Use of acid suppressive medications during infancy and early childhood and its association with Type 1 diabetes
Menon,S., Umaphathi,K.K., Thavamani,A., Bora,G., Davis,A.
MetroHealth Medical Center affiliated with Case Western Reserve University School of Medicine, Cleveland, Ohio

Background
- Type 1 diabetes is a multifactorial, immune mediated disease whose incidence has been increasing worldwide.
- These changes in prevalence cannot be explained by genetic susceptibility alone and several lifestyle changes have been linked to the rising incidence including obesity, diet and mode of delivery.
- Many of these environmental factors influence the composition of the gut microbiome which interacts with the immune system as well as affects gut permeability, thus facilitating exposure to potentially diabetogenic antigens and possibly playing a role in initiating autoimmunity against islet cells.
- Acid suppressive medications have been linked to intestinal dysbiosis, however there is no data analyzing the role of acid suppressant use and development of type 1 diabetes.
- In addition to causing intestinal dysbiosis, acid-suppressive medications may increase sensitization to ingested antigens by decreasing protein breakdown in the stomach.

Objective
To determine if there is an association between receiving treatment with acid suppressive medications (proton pump inhibitors or H2-receptor blockers) in early childhood and the incidence of Type 1 diabetes.

Methods
- Study design: A retrospective case control study was conducted using the “Explorys” database, an open private cloud platform that electronically integrates de-identified patient data used by major health systems in the United States comprising of almost 50 million patients.
- Methodology: We queried the database for patients who were (cases) and were not (controls) diagnosed with Type 1 Diabetes between the ages of 5 and 24. We used Type 1 diabetes and included 8 other sub-diagnosis based on SNOMED (Systematized Nomenclature of Medicine - Clinical Terms) classification of diseases.
- We excluded patients with a diagnosis of neonatal diabetes and Type 2 diabetes.
- The number of patients in each group who received a prescription for acid suppressive medications (proton pump inhibitor or H2-receptor blocker) before the age of 4 were compared.
- Data was analyzed using SPSS software.

Results
The study population consisted of almost 10.3 million patients between ages 5 to 24. 40840 of these patients had a diagnosis of type 1 diabetes. Of those with type 1 diabetes, 380 patients had received a prescription for a proton pump inhibitor or a H2-receptor blocker before the age of 4.

<table>
<thead>
<tr>
<th>Exposed to PPI/H2B</th>
<th>CASES- TYPE 1 DIABETES (N=40460)</th>
<th>CONTROLS- NO TYPE 1 DIABETES (N=10,279,290)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>380</td>
<td>87720</td>
</tr>
<tr>
<td>No</td>
<td>40460</td>
<td>10,191,570</td>
</tr>
</tbody>
</table>

- Exposure to either PPI or H2B before the age of 4 was not significantly associated with a future risk of developing Type 1 diabetes between the ages of 5 and 24 (OR = 1.09; CI-0.99 to 1.2, p value=0.09).
- Exposure to only PPI (OR = 1.05; CI- 0.96 to 1.11, p value=0.07) or only H2B (OR= 0.94; CI- 0.82 to 1.07, p value=0.3) also did not show a significant association with the development of Type 1 diabetes.

Conclusion
- Treatment with acid suppressive medications such as proton pump inhibitors and H2-receptors blockers during infancy and early childhood is not significantly associated with higher odds of developing type 1 diabetes.
- No prior data is available looking at the possible association between acid suppressive medications in pancreatic islet cell autoimmunity and Type 1 diabetes. Further studies are necessary to better understand the effects of these medications on gut micro biome composition, gut integrity and possible alterations to the immune system.

Disclosure
We declare that we have no potential conflicts of interest.

References