Identifying Sub-Phenotypes of ASD and the Etiological Association of Maternal Immune Disease: Advocating for Health Equity among Population with ASD

Jacqueline Cabral¹, Bibiana Restrepo, MD², Christine Wu Nordahl, Ph.D³

¹ Kennedy Krieger Institute/Maternal Child Health Careers/ Research Initiatives for Student Enhancement-Undergraduate Program, ²University of California, Davis MIND Institute

INTRODUCTION

• Autism spectrum disorder (ASD) is an emerging public health concern as its prevalence rapidly continues to increase (CDC, 2018).
• The increase in ASD prevalence augments the demand for services, resulting in a lack of developmental services, treatments, and prevention efforts (Newscaffer & Kresch, 2003).
• The plethora of etiologies points to potential sub-phenotypes of ASD, which can lead to tailored treatments for subsets of ASD population (Amaral et al., 2012).
• Medical comorbidities may influence the behavioral and developmental presentation of ASD (Jyonouchi, 2010).
• Health care professionals must cover the gaps in treatment, services, and prevention.

OBJECTIVE

We aim to address the following questions:
1. Determine how GI symptoms correlate with various phenotypes of ASD based on behavioral and developmental measures. Assess how frequent children with ASD experience GI symptoms.
2. Explore the association between maternal diabetes, autoimmune, and immune mediated disease and the presence of GI symptoms among the ASD population.

PUBLIC HEALTH FRAMEWORK

By exploring these questions, we seek to:
1. Advocate for health equity by raising awareness for the need of tailored treatments and resources
2. Inform prevention efforts

METHODS

Participants
• 388 participants recruited through Autism Phenome Project (APP)
• 259 children with ASD; 129 children typically developing (TD)

Measures
• APP evaluated da and developmental and behavioral outcomes.
• GI History Parent Questionnaire was used to determine the presence of GI symptoms.
• Autoimmune Survey used to assess history of maternal diabetes, autoimmune, and immune-mediated disease.

Variables
• Behavioral outcomes: motor, repetitive behaviors, social communication and interaction, aggressive behaviors
• Developmental outcomes: repetitive and expressive language

Data Analysis
• Chi – squared tests; Two – Way ANOVA

RESULTS

Table 1. Frequency of gastrointestinal symptoms among ASD and TD groups.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>ASD, n (%)</th>
<th>TD, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal Pain</td>
<td>30 (22.6)</td>
<td>5 (17.2)</td>
</tr>
<tr>
<td>Gaseousness or Bloating</td>
<td>39 (29.3)</td>
<td>9 (31.0)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>47 (35.3)</td>
<td>8 (27.6)</td>
</tr>
<tr>
<td>Constipation</td>
<td>52 (39.0)</td>
<td>8 (27.6)</td>
</tr>
<tr>
<td>Pain on Stooling</td>
<td>37 (29.3)</td>
<td>3 (19.3)</td>
</tr>
<tr>
<td>Sensitivity to Foods</td>
<td>64 (48.1)</td>
<td>30 (34.5)</td>
</tr>
<tr>
<td>Total Gastrointestinal Symptoms</td>
<td>133 (51.2)</td>
<td>29 (22.5)</td>
</tr>
</tbody>
</table>

Table 2. Maternal Autoimmune Diseases, Immune-Mediated Diseases, and Diabetes among ASD and TD Subgroups.

<table>
<thead>
<tr>
<th>Disease Type</th>
<th>Cases of ASD with GI Symptoms</th>
<th>Cases of ASD without GI Symptoms</th>
<th>χ² P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autoimmune</td>
<td>22</td>
<td>100</td>
<td>0.016*</td>
</tr>
<tr>
<td>Immune-Mediated Diabetes</td>
<td>15</td>
<td>90</td>
<td>0.020</td>
</tr>
<tr>
<td>Diabetes</td>
<td>8</td>
<td>92</td>
<td>0.380</td>
</tr>
</tbody>
</table>

Table 3. Association of GI prevalence in relation to history of maternal autoimmune, immune-mediated, and diabetic diseases among the ASD population.

<table>
<thead>
<tr>
<th>Disease Type</th>
<th>Cases of ASD with GI Symptoms</th>
<th>Cases of ASD without GI Symptoms</th>
<th>χ² P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autoimmune</td>
<td>22</td>
<td>100</td>
<td>0.016*</td>
</tr>
<tr>
<td>Immune-Mediated Diabetes</td>
<td>15</td>
<td>90</td>
<td>0.020</td>
</tr>
<tr>
<td>Diabetes</td>
<td>8</td>
<td>92</td>
<td>0.380</td>
</tr>
</tbody>
</table>

Figure 1. Behavioral scores among ASD groups with and without GI symptoms.

Figure 2. Developmental scores among ASD groups with and without GI symptoms.

SUMMARY

• Children with ASD experienced GI symptoms more frequently than typically developing children.
• Most frequent symptoms among children with ASD were sensitivity to foods, constipation, and diarrhea.
• Maternal immune mediated diseases are associated to the diagnosis of ASD (p < 0.05).
• Among the ASD population, children with GI symptoms had consistently higher behavioral scores than children without GI symptoms. When comparing differences in developmental measures, both groups reported similar scores.
• There were no significant associations between behavioral and developmental scores and the interaction of GI symptoms and ASD diagnosis.

CONCLUSIONS

• Children with ASD experience GI symptoms more than TD children. Practitioners should ask for presence of GI symptoms as they influence behaviors in children with ASD.
• Medical comorbidities may be related to behavioral profiles of ASD. No behavioral sub-phenotypes were observed in correlation with comorbidities.
• The association between maternal immune mediated disease and ASD diagnosis should be explored further.
• Our data suggests that we need more research on the possible correlation between medical comorbidities and sub-phenotypes of ASD.

STRENGTHS & LIMITATIONS

• APP provides longitudinal analysis data of children with ASD; thus, prospective studies on the effects of comorbidities on prognosis of ASD are possible.
• The research addresses the gap between public health and translational research.
• The sample did not report demographic data – weakening the generalizability of the results.

ACKNOWLEDGEMENTS

This research would not have been possible without the support of Dr. Restrepo, the APP team, and Dr. Taylor.