**Supplemental Digital Content**

**Table 1.** Literature Review of comorbidities associated with celiac disease and the types of studies conducted.

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| --- | --- | --- |
|  |  | **Example Recent Study** |
| **Comorbidities** | **Prevalence of Comorbidity in Patients with Celiac Disease (Adult and Pediatric populations)** | **Author (Year)** | **Type of Study** | **Size** | **Finding** |
| **Diabetes Mellitus Type 1** | Range: 2.2% -12.6%1,2 | Viljamaa (2005)1,3 | Adult + Pediatric Population, Retrospective Chart Review, Hypothesis Driven | 703 CD[[1]](#footnote-1) Cases, matched with 299 controls | Prevalence of Type I Diabetes in CD=12.6% (Significant) |
| **Autoimmune Thyroiditis**  | Range: 5.95% - 17.6%1,4  | Cosnes (2008)5 | Adult + Pediatric Population, Retrospective Cross-sectional Study, Hypothesis Driven | 924 CD patients | Prevalence of Autoimmune Thyroiditis in CD=5.95% |
| **Autoimmune Thyroid Disorders**  | Range: 4.8%- 10.2%6 | Canova (2016)7,8 | Pediatric population, Population-Based Cohort Study,Hypothesis Driven | 1251 CD cases, 5:1 matching on age and gender | Prevalence of ATD[[2]](#footnote-2) in CD = 4.8% (not significant); Hazard Ratio = 4.64 (Significant) |
| **Systemic Lupus Erythematosus** | Range: 1.4% - 2.4%1 | Freeman (2008)9 | Adult Population, Cross-Sectional Study, Hypothesis Driven | 246 CD Cases | Prevalence of Systemic Lupus Erythematosus in CD=2.4% |
| **Juvenile Arthritis** | Range: 2.8% -6.6% (This is the range of CD found in patients with Juvenile Arthritis)10,11 | Stagi (2005)10 | Pediatric Population, Cohort Study, Hypothesis Driven | 151 Juvenile Idiopathic Arthritis Cases, matched with 158 controls | Prevalence of CD in Juvenile Arthritis cases=6.6% (Significant) |
| **Dermatologic Herpetiformis** | Range: 2.9% - 25%12,13 | Iqbal (2013)14 | Adult + Pediatric Population, Cross-Sectional Cohort Study | 360 CD Cases matched with 234 controls | Prevalence of Dermatologic Herpetiformis in CD=13.5% |
| **Alopecia Areata** | Range: 0.9% - 3.5%1 | Ventura (1999)12 | Adult + Pediatric Population, Retrospective Cohort Study, Hypothesis Driven | 909 CD Cases, matched with 1268 controls | Prevalence of Alopecia Areata in CD=1.1% in patients aged 2-10 years; =3.5% in patients aged 10+ (Significant) |
| **Psoriasis** | Range: 4.1% - 12.9%1,14  | Ludvigsson (2011)15 | Adult + Pediatric Population, Cohort Study, Hypothesis Driven | 28,958 CD Cases, matched with 143,910 controls | Hazard Ratio=1.72  |
| **Inflammatory Bowel Disease** |  Range: 2.2% | Yang (2005)16 | Adult + Pediatric Population, Cross Sectional Study, Hypothesis Driven | 455 CD cases | Prevalence of IBD in CD=2.2% |
| **Autoimmune Hepatitis** | Range: 2.0%-12.5%17 | Najafi (2014)18 | Pediatric Population, Cross Sectional Study, Hypothesis Driven | 32 CD Patients | Prevalence of Autoimmune Hepatitis in CD= 12.5%  |
| **Selective IgA Deficiency** | Range: 1.7% - 2.6%1,19,20 | Cataldo (1997)19 | Pediatric + Adult Population, Cross-Sectional Study, Hypothesis Driven | 688 CD Cases | Prevalence of IgA Deficiency in CD=1.7%  |
| **Down Syndrome[[3]](#footnote-3)** | Range: 1.4% - 4.8%21  | Khatib (2016)22 | Pediatric Population, Cross-Sectional Study | 177 CD cases | Prevalence of Down Syndrome in CD=4.8% |
| **ADHD** | Range: 0.86% - 2.94%23 | Dazy (2013)24 | Pediatric + Adult Population, Case-Control Study, Hypothesis Driven | 281 CD cases matched with 301 controls | Prevalence of ADHD in CD-2.94%(Not significant) |
| **Turner****Syndrome[[4]](#footnote-4)** |  Range: 0.26% - 0.3%25 | Marild (2016)26 | Pediatric + Adult Population, Case-Control Study, Hypothesis Driven | 7,548 CD cases matched with 34,492 controls | Prevalence of Turner’s Syndrome in CD=0.26% (Not significant) |

**Table 2**. Expansion of significant ICD-10 Level 1 Hierarchy Codes into their detailed subtypes.

**Expected Diseases**

|  |  |
| --- | --- |
| **ICD 10 Code** | **Frequency (Cases, Controls)** |
| **Other diseases of stomach and duodenum (K31)** |
| Disease of stomach and duodenum, unspecified (K31.9) | 82,5 |
| Gastroparesis (K31.84) | 1,3 |
| Fistula of stomach and duodenum (K31.6) | 1,1 |
| **Gastritis and duodenitis (K29)** |
| Acute gastritis without bleeding (K29.00) | 1,2 |
| Chronic atrophic gastritis without bleeding (K29.40) | 9,6 |
| Unspecified chronic gastritis without bleeding (K29.50) | 3,2 |
| Other gastritis without bleeding (K29.60) | 5,6 |
| Gastritis, unspecified, without bleeding (K29.70) | 11,14 |
| Duodenitis without bleeding (K29.80) | 36,1 |
| Gastroduodenitis, unspecified, without bleeding (K29.90) | 8,11 |
| **Other anemias (D64)** |
| Anemia, unspecified (D64.9) | 35,62 |
| **Immunodeficiency with predominantly antibody defects (D80)** |
| Selective deficiency of immunoglobulin A [IgA] (D80.2) | 8,2 |
| **Other hypothyroidism(E03)** |
| Hypothyroidism, unspecified (E03.9) | 13,30 |
| Other specified hypothyroidism (E03.8) | 7,10 |
| Congenital hypothyroidism without goiter (E03.1) | 3,5 |
| Hypothyroidism due to meds and other exogenous substances (E03.2) | 1,0 |

**Expected Symptoms**

|  |  |
| --- | --- |
| **ICD 10 Code** | **Frequency (Cases, Controls)** |
| **Other symptoms and signs involving the digestive system and abdomen (R19)** |
| Diarrhea, unspecified (R19.7) | 122,161 |
| Other fecal abnormalities (R19.5) | 12,11 |
| Other symptoms and signs involving the digestive sys and abdomen (R19.8) | 7,9 |
| Right lower quadrant abdominal swelling, mass and lump (R19.03) | 1,0 |
| **Other functional intestinal disorders (K59)** |
| Constipation, unspecified (K59.00) | 120,357 |
| Other constipation (K59.09) | 20,21 |
| Slow transit constipation (K59.01) | 4,6 |

**Potential Novel Findings**

|  |  |
| --- | --- |
| **ICD 10 Code** | **Frequency (Cases, Controls)** |
| **Family history of other specific disorders (Z83)** |
| Family history of other diseases of the digestive system (Z83.79) | 15,3 |
| Family history of endocrine, nutritional and metabolic diseases (Z83.49) | 6,8 |
| Family history of diabetes mellitus (Z83.3) | 9,24 |
| Family history of disorders of the blood/immune mechanism | 1,11 |
| **Abnormal serum enzyme levels (R74)** |
| Nonspecific elevated of levels of transaminase & lactic acid dehydrogenase (R74.0) | 27,21 |
| Abnormal levels of other serum enzyme levels (R74.8) | 6,12 |
| **Persons encountering health services for counseling and medical advice, not elsewhere classified (Z71)** |
| Dietary counseling and surveillance (Z71.3) | 82,9 |
| Other specified counseling (Z71.89) | 57,11 |
| Counseling, unspecified (Z71.9) | 1,0 |
| **Esophagitis (K20)** |
| Eosinophilic esophagitis (K20.0) | 12,15 |
| Esophagitis unspecified (K20.9) | 6,5 |
| **Other joint disorder, not elsewhere classified (M25)** |
| Pain in knee (M25.56) \*Includes (M25.561) (M25.562) (M25.569) | 26,110 |
| Pain in ankle and joints of foot (M25.57) \*Includes (M25.571) (M25.572) (M25.579) | 16,60 |
| Pain in unspecified joint (M25.50) | 20,34 |
| Pain in hip (M25.55) \*Includes (M25.551) (M25.552) (M25.559) | 9,50 |
| Pain in wrist (M25.53) \*Includes (M25.531) (M25.532) (M25.539) | 9,32 |
| Pain in shoulder (M25.51) \*Includes (M25.511) and (M25.519) | 7,39 |
| Pain in elbow (M25.529) | 6,17 |
| Effusion, ankle and foot (M25.47) \*Includes (M25.472) (M25.473) (M25.476) | 2,9 |
| Effusion, wrist (M25.432) | 2,0 |
| Effusion, unspecified joint (M25.40) | 3,0 |
| Effusion, elbow (M25.429) | 3,5 |
| Effusion, knee (M25.469) | 2,18 |
| **Other systemic involvement of connective tissue (M35)** |
| Hypermobility syndrome (M35.7) | 6,6 |
| Systemic involvement of connective tissue, unspecified (M35.9) | 4,0 |
| Other specified systemic involvement of connective tissue (M35.8) | 1,0 |
| Other overlap syndromes (M35.1) | 1,0 |
| **Other diseases of anus and rectum (K62)** |
| Hemorrhage of anus and rectum (K62.5) | 13,16 |
| Other specified diseases of anus and rectum (K62.89) | 3,3 |
| Rectal prolapse (K62.3) | 1,4 |
| Anal sphincter tear (healed) (non-traumatic) (old) (K62.81) | 1,0 |
| Disease of anus and rectum, unspecified (K62.9) | 1,0 |
| **Allergy status to drugs, medicaments and biological substances (Z88)** |
| Allergy status to penicillin (Z88.0) | 12,64 |
| Allergy status to other anti-infective agent’s status (Z88.3) | 10,35 |
| Allergy status to other antibiotic agent’s status (Z88.1) | 8,25 |
| Allergy status to other drug/meds/biological substance status (Z88.8) | 6,34 |
| Allergy status to narcotic agent status (Z88.5) | 3,8 |
| Allergy status to sulfonamides status (Z88.2) | 2,15 |
| Allergy status to anesthetic agent status (Z88.4) | 2,1 |
| Allergy status to analgesic agent status (Z88.6) | 2,6 |

**Table 3**. Characteristics of comorbid celiac disease and eosinophilic esophagitis cases.

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| --- | --- | --- | --- | --- | --- |
| **Eosinophilic Esophagitis Cases** | **Gender** | **Race** | **Age at Diagnosis of Celiac Disease (years)** | **Confirmed Eosinophilic Esophagitis (With Biopsy)** | **Other Comorbidities** |
| 1 | M | White | 11.3 | Yes | Sensorineural hearing loss, Congenital preauricular pit, Asthma, Hydronephrosis |
| 2 | F | Biracial/Multiracial  | 9.6 | Yes | Calcaneal apophysitis, Instability of right shoulder joint, Asthma, Eczema, Food Allergies |
| 3 | M | White | 5.6 | Yes | Food Allergy, Feeding difficulties, Poor weight gain, Anxiety disorder of childhood, ADHD predominantly hyperactive impulsive type, Raynaud's Syndrome, Asthma, GERD, Constipation, Wheezing, Otitis Media |
| 4 | F | White | 17.4 | Yes | Pain in joint, multiple sites, High BMI |
| 5 | M | White | 13.3 | Yes | Periumbilical abdominal pain, Obesity, Acanthosis, Acne, Bloating, Fecal Urgency, Anxiety, Panic Attack, Concussion, Anemia |
| 6 | M | White | 11.0 | Yes | Allergic rhinitis, GERD |
| 7 | F | White | 10.4 | Yes | Abdominal Pain, Otitis Media |
| 8 | F | White | 14.8 | Yes | Peanut Allergy, Dysphagia, Depression, Asthma |
| 9 | M | White | 13.3 | Yes | Elevated IgA level |
| 10 | M | White | 9.6 | Yes | Dysphagia, Finger sprain |
| 11 | M | White | 8.2 | Yes | Congenital renal dysplasia, Hypospadias, RSV infection as an infant, Constipation |
| 12 | F | White | 5.4 | Yes | Dysphagia, Microcytosis, GERD |

**Table 4**. Investigation of “Overweight and obesity” (E66) finding via BMI analysis

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Age Group (years)** | **Average BMI of Celiac Disease Cases** | **Number of Cases[[5]](#footnote-5)** | **Average BMI of Matched Controls** | **Number of Control Matched Entries[[6]](#footnote-6)** |
| 0 - 5 | 15.60 | 81 | 16.50 | 520 |
| 5 - 10 | 16.27 | 151 | 17.73 | 671 |
| 10 - 15  | 19.05 | 123 | 21.96 | 704 |
| 16 - Older | 22.90 | 77 | 25.24 | 406 |

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1. CD = Celiac Disease [↑](#footnote-ref-1)
2. ATD = Autoimmune Thyroid Disease [↑](#footnote-ref-2)
3. The prevalence of celiac disease in patients with Down syndrome has been better established than the inverse relationship [↑](#footnote-ref-3)
4. This study demonstrated an increased risk of developing CD in Turner Syndrome, but not the inverse relationship [↑](#footnote-ref-4)
5. Excluded one case of a missing BMI value [↑](#footnote-ref-5)
6. Excluded 2,022 controls of missing BMI values [↑](#footnote-ref-6)