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Table of Contents

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Case Report

Pancreatic Rest Complicated by Actinomyces Gastric Abscess in a Young Male: A Case Report

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ABSTRACT

Pancreatic rest, or ectopic pancreatic tissue, is a rare condition. It is characterized by pancreatic tissue outside its usual location, most commonly in the gastric antrum or proximal small intestine. We present a rare case of a 21-year-old male with recurrent epigastric pain, vomiting, and fever. Imaging and endoscopic ultrasound (EUS) identified a subepithelial lesion with features consistent with pancreatic rest. Subsequent fine-needle aspiration (FNA) grew Actinomyces and Streptococcus. Given persistent symptoms and incomplete resolution despite prolonged antibiotics, he underwent partial gastrectomy. This case highlights an unusual infectious complication of pancreatic rest with Actinomyces and underscores the need to consider surgical intervention in cases refractory to medical therapy.

1. Introduction

Pancreatic rest is a condition where pancreatic tissue is located outside its usual anatomical site. It is also called ectopic, heterotopic, or aberrant pancreatic tissue. This tissue lacks an anatomical or vascular connection to the main pancreas yet retains its own separate blood and nerve supply [1, 2]. This condition predominantly affects the gastrointestinal tract, particularly the gastric antrum and proximal small intestine, with an incidence ranging from 0.55% to 13% in autopsy series [1]. While pancreatic rests are often asymptomatic and discovered incidentally during endoscopic or imaging studies, common symptoms include nausea, vomiting, epigastric pain, weight loss, gastrointestinal bleeding, and gastric outlet obstruction. Rarely, it can lead to complications such as gastric ulceration, pancreatitis, obstructive jaundice when near the Ampulla of Vater, or even acute perforation due to inflammation in the stomach or duodenum [2, 3]. Gastric abscesses secondary to pancreatic rest are particularly rare, with few reported cases describing this phenomenon [4, 5]. These abscesses are believed to result from localized inflammation or necrosis of ectopic acinar tissue. Identifying pancreatic rest as the source of a gastric abscess is clinically challenging, particularly when the initial presentation mimics more common gastric subepithelial lesions such as gastrointestinal stromal tumors (GISTs) or duplication cysts [2, 6]. Malignant transformation is uncommon, occurring in 0.7% to 1.8% of cases [3]. For example, a case report highlighted a pancreatic rest presenting as a subepithelial nodule, with histological analysis revealing pancreatic intraepithelial neoplasia [7]. We report a rare case of a young male with recurrent gastric abscess formation due to pancreatic rest, complicated by Actinomyces and alpha-hemolytic Streptococcus infection. To our knowledge, this is among the few reported cases of infected pancreatic rest and the first with hematogenous Actinomyces seeding from dental work.

2. Case Presentation

A 21-year-old male with no significant past medical history initially presented to the emergency department (ED) with epigastric abdominal pain radiating to the back, early satiety, and vomiting. Laboratory workup showed white blood cells (WBC) 15×10^3, lipase 26 U/L, and alanine aminotransferase 16 U/L. A computed tomography (CT) scan of the abdomen and pelvis was done, and it showed mild edematous and inflammatory stranding adjacent to the distal stomach. He was discharged with a prescription for omeprazole and metoclopramide and advised to follow up with gastroenterology. One week later, he returned with worsening symptoms and a fever (101°F). Repeat labs showed leukocytosis 18×10^3, Lipase 26 U/L, an alkaline phosphatase of 76 U/L, aspartate aminotransferase of 23 U/L, alanine aminotransferase of 29 U/L, and lipase of 26 U/L. A repeat CT scan with contrast demonstrated mass-like thickening of the gastric antral wall with luminal compression and adjacent stranding, suggesting an inflammatory phlegmon with no drainable collection (**Figure 1**). He was admitted and started on ceftriaxone and Metronidazole. Esophagogastroduodenoscopy (EGD) revealed large subepithelial extrinsic compression in the antrum, with the suspected fluid collection, possibly a walled-off abscess (**Figure 2**). No ulceration was observed, and biopsies were not obtained due to the soft consistency of the lesion. He was discharged on Metronidazole and Cefdinir for 7 days with plans for a repeat CT scan and EGD in 6 weeks. A follow-up CT scan

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showed interim resolution of the antral mass. The EGD showed a 15 mm submucosal nodule along the greater curvature of the antrum concerning pancreatic rest. EUS revealed an extended area of heterogenous echotexture extending from the muscularis propria to the submucosa, consistent with pancreatic rest **(Figure 3)** . Five months later, the patient presented to the ED with recurrent epigastric pain, nausea, and diarrhea. Labs showed WBC $15 \times 10^3/\mu$L, lipase 26 U/L, and amylase 43 U/L. An abdominal-pelvic CT scan with contrast showed a 2.4 cm fluid-containing structure in the anterior/caudal wall of the gastric antrum near the pylorus, suspicious of an abscess versus a walled-off ulcer **(Figure 4)**. Ceftriaxone and metronidazole were reinitiated. A repeat EUS showed an irregular, oval, and anechoic cyst measuring 27 mm x 21 mm, with debris present and well-defined, smooth margins **(Figure 5)**. Fine-needle aspiration revealed no malignant cells, with abundant neutrophils and histiocytes. Culture grew alpha-hemolytic Streptococcus and Actinomyces species. He was discharged on a 7-day course of cefpodoxime and metronidazole. A repeat CT scan four weeks later showed reduced size of the gastric wall fluid collection, with no new findings. Due to persistence, he was referred to Infectious Diseases and started on cefdinir and doxycycline. Imaging showed a 2.2 × 1.9 cm gastric antral mass without fluid two months later. Cefdinir was stopped, and doxycycline was continued for six months to treat Actinomyces. He later reported a recent root canal prior to symptom onset, suggesting an odontogenic source. Given the persistence of the lesion despite multiple courses of antibiotics and concerns over prolonged antibiotic use in a young patient, he underwent partial gastrectomy. Preoperative CT showed a persistent submucosal mass measuring 2.3 × 2.0 × 2.0 cm. A surgical biopsy showed a submucosal abscess involving a small bowel and stomach with foreign-body giant cells and clear margins **(Figure 6)**. At the one-year follow-up, the patient remained asymptomatic and denied any gastrointestinal symptoms, and no follow-up imaging was performed due to the absence of clinical concerns.

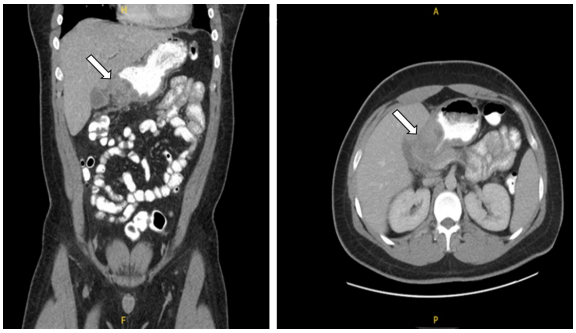

Figure 1: Mass-like thickening of the wall of the gastric antrum with luminal compression and adjacent stranding.

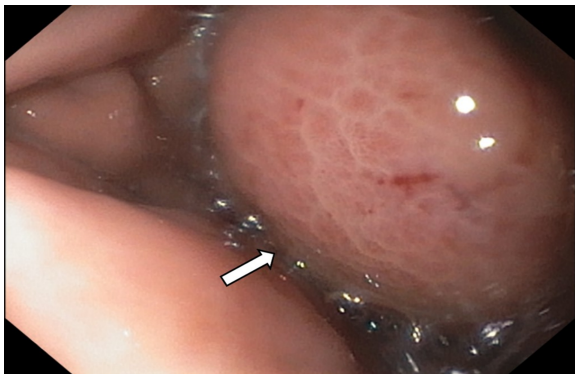

Figure 2: Large subepithelial extrinsic compression towards the antrum. Suspected fluid collection, possibly a walled-off abscess on the other side of this. No clear ulceration was seen.

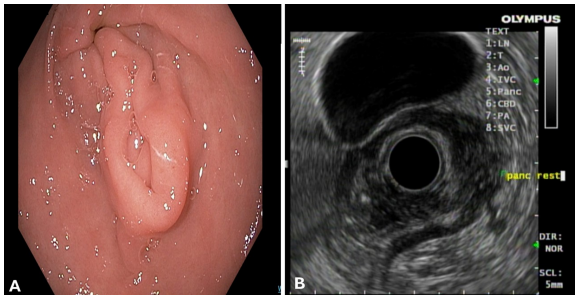

Figure 3: A: Antral nodule with redundant folds General appearance consistent with pancreatic rest. B: Area of thickened fold. The muscularis propria thickened to 12 mm with an extended area of heterogenous echotexture extending from the muscularis propria to the submucosa, consistent with pancreatic rest.

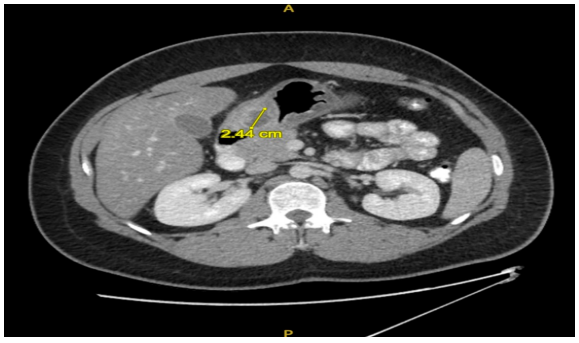

Figure 4: Rim-enhancing 2.4 cm fluid-containing structure is observed, including the anterior/caudal wall of the antrum of the stomach near the pylorus.

3. Discussion

Pancreatic rest is typically found incidentally during endoscopic imaging and is considered a gastric subepithelial lesion when found incidentally in the stomach. The differential for gastric subepithelial lesions can be broad, but it is important to consider pancreatic rest. Pancreatic rest can be found throughout the gastrointestinal tract; however, it is more commonly found in the stomach, particularly in the distal stomach along the greater curvature of the antrum [7]. Our patient's endoscopic ultrasound revealed a submucosal nodule with heterogenous echotexture extending from the muscularis propria to the submucosa of the greater curvature of the antrum of the stomach consistent with pancreatic rest. The classic appearance of pancreatic rest on endoscopic ultrasound is described as hypoechoic or mixed echogenicity with heterogeneity within the second, third, or fourth layer (muscularis mucosa, submucosa, and muscularis propria, respectively) [4]. The heterogenous appearance is attributed to the presence of acini within the ectopic pancreatic tissue [7]. EUS is the preferred imaging study of choice to distinguish pancreatic rest from other gastric sub-mucosal lesions, with GISTs and leiomyomas being the most common [5]. The finding within the stomach can commonly be mistaken for malignancy; however, malignant features of an intramural lesion seen on EUS are typically greater than 4 cm in size, echogenic foci greater than 3 mm, cystic areas within the lesion, irregular borders, and the

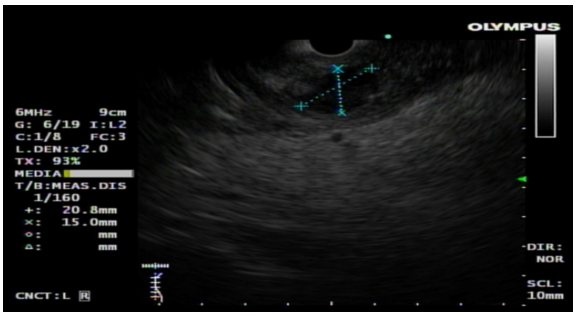

Figure 5: Irregular, oval, and anechoic cyst measuring 27 mm x 21 mm with debris present, well-defined margins, and smooth margins.

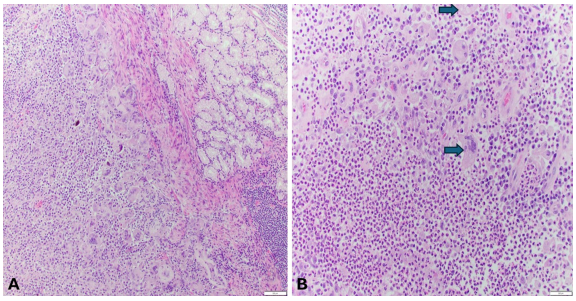

Figure 6: A: HE, 10X: Brunner glands of the duodenum (upper right) with adjacent acute and chronic inflammation, including multinucleated giant cells consistent with abscess. B: HE, 20X; Abundant neutrophils with scattered multinucleated giant cells (arrow).

presence of adjacent lymph nodes with malignant pattern [6]. Our patient did not have any of these malignant features. Although pancreatic rest is typically asymptomatic, it can result in complications, including acute or chronic pancreatitis, pancreatic necrosis, pseudocyst, abscess, gastric outlet obstruction, and carcinoma [5, 8]. Gastric abscess formation secondary to pancreatic rest has been reported only in a few cases. Alastal et al. reported a patient with an ectopic pancreas complicated by recurrent abscess and pancreatitis, ultimately requiring surgical intervention [9]. Similarly, Berry et al. described a heterotopic pancreas initially mistaken for malignancy, necessitating resection [10]. However, neither case identified Actinomyces or a suspected odontogenic source. Our case is unique in that the abscess was polymicrobial, including Actinomyces, and may have originated from hematogenous spread following a recent root canal procedure, a mechanism not previously reported. Furthermore, while Alastal's case involved abscesses in the setting of ectopic pancreatitis [9], our patient lacked clinical or imaging features of pancreatitis. Instead, recurrent abscesses formed without enzymatic inflammation, possibly due to localized tissue necrosis and infection within the pancreatic rest itself. Histopathology supported the diagnosis, with foreign-body giant cells reflecting chronic inflammation indicative of a prolonged immune response. Their presence suggests the body's attempt to wall off or isolate the ectopic pancreatic tissue, further supporting the chronicity and infectious etiology of the lesion. These cells form granulomas that may occur in response to tissue injury in ectopic pancreatic rests[11]. Management of such cases typically begins with antibiotic therapy, as was initially attempted in our patient. However, despite multiple courses of antibiotics and temporary clinical improvement, imaging showed persistence of the lesion, ultimately necessitating partial gastrectomy. This case underscores the importance of recognizing rare infectious complications of pancreatic rest. It demonstrates how multidisciplinary evaluation, including imaging, endoscopy, pathology, infectious disease, and surgical intervention, can lead to successful outcomes. It also contributes to a better understanding of Actinomyces-associated gastric abscesses, which are exceedingly rare and may present in atypical ways. This case report is limited by the lack of histological confirmation of pancreatic acini in the initial diagnosis, although imaging and clinical features were consistent. Additionally, follow-up beyond one year would be beneficial to assess for long-term recurrence.

4. Conclusions

This case illustrates a rare but clinically significant complication of pancreatic rest and highlights the need for timely recognition and coordinated care. Awareness of atypical infectious presentations can guide appropriate interventions and improve patient outcomes.

Conflicts of Interest

The authors declare that they have no competing interests that could have influenced the objectivity or outcome of this investigation.

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Informed consent statement

Consent was obtained from the patient and family to publish this case report and images. All relevant information and confidentiality rights were explained, and identifying details have been anonymized.

Large Language Model Statement

None

Authors Contribution Statement

AO provided study leadership and led manuscript writing and editing; FL and AB contributed to manuscript writing; LoS supervised the project and reviewed the manuscript; SK and GS performed advanced scoping for the case and reviewed the manuscript and figures; LiS reviewed pathology slides and provided their descriptions. All authors reviewed and approved the final manuscript and ensured its accuracy and integrity.

Data Availability Statement

All information presented in this case report is included within the manuscript. If further details are required, please contact the corresponding author.

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Original Article

Alternative Gastrointestinal Conditions Identified in Patients Meeting Rome IV Criteria for Irritable Bowel Syndrome or Functional Diarrhea Referred to Secondary Care: A Prospective Study

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ABSTRACT

Introduction: Organic gastrointestinal (GI) disorders can be missed in individuals with irritable bowel syndrome (IBS). This study investigated the frequency of organic disorders in patients with diarrhea-predominant IBS or functional diarrhea and the impact of treatment for any identified alternative diagnoses.
Methods: Between April 2019 and March 2020, the results of comprehensive investigations, including blood and fecal tests, a ^{75}Se-homocholic acid taurine (SeHCAT) scan, a breath test, and endoscopies performed on consecutive eligible patients, were recorded. Symptom burden was reassessed after treatment for any GI conditions identified.
Results: 66 consecutive patients (15 males) were included. Two patients (3%) were diagnosed with colonic malignancy; 21 (38%) had bile acid diarrhea; one (1%) had pancreatic exocrine insufficiency; and 31 (54%) had small intestinal bacterial overgrowth. 21 patients (32%) had at least two GI diagnoses. Significant improvement in symptoms occurred following treatment ($p<0.0001$).
Conclusions: Multiple co-existing conditions were detected in many of these patients, with one-third of the cohort having more than one abnormal test. When these alternative diagnoses were treated, patients reported significant symptomatic improvement. Larger studies are required to validate our findings, and these patients' investigative and management pathways should be amended accordingly.

1. Introduction

Although international consensus-derived criteria recommend that patients can be diagnosed with irritable bowel syndrome (IBS) if they have specific symptoms, 'red flags' are absent. There is no serological evidence of inflammation or coeliac disease, many studies suggest that an alternative gastrointestinal (GI) disorder can frequently be identified in patients confidently diagnosed with IBS. These include bile acid diarrhea (BAD), cancer, carbohydrate malabsorption, coeliac disease, infectious diarrhea, inflammatory bowel disease, microscopic colitis, pancreatic exocrine insufficiency (PEI), and small intestinal bacterial overgrowth (SIBO). However, studies report widely differing prevalences of these conditions [1].

There are no published studies on people whose symptoms meet diagnostic criteria for IBS that investigate participants for all the conditions listed above and report the change in symptoms using patient-reported outcome measures when such a condition is diagnosed and treated.

In this study, we recorded the alternative diagnoses detected in a consecutive series of patients with diarrhea-predominant IBS (IBS-D) and functional diarrhea (FD) following comprehensive investigations. We also measured changes in their symptoms and quality of life, prospectively following lifestyle advice when necessary and standard treatment of all alternative conditions detected.

2. Methods

Our Clinical Governance and Research and Innovation Departments of the United Lincolnshire Hospitals National Health Service Trust approved this study as a prospective clinical service evaluation. It was not considered to require written informed consent by the patients as all tests conducted fall within the standard investigative pathway comprehensively to look for potential aetiologies in chronic diarrhea in these patients.

We recorded investigation results and outcomes following intervention in patients newly referred to our "diarrhea clinic" by their GPs for secondary care management of persistent GI symptoms.

Between April 2019 and March 2020, we identified consecutive adults prospectively aged $\geq$ 18 and $\leq$ 50 years old who had symptoms fulfilling the Rome IV criteria for IBS-D or FD but no

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Table 1: First and Second-Line Investigations

First-line Investigations
Blood Tests
Full blood count
Bone profile
C-reactive protein
Erythrocyte sedimentation rate
Liver function tests
Tissue transglutaminase antibody with immunoglobulins
Thyroid function tests
Urea and electrolytes
Vitamin B12 and folate
Stool Tests
Microbiological culture
Pancreatic faecal elastase-1
Faecal calprotectin
Guaiac faecal occult blood (FOB)
Breath Tests and Imaging
Lactulose hydrogen breath test (HBT)
SeHCAT scan
Gastroscopy with duodenal biopsies (if no upper GI endoscopic investigation within past 12 months)
Endoscopy-Based Tests
Flexible sigmoidoscopy with left-sided mucosal biopsies (if no lower GI endoscopic investigation within past 12 months), if:
• Negative FOB, and
• Faecal calprotectin < 50 µg/g
Or Colonoscopy with colonic biopsies, if:
• Positive FOB, or
• Faecal calprotectin > 250 µg/g
Second-line Investigations
Lactose hydrogen breath test
Fructose hydrogen breath test
Fasting gut hormone profile

FOB, Faecal occult blood; HBT, Hydrogen breath test.

"red flag" symptoms at the time of their first clinic visit in Lincoln County Hospital, UK. Patients were excluded from this study if they had undergone any previous abdominal surgery (except appendicectomy, inguinal/femoral hernia repair, or Caesarean section). Patients were also excluded if they were pregnant or breastfeeding or had a history of coeliac disease, cancer, inflammatory bowel disease, or pancreatic disease.

All clinic patients were investigated similarly, so this study did not reflect a change in clinical practice. If the physical examination was unremarkable, first and second-line investigations were arranged accordingly **(Table 1)**.

Before each appointment, all patients completed a Patient Reported Questionnaire and the Gastrointestinal Symptom Rating Scale (GSRS), **(Supplemental material)**. This questionnaire is validated for patients with functional bowel symptoms [2, 3, 4]. In this study, a (≥30% reduction in the overall GSRS score is considered a good response to treatment with significant symptom improvement [5]. The GSRS questionnaire was modified by adding two 11-point visual analog scales evaluating the quality of life and the impact of GI symptoms on quality of life and a Bristol Stool Chart assessing the patient's 'best' and 'worst' bowel frequencies and stool forms. In addition, to avoid missing relapsing and remitting symptoms [6], we asked patients to complete the questionnaire based on their symptoms over the preceding month rather than the two weeks originally specified. Some questions were shortened, and 17 additional symptoms were added to allow for a more holistic assessment. All these additional items were deemed clinically relevant, and their inclusion allowed a more holistic assessment of the patient's overall symptom burden. They can be categorized into three major domains – upper GI, lower GI, and perianal symptoms. In addition, two visual analog scales evaluating the quality of life and the impact of GI symptoms on quality of life and a Bristol Stool Chart assessing the patient's 'best' and 'worst' bowel frequencies and stool forms were included in the questionnaire. All these modifications made to the original questionnaire give a better reflection of patients' overall GI burden and have been adopted in clinical practice by Professor Andreyev, an experienced clinician and Professor in gastroenterology.

2.1. Dietary factors

The dietary fiber intake of all patients was assessed at the baseline using a questionnaire that contains 31 items **(Supplemental material)**. A potential maximum of 41 points can be scored; one point is approximately equivalent to 1.5g of fiber; therefore, a score (≤10 suggests a low dietary fiber intake, whereas a score (≥20 indicates a high dietary fiber intake. Recommendations were made, and leaflets on dietary fiber were given to those with a low or high dietary fiber intake.

A questionnaire Supplemental material assessed total daily caffeine intake. An intake of (≥400 mg/day was considered high, and these patients were advised to try reducing their caffeine intake.

All patients were asked to complete an Alcohol Use Disorders Identification Test (AUDIT), a validated screening tool detecting early signs of excessive alcohol use [7]. Patients who scored (≥8 on the questionnaire were recommended to reduce their alcohol intake.

2.2. Treatments used

All patients were provided with written information for all treatments prescribed and were given a face-to-face follow-up appointment one month after starting treatment to assess response until the start of the first national lockdown following the outbreak of coronavirus 2019, when follow-up appointments were conducted via telephone.

All patients with BAD were recommended to reduce their total daily fat intake to 20% of their daily calorie intake [8, 9]. With moderate to severe BAD (SeHCAT 7-day retention 0% to <10%), patients were also prescribed cholestyramine 4 g sachets and asked to titrate the dose up to a maximum of three sachets a day, taken with food, according to the response. If not tolerated, colesevelam was offered instead, starting with one 625 mg tablet with food and titrating up to a maximum of seven tablets daily in split doses. Patients with mild or borderline BAD (SeHCAT 7-day retention 10-20%) were initially treated with diet alone; if that was not adequate or could not be maintained long-term, a sequestrant was offered [10].

Table 2: Baseline Characteristics of the 66 Patients in the 'Diarrhea' Clinic

Characteristic	Male	Female	Total
Number of patients (n)	15	51	66
Age, median (range)	34 (20–50)	34 (18–50)	34 (18–50)
BMI, mean (± SD)	27.7 (±5.6)	29.4 (±6.4)	29.0 (±6.3)
Ethnicity			
White	13	50	63 (95%)
Asian	1	1	2 (3%)
Black	1	0	1 (2%)
Rome IV Criteria			
IBS-D	10	34	44 (67%)
FD	5	17	22 (33%)
Duration of symptoms (months), median (range)	60 (6–240)	36 (6–360)	36 (6–360)
Questionnaires			
Fibre intake (points), mean (±SD)	14.4 (±4.3)	12.5 (±4.4)	13.2 (±4.3)
Caffeine intake (mg), median (range)	200 (16.25–1725)	206.5 (9.75–780)	201.25 (9.75–1725)
AUDIT score, median (range)	4 (1–11)	2 (0–14)	3 (0–14)

Patients diagnosed with PEI were prescribed 25,000-unit Creon® (pancrelipase) capsules and advised to take 50,000–75,000 units with main meals and 25,000–50,000 units with snacks or any drinks except for water, black tea, and black coffee.

If SIBO was diagnosed following a breath test, patients were offered seven days of rifaximin 550 mg twice daily for hydrogen (H2) positive tests or rifaximin 550 mg and neomycin 500 mg twice daily for methane (CH4) positive tests [11, 12].

Patients diagnosed with villous atrophy were advised to follow a gluten-free diet. Those diagnosed with lactose or fructose malabsorption were advised to avoid lactose or fructose from their diet. Both groups were also referred to the dieticians for further advice.

Overflow diarrhea was treated with two doses of Picolax® sachets followed by a 7g sachet of Normacol® granules (sterculia), to be taken once or twice daily long term.

2.3. Statistics

Descriptive statistics were used to describe the identified baseline demographics and prevalence rates of GI conditions. For both categorical and continuous variables, normally distributed data were expressed as mean (SD), and non-normally distributed data were expressed as median (range). Paired scores were compared using Wilcoxon non-parametric tests to determine changes in total GSRS, quality of life, and impact of GI symptoms on life quality between baseline and follow-up. All statistical analyses were conducted using Stata SE 16 (StataCorp LLC, USA). A two-sided alpha level of 0.05 was used to test for statistical significance.

3. Results

3.1. Patient Demographics

Between April 2019 and March 2020, 66 consecutive patients were included, 44 (67%) meeting the Rome IV criteria for IBS-D and 22 (33%) FD. The majority were female (77%), with a median age 34 years old; they had been symptomatic for a median of three years at presentation. Four patients had a high dietary fiber intake (range 20-22), and 18 had a low dietary fiber intake (range 2-10). 15 patients consumed>400 mg/day of caffeine (median 517.25 mg/day, range 450-1725). Eight patients scored ≥ 8 (range 9-14) on the AUDIT questionnaire **(Table 2)**.

The mean total GSRS baseline symptom score was 31 ± 12. Abdominal pain, bloating, diarrhea, fecal urgency, and a sense of incomplete emptying were the dominant symptoms. The prevalence of baseline individual GI symptoms and bowel frequencies are shown in **(Figure 1)** and **(Figure 2)**. Baseline stool forms varied between types 4 and 7. Almost all patients with predominant type 7 stool had occasions when they passed type 4 stool.

3.2. Investigation Findings and Outcomes of Treatments (Table 3) (Supplemental material)

3.2.1. Blood tests

All blood tests were normal except for one patient with iron deficiency anemia. Urinalysis, upper and lower GI endoscopies, and small bowel capsule endoscopies were normal. His anemia was attributed to his poor diet.

3.2.2. Stool tests

Stool samples for microbiology and calprotectin were produced by 64 patients. None grew pathogens. Three patients had a raised fecal calprotectin between 100 and 250 µg/g in their initial and repeat stool samples, but no endoscopic evidence of inflammatory bowel disease was found.

Two FOB tests were positive. At colonoscopy, one patient had an adenocarcinoma in her sigmoid colon. No cause for the positive FOB was found in the other.

3.2.3. Pancreatic FE-1 < 500 ug/g

65 patients had their FE-1 level tested; one (1.5%) had severe PEI (FE-1 (≤100 µg/g). The CT scan of her pancreas was unremarkable. This patient also had moderate BAD. 11 patients (17%) had an equivocal FE-1 (200-500 µg/g). Of the 12 patients, 10 (83%) had IBS-D, and two (17%) had FD. They had a mean (SD) body

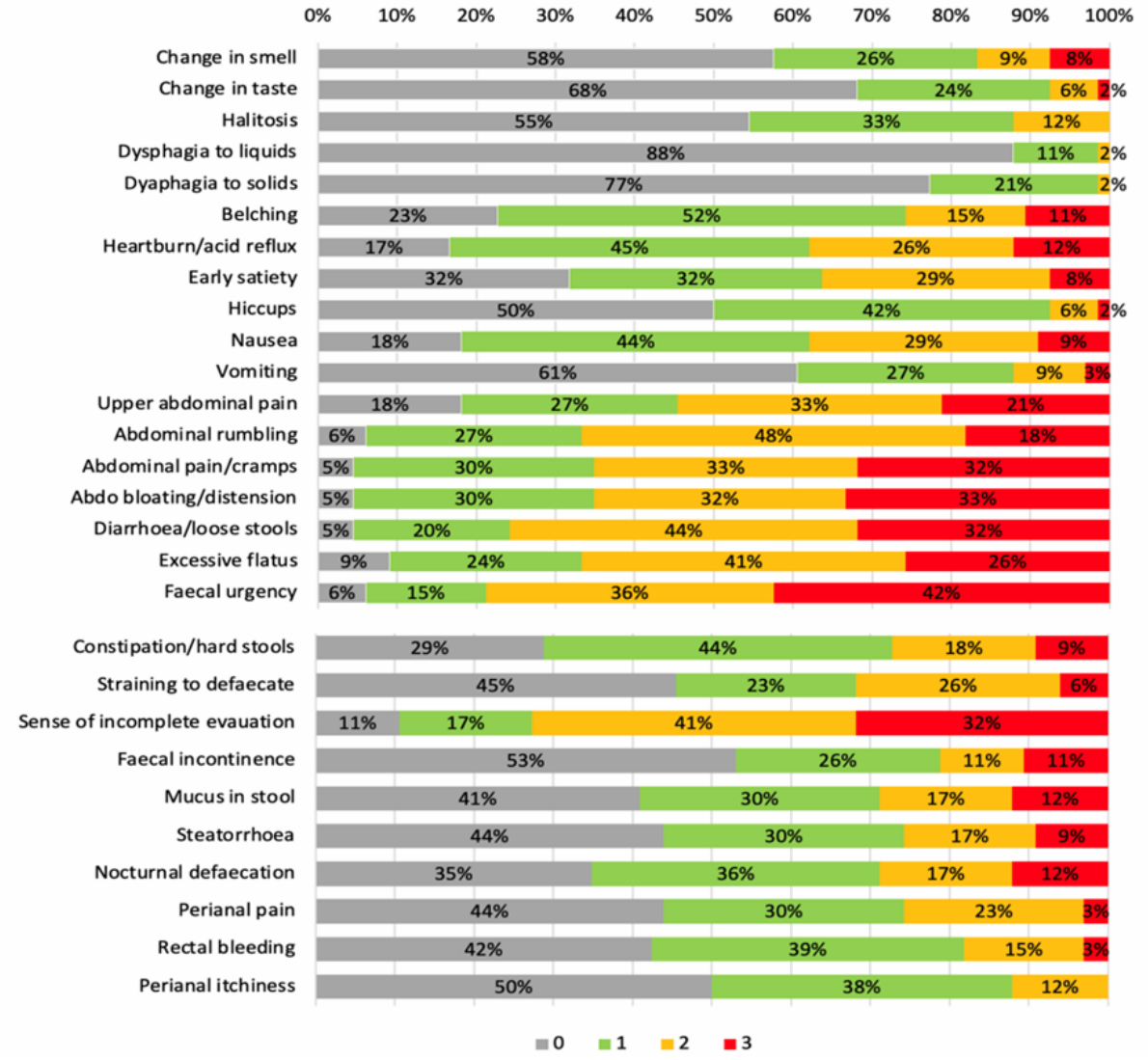

Figure 1: The GI symptoms and function reported by the 66 patients at baseline. GSRS, Gastrointestinal Symptom Rating Scale.

mass index of 29.3 (7.4). Four also had SIBO, and four were also diagnosed with BAD.

Of interest was that four of the ten patients with a FE-1 of 200-500 µg/g treated with Creon® reported a good clinical response **(Supplemental material)**. The median GSRS score reported by the patients benefiting from Creon® reduced from 38 (range 27-48) at baseline to 32 (range 10-42) at follow-up (p= 0.04). Changes in quality of life score and the impact of GI symptoms on quality of life were not statistically significant (p= 0.24 and 0.15, respectively).

3.2.4. Lactulose HBT

57 patients underwent lactulose HBT, and 31 (54%) were positive, 52% with a rise in H2, 39% with a rise in CH4, and a 3% rise in both gases. Of the patients with an abnormal HBT, 24 (77%) met the criteria for IBS-D and seven (23%) for FD. A second diagnosis was made in 18 patients: ten had BAD, seven PEI and one villous atrophy.

Following first-line antibiotic treatment, 12 (39%) patients with an abnormal HBT reported improvement in GI symptoms **(Supplemental material); the total** GSRS reduced from 30 (range 10-50) at baseline to 16 (range 1-47) (p= 0.0002). Quality of life and impact of GI symptoms on quality of life improved from a median baseline score of 5 (range 0-8) to 7 (range 2-10) (p= 0.004) and from a median baseline score of 8 (range 3-10) to 6 (range 1-10) (p= 0.001), respectively.

3.2.5. SeHCAT scan

56 patients underwent two scans, and 25 (45%) had a retention rate of (≤20% after one week. Three patients (5%) had severe BAD, nine (16%) had moderate BAD, nine (16%) had mild BAD, and four (7%) had borderline BAD. Of these 25 patients, 22 patients (88%) met the criteria for IBS-D and three (12%) for FD. A second diagnosis was made in 14 patients: four had PEI, and 10 had SIBO.

Improvement was reported by 18 of 23 treated patients **(Supplemental material)**. The median baseline GSRS of 35 (range 10-48) dropped to 17 (range 3-39) (p= 0.0005). The quality of life improved from a baseline median score of 6 (range 1-10) to 8 (range 3-10) (p= 0.0002); the impact of GI symptoms on life

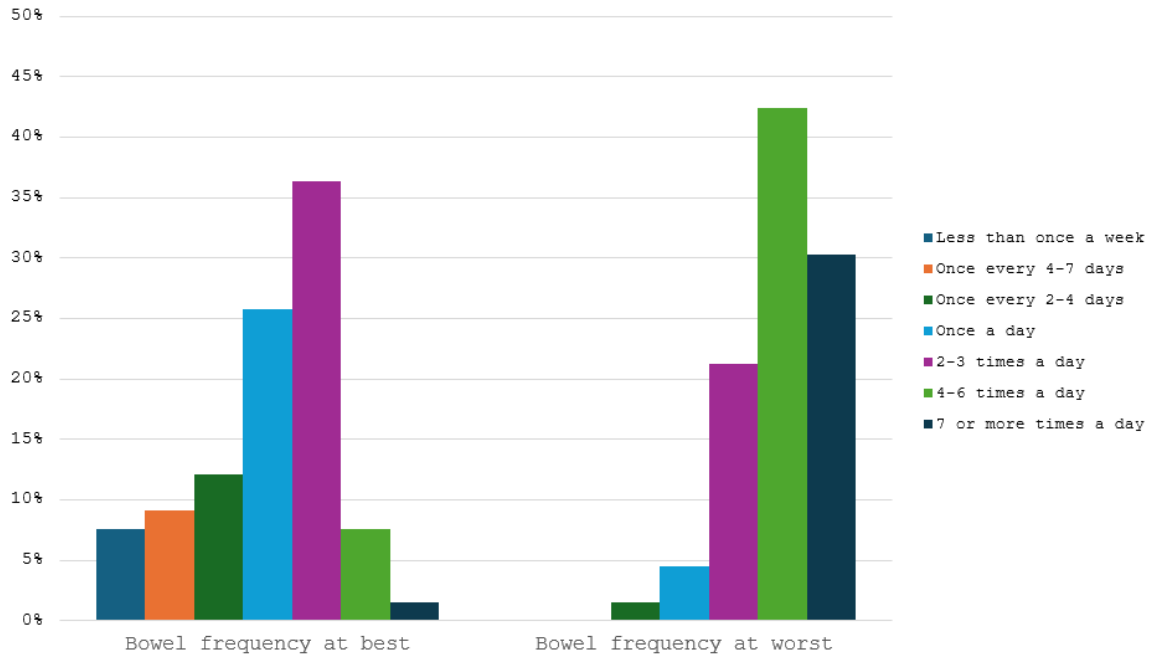

Figure 2: Bowel frequency reported by the 66 patients at baseline.

quality reduced from 8 (range 4-10) at baseline to 4 (range 0-8) ($p< 0.0001$).

3.2.6. Endoscopic assessment

Thirty-eight patients underwent gastroscopy with duodenal biopsies, 33 had flexible sigmoidoscopies, and 10 had colonoscopies. Twenty-eight patients had their endoscopies canceled due to the coronavirus pandemic.

Two patients (3%) had negative coeliac serology but histological features of crypt hyperplasia with marked villous atrophy consistent with Marsh type 3b on the duodenal biopsies. Both patients reported a good symptomatic response after switching to a gluten-free diet, with their baseline GSRS improving from 39 to 11 and 40 to 27, respectively. Their quality of life also improved from 5 to 7 and from 2 to 5, respectively.

Two patients (3%) were found to have a Dukes B sigmoid adenocarcinoma, although only one initial FOB test was positive, and neither patient was anemic nor iron deficient. Both patients underwent curative surgical resection of their tumors, and follow-up appointments were arranged with the surgical team. No follow-up data were available for both patients.

3.3. Other findings

Overall, 21 (32%) patients had more than one cause found for their symptoms. 16 patients with unremarkable initial investigations underwent second-line investigations, with one patient identified with fructose malabsorption and referred for dietetic input. Lactose HBTs and tests for neuroendocrine tumors in the other 15 patients were unremarkable.

On revisiting the symptoms of these 15 patients at follow-up, eight patients gave a history of intermittent straining to defecate, a sense of incomplete emptying, and a short period of symptom relief after having the bowel preparation for their lower GI endoscopy. An abdominal X-ray was performed on these patients; three had colonic fecal loading. Overflow diarrhea with severe fecal impaction was diagnosed. Two of the patients were also found to have grade III hemorrhoids during their lower GI endoscopy and were referred for potential surgical intervention.

12 (21%), ten with IBS-D and two with FD had no abnormal tests. Two patients were started on amitriptyline with a good clinical response. Four were referred to dieticians for a trial of a diet low in fermentable oligo-, di-, mono-saccharides, and polyols. The other six did not want further input as their symptoms had spontaneously improved.

4. Discussion

This study demonstrates that a significant proportion of patients who fit the Rome IV diagnostic criteria for IBS-D or FD referred to a secondary care “diarrhea clinic” have at least one alternative diagnosis potentially accounting for their symptoms. Standard first-line therapies led to the alleviation or abolition of symptoms in many patients. Treating all identified alternative diagnoses was often required to achieve clinical improvement.

Many previous studies have examined the co-existence of one specific organic GI condition in patients with IBS-type symptoms, predominantly BAD and SIBO [1]. However, this is the first study that looks for a wide range of potential diagnoses. Our study has also considered the role of significant dietary indiscretion in contributing to symptoms, be it fiber, caffeine, or alcohol. In addition, our study is unique in objectively assessing treatment outcomes using patient-reported measures if any of these new diagnoses are made.

The prevalence of most of the conditions we identified is similar to data reported elsewhere in studies that have looked for the co-existence of one specific organic GI condition in patients with IBS-type symptoms [1]. The fact that the majority of patients reported a clinical response after appropriate treatments also suggests that the conditions were correctly identified. Thirdly, the response rates

Table 3: Investigations Undertaken and Number of Abnormalities Detected

Investigation	No. of Patients	Abnormalities Detected
First-line Investigations		
Baseline blood tests	66	1 iron deficiency anaemia
Stool Tests		
Microbiological culture	64	0
Faecal calprotectin	64	3
Pancreatic faecal elastase-1 (FE-1)	65	1 severe PEI ((≤100 μg/g)
Guaiac faecal occult blood (FOB)	64	2 positive
SeHCAT scan	56	25 BAD (7-day retention (≤20%)
Lactulose hydrogen breath test (HBT)	57	31 positive
Endoscopy		
Gastroscopy	38	2 villous atrophy on duodenal biopsies
Flexible sigmoidoscopy	33	2 sigmoid adenocarcinoma
Colonoscopy	10	0
Second-line Investigations		
Fructose HBT	16	1
Lactose HBT	15	0
Fasting gut hormone profile	15	0
Other Tests		
Abdominal X-ray	8	3 with radiological evidence of faecal loading*
Small bowel capsule endoscopy	1**	0

*Only three patients were treated with laxatives as they reported intermittent constipation-type symptoms with evidence of faecal impaction on abdominal X-ray.
**The one patient with iron deficiency anaemia underwent a small bowel capsule endoscopy.

we saw are similar to other large studies that have looked at the response of these individual conditions to treatment [10, 13, 12, 14].

An important finding was a relatively high response rate to treatment in patients with "borderline" SeHCAT results (between 15-20% 7-day retention) and in almost half of patients with a pancreatic FE-1, which lies between 200-500 μg/g. Many clinicians would consider these a normal result; however, these response rates support previously published data challenging the view that a SeHCAT scan is significant only if the level is below 10% or 15% 7-day retention [10, 15, 9]. Also, a recent study has confirmed that a significant proportion of patients with a FE-1 level of between 200-500 μg/g may also respond to pancreatic enzyme replacement therapy[16]; however, while experts do acknowledge that this is possible, clinical data are lacking [17].

One limitation of our findings is that this was a non-randomized study, and symptom scores were compared to baseline in the same individual. There were no matched controls. Therefore, improvements may be related to placebo effects, although many patients had had a variety of previous treatments in primary care that had no benefit. The patient population captured in this study likely represents more complex cases and may not represent the broader IBS population.

A second limitation was that the coronavirus outbreak in March 2020 caused major disruptions to clinics and non-urgent investigations, resulting in some patients in this study not having complete investigations. It is, therefore, likely that GI diagnoses were missed in some. Lockdowns may also have minimized symptoms for other patients as they stayed home. Others may not have received full or appropriate treatment due to delayed or telephone follow-up. Therefore, the findings generated from this study with a small sample size should be interpreted cautiously.

A third limitation is that a number of patients received multiple interventions, particularly with respect to any detected dietary indiscretion, and this study did not assess specifically the impact of advice given to correct these, particularly when another cause was also treated. So, some of the measured improvements in outcomes may have been related to wider lifestyle changes than just a specific prescribed medication.

The follow-up period varied and ideally would have been longer – those with only one alternative GI condition identified and reporting an excellent treatment response stayed in this study for a much shorter period than those who required more than one form of treatment for multiple GI diagnoses.

After first-line antibiotic therapy for SIBO, improvement was only seen in four in ten treated patients. Our normal practice in people with a positive HBT is to try a first-line treatment and then, if there is no response, a second-line treatment. If HBT is still positive and the patient remains symptomatic, a small bowel aspirate is performed to attempt to grow the organisms causing SIBO and obtain antibiotic sensitivities. This meticulous approach was discarded as a result of the pandemic. Important data suggest that normalization of a HBT following antibiotics correlates with good treatment outcome [18], so appropriate treatment for SIBO should

be the goal. Our data also show that it is essential to measure both H2 and CH4 during the HBT.

Our three patients diagnosed with overflow diarrhea did well after treatment. However, fecal loading is a subjective diagnosis with no clearly defined X-ray features, and it remains unclear whether the presence of fecal loading captured on a single abdominal film correlates well with symptoms.

Finally, although the validity of the GSRS is well-documented, we used a modified version which has not been validated. Nonetheless, the modified GSRS was repeated to assess all patients at baseline and following treatment, and this uniform assessment provides an objective short-term trajectory for each patient's symptoms.

5. Conclusions

Despite these limitations, our data suggest that organic GI conditions can be detected in a large proportion of patients who could be easily misdiagnosed as having IBS. This can be detrimental not only to the patients but also to healthcare and society. If our data are reproduced by others, this would require a fundamental reappraisal of clinicians' use of symptom-based diagnostic criteria.

Conflicts of Interest

The authors declare that they have no competing interests that could have influenced the objectivity or outcome of this investigation.

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Institutional Review Board (IRB)

This study was registered and approved as a prospective clinical service evaluation and quality improvement project (Registration No. L0141) by the Clinical Governance and Research and Innovation Departments of United Lincolnshire Hospitals National Health Service Trust on 27 March 2019. The study was also approved by the specialty Audit Lead on 21 March 2019. As this was classified as a service evaluation using standard investigative pathways for chronic diarrhea, formal research ethics committee approval was not required under NHS Health Research Authority guidance.

Large-Language Model

None

Authors Contribution

DP designed the study, collected and interpreted data, and drafted and revised the manuscript; GM designed the study and drafted and revised the manuscript; JA designed the study and drafted and revised the manuscript. All authors reviewed and approved the final manuscript.

Data Availability

All data generated or analyzed in this study are included in this published article.

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Case Report

An Unusual Case of Disseminated Hydatid Disease: A Laparoscopic Wonder

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ABSTRACT

Human echinococcosis, caused by Echinococcus tapeworms, is a zoonotic disease in which ingested eggs of the tapeworm form cysts in the organs known as Hydatid cysts. These cysts are commonly found in the Liver and lungs, but in rare cases, they can also be found in the spleen, ovaries, round ligament, and peritoneal cavity. Treatment typically involves surgery. This is a case of a 32-year-old female who presented with chief complaints of pain in the abdomen for 2 months, which was associated with nausea, vomiting, reduced appetite, and increased size of mass per abdomen. Further investigations revealed the presence of multiple disseminated hydatid cysts in the upper abdomen and the peritoneal cavity. This was a rare unusual entity that was meticulously managed by minimally invasive laparoscopic surgery. Echinococcosis can occur anywhere in the body, with concurrent localizations in the liver, spleen, round ligament, ovaries, and peritoneal cavity, which are rare and pose a diagnostic as well as a surgical management challenge. The inconvenience of multiple localization and the risk of contamination usually lead to open surgery in these cases. The presented case is unique due to the laparoscopic approach to the multiple localizations of hydatid disease, advocating for a minimally invasive first-line approach even in these particular localizations.

1. Introduction

Human echinococcosis is a zoonotic disease caused by Echinococcus tapeworms. Transmission occurs through ingesting eggs, releasing oncospheres in the intestine that migrate and form hydatid cysts in organs. Rarely, cyst rupture spreads protoscolices, causing secondary cyst formation, known as secondary or disseminated echinococcosis. Disseminated hydatid disease is uncommon, even in endemic areas, with an incidence of 1% to 8% [1]. The spleen, kidney, peritoneal cavity, skin, and muscles each have about a 2% involvement rate, while the heart, brain, vertebral column, ovaries, pancreas, gallbladder, thyroid gland, breast, and bones each have about a 1% involvement rate [2]. Management typically involves open or laparoscopic surgery. Surgical treatment depends on the cysts' size and spread, requiring either an open or laparoscopic approach. Laparoscopic surgery offers shorter operative duration, fewer intraoperative complications, less pain, shorter hospital stays, and better cosmesis [3]. This report aims to enhance understanding of the atypical presentation and management of disseminated hydatid disease involving multiple tissues like the liver, spleen, ovaries, round ligament, and peritoneal cavity. This case report seeks to contribute valuable insights to the knowledge on managing disseminated hydatidoses, ultimately guiding future clinical interventions.

2. Case Presentation

A 32-year-old woman presented to the outpatient clinic with a primary complaint of abdominal pain persisting for two months. The pain had a sudden onset, was severe in intensity, radiated to the flanks, and was accompanied by a progressively enlarging abdominal mass located in the epigastric region, which had been present for six years. Additionally, the patient reported experiencing nausea, vomiting, and anorexia over the past month. She denied any history of fever, significant weight loss, melena, or rectal bleeding. There was no prior use of medications before the presentation. The patient had no known comorbidities and no history of diabetes mellitus, hypertension, tuberculosis, bronchial asthma, epilepsy, or any significant medical or surgical conditions. She also reported no known allergies to food or medications. There was no relevant family history or any similar complaints in the past. She denied having any domestic animals, including dogs. On physical examination, a round, tender mass of approximately 10 × 10 cm was palpated in the epigastric region, with associated guarding and rigidity. The patient had remained asymptomatic until two months prior, when the onset of severe abdominal pain likely delayed medical consultation. There was no prior history of diagnostic imaging or medical treatment. Initial investigations, summarized in **(Table 1)**, revealed mildly decreased hemoglobin levels, a normal white blood cell count, slightly elevated liver enzymes, and renal function tests within normal limits. Viral markers, including HCV, HBsAg, and HIV, were non-reactive. CT imaging revealed multiple characteristic features consistent with disseminated hydatid disease. As shown

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in **(Figure 1)** 1A, a cystic lesion was observed in segment IV of the liver, classified as WHO Stage CE-4. Adjacent to this, a large exophytic hypodense cyst was visualized, consistent with WHO Stage CE-2, and containing multiple peripheral daughter cysts. **(Figure 1)** 1B demonstrated a focal loculated extension of this hepatic cyst along its infero-medial wall. **(Figure 2)** displays axial CT sections revealing well-defined cysts in the recto-uterine pouch and left adnexa, in addition to the infero-medial extension of the hepatic cyst.

Surgery was planned based on these findings. Under General anesthesia, the patient was painted and draped. An infra-umbilical curvilinear incision was given, and Carbon dioxide pneumoperitoneum was created. Laparoscopic exploration (using a 30° laparoscope) was carried out through trocar placement, with a 12 mm trocar infra-umbilically and two 5mm working ports in the right and left mid-clavicular line. Approx. 5 intact cysts (measuring approx. 3-5cm in size) were identified in the cul-de-sac (anterior to the rectum), right fornix, and left fornix. One ruptured hydatid cyst was also identified in the right fornix with intact membranes **(Figure 3)**. Another cyst, which was arising from the round ligament on the left side (approx. 4cm in size), was identified. All the cysts were meticulously dissected and excised intact using harmonic shears **(Figure 4)**. After pelvic clearance, the upper abdomen was examined, which showed extensive omental adhesions that were adhered to the anterior abdominal wall as well as the underlying cyst. It was found out that the omentum was wrapped around a large liver hydatid cyst (measuring approx. 15cm), replacing the entire left liver lobe and causing pressure atrophy of the lobe. Adhesiolysis was done, and it was found that this cyst was also adhered to the surface of the spleen **(Figure 5)**. After meticulous adhesiolysis, the cyst was carefully punctured, and the fluid inside the cavity was aspirated before keeping povidone iodine-soaked gauze around the cyst to prevent recurrence due to spillage. The cyst was then de-roofed, along with the instillation of 3% hypertonic saline in the cavity, and was excised using a harmonic scalpel. The cystic content was taken out in an endo bag along with the excised pelvic cysts **(Figure 6)**. A Bile leak was identified over the edge of the left lobe (possibly a cysto-biliary fistula), the source was identified (Branch of left hepatic duct) and was ligated using ligaclip 400 & 4-0 vicryl suture. Biliostasis was achieved. Another cyst (measuring approx. 3cm) was identified over segment IV of the liver (behind the gall bladder), which was de-roofed, and all the contents were aspirated out **(Figure 7)**. Romovac drain was placed in the upper left quadrant through the 5mm port, and for postoperative pain management, a local anesthetic agent, Bupivacaine, was administered in the subcutaneous plane. Closure of 12mm ports was performed using polyglactin 910 (vicryl) sutures, and the skin of the port entry site was approximated with a skin stapler **(Figure 8)**. The patient was extubated successfully and was shifted to the ward. The post-op period was uneventful, and the patient was ambulatory & accepting diet per oral within post-op Day 1. The patient was monitored for another 3 days for any anaphylactic reactions, and the patient was discharged on Day 4 as the patient became asymptomatic and fit for discharge. The patient was put on 4-week anthelminthic medication of 400mg Albendazole, and the follow-up ultrasound in the 6th week showed no residual disease. Histopathological features were consistent with a clinical diagnosis of Hydatid disease. Examination of the cyst revealed acellular laminated membranes with debris, scolex, and protoscolices. Cyst wall tissue was lined by cuboidal lining epithelium, with mixed inflammatory infiltrates comprising lymphocytes, eosinophils, and plasma cells underneath. Areas of fibrosis, calcification, congested blood vessels, and necrosis were discernible **(Figure 9)**.

Table 1: Initial Laboratory Investigations

Investigations	Value	Normal Range
Haemoglobin	11.2 g/dl	13.0-17.0
Total Leukocyte Count (TLC)	7.2×10^3/uL	4.0-10.0
Platelet	285 *times* 10^3/uL	150.0-410.0
Liver Function Tests		
Serum Glutamic-Oxaloacetic Transaminase (SGOT)	37 IU/L	0.0-35.0
Serum Glutamic Pyruvic Transaminase (SGPT)	46 IU/L	0.0-41.0
Alkaline Phosphatase (ALP)	127 IU/L	40.0-129.0
Albumin	5.5 g/dl	3.5-5.2
Bilirubin	0.2 mg/dl	0.1-1.2
Renal Function Tests		
Serum urea	13 mg/dl	17.0-43.0
Serum Creatinine	0.7 mg/dl	0.6-1.1
International Normalized Ratio (INR)	1.05	0.8-1.2
Serum Sodium (Na^+)	140 mmol/L	136.0-145.0
Serum Potassium (K^+)	3.9 mmol/L	3.5-5.0
Viral Markers		
Hepatitis C virus (HCV)	Non-Reactive	
Hepatitis B surface antigen (HBsAg)	Non-Reactive	
Human Immunodeficiency Virus (HIV)	Non-Reactive	

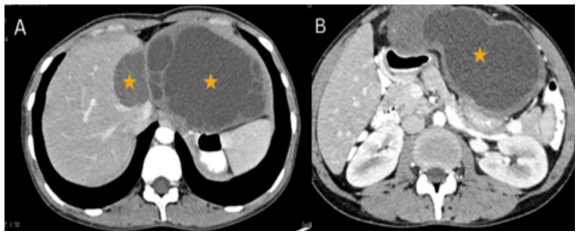

Figure 1: (A) Cystic structure visualized in segment IV (WHO Stage CE-4) of the liver. Another large exophytic hypodense cyst (WHO Stage CE-2) with multiple small locations scattered at its periphery (s/o daughter cysts). (B) A focal loculated extension of the Hepatic cystic lesion along its infero-medial wall.

3. Discussion

Disseminated hydatid disease is a rare condition, with an incidence ranging from 1% to 8% [1]. Involvement of sites other than the liver and lungs is uncommon. Clinical presentation varies depending on the size, location, and presence of complications related to the cysts. Involvement of organs such as the spleen, ovaries, round

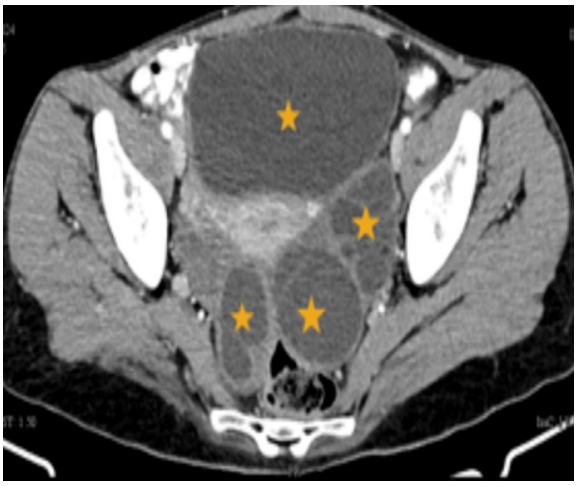

Figure 2: Axial section presence of well-defined cysts in the Recto-uterine pouch, Left Adnexa, and infero-medial extension of the Hepatic cyst.

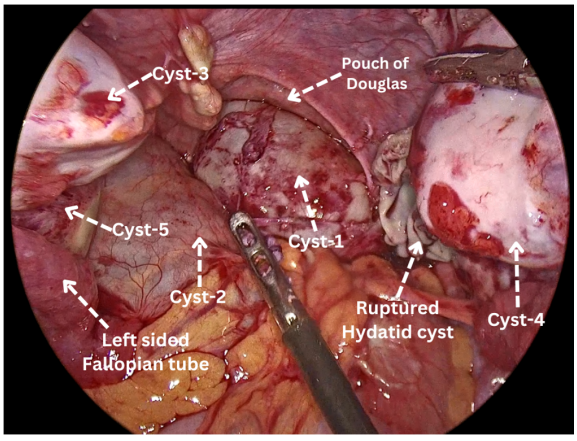

Figure 3: Intra-operative findings- Multiple cysts identified in the cul-de-sac, right and the left fornix which were excised using harmonic. One ruptured hydatid cyst was also identified in the right fornix with intact membranes.

ligament, and peritoneum typically occurs secondary to the rupture of a primary hepatic hydatid cyst. Ultrasound serves as the first-line diagnostic modality for hydatid disease [4]; however, computed tomography (CT) has significantly enhanced both diagnostic accuracy and treatment planning. Surgical intervention remains the cornerstone of treatment and may be performed via open or laparoscopic approaches. Laparoscopic surgery offers several advantages, including reduced operative time, fewer intraoperative complications, diminished postoperative pain, shorter hospital stays, and superior cosmetic outcomes.

Preoperative and postoperative administration of albendazole for one month is recommended to sterilize the cyst and reduce the risk of recurrence. Nonetheless, laparoscopic procedures have inherent limitations, such as dependence on the surgeon's expertise and the potential risk of cyst content spillage, which may lead to intraoperative anaphylaxis and recurrence.

The strength of this case report lies in its documentation of a rare and atypical manifestation of hydatid disease, successfully

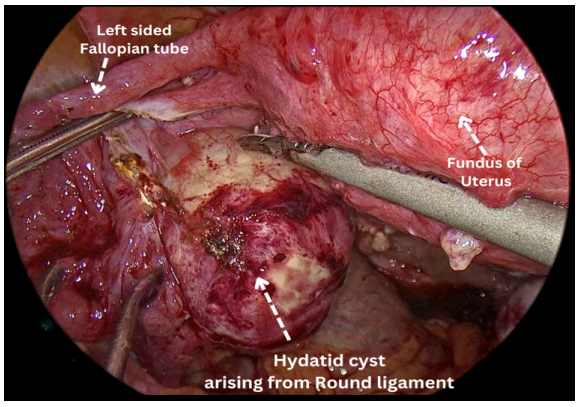

Figure 4: Intra-operative findings- Another cyst was identified arising from round ligament which was meticulously dissected.

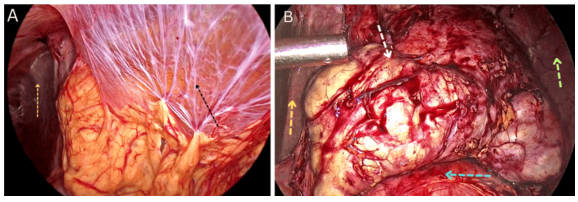

Figure 5: Intra-operative findings- (A) Extensive omental adhesion adhered to the anterior abdominal wall visualized (Black arrow). Right lobe of liver was also visible (Yellow arrow). (B) Cyst visualized after adhesiolysis (White arrow), Spleen (Green arrow), Right Liver lobe (Yellow arrow), Transverse Colon (Blue arrow).

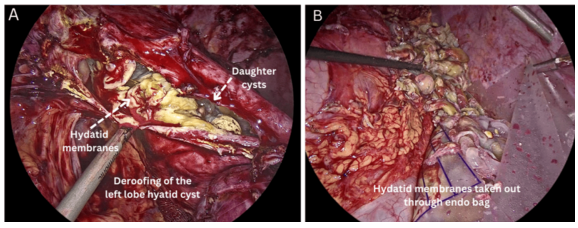

Figure 6: Intra-operative imaging- (A) Visible intact Hydatid membranes and Daughter cysts. (B) Cyst membranes, along with daughter cysts, are delivered out using an Endo bag.

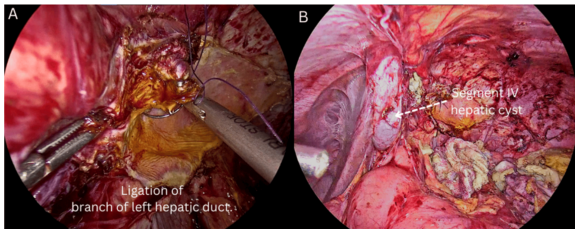

Figure 7: Intra-operative findings (A) Bile leak identified over the tissue of left lobe, which was ligated using ligaclip 400 vicryl suture. (B) Another cyst was identified in segment IV of the liver.

managed through a laparoscopic approach. Initial diagnostic laparoscopy confirmed the feasibility of a minimally invasive surgical strategy. This approach offered superior intraoperative visualization, facilitated by advanced 4K imaging technology, which allowed for enhanced anatomical detail beyond the capabilities of direct visualization in open surgery. As a result, a large incision

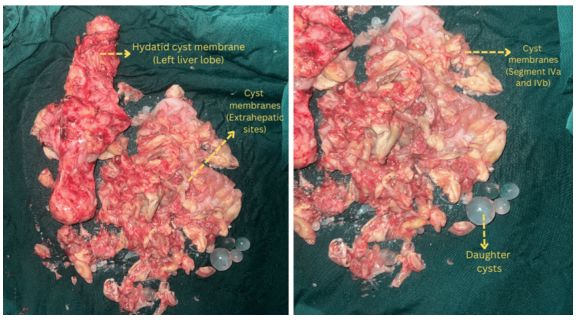

Figure 8: Specimen- Hydatid cyst can be visualized with intact membranes and daughter cysts.

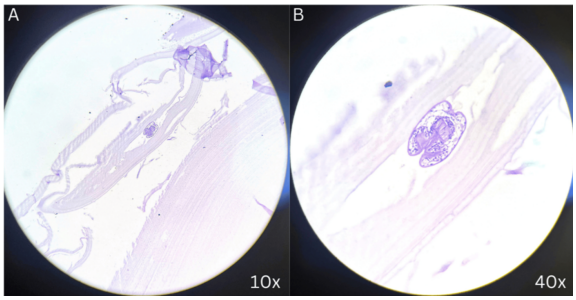

Figure 9: (A) Examination under 10x magnification revealed cyst wall tissue lined by cuboidal lining epithelium with mixed inflammatory infiltrates. (B) Examination under 40x magnification revealed scolices, protoscolioses, and acellular laminated membranes with debritic material

was avoided in a young patient, leading to improved surgical outcomes such as minimal blood loss, reduced postoperative pain, a shorter hospital stay—which lowers the risk of hospital-acquired infections—and improved cosmetic results due to minimal scarring. Collectively, these factors contributed to an overall enhanced surgical experience. An extensive literature review indicates that, to our knowledge, this is among the first documented cases of its kind globally, underscoring the uniqueness of the cysts' size and location and the laparoscopic approach used in management. However, a key limitation of this report is that it describes a single case, which restricts the generalizability of its findings.

A comprehensive review of documented cases involving disseminated and atypical sites of hydatid disease was conducted. Mihetiu A. et al. [5] reported 49 cases with unusual abdominal localizations, among which only one involved the round ligament [6]. Of these 49 cases, merely two were managed laparoscopically, reinforcing our case report's significance. El Bakaouri et al. [7] described a rare case involving the liver, spleen, and peritoneum, managed through cystectomy combined with splenectomy; the patient was discharged on the sixth postoperative day, suggesting a relatively extended hospital stay.

Ziad F. et al. [1] also reported a similar case with hydatid cysts localized to comparable sites, with cyst sizes ranging from 3 to 10 cm. That case was managed via a median laparotomy and had an uneventful postoperative course. In contrast, our case demonstrates the successful application of a minimally invasive laparoscopic approach to similar anatomical sites despite the presence of even larger cysts. This highlights the feasibility and advantages of laparoscopy in managing such complex presentations.

A rare case presented by Achraf S et al. [8] shows how a patient with multiple hepatic as well as extrahepatic hydatid cysts was managed by resection of the cysts but died on postoperative day 15, further strengthening our case, which was managed laparoscopically.

A recent case reported by Kandel et al. [9] described multiple primary intraperitoneal cysts ranging in size from 2 to 15 cm, which were managed through an open surgical approach. In contrast, our report offers valuable insights into managing similarly complex cases of hydatid disease using a minimally invasive laparoscopic technique.

A comparable case by Zayati M. et al. [10] also demonstrated similar localization of hydatid cysts, with sizes ranging from 3 to 6 cm—closely resembling those in our case. Notably, they reported the presence of a cysto-biliary fistula, a complication also identified in our patient. However, while their case was managed via open surgery, our case highlights the successful laparoscopic management of the same, further reinforcing our approach's strength.

A comprehensive literature review also identified a rare case of disseminated hydatid disease reported by Babiker et al. [11], involving cysts localized to the lungs, liver (5 cm), and spleen (7.5 cm). Although this case was successfully managed laparoscopically, the degree of dissemination and the cyst sizes were notably smaller than those observed in our report.

The literature review indicates that only a limited number of cases have utilized laparoscopy as the primary modality for managing hydatid disease. One such case was reported by Obeid M. et al. [12], where hydatid cysts were localized to the liver and the small intestine mesentery, with the largest measuring 10 cm. This case was successfully managed laparoscopically. Similarly, Jangjoo et al. [13] described a large cyst measuring 10 × 5 cm located in the greater omentum, which was also treated via a laparoscopic approach. These reports further support the uniqueness of our case, both in terms of presentation and the successful use of minimally invasive management.

In contrast, Baimakhanov et al. [14] documented a rare instance of disseminated hydatid disease involving multiple organs—including the liver, spleen, kidneys, and pancreas—with cyst sizes ranging from 1 to 6 cm. This case was managed using open surgery. Likewise, Ranjan R. et al. [15] reported a mesenteric hydatid cyst measuring 12 × 10 cm, which was also treated through an open surgical approach. Delis SG et al. [16] reported a case series of patients presenting with unusual localization of hydatid cysts for which complete cyst excision in most patients was performed, along with omentoplasty in a few cases of hydatid extension into vertebrae.

G. Ozturk et al. [17] conducted a study involving twenty patients with post-traumatic ruptured liver hydatid cysts, all of whom were managed surgically. The authors advocated for a conservative surgical approach—primarily involving de-roofing and various techniques to manage the residual cavity—over more radical procedures such as hepatic resection or pericystectomy. This study also highlights the pivotal role of computed tomography (CT) in transforming the diagnosis and management of hydatid disease.

Mushtaque M. et al. [18] further emphasized that surgery remains the cornerstone of hydatid disease treatment. Among the surgical options available, laparoscopic intervention is generally preferred over traditional open surgery. The PAIR technique (Puncture, Aspiration, Injection, and Reaspiration/Removal) is commonly used in laparoscopic procedures, as it facilitates the conversion of the cyst into a non-dependent cavity. This approach offers several advantages, including a shorter hospital stay, reduced postoperative pain, and improved cosmetic outcomes.

Evidence indicates that surgical intervention remains the cornerstone in managing complex cases of hydatid disease. While the optimal surgical approach continues to be a topic of discussion, multiple studies have demonstrated that laparoscopic techniques offer superior outcomes, including reduced hospital stays, lower complication rates, and improved prognoses compared to open surgery. Our case underscores that even rare and atypical presentations of hydatid disease can be effectively managed through minimally invasive methods. This supports the growing body of evidence advocating for laparoscopic surgery as a transformative approach in treatment guidelines, ultimately enhancing patient care. We advocate for adopting minimally invasive techniques, even in cases involving large cysts or multiple localizations, to optimize patient outcomes and avoid unnecessary open procedures when not explicitly indicated. In managing sizable cysts, de-roofing combined with the instillation of sporicidal agents such as hypertonic saline have improved surgical outcomes. Additionally, using povidone-iodine-soaked gauze during surgery can effectively prevent spillage of cystic contents, thereby reducing the risk of recurrence. Laparoscopy, as a novel surgical modality, offers numerous advantages, including shorter hospital stays, enhanced cosmetic results, and the avoidance of large incisions associated with open surgery. These benefits contribute to improved overall patient experiences and outcomes.

4. Conclusions

Echinococcosis can occur anywhere in the body, with concurrent localizations in the liver, spleen, round ligament, peritoneum, mesentery, and omentum. It is rare and poses a diagnostic as well as a surgical management challenge. The inconvenience of multiple localization and the risk of contamination usually lead to open surgery in these cases. A thorough literature review suggested that our case was unique in various aspects, including variable localization of the cysts, cyst size, and the laparoscopic approach to such complex cases of hydatid disease, advocating for a minimally invasive first-line approach even in these types of cases.

Conflicts of Interest

GB, RB, VS, and RK declare that they have no financial or non-financial competing interests related to the content of this article. No conflicts of interest, financial ties, or funding sources have influenced the results or interpretations presented in this manuscript.

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Patient consent

This study was conducted in accordance with the Declaration of Helsinki. Ethical approval was waived by the Institutional Review Board (IRB) for the case reports/case series. Written informed consent was obtained from the patient to participate in the study and publish their clinical information and images. No identifiable patient information is included in this publication.

Large-Language Model

None

Author's contribution

GB and RB supervised, conceptualized, designed methodology, provided resources, investigated, drafted the original manuscript, and reviewed and edited the draft; VS and RK reviewed and edited the draft. All authors contributed to the manuscript's text and content, approved the final version, and agreed to be accountable for the work.

Data Availability

All data are included in this published article.

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ASIDE Gastroenterology

Original Article

A Systematic Review and Meta-Analysis of Liver Transplant Outcomes in Lean Versus Non-Lean Metabolic Dysfunction-Associated Steatotic Liver Disease Patients

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Lean MASLD

ABSTRACT

Introduction: Metabolic dysfunction-associated steatotic liver disease (MASLD) is a prevalent hepatic disease with metabolic dysfunction-associated steatohepatitis (MASH) as its severe necro-inflammatory subtype. At present, it is the second leading cause of liver transplant. A systematic literature review (SLR) was conducted to assess the effect of lean vs non-lean BMI on clinical outcomes after transplant in MASLD patients.
Methods: A systematic search of PubMed, Cochrane Library, and Google Scholar databases was executed. Review Manager 5.4.1 was used for statistical analyses. A random-effects model was used with the results reported as Odds Ratio (OR) and 95% confidence interval (CI). A narrative approach was used where it was not feasible to conduct a meta-analysis.
Results: Eleven observational studies were included in the SLR. Pooled results from three studies showed no significant difference in mortality between lean and non-lean patients at 1 year (OR= 0.78, p= 0.76), 2 years (OR= 0.83, p= 0.24), and 5 years (OR= 1.07, p= 0.51) post-transplant. There was also no significant relation of lean and non-lean BMI in graft survival, observed over 30 days (OR= 1.34, p= 0.27), 1 year (OR= 0.75, p= 0.25), 2 years (OR= 1.20, p= 0.45), and 5 years (OR= 1.07, p= 0.60) post-transplant. Qualitative analysis suggested morbid obesity is linked with higher waitlist dropout in MASH patients.
Conclusion: The qualitative analysis of eight studies indicates a trend towards poorer outcomes in the non-lean group. There is a need for further investigations to comprehensively examine the factors influencing the relationship between BMI and post-transplant outcomes.

1. Introduction

Metabolic dysfunction-associated steatotic liver disease (MASLD) is a prevalent hepatic condition characterized by a build-up of macrovesicular steatosis in ≥5% of hepatocytes, occurring without significant alcohol or drug consumption [1]. A recent review of 72 records described the overall prevalence of MASLD worldwide increased significantly over time, from 25.5% before 2006 to 37.8% in 2016 or later [2]. Given the prevalence estimate, MASLD stands as the primary cause of chronic liver disease worldwide [3]. MASLD shares metabolic risk factors, including type 2 diabetes mellitus, obesity, and hypercholesterolemia, with metabolic syndrome [1]. Diagnosis involves identifying steatosis on ultrasound, often prompted by elevated liver transaminases [1]. Management of MASLD focuses on addressing modifiable risk factors such as blood pressure, body mass index (BMI), cholesterol, and blood sugar levels, with weight reduction being notably associated with decreased fibrosis among patients [4].

Metabolic dysfunction-associated steatohepatitis (MASH) is defined as a severe necro-inflammatory subtype of MASLD, which involves hepatic steatosis accompanied by inflammation and hepatocellular ballooning, which can progress to hepatocellular carcinoma (HCC) [5]. MASH frequently leads to complicated liver cirrhosis or failure, making liver transplantation the primary treatment option and a preventive measure against HCC [6]. MASH has an estimated global prevalence of 5.27% [6] and is currently the second leading indication for liver transplantation [7, 8].

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Although obesity can predispose individuals to various clinical comorbidities and post-operative complications, the impact of obesity on survival and transplantation outcomes in liver transplant patients remains uncertain. The American Society of Transplantation describes morbid obesity (BMI $\geq$ 40 kg/m^2) as a potential contraindication for liver transplant due to the heightened risk of post-transplant complications. A previous study conducted by Barone et al. assessed post-transplant outcomes in obese patients [9], which observed that a BMI $\geq$ 40 was linked to a greater risk of mortality, while a BMI $\geq$ 30 led to significantly more post-transplant complications [9]. When comparing outcomes in MASH versus non-MASH patients, a meta-analysis by Wang et al. comparing post-transplant outcomes, survival, and mortality rates in liver transplant patients with and without MASH reported similar mortality rates at 1, 3, and 5 years between the two groups, with cardiovascular complications being more common in the MASH group [10]. Another study published in 2022 concluded no significant difference in post-transplant survival between the MASH and non-MASH groups. However, the MASH group exhibited higher sepsis-related mortality and better graft survival [11].

Given the current conflicting data and lack of consensus on the impact of obesity on liver transplant patients, our systematic literature review (SLR) and meta-analysis aim to compare post-transplant outcomes in lean and non-lean MASLD patients who underwent liver transplantation.

2. Methods

2.1. Data sources and search strategy

A SLR and meta-analysis following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [12] was conducted. PubMed, Cochrane Library, and Google Scholar were searched from inception to April 22, 2023. To update the search for any potential new relevant publications, hand searching was performed on November 30, 2024, to identify any additional studies published since the last search date. The search strategy comprised both older and newer terminologies for the disease, including Non alcoholic fatty liver disease (NAFLD), Non-alcoholic fatty steatohepatitis (NASH), MASH, and MAFLD. The search string used was: (NAFLD OR nonalcoholic fatty liver disease OR NASH OR MASLD OR MASH OR non-alcoholic Steatohepatitis OR non-alcoholic cirrhosis) AND (transplant* OR post-transplant*) AND (lean OR BMI OR obese). Additionally, we cross-referenced any identified SLRs to ensure comprehensive coverage.

2.2. Eligibility criteria

The eligibility criteria were formulated using the PECO framework: P (Patients): nonalcoholic fatty liver disease patients or non-alcoholic steatohepatitis patients who underwent transplantation; E (Exposure): BMI $\geq$ 25 kg/m^2 pre-transplantation; C (Control): BMI $\leq$ 25 kg/m^2 pre-transplantation; O (Outcome): mortality and graft survival/loss. Lean was defined as BMI $\leq$ 25 kg/m^2, and non-lean was defined as BMI $\geq$ 25 kg/m^2 [13].

2.3. Screening, data extraction, and quality assessment of studies

Two independent reviewers conducted electronic database searches. The retrieved studies were exported to EndNote Reference Library version 20.0.1 software for screening after deduplication. The screening was conducted in duplicate by two reviewers (FP and UH) at the title/abstract and full text stages. Any disagreements or conflicts were resolved through discussion or by a third reviewer (MKG), if needed. Two reviewers (FJ and DSD) independently extracted data and further assessed the risk of bias in the included studies. The variables extracted included study author names, year of publication, study duration, country of origin, total number of patients, BMI, male proportions, mean age, and outcomes reported.

The Newcastle-Ottawa Scale (NOS) was used to assess the quality of cohort studies. NOS score of 1-5 was considered at high risk of bias, 6-7 indicated moderate risk, and scores greater than 7 were considered low risk of bias **(Table 1)**.

2.4. Statistical analysis

All statistical analyses were performed using Review Manager (version 5.4.1; Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2020). The extracted data were pooled using a random-effects model. Odds ratios (OR) with corresponding 95% confidence intervals (CI) were calculated to analyze the results. The chi-square test was used to assess any subgroup differences. Heterogeneity was evaluated using the Higgins et al. scale: I^2 = 25–60% (moderate), 50–90% (substantial), and 75–100% (considerable heterogeneity) [14]. A p-value < 0.05 was considered statistically significant. A qualitative synthesis was performed on studies that met the inclusion criteria but did not provide data suitable for quantitative analysis.

3. Results

The comprehensive search of electronic databases yielded a total of 1,361 records. After removing duplicates, 946 records underwent title and abstract screening. Out of these, 135 records underwent eligibility assessment based on full-text. Finally, 11 studies [15, 16, 17, 18, 19, 20, 21, 22, 23, 24] were selected for inclusion in the SLR, with evidence from eight studies [18, 19, 20, 21, 22, 23, 24, 25] synthesized qualitatively and three [15, 16, 17] feasible to be included in meta-analysis. The PRISMA flowchart illustrating the study selection process is shown in **(Figure 1)**.

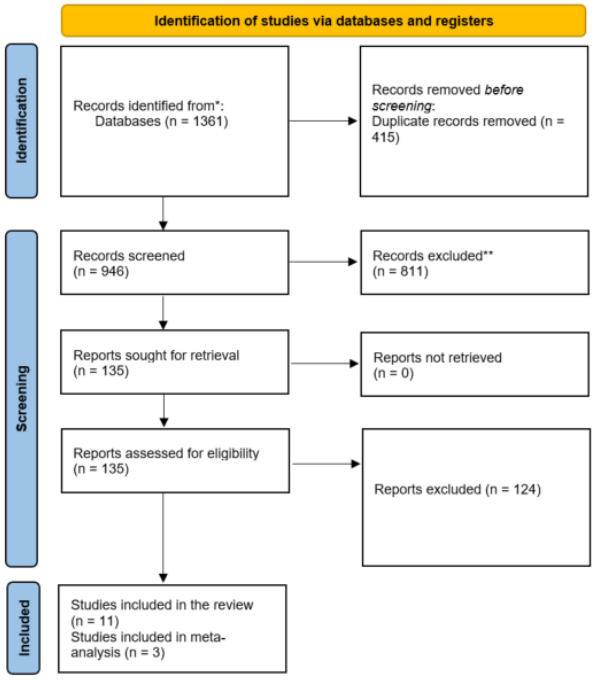

Figure 1: PRISMA flow diagram of systematic review process

Table 1: Quality assessment of included studies

Study	Selection (Maximum 4)				Comparability (Maximum 2)	Outcome (Maximum 3)			Total Score
	Representative of the Exposed Cohort	Selection of the Non-Exposed Cohort	Ascertainment of Exposure	Demonstratio That Outcome of Interest Was Not Present at Start of Study	Comparability of Cohorts on the Basis of the Design or Analysis	Assessment of Outcome	Was Follow-Up Long Enough for Out-comes to Occur	Adequacy of Follow Up of Cohorts	
Malik et al.	1	1	1	1	2	1	1	1	9
Leonard et al.	1	1	1	1	2	1	1	1	9
Heuer et al.	1	1	1	1	2	1	1	1	9
Kenedy et al.	1	1	1	1	2	1	1	1	9
Conzen et al.	1	1	1	1	2	1	1	1	9
Kardashian et al.	1	1	1	1	2	1	1	1	9
Halder et al.	1	1	1	1	2	1	1	1	9
Eshraghian et al.	1	1	1	1	2	1	1	1	9
Satapathy et al.	1	1	1	1	2	1	1	1	9
Qazi-Arisar et al.	1	1	1	1	2	1	1	1	9

The selected studies, comprising 18,783 patients, were all observational studies. **(Table 2)** provides an overview of the baseline characteristics of the included articles [15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25]. These studies were conducted in various geographical regions, including six in the USA, two in Iran, and one each in Europe, Canada, and Germany. The mean age of the patients was 50.8 years.

3.1. Publication Bias and Quality Assessment

Due to the limited number of articles available for quantitative analysis, it was impossible to assess publication bias. However, all the included studies demonstrated a low risk of bias, as assessed by the NOS, as shown in **(Table 1)**.

3.2. Quantitative Analysis

Only three studies [15, 16, 17] were feasible to be included in the meta-analysis. Eight studies [18, 19, 20, 21, 22, 23, 24, 25] could not be included in the quantitative analysis due to heterogeneity of analysis parameters, outcome endpoints, and different BMI cutoffs to classify lean and non-lean patients.

3.2.1. Patient Mortality

Three studies were included in the quantitative analysis to evaluate patient mortality based on pre-transplant BMI [15, 16, 17]. No significant difference was observed in mortality between lean and non-lean patients at 1 year (OR= 0.78 [CI 0.15, 4.01]; p= 0.76; I^2= 81%), 2 years (OR= 0.83 [CI 0.62, 1.13]; p= 0.24; I^2= 57%), and 5 years (OR= 1.07 [CI 0.87, 1.31]; p= 0.51; I^2= 38%) post-transplant **(Figure 2)**.

3.2.2. Graft Survival

Three studies were included in the quantitative analysis to assess graft survival based on pre-transplant BMI [15, 16, 17]. The results showed no statistically significant relationship of BMI with graft survival at 30 days (OR= 1.34 [CI 0.79, 2.26]; p= 0.27), 1 year (OR= 0.75 [CI 0.46, 1.22]; p= 0.25; I^2= 24%), 2 years (OR= 1.20 [CI 0.75, 1.91]; p= 0.45; I^2= 76%), and 5 years (OR= 1.07 [CI 0.84, 1.35]; p= 0.60; I^2= 0%) post-transplantation **(Figure 3)**.

3.3. Qualitative Analysis

Eight studies were included in the qualitative analysis, which examined the impact of BMI on clinical outcomes [18, 19, 20, 21, 22, 23, 24, 25]. The studies provided varied outcomes assessing the association between BMI and post-transplant outcomes. Eshraghian et al. [25] found an increased risk of hepatic steatosis after liver transplant in patients with a higher BMI. Haldar et al. [19] observed that high BMI (>40 kg/m^2) independently predicted death in patients transplanted for NASH without HCC. Kardashian et al. [20] reported that morbid obesity was significantly linked to waitlist dropout in MASH patients with and without ascites (hazard ratio (HR) = 1.27 [1.20, 1.36]). Heur et al. [22] observed that sustained obesity and features of the metabolic syndrome in patients were associated with worse 1-year mortality. Kennedy et al. [23] noted worse survival in the high-risk cohort (age >60 years, BMI >30 kg/m^2, and the presence of both diabetes and hypertension). Meanwhile, Satapathy et al. [21] described lean NASH patients to have lower graft and patient loss at 10 years follow-up than their obese counterparts. A sub-analysis from Malik et al. [24] revealed that patients transplanted for NASH cirrhosis who died within the first year post-transplant were older (≥60 years), more obese (BMI ≥30 kg/m^2), and had pre-transplant DM and HTN. Eshragian et al. [18] observed a higher BMI to be marginally associated with NASH occurrence in non-obese compared to those without NASH (P=0.05). BMI-related results in these studies were often available without complete raw data, and with variable follow-up durations and outcomes; therefore, they could not be added to the meta-analysis.

Table 2: Characteristics of Included Studies

Study	Year	Study design	Duration	Country	Total patients (n)	BMI <25 kg/m^2 (n)	BMI ≥25 kg/m^2 (n)	Male (%)	Mean Age (years)	Qualitative or Quantitative	Outcomes reported	Risk of Bias
Malik et al.	2009	Cohort	July 1997-June 2008	USA	98	N/A*	N/A*	44.9	59.8	Qualitative	Mortality	Low Risk
Leonard et al.	2008	Cohort	April 1990-June 1994	USA	1313	628	685	60.4	50.8	Quantitative	Patient mortality, Graft survival	Low Risk
Heuer et al.	2012	Cohort	Oct 2007-Jan 2011	Germany	40	4	36	60	N/A*	Qualitative	Mortality, Graft failure	Low Risk
Kenedy et al.	2012	Cohort	1999-2009	USA	129	N/A*	N/A*	47	57	Qualitative	Patient survival	Low Risk
Conzen et al.	2015	Cohort	Jan 2002-Dec 2012	USA	785	219	566	67.2	N/A*	Quantitative	Patient mortality, Graft survival	Low Risk
Kardashian et al.	2018	Cohort	March 2002-Dec 2013	USA	10001	N/A*	N/A*	66.3	N/A*	Qualitative	Waitlist dropout	Low Risk
Halder et al.	2019	Cohort	Jan 2002-Dec 2016	Europe	2741	N/A*	N/A*	71.1	N/A*	Qualitative	Patient survival	Low Risk
Eshraghian et al.	2020	Cohort	July 2012-Oct 2018	Iran	310	246	64	42	32.64	Qualitative	Prevalence	Low Risk
Eshraghian et al.	2020	Cohort	March 2010-March 2017	Iran	462	N/A*	N/A*	65.5	46.9	Qualitative	Graft rejection	Low Risk
Satapathy et al.	2020	Cohort	Jan 2002-June 2013	USA	2728	278	2450	54.3	57.9	Qualitative	Patient survival and Graft loss	Low Risk
Qazi-Arisar et al.	2022	Cohort	Nov 2012-May 2019	Canada	176	54	122	53.9	N/A*	Quantitative	Patient mortality, Graft survival	Low Risk

N/A*= Not Available

4. Discussion

The current SLR and meta-analysis evaluated the role of BMI in post-transplant outcomes in patients with MASLD who underwent liver transplantation. Our analysis included both quantitative and qualitative evidence synthesis. The quantitative analysis did not find a significant association between long-term mortality rates and graft survival when comparing lean and non-lean patients [15, 16, 17]. While the qualitative analysis of eight studies observed a trend towards poorer outcomes in the non-lean patients [18, 19, 20, 21, 22, 23, 24, 25], statistical association could not be assessed. These findings align with previous studies that have shown a relationship between obesity and poorer outcomes following liver transplantation. Evidence in the literature is mixed regarding any differences in outcomes between lean and non-lean patients. One of the initial studies conducted by Nair et al. served as the basis for the American Association for the Study of Liver guidelines in 2005, which contraindicated liver transplantation for morbidly obese individuals. Subsequent studies, such as those by Beckmann et al., further supported this association, showing worse survival and graft survival rates in patients with a pre-transplant BMI higher than 30 kg/m^2 [26, 27]. However, variations in study populations and primary causes of transplantation introduced heterogeneity in the results.

Interestingly, when accounting for concomitant comorbidities, studies have not consistently established an independent link between obesity and liver transplantation outcomes. Wong et al. demonstrated that when diabetes was considered, the survival rates between obese and non-obese patients were similar [3]. Additionally, some studies reported improved survival rates in patients with moderately elevated BMI, highlighting the potential confounding effect of being underweight on post-transplant survival [28, 29].

To explain the heterogeneity observed in study results, further analysis is needed regarding the definition of BMI and its relationship to MASLD/MASH patients. The use of BMI as an estimate of body adiposity has limitations, as it does not account for variations in body composition. In MASLD/MASH patients, ascites or volume overload may lead to overestimating body weight [26, 30]. Moreover, racial disparities in BMI cutoffs, particularly in the Asian population, may contribute to discrepancies in outcomes among liver transplant patients [31].

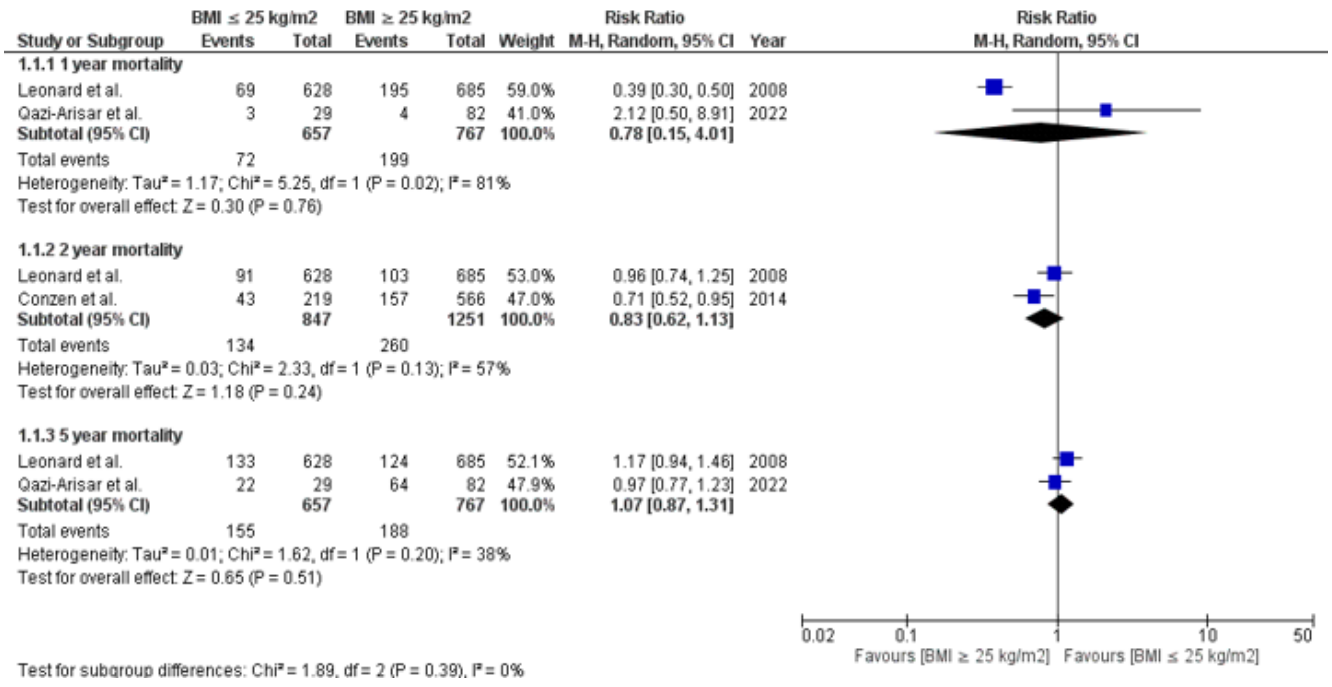

Figure 2: Forest plot of Mortality in lean vs. non-lean patients.

Furthermore, post-transplant mortality in MASLD patients can result from various factors, including disease recurrence, allograft rejection, progression to MASH cirrhosis or HCC, and metabolic syndrome [17, 32]. Higher BMI is associated with an increased risk of cardiovascular incidents and metabolic symptoms, which may confound the association between high BMI and survival [33, 34].

Our study also did not find a statistically significant association between BMI and graft survival. However, graft survival is multifactorial and depends on factors such as compliance with immunosuppressive therapy [35]. Previous studies have reported conflicting results, with some suggesting that obesity significantly impacts graft survival while others have found no significant differences [15, 17, 29]. The inconsistency in results can be attributed to variations in the definition of obesity and the inclusion of fluid overload rather than true obesity in some studies.

It is worth mentioning that some studies have associated BMI with HCC, potentially due to pro-inflammatory cytokine production by adipose tissue [17, 36, 37, 38]. However, the mechanism underlying this association remains unclear.

4.1. Strengths and Limitations

Our study's strengths include searching multiple databases to ensure comprehensive coverage and the inclusion of several studies with larger sample sizes and longer follow-up periods. Furthermore, while previously published meta-analyses do not determine the transplant outcomes regarding BMI in MASLD patients or MASH patients, we specifically focused on both subgroups, which consist of a substantial number of liver transplant patients.

The findings of this review require cautious interpretation due to some limitations. Firstly, only three studies were included in the quantitative analysis due to a lack of studies reporting sufficient raw data and heterogeneity in BMI classifications, outcome endpoints, and their durations, limiting the feasibility of producing pooled estimates. Furthermore, the low number of studies and the limited sample size in the quantitative analysis may underestimate the important effects that could have emerged better in larger and uniform datasets, reduce the statistical power of the pooled estimates, and limit the generalizability of findings. This limitation stresses the urgent need for future research to adopt standardized BMI classifications and outcome definitions. Secondly, all included studies were observational, which may introduce potential selection, reporting, and confounding biases that are inherent to non-randomized study designs. Thirdly, normal weight and underweight patients were pooled as "lean" (BMI 25 kg/m^2) and all overweight and obese patients grouped as "non-lean" (BMI $\geq$ 25 kg/m^2), potentially obscuring important differences within these groups. Lastly, the quantitative analysis focused primarily on mortality and graft survival, not extensively analyzing other important post-transplant outcomes such as length of hospital stay, complications, quality of life, or disease recurrence, which can be critical for understanding transplant success in these patients.

Future research requires focusing on a few critical areas, including conducting larger, multicenter, international studies to gather representative data on MASLD patients across various racial and geographical backgrounds. Investigating any pathophysiological mechanisms driving MASLD progression in lean versus non-lean patients, which can include metabolic and genetic factors that may potentially influence liver transplant outcomes, and moving beyond BMI-based classifications to include other analyses of body composition (e.g., muscle mass, fat distribution) and their effect on post-transplant outcomes should be considered. Prospective multicentric studies with standardized BMI classifications can be conducted for appropriate comparability across studies. Additionally, future analyses can stratify outcomes by the different categories of BMI and control for confounding comorbidities. A shared data registry with uniform definitions, follow-up durations, and outcomes can facilitate pooled analyses of a larger cohort of patient data across multiple centers. Although the quantitative analysis from three studies did not identify any relation of BMI

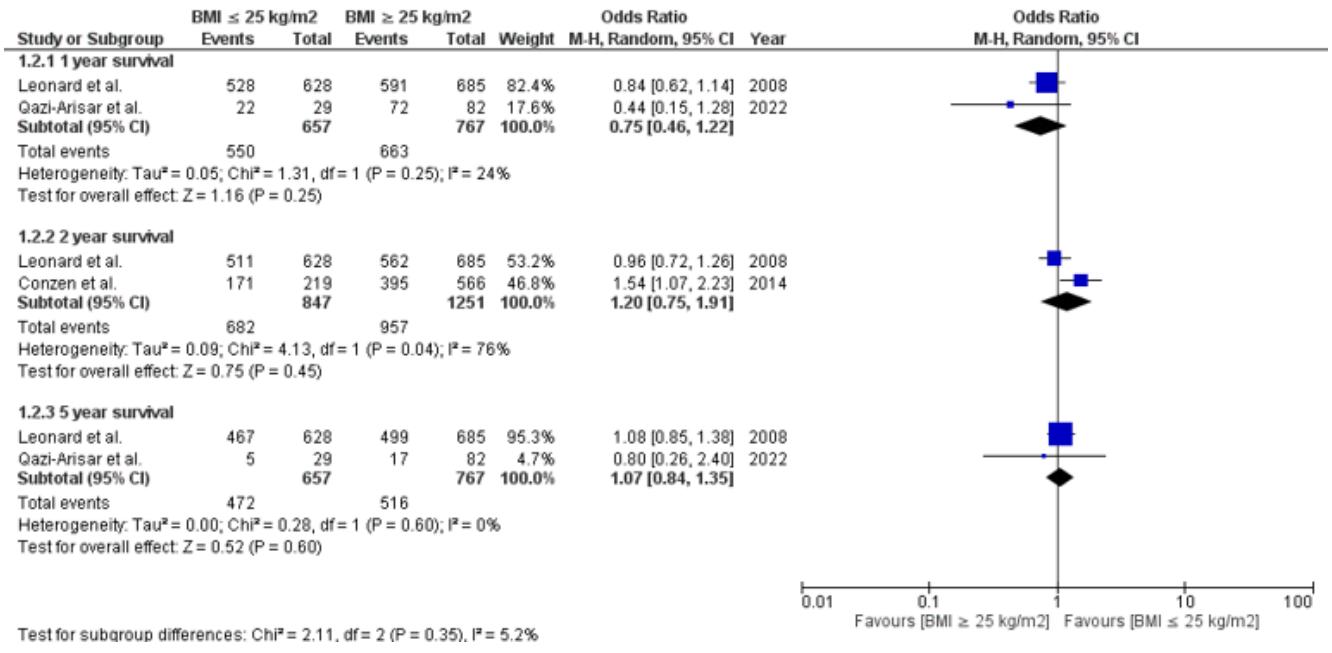

Figure 3: Forest plot of Graft Survival in lean vs. non-lean patients

with post-transplant outcomes, transplant centers can move beyond BMI when assessing the candidacy of MASLD patients for liver transplant. The clinical assessment and decision-making can incorporate additional clinical factors, including metabolic health, other comorbid conditions, and functional status [39].

5. Conclusions

In conclusion, the quantitative analysis did not demonstrate a significant impact of BMI on post-transplant outcomes in MASLD patients. However, the qualitative analysis indicated a trend towards an association between higher BMI and poor post-transplant outcomes, although statistical conclusions could not be definitively drawn. Our study is useful as it plays a pivotal role in presenting and summarizing all the available evidence, highlighting the existing dichotomy in the literature, and its potential causes. It also emphasizes the need for future investigations to consider key parameters that may influence the relationship of BMI with post-transplant outcomes.

Conflicts of Interest

The authors declare no conflict of interest.

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None

Authors Contributions

Author contributions: MGSDS and MKG conceptualized the study design and objectives. MA, FP, DSD, UH, FJ, HA, and SI conducted the literature search, study screening, selection, and data extraction. MKG, OI, and MA designed the data extraction template, extracted data, and carried out data analysis. OI, MA, FP, DSD, UH, FJ, HA, and SI drafted the initial manuscript. MKG, SI, and MGSDS critically reviewed and revised the final manuscript. MGSDS is the guarantor, and the manuscript has been critically reviewed. All authors approve the final manuscript as submitted for publication.

Data Availability

All studies used in the research are available in various databases.

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Case Report

Annular pancreas in adults presenting as chronic pancreatitis and duodenal obstruction: A review of literature and a rare case report

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ABSTRACT

Background: Annular pancreas is a rare congenital anomaly with an estimated incidence of 3.4 per 1,00,000 live births. It is more commonly diagnosed in infants. Its occurrence in adults is exceptionally rare but clinically significant, as seen in our case, where it presented as a duodenal obstruction.
Case presentation: We present a case of an adult male who presented with a 3-week history of projectile bilious vomiting associated with postprandial abdominal pain and early satiety. Imaging studies revealed a segment of the pancreas encircling the second part of the duodenum, along with pancreatolithiasis. Based on the diagnosis of annular pancreas with chronic calcific pancreatitis, the patient underwent pylorus-preserving pancreatoduodenectomy.
Materials and Methods: A structured literature review was performed using PubMed and Scopus databases, covering the period from 2018 to 2024. A total of 24 case reports were analyzed.
Results: The review confirms that annular pancreas remains a rare condition, often undiagnosed in asymptomatic individuals with abdominal pain (83.3%) and vomiting (41.6%) as the most common symptoms. The most common diagnostic modality is the CT scan (computed tomography), at 64.1%, and surgical procedures, such as gastrojejunostomy, are the most common treatment modality, at 46.5%.
Conclusions: It is a rare congenital condition that usually remains undiagnosed in asymptomatic individuals but typically presents with abdominal pain and vomiting when symptomatic. Diagnosis relies primarily on CT imaging. Conservative management is preferred for asymptomatic cases, and surgery is for symptomatic patients. Further research is needed to develop standardized management protocols.

1. Introduction

The annular pancreas (AP) is a rare congenital anomaly characterized by pancreatic tissue partially or completely encircling the second part of the duodenum. This results from the aberrant migration of the ventral pancreatic bud during embryogenesis. This condition was first described by Tiedemann in 1818 and later termed "annular pancreas" by Ecker [1]. Between the fourth and eighth week of embryonic growth, the pancreas typically forms through the rotation and merging of the dorsal and ventral pancreatic buds, driven by the duodenum's expansion. Thereafter, the ventral bud gives rise to the lower portion of the pancreatic head and the uncinate process, while the dorsal bud develops into the body and tail of the pancreas [2]. The majority of cases of AP are identified in the pediatric population, exhibiting signs of gastric outlet obstruction [3]. Common symptoms in adults include abdominal discomfort, vomiting, and hematemesis in patients [4]. A recent population-based study in the United States analyzed data from 6,162,600 patients who underwent abdominal imaging, identifying 210 cases of AP. This finding suggests an estimated prevalence rate of 3.4 per 100,000 individuals [5]. It impacts both sexes, with a modest predominance towards males [6]. The current standard for diagnosing AP relies on abdominal imaging techniques, including ultrasound, computed tomography (CT) scans, barium studies, endoscopic retrograde cholangiopancreatography (ERCP), and magnetic resonance cholangiopancreatography (MRCP) [7]. Approximately 40% of cases necessitate surgical interventions, such as duodenoduodenostomy or duodeno-jejunostomy, to circumvent the blocked duodenal section. Pancreatoduodenectomy is advised only in instances where the AP coexists with pancreatolithiasis and is further complicated by chronic pancreatitis [4]. This report condenses a meticulous review of 24 recently published case reports (2018–2024), providing a contemporary overview of symptomatic adult AP, along with a case report that further contributes to its clinical significance.

2. Objective

This paper aims to advance the understanding of AP presentation in adults, a rare condition with limited published research. Through

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a case report and a comprehensive literature review, we seek to provide valuable insights that enhance the current knowledge of this pathology.

3. Case Description

A 50-year-old male presented to the outpatient clinic with chief complaints of vomiting and abdominal pain for 3 weeks. The pain was intermittent, moderate to severe in intensity, poorly localized in the upper abdomen, radiating to the back, and was relieved by vomiting. There was a history of projectile bilious vomiting associated with post-prandial abdominal pain and fullness for 3 weeks. The patient also had a history of chronic smoking and alcohol intake for 20 years. There was no history of weight loss, fever, or melena. There were no co-morbidities associated, including no history of diabetes mellitus, hypertension, tuberculosis, bronchial asthma, or epilepsy, and no significant past medical or surgical history was reported. There was no history of similar complaints in the past. On examination, the abdomen was distended and tender, along with guarding and rigidity. No mass was palpable per abdomen. No significant findings in per rectal examination.

Initial investigations, as detailed in **(Table 1)**, revealed slightly decreased hemoglobin levels, an elevated white blood cell count, elevated random blood sugar, and slightly deranged liver enzymes. Renal function tests were within normal limits. Electrolytes were slightly deranged, and pancreatic enzymes were highly elevated. Viral markers, including HCV, HBsAg, and HIV, were non-reactive.

Further, the patient was investigated, and a CT scan of the abdomen revealed an abnormal configuration of the head of the pancreas with features suggestive of (F/S/O) chronic calcific pancreatitis (CCP) and a triangular segment of the pancreatic tissue encircling the second part of the duodenum (D2), causing complete obstruction. A few foci of calcification were also noted in the head of the pancreas (HOP) along with stranding of peripancreatic fat and dilated pancreatic duct with no evidence of malignancy or necrosis **(Figure 1)**.

Table 1: Initial investigations

Investigations	Value	Normal Range
Haemoglobin	9.5 g/dl	13.0–17.0
TLC	18 $\times 10^3$/uL	4.0–10.0
RBS	155 mg/dL	80.0–140.0
Liver Function Tests		
SGOT	89 IU/L	0.0–35.0
SGPT	92 IU/L	0.0–41.0
Alkaline Phosphatase (ALP)	109 IU/L	40.0–129.0
Albumin	3.2 g/dl	3.5–5.2
Bilirubin	2.5 mg/dl	0.1–1.2
Renal Function Tests		
Serum urea	42 mg/dl	17.0–43.0
S. Creatinine	1.4 mg/dl	0.6–1.1
INR	0.91	0.8–1.2
Electrolytes		
S. Na^+	135 mmol/L	136.0–145.0
S. K^+	4.1 mmol/L	3.5–5.0
S. Ca^{2+}	6.2 mg/dl	8.6–10.3
Pancreatic Enzymes		
S. Lipase	2850 U/L	13.0–60.0
S. Amylase	1549 U/L	22.0–80.0
Viral Markers		
HCV	Non-Reactive	–
HBsAg	Non-Reactive	–
HIV	Non-Reactive	–

Hb, Haemoglobin; TLC, Total Leukocyte Count; RBS, Random Blood Sugar; SGOT, Serum Glutamic Oxaloacetic Transaminase (AST); SGPT, Serum Glutamic Pyruvic Transaminase (ALT); ALP, Alkaline Phosphatase; INR, International Normalized Ratio; S. Na, Serum Sodium; S. K, Serum Potassium; S. Ca^2, Serum Calcium; S. Lipase, Serum Lipase; S. Amylase, Serum Amylase; HCV, Hepatitis C Virus; HBsAg, Hepatitis B Surface Antigen; HIV, Human Immunodeficiency Virus.

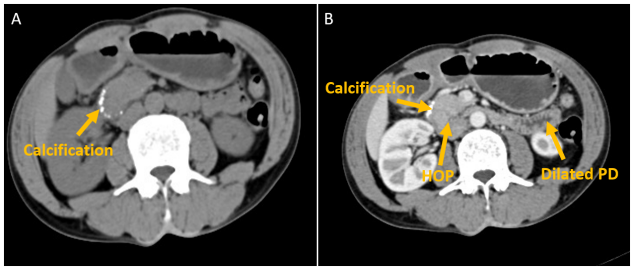

Figure 1: Axial sections: A) Plain CT scan showing presence of hyperdense calcific lesion in the head of the pancreas. B) CECT showing bulky head of pancreas (HOP) with features suggestive of chronic calcific pancreatitis, dilated pancreatic duct, and presence of foci of calcification.

Based on the diagnostic findings, surgical intervention was planned. The patient underwent pylorus-preserving pancreatoduodenectomy under general anesthesia with endotracheal tube intubation. After proper painting and draping, a nasogastric tube was inserted for gastric decompression. An extended right subcostal incision was given to access the abdominal cavity. Intraoperatively, the first part of the duodenum (D1) was found to be dilated **(Figure 2)**, with annular pancreatic tissue encircling the second part (D2), causing its narrowing **(Figure 3)**) – findings consistent with the preoperative radiological imaging findings. Intra-operatively, a mass-forming lesion was palpated in the HOP. A stapler was fired along the distal part of the stomach, and another was fired approximately 20 cm distal to the ligament of Treitz. A jejunal loop was then brought up retrocolically, and an end-to-side anastomosis was performed, resulting in pancreatojejunostomy, hepaticojejunostomy, and gastrojejunostomy. The specimen was then resected, and the area post-resection was visualized. The macroscopic inspection of the gross specimen by observing the cut section revealed the presence of a stone in the HOP (pancreatolithiasis) **(Figure 4)**. The postoperative course was uneventful, with mild abdominal pain and minimal serosanguinous discharge from the drain. The patient was discharged on postoperative day 7 in a stable condition.

Microscopic examination of the resected specimen revealed chronic inflammatory infiltrates with interlobular fibrosis, confirming the diagnosis of chronic calcific pancreatitis. Pancreatic duct dilation and pancreaticolithiasis were noted without evidence of dysplasia or malignancy.

At 6-month postoperative follow-up, the patient remained asymptomatic with complete resolution of vomiting and abdominal pain. No signs of recurrence or complications were observed on CT imaging and labs.

All procedures performed in this study adhered to the ethical standards of the institutional and national research committee and the Helsinki Declaration. Informed written consent was obtained from the patient for the publication of this case report and accompanying images. No identifiable patient information is included in this publication. Ethical approval was waived by the Institutional Review Board (IRB) for the case reports.

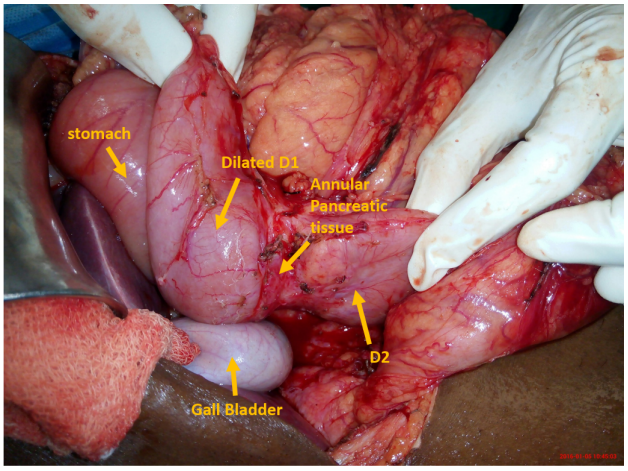

Figure 2: Intra-operative imaging showed dilated D1 due to distal compression by the annular pancreatic tissue encircling D2.

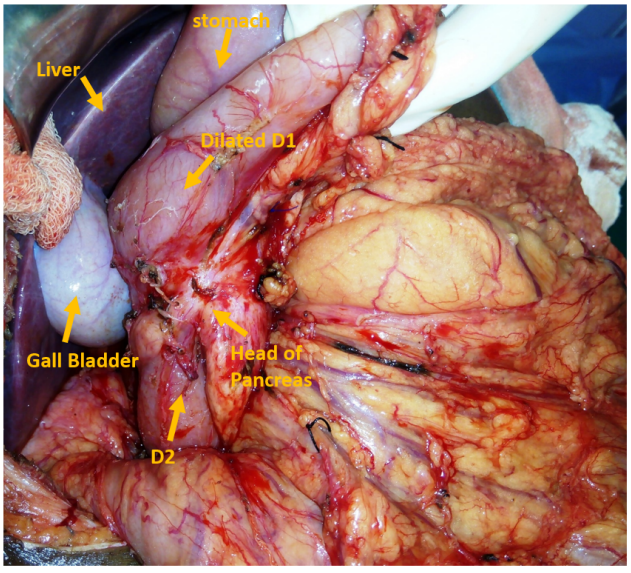

Figure 3: Intra-operative finding- Imaging showing annular pancreatic tissue encircling the duodenum, causing dilation in the proximal part along with other visible visceral organs.

4. Discussion

AP is a rare congenital anomaly resulting from an embryological error during the fifth to seventh weeks of gestation, wherein the ventral pancreatic bud fails to rotate properly, leading to partial or complete encasement of the duodenum. This case illustrates the

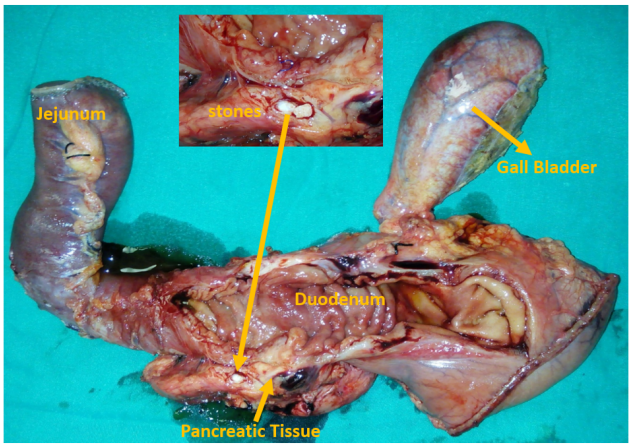

Figure 4: Macroscopic investigation- The cut-section of the resected specimen revealed the presence of a stone in the annular pancreatic tissue (pancreato-lithiasis) along with the resected gall bladder and jejunum. Stapler lines are visible in the specimen.

elusive nature of the condition, consistent with historical autopsy-based prevalence estimations of approximately 1 in 20,000, although more recent radiological studies suggest higher rates [8]. These discrepancies underscore the underrecognized burden of AP, particularly in adults, where incidental diagnoses often mask symptomatic presentations. In our patient, the diagnosis of AP with CCP highlights the clinical challenges posed by its nonspecific symptoms—most commonly abdominal pain, nausea, and vomiting, and less frequently hematemesis. In a large single-institutional cohort study, Nagpal et al. [9] reported that 59.6% of adults with AP were asymptomatic; among symptomatic patients, abdominal pain was the most frequently observed symptom (50%).

To better contextualize our case and understand current trends, we conducted a structured literature review focusing on adult patients with symptomatic annular pancreas who underwent surgical intervention, particularly pancreatoduodenectomy. This review aimed to compare presenting symptoms, diagnostic modalities, and treatment approaches in recently reported cases.

5. Methodology

A structured literature review was performed using PubMed and Scopus databases, covering the period from 2018 to 2024. The following Boolean keyword string was applied: (“Annular pancreas” OR “pancreatic ring”) AND (“adult” OR “adult presentation”) AND (“case report” OR “case series”). Filters included: English language, human studies, and adult subjects (aged 18 years or older). The review process was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure transparency, reproducibility, and methodological rigor. A PRISMA flow diagram detailing the selection process has been included to summarize the article screening and inclusion process.

5.1. Eligibility criteria and study selection

Studies were included if they reported symptomatic adult cases of AP confirmed by imaging or intraoperative findings and provided clinical details including symptoms, diagnostics, and treatment. Exclusion criteria included pediatric-only data, asymptomatic incidental findings with minimal clinical description, and editorials

without primary data. Two independent reviewers extracted data including age, gender, presenting symptoms, diagnostic modality, treatment modality, and outcomes. Any discrepancies were resolved through consensus.

5.2. Data extraction

Summary statistics were generated using Microsoft Excel. Descriptive percentages were calculated for the following categorical variables: (a) Symptoms, (b) Diagnosing modality, (c) Modality of intervention

5.3. Risk of Bias assessment

The methodological quality of the included case reports and case series was assessed using the Joanna Briggs Institute (JBI) Critical Appraisal Checklists, specific to each study design. These standardized tools were used to evaluate the risk of bias and ensure the inclusion of methodologically sound studies in the review.

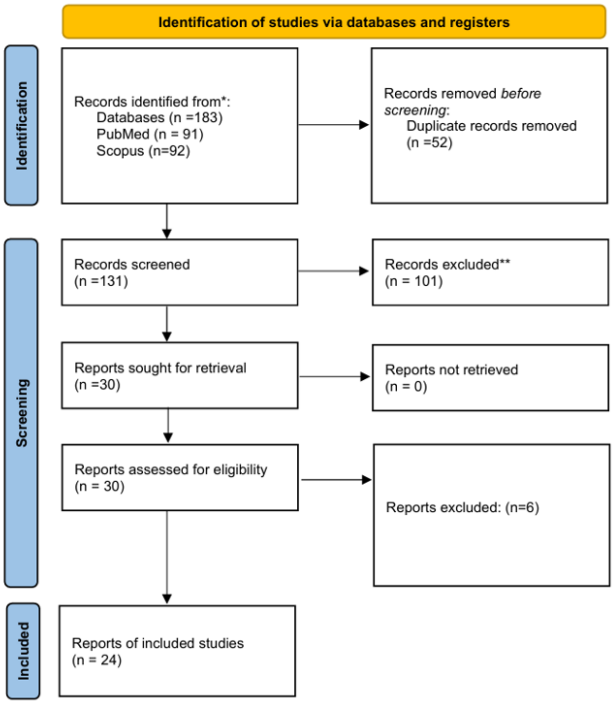

Figure 5: PRISMA Flow Diagram Illustrating the Study Selection Process for the Literature Review.

We reviewed 24 published cases (n = 24) of AP since 2018 and found that patients exhibited abdominal pain (83.3%), vomiting (41.6%), early satiety (16.6), weight loss (16.6%), melena (4.16%), dyspepsia (4.16%), hematochezia (4.16%), and diarrhea (4.16%) – **(Table 2) (Figure 5)**. These manifestations, often mimicking peptic ulcer disease, pancreatitis, or gastric outlet obstruction, emphasize the need for a high index of suspicion among clinicians.

The embryological theories proposed by Leeco and Baldwin [25] offer a foundational framework for understanding the development of AP. Leeco hypothesized that the ventral pancreatic bud adheres to the duodenal wall, while Baldwin suggested that persistent anomalies of the left ventral bud result in the formation of a pancreatic ring—both mechanisms potentially explaining the annular configuration observed in this patient. Imaging studies played a critical role in diagnosis, with CT scan revealing pancreatic tissue posterolateral to the second portion of the duodenum—a

Table 2: Variable symptoms present in patients with annular pancreas [10, 11, 12, 13, 14, 15, 6, 16, 17, 18, 19, 20, 21, 22, 4, 23, 1, 24].

No. of patients (n = 24)

Symptoms	No. of patients	Percentage (%)
Abdominal pain	20	83.3% No. of patients (M)elena
1	4.16%	
Dyspepsia	1	4.16%
Hematochezia	1	4.16%
Diarrhea	1	4.16%

Table 3: Diagnostic modalities used to diagnose annular pancreas [10, 11, 12, 13, 14, 15, 6, 16, 17, 18, 19, 9, 20, 21, 22, 4, 23, 1, 24]

(No. of patients n = 223)

Modality	No. of patients	Percentage (%)
Computed Tomography (CT) scan	143	64.1%
Magnetic Resonance Cholangiopancreatography (MRCP)	52	23.3%
Intraoperative finding	15	6.72%
Endoscopic ultrasound	8	3.58%
Endoscopic Retrograde Cholangiopancreatography (ERCP)	5	2.2%
Total	**223**	**100%**

finding reported to have 92% sensitivity and 100% specificity for annular pancreas [25]. Complementary modalities such as ERCP and MRCP further improve diagnostic accuracy, although their routine use may be limited by cost and availability.

In our analysis of 24 published case reports comprising 223 patients, CT was the most frequently employed imaging modality for diagnosing annular pancreas. By integrating data from Nagpal et al. [9] with our case series, we summarized the diagnostic tools utilized in **(Table 3)**. In the present case, the supra-papillary obstruction corresponded with the literature, which notes involvement of the second portion of the duodenum in approximately 74% of cases, underscoring the anatomical consistency of AP across patient populations [26].

Management of the AP remains individualized, as no universal treatment protocol exists. Among patients requiring surgical intervention, gastrojejunostomy is the most frequently performed procedure. By synthesizing data from Nagpal et al [9]with our reviewed case reports, the most common surgical approaches are presented **(Table 4)**. In our patient, pancreatoduodenectomy effectively alleviated the obstruction and the symptoms.

This case adds to the limited body of literature on adult presentations of AP, where symptomatic manifestations remain less well understood compared to the extensively documented neonatal counterpart. Prevalence estimates vary widely—from 0.0005% to 0.0015% in autopsy series to 3.4 per 100,000 in recent U.S. population-based imaging studies [5]. The true incidence of AP likely lies between these extremes, obscured by asymptomatic

Table 4: Different treatment modalities in patients [10, 11, 12, 13, 14, 15, 6, 16, 17, 18, 19, 9, 20, 21, 22, 4, 23, 1, 24]

No. of patients (N = 43)

Treatment Modalities	No. of patients	Percentage (%)
Gastrojejunostomy	20	46.5%
Pancreatoduodenectomy	10	23.2%
Duodenoduodenostomy	5	11.6%
Duodenojejunostomy	4	9.3%
30	2	4.6%
Annular ring resection	1	2.3%
Total pancreatectomy	1	2.3%
Total	**43**	**100%**

cases and variability in diagnostic practices. A slight male predominance has been observed among symptomatic adults, consistent with our patient's profile.

This report highlights the value of advanced imaging and individualized surgical intervention in managing AP along with CCP, while emphasizing its diagnostic complexity and clinical heterogeneity. As a rare entity, AP continues to present diagnostic and therapeutic challenges, warranting further research to clarify its natural history and optimize treatment strategies, especially in adults, for whom timely diagnosis significantly impacts quality of life.

The case described here is noteworthy for several distinctive features that differentiate it from most reported instances. Unlike the typical neonatal presentation marked by early duodenal obstruction or incidental findings in asymptomatic adults, this 50-year-old male presented with a three-week history of projectile bilious vomiting, postprandial fullness, and abdominal pain. This delayed and atypical symptomatic profile stands out, particularly given the presence of CCP findings that are infrequently emphasized in existing literature. CT Scan confirmed the diagnosis, revealing both annular pancreatic tissue and pancreatic calcification, causing duodenal obstruction—an uncommon constellation. The likely mechanism of obstruction may involve ulceration secondary to compression by the annular tissue in the setting of chronic inflammation.

This combination of a subacute presentation, diagnostic complexity, and the use of an uncommon operative approach —namely, pylorus-preserving pancreatoduodenectomy (Whipple procedure) —distinguishes this case and broadens the current understanding of adult annular pancreas presentations and management.

What sets our review apart from prior studies is its targeted synthesis of 24 recently published case reports (2018–2024), offering a contemporary overview of symptomatic adult AP. We also provide a detailed account of less frequently reported symptoms, such as melena, hematochezia, and dyspepsia, which are often underrepresented in broader reviews. Furthermore, by integrating cohort-level data from Nagpal et al., we enhance the understanding of these symptoms.[9] with our findings, we present a more comprehensive analysis of diagnostic trends and treatment modalities, summarized in Tables 2 and 3. This layered approach enhances both the granularity and relevance of our review compared to earlier, more generalized surveys of the condition.

6. Conclusion

A review of recent case reports confirms that AP remains a rare condition, often undiagnosed in asymptomatic individuals. Symptomatic patients typically present with abdominal pain and vomiting, though additional symptoms such as weight loss and early satiety may also occur. Abdominal imaging serves as the cornerstone of diagnosis, with CT scans being the most commonly employed modality to confirm the condition. Asymptomatic cases of AP generally require no intervention and are managed conservatively. In contrast, surgical treatment is the primary approach for symptomatic patients, with the specific procedure tailored to the individual's anatomy and the severity of the pathology. Further timely research is needed to establish standardized protocols for the diagnosis and management of AP.

Conflicts of Interest

GB, SP, RK, and RB declare that they have no financial or non-financial competing interests related to the content of this article. No conflicts of interest, financial ties, or funding sources have influenced the results or interpretations presented in this manuscript.

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Institutional Review Board (IRB)

This study was conducted in accordance with the Declaration of Helsinki. Ethical approval was waived off by the Institutional Review Board (IRB) for the case reports/case series. Written informed consent was obtained from the patient to participate in the study and publish their clinical information and images. No identifiable patient information is included in this publication.

Large-Language Model

None

Authors' Contribution

GB and RB supervised, conceptualized, designed methodology, provided resources, investigated, drafted the original manuscript, and reviewed and edited the draft; SP and RK assisted in writing original draft, reviewed and edited the draft. All authors contributed to the manuscript's text and content, approved the final version, and agreed to be accountable for the work.

Data Availability

All data are included in this published article.

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