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A Link Between Type I Diabetes Mellitus and Microscopic Colitis: A State-Wide Retrospective Analysis

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1. Abstract

Type 1 diabetes mellitus (T1DM) and microscopic colitis (MC) share autoimmune mechanisms. A retrospective study at UAMS found 22 MC cases among 2,978 T1DM patients, predominantly in Caucasian females aged 60-80. Collagenous colitis (CC) was more common than lymphocytic colitis (LC). A Swedish study confirmed a nearly 80% increased MC risk in T1DM. Shared immune dysregulation, gut permeability, and medication effects may contribute. Screening for MC in T1DM patients with chronic diarrhea is advised. Integrated care is crucial, as treatment interactions can complicate management. Further research on genetic and microbial factors is needed for better prevention and treatment.

2. Introduction

Type 1 diabetes mellitus (T1DM) is an autoimmune condition characterized by the destruction of pancreatic β-cells, causing insulin deficiency, and hyperglycemia [1]. Microscopic colitis (MC) is a chronic inflammatory condition of the colon, subdivided into two main subtypes: lymphocytic colitis (LC) and collagenous colitis (CC)[2]. Both disorders are linked to autoimmune dysregulation, suggesting a potential overlap in their pathogenesis. This report examines the association between T1DM and MC, drawing on recent studies to explore epidemiological evidence, possible mechanisms, and clinical implications.

3. Population and Methods

A retrospective analysis was conducted state-wide at the University of Arkansas for Medical Sciences (UAMS). All patients studied had a confirmed diagnosis of T1DM and MC confirmed via biopsy. Patients were then subdivided via age, sex, race. The results were then subdivided into microscopic colitis subtypes, lymphocytic colitis and collagenous colitis.

4. Results

At UAMS, a total of 2,978 patients were identified to have T1DM between January 2020 through November 2024. Of those 2,978 patients, 1283 were male (43.1%) and 1,695 were female (56.9%). Three-hundred twenty-one patients underwent gastric, small intestinal, or colonic biopsy regardless of whether they demonstrated symptoms of microscopic colitis. Of the 321 biopsies, 183 were female and 138 were male (Figures 1-3), which resulted in a total of 22 patients diagnosed with microscopic colitis. The odds ratio for MC was 2.72 for females, with a 95% CI of 0.98 to 7.56. Although this result did not reach statistical significance, it suggests a clinically meaningful trend towards higher odds of MC in females.Of the 22 patients, the summation of all age groups showed a significant bias towards females (77.3%) and the Caucasian race (95.5%). 50% of all patients were within the age range of 60-80 years old at disease onset (Table 1).When the patients are subdivided into the subtypes of microscopic colitis, including collagenous colitis and lymphocytic colitis, there is a significant bias towards collagenous colitis (68.2%) vs lymphocytic colitis (31.8%). When the age of onset is < 60 years of age, there is a predominance of lymphocytic colitis (71.4%) vs collagenous colitis (28.6%). However, when comparing patients with onset ≥ 60 years old, there is a significant shift in the incidence of collagenous colitis (80%) vs lymphocytic colitis (13.3%) (Table 1).Irrespective of age, both men and women had comparable rates of developing collagenous colitis vs lymphocytic colitis (women 70.6%; men 60%) (Table 2).The lack of statistical significance is likely due to the small sample size of patients diagnosed with colitis at UAMS (22 cases), the imbalance in group sizes between females and males, and the low event rate of microscopic colitis in the study population. These factors contributed to a wider CI and limited statistical power, but the observed trend may warrant further investigation in larger studies.

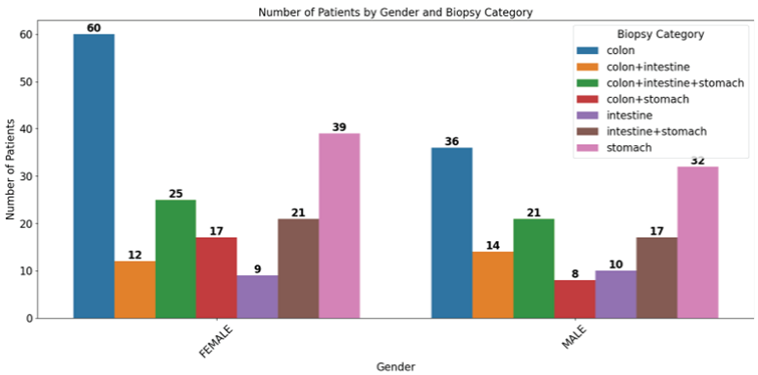

Figure 1: Bar graph demonstrating the types of biopsies taken by each patient organized by gender.

Figure 2: Venn diagram demonstrating the types of biopsies taken in the female patient population.

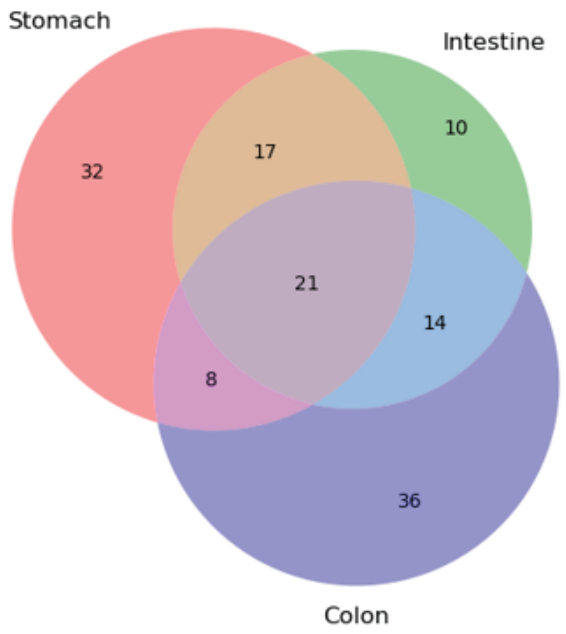

Figure 3: Venn diagram demonstrating the types of biopsies taken in the male patient population.

5. Epidemiological Evidence

A large, nationwide matched case-control study conducted in Sweden based on the ESPRESSO cohort provides significant evidence correlating T1DM and MC. This study analyzed 9,600 MC patients diagnosed via biopsy and compared them to 47,870 population controls matched for age, sex, and other factors. Among MC patients, 352 (3.7%) had a prior T1DM diagnosis, compared to 945 (2.0%) in controls, yielding an odds ratio (OR) of 1.79 (95% CI: 1.56-2.05). This indicates a nearly 80% increase in likelihood in the development of MC amongst patients with T1DM when compared with the general population [3].Subgroup analysis varied by MC subtype and sex. For collagenous colitis, the OR was higher (OR 2.06, 95% CI: 1.67-2.54) than for lymphocytic colitis (OR 1.60, 95% CI: 1.31-1.94), suggesting a stronger link with CC. In addition, The association was consistent across sexes, with an OR of 1.76 (95% CI: 1.46-2.12) for males and 1.81 (95% CI: 1.51-2.18) for females revealed that the association was consistent across sexes.1 It should be noted, however, that the association among females was attenuated after adjusting for statin use (OR 1.62, 95% CI: 1.25-2.11), suggesting potential confounding by medication [3].When controlled for shared genetic and environmental factors, sibling comparisons showed a weaker but still significant association (OR 1.43, 95% CI: 1.02-2.01), reinforcing the link beyond familial confounding. Polypharmacy in T1DM may partially mediate the relationship as adjustments for medications commonly associated with MC (e.g., proton pump inhibitors, NSAIDs, SSRIs, and statins) further attenuated the OR to 1.46 (95% CI: 1.14-1.88) [3].

6. Potential Mechanisms

The association between T1DM and MC likely arises from shared autoimmune and inflammatory pathways, as both conditions are linked to immune dysregulation:

- Autoimmune Overlap: T1DM is driven by autoreactive T-cells targeting pancreatic β-cells, while MC is associated with mucosal immune responses to luminal antigens. Concomitant autoimmune diseases are seen in up to 30-50% of MC, including T1DM, celiac disease, and thyroid disorders.4 A genetic predisposition is suggested as Human leukocyte antigen (HLA) variants, such as HLA-DR3-DQ2, implicated in T1DM, have also been linked to MC [5].
- Gut Permeability and Microbiota: Abnormal gut motility and permeability due to autonomic neuropathy and hyperglycemia secondary to T1DM potentially increases exposure to luminal antigens that trigger MC [6]. As observed in both MC and T1DM, changes in the gut microbiome may exacerbate inflammation [7].
- Medication Effects: Medications such as PPIs and NSAIDs, which are commonly used amongst patients with T1DM are known risk factors for MC, with the Swedish study highlighting higher usage of these drugs among T1DM patients with MC, further suggesting a contributory role [3].

7. Clinical Implications

The association between T1DM and MC has significant, and practical implications for patient care:

- **Screening:** Given the increased risk, clinicians should screen for

Table 1: Summary showing correlation between race, sex, and age for a confirmed diagnosis of Type 1 Diabetes Mellitus and Microscopic Colitis.

Age of Onset/Diagnosis of Microscopic Colitis	Number of Diagnosis	Female: Male Ratio	Caucasian: Black Ratio: Other Race	Collogenous Colitis: Lymphocytic Colitis
≤ 30 years of age	1	0:1	1:0:0	0:1
31-59 years old	6	5:1	6:0:0	2:4
60-80 years old	11	8:3	10:1:0	8:2
≥ 81 years old	4	4:0	4:0:0	4:0
Total	22	17:5	21:1:0	15:7

Table 2: Confirmed diagnosis of collagenous colitis vs lymphocytic colitis based on sex.

	Collagenous Colitis	Lymphocytic Colitis
Male sex	3	2
Female Sex	12	5
Total	15	7

MC in T1DM patients presenting with chronic watery diarrhea, especially if refractory to standard treatments [8]. Conversely, T1DM screening should be considered in MC younger patients with suggestive symptoms, as T1DM is more often diagnosed in younger patients.

- **Management Challenges:** Management can be challenging as treatments for MC, such as budesonide, are effective but may complicate glycemic control in T1DM [8]. As suggested earlier, polypharmacy in T1DM patients requires careful monitoring to avoid exacerbating MC risk.
- **Prognosis:** Although the long-term prognosis is good, the coexistence of MC with T1DM may cause an exacerbation of gastrointestinal symptoms and reduce quality of life, necessitating integrated care approaches [4].

8. Comparison with Other Autoimmune Associations

In addition to T1DM, MC is associated with other autoimmune diseases, including celiac disease in 2-20% of MC patients, with a pooled event rate of 6.2% in celiac patients developing MC [4]. This association, although weaker, is still notable when compared to the 3.7% prevalence of T1DM in MC patients [3]. The association between MC and T1DM appears to be more influenced by environmental and medication-related factors in adults, unlike inflammatory bowel diseases (IBD) which show stronger genetic overlap with T1DM in pediatric populations [9].

9. Critical Analysis of Prior Studies

While the Swedish study provides compelling evidence, limitations exist, including the reliance on registry data that may underestimate existing cases. In addition, the attenuation of the association with medication adjustment raises questions about causality versus confounding.3 The stronger association with CC than LC suggests subtype-specific mechanisms that warrant further exploration. Furthermore, the role of gut microbiota and specific HLA alleles remains underexplored, necessitating targeted genetic and microbiome studies [5,7].

8. Conclusion

The association between T1DM and MC is well-supported by epidemiological data, with an increased risk of approximately 80% in T1DM patients [3]. Our data showed a significant bias towards females (77.3%) vs males (22.7%), with the most significant incidence occurring between the ages of 60-80 years of age (50%) and amongst Caucasians (95.5%). Shared autoimmune mechanisms, altered gut physiology, and medication effects likely contribute to this relationship. Clinicians should be vigilant for MC in T1DM patients with diarrhea, and future research should focus on elucidating genetic and microbial drivers to refine prevention and treatment strategies. This interplay underscores the complexity of autoimmune comorbidities and the need for holistic patient management.

9. Future Directions

Conduct prospective cohort studies to confirm causality and assess temporal relationships. Investigate specific HLA alleles and microbiome profiles in T1DM-MC patients [5,7]. Develop guidelines for screening and managing dual diagnoses to optimize outcomes [8].

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