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Diagnostic Yield of Routine Distal Duodenal Biopsy in a Tertiary Care Centre in South India (Tamilnadu) - A Retrospective Study

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Abstract: ***Background: Patients with non-diarrheal disease, are highly suspicious for coeliac diseases (CD). To get a clear picture, descending duodenum biopsy remains exclusive. Objectives: To determine the diagnostic yield of routine distal duodenal biopsies in patients with suspected coeliac disease attending a tertiary care centre in Tamil Nādu. Materials and methods: A Retrospective study was conducted at department of gastro-enterology at a tertiary care centre in Tamil Nādu from January 2018 to June 2021 among 516 suspected CD patients. Demographics, indication for the procedure, preoperative investigations (including complete blood count, and iron studies), endoscopic and histologic findings were collected from medical records. Duodenal biopsies were performed with standard technique using 2.8 mm biopsy taken from D2 second part of duodenum. Data was analysed using SPSS version 22. Results: The mean age was 46.35 ± 14.6 years. There were more proportion of females in the study with 52.52% (271 out of 516). Anemia was reported with high prevalence in 86.82% followed by Diarrhoea 5.81% and Anemia+ diarrhoea in 4.07%. As per endoscopy findings 489 (94.77%) had normal mucosa and scalloping was reported in 19 cases (3.68%). As per the biopsy report 436 (84.50%) cases showed normal mucosa flattening of villi in 5 (0.97%) cases. In abnormal endoscopy 9 (33.33%) cases were suggestive of CS. The difference between biopsy report and endoscopy findings was statistically significant (P value=0.009). The sensitivity of biopsy in predicting celiac was 33.33% (95% CI 16.52, 53.96), specificity was 85.48% (95% CI 82.04, 88.48%) and diagnostic accuracy was 82.75% (79.21, 85.91). Conclusion: Distal duodenal biopsy showed diagnostic accuracy of 82.75% and can be considered in diagnosing suspected CD cases.***

Keywords: Iron deficiency anaemia, duodenum, biopsy, endoscopy, small intestine

1. Introduction

Celiac disease (CD) is a common yet under diagnosed immune-mediated small intestinal enteropathy triggered by gluten in genetically susceptible individuals. [1] Seroprevalence of CD in Asia is found to be 1.6% in Asia (Iran, Turkey, Israel and India). [2] There are two requisites for the development of CD in a population: a pool of individuals who are capable of expressing the human leukocyte antigen (HLA)-DQ antigens 2 or 8 and consumption of wheat, which is the major gluten-containing grain associated with the development of CD. [3] Wheat is the staple grain used in the northern and western states of India, whereas rice is the staple grain in eastern and southern states of India. Thus CD with histological change is present in nearly 1% of the population of the northern Indian states, whereas it is much less prevalent in the southern states. [4]

Typically, patients with CD demonstrate small intestinal inflammation and villous atrophy, and this may result in malabsorption of both calories and micronutrients including iron. Major guidelines for both management of CD and iron-deficiency anaemia (IDA) point out the association between these two diseases and the need to test patients with unexplained IDA for CD. [5] It was found that approximately 1 in 31 patients with IDA have histologic evidence of CD that justifies the practice of testing patients with IDA for CD. [6]

Celiac disease may be associated with a multitude of symptoms and presentations such as bloating, diarrhoea, abdominal discomfort, fatigue, weight loss, iron deficiency anaemia, bone disease, skin disorders and abnormal liver function tests. [7] Patients may also be completely asymptomatic but, such patients generally do not present for upper endoscopy. While the prevalence of celiac disease continues to increase globally, a significant proportion of celiac disease patients remain undiagnosed. The diagnosis mainly consists of serological screening of antitissue trans-glutaminase (anti-TTG) level and upper gastrointestinal endoscopy with multiple duodenal biopsies. [8]

The ACG guidelines 2013 require medical history, physical examination, serology, and upper endoscopy with histological analysis of multiple biopsies of the duodenum for the confirmation of a diagnosis of CD. [9] Presently duodenal biopsy remains the gold standard in diagnosing CD patients. There is also good evidence to support refining our biopsy practice to increase diagnostic yield [10]. Recent study have shown that a bulb biopsy in addition to four biopsies in the second part of the duodenum increased the yield of celiac disease detection by 10–18% and such practice is recommended by National Institute of Clinical Excellence

and European Society for Pediatric Gastroenterology, Hepatology, and Nutrition guidelines. [11], [12], [13]A previous study by Sharma A et al found CD changes limited to the duodenal bulb only among children. To improve the diagnostic yield of duodenal bulb biopsy the study recommended to routinely include duodenal biopsies in children suspected with CD. [14]

There are very limited studies showing benefit and outcome of performing biopsy of duodenum for patients with suspected celiac diseases. Therefore, the purpose of this study was to examine the diagnostic yield of both normal appearing duodenal mucosa and abnormal mucosa such as scalloping, freckling for investigation of suspected celiac disease with particular attention to biopsy results that help in clinical management.

Aims and objectives:
To determine the diagnostic yield of routine distal duodenal biopsies in patients with suspected coeliac disease attending a tertiary care centre in Tamil Nādu

2. Materials and Methods

Study design: A Retrospective study

Study setting: The study was conducted at department of gastro-enterology at a tertiary care centre in Tamil Nādu

Source population: The study was conducted at department of gastro-enterology at a tertiary care centre in Tamil Nādu

Study population: The study was conducted at department of gastro-enterology at a tertiary care centre in Tamil Nādu

Study period: From January 2018 to June 2021.

Sample size: A total of 516 subjects were selected as sample size.

Ethical and informed consent: Institutional ethics committee approval was taken with a waiver of consent as the study was record based.

Inclusion criteria:
- Patients with Iron deficiency Anaemia (<12gm/dl in women and <13gm/dl in men with low MCV and / or
- Chronic diarrhoea (>4 weeks) or
- Significant weight loss (>5% in 6 months) or
- Combination of these above symptoms

Exclusion criteria:
- Age less than 18 years
- Known celiac disease
- Positive celiac serology
- Patient with an overt bleed, or an obvious source of bleed identified on endoscopy
- Residence outside of Tamil-Nadu

Data collection
Clinical and endoscopic data was obtained from electronic medical records and an electronic endoscopy database. In particular, the variables collected included patients' demographics, the indication for the procedure, preoperative investigations (including complete blood count [CBC], and iron studies), endoscopic and histologic findings. Duodenal biopsies were performed with standard technique using 2.8 mm biopsy taken from D2 second part of duodenum (distal). At least two duodenal biopsies were taken. The unfixed specimen was sent immediately for interpretation by pathologist.

Study variables
Predictive validity of duodenal biopsy was considered as primary outcome variable.

Statistical analysis
Summary statistics like mean, 95% confidence interval (CI; lower and upper bounds), median, minimum and maximum, and percentage were reported for continuous parameters like age, haemoglobin and categorical parameters like gender and symptoms. The association between explanatory variables and categorical outcomes was assessed by cross tabulation and comparison of percentages. The sensitivity, specificity, predictive values and diagnostic accuracy of the screening test along with their 95% CI were presented. P value < 0.05 was considered statistically significant. Data was analyzed by using SPSS software, V.22. [16]

3. Results

A total of 516 subjects were included in the final analysis.

The mean age was 46.35 ± 14.6 ranged between 18 to 83 years. There were more proportion of females in the study with 52.52% (271 out of 516). The mean haemoglobin% was 8.57 ± 2.29. Anemia was reported with high prevalence in 86.82% (448 out of 516) followed by Diarrhoea 5.81% and Anemia+ diarrhoea in 4.07% (21 out of 516). (Table 1)

As per Endoscopy findings scalloping was reported in 19 cases (3.68%) followed by reduced folds (0.58%), helminth (0.39%), nodularity (0.39%) and erythema (0.19%). As per the biopsy report, BGH was in 57 cases (11.05%) followed by peptic duodenitis 6 (1.16%), flattening of villi 5 (0.97%) etc., (Table 2)

In abnormal endoscopy 9 (33.33%) cases were suggestive of celiac and 18 (66.67%) were not suggestive of celiac. The difference between biopsy report and endoscopy findings was statistically significant (P value=0.009). (Table 3)

The sensitivity of biopsy in predicting celiac was 33.33% (95% CI 16.52, 53.96), specificity was 85.48% (95% CI 82.04, 88.48%) and diagnostic accuracy was 82.75% (79.21, 85.91). (Table 4)

Table 1: Summary of baseline parameter (N=516)

Parameter	Summary
Age (in years)	46.35 ± 14.6 (ranged 18 to 83)
Gender	
Male	245 (47.48%)
Female	271 (52.52%)
Haemoglobin %	8.57 ± 2.29 (ranged 2.60 to 16.10)
Symptoms	

Anemia	448 (86.82%)
Anemia+ diarrhoea	21 (4.07%)
Anemia+ weight loss	8 (1.55%)
Diarrhoea	30 (5.81%)
Diarrhoea + weight loss	1 (0.19%)
Weight loss	8 (1.55%)

Table 2: Summary of D2 endoscopy and Biopsy parameter (N=516)

Parameter	Summary
D2 Endoscopy	
Normal	489 (94.77%)
Scalloping	19 (3.68%)
Reduced folds	3 (0.58%)
Helminth	2 (0.39%)
Nodularity	2 (0.39%)
Erythema	1 (0.19%)
D2 Biopsy	
Normal	436 (84.50%)
BGH	57 (11.05%)
peptic duodenitis	6 (1.16%)
flattening of villi	5 (0.97%)
focal erosion	3 (0.58%)
Hookworm	2 (0.39%)
Lymphangiectasia	2 (0.39%)
Strongyloides	2 (0.39%)
Eosinophilic duodenitis	1 (0.19%)
CMV vasculitis	1 (0.19%)
Gastric heterotopia	1 (0.19%)

Table 3: Comparison of D2 Endoscopy with D2 Biopsy (N=516)

D2 Biopsy	D2 Endoscopy		Chi square	P value
	Abnormal (N=27)	Normal (N=489)		
Suggestive of celiac	9 (33.33%)	71 (14.52%)	6.914	**0.009**
Not suggestive of celiac	18 (66.67%)	418 (85.48%)		

Table 4: Predictive validity of D2 Biopsy in predicting CD (N=516)

Parameter	Value	95% CI	
		Lower	Upper
Sensitivity	33.33%	16.52%	53.96%
Specificity	85.48%	82.04%	88.48%
False positive rate	14.52%	11.52%	17.96%
False negative rate	66.67%	46.04%	83.48%
Positive predictive value	11.25%	5.28%	20.28%
Negative predictive value	95.87%	93.55%	97.54%
Diagnostic accuracy	82.75%	79.21%	85.91%

4. Discussion

This study from India, determined the role of distal duodenum biopsy among suspected CD patients visiting tertiary care centre. The study reported a sensitivity of 33.33% specificity of 85.48% and diagnostic accuracy of 82.75% of distal duodenum biopsy in predicting CD cases. The difference between biopsy report and endoscopy findings was statistically significant (P value=0.009).

CD is believed to be largely under diagnosed because of patchy nature of mucosal changes in CD, yield of biopsy samples that are inadequate for histological analysis and variability in histopathology reporting. submission of an adequate number of duodenal biopsies are to be submitted for histopathological analysis in diagnosing CD. [17] In the present study at least two duodenal biopsies were taken. Husnoo N, et al [18] suggested of taking <4 duodenal biopsy specimens in assessing for the presence of CD. The British Society of Gastroenterology (BSG) recommends taking at least four biopsy specimens if CD is suspected at the time of endoscopy. [19]

The mean age of the participants in the present study was 46.35 ± 14.6 years with 52.52% (271 out of 516) females compared to males. Pitman M et al [20] found patients under 50 years old, and 61% women more likely than men, to undergo duodenal biopsy, similar to present study. In the current study, anaemia was reported with high prevalence in 86.82% followed by anaemia and diarrhoea in 4.07%. Young E et al [21] found iron deficiency anemia in females as the strongest indicators for celiac disease which was in consistent to present study. Chellat H et al [22] found that routine duodenal biopsy gives an additional 6.63% diagnostic benefit of CD in anemia patients.

In the present study the biopsy report flattening of villi in 5 (0.97%) cases. In contrast, Dhandhu BSet al [23] found no evidence of villous atrophy in eight patients where distal duodenum biopsy was done and correct diagnosis of CD was made by bulb biopsy. McCarty Tret al [24] in his systematic review and meta-analysis, found duodenal bulb biopsy improved diagnostic yield of celiac disease by 5%. Biopsy and histologic examination of duodenal bulb during routine upper endoscopy increases diagnostic yield and aid in the diagnosis of celiac disease. This finding was contrasting the present study finding, where distal part of duodenum was considered for diagnosing CD. Similarly, Khadka M. et al [25] found distal duodenal biopsy useful for the diagnosis of CD in patients with inflammatory bowel syndrome.

Our findings highlight that routine duodenal biopsy can detect the majority of CD cases. The findings can help in providing interventions in managing CD and increasing compliance with existing guidelines. Despite the availability of easy and accurate serological tests, majority of CD patients remain undiagnosed due to is subtle symptoms. Diet modification treatment and other additional approaches are needed in tackling this challenge of undiagnosed CD patients presenting in a healthcare setting.

Small bowel biopsy still holds the position of the gold standard for evaluating the mucosal pathologies in patients with CD, especially in adults, and for evaluation of mucosal healing in follow up biopsies. As the histological changes in CD are not specific, access to clinical, endoscopic findings and serological titer will improve the pathology reporting. Pathologists should make effort to rule out all mimickers of CD and follow the laid down reporting format for uniformity. [26]

5. Limitations

The present study was retrospective in nature. The data was collected from medical records which excludes a temporal and causal relationship. Also, it was a single centre, nonrandomised study limiting its application to wider

population group. We did not have complete data on gross endoscopic findings. A comparative group study would be advisable. Further multicentric prospective studies are recommended in supporting the findings of present study.

6. Conclusion

The sensitivity of distal duodenal biopsy in predicting celiac was only 33.33%. But the specificity was 85.48% and diagnostic accuracy was 82.75%. Distal duodenal biopsy can be considered in diagnosing suspected CD cases. Anaemia was most prevalent in this study and patients presenting with unexplained anaemia are to be diagnosed for CD. More efforts are warranted to improve awareness on CD features among physicians of different medical specialties. Health care professionals need to take measures in increasing awareness and improving local compliance in diagnosing CD**.** Validated indications for endoscopy and duodenal biopsy among patients with common upper gastrointestinal symptoms need to be explored.

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