Celiac disease (CD) is an autoimmune systemic disorder triggered by ingestion of gluten in genetically susceptible individuals. It affects 1% of the population\(^1,2\) but only about 20% of patients are currently diagnosed.\(^3,4\) Most of the patients remain undiagnosed because they are either asymptomatic (silent forms) or have vague unspecific symptoms (recurrent abdominal pain, abdominal distension) which are mislabeled as irritable bowel syndrome (IBS), or have extradigestive manifestations (depression, ataxia, neuropathy, infertility, osteoporosis). The latter group, those with nongastrointestinal presentation, is usually treated symptomatically or pathogenically without considering CD as a possible etiology. Given the fact that symptoms of CD or IBS can overlap with those of an inflammatory bowel disease (IBD) activity flare, IBD is also considered in front of a patient presenting with abdominal pain, bloating, or bowel movement changes.

CD serum antibody tests are helpful in case-finding programs for at-risk individuals, but they are quite costly and not easily available. The low diagnostic rate has set a need for developing additional tools which can select patients who warrant confirmatory CD specific tests (serology, upper gastrointestinal endoscopy with duodenal biopsy).

Splenic atrophy and dysfunction and increased red blood cell distribution width (RDW) have been previously reported as being commonly encountered in adult CD patients, but currently available guidelines are not frequently reporting it.\(^5-7\) Besides CD, a small spleen with functional hyposplenism can also occur in sickle cell anemia,\(^10\) a low prevalence condition in whites. While splenic hypofunction may improve with a gluten-free diet, in CD patients morphologically the spleen size seems to be irreversible.\(^11\)

RDW is a measure of size variation within the red blood cell (RBC) population, which is reported as part of the standard complete blood count (CBC) by automated hematology analyzers, without any additional costs. RDW is considered a sensitive indicator of nutritional deficiencies affecting RBC production and formation of a heterogeneous RBC population, with variation in cell volume.\(^12\)

Increased RDW even in the presence of normal hemoglobin values has been considered to be a sensitive predictor for CD.\(^13,14\) but it lacks specificity.\(^15\) In CD, RDW can also be used to monitor the dietary efficacy and compliance, as it should normalize in response to the gluten-free diet.\(^16-18\)

In this study, we propose the use of a simple, noninvasive, widely available score—the ratio of spleen diameter to RDW—to detect individuals with probability of CD, who may benefit from further testing. The assumption of using this score is the

**INTRODUCTION**

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In this study, we propose the use of a simple, noninvasive, widely available score—the ratio of spleen diameter to RDW—to detect individuals with probability of CD, who may benefit from further testing. The assumption of using this score is the
fact that both high RDW and splenic atrophy are noted in CD patients and a proportion of a low numerator to a high nominator augments the value of each component used separately.

METHODS

Study Population

We consecutively evaluated 15 newly diagnosed, antibody-positive, biopsy-proven CD adults, 52 IBD patients (20 with Crohn disease and 32 with ulcerative colitis), and 35 IBS patients admitted to our clinic over a period of 24 months, between June 1, 2012, and May 31, 2014. The CD, IBD, and IBS patients were diagnosed based on currently available guidelines.6,18,19 Patients with coexisting disease associated with celiac disease, IBS—irritable bowel syndrome, RDW—red blood cell distribution width, SD—standard deviation.

RESULTS

Of the 52 patients with IBD, 24 (46%) were women, with a mean age of 41 ± 14.1 years. Among the 35 IBS subjects, 19 (54%) were women, with a mean age of 37.9 ± 12.2 years. There was a significant higher proportion of women (80%) in the CD group in our cohort. The patient characteristics are shown in Table 1.

Crohn disease patients were more likely to be anemic than the other 3 groups, as seen by the mean hemoglobin (Hb) values (the difference, however, did not reach statistical significance). Spleen diameter, RDW, and their ratio values in the study groups are shown in Table 2.

The proportion of CD and Crohn disease patients with elevated RDW (defined as over 14) was significantly higher than those with ulcerative colitis or IBS—67%, 85% versus 37.5% and 9%, respectively. A small spleen (<95 mm) was most frequently seen in CD patients (80%) and less in ulcerative colitis (21.87%), Crohn disease (10%), or IBS (9%).

A spleen diameter to RDW ratio under 6 had a sensitivity of 73.3%, specificity of 88.5%, positive predictive value of 52.4%, and negative predictive value of 95.1% in detecting CD. The AUC (area under the curve) for predicting CD was 0.737 (95% CI: 0.597–0.877) (Figure 1). Only 1 out of 35 (3%) of IBS control subjects had a ratio under 6.

DISCUSSION

In the current study, we evaluate the usefulness of a simple score to detect patients with likelihood of CD. Made up of 2 widely available, inexpensive parameters (RDW is available from routine CBC and spleen size from routine US), this score can be easily calculated in daily clinical practice.

A small spleen (less than 95 mm in longitudinal axis) was noted in a large proportion of CD patients in our study (80%). Previous research has reported similar frequencies in celiac patients, significantly higher than in healthy subjects (78.3%...
and 26.1%, respectively). The paper of Eid et al8 also demonstrated significant lower splenic volumes in CD patients, compared to healthy population: 162 cm³ (range 37–321 cm³) to 215 cm³ (107–341 cm³), respectively. The mechanism of splenic atrophy in CD might be related to autoantibody targeting of lymphoid tissue, as shown by Korponay-Szabo et al22 Considering that splenic length correlates best with body height23 and that celiac patients are shorter relative to the general population,24 we also tested the difference in spleen diameter in the 3 groups after adjusting for height and revealed that the difference persisted. There was no statistically significant difference in body weight between the four groups (mean body weight 63.5 kg in CD, 64.5 kg in Crohn, 67.5 in UC, and 65.7 in IBS).

The second parameter included in this score, RDW, has proven to be a sensitive predictor of CD in previous research. As a marker of anisocytosis due to decreased erythropoiesis, a high RDW is one of the earliest signs of iron deficiency preceding a drop in Hb or low MCV). RDW is one of the earliest signs of iron deficiency (preceding a marker of anisocytosis due to decreased erythropoiesis, a high RDW was proven to be a sensitive predictor of CD in previous research. As a marker of anisocytosis as shown by Korponay-Szabo et al22 considering that splenic length correlates best with body height23 and that celiac patients are shorter relative to the general population,24 we also tested the difference in spleen diameter in the 3 groups after adjusting for height and revealed that the difference persisted. There was no statistically significant difference in body weight between the four groups (mean body weight 63.5 kg in CD, 64.5 kg in Crohn, 67.5 in UC, and 65.7 in IBS).

By combining these 2 sensitive parameters we can easily determine a ratio useful to detect patients who warrant serologic and histological confirmatory investigations for CD diagnostic. Regarding its sensitivity and specificity, the ratio proved to be better than other daily routine laboratory indices, such as neutrophil-to-lymphocyte ratio (Sn 80%, Sp 41%).

The main limitation of this study is the small sample size. Studies on larger cohort of untreated CD patients would be needed to validate our results and to establish the best cutoff of spleen diameter/RDW ratio.

CONCLUSIONS

Spleen diameter to RDW is a simple, readily available, and reliable score, which can be used to indicate patients with probability of CD. We report for the first time the usefulness of spleen diameter to RDW ratio in selecting patients for CD diagnosis. Further studies with larger samples of CD are needed to validate the diagnostic value of this ratio.

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FIGURE 1. Area under the curve (AUC) for a ratio of spleen diameter/RDW under 6 in predicting CD.
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