Individuals and Organizations Completing Research in the IMEDS Research Lab

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Research Objectives and Aims: Patients with Juvenile Idiopathic Arthritis (JIA) often present with multiple comorbid conditions. The spectrum of comorbidities in these patients is poorly understood. We aim to: (1) identify diseases comorbid with Juvenile Idiopathic Arthritis (JIA), and (2) study the potential effects of medications on the development of comorbidities.

Scope/Proposed Approach: We will conduct a retrospective analysis of claims provided through the iMeds platform. Study participants will include individuals with a first diagnosis of JIA at 0-16 years old. A control population of children without JIA will be formed. Diagnosis data for these children will be extracted to identify the comorbid conditions that are over-represented in children with JIA. Exposures to common medications for treating JIA will also be extracted from claims, and their effects on comorbidities examined.

Identification of JIA patients. Children with JIA are identified using the International Classification of Disease, 9th Revision (ICD-9) codes, including the following JIA categories:

- Polyarticular JIA (714.30, 714.31)
- Oligoarticular JIA (714.32, 714.33)
- Psoriatic JIA (696.0)
- Enthisitis Related Arthritis (720.*, 721.*, 726.*)

Children who had 2 or more JIA ICD-9 codes from outpatient and inpatient claims within a period of 2 years will be included.

Identification of comorbidities. Comorbidities will be identified using ICD-9 codes. Children who had 2 or more ICD-9 codes associated with a comorbidity within a period of 2 years will be included. We will initially focus on the following comorbidities:

- Celiac disease (579.0)
- Food allergy (V15.0*, 579.8, 995.6*, 995.7)
- Allergic gastrointestinal disorders (530.13, 535.7*, 558.3, 558.4*)

Medication exposures. We define 5 classes of therapeutic agents:

- Prescription NSAIDs (e.g. celecoxib, diclofenac, ibuprofen, indomethacin, meloxicam, naproxen, pyroxicam, tolmetin, etc.)
- Conventional DMARDS (Methotrexate or leflunomide)
- Other non-biologic immune-modulatory agents (e.g. azathioprine, cyclophosphamide, cyclosporine, IVIG, 6-mercaptopurine, mycophenolate mofetil, tacrolimus)
- TNF inhibitors (etanercept, infliximab, adalimumab, golimumab, certolizumab pegol)
- Other biologics (e.g. abatacept, anakinra, canakinumab, rilonacept, rituximab, tocilizumab)

We will assess the risk of comorbidities in JIA patients who were exposed to each medication class, compared to JIA patients who were not exposed to the medication class. We will consider only comorbidities that developed after the medications were prescribed, up to a period of 5 years. Effects of medications will be examined both as a dichotomous variable (ever exposed/never exposed), and a continuous variable (dose-response relationship).

Statistical analysis. Regression analysis will be used to calculate the risk of developing comorbidities in JIA patients. Survival analysis will be applied to examine the effects of medication exposures on comorbidities. We will adjust all analyses by age, gender and race.

Validation. We will cross-validate our findings on multiple claims datasets, and electronic medical records at Boston Children's Hospital, Tufts Medical Center and Beth Deaconess Israel.

Impact: Knowledge generated from this study may assist in the identification and understanding of the patterns of comorbid conditions in children with these chronic diseases. This will in turn lead to improved recognition and screening for such comorbid conditions in individuals with pediatric-onset rheumatic diseases.

Experience: Trevor E. Davis, Attending, Pediatric Rheumatology, Floating Hospital for Children at Tufts Medical Center and Research Fellow, Beth Deaconess Israel Medical Center; Marc Natter, Staff Scientist, Boston Children's Hospital and Instructor, Harvard Medical School; Mei-Sing Ong, Research Fellow, Boston Children's Hospital.

Timeline: 12 months (from August 2014).

Preliminary Study:
We have previously identified a heightened risk of food allergy and celiac disease in children with JIA, using electronic medical records from Boston Children's Hospital (abstract submitted to the 2014 American College of Rheumatology Annual Meeting). We hope to validate and expand our findings on multiple datasets.