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Spectrum of Duodenal & Small Intestinal Diseases in Quetta: A Hospital-Based Study

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Author`s Contribution

[1,3]Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work, [1,2,5]Drafting the work or revising it critically for important intellectual content, Literature review, [4,6]Data analysis

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ABSTRACT

Objective: To determine the spectrum of inflammatory and neoplastic diseases affecting the duodenum and small intestine in patients presenting at a tertiary care hospital in Quetta, Balochistan.

Methodology: This is a retrospective observational study. It was conducted in a tertiary care hospital from April 2021 to January 2025 in Quetta. A total of 152 patients of all ages and both genders who underwent duodenal or small intestinal biopsy were included in the study. Those cases with complete clinical, endoscopic, and histopathological data were analyzed. Histological findings of endoscopic biopsies, incisional biopsies, and excision specimens were assessed. Celiac disease was classified using the Marsh classification. Data was analysed using SPSS version 20. Associations between variables were calculated using Chi-square and Fisher's exact tests. Statistical significance was set at $p<0.05$.

Results: The mean age of patients was 31.53 ± 13.81 years, with a male predominance (70.4%). The most common presenting symptoms were anemia (39.5%) and chronic diarrhea (19.1%). Inflammatory and benign conditions accounted for 95.4% of cases, while malignant lesions comprised 4.6%. The most common histopathological finding was chronic non-specific inflammation (61.2%). Celiac disease was reported in 19.7% of cases, predominantly in males, with Marsh stage 1 and stage 3b being the most common subtypes. Giardiasis and Meckel's diverticulum were each diagnosed in 1.3% of cases. Adenocarcinoma was most common malignant lesion (2%), followed by intestinal lymphomas and gastrointestinal stromal tumors (GISTs).

Conclusion: Inflammatory conditions, especially chronic non-specific inflammation and celiac disease, represent the majority of duodenal and small intestinal pathologies in this area. Although uncommon, malignant lesions remain clinically significant. Histopathological examination of biopsies plays a crucial role in accurate diagnosis and appropriate management.

Keywords: Celiac disease, Duodenal diseases, Small intestine diseases.

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Introduction

Duodenal and small intestinal diseases contribute significantly to the global burden of gastrointestinal disorders. The prevalence of inflammatory bowel disease (IBD) has been increasing worldwide, with the global incidence rate raising from 4.22 per 100,000 in 1990 to 4.45 per 100,000 in 2021.[1] In 2019, the global cases of IBD were approximately 4.9 million, with highest number of cases in China and USA.[2] Important conditions affecting duodenum and small intestine include duodenitis, duodenal perforation, celiac disease, giardiasis, and various neoplasms including gastrointestinal stromal tumors (GISTs) and adenocarcinomas.[3] These disorders can be asymptomatic or present with symptoms like epigastric discomfort, bleeding, anemia, weight loss, and chronic diarrhea. These diseases vary by geographic location, dietary habits of people, socioeconomic conditions, Helicobacter pylori infection rates, and accessibility of people to healthcare. For example, peptic ulcer disease, caused by

pylori infection, is still a major cause of duodenitis, duodenal strictures, and gastric outlet obstruction.[3]

Among inflammatory conditions, H. pylori is the primary cause of duodenitis and peptic ulcers, followed by Giardia lamblia infection, which is more common in developing countries of South Asia. In Pakistan, there is a high incidence of giardiasis (15–20%).[4] Drugs like Non-steroidal anti-inflammatory drugs can damage duodenal epithelium and are the major cause of duodenitis in patients using these drugs.[5]

Worldwide, Celiac disease affects approximately 40-60 million individuals.[6] Previously, it was thought to be uncommon in South Asia, but its incidence is increasing in India and Pakistan.[7] The increasing prevalence of celiac disease and other related disorders in Asia, in many instances, is misclassified as irritable bowel syndrome due to similar symptoms.[7]

Duodenal neoplasms are uncommon worldwide (1–2% of gastrointestinal cancers).[8] In Asia, there is an increasing incidence of adenocarcinomas and GISTs, attributed to genetic and dietary factors.[6] Frequency of lymphomas secondary to chronic inflammation is also on the rise.[8] According to GLOBOCAN 2020 data, there are 24,000 new cases of duodenal cancer annually worldwide, emphasizing the importance of early diagnosis.[9]

Diagnosis through endoscopic biopsies plays an important role in diagnosis, especially in-patient groups where alternative diagnoses need to be excluded. Gastroenterologists consider endoscopic biopsies to be the most reliable method for obtaining final diagnoses in suspected gastrointestinal pathologies.[9] This is especially important in settings where advanced imaging techniques are not available, making endoscopy and biopsy the most practical diagnostic approach.

Data specifically focusing on the burden of duodenal and small intestinal diseases is limited in Pakistan. This highlights the need for more focused research in this area. Our study focuses on examining regional differences in diseases of the gastrointestinal tract and their association with various etiological factors. This will improve diagnostic accuracy by identifying common diseases, particularly in the duodenum and small intestine, such as celiac disease and infections. This will contribute to developing local clinical guidelines and ultimately lead to improved patient care and healthcare policy formulation.

Methodology

This retrospective study was conducted at a tertiary care hospital in Quetta from April 2021 to January 2025. The study population included adults of both genders and all ages who presented with gastrointestinal symptoms such as anemia, chronic diarrhea, pain abdomen, weight loss, dyspepsia, hematemesis, and vomiting. Patients with complete clinical, endoscopic, and histopathological data were included. Endoscopic biopsies, Incisional biopsies, and excision specimens were included. Patients with incomplete biopsy data or inadequate tissue samples for histological evaluation were excluded, as were poorly fixed specimens.

A sample size of 152 was calculated using the WHO sample size calculator, with a 95% confidence interval, anticipated population of 15%[10], and 6% absolute precision. Data was collected from hospital electronic records and histopathology archives after ethical approval by the institutional review board (XXXQTA-IERB/97/2025).

Outcome variables included clinical symptoms and histopathological results, which included diagnosis, degree of inflammation, villous atrophy, crypt hyperplasia, and Intraepithelial lymphocytes and their association with patients' age and gender. Histological changes in cases suspected of Celiac disease (CD) were classified using the Marsh Classification system. [11] Marsh 1 cases showed increased intraepithelial lymphocytes (IELs) (>30 per 100 enterocytes), with normal villous architecture, Marsh 2 cases exhibited increased IELs and crypt hyperplasia, and normal villi. Marsh 3 has increased IELs with crypt hyperplasia and villous atrophy, which is subclassified into 3 a,b, and c depending upon the severity of villous atrophy.

Cases lacking a definitive cause but displaying mild inflammation were categorized as chronic non-specific inflammation. The obtained data were entered and subjected to descriptive statistical analyses using SPSS version 20. Furthermore, the association of diagnosis was seen with various other variables, including age and gender, using the Chi-square test, Fisher’s exact test and Mann-Whitney U test. To determine the association between the patient's age and gender, they were divided into four groups. Group I included patients aged < 20 years, group II included those aged 21–40 years, group III included those aged 41–60 years, and group IV included those aged > 60 years. Statistical significance was set at $P < 0.05$.

Results

The age range of patients in the study was 7 to 76 years, with a mean age of 31.53 years ±13.81. Overall, the age distribution reflects a predominance of participants between 20 and 45 years. Males were the majority, representing 70.4% (n=107) of the sample, while females accounted for 29.6% (n = 45). Majority of biopsies were obtained from the duodenum, with the remainder taken from the jejunum and ileum.

The most prevalent symptom among patients was anemia (39.5%, n=60), followed by chronic diarrhea (19.1%, n=29), dyspepsia (15.8%, n=24), abdominal pain (8.6%, n=18), and weight loss (8.5%, n=13). Less common symptoms included vomiting, hematemesis, and intestinal obstruction, as depicted in Figure 1.

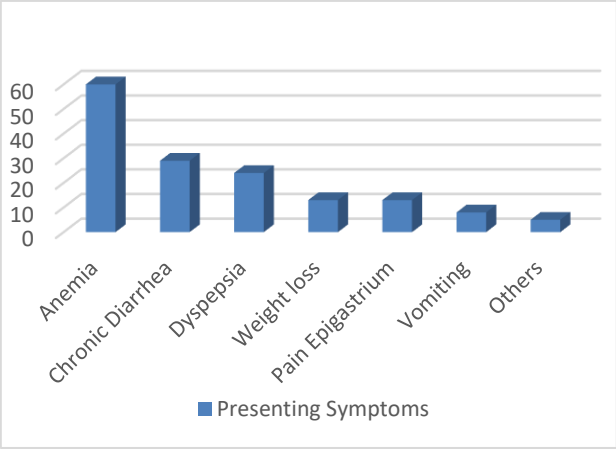

Figure 1. Frequency of presenting symptoms among patients. (n=152)

Age groups and symptoms were correlated with gender to look for any significant association. The majority of the cases were in group II (age 21-40 years), predominantly affecting males. The results showed a significant association between male gender and age group-I with a p-value less than 0.05. No significant association was found with other age groups. While analyzing symptoms, anemia was found to be the most common presenting symptom in both genders, followed by chronic diarrhea and weight loss. However, chronic diarrhea and weight loss are the predominant symptoms in patients with celiac disease. No significant association was found with the gender of the patients. These findings are summarized in Table I.

Out of all cases, 95.4% (n=145) were diagnosed with inflammatory and benign conditions, while 4.6% (n=7) were identified as neoplasms. Normal morphology was observed in 11.8% (n=18) of cases, whereas 88.2% (n=134) of cases exhibited duodenal pathology.

Table I: Correlation of Gender with different age groups and Symptoms. (n=152)

Variable		Gender		Total	p-value
		Male	Female		
Age Groups	≤20 Years	14 (48.3%)	15 (51.7%)	29 (19.1%)	0.006
	21-40 Years	71 (75.5%)	23 (24.5%)	94 (61.8%)	0.10
	41-60 Years	15 (75%)	5 (25%)	20 (13.2%)	0.794
	>60 Years	7 (77.8%)	2 (22.2%)	9 (5.9%)	1.00
	Total	107 (70.4%)	45 (29.6%)	152 (100%)	
Symptoms	Anemia	38 (65.5%)	20 (34.5%)	58 (38.2%)	0.361
	Chronic Diarrhea	24 (80%)	6 (20%)	30 (19.7%)	0.124
	Dyspepsia	14 (70%)	6 (30%)	20 (13.2%)	1.00
	Pain epigastrium	7 (58.3%)	5 (41.7%)	12 (5.3%)	0.675
	Weight loss	13 (100%)	0	13 (8.6%)	0.068
	Vomiting	3 (37.5%)	5 (62.5%)	8 (5.3%)	0.342
	Others	8 (72.7%)	3 (27.3%)	11 (7.2%)	-
	Total	107 (%)	45 (%)	152 (100%)	

The predominant histological finding was chronic non-specific inflammation, present in 61.2% (n=93) of cases. Out of the examined cases, 19.7% (n=30) were diagnosed as Celiac disease (CD) and were subsequently classified using the Marsh Classification system.[10] They were further categorized as Marsh stage 1, which accounted for 7.2% (n=11) of cases, Marsh stage 2 represented 0.7% (n=1), Marsh stage 3a comprised 3.3% (n=5), stage 3b made up 6.6% (n=10), and stage 3c constituted 2% (n=3) of cases. A higher prevalence was observed in males (63.3%, n=19) compared to females (36.7%, n=11). This gender disparity was statistically significant only for chronic non-specific inflammation. Furthermore, the study identified 1.3% (n=2) cases of Meckel's diverticulum in the ileum and an equal percentage (1.3%, n=2) of giardiasis cases exhibiting mild villous atrophy. A comprehensive overview of these results is provided in Table II.

Malignant neoplasms were identified in 4.6% (n=7) of the examined cases. Among these, adenocarcinomas constituted 2% (n=3), with 1.3% (n=2) being well-differentiated and 0.7% (n=1) poorly differentiated. Intestinal lymphomas were observed in 1.3% (n=2) of cases, comprising enteropathy-associated T-cell lymphoma and diffuse large B-cell lymphoma, each at

0.7% (n=1). Additionally, 1.3% (n=2) of cases exhibited gastrointestinal stromal tumors classified as intermediate risk as shown in Table II.

Table II: Summary of all histological findings in duodenal & Small intestinal biopsies. (n=152)

Diagnosis	Gender		Total	P-Value
	Male	Female		
Benign				
Unremarkable	13 (72.2%)	5 (27.8%)	18 (11.8%)	
CNS inflammation	67 (72%)	26 (28%)	93 (61.2%)	0.037
Celiac Disease	19 (63.3%)	11 (36.7%)	30 (19.7%)	0.281
Marsh 1	5 (50 %)	5 (50 %)	10 (6.6 %)	
Marsh 2	1 (100%)	0	1 (0.7%)	
Marsh 3a	4 (66.7 %)	2 (33.3%)	6 (3.9%)	
Marsh 3b	6 (60%)	4 (40 %)	10 (6.6%)	
Marsh 3c	3 (100%)	0	3 (2%)	
Meckel's Diverticulum	2 (100%)	0	2 (1.3%)	-
Giardiasis	1 (50%)	1 (50%)	2 (1.3%)	-
Tumors	5 (71.4%)	2 (28.6%)	7 (4.6%)	1.00
GIST	1 (50%)	1 (50%)	2 (1.3%)	
Lymphoma			2 (1.3%)	
EATL	1 (0.7%)	0	1 (0.7%)	
DLBCL	1 (0.7%)	0	1 (0.7%)	
Adenocarcinoma Well Differentiated	1 (0.7%)	1 (0.7%)	3 (2%) 2 (1.3%)	
Poorly differentiated	0	1 (0.7%)	1 (0.7%)	

The histological changes in patients with Celiac disease (CD) were further analyzed for any correlation with gender. Villous atrophy was found in 15.1% (n=23) patients. Among these mild (3.9%, n=6) to moderate (7.2% n=11) villous atrophy was observed in most cases, while severe villous atrophy was seen in 3.9 % (n=6) of cases. Crypt hyperplasia ranged from mild (7.2%, n=11) to moderate (2%, n=3) in most cases. Inflammation was categorized as mild in 64.5% (n=98) cases, moderate in 15.1% (n=23) cases, and severe in 8.5% (n=13) cases. No inflammation was observed in 11.8% (n=18) of the cases. Intraepithelial lymphocytosis was noted in 19% (n=29) of cases. These findings were also correlated with gender, but there was no significant correlation, as shown in Table III.

Table III: Histological changes in duodenal biopsies. (n=152)

Histological Changes		Gender		Total	p-value
		Male	Female		
Villous Atrophy	Not Seen	91 (70.5%)	38 (29.5%)	129 (84.9%)	0.843
	Mild	4 (66.7%)	2 (33.3%)	6 (3.9%)	
	Moderate	7 (63.6%)	4 (36.4%)	11 (7.2%)	
	Severe	5 (83.3%)	1 (16.7%)	6 (3.9 %)	
	Total	107 (70.4%)	45 (29.6%)	152 (100%)	
Crypt Hyperplasia	Not Seen	96 (69.6%)	42 (30.4%)	138 (90.8%)	0.461
	Mild	8 (72.7%)	3 (27.3%)	11 (7.2%)	
	Moderate	3 (100%)	0	3 (2%)	
	Severe	0	0	0	
	Total	107 (70.4%)	45 (29.6%)	152 (100%)	
Inflammation	Not Seen	13 (72.2%)	5 (27.8%)	18 (8.6%)	0.626
	Mild	70 (36.4%)	28 (28.6%)	98 (64.5%)	
	Moderate	15 (65.2%)	8 (34.8%)	23 (15.1%)	
	Severe	9 (69.2%)	4 (30.8%)	13 (8.6%)	
	Total	107 (70.4%)	45 (29.6%)	152 (100%)	
IELs	<30	88 (71.5%)	35 (28.5%)	123 (81%)	0.524
	>30	19 (65.5%)	10 (34.5%)	29 (19%)	
	Total	107 (70.4%)	45 (29.6%)	152 (100%)	

Discussion

Globally, the diseases of the small intestine, especially the duodenum, represent significant health challenges in people. They are difficult to diagnose, and if they remain untreated, they can cause significant complications. The symptoms caused by these diseases are variable depending on the cause of the underlying disease.

In this study, the patients showed a variety of symptoms, which include epigastric pain, vomiting, and unexplained weight loss, which is comparable to findings from Frissora et al. and Da Rosa Mesquita et al., who reported chronic diarrhea and abdominal discomfort as major symptoms.[12,13] These findings point to the important role of endoscopic examination and histological assessment. Endoscopic findings may be less specific; therefore, histopathological evaluation of biopsy becomes critical in reaching the final diagnosis, staging of disease, and also guiding clinicians for appropriate treatment strategies. This integrated approach is especially important to differentiate between inflammatory, infectious, and neoplastic conditions affecting the duodenum and small intestine

Duodenal diseases, including both inflammatory and neoplastic lesions, were more prevalent in males as compared to females in our study. Similar findings are also seen at the global level, as confirmed by a study done from 1990 to 2019, which showed a higher burden of intestinal diseases in males across different sociodemographic regions.[14] While acknowledging that gender-related differences can vary based on specific conditions, age groups, and location, our study shows a male predominance in all age groups, with statistical significance observed in age group I. Furthermore,

chronic non-specific inflammation was found to be more prevalent in males. These differences based on gender need further studies to look into possible contributing factors, which may include hormonal influences, lifestyle factors, and genetic predispositions.

Our study revealed non-specific inflammation to be the common histological finding, as it was identified in 93 cases, while 18 cases were unremarkable. Studies on non-specific duodenitis and unremarkable duodenal biopsies highlight the importance of recognizing subtle histological features and their diagnostic significance. They show that even if there are no overt villous abnormalities, studies on non-celiac gluten sensitivity have shown characteristic changes in the duodenal mucosa, such as reduced villous length and increased intraepithelial lymphocyte counts. Such findings suggest that even when inflammation is non-specific or biopsies appear unremarkable, mild histological changes, as seen in non-celiac gluten sensitivity, may still provide important diagnostic information. Non-specific duodenitis can show mild changes in villous architecture and IEL counts, apparently normal biopsies might still show alterations in specialized cell populations such as tuft cells.[15]

Worldwide Celiac disease affects 40-60 million individuals, with increasing prevalence in certain Asian countries, including Pakistan.[16] Its occurrence varies over different regions, with incidence ranging from 0.1% to 3.2% in Arab countries.[17] Our study showed 19.7% cases of Celiac disease. These results suggest significant presence of CD in our study population, which is consistent with findings in local and international studies. Various factors can be responsible for these findings which include genetic predisposition, gluten intake, and improved diagnostic methods.[18] Additional research is required to determine the precise prevalence rates in Pakistan. Our study observed an increased incidence of CD in males 63.3%, as compared to females, 36.7%. This is important, as females are more likely to have persistent disease, as reported by Veeraraghavan et al., who found that female children were more prone to experience non-responsive celiac disease than males.[19] This finding indicate a potential gender-related correlation in the persistence of celiac disease symptoms even if these patients adhere to a gluten-free diet.[19] In South Asia, the prevalence of CD and associated malabsorption syndrome is not well-documented, although its recognition is increasing. The causes for this may be due to the broad clinical spectrum of CD presentation, which range from asymptomatic cases to severe manifestations. This leads to its underdiagnosis, especially in areas with low awareness about the diseases.[20]

Although, duodenal biopsies are not typically performed for diagnosing giardiasis, our study showed two cases, however this diagnosis is very important, especially in treatment-resistant cases. Giardiasis remains a common cause of diarrhea and intestinal enteropathy worldwide, affecting low-income and people in developing countries.[21] Recent studies indicate a concerning rise in treatment-refractory giardiasis, with up to 50% of cases which do not respond to initial 5-nitroimidazole treatment.[21] This finding signifies the need for increased awareness and alternative treatment strategies for giardiasis.

Neoplasms affecting the duodenum and small intestine are less common and constitute less than 5% of all gastrointestinal tumors worldwide, but their occurrence has been rising.[22] In our research, adenocarcinomas were found to be the most common malignancy growths, with two cases located in the periampullary region. Other tumors found in our study included intestinal lymphomas and Gastrointestinal Stromal Tumors (intermediate-risk). These findings correlate with regional and international studies, such as that by Gelsomino et al., which showed that adenocarcinomas of the small intestine predominantly originate in the duodenum in 40% of cases.[23] The relatively high proportion of adenocarcinomas in our study signifies the importance of endoscopic evaluation in patients with related symptoms, like abdominal pain, weight loss, or gastrointestinal bleeding. A study in Egypt reported that 58.8% of small intestinal GISTs were located in the ileum and 41.2% in the jejunum.[24] In literature, there is no specific data on duodenal GIST prevalence in South Asia. Because of the scarcity of these tumors, there is limited research available on these tumors, but recent genetic and molecular investigations offer new perspectives on their unique profiles and potential targeted therapies.[23] Small intestinal cancer revealed a higher incidence in males as compared to females. The global impact was found to be greater in men, with similar increasing patterns observed in both genders over time.[25] This increase was more pronounced in the older population aged 50-74 years compared to younger adults.

Limitations: It is important to acknowledge the limitations of this study, primarily the fact that it was conducted at a single tertiary care hospital. This may limit the generalizability of our findings to the broader population.

Conclusion

In conclusion, our study highlights the importance of integrating endoscopic findings with histological examination of biopsy samples for accurate diagnosis and management of duodenal diseases. This comprehensive approach improves patient outcomes and reduces the need for more invasive procedures, and prevents complications.

References

1. Lin D, Jin Y, Shao X, et al. Global, regional, and national burden of inflammatory bowel disease, 1990–2021: insights from the Global Burden of Disease 2021. *Int J Colorectal Dis.* 2024;39(1). https://doi.org/10.1007/s00384-024-04711-x
2. Wang R, Li Z, Liu S, Zhang D. Global, regional and national burden of inflammatory bowel disease in 204 countries and territories from 1990 to 2019: a systematic analysis based on the Global Burden of Disease Study 2019. *BMJ Open.* 2023;13(3):e065186. https://doi.org/10.1136/bmjopen-2022-065186
3. Kurniawan A, Tan C. Peptic duodenal stricture causing gastric outlet obstruction: a case report. *Indones J Gastroenterol Hepatol Dig Endosc.* 2023;24(2):176-181. https://doi.org/10.24871/2422023176-181
4. Khan A, Khatoon N, Shaukat SS, Waheed S, Khan A, Nil R. Helminth associated infections among residents of Karachi. *RADS J Biol Res Appl Sci.* 2020;11(2):96-101.
5. Chey WD, Leontiadis GI, Howden CW, Moss SF. ACG clinical guideline: treatment of *Helicobacter pylori* infection. *Am J Gastroenterol.* 2017;112(2):212-239. https://doi.org/10.1038/ajg.2016.563
6. Mohta S, Ahuja V, Makharia GK, Rajput MS. Emergence of celiac disease and gluten-related disorders in Asia. *J Neurogastroenterol Motil.* 2021;27(3):337-346. https://doi.org/10.5056/jnm20140
7. Shirwaikar Thomas A, Schwartz M, Quigley E. Gastrointestinal lymphoma: the new mimic. *BMJ Open Gastroenterol.* 2019;6:e000320. https://doi.org/10.1136/bmjgast-2019-000320
8. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2021;71(3):209-249. https://doi.org/10.3322/caac.21660
9. Machiwal K, Menghani B, Kasliwal N, Sharma M. Histopathological spectrum of lesions in gastrointestinal endoscopic biopsies in Jawahar Lal Nehru Medical College and associated group of hospitals, Ajmer, Rajasthan. *Int J Res Med Sci.* 2022;10(12):2831. https://doi.org/10.18203/2320-6012.ijrms20223084
10. Patel N, Pai R, Leffler D, et al. Clinical data do not reliably predict duodenal histology at follow-up in celiac disease: a 13-center correlative study. *Am J Surg Pathol.* 2024;48(2):212-220. https://doi.org/10.1097/PAS.0000000000002150
11. Yasin MA, Farooq MA, Uddin N, Parveen B, Asghar A, Ahsan J. Spectrum of histopathological patterns of duodenal biopsies in patients with unexplained anemia and chronic diarrhea and their correlation with endoscopic findings and serological markers. *Pak Armed Forces Med J.* 2021;71(5):1893-1896. https://doi.org/10.51253/pafmj.v71i5.6145
12. Frissora CL, Schiller LR. Getting the BS out of irritable bowel syndrome with diarrhea (IBS-D): let's make a diagnosis. *Curr Gastroenterol Rep.* 2024;26(1):20-29. https://doi.org/10.1007/s11894-023-00909-1
13. Da Rosa Mesquita R, Galdino Dos Santos AG, Salgueiro De Aquino SH, et al. Clinical manifestations of COVID-19 in the general population: a systematic review. *Wien Klin Wochenschr.* 2021;133(7-8):377-382. https://doi.org/10.1007/s00508-020-01760-4
14. Wang R, Zhang D, Liu S, Li Z. Global, regional, and national burden of 10 digestive diseases in 204 countries and territories from 1990 to 2019. *Front Public Health.* 2023;11:1061453. https://doi.org/10.3389/fpubh.2023.1061453
15. Rostami K, Jericho H, Ciacci C, et al. Gluten induces subtle histological changes in duodenal mucosa of patients with non-coeliac gluten sensitivity: a multicentre study. *Nutrients.* 2022;14(12):2487. https://doi.org/10.3390/nu14122487
16. Mohta S, Ahuja V, Makharia GK, Rajput MS. Emergence of celiac disease and gluten-related disorders in Asia. *J Neurogastroenterol Motil.* 2021;27(3):337-346. https://doi.org/10.5056/jnm20140
17. El-Metwally A, Alsaqabi MK, Toivola P, et al. The epidemiology of celiac disease in the general population and high-risk groups in Arab countries: a systematic review. *Biomed Res Int.* 2020;2020:6865917. https://doi.org/10.1155/2020/6865917
18. Jansson-Knodell CL, Weekley K, Lyu R, et al. Relationship between gluten availability and celiac disease prevalence: a geo-epidemiologic systematic review. *J Gastroenterol Hepatol.* 2023;38(10):1695-1709. https://doi.org/10.1111/jgh.16260
19. Veeraraghavan G, Kelly CP, Therrien A, et al. Non-responsive celiac disease in children on a gluten-free diet. *World J Gastroenterol.* 2021;27(13):1311-1320. https://doi.org/10.3748/wjg.v27.i13.1311
20. Bolia R, Thapar N. Celiac disease in children: a 2023 update. *Indian J Pediatr.* 2024;91(5):481-489. https://doi.org/10.1007/s12098-023-04659-w
21. Mørch K, Hanevik K. Giardiasis treatment: an update with a focus on refractory disease. *Curr Opin Infect Dis.* 2020;33(5):355-364. https://doi.org/10.1097/QCO.0000000000000668
22. Zhao Z, Guo S, Yang S, et al. Endoscopic diagnosis and treatment of superficial non-ampullary duodenal epithelial tumors: a review. *J Transl Intern Med.* 2023;11(3):206-215. https://doi.org/10.2478/jtim-2023-0102
23. Gelsomino F, De Lorenzo S, Garajová I, Balsano R. Small bowel adenocarcinoma: from molecular insights to clinical management. *Curr Oncol.* 2022;29(2):1223-1236. https://doi.org/10.3390/curroncol29020104
24. Hamed H, Elmahdy Y, Wahab MA, El-Wahab RMA, El-Magd ESA. Gastrointestinal stromal tumors of the small intestine: the challenge of diagnosis and the outcome of management. *World J Surg Oncol.* 2023;21(1):129. https://doi.org/10.1186/s12957-023-02968-0
25. Huang J, Elcarte E, Lin X, et al. Incidence, risk factors, and temporal trends of small intestinal cancer: a global analysis of cancer registries. *Gastroenterology.* 2023;165(3):600-612. https://doi.org/10.1053/j.gastro.2023.05.043