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COMPARATIVE EVALUATION OF SEROLOGICAL MARKERS AND DUODENAL HISTOPATHOLOGY IN DIAGNOSING CELIAC DISEASE AND OUTCOMES OF GLUTEN-FREE DIET

Uzma Batool [1*],Aliya Batool[2],Zholdasbekova Ainur[3],Bushra Anwar[4]

[1*]Consultant Physician MBBS,FCPS. Department of Medicine. PAEC General hospital.
[2]Assistant Professor MBBS,DCP,FCPS. Department of Pathology .Islamabad Medical & Dental College/Akbar Niazi Teaching Hospital.
[3] Senior Registerar, MBBS,FCPS.Deparment of Peadiatrics. Islamabad Medical & Dental College/Akbar Niazi Teaching Hospital.
[4]Associate Professor. MBBS,DCP,M-phil .Fazaia Medical college,Air University Islamabad.

***Corresponding Author:**Aliya Batool
*E mail: Aliya.batool@imdcollege.edu.pk
Cell No:0301-5140525

Abstract

Background: Celiac disease (CD) is a long-lasting autoimmune enteropathy activated by gluten in genetically susceptible human beings. Timely and proper diagnosis and gluten-free diet (GFD) are essential to be controlled.

Objectives: To evaluate and compare diagnostic value of serological biomarkers (anti-tTG) and duodenal biopsy in CD along with patient improvement over time with a GFD.

Methods: In this study, the cross-sectional design took place in June 2020 through December 2021 at Pakistan Atomic Energy Commission (PAEC) General Hospital. One-hundred and fifty patients with either clinically suspected or confirmed CD were recruited. Duodenal histology, serology and clinical symptoms were assessed. Patients were monitored upto six months in order to determine the GFD adherence and response.

Study Design: A Cross sectional study. Place and Duration of study. June 2020 through December 2021 at Pakistan Atomic Energy Commission (PAEC) General Hospital, Islamabad.

Results: Among 150 patients with mean age of 28.5± 9.7 years, 63% were female patients.68% patients presented with diarrhea, 54% abdominal pain, and 48% with weight loss.94 % had high anti-tTG (mean: 55.6 ±12.4 U/mL) and 88% had a biopsy-proven villous atrophy ($p < 0.01$). At six months of GFD, 76 % of patients showed symptomatic improvement, and 84 % had normalized serological markers ($p < 0.001$).

Conclusion: Serological markers (anti-tTG) are sensitive diagnostic markers and show high concordance with duodenal biopsy and are also useful screening tests. A strict GFD is effective in enhancing clinical and laboratory outcomes. There should be gender-specific management strategies.

Keywords: Celiac disease, anti-tTG antibodies, duodenal biopsy, gluten-free diet, serological markers

Introduction

Celiac disease (CD) is a long-into the past, autoimmune enteropathy that is caused by dietary gluten in genetically inclined persons. It is estimated to occur in about 1 percent of the world population and it manifests with a variety of gastrointestinal and extraintestinal symptoms, which can sometimes be problematic in making the diagnosis[1,2].Certain genetic markers have astrong relationship with the disease and include the HLA-DQ2 and the HLA-DQ 8 haplotypes in more than 95 percent of the patients [3]. Developmental origins of disease have also been reported to play a role in the pathogenesis of the disease, including early infections and gut microbiota changes [4,5].The defining features of CD include immune-mediated destruction of the small intestinal mucosa that leads to villous atrophy, an expansion of the crypt and intraepithelial lymphocytosis [6]. Malabsorption is a result of these histological modifications, which are characterized by corresponding symptoms of diarrhea, belly pain, weight loss, anemia, osteoporosis, and in others infertility and neurological disturbances [7,8]. It has a wide and nonspecific clinical presentation, particularly in adults; thus the diagnosis might be missed or delayed. The actual gold standard in the diagnosis of CD is acombinationofserologicaltestingandhistopathologicalconfirmationby asmallintestinal(duodenal) biopsy. Anti-tissuetransglutaminase(anti-tTG) and anti-endomysial antibodies (EMA) are serological markers, which are highly sensitive and specific in nature and are commonly used in screening [9,10]. Nevertheless, biopsy is still needed as the only way to determineadefinitediagnosisinparticularsettings,e.g.inseronegativeorlatentcasesofCD[11]. Intheseinstances,wegettousetheMarsh-Oberhuberclassificationsystemtocategorizethelevel ofmucosadamages[12].TheonlyknowneffectivetreatmentofCDisthelifelongstrictadherence to a gluten-free diet (GFD). The compliance with GFD is most likely to resolve the symptoms, regulate the serological markers, and heal the histologic intestinal mucosa [13]. Yet, such factors as socioeconomic, cultural and psychological barriers can render compliance difficult [14]. Structured education and dietary counseling havebeen proven to havea significantimprovement of adherence and clinical outcomes [15].The older literature on gender differences in the disease presentation has also been pointed out as females having greater extraintestinal presentation compared to the males who often present with anemia or silent diseases [16]. In addition, the development of non-responsive CD (NRCD) worsens the control of the disease and additional measures are needed, including immunosuppressive treatment or nutritional assistance [17].The proposed study is necessary to fully compare the diagnostic value of serological markers to correlatewith thehistopathologicalsituations in CD, as wellas to analyzesex-related symptoms, andcomparetheeffectsofGFDonsymptomaticandserologicalimprovement.Thisstudyaimsto providetheevidencebaseonwhichtomakebetterdiagnosticandtherapeuticdecisionsespecially in low-resource environments by combining serological and histological information.

Methods

It was a cross-sectional study carried out at the Medicine Department of Pakistan Atomic Energy Commission (PAEC) General Hospital,Islamabad.One hundred and fifty adult patients with a suspected or known celiac disease whose age was equal to or above 18 years old were selected. The presence of antibody -anti-tTG in serology and histopathologic finding of duodenal biopsies after upper gastrointestinal endoscopy proved the diagnosis. The Marsh-Oberhuber system was used to determine and measure biopsies. The clinical and serological response to gluten-free diet was also evaluated six months after the intervention. The patients received structured dietary counseling and this was monitored to check its adherence.

Inclusion Criteria

The patients were patients 18 years and older with clinical suspicion of celiac disease and confirmed either by serological positivity (anti- tTG/EMA) or histologic detection of histologic changes due to CD with biopsy.

Exclusion Criteria
Other autoimmune disorders, previous surgery in the gastrointestinal tract, incomplete medical history, and refusal of endoscopic biopsy or gluten free dietary advice were exclusion criteria.

Data Collection
Structured proformas were used to enter the demographics, presenting symptoms, serological titers, and biopsy results of patients. Repeat serology and symptom evaluation of repeat GFD adherence were done after a period of six months. Compliance was measured through interviews of patients when visiting the outpatients and through dietary recall.

StatisticalAnalysis
The SPSS version 24.0 was used to analyze data. The demographic data was analyzed by means of descriptive statistics. Categorical variables were evaluated by using chi-square tests. The relationship between serology and biopsy results was determined by Pearson correlation coefficient. All inferential tests were set at a p-value of <0.05 that was taken as significant.

Results
One hundred and fifty of the enrolled patients were involved,with a mean ageof28.5+/-9.7years, and a female abundance (63 percent). The most frequently reported symptoms were diarrhea (68%),abdominal pain (54%)and weight loss(48%).The rate of anti-tTGantibodies was high in 94% of the patients with an average score of 55.6 12.4 U/mL. A duodenal biopsy determined villousatrophyconsistentwithMarshgrade3lesionsin88percentofpatients(p<0.01),showing strong concordance with the serological results. After six months of follow-up after commencement of gluten-free diet, 76 percent of patients said they had greatly improved with symptoms. In addition, 84 percent exhibited normalized anti-tTG ($p < 0.001$). It is worth noting that adherence and outcomes were superior among patients who received structured dietary counseling stratum vs. patients who received no counseling ($p = 0.02$). The results confirm the value of serological and histopathological analysis in diagnosis,and emphasise the efficacy of dietary alternatives especially with education support.

Chart01:CommonSymptomsinCeliacDisease

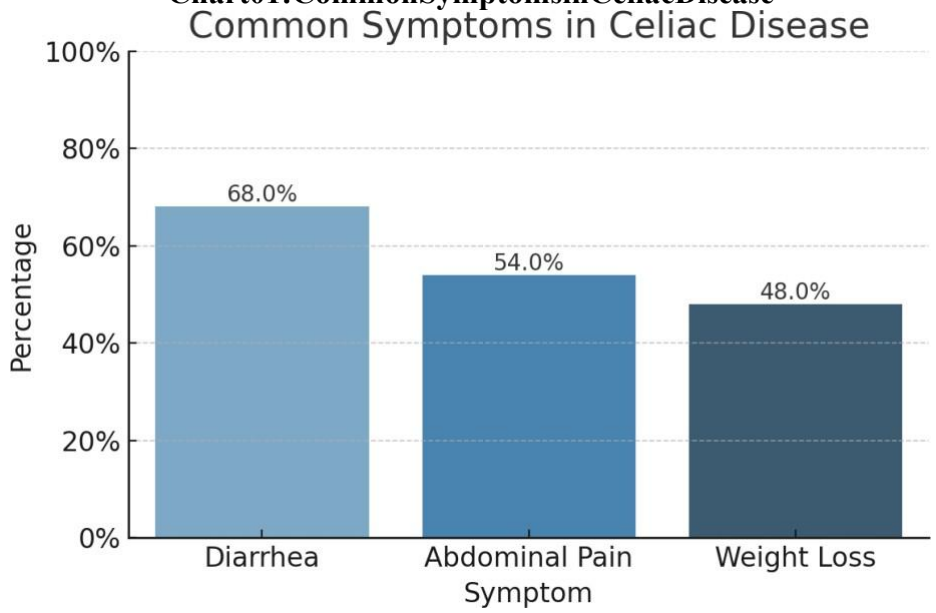

Chart02:DiagnosticFindingsinCeliacDisease

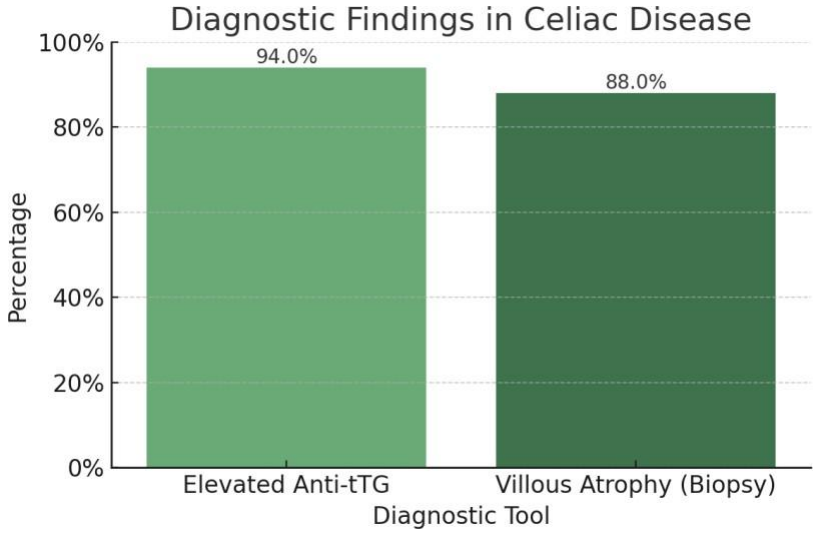

Table1:Demographics

Category	Value
TotalPatients	150
MeanAge (Years)	28.5 ±9.7
FemalePatients(%)	63%

Table2:Common Symptoms

Symptom	Percentage(%)
Diarrhea	68
AbdominalPain	54
WeightLoss	48

Table3:DiagnosticFindings

DiagnosticTool	Percentage(%)
ElevatedAnti-tTG	94
VillousAtrophy(Biopsy)	88

Discussion

The results of the present study support the accuracy in the serological diagnosis of celiac disease (CD) throughtheuseofserologicalmarkers,specificallyanti-tTGalongwiththehistopathologicalconfirmation. High anti-tTG levels were found in 94% of patients, and duodenal biopsies confirmed villous atrophy in
88% of cases also,which is in line with the previous studies,which on CD diagnosis reported a high level of concordance between serological markers and intestinal histology[18].
Ourfindingsalignwithwhatwasdoneby Kurppa etal.,inthattheyachievedastrongassociationbetween high anti- tTG titers and Marsh 3 lesions but they also proposed that biopsies could be foregone in a few high-titer patients¾ finding that supports our study conclusions. But the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) nevertheless continues to recommend biopsy confirmation in the majority of cases, because of individual

variability in serological response, especially in an adult patient[20].
ClinicaldifferencesbetweengendersinCD,asithasbeenreflectedinourcohort,refertopreviousresults. Female subjects were more likely to present with fatigue, neurological manifestations and infertility whereasanemiawasmoreprevalentinmales.Similartrendsinsex-basedvariationinclinicalpresentation werealsoreportedbyGreenetal.Theyfocusedonsuchfactorsasthepresenceofmaleorfemalehormone influence and immunological parameters[21]. Such evidence points to the need of gender-sensitive diagnosis approaches.
Our study findings of the positive clinical response to a gluten-free diet (GFD) with an improvement of symptoms in 76 percent and normalization of serological markers in 84 percent reinstate GFD as the mainstay of CD management. It is already determined by Rubio-Tapia et al. and others that strict GFD adherence is associated with significant clinical and histological outcomes on part of this issue[22]. Nonetheless, complianceisaproblembecauseofculturalandsocioeconomicfactorsashighlightedbyHall etal.,whoconcludedthatmore thana quarter of the patientswere notincompliance,manywere unaware or had limited access to gluten-free food supply[23].
Notably, the effect of dietary counseling on compliance and the outcomes was improved in our research. Our resultissimilar toone by Case etal.,whoillustratedthe presence of structurededucationandfollow- up to bring about significant GFD adherence and quality of life in CD individuals[24].
Still, non-responsive CD (NRCD) is a serious issue. It has beenspeculated byTacket al.andAbdulkarim etal.thatcontinuingsymptomsdespiteaGFDcanbeduetoeitherinadvertentglutenexposure,concomitant conditionslikeIBS,orrefractoryCD[25,26].Thesecasesdeservefurtherresearchtofindandhandlethem effectively.
There are potential add-ons to dietary therapy such as emerging therapeutic interventions such as enzyme supplementation, immunomodulators, and vaccines. Lebwohl et al. and Schuppan have stressed that new treatment options are required to overcome GFD shortcomings and enhance long-lasting management of the disease[27,28].

Conclusion:

Thisinvestigationproveshighlevelofdiagnosticprecisionofanti-tTGserologyincombinationwithbiopsyofduodenum.Theclinicalsymptomsshowsubstantialimprovementduringthegluten-freedietalongwith the serological indices. Gender differences in presentations point to the importance of individualized diagnosing and treatment strategies in the effective management of celiac disease.

Limitations:

The cross-sectional design of the study is restrictive to the determination of long-term compliance and mucosal healing. It is also a single-center; generalizability is limited. Also, possible recall bias with reporting dietary compliance by patients will underestimate the prevalence of non-compliance and its effects on the course of the disease and patient response to treatment.

Future Findings:

Multicenter longitudinal studies measuring long-term outcome of gluten-free dietadherence andresponse should be conducted in the future. Research is required into non-responsive celiac disease, starting with genetic/immunologic markers.Itis alsopossible thatby exploringadjunctive therapies,e.g.withenzyme- based or immunologic approaches, treatment options beyond using dietary restriction exclusively may be available.

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