)</td>
<td>128 (85.3%)</td>
<td>130</td>
</tr>
<tr>
<td>No (n=130)</td>
<td>32 (24.1%)</td>
<td>96 (71.7%)</td>
<td>128</td>
</tr>
</tbody>
</table>

• Non-White races when compared to White, and those with lower household median income have a significantly higher prevalence of being diagnosed with LN. (P < 0.05).
• Among cSLE patients, neuropsychiatric manifestations are more prevalent in patients with LN (5.9% vs 1.5%).
• Among cSLE patients, the distribution of age and sex is similar among those diagnosed with LN and those who were not.
• cSLE patients with LN have a significantly (P = .017) higher SLEDAI-2K mean (standard deviation) score of 8.0 (9.4) in comparison to a cSLE patient without LN, in which the score is 3.8(4.5).

Discussion

- In our study, neuropsychiatric manifestations were more prevalent in patients with LN compared to those without LN.
- Socioeconomic factors such as household income and race individually play a significant role in LN risk.
- We did not find significant age differences in risk of LN in our study population.
- Although some previous studies report a males with cSLE have a higher frequency of LN, our study did not show a significant difference in prevalence of LN by sex.

Limitations / Future Direction

Limitation:
- Low number of neuropsychiatric diseases due to limited sample size.
- Median income is not directly collected by obtained mapping zip code to census data.

Future Directions:
- Complete review of patient charts of those diagnosed with cSLE including those above the age of 25 years old at the time of data extraction.
- Assess each neuropsychiatric disease individually with a larger sample size.
- Further assess specific socioeconomic and environmental factors that contribute to neuropsychiatric complications of cSLE.

References


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