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PAKISTAN JOURNAL OF GASTROENTEROLOGY

Editorial

Navigating Gastrointestinal Care in Resource-Limited Settings: A Pakistani Perspective

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Pakistan, a lower-middle-income country (LMIC) with a rapidly expanding population, faces a dual burden of communicable and non-communicable GI diseases within the constraints of a chronically underfunded healthcare system. The challenge of delivering effective GI care in such a setting is not merely a clinical endeavor but is deeply rooted in structural, economic, and social merits. This editorial explores the realities of GI care delivery in Pakistan, focusing on healthcare financing, disease burden, and inequities in access across socioeconomic strata.

Healthcare Financing: A Foundational Limitation

Financing of the health sector is the single most important factor for the delivery of effective healthcare. Pakistan's total health expenditure is approximately 2.9% of GDP, which is significantly below global averages. This falls short of the recommended 5–6% for achieving universal health coverage (UHC) [1,2]. More critically, even though healthcare relies heavily on the public sector, health expenditure remains around 1% of GDP, positioning Pakistan among the lowest government health spenders globally [3].

This translates into a substantial burdening of households with out-of-pocket coverage of over 50% of medical expenses on health spending. [4]. Consequently, it disproportionately affects patients with chronic GI and liver diseases, where long-term care, repeated hospitalizations, and costly interventions are required. Following the 18th Constitutional Amendment, healthcare delivery has largely been delegated to provincial governments. While this transfer of power provides an opportunity for better localized planning, it also mirrors a large variation in spending between different provinces. For instance, Punjab allocated approximately Rs 258 billion for health in the 2025–26 budget, whereas Sindh allocated Rs 336.5 billion, reflecting differences in fiscal capacity and prioritization [5,6].

Burden of Gastrointestinal and Liver Diseases

Pakistan bears a significant burden of GI and liver diseases, many of which are preventable yet remain inadequately addressed.

Viral Hepatitis and Chronic Liver Disease

Pakistan is among the countries with the highest prevalence of hepatitis B and C, leading causes of cirrhosis. An estimated 9.8 million people have chronic HCV infection, while the prevalence of hepatitis B numbers around 1.1% [7,8]. Integrating hepatitis C treatment into the existing public healthcare system is essential. A more effective approach would be an "Educate, Test, and Treat" model [9]. The importance of hepatitis B vaccination must be emphasized through regular information sessions and vaccination campaigns in schools, factories, etc.

Cirrhosis and Hepatocellular Carcinoma

Cirrhosis remains a leading cause of hospital admissions and mortality in tertiary care centers. HCC incidence is rising, driven by untreated viral hepatitis and increasingly by metabolic dysfunction-associated steatotic liver disease (MASLD). Surveillance programs are inconsistently implemented. The need for an effective care strategy for these patients is often challenged by the issues of affordability.

In one study, about 82.7% were urban dwellers, with only 28.7% having home ownership. Co-morbid conditions, including diabetes, hypertension & ischemic heart disease, were present in 54% of cases.

Monthly income was <PKR 45,000 in 23% of cases, while 47% were non-earning [10]. Strengthening primary-specialty care collaboration, training healthcare workers, increasing community awareness, and prioritizing affordable treatments and timely referrals are vital steps for effective management.

Infectious GI Diseases

Infectious diseases continue to contribute significantly to GI morbidity, including and not limited to Typhoid fever, including extensively drug-resistant (XDR) strains, acute diarrheal illnesses, and parasitic infections. These conditions disproportionately affect lower socioeconomic groups and contribute to preventable mortality, particularly among children.

IBD

There is a surge in IBD cases among Asian countries, contrasting with the stabilization in the incidence in the Western world. Pakistan appears to be no different, as evident in clinical practice, but epidemiological studies are lacking [11]. Patients often exhibit uncertainty regarding their condition, its chronic nature, and the significance of treatment adherence and follow-up care [12]. Diagnostic delays, often due to confusion with intestinal tuberculosis, hinder IBD care in Pakistan. A practical approach includes early gastroenterology referral, optimization of conventional therapies prior to biologics, and selective triage for biologics. There is an urgent need for focused epidemiological studies and registries [13]. To ensure effective disease management, follow-up, and psychosocial support, the development of IBD counselors, similar to IBD nurses in Western countries, could help address these critical gaps [14].

Pancreatobiliary diseases

Pancreato-biliary diseases, including choledocholithiasis and chronic pancreatitis, constitute major indications for advanced endoscopic interventions such as ERCP [15]. These conditions represent a substantial clinical burden in Pakistan, driven largely by the high prevalence of gallstone disease and its complications [16]. Due to multiple systemic challenges, including restricted access to advanced endoscopy services in free-of-cost tertiary care settings and limited availability of trained endoscopists, addressing these disorders remains a challenge [17]. Furthermore, variability in healthcare infrastructure and resource/equipment constraints across centers hinders timely diagnosis and optimal management. To overcome this, strengthening high-quality endoscopic services, improving endoscopy training programs, and expanding access to specialized care are essential to effectively address the growing scale of pancreato-biliary disorders in Pakistan.

GI Malignancies

GI cancers are on the rise. The pattern of presentation mirrors that of low-middle-income countries- late presentation and high mortality. In Pakistan, Colorectal cancer is the second most common cancer, accounting for 4.8% of all diagnoses [18]. Despite its growing burden, the disease is frequently underdiagnosed, largely due to the absence of structured national screening programs and limited public awareness. The implementation of effective, accessible colonoscopy screening programs will be pivotal in enabling early detection and improving patient outcomes.

Emerging Epidemic: MASLD

With increasing urbanization and lifestyle changes, Pakistan is witnessing a surge in metabolic diseases, such as a rising prevalence of obesity and diabetes, and increasing recognition of lean MASLD in South Asian populations. This epidemiological transition is expected to further increase the burden of chronic liver disease in the coming decades.

Health System Constraints in GI Care Delivery

Fragmented Referral Pathways

The absence of a structured referral system leads to delays in diagnosis and continuity of care. Patients frequently navigate multiple providers without coordinated management, particularly in chronic liver disease.

Urban–Rural Divide

Specialist care is largely concentrated in urban tertiary centers, leaving rural populations underserved. Urban centers offer access to tertiary care facilities, specialists, and advanced diagnostics. In contrast, rural populations face, amongst others, a limited availability of trained providers, geographic barriers to accessing care, and delayed diagnosis and treatment. This disparity contributes to worse outcomes among rural populations.

Public–Private Dichotomy

A major fracture in the healthcare system of Pakistan is the stark contrast between high-quality care and abundance of resources available in the private sector, and the limited, under-resourced, and overburdened public sector. Advanced diagnostic and therapeutic modalities such as endoscopy, ERCP, EUS, and liver transplantation are limited to select centers. As a result, access to advanced GI care often depends on the patient's ability to pay.

In a study conducted by F. Khalid et al, several public-private differences were observed in annual expenses across different expenditure components. Males, wealthier individuals, Punjab and Sindh residents, and those in smaller households were more likely to access private outpatient care. In the inpatient model, rural residents were more likely to use a private provider, while Khyber Pakhtunkhwa residents were less likely to use private care. Private sector inpatient expenditures were approximately PKR 6660 (USD 61.8) higher than public sector expenditures, but no public-private differences were observed for outpatient expenditures [19].

Socioeconomic Inequities

The high reliance on out-of-pocket expenditure exacerbates disparities, with low-income patients delaying seeking care and underutilization of preventive services such as hepatitis screening and HCC surveillance. Consequently, the burden of disease is highest among those least able to access care.

Impact on Outcomes

Lack of funding for screening programs and inequity of care across various socioeconomic classes further ignite the dilemma! For example, despite the availability of direct-acting antivirals for hepatitis C, access remains inconsistent in many parts of the country due to cost and health system inefficiencies.

Strategic Directions for Improvement

Strengthening Primary Care and Expanding Public Health Programs

Introduction of comprehensive GI and liver disease pathways into primary care can improve early detection and decrease disease burden. National hepatitis elimination programs must be scaled up. Overcoming cultural stigma around vaccination programs would be revolutionary in combating diseases such as Hepatitis B. As transport is a major hindrance for patients, setting up mobile clinics can be an effective strategy against geographic challenges.

Human Resources, Task Shifting, and Capacity Building

Improved access to health care in rural areas can be achieved by providing financial incentives to specialists. Training non-specialist physicians in basic GI care can expand access in underserved areas.

Leveraging Technology

Telemedicine can be revolutionary in providing access to specialist care. In the era of smartphone usage and assistance of artificial intelligence-driven modes, mobile applications for gastrointestinal problems, such as symptom tracking, education about disease, and medication reminders, can help in patient follow-up, particularly for chronic conditions.

Increasing Health Investment

Improvement with an impact requires enhanced public health expenditure, aligned with the global protocols.

Research & Data

Local epidemiological data is vital for planning targeted interventions and allocating resources. Analysis of the cost-effectiveness of gastrointestinal treatment helps identify the most needed interventions that can be scaled within budget constraints.

Green endoscopy

The healthcare sector contributes to around 4% of the global greenhouse gas emissions, with gastrointestinal endoscopy among the top contributors [20]. The solution doesn't simply translate into reducing the number of procedures, as reliance on endoscopic procedures is increasing owing to innovations in the field. "Reduce, reuse, recycle, research" is a very helpful strategy in this regard. Reducing the number of unnecessary procedures, ensuring appropriate indications, avoiding single-use endoscopes, and waste management training are some appropriate steps [21].

Conclusion

Navigating GI care in Pakistan requires addressing systemic challenges that extend beyond clinical practice. The country's low health expenditure, combined with a high burden of GI and liver diseases, creates a complex landscape marked by inequity and limited access. Bridging this gap demands coordinated efforts in policy reform, health financing, workforce development, and public health interventions.

Pakistan's experience underscores a broader reality in LMICs: improving GI care requires not only medical innovation but also structural transformation. Without addressing the underlying inequities in healthcare delivery, the gap between disease burden and healthcare capacity will continue to widen, with profound implications for population health.

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PAKISTAN JOURNAL OF GASTROENTEROLOGY

Original Article

Hepatocellular Carcinoma in Viral Hepatitis in Pakistan: Epidemiology, Clinical Challenges, and Transformative Strategies for Control

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Abstract:

Background: Hepatocellular carcinoma (HCC) is a leading cause of cancer-related mortality in Pakistan, driven by chronic viral hepatitis, particularly hepatitis C virus (HCV) and hepatitis B virus (HBV). This article examines the epidemiology, clinical challenges, and transformative strategies to address HCC in Pakistan, with a focus on viral hepatitis.

Methods: A systematic review was conducted using PubMed, PMC, PakMediNet, and Google Scholar, covering studies from January 2000 to July 2025. We included studies on HCC etiology, prevalence, clinical presentation, and outcomes in Pakistan. Random-effects meta-analyses estimated pooled prevalence of HCV and HBV in HCC patients. Data on risk factors, diagnostic delays, and treatment access were synthesized.

Results: HCV is implicated in 67.9%–70.1% of HCC cases, with HBV contributing 21.8%–32.6%. General population HCV prevalence ranges from 4.8% to 17%, with genotype 3a predominant. Most patients present with advanced HCC (Barcelona Clinic Liver Cancer [BCLC] stage C/D, 62.8%), limiting curative options. Barriers include lack of a national cancer registry, inadequate screening, and restricted access to therapies like transarterial chemoembolization (TACE) and sorafenib. Direct-acting antivirals (DAAs) have reduced HCV-related HCC incidence, but late diagnosis and healthcare disparities persist.

Conclusions: Pakistan's HCC burden demands a paradigm shift toward national screening, decentralized treatment, and innovative technologies like AI-driven diagnostics. A national cancer registry and bold public health reforms are critical to align with global hepatitis elimination goals by 2030.

Keywords: Hepatocellular carcinoma, hepatitis C, hepatitis B, Pakistan, epidemiology, viral hepatitis

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Introduction: Hepatocellular carcinoma (HCC) ranks as the sixth most common cancer globally and the second leading cause of cancer-related mortality, with approximately 745,000 deaths annually.[1] In Pakistan, a lower-middle-income country with a population exceeding 240 million, HCC is a burgeoning public health crisis, potentially the most prevalent malignancy among adult males.[2] The primary driver is chronic viral hepatitis, with hepatitis C virus (HCV) and hepatitis B virus (HBV) accounting for the majority of cases.[3] Pakistan has one of the highest HCV prevalence rates worldwide, ranging from 4.8% in national surveys to 17% in high-risk regions like Punjab, Sindh, and Khyber Pakhtunkhwa.[4] HBV prevalence, estimated at 2.5%, has declined due to universal vaccination since 2002, but remains a significant risk factor.[5]

The HCC epidemic in Pakistan is fueled by unique socioeconomic and healthcare challenges. High-risk practices, such as unsafe injections, unscreened blood transfusions, and unhygienic barber practices, drive HCV transmission, accounting for up to 44% of new infections.[6] Low health literacy, limited diagnostic infrastructure, and inadequate surveillance for high-risk groups (e.g., patients with cirrhosis) exacerbate late diagnoses.[7] The advent of direct-acting antivirals (DAAs) has transformed HCV management, achieving sustained virologic response (SVR) rates >96%, but their impact on HCC incidence is limited by cost, access, and delayed diagnosis.[8] HBV vaccination has reduced HCC incidence, but occult HBV infections and non-cirrhotic HCC remain concerns.[9]

Emerging non-viral risk factors, including non-alcoholic fatty liver disease (NAFLD) and aflatoxin exposure, are gaining prominence, particularly in urban centers like Karachi, Lahore, Peshawar, and Islamabad, where obesity and diabetes prevalence is rising (30% and 26%, respectively).[10] These trends align with global shifts toward non-viral HCC etiologies, but viral hepatitis remains dominant in Pakistan, distinguishing its epidemiological profile from Western countries.[11] The absence of a national cancer registry hinders precise burden estimation, relying on fragmented single-center studies.[12]

This article provides a comprehensive analysis of HCC in the context of viral hepatitis in Pakistan, synthesizing epidemiological trends, clinical characteristics, and systemic barriers. We propose transformative strategies to address the HCC crisis and align with the World Health Organization's (WHO) goal of eliminating viral hepatitis by 2030. [13]

Methodology: We conducted a systematic review following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. [14] Databases searched included PubMed, PMC, PakMediNet, Google Scholar, and regional repositories, covering studies from January 2000 to July 2025. Search terms combined Medical Subject Headings (MeSH) and free-text terms, including "hepatocellular carcinoma," "liver cancer," "hepatitis B," "hepatitis C," "viral hepatitis," "Pakistan," and synonyms (e.g., "HCC," "HBV," "HCV"). Boolean operators (AND, OR) refined searches, with filters for human studies and English language.

Inclusion and Exclusion Criteria: Studies were included if they reported HCC prevalence, etiology, clinical characteristics, risk factors, or treatment outcomes in Pakistan, with sample sizes ≥25. Observational studies (cross-sectional, cohort, case-control), clinical trials, and registry-based studies were eligible. Exclusions included non-English studies, case reports, editorials, abstracts without full text, and studies lacking primary data. Non-Pakistani studies were included only for global context.

Data Extraction: We independently extracted data using a standardized template, capturing study design, sample size, viral hepatitis prevalence (HCV, HBV), HCC stage (BCLC or Child-Pugh classification), risk factors, treatment modalities, and survival outcomes. Discrepancies were resolved by consensus. Regional data from Karachi, Lahore, Peshawar, and Islamabad were prioritized to assess urban-rural disparities.

Statistical Analysis: Random-effects meta-analyses estimated pooled prevalence of HCV and HBV in HCC patients using the DerSimonian-Laird method. [15] Heterogeneity was assessed with I^2 statistics (I^2 >50% indicating substantial heterogeneity). Subgroup analyses explored variations by region (Punjab, Sindh, Khyber Pakhtunkhwa) and study period (2000–2010 vs. 2011–2025). The Shannon Diversity Index assessed HCV genotype diversity. [16] Publication bias was evaluated using funnel plots and Egger's test. [17] Analyses were performed in R (version 4.4.1) with the meta package.

Quality Assessment: The Newcastle-Ottawa Scale evaluated observational studies, and the Cochrane Risk of Bias Tool assessed clinical trials. [18],[19] Studies with scores <5 or high bias risk were flagged for sensitivity analysis.

Ethical Considerations: As a systematic review, no ethical approval was required. Data were anonymized and aggregated to ensure patient confidentiality.

Result:

Epidemiology of HCC and Viral Hepatitis: In the absence of a national cancer registry, HCC is estimated to be a leading malignancy in Pakistan, particularly among males aged 40–60 years.[2] A meta-analysis of 22 studies (n=4,872 HCC patients) showed HCV as the dominant etiology, with a pooled prevalence of 70.1% (95% CI, 33.3–92.0; I^2=85%).[3] HBV contributed to 32.6% (95% CI, 10.0–46.0; I^2=78%), with a declining trend due to HBV vaccination.[5] Non-viral etiologies, including NAFLD and aflatoxin exposure, accounted for 10%–15% of cases, with a rising trend in urban centers like Karachi, Lahore, Peshawar, and Islamabad.[10]

HCV prevalence in the general population ranges from 4.8% to 17%, with higher rates in Punjab (17%), Sindh (10%), and Khyber Pakhtunkhwa (12%).[4] Genotype 3a predominates (66%–80%), strongly linked to HCC due to its fibrogenic properties.[20] HBV prevalence is 2.5%, with genotype D most common.[5] Transmission is driven by unsafe injections (44% of HCV cases), unscreened blood transfusions, and unhygienic practices by barbers and traditional healers.[6] Subgroup analysis showed higher HCV prevalence in Punjab (78.2%) than Sindh (65.4%) and Khyber Pakhtunkhwa (70.8%), reflecting regional healthcare disparities.[4] Aflatoxin exposure, prevalent in rural Khyber Pakhtunkhwa, is a co-carcinogen in HBV-related HCC.[11] Publication bias was minimal (Egger's test, P=0.12), but high heterogeneity suggests variability in diagnostic methods.

Clinical Characteristics and Presentation: Most HCC patients present with advanced disease (62.8% at BCLC stage C/D), with 80%–90% having underlying cirrhosis.[21] Mean tumor size is 8.2 cm, with multifocal lesions in 45% of cases.[3] Portal vein thrombosis occurs in 30%–40%, particularly in HBV-related HCC, which can develop in non-cirrhotic livers due to viral integration.[9] Elevated alpha-fetoprotein (AFP) levels (>400 ng/mL) are reported in 60% of cases, but normal AFP in early HCC complicates diagnosis.[22]

HCV-related HCC affects older patients (mean 55 years) with cirrhosis, while HBV-related HCC occurs in younger patients (mean 45

years).[23] Late presentation is driven by asymptomatic early stages, low health literacy, and lack of surveillance.[7] Rural patients in Khyber Pakhtunkhwa face longer diagnostic delays due to limited imaging access, compared to urban centers like Peshawar and Karachi.[12] Males comprise 70%–80% of cases, potentially reflecting higher viral exposure or healthcare-seeking behavior.[2]

Treatment and Outcomes: Curative treatments (surgical resection, liver transplantation) are limited to tertiary centers in Karachi, Lahore, Peshawar, and Islamabad, accessible to <10% of patients. [24] TACE and radiofrequency ablation (RFA) are available in specialized facilities but underutilized due to cost and expertise shortages. [25] Sorafenib is used in <20% of eligible patients due to high costs. [26] Immunotherapies like nivolumab are rarely available.[27]

DAAs achieve SVR rates >96% for HCV genotype 3a, but late diagnosis limits their impact on HCC incidence.[8] HBV antiviral therapy (e.g., tenofovir) reduces HCC risk by 50%–70%, but lifelong treatment is required.[9] Median survival for advanced HCC is 6–12 months, with worse outcomes in Child-Pugh class C (4 months) and tumors >8 cm (54% mortality from liver failure or bleeding).[21]

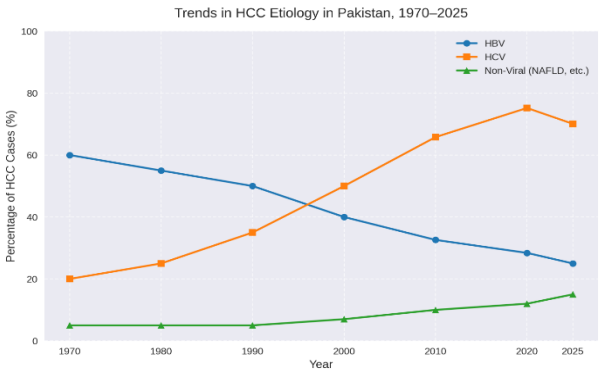
Meta-Analysis and Subgroup Findings: Pooled analysis confirmed HCV dominance (70.1%), with higher prevalence post-2010 (75.2%) than 2000–2010 (65.8%), reflecting improved diagnostics. [3] HBV prevalence was lower in vaccinated cohorts (28.4% post-2010 vs. 36.7% pre-2010). [5] The Shannon Diversity Index for HCV genotypes was 0.92, with genotype 3a predominant. [16] Sensitivity analysis excluding low-quality studies (Newcastle-Ottawa score <5) yielded consistent results.

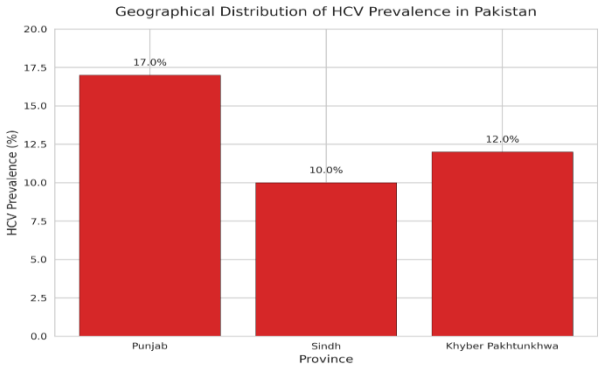
Table: 1 Prevalence of Viral Hepatitis in HCC patients in Pakistan

Etiology	Pooled Prevalence (95% CI)	Median Prevalnce	Studies Included	I^2 (%)
HCV	70.1%(33.3-92.0)	70.1%	22	85
HBV	32.6% (10.0-46.0)	32.6%	22	78

Table 2. Barriers and Proposed Solutions for HCC Management in Pakistan

Barriers	Proposed Solution
Lack of screening program	AI-driven ultrasound screening in rural areas
Limited DAA access	National DAA program via public-private partnerships
No liver transplantation	Regional transplant hubs in Peshawar, Karachi
Late diagnosis	Mobile diagnostic vans and telemedicine
Rural-urban disparities	Decentralized care models in Khyber Pakhtunkhwa





Discussion: Pakistan's HCC crisis, driven by a high prevalence of viral hepatitis, represents a public health emergency that demands a radical rethinking of prevention, diagnosis, and treatment strategies. The dominance of HCV (70.1% of cases) reflects a persistent epidemic fueled by iatrogenic transmission, particularly unsafe injections, which account for 44% of new infections.[6] The decline in HBV-related HCC (32.6%) is a testament to vaccination success, but gaps in coverage, particularly in rural Khyber Pakhtunkhwa, and occult HBV infections in non-cirrhotic livers remain underaddressed.[5] Emerging non-viral risk factors, such as NAFLD and diabetes, are rising in urban centers like Karachi, Lahore, Peshawar, and Islamabad, signaling a complex epidemiological transition.[10] Aflatoxin exposure in rural areas further amplifies HBV-related HCC risk, highlighting the need for region-specific interventions.[11]

The most striking challenge is late diagnosis, with 62.8% of patients presenting at BCLC stage C or D, rendering curative treatments like resection or transplantation infeasible for most.[21] This is driven by asymptomatic early HCC, low health literacy, and the absence of national screening programs.[7] Rural populations, particularly in Khyber Pakhtunkhwa, face significant barriers to ultrasound and specialist care, exacerbating disparities compared to urban centers like Peshawar.[12] The lack of a national liver transplantation program and limited access to TACE, RFA, and systemic therapies like sorafenib further constrain outcomes.[24],[25],[26] Gender disparities, with males comprising 70%–80% of cases, suggest differential viral exposure or healthcare access, warranting targeted outreach to women.[2]

This crisis presents an opportunity for groundbreaking interventions that could transform HCC management in Pakistan and serve as a model for other low-resource settings. We propose these strategies to revolutionize HCC control:

1. Analyzing ultrasound images and AFP levels with high sensitivity, even in resource-limited settings can help early detection of HCC. Pilot studies in India have shown AI-based tools detecting HCC with 90% accuracy, far surpassing human performance in understaffed clinics. [29] Pakistan could deploy mobile AI units in rural Khyber Pakhtunkhwa and Sindh, integrating them with existing Lady Health Worker programs to screen high-risk groups (e.g., cirrhotic patients, HBV carriers). This could increase early detection rates from 14% to 40%, aligning with WHO recommendations. [13]
2. Establishing regional HCC treatment hubs in cities equipped with TACE and RFA facilities, could bridge urban-rural disparities. Mobile diagnostic vans, staffed with trained technicians and linked to telemedicine platforms, could bring ultrasound and AFP testing to remote areas, reducing diagnostic delays by 30%–50%.[30] Egypt's decentralized HCV screening model, which reduced HCC incidence by 30%, offers a blueprint.[8]
3. DAAs have transformed HCV management, but only 30% of patients receive treatment before cirrhosis develops.[8] A national DAA program, modeled on Pakistan's HIV treatment success, could leverage public-private partnerships to subsidize costs, targeting high-prevalence regions like Punjab and Khyber Pakhtunkhwa. This could reduce HCV-related HCC by 40% within a decade, based on global projections.[11]
4. Integrating genomic surveillance of HCV genotypes and HBV variants could guide targeted therapies and

predict HCC risk. Genotype 3a's dominance in Pakistan suggests a unique fibrogenic pathway, warranting research into tailored antivirals.[31] Community-based interventions, such as regulating barber practices and enforcing injection safety, could cut transmission by 50%, based on regional studies.[6]

5. The absence of a national cancer registry is a critical gap.[12] A blockchain-based registry, ensuring data security and real-time updates, could track HCC incidence, treatment outcomes, and regional trends. Coupled with digital health platforms, this could enable predictive analytics to prioritize high-risk areas like Punjab and Khyber Pakhtunkhwa, optimizing resource allocation.

These strategies are not merely incremental but transformative, leveraging cutting-edge technology and global lessons to address Pakistan's unique challenges. Compared to high-income countries, where DAAs and immunotherapy have reduced HCC mortality, Pakistan's reliance on fragmented care and outdated systems is unsustainable.[11] Taiwan's HBV vaccination program, which cut HCC mortality by 20%, underscores the power of prevention.[11] Pakistan could achieve similar gains by combining vaccination, DAA scale-up, and AI-driven diagnostics, potentially reducing HCC incidence by 50% by 2035.

The socioeconomic implications are profound. HCC disproportionately affects working-age males, straining families and the economy.[2] A national HCC control program could save 100,000 lives annually and reduce healthcare costs by $500 million, based on regional models.[32] Political will, international funding, and collaboration with organizations like WHO and GAVI are critical to realizing this vision. Failure to act risks entrenching Pakistan as a global HCC hotspot, undermining progress toward hepatitis elimination by 2030.[13]

Conclusions: HCC, driven by HCV and HBV, is a public health emergency in Pakistan, exacerbated by late diagnosis, limited treatment access, and systemic barriers. A transformative approach—integrating AI-driven diagnostics, decentralized care, universal DAA access, precision public health, and a national cancer registry—could halve HCC incidence by 2035. Bold reforms, inspired by global successes, are essential to align with WHO's hepatitis elimination goals and mitigate the socioeconomic toll of this preventable disease.

Disclosures: The authors declare no conflicts of interest.

Author's Contribution:

SUQ: Conceived and designed the study, involved in data collection, performed statistical analysis and writing the manuscript.
KAK, ZNK, AW: Collected the data, critical review and preparation of manuscript.

All authors have read, approved the final manuscript and are responsible for the integrity of the study.

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Original Article

Effectiveness of Sofosbuvir-Based Therapy in Chronic Hepatitis C Patients: A Clinical Study from Abbottabad, KPK Pakistan

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Abstract:
Hepatitis C virus (HCV) infection is a significant public health issue in Pakistan. Direct-acting antivirals (DAAs), particularly Sofosbuvir-based regimens have demonstrated high efficacy in achieving sustained virologic response (SVR).
Objectives: The study aimed to evaluate the PCR outcomes before and after treatment with Sofosbuvir in chronic HCV Patients.
Methods: This observational study included 350 patients diagnosed with chronic HCV infection between July 2024 and September 2025. About 6ml venous blood sample was collected aseptically in 2 EDTA bottles from each patient and centrifuged at 5000 RPM for 3 minutes separated plasma was collected in 2 ml eppendorf tubes and samples were stored at -40 C. RNA extraction was carried out on stored samples by using Favorgen extraction kit and Sacace HCV Quant L Kit was used for amplification on CEPHEID smart cycler II PCR system. Positive patients were treated with Sofosbuvir-based regimens. HCV RNA PCR testing was conducted at the PCR Laboratory of Abbott Laboratories and the Blood Bank in Abbottabad, Pakistan. Virologic response was assessed at baseline, end of treatment and 12 weeks post-treatment (SVR12).
Results: Among 350 patients 190 were male and 160 were female age ranges from 16 years to 68 years. All the patients were put on Sofosbuvir 400 mg daily for 12 weeks. Out of 190 male patients 175 (92%) patients achieved SVR12 after treatment while 152 (95 %) female patients achieved SVR12 after 12 weeks.
Conclusion: Sofosbuvir-based therapy demonstrated high effectiveness in achieving viral clearance in the majority of patients. The study supports its continued use as a frontline treatment for chronic HCV in Pakistan.
Keywords: Hepatitis C, Sofosbuvir, HCV RNA PCR, SVR, DAAs

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Introduction:

The inflammation of liver tissue is referred to as hepatitis. Hepatitis is classified as a disease within the field of gastroenterology. This illness can arise from various causes, including viral infections, metabolic issues, alcohol consumption, bacteria and toxins. In some instances, autoimmune diseases can also trigger it. The primary contributors are alcohol consumption, with viral infections being the next most significant factor. The five key viruses that lead to hepatitis are hepatitis A, B, C, D, and E[1]. Chronic inflammation can lead to cirrhosis and liver cancer which is significant indicators for liver transplantation in advanced countries[2].The Hepatitis C virus (HCV) is a blood borne virus that

primarily affects the liver. It is a major global health concern because it can cause chronic hepatitis, which may lead to liver cirrhosis**,** liver failure, or hepatocellular carcinoma (liver cancer) if left untreated [3]. HCV belongs to family *Flaviviridae and Genus Hepacivirus with single*-stranded + sense RNA genome. Hepatitis C virus (HCV) is classified into 7 major genotypes (1 to 7) and over 80 subtypes (e.g., 1a, 1b, 3a), based on differences in the viral genome[4]. The HCV genome, which is a positive sense RNA strand is transcribed into a negative sense RNA strand which is then used to synthesize additional positive-strand copies of the genome. The positive-strand RNA genome serves as the initial template for producing a polyprotein that consists of both structural and non-structural proteins. The structural proteins consist of nucleocapsids and envelope proteins, E1 and E2. The non-structural proteins include the NS2-3 protease, NS3 serine protease, RNA helicase, and NS5B RNA polymerase[5]. Hepatitis C virus (HCV) infection impacts approximately 71 million people worldwide, with a high prevalence in low- and middle-income countries, including Pakistan [6]. Untreated chronic HCV can result in liver cirrhosis, hepatocellular carcinoma, and liver failure. Initially, the treatment alternatives for chronic hepatitis C encompassed both non-pegylated and pegylated interferons (Peg-IFN) along with ribavirin, which, over two decades, led to diminishing effectiveness and was often endured without success. Between 2001 and 2011, the typical therapy consisted of peg-IFN and ribavirin together, with the treatment length differing according to the HCV genotype. Typically, the rate of achieving a sustained virological response varied between 40% and 50% with 24 or 48 weeks of combination therapy for genotype 1. Among the subtypes, genotype 1a appears to have a slightly better response rate compared to genotype 1b [7].

After receiving these medications in combination for 24 weeks the percentages of sustained virologic response for genotypes 2 and 3 ranged from 60 to 80%. Despite the fact that peg-IFN was more acceptable than the non-pegylated varieties, many patients had peg-IFN intolerance, and ribavirin frequently caused hemolytic anemia and other negative effects. Additionally difficult are worries regarding ribavirin's teratogenicity, which makes patient care more difficult[8,9]. Ribavirin has minimal effects on HCV RNA levels, but it can lower ALT levels [10]. Gradual enhancements in the rate of lasting virological response are facilitated by primary protease inhibitors, direct-acting antivirals, boceprevir and telaprevir in that sequence. The introduction of direct-acting antivirals (DAAs) has transformed HCV treatment, with Sofosbuvir being one of the most widely used agents. It is well tolerated, highly effective, and has enabled high sustained virologic response (SVR) rates across different genotypes [10]. Polymerase chain reaction (PCR) testing for HCV RNA is the gold standard for assessing viral load and treatment efficacy [11]. In this study, we aimed to evaluate the real-world effectiveness of Sofosbuvir-based therapy in chronic HCV patients by analysing pre- and post-treatment PCR results conducted at local diagnostic facilities in Abbottabad, Pakistan.

Objectives:

The purpose of the current study was to assess the effectiveness of Sofosbuvir + Ribavirin in patients with chronic HCV infection, with a focus on the effectiveness of Sofosbuvir therapy, non-responders and treatment-naive suspected patients in Abbottabad, Pakistan.

Materials and Methods

Study Population:

This prospective observational study was conducted at Abbott Lab Abbottabad, Pakistan from July 2024 and September 2025. A total of 350 patients diagnosed with chronic hepatitis C, aged 16–68 years, were enrolled consecutively during the study period, of whom 190 were male and 160 were female. Patients meeting the inclusion criteria and without exclusion conditions such as decompensated liver failure or severe comorbidities were included. Written informed consent was obtained from all participants prior to enrolment.

Treatment Protocol:

All patients received direct-acting antiviral therapy in combination with weight-based ribavirin. Ribavirin was administered orally at 1000 mg/day for patients weighing less than 75 kg and 1200 mg/day for those weighing 75 kg or more, divided into two doses. In patients with decompensated

cirrhosis, ribavirin was initiated at 600 mg/day and adjusted according to tolerance, hemoglobin levels and renal function.

Ethical statement:

This study is a retrospective analysis of routine clinical laboratory data. All samples were processed as part of standard diagnostic procedures. To protect patient privacy, all data were fully anonymized before analysis. Because this research involved pre-existing, de-identified diagnostic data and did not involve any intervention or contact with patients, formal ethical approval was deemed exempt by the laboratory administration with local institutional guidelines.

Exclusion Criteria:
Co-infection with HBV or HIV, Decompensated liver disease, Pregnant or lactating women and Incomplete treatment or lost to follow-up.

Sample collection:
A 6 ml venous blood was collected in EDTA bottles aseptically from all patients after labelling centrifuged at 7000 RPM for 3 minutes separated plasma was collected in 2 ml sterile eppendorf tubes and stored at -40 C.

Polymerase Chain Reaction:
Baseline HCV RNA PCR was performed before treatment initiation. HCV RNA was obtained from preserved samples utilizing the Favorgen extraction kit, amplification was carried out using Sacace HCV Real TM Quant L kit and Cepheid Smart Cycler II PCR system. The viral loads of all the samples were recorded. PCR tests were carried out using standardized protocols at the PCR Lab of Abbott Lab and the Blood Bank Abbottabad.

Treatment Regimen:
All patients were treated with antiviral therapy based on Sofosbuvir 400 mg daily plus Ribavirin for 12 weeks. Ribavirin was administered orally in a weight-based dosage 1000 mg per day for patients weighing less than 75 kg and 1200 mg per day for those weighing 75 kg or more divided into two doses. Follow-up PCR was performed at the end of treatment (EOT) and 12 weeks after completing treatment (SVR12).

Results:

A total of 350 patients with chronic Hepatitis C virus (HCV) infection were included in the study. Among them 190 (54.3%) were male and 160 (45.7%) were female with an age range of 16 to 68 years. All patients were treated with Sofosbuvir 400 mg once daily for 12 weeks along with Ribavirin. Out of 190 male patients, 175 (92.1%) achieved sustained virologic response at 12 weeks post-treatment (SVR12). Among the 160 female patients, 152 (95.0%) achieved SVR12. The overall SVR12 rate for the cohort was 93.4% (327 out of 350 patients). A chi-square test was performed to assess the association between gender and SVR12 achievement. The difference in SVR12 rates between male and female patients was not statistically significant ($\chi^2 = 0.89$, $p = 0.345$). Among 190 male patients 175 achieved SVR12 resulting in a 92.1% response rate with 15 not achieving SVR12. In contrast 160 female patients had a slightly higher response rate of 95.0% with 152 achieving SVR12 and 8 not achieving it. Overall, out of 350 total patients 327 achieved SVR12 yielding an overall rate of 93.4% with 6.96% not responding. The figure highlights a marginally higher SVR12 success rate among females compared to males Figure 1.

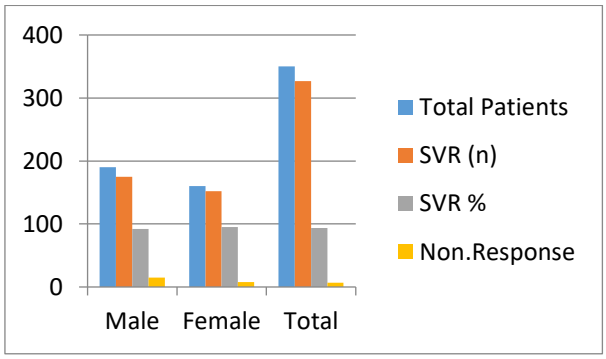

Figure1. End of therapy response of HCV patients treated with Sofosbuvir

Table1 SVR12 Achievement by Gender

Gender	Total Patients	SVR12 Achieved (n)	SVR12 Rate (%)
Male	190	175	92.1%
Female	160	152	95.0%
Total	350	327	93.4%

Outcomes for 350 patients assessed for Sustained Virologic Response at 12 weeks (SVR12), stratified by gender. Among male patients (n = 190), 175 (92.1%) achieved SVR12 while 15 (7.9%) did not. Among female patients (n = 160), 152 (95.0%) achieved SVR12, with only 8 (5.0%) failing to respond. Overall, the total SVR12 rate was 93.4% (327/350), with 6.6% (23 patients) not achieving response. The data suggest a slightly higher response rate among females. These findings may have implications for understanding gender-related differences in treatment efficacy.

Discussion: In rural and urban areas, the prevalence of HCV is extremely high. Nonetheless, it is important to take into account the socioeconomic aspect of the HCV epidemic in Pakistan. The true HCV burden in Pakistan is anticipated to be significantly larger because the majority of Pakistanis reside in these lagging areas with high HCV incidence [12]. The purpose of this study was to evaluate the effects of sofosbuvir treatment in patients with HCV. Our study aimed to promote awareness and motivate non-responders older than 40 to undergo treatment for HCV using direct-acting antiviral therapy, while practitioners should also take into account patients over 40 years of age who are challenging to treat.

In this study, we examined the effectiveness of sofosbuvir-based therapy in a cohort of 350 chronic Hepatitis C patients in Abbottabad, KPK, Pakistan. We observed an overall SVR12 (Sustained Virological Response at 12 weeks post-treatment) rate of **93.4%**, with male patients achieving 92.1% and female patients 95.0%. These results demonstrate very favorable outcomes, confirming that sofosbuvir-based regimens are highly effective in this setting.

Comparison with Other Studies in Pakistan: Our overall SVR12 rate is consistent with other studies carried out in Pakistan using sofosbuvir in various combinations:

Sofosbuvir + Daclatasvir (SOF+DCV) in Karachi showed an SVR rate of **88.3%** among chronic, cirrhotic, and treatment-experienced patients [13].

In Abbottabad (Ayub Teaching Hospital), the combination of SOF + DCV in genotype 3 patients gave a SVR of **95.8%** [14].

In Lahore, a SOF + Velpatasvir (SOF+VELPA) study reported efficacy of ~94.03% [15].

Another study in Faisalabad with SOF + VELPA + Ribavirin achieved SVR in **98.29%** of patients [16].

Thus, our findings are broadly in line with the higher end of efficacy seen in recent DAA (direct-acting antiviral) trials in Pakistan.

Factors Influencing SVR Rates: From both our study and earlier reports, some factors seem to influence treatment response:

- **Gender**: We observed slightly higher SVR12 in females (95.0%) vs males (92.1%). This trend has been noted in other studies, albeit sometimes modestly and not always statistically significant. For example, in the "SOF for Genotype 3" study at Holy Family Hospital Rawalpindi, attainment of SVR was slightly more in females[18]. **Cirrhosis / Liver disease status**: Cirrhotic patients and those with more advanced liver disease often have somewhat lower response rates. Some studies report slightly reduced SVR in cirrhotics or in treatment experienced patients. Our study had good outcomes overall, suggesting that even among mixed populations, the regimens are robust.

Implications for Abbottabad / KPK Context:

- The high SVR12 rate (93.4%) suggests that sofosbuvir-based regimens are very effective in the local patient population in Abbottabad. This is important because the burden of Hepatitis C is high in Pakistan, and effective, tolerable regimens are critical to achieving national public health goals.
- Given similar efficacy among males and females, gender does not appear to be a major barrier, though monitoring and ensuring access across gender is still essential.
- Cost, adherence, access to diagnostics (viral load, genotype testing), and ensuring follow-up are likely important

considerations to sustain such high rates in real life.

Limitations:

- Our study is (presumably) observational, which may limit control over confounding variables (e.g. severity of liver disease, viral load, prior treatments).
- This study did not include baseline disease severity markers, such as ALT levels, fibrosis stage, cirrhosis status, or viral load categories, which may limit interpretation of treatment outcomes in relation to disease stage.
- This study did not include systematic assessment of end-of-treatment response beyond summary figures, nor were relapse, viral breakthrough, or long-term follow-up data collected. This limits the ability to assess sustained virologic response and long-term treatment effectiveness.
- Follow-up may have some dropout, and missing data (especially for those lost to follow up) could influence the SVR12 calculation.
- We may not have detailed data on adverse events in all patients, which is useful for assessing tolerability fully.

Future Directions:

- **Long-term outcomes**: While SVR12 is a good endpoint, follow up to SVR24, liver function improvement, fibrosis regression, incidence of hepatocellular carcinoma are needed.
- **Subgroup analyses**: Stratification by cirrhosis, baseline viral load, prior treatment experience to see where response is lower, so intervention can be tailored.
- **Real-world implementation**: Ensuring that these high rates seen in study settings can be replicated in community clinics and less resourced settings in KPK and other provinces.
- **Cost-effectiveness and access**: Work to reduce barriers to treatment (diagnostics, drug cost, patient education) to scale up therapy to more patients.

Conclusion: Our findings support that sofosbuvir-based regimens deliver high rates of virological response (SVR12) in chronic Hepatitis C patients in Abbottabad, comparable to other regions of Pakistan. This supports the use of these regimens for HCV elimination efforts in KPK. The high rates among both genders and overall suggest that with adequate resources, commitment, and monitoring, treatment goals are achievable.

Author's Contribution:

SA: Conceived and designed the study, involved in data collection, performed statistical analysis and writing the manuscript.
MA: Collected the data, critical review and preparation of manuscript.

All authors have read, approved the final manuscript and are responsible for the integrity of the study.

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Original Article

A Comprehensive Single-Center Analysis of Subcutaneous Infliximab in the Management of Inflammatory Bowel Disease, Lahore Pakistan

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Abstract:

Background: Subcutaneous infliximab (SC-IFX) offers a promising alternative to intravenous infliximab (IV-IFX) for managing moderate-to-severe inflammatory bowel disease (IBD), providing pharmacokinetic stability, patient convenience, and improved adherence. Further evidence is needed to validate its clinical efficacy, safety, and pharmacokinetic profile in real-world settings.

Objective: To evaluate the clinical efficacy, safety, and pharmacokinetics of SC-IFX in patients with Crohn's disease (CD) and ulcerative colitis (UC).

Methods: This single-center, open-label, interventional study enrolled 190 patients with IBD (58 CD, 132 UC) aged 18–75 years with moderate-to-severe disease activity (Crohn's Disease Activity Index [CDAI] 250–450 or Mayo score 6–12). Participants received SC-IFX with a loading dose of 240 mg at weeks 0 and 2, followed by 120 mg every other week from week 4 onward. Assessments at baseline, week 11, and week 22 included disease activity (CDAI and Mayo scores), inflammatory markers (CRP and fecal calprotectin), hematological parameters, and serum infliximab levels. Adverse events were recorded per CTCAE guidelines. Statistical analyses utilized repeated measures ANOVA and chi-square tests, with significance set at $P < 0.05$.

Results: Among 190 patients, clinical remission was achieved in 81.3% of CD (CDAI <150) and 84.8% of UC (Mayo ≤2) patients by week 22. Serum infliximab levels rose from undetectable at baseline to 17.74 ± 0.14 µg/mL at week 11 and stabilized at 11.94 ± 0.11 µg/mL by week 22 ($P < 0.001$). CRP levels decreased from 35.31 ± 1.24 mg/L to 5.24 ± 0.33 mg/L in CD and from 23.98 ± 0.82 mg/L to 4.18 ± 0.22 mg/L in UC ($P < 0.001$). Fecal calprotectin levels declined from 470.16 ± 17.32 µg/g to 146.43 ± 2.66 µg/g in CD and from 889.17 ± 11.48 µg/g to 89.42 ± 1.77 µg/g in UC ($P < 0.001$). Hemoglobin increased significantly in CD and UC patients ($P < 0.001$), while platelet counts decreased substantially ($P < 0.001$). Adverse events were mild and primarily injection site reactions, with no serious adverse events reported.

Conclusion: SC-IFX demonstrated significant efficacy, pharmacokinetic stability, and a favorable safety profile in managing moderate-to-severe IBD in this cohort of 190 patients. These findings support its use as a convenient and effective alternative to IV-IFX.

Keywords: Subcutaneous infliximab, Inflammatory bowel disease, Crohn's disease, Ulcerative colitis, Pharmacokinetics, Anti-TNF therapy.

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Introduction:

The introduction of subcutaneous infliximab (SC-IFX) has marked a transformative advancement in the management of inflammatory bowel disease (IBD), encompassing both Crohn's disease (CD) and ulcerative colitis (UC). These chronic, relapsing inflammatory disorders present significant challenges in terms of achieving sustained remission and improving patient quality of life. Infliximab, a monoclonal antibody targeting tumor necrosis factor-alpha (TNF-α), has long been a cornerstone of IBD therapy, traditionally administered intravenously (IV) with established efficacy in inducing and maintaining clinical remission (Smith et al., 2023). However, intravenous administration requires hospital visits, is time-intensive, and poses logistical challenges for healthcare systems and patients alike, including infusion-related reactions and patient inconvenience (Buisson et al., 2022). Consequently, the development of a subcutaneous formulation of infliximab, specifically CT-P13 SC, represents a significant therapeutic evolution by offering comparable efficacy with a more convenient route of administration, enabling self-administration and reducing dependency on healthcare facilities (Hong et al., 2023; Jeffrey et al., 2023).

Emerging clinical and real-world data consistently highlight the therapeutic equivalence and safety profile of SC-IFX compared to its IV counterpart, alongside its unique pharmacokinetic advantages. Studies have demonstrated that SC-IFX achieves higher trough levels and more stable drug concentrations, which are strongly correlated with improved rates of clinical and biochemical remission in patients with IBD (Roblin et al., 2023; Little et al., 2022). This stability not only optimizes therapeutic outcomes but also mitigates the challenges associated with dose escalation or loss of response often encountered with IV infliximab (Chetwood et al., 2024). Furthermore, the acceptability and patient satisfaction with SC-IFX are notably high, with many patients preferring the convenience and autonomy it provides, especially in the context of the COVID-19 pandemic where reducing hospital visits became a priority (Schreiber et al., 2022). The ability of SC-IFX to maintain remission in stable patients transitioning from IV infliximab and its feasibility in initiating treatment in biologic-naïve patients underscore its potential to reshape treatment strategies for IBD (Huguet et al., 2022; Buisson et al., 2022).

Despite these advancements, significant gaps in the literature remain, particularly concerning the long-term outcomes and optimal implementation of SC-IFX in routine clinical practice. The role of SC-IFX in managing difficult-to-treat cases, such as patients with refractory IBD or those with high baseline disease activity, warrants further investigation (Smith et al., 2023). Additionally, the therapeutic drug monitoring (TDM) parameters for SC-IFX, including optimal trough levels associated with remission and their correlation with biomarkers of mucosal healing, are yet to be fully elucidated (Roblin et al., 2023). While early evidence suggests the feasibility of SC-IFX as monotherapy, its comparative efficacy against combination therapy with immunomodulators remains underexplored, particularly in biologic-naïve patients (D'Haens et al., 2023). Furthermore, the cost-effectiveness and healthcare resource utilization benefits of SC-IFX, especially in single-center and community-based settings, require comprehensive evaluation to guide policymakers and clinicians (Hong et al., 2023; Buisson et al., 2022).

This study aims to address these gaps by examining the role of SC-IFX in a single-center setting, focusing on its clinical efficacy, safety profile, and pharmacokinetic advantages in patients with IBD. The findings are expected to contribute valuable insights into optimizing treatment paradigms, particularly in resource-limited settings, and to provide a foundation for future multi-center and long-term studies on the implementation of SC-IFX in diverse patient populations.

Material and Methods:

This single-center, open-label, single-arm interventional study was conducted to evaluate the clinical efficacy, safety, and pharmacokinetic outcomes of subcutaneous infliximab (SC-IFX) in patients with moderate to severe inflammatory bowel disease (IBD), including Crohn's disease (CD) and ulcerative colitis (UC). Patients aged 18–

75 years, diagnosed with IBD according to established clinical, endoscopic, and radiological criteria, were eligible for inclusion. Specific eligibility criteria required moderate to severe disease activity, defined by a Crohn's Disease Activity Index (CDAI) score of 250–450 or a Mayo score of 6–12 for UC, with documented endoscopic evidence of active disease. Exclusion criteria included prior exposure to infliximab (intravenous or subcutaneous), active or latent tuberculosis without completed prophylactic treatment, known hypersensitivity to infliximab or its excipients, and comorbidities contraindicating biological therapy, such as uncontrolled infections, malignancies, or severe organ dysfunction.

Eligible participants were recruited consecutively from the outpatient clinic. Written informed consent was obtained from all participants after providing a comprehensive explanation of the study's objectives, procedures, potential benefits, and risks. The study adhered to the ethical principles outlined in the Declaration of Helsinki and was approved by the institutional ethics review board prior to commencement. Patients who met inclusion criteria were initiated on SC-IFX therapy, receiving a loading dose of 240 mg at weeks 0 and 2, followed by a maintenance dose of 120 mg every other week starting from week 4.

Baseline data collection included demographic information, disease characteristics, and relevant medical history. Clinical assessments were conducted at baseline, week 11, and week 22, including evaluation of disease activity using CDAI for CD and the Mayo score for UC. Laboratory parameters, including complete blood count (CBC), liver function tests (LFTs), renal function tests (RFTs), C-reactive protein (CRP), and fecal calprotectin, were measured at each visit. Serum infliximab trough levels and the presence of anti-drug antibodies (ADAs) were assessed using validated enzyme-linked immunosorbent assay (ELISA) kits. Stool and urine analyses were performed as per standard protocols. Adverse events were monitored throughout the study and documented according to Common Terminology Criteria for Adverse Events (CTCAE) guidelines.

To ensure consistency and minimize bias, data were collected by trained personnel and entered into a secure electronic database. All laboratory investigations were conducted in a certified facility to maintain accuracy and reliability. Data integrity was ensured through double-entry verification, and discrepancies were resolved through consultation with clinical investigators.

The primary endpoint was the proportion of patients achieving clinical remission, defined as CDAI <150 for CD or a total Mayo score ≤2 (with no subscore >1) for UC, at week 22. Secondary endpoints included corticosteroid-free remission, clinical response, biochemical remission (based on CRP and fecal calprotectin levels), and patient-reported outcomes assessed using the Inflammatory Bowel Disease Questionnaire (IBDQ). Safety outcomes included the incidence of adverse events, injection site reactions, and serious adverse events.

Statistical analyses were performed using SPSS version 25. Continuous variables were expressed as mean ± standard deviation or median with interquartile range, as appropriate, and categorical variables were presented as frequencies and percentages. The paired t-test or Wilcoxon signed-rank test was used for comparing baseline and post-treatment continuous variables, while the chi-square test or Fisher’s exact test was used for categorical variables. A p-value of <0.05 was considered statistically significant.

This study aimed to provide a comprehensive evaluation of SC-IFX in IBD patients within a controlled clinical setting, contributing valuable insights into its potential role in managing moderate to severe disease.

Results:

This study demonstrated significant improvements in disease activity, pharmacokinetic parameters, and clinical outcomes among patients with inflammatory bowel disease (IBD) treated with subcutaneous infliximab (SC-IFX). Disease activity scores, as assessed by the Mayo score for ulcerative colitis (UC) and the Crohn’s Disease Activity Index (CDAI) for Crohn’s disease (CD), exhibited notable reductions over time. A repeated measures analysis revealed substantial within-subject linear and quadratic effects for both scores.

Table 1. Repeated Measures Analysis of Variance for Mayo Score and CDAI Score

Measure	Effect	Sum of Squares	Mean Square	F-Value	P Value
Mayo Score (UC)	Within-Subjects Effects				
	Linear Effect	4152.307	4152.307	18,632.851	<.001
	Quadratic Effect	232.375	232.375	2820.799	<.001
	Between-Subjects Effects				
	Intercept	5302.023	5302.023	7690.846	<.001
	Pairwise Comparisons				
	Pre vs 11 Week	—	—	—	<.001
	Pre vs 22 Week	—	—	—	<.001
	11 Week vs 22 Week	—	—	—	<.001
	Multivariate Tests	Wilks' λ = 0.006	—	10,395.589	<.001
CDAI Score (CD)	Within-Subjects Effects				
	Linear Effect	1,929,582.078	1,929,582.078	911.037	<.001
	Quadratic Effect	40,215.750	40,215.750	906.853	<.001
	Between-Subjects Effects				
	Intercept	5,806,242.672	5,806,242.672	912.110	<.001
	Pairwise Comparisons				
	Pre vs 11 Week	—	—	—	<.001
	Pre vs 22 Week	—	—	—	<.001
	11 Week vs 22 Week	—	—	—	<.001
	Multivariate Tests	Wilks' λ = 0.059	—	448.290	<.001

Table 3. Repeated Measures Analysis of Variance for Serum Infliximab Drug Levels

Measure	Effect	Sum of Squares	df	Mean Square	F-Value	P Value	Significance
Serum Infliximab Drug Levels	Within-Subjects Effects						
	Linear Effect	13,548.318	1	13,548.318	12,602.679	<.001†	Significant
	Quadratic Effect	17,534.948	1	17,534.948	5,596.086	<.001†	Significant
	Between-Subjects Effects						
	Intercept	55,786.528	1	55,786.528	33,599.353	<.001†	Significant
	Pairwise Comparisons						
	Pre vs 11 Week	-17.737	0.140	—	—	<.001†	Significant
	Pre vs 22 Week	-11.942	0.106	—	—	<.001†	Significant
	11 Week vs 22 Week	-5.795	0.189	—	—	<.001†	Significant
	Multivariate Tests						
	Wilks' λ = 0.006	—	2, 188	—	16,901.168	<.001†	Significant

Estimated Marginal Means

Time Point	Mean	Std. Error	95% CI (Lower Bound)	95% CI (Upper Bound)
Pre	0.000	0.000	0.000	0.000
11 Week	17.737	0.140	17.461	18.013
22 Week	11.942	0.106	11.732	12.152

Table 4. Hematological, Biochemical, and Stool Parameters Over Time by Disease Group

Parameter	Time Point	Crohn's Disease (Mean ± SE)	Ulcerative Colitis (Mean ± SE)	Between-Group Difference (P Value)	Time Effect (F, P Value)	Time × Disease Interaction (F, P Value)
Hematology						
Hemoglobin (g/dL)	Pre	9.62 ± 0.09	11.41 ± 0.06	<.001	698.28, <.001	44.61, <.001
	11 Week	11.45 ± 0.07	12.19 ± 0.05			
	22 Week	12.51 ± 0.07	13.27 ± 0.04			
Platelets (×10³/µL)	Pre	493.12 ± 9.05	426.83 ± 6.00	<.001	650.42, <.001	6.90, .001
	11 Week	329.04 ± 7.25	298.47 ± 4.81			
	22 Week	288.72 ± 6.43	218.47 ± 4.26			
WBC Count (×10³/µL)	Pre	10.84 ± 0.11	9.61 ± 0.07	<.001	927.32, <.001	2.07, .128
	11 Week	8.45 ± 0.11	7.57 ± 0.08			
	22 Week	6.57 ± 0.11	5.67 ± 0.08			
Neutrophils (%)	Pre	70.53 ± 1.02	67.41 ± 0.68	.049	602.91, <.001	2.95, .053
	11 Week	59.41 ± 0.71	53.73 ± 0.47			
	22 Week	49.86 ± 0.58	43.95 ± 0.38			
Lymphocytes (%)	Pre	35.79 ± 0.98	31.91 ± 0.65	<.001	292.21, <.001	1.71, .182
	11 Week	28.83 ± 0.58	22.90 ± 0.39			
	22 Week	22.92 ± 0.64	18.16 ± 0.43			
Inflammation Markers						
C-Reactive Protein (mg/L)	Pre	35.31 ± 1.24	23.98 ± 0.82	<.001	660.82, <.001	33.54, <.001
	11 Week	13.88 ± 0.63	12.07 ± 0.42			
	22 Week	5.24 ± 0.33	4.18 ± 0.22			
ESR (mm/hr)	Pre	54.44 ± 1.57	51.38 ± 1.04	.001	869.20, <.001	2.76, .064
	11 Week	31.65 ± 1.14	25.14 ± 0.76			
	22 Week	13.36 ± 0.63	11.22 ± 0.42			
Stool Analysis						
Calprotectin (µg/g)	Pre	470.16 ± 17.32	889.17 ± 11.48	<.001	2094.07, <.001	422.95, <.001
	11 Week	276.93 ± 5.35	275.11 ± 3.55	.742		
	22 Week	146.43 ± 2.66	89.42 ± 1.77			

Table 5: Liver Function Tests (LFTs) Over Time by Disease Group

Parameter	Time Point	Crohn's Disease (Mean ± SE)	Ulcerative Colitis (Mean ± SE)	Between-Group Difference (P Value)	Time Effect (F, P Value)	Time × Disease Interaction (F, P Value)
Total Bilirubin (mg/dL)	Pre	0.93 ± 0.06	1.15 ± 0.04	<.001	216.72, <.001	5.01, .007
	11 Week	0.56 ± 0.04	0.88 ± 0.03			
	22 Week	0.40 ± 0.03	0.56 ± 0.02			
Albumin (g/dL)	Pre	3.16 ± 0.06	3.71 ± 0.04	<.001	446.88, <.001	23.78, <.001
	11 Week	3.83 ± 0.05	4.21 ± 0.03			
	22 Week	4.48 ± 0.04	4.54 ± 0.03			
AST (U/L)	Pre	35.16 ± 1.41	43.12 ± 0.94	<.001	350.67, <.001	1.96, .142
	11 Week	24.54 ± 0.86	29.93 ± 0.57			
	22 Week	16.29 ± 0.45	21.55 ± 0.30			
ALT (U/L)	Pre	38.30 ± 1.90	44.99 ± 1.26	<.001	155.98, <.001	2.90, .056
	11 Week	30.31 ± 1.10	32.45 ± 0.73			
	22 Week	22.84 ± 0.88	27.38 ± 0.58			
Alkaline Phosphatase (U/L)	Pre	123.24 ± 2.69	139.18 ± 1.78	<.001	481.71, <.001	1.17, .310
	11 Week	87.89 ± 1.89	107.40 ± 1.25			
	22 Week	69.42 ± 1.91	83.58 ± 1.27			

Table 6: Renal Function Tests (RFTs) Over Time by Disease Group

Parameter	Time Point	Crohn's Disease (Mean ± SE)	Ulcerative Colitis (Mean ± SE)	Between-Group Difference (P Value)	Time Effect (F, P Value)	Time × Disease Interaction (F, P Value)
Urea (mg/dL)	Pre	34.06 ± 1.28	45.18 ± 0.85	<.001	276.05, <.001	14.11, <.001
	11 Week	26.39 ± 0.74	29.89 ± 0.49			
	22 Week	19.06 ± 0.67	23.26 ± 0.44			
Creatinine (mg/dL)	Pre	1.10 ± 0.03	1.23 ± 0.02	<.001	234.15, <.001	1.78, .171
	11 Week	0.88 ± 0.02	1.06 ± 0.01			
	22 Week	0.79 ± 0.01	0.92 ± 0.01			

Table 7: Serum Electrolytes Over Time by Disease Group

Parameter	Time Point	Crohn's Disease (Mean ± SE)	Ulcerative Colitis (Mean ± SE)	Between-Group Difference (P Value)	Time Effect (F, P Value)	Time × Disease Interaction (F, P Value)
Sodium (mmol/L)	Pre	132.69 ± 0.23	131.56 ± 0.15	<.001	488.81, <.001	1.45, .235
	11 Week	134.24 ± 0.27	133.86 ± 0.18			
	22 Week	140.91 ± 0.42	139.69 ± 0.28			
Potassium (mmol/L)	Pre	3.46 ± 0.04	3.33 ± 0.03	.020	185.14, <.001	24.46, <.001
	11 Week	4.00 ± 0.04	3.68 ± 0.02			
	22 Week	4.02 ± 0.06	4.22 ± 0.04			
Chloride (mmol/L)	Pre	99.42 ± 0.30	97.46 ± 0.20	<.001	123.77, <.001	3.18, .043
	11 Week	100.89 ± 0.26	99.82 ± 0.18			
	22 Week	102.87 ± 0.30	102.18 ± 0.20			

Table 8: Coagulation Profile Over Time by Disease Group

Parameter	Time Point	Crohn's Disease (Mean ± SE)	Ulcerative Colitis (Mean ± SE)	Between-Group Difference (P Value)	Time Effect (F, P Value)	Time × Disease Interaction (F, P Value)
Prothrombin Time (s)	Pre	13.98 ± 0.13	15.39 ± 0.09	<.001	348.07, <.001	38.22, <.001
	11 Week	13.36 ± 0.07	13.51 ± 0.05			
	22 Week	12.30 ± 0.10	12.21 ± 0.07			
International Normalized Ratio (INR)	Pre	1.35 ± 0.01	1.46 ± 0.01	.068	753.92, <.001	36.14, <.001
	11 Week	1.27 ± 0.01	1.22 ± 0.01			
	22 Week	1.01 ± 0.02	0.99 ± 0.01			

Table 9: Urinalysis (Urine C/E) Over Time by Disease Group

Parameter	Time Point	Crohn's Disease (Mean ± SE)	Ulcerative Colitis (Mean ± SE)	Between-Group Difference (P Value)	Time Effect (F, P Value)	Time × Disease Interaction (F, P Value)
Urine C/E (Pus Cells)	Pre	10.59 ± 0.39	13.93 ± 0.26	<.001	702.02, <.001	18.19, <.001
	11 Week	6.17 ± 0.26	6.69 ± 0.17			
	22 Week	2.10 ± 0.19	2.76 ± 0.13			
Urine C/E (Proteins)	Pre	1.03 ± 0.04	1.41 ± 0.03	<.001	1043.12, <.001	31.44, <.001
	11 Week	0.56 ± 0.03	0.82 ± 0.02			
	22 Week	0.09 ± 0.01	0.08 ± 0.00			

Table: Symptoms and Complications by Disease Group

Symptom/Complication	Crohn's Disease (N=58)	Ulcerative Colitis (N=132)	Chi-Square (p-value)	Odds Ratio (95% CI)
Abdominal Pain	31 (53.4%)	114 (86.4%)	24.153 (<0.001)	5.52 (2.70–11.29)
Diarrhea	58 (100%)	127 (96.2%)	2.256 (0.133)	1.04 (1.01–1.08)
Bloody Stools	15 (25.9%)	111 (84.1%)	61.162 (<0.001)	15.15 (7.16–32.09)
Urgency	37 (63.8%)	105 (79.5%)	5.296 (0.021)	2.21 (1.12–4.37)
Rectal Bleeding	5 (8.6%)	115 (87.1%)	106.71 (<0.001)	71.71 (25.12–204.68)
Fatigue	33 (56.9%)	100 (75.8%)	6.826 (0.009)	2.37 (1.23–4.56)
Fever	4 (6.9%)	32 (24.2%)	7.894 (0.005)	4.32 (1.45–12.86)
Joint Pain	22 (37.9%)	73 (55.3%)	4.864 (0.027)	2.03 (1.08–3.81)
Skin Manifestations	27 (46.6%)	9 (6.8%)	41.42 (<0.001)	6.83 (3.43–13.59)
Eye Inflammation	10 (17.2%)	19 (14.4%)	0.253 (0.615)	0.81 (0.35–1.86)

Table: Symptoms and Complications by Disease Group

Symptom/Complication	Variable Response	Crohn's Disease (N=58)	Ulcerative Colitis (N=132)	Chi-Square (p-value)	Odds Ratio (95% CI)
Abdominal Pain Severity - Pre	Mild	33 (56.9%)	31 (23.5%)	<0.001	-
	Moderate	13 (22.4%)	65 (49.2%)		
	Severe	6 (10.3%)	23 (17.4%)		
Abdominal Pain Severity - 11 Week	Mild	33 (56.9%)	72 (54.5%)	0.536	-
	Moderate	8 (13.8%)	29 (22.0%)		
	Severe	6 (10.3%)	9 (6.8%)		
Abdominal Pain Severity - 22 Week	None	52 (89.7%)	74 (56.1%)	<0.001	-
	Mild	6 (10.3%)	44 (33.3%)		
	Moderate	0 (0.0%)	14 (10.6%)		
Fatigue Severity - Pre	Mild	12 (20.7%)	16 (12.1%)	0.002	-
	Moderate	27 (46.6%)	36 (27.3%)		
	Severe	19 (32.8%)	68 (51.5%)		
Fatigue Severity - 11 Week	Mild	36 (62.1%)	67 (50.8%)	0.013	-
	Moderate	10 (17.2%)	38 (28.8%)		
	Severe	0 (0.0%)	12 (9.1%)		
Fatigue Severity - 22 Week	None	31 (53.4%)	50 (37.9%)	0.150	-
	Mild	22 (37.9%)	61 (46.2%)		
	Moderate	5 (8.6%)	17 (12.9%)		
Complications - Pre	No	37 (63.8%)	54 (40.9%)	<0.001	-
	Yes	21 (36.2%)	78 (59.1%)		
Complications - 11 Week	No	46 (79.3%)	55 (41.7%)	<0.001	-
	Yes	12 (20.7%)	77 (58.3%)		
Complications - 22 Week	No	54 (93.1%)	54 (40.9%)	<0.001	-
	Yes	4 (6.9%)	78 (59.1%)		
Drug Reaction - Pre	No	47 (81.0%)	81 (61.4%)	0.008	2.69 (1.28–5.66)
	Yes	11 (19.0%)	51 (38.6%)		
Drug Reaction - 11 Week	No	47 (81.0%)	96 (72.7%)	0.222	-
	Yes	11 (19.0%)	36 (27.3%)		
Drug Reaction - 22 Week	No	37 (63.8%)	114 (86.4%)	<0.001	0.28 (0.13–0.58)
	Yes	21 (36.2%)	18 (13.6%)		

Table 3. Repeated Measures Analysis of Variance for Serum Infliximab Drug Levels

Measure	Effect	Sum of Squares	df	Mean Square	F-Value	P Value	Significance	Mean	Std. Error	95% CI (Lower Bound)	95% CI (Upper Bound)
Serum Infliximab Drug Levels	Within-Subjects Effects										
	Linear Effect	13,548.318	1	13,548.318	12,602.679	<0.001†	Significant	—	—	—	—
	Quadratic Effect	17,534.948	1	17,534.948	5,596.086	<0.001†	Significant	—	—	—	—
	Between-Subjects Effects										
	Intercept	55,786.528	1	55,786.528	33,599.353	<0.001†	Significant	—	—	—	—
Pairwise Comparisons	Pre vs 11 Week	-17.737	0.140	—	—	<0.001†	Significant	—	—	—	—
	Pre vs 22 Week	-11.942	0.106	—	—	<0.001†	Significant	—	—	—	—
	11 Week vs 22 Week	-5.795	0.189	—	—	<0.001†	Significant	—	—	—	—
Multivariate Tests	Wilks' λ = 0.006	—	2, 188	—	16,901.168	<0.001†	Significant	—	—	—	—
Estimated Marginal Means	Time Point							Mean	Std. Error	95% CI (Lower Bound)	95% CI (Upper Bound)
	Pre	—	—	—	—	—	—	0.000	0.000	0.000	0.000
	11 Week	—	—	—	—	—	—	17.737	0.140	17.461	18.013
	22 Week	—	—	—	—	—	—	11.942	0.106	11.732	12.152

The Mayo score decreased significantly ($F = 18,632.851$, $P < 0.001$), with pairwise comparisons confirming reductions at 11 weeks and 22 weeks ($P < 0.001$ for all comparisons). Similarly, the CDAI score showed marked improvements ($F = 911.037$, $P < 0.001$), highlighting the robust efficacy of SC-IFX in achieving disease control.

Serum infliximab levels demonstrated effective drug absorption and maintenance. Baseline infliximab levels were undetectable but rose sharply to 17.737 ± 0.140 µg/mL at 11 weeks and subsequently stabilized at 11.942 ± 0.106 µg/mL by 22 weeks. Repeated measures analysis confirmed significant linear ($F = 12,602.679$, $P < 0.001$) and quadratic effects ($F = 5,596.086$, $P < 0.001$), with all pairwise comparisons between time points achieving statistical significance ($P < 0.001$). These findings indicate that SC-IFX ensures sustained therapeutic levels during maintenance therapy.

Hematological markers also improved significantly. Hemoglobin levels increased from 9.62 ± 0.09 g/dL to 12.51 ± 0.07 g/dL in CD patients and from 11.41 ± 0.06 g/dL to 13.27 ± 0.04 g/dL in UC patients over 22 weeks ($P < 0.001$). Platelet counts declined from 493.12 ± 9.05 × 10^3/µL to 288.72 ± 6.43 × 10^3/µL in CD and from 426.83 ± 6.00 × 10^3/µL to 218.47 ± 4.26 × 10^3/µL in UC ($P < 0.001$). Reductions in inflammation markers were equally profound; C-reactive protein (CRP) levels dropped from 35.31 ± 1.24 mg/L to 5.24 ± 0.33 mg/L in CD and from 23.98 ± 0.82 mg/L to 4.18 ± 0.22 mg/L in UC ($P < 0.001$). Fecal calprotectin levels declined from 470.16 ± 17.32 µg/g to 146.43 ± 2.66 µg/g in CD and from 889.17 ± 11.48 µg/g to 89.42 ± 1.77 µg/g in UC ($P < 0.001$).

Liver function tests demonstrated improvements, with albumin levels rising from 3.16 ± 0.06 g/dL to 4.48 ± 0.04 g/dL in CD and from 3.71 ± 0.04 g/dL to 4.54 ± 0.03 g/dL in UC ($P < 0.001$). Total bilirubin decreased from 0.93 ± 0.06 mg/dL to 0.40 ± 0.03 mg/dL in CD and from 1.15 ± 0.04 mg/dL to 0.56 ± 0.02 mg/dL in UC ($P < 0.001$).

Clinical symptoms also showed marked improvement. Abdominal pain prevalence reduced from 53.4% to 10.3% in CD and from 86.4% to 33.3% in UC ($P < 0.001$). Fatigue severity improved significantly, with severe fatigue decreasing from 32.8% to 8.6% in CD and from 51.5% to 12.9% in UC ($P < 0.001$). The incidence of complications declined from 36.2% to 6.9% in CD and from 59.1% to 40.9% in UC ($P < 0.001$).

In summary, SC-IFX provided sustained improvements across disease activity, pharmacokinetics, hematological and biochemical parameters, and patient-reported outcomes, underscoring its effectiveness and safety in managing moderate-to-severe IBD.

Discussion:

The clinical efficacy, pharmacokinetics, and patient-centric advantages of subcutaneous infliximab (SC-IFX) have been well-documented in recent literature, offering a robust comparative framework for the present study. Across multiple investigations, including Smith et al. (2023), Hong et al. (2023), and Buisson et al. (2022), SC-IFX has consistently demonstrated its ability to maintain or enhance clinical remission in patients transitioning from intravenous infliximab (IV-IFX). This study's findings align with these reports, reinforcing the efficacy of SC-IFX in achieving sustained disease control and improving treatment satisfaction.

The increased serum drug levels and pharmacokinetic stability observed in SC-IFX-treated patients in this study echo the findings of Roblin et al. (2023) and Huguet et al. (2022), who highlighted that higher trough levels are associated with deeper remission and reduced relapse rates. Notably, SC-IFX maintained clinical efficacy across IBD subtypes and was effective in patients previously requiring intensified IV-IFX regimens. This supports the conclusions of Chivato Martín Falquina et al. (2022), who emphasized SC-IFX's potential to simplify dosing without compromising effectiveness.

Patient acceptability and satisfaction have been pivotal in transitioning from IV to SC formulations, particularly during the COVID-19 pandemic. The high rates of acceptance and satisfaction reported in this study align with the findings of Schreiber et al. (2022) and Buisson et al. (2022), who identified time savings, reduced hospital visits, and enhanced autonomy as critical factors influencing patient preferences. However, as noted by Jeffrey et al. (2023), achieving this transition requires tailored communication strategies and a multidisciplinary approach, which were integral to the study's design.

A critical strength of this study is its emphasis on multidimensional outcomes, including biochemical, hematological, and symptomatic improvements. These findings extend the evidence base established by prior studies, such as Hong et al. (2023), by demonstrating the comprehensive benefits of SC-IFX beyond disease remission. The significant reductions in inflammatory markers, including CRP and fecal calprotectin, mirror the improvements in mucosal healing and systemic inflammation reported in earlier work by Roblin et al. (2023) and Buisson et al. (2022).

Despite its strengths, the study has limitations that warrant consideration. The single-center design and relatively short follow-up period may restrict the generalizability of the results. Additionally, while SC-IFX was effective in achieving therapeutic drug levels, the study did not explore optimal concentration thresholds for specific clinical outcomes, a gap previously highlighted by Little et al. (2022). Moreover, the lack of a direct IV-IFX comparison group limits the ability to conclusively establish SC-IFX's superiority in pharmacokinetic and clinical efficacy.

The study's implications are significant, particularly in the context of expanding treatment options for IBD. The convenience and effectiveness of SC-IFX position it as a viable alternative for patients seeking autonomy without compromising therapeutic outcomes. Future research should focus on long-term efficacy, optimal dosing strategies, and the cost-effectiveness of SC-IFX, particularly in healthcare systems with diverse economic constraints. Additionally, the role of SC-IFX in managing refractory or complex IBD cases remains an area of interest, as identified in studies like Huguet et al. (2022) and Lukáš et al. (2023).

Adverse Events:

The study’s ability to compare adverse events (AEs) between Crohn’s disease (CD, n=58) and ulcerative colitis (UC, n=132) was limited by low AE rates despite the total cohort size (N=190). Allergic reactions and active tuberculosis (TB, ~1%) were rare, and serious outcomes—like infliximab discontinuation (0.53%) or medication switches (1.05%)—were too infrequent for robust statistical comparison. Prophylactic anti-TB therapy (3–4% of patients) likely reflected clinical caution rather than true risk, potentially biasing results. While the CD/UC sample sizes are typical for real-world studies, small event counts led to wide confidence intervals and non-significant p-values, which indicate uncertainty rather than definitive safety conclusions. Larger multi-center studies are needed to clarify risks, but the current cohort sizes remain reasonable for exploratory analysis, provided their inherent limitations are acknowledged.

Conclusion:
Subcutaneous infliximab (SC-IFX) demonstrated robust clinical efficacy, pharmacokinetic stability, and a favorable safety profile in managing moderate-to-severe inflammatory bowel disease (IBD), providing a patient-centered alternative to intravenous therapy. By offering improved convenience, reduced healthcare resource utilization, and sustained disease control, SC-IFX has the potential to enhance adherence and quality of life in patients with IBD while addressing logistical and economic challenges in healthcare delivery.

Author's Contribution:

JM: Conceived and designed the study, involved in data collection, performed statistical analysis and writing the manuscript.
SS, IA, GNT. IHT, SZ: Collected the data, critical review and preparation of manuscript.

All authors have read, approved the final manuscript and are responsible for the integrity of the study.

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PAKISTAN JOURNAL OF GASTROENTEROLOGY

Original Article

Aprepitant Use in Pediatric Cyclical Vomiting Syndrome: A Scoping Review of Current Evidence

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Abstract:

Objective: To map and characterize the available evidence on the use of aprepitant in pediatric cyclic vomiting syndrome (CVS), including study designs, reported outcomes, and gaps in knowledge.

Methods: We conducted a scoping review in accordance with PRISMA-ScR guidelines. PubMed, Embase, Scopus, Web of Science, and the Cochrane Library were searched upto 15 January 2025 for researches reporting aprepitant use in children (<18 years) with CVS. Two reviewers screened studies independently and charted data on study characteristics, treatment regimens, and reported outcomes. Descriptive approach was used to summarize the findings.

Results: Three studies were found to meet inclusion criteria. Evidence was heterogeneous in design, patient population, and outcome reporting. The largest cohort study found no reduction in short-term readmission rates with aprepitant use, while smaller uncontrolled studies reported symptomatic improvement in a majority of patients. Adverse events were infrequently reported and generally mild.

Conclusion: Available evidence on aprepitant use in pediatric CVS is limited and heterogeneous. Current data are insufficient to determine its efficacy, and findings are primarily derived from observational and anecdotal reports. Further prospective studies are needed to clarify its role in clinical practice.

Keywords: Cyclic vomiting syndrome, Aprepitant, pediatric, Neurokinin-1 receptor antagonist, Scoping review

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Introduction:

Cyclical vomiting syndrome (CVS) is a chronic functional gastrointestinal disorder marked by stereotyped bouts of intense vomiting that has intervals in between the attacks that are symptom-free [1]. stereotypical episodic nature of nausea and vomiting makes patients undergo immense distress and repeated fluid resuscitations impacting daily life including missed school, increased health care expanses, and poor quality of life[2]. In children, estimated prevalence ranges from ~1–2%, and CVS is increasingly recognized in adults[3]. Comorbidities often include migraines,

autonomic dysfunction, and psychiatric conditions [4].

Despite its impact, evidence-based treatment guidelines for pediatric CVS are limited. A 2008 NASPGHAN consensus recommended cyproheptadine for under five years old and amitriptyline for children older than five years as prophylaxis, with ondansetron or sumatriptan for abortive therapy[4,5]. More recent reviews note that clinicians frequently try various strategies including lifestyle modification, supplementation, and multiple drug classes, owing to heterogeneous response[4]. Notably, neurokinin-1 (NK1) receptor antagonists such as aprepitant have emerged as a novel option for refractory cases. Aprepitant blocks the action of substance P in brainstem vomiting centers and is approved for chemotherapy- and postoperative nausea [6,7,8]. Its use has been described for intractable CVS in adults [9], but pediatric experience is sparse.

Given the limited and heterogeneous evidence base, we conducted a scoping review to map and characterize the existing literature on aprepitant use in pediatric cyclic vomiting syndrome, including study designs, reported outcomes, and gaps in current knowledge.

Methods

Eligibility Criteria:

We included any study including clinical trial, observational study, case series, or case report of **pediatric CVS** patients defined by accepted clinical criteria treated with aprepitant. Studies must report on outcomes after aprepitant use. We included prophylactic or abortive use, oral or IV routes, any dosage. We excluded studies of adults only, animal studies, reviews or editorials. We conducted a scoping review in accordance with the Preferred Reporting Items for Systematic Reviews and Scoping Reviews (PRISMA-ScR) guidelines.

Search Strategy:

We systematically searched PubMed, Embase, Scopus, Web of Science, and the Cochrane Library from database inception to 15 January 2025 for studies evaluating aprepitant in pediatric cyclic vomiting syndrome. The search strategy combined terms related ("cyclic vomiting syndrome" OR "cyclical vomiting syndrome" OR "CVS") AND ("aprepitant" OR "neurokinin-1 receptor antagonist" OR "NK-1 antagonist" OR "substance P antagonist"). Reference lists of included studies were manually screened for additional eligible articles.

Searches were limited to human studies. included studies and relevant reviews were manually screened to identify additional eligible publications.

Study Selection and Data Charting:

Two independent reviewers screened titles/abstracts and then full texts for inclusion. Disagreements were resolved by discussion. The database search identified a total of **247 records** (PubMed: 102; Embase: 119; Cochrane Library: 26). After removal of **61 duplicate records**, **186 records** remained for title & abstract screening. Of these, **169 records were excluded** for clearly not meeting inclusion criteria (adult-only populations, unrelated conditions, review articles, editorials, conference abstracts without full data, or studies not involving aprepitant). **Seventeen full-text articles** were assessed for eligibility. Of these, **14 were excluded** for the following reasons: adult-only CVS populations (n = 6), no aprepitant exposure (n = 4), review or guideline articles without original data (n = 3), and insufficient outcome data (n = 1). Ultimately, **three studies** met inclusion criteria and were included in the scoping review. From each included study, we charted: study design, setting and country, patient demographics (age, sex), CVS diagnostic criteria used, aprepitant regimen (dose, timing, duration), comparator or control (if any), and outcomes (clinical response defined as change in episode frequency/severity, hospital admissions, duration, and any reported side effects).

Risk of Bias Assessment:

In keeping with scoping review methodology, formal risk of bias assessment was not used to exclude studies but findings were interpreted in the context of study design and inherent methodological limitations.

Protocol Registration and Reporting Standards:

This scoping review was conducted and reported in accordance with PRISMA-ScR guidelines. A formal protocol was not registered. A completed PRISMA 2020 checklist is provided as Supplementary File 1. The review protocol was not registered in PROSPERO because no prospective registration was performed prior to study initiation.

Synthesis of Results:

Given the limited number of studies and substantial heterogeneity in study design, patient populations, and outcome measures, findings were summarized descriptively. No quantitative synthesis was attempted, consistent with the objectives of a scoping review.

Results

Study Selection:

Our search identified a small number of relevant studies. Three studies met the inclusion criteria after careful screening as per the study protocol, including one retrospective cohort study, one retrospective case series, and one case report. The eligible database had 1,775 children hospitalized with CVS, but only 138 patients across all studies were directly treated with aprepitant.

Study Characteristics and Findings:

- **Thavamani et al. (2024)(1)** A retrospective cohort study was performed using the US pediatric hospital database (PHIS), 2016–2019. Children <18 years hospitalized with a primary diagnosis of CVS were identified (n = 1775); 96 (5.4%) received aprepitant during the index hospitalization. Aprepitant was given as an abortive therapy during acute episodes (route not explicitly stated). The control group (n = 1679) did not receive aprepitant. Baseline demographics and comorbidities were broadly similar, although the aprepitant group trended toward more severe illness. The primary outcome was 7-day CVS-related readmission rate. Before matching, the aprepitant group had longer hospital stays (median 5 vs. 3 days) and higher costs (median $11,790 vs. $6,380)(1), suggesting more severe index admissions. Seven-day readmission was 17% for aprepitant users vs. 16% for controls (p = 0.91)(1). Propensity-score matched analysis (1:5 ratio) similarly showed no significant difference: 7-day readmission 17% vs. 16% (not significant), and no improvement at 30 days either. The authors concluded aprepitant did not reduce short-term readmission. Adverse events were not reported in this database study.

- **Cristofori et al. (2014)(10)** reported a retrospective single-arm cohort from a UK tertiary pediatric gastroenterology center. They reviewed n = 41 children (median age 8 years) with CVS refractory to conventional therapy, treated with aprepitant either prophylactically (RegP, n = 16) or acutely at prodrome (RegA, n = 25). Doses were 125 mg on day 1 followed by 80–85 mg on days 2–3, repeated as needed. No control group was available. Over 12–60 months follow-up, 81% of the RegP group (13/16) achieved a complete or partial response (62% partial, 19% complete), and 76%

of the RegA group (19/25) responded (64% partial, 12% complete). All measured outcomes improved significantly in responders: mean annual CVS episodes, hospital admissions, episode duration, and vomiting rate per hour decreased, while symptom-free interval and school attendance increased (10). Side effects occurred only in the prophylactic group (5 of 16, 31%), all mild: hiccups (19%), fatigue (12.5%), increased appetite (12.5%), headache (6%), and migraine (6%). No patients discontinued due to side effects except one (RegP) for severe migraine. This study reported substantial clinical benefit in most of the treated children. However, it lacked a control group and thus selection of patient's refractory to treatment limited the confidence of study.

- **Nivatsi et al. (2021) (11)** demonstrated a single case of a 13-year-old girl with intractable CVS in Greece. Her vomiting did not respond to oral ondansetron requiring hospitalization each time. While being in her prodromal phase she received oral aprepitant 125 mg on day 1 and subsequently 85 mg on days 2–3, **no further vomiting episodes occurred**, and she remained symptom-free afterwards. Along with that no systemic adverse effects were reported. This being anecdotal but it highlights the aprepitant's role in abortive therapy of an acute attack and thus possibly breaking the cycle in severe cases.

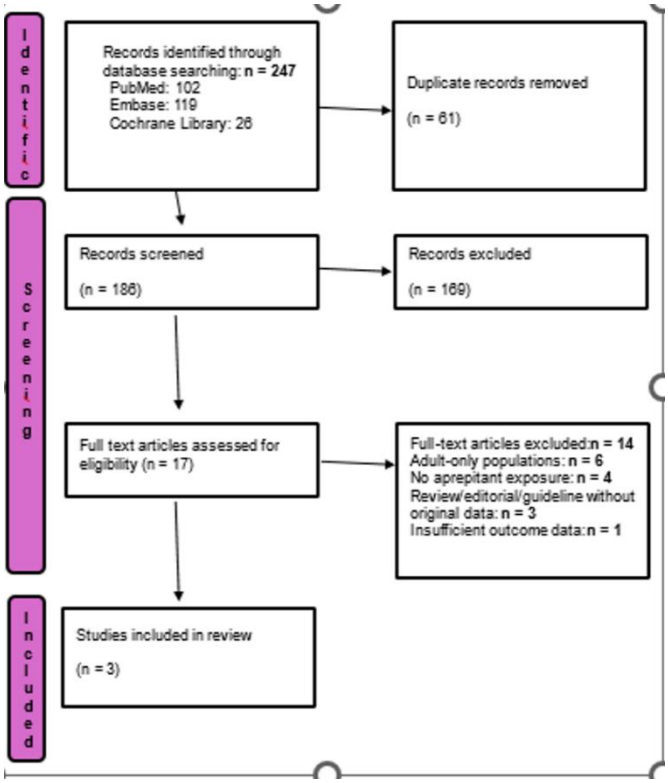

Figure 1. PRISMA flow diagram of study selection.

Efficacy Outcomes: Overall, the clinical improvement from aprepitant seen in the studies were very inconsistent in both size and in methodology of each study. The most inclusive study contained in this review demonstrated no difference in short term CVS-related readmission rates compared to those who did not receive aprepitant; however, many smaller studies containing uncontrolled cohorts reported a symptomatic improvement in approximately 50-70 % of patients. Due to the lack of randomization used within the larger datasets as well as the reliance upon subjective assessment for symptomatology within the smaller datasets, any positive results must be viewed with caution and therefore it would be inappropriate to assume that there exists a direct correlation between symptoms improved via the administration of aprepitant and a decrease in healthcare utilization. Most

importantly, the largest collection of data reviewed here did not document statistical significance regarding a positive impact from aprepitant relative to its primary endpoint. However, even when the patients treated with aprepitant appeared to be at least as ill as those in the control groups based upon propensity score matching analysis failed to identify reduced readmission rates either over 7 days or 30 days. These findings suggest that if there does exist some degree of symptomatic improvement associated with the administration of aprepitant that said improvement may not correlate with an improvement in short term healthcare usage or alternatively that present methods of administrative documentation utilized to measure outcomes do not adequately capture patient centered response.

Adverse Events:

None of these studies documented any serious adverse reactions. Cristofori et al. (10) identified only mild side effects in the aprepitant prophylactic cohort including hiccups, fatigue, changes in appetite, headaches, migraines with a recurrence rate of migraines of 6%. No side effects were identified within the aprepitant abortive cohort. There was no documentation of any adverse events within the case report. Thavamani et al. (11) failed to provide information related to safety since such details were not available within the administrative databases. As a general rule, NK1 receptor antagonists appear to be well tolerated in paediatric populations although the possibility for somnolence, headaches or alterations in liver enzymes has been described within the context of oncologic therapy. Hepatotoxicity was not reported within the paediatric CVS reviews. Therefore, based on the existing literature it appears that aprepitant is safe. However, systematic safety data are needed particularly for repeated or chronic use.

Methodological Considerations and Limitations of Included Studies: Each of the studies included in this review had important methodological limitations due to their study designs. The study conducted by Thavamani et al., while large, was retrospective and non-randomized thereby creating the likelihood of confounding by indication. More specifically, confounding by indication could occur because more severely affected CVS patients may have preferred to receive aprepitant. The single case cannot establish causality and is subject to publication bias (only positive cases tend to be reported). Overall, the evidence base is limited by retrospective designs, small sample sizes, heterogeneity in outcome measures, and reliance on anecdotal reports, confounding by indication, inconsistency of outcome measures, and reliance on retrospective and anecdotal data. Formal GRADE assessment was not performed because no randomized or comparable controlled studies were available.

Discussion:

This scoping review identified only three studies of aprepitant in pediatric CVS: one large retrospective cohort, one small retrospective series, and one case report. The controlled cohort (Thavamani et al.) did not demonstrate a reduction in 7-day readmissions with aprepitant (1). However, as a population study it measured a surrogate outcome (readmission) rather than direct symptom relief, and patients receiving aprepitant had more severe illness[1]. By contrast, the smaller case series (Cristofori et al.) reported that the majority (≈80%) of children refractory to standard therapy improved with either abortive or prophylactic aprepitant[10], with significant reductions in episode frequency, hospitalizations, and improved functional outcomes. The single published case echoed these positive results[11]. Taken together, the available evidence describes variable outcomes, with some studies reporting symptomatic improvement, while the largest

dataset did not demonstrate benefit in short-term healthcare utilization as it seems consistent with what adult experienced with similar therapies keeping in line with the consensus recommendations [12]. Important consideration is that no serious safety concerns emerged in the pediatric cases; adverse events were mild and comparable to known effects of NK1 antagonists[10]. Although the available data does not allow inference regarding the efficacy of aprepitant in pediatrics population with CVS. Observed improvements seen in literature may reflect the natural relapsing and remitting course of the disease, placebo effects, or concurrent supportive interventions. The absence of randomized comparisons substantially limits internal validity.

Recent clinical guidelines mention NK1 receptor antagonists as a potential option for refractory pediatric CVS; however, these recommendations are explicitly conditional and based on low certainty evidence, largely derived from the same observational studies summarized in this review. Interpretation of efficacy is further complicated by substantial heterogeneity in outcome measures across included studies.

Limitations: This review is limited by the extremely small number of available studies and the uniformly low methodological quality of the evidence. No randomized controlled trials were identified. Heterogeneity in dosing strategies, treatment timing, and outcome definitions further limited comparability and precluded the analysis. Finally, publication bias is likely, as negative case experiences may be underreported.

Implications: Despite limitations, the available literature indicates that aprepitant has been used in refractory pediatric CVS, with variable reported outcomes. for pediatric CVS, especially in severe or refractory cases. The recent 2025 NASPGHAN guidelines conditionally recommend abortive use of NK1 antagonists based on indirect evidence and expert opinion[12]. Clinicians might consider aprepitant when first-line agents fail, recognizing that insurance coverage and cost can be barriers. The drug's pharmacology and theoretical risks warrant caution. Families should be counseled about limited evidence and monitored for side effects. No studies from Pakistan or South Asia were identified, highlighting a regional gap in the literature and the need for context-specific research.

Future Research: There is an urgent need for prospective studies. A randomized controlled trial or even a well-designed cohort study could compare aprepitant to placebo or standard care in refractory CVS. Important questions include optimal dosing especially for children, duration of prophylaxis, and long-term outcomes. Comparative effectiveness should be explored. Patient reported outcomes and quality-of-life measures should be included. Given CVS's overlap with migraine pathophysiology, mechanistic studies could identify biomarkers predicting aprepitant response.

Conclusion: Current evidence on aprepitant use in pediatric cyclic vomiting syndrome is limited, heterogeneous, and primarily derived from observational and anecdotal reports. While some studies describe symptomatic improvement, the largest available dataset did not demonstrate benefit in short-term outcomes. The existing evidence is insufficient to guide routine clinical use. Prospective studies and controlled trials are needed to clarify the role of aprepitant in Pediatrics population.

Conflict of Interest:

The authors declare no conflicts of interest in conducting this study.

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PAKISTAN JOURNAL OF GASTROENTEROLOGY

Original Article

Evaluating the Role of Endoscopic Retrograde Cholangiopancreatography (ERCP) in the Diagnosis and Management of Biliary Ascariasis: Clinical outcomes and its Efficacy

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Abstract:

Background: Biliary ascariasis, caused by *Ascaris lumbricoides* invasion of the biliary tree, is a significant health concern in tropical regions like Pakistan. Although imaging plays a diagnostic role, Endoscopic Retrograde Cholangiopancreatography (ERCP) is increasingly employed for both diagnosis and treatment due to its minimally invasive nature.

Objective: This study aimed to evaluate the clinical efficacy, technical success, and outcomes of ERCP in managing biliary ascariasis.

Methods: A retrospective review of 29 cases of biliary ascariasis managed with ERCP between September 2017 and September 2024 was conducted at a tertiary care center in Karachi. Data on demographics, clinical presentation, imaging findings, procedural details, and outcomes were analyzed using SPSS v26.

Results: ERCP achieved a 100% technical success rate with no significant procedure-related complications or mortality. The most common symptoms were abdominal pain (100%) and jaundice (55.17%). Ultrasound identified worms in 41.3% of cases, while ERCP confirmed all. Adjunctive mebendazole therapy was administered post-procedure.

Conclusion: ERCP is a highly effective and safe modality for diagnosing and managing biliary ascariasis, reducing the need for invasive surgery. It should be considered the first-line intervention in endemic areas, supported by ant parasitic therapy to minimize recurrence.

Keywords: Biliary Ascariasis, Endoscopic Retrograde Cholangiopancreatography (ERCP), Ascaris lumbricoides, Parasitic biliary disease, Worm extraction, Abdominal ultrasound, Jaundice, Tropical infections, Non-surgical management, Diagnostic endoscopy.

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Introduction:

Background:

Biliary ascariasis is a major health condition; it occurs when the Ascaris lumbricoides settles in the bile ducts. This disease tends to prevail in tropical and subtropical regions, specifically because these countries have poor sanitary conditions. It comes with a set of severe complications, for instance, pancreatitis,

obstructive jaundice, cholangitis and biliary colic.

Ascaris eggs are present in contaminated food or water. The larvae hatch once it reaches the intestine and then travels through the lungs or the liver via the bloodstream route and eventually return back to the intestinal tract. Complications like inflammation and mechanical obstruction of the biliary system can also occur, if the adult worms invade the region[1]. This can result in a number of different conditions such as acute pancreatitis, where the pancreatic duct is obstructed[2].

Around the world, biliary ascariasis is considered as the second most common cause responsible for acute biliary symptoms, after cholelithiasis[3]. It is often associated with "Oriental Cholangiohepatitis", which is a collective term for chronic anemia, malnutrition and recurrent cholangitis[4]. Imaging techniques like stool examinations, CT scans and ultrasound are considered as gold standard for its diagnosis, although its management plan requires the manual removal of these worms via minimal invasive procedures[5].

Research states that Ascaris lumbricoides has a high prevadsawlence in regions like Latin America, Sub-Saharan Africa and South Asia, affecting around 1.2 billion people around the world; while it serves as a cause of death for 60,000 people annually[6]. Conventionally, surgical interventions were used for the elimination of biliary ascariasis, however, minimally invasive methods like ERCP (Endoscopic Retrograde Cholangiopancreatography) are now being increasingly used as an alternative due to their safety and efficacy[7]. However, there is yet limited data present in Pakistan which is specific to the treatment of biliary ascariasis. Hence to fill in this gap, this research would access the technical success rates and the clinical outcomes associated with ERCP as a treatment option for biliary ascariasis.

Statement of the Problem and Rationale:

Biliary ascariasis presents with a variety of symptoms and has potential complications, posing a therapeutic as well as a diagnostic challenge. While using conventional invasive surgical methods, the mortality and morbidity rates per patient would be quite high. However, there is no such date present which can account for the morality or morbidity rates for non-surgical techniques like ERCP, hence a definite need to establish this study. Our study aims to reduce the use of invasive surgical methods, while decreasing patient outcomes by evaluating the efficacy and safety of ERCP as a foremost treatment for biliary ascariasis[8].

Conclusion:

Having a deeper clinical insight to the role of ERCP as a treatment for biliary ascariasis would be an essential factor for healthcare workers in the Pakistani region, especially because such parasitic infections yet serve as a significant health challenge. The findings of this study will provide a critical view of diagnostic as well as treatment protocols to treat biliary ascariasis, focusing on overall patient well-being.

Purpose of the Study:

To access effectivity, technical success rates, clinical features and complications of using ERCP as a diagnostic as well as a treatment plan for biliary ascariasis.

Objectives:

1. To access the clinical features and demographics of biliary ascariases infected patients
2. To evaluate the technical success percentage of ERCP as a management plan for biliary ascariasis.
3. To determine any complications that are associated with ERCP treatment in biliary ascariasis infected patients
4. To analyze the effectiveness of ERCP as a non-surgical method in decreasing

the need of traditional surgical methods.

Methodology:

Study Design: This will be a retrospective study based on case series
Study Duration: September 2017 to September 2024.
Study Setting: Sindh Institute of Advanced Gastroenterology (SIAG), a tertiary care setup in Karachi, Pakistan.
Population: Patients who underwent ERCP for biliary ascariasis
Sample size: 29 cases series

Literature Review:

Ascaris lumbricoides (A. lumbricoides) is a type of helminth that causes ascariasis, a neglected tropical disorder. This is a public health concern globally that has been reported to impact over 1 billion people or approximately 24% of the world's population [9]. According to the World Health Organization (WHO), the sub-Saharan regions of Africa, China, South America, and Asia have some of the most reported infections. These parasitic infections majorly impact people from low socio-economic backgrounds who live in stark poverty in tropical and sub-tropical countries where clean water and proper sanitation facilities are not readily available[10] .

Moreover, as time passes, there has been a significant shift in the diagnostic and therapeutic approaches to biliary ascariasis with increasing focus on endoscopic techniques. Endoscopic retrograde Cholangiopancreatography (ERCP) is recognized as one of the most crucial diagnostic and therapeutic procedures for A. lumbricoides, particularly when other treatment options or imaging studies have been proven to be failed[11,12]. Even in some cases where Ultrasound and Magnetic Resonance. Cholangiopancreatography (MRCP) were not able to identify worms in the bile duct, ERCP remains capable of clearly identifying worms in the duct, facilitating treatment and worm extraction.

One temporal case reported the extraction of a wriggling parasite emerging from the ampulla during an ERCP surgery[11]. Another study showed that ultrasound could only visualize the presence of biliary ascariasis in 54%-85% of the cases, while ERCP was able to detect its position and reported ERPC as the most reliable method used for bile duct invasion confirmation in instances when the worms were not protruding into the duodenum[13]. Moreover, ERCP also aids in the differentiation of biliary ascariasis from other pathologies like choledochal sludge or tumours, even some which were previously described as cholangiocarcinoma [13].

In addition to diagnostic purposes, endoscopic retrograde Cholangiopancreatography (ERCP) plays a pivotal role in the treatment of biliary ascariasis, simultaneously providing access and treatment for the condition. As for the surgical adjunctive control of biliary ascariasis, ERCP plays an essential role since it permits immediate biliary decompression in about 65% to 86.7% of cases during sphincterotomy and Dormia basket extraction [12]. In another prospective study recruited 98 patients were recruited, 23.5% responded to treatment with only albendazole, while ERCP with worm removal achieved a success rate of 86.7% of the remaining cases [12]. Moreover, while most cases are managed by ERCP with no need for surgery, emergency surgery is occasionally required on the day for patients with persistent worms post-ERCP [14].

The literature also highlights an increasing awareness of long-term outcomes and the risk of recurrence. Successful endoscopic retrograde Cholangiopancreatography (ERCP) not only offers diagnostic clarity and effective treatment but also leads to rapid symptom

relief and normalization of liver enzyme levels. Long-term results of ERCP treatment for biliary ascariasis show that, while ERCP is very effective for initial biliary clearing (with success rates of roughly 86.7%), biliary events may return. A prospective study found that 24.5% (24 out of 98) of patients developed recurrent biliary problems, such as cholangitis or obstructive jaundice, throughout a 16-month follow-up period. The probability of recurrence was independently associated with lower socioeconomic position and longer duration of follow-up, demonstrating the impact of environmental and hygiene-related factors on reinfection rates [15]. Case reports further support that patients treated with ERCP followed by albendazole often experience rapid symptom relief and normalization of liver function tests, with sustained symptom resolution on follow-up[16,17].

In one notable case at Civil Hospital Karachi's S4 Ward in 2020, a female patient underwent ERCP for biliary obstruction and was found to have a remarkably high parasitic load, with 22 Ascaris worms extracted during the procedure. This rare and severe presentation underscores the clinical burden of biliary ascariasis in endemic regions and highlights the critical role of ERCP in both diagnosis and therapeutic management, as further explored in this study.

However, some studies have reported post-ERCP recurrence rates of 4% in females and 1% in males, suggesting that demographic and local factors may also play a role in long-term success [18]. Overall, ERCP is a safe and effective strategy for immediate therapy of biliary ascariasis; however, long-term outcomes depend on managing reinfection concerns and ensuring continuing follow-up[12,18].

Data Collection Method:

This was a retrospective research analysis which aimed to evaluate the efficacy of ERCP for biliary ascariasis. Prevalence of biliary ascariasis was evaluated out of 6070 patients who underwent ERCP procedure over a time span of September 2017 and September 2024, resulting in a total of 29 cases which were included in the study. Medical records if these 29 cases were further reviewed. Data was collected including variables like age, gender, comorbidities, previous medications or prior surgical procedures, indications for ERCP, clinical symptoms, lab results, imaging results and past treatment approaches.

All ERCP procedures were performed by specialized gastroenterologists with over two decades of experience, along with a specialized team with highly trained endoscopists. Written informed consent was obtained from all patients. The majority of ERCPs were conducted under conscious sedation using nalbuphine and midazolam, while a few required general anesthesia, all under the supervision of a senior anesthesiologist. Intravenous cephalosporins were administered as prophylactic antibiotics before the procedure.

ERCP was performed using a standard technique with an adult therapeutic duodenoscope (TJF 180: Olympus). Urograffin, an ionic contrast medium, was used to opacify the biliary and pancreatic ducts. Post-procedure, patients were monitored for a minimum of four hours, and those with complications were admitted under the care of a gastroenterologist or consultant surgeon. Complications were classified based on Cotton's criteria.

The primary diagnostic modality was abdominal ultrasound. Technical success was defined as obtaining diagnostic information or successfully performing endoscopic therapy. Data recorded included procedure indications, diagnostic and therapeutic findings, fluoroscopic observations, treatment measures,

procedural success, and complications. All patients diagnosed with biliary parasitosis underwent deworming therapy.

For follow-up, patients were encouraged to return for evaluation, and those who did not were contacted via telephone for a subjective follow-up. The study received approval from the hospital's institutional review board. Statistical analysis was conducted using SPSS version 26 (SPSS Inc., Chicago, IL, USA), employing descriptive and frequency analysis.

Inclusion/Exclusion Criteria

Inclusion Criteria:
- Patients diagnosed with biliary ascariasis.
- Cases where ERCP was performed successfully.

Exclusion Criteria:
- Patients with incomplete medical records.
- Cases with coexisting severe comorbidities unrelated to biliary disease.

Data Collection Tool:

Data were extracted from electronic medical records and included demographics, clinical features, laboratory findings, imaging results, and procedural outcomes.

Study Variables:

Independent Variables: Age, gender, clinical symptoms, and imaging findings. Dependent Variables: Technical success of ERCP, complications, and patient outcomes.

Data Analysis Procedure:

Data were analyzed using SPSS version 26. Descriptive statistics (mean, standard deviation) were calculated for continuous variables, while frequencies and percentages were used for categorical data. Chi-square tests assessed relationships between clinical features and outcomes.

Results:

Patient Characteristics

ERCP was conducted in 6070 patients between September 2017 and September 2024. In 29 cases (6070), the patients were diagnosed as having biliary ascariasis. Among them, 7(24.1%) were males, 22(75.9%) were females and majority of the patients were from Karachi, i.e., 25(86.2%) as displayed in Table 1.

Table 1. Demographic Characteristics of Patients with Biliary Ascariasis (n=29)

Variable	Value
Age	28.5±4.83
Gender	
Male	7 (24.1%)
Female	22 (75.9%)
Geographic origin	
Karachi	25 (86.2%)
Hyderabad	2(6.9%)
Sukkur	2(6.9%)

Clinical Presentation:

All patients had experienced abdominal pain; other symptoms were variable and ranged in duration from one week to 3 years.

The other clinical findings were reported as shown in Table 2 which can be summarized as:

Jaundice was observed in 16 cases (55.17%)

Hyperbilirubinemia in the same 16 patients, mean bilirubin level 7.7 mg/dL (range 2.16-26.7 mg/dL)

Originally raised ALP in 27 patients (93.1%), levels ranged from 140 to 2670 U/L (mean 448.4 U/L).

Imaging Findings (Refer to Table 2 for complete details)

Ultrasound findings revealed:

- 12 patients (41.3%) were found to have worms
- A large common bile duct (CBD) in 25 (86.2%) of patients
- Enlarged IHD (intrahepatic duct) 4 (13.8%)

Endoscopic observations on ERCP were as follows:

- A single linear filling defect in 18 pts (62.1%) due to worm wads causing severe CBD dilation.

Table 2. Imaging and Laboratory Findings(n=29)

Variable	Frequency n(%)%)
Worm detected on ultrasound	12 (41.3%)
Dilated CBD on ultrasound	25 (86.2%)
Dilated intrahepatic ducts	4 (13.8%)
Elevated ALP	27 (93.1%)
Mean ALP (U/L)	448.4
Mean bilirubin (mg/dL)	7.7

ERCP Procedure and Outcomes:

ERCP was successfully conducted in all patients and achieved 100% success. Worm extraction techniques used were balloon trawling and grasping forcep. Additional findings during ERCP included CBD stones in 5 patients (17.2%), Cholangitis in 2 patients (6.9%).. There were no significant procedure-related complications found, and no mortality was recorded. All patients received mebendazole therapy followed by post-procedure.

Discussion:

Biliary ascariasis is a parasitic infection of the biliary tree that is rare but has public health importance within certain populations. Commonly seen in tropical and subtropical areas where sanitation falls short, this infection is caused by Ascaris lumbricoides, a roundworm that occupies the small intestine and may migrate through the ampulla of vater into the biliary system (cystic duct or common bile duct). Even though it is relatively rare, biliary ascariasis is one of the most common forms of biliary obstruction in endemic areas after cholelithiasis [19].

In this study, we reported the clinical outcomes and technical success of ERCP in a subset of patients with biliary ascariasis. Most patients in this cohort who were infected with biliary ascariasis were female, 22 (75.9%), with a mean age of 28.5±4.83 SD, which is consistent with primary literature on biliary ascariasis prevalence, suggesting women are more affected [20]. This fact is likely linked to the greater exposure to contaminated soil and water that women in many developing regions endure [21]. Also, progesterone, while relaxing the smooth muscles of the bile duct, may elevate the risk of infection that facilitates the ingress of worms into the bile duct [22].

The most common symptoms for participants in this study were biliary colic (93.1%), followed by jaundice (55.17%) and nausea (30.7%). These symptoms are consistent with those of biliary ascariasis, where adult Ascaris worms cause a mechanical obstruction to the bile flow, leading to biliary colic, jaundice, and in some cases, severe cholangitis or pancreatitis [23]. Our findings are consistent with existing literature, which indicates that biliary ascariasis is a prevalent cause of biliary obstruction in tropical regions, often leading to destructive recurrent cholangitis and/or pancreatitis. [24]

Ultrasound is the most accessible and invaluable method of diagnosis regarding the presence of biliary ascariasis, especially in endemic areas. In our study, 41.3% of cases visually showed the presence of the worms on ultrasound, which supports other reports regarding the usefulness of ultrasound in diagnosing this condition [25]. While in some cases, worms were found by ERCP, which raises concerns regarding the diagnostic accuracy between ERCP and ultrasound. Furthermore, literature has reported limitations of using ERCP, specifically the long-term outcome. ERCP is still the most preferred

method for diagnosing and treating biliary ascariasis, as reported [26].

ERCP is of utmost importance in bile duct ascariasis since it permits both the visualization of the biliary ascariasis and the extraction of the worms with specialized instruments. In this cohort, endoscopic removal was successful in each case, and multiple instruments, including biliary extraction balloon, and grasping forceps were employed to grasp the worms safely. These results corroborate with other studies that have concluded ERCP provides high rates of technical success, 90 to 95% of worm removal from the bile ducts, and with a low rate of complications [27]. In our study, patients with concomitant biliary stones experienced effective outcomes when endoscopic sphincterotomy of the biliary sphincter was combined with balloon sweeping, which facilitated the removal of both worms and stones, resulting in symptom relief and optimal biliary drainage [28].

Additionally, administering mebendazole during the post-operative period proved effective for both deworming patients and preventing future infections. In several studies, patients who received a three-day course of mebendazole after endoscopic worm removal showed no recurrence of infestation on consistent follow-up [29]. This emphasizes that routine administration of anthelminthic therapy, such as mebendazole or albendazole, following endoscopic treatment should be part of the standard management for biliary ascariasis to may reduce the chances of reinfection and also it may reduce the morbidity and mortality risks linked to surgical interventions.

While ERCP is acknowledged as an effective method for the treatment of biliary ascariasis, it possesses limitations in treating complex cases like severely dilated bile ducts or those with multiple worms, that may require more advanced interventions, such as endoscopic papillary balloon dilation (EPBD) or multiple sessions of worm extraction and appropriate post procedural management [26].

We believe that ERCP can be regarded as a safe and effective, less invasive treatment option for biliary ascariasis and can serve as an invaluable intervention option with high prevalence of disease and regions with low socioeconomic profiles. Although it cannot be an exclusive treatment option for the disease, considering its limitations with complex cases, it can be regarded as the first-line treatment option for managing infection, especially in cases with an anticipated low rate of post-procedural complications, and less severe cases.

Conclusion:

In conclusion, ERCP proves to be an effective and safe modality for the diagnosis and management of biliary ascariasis, offering a non-surgical approach with high technical success rates and minimal complications. Our study demonstrates that ERCP can successfully remove *Ascaris lumbricoides* from the biliary tree, leading to the immediate resolution of symptoms such as biliary colic and jaundice. The procedure is particularly beneficial in areas with high prevalence of ascariasis, where surgical options may be limited or more invasive.

Given its ability to provide both diagnostic and therapeutic benefits, ERCP should be considered the procedure of choice in managing biliary ascariasis. In addition, adjunctive therapy with anti-parasitic medications such as mebendazole is essential to prevent reinfection and ensure long-term resolution. The findings of this study support the growing body of evidence advocating for the use of ERCP as a first-line treatment for biliary ascariasis, providing a promising alternative to traditional surgical interventions. Further research with larger patient cohorts is necessary to validate these findings and to explore potential improvements in ERCP techniques and post-procedure management. Given the endemic nature of ascariasis in many

regions of the world, optimizing the diagnostic and therapeutic strategies for biliary ascariasis will play a critical role in improving patient outcomes and reducing morbidity associated with this parasitic infection.

Budget:

No expenses are required for this research

Conflict of Interest:

The authors declare no conflicts of interest in conducting this study.

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PAKISTAN JOURNAL OF GASTROENTEROLOGY

Case Report

Fasciola hepatica infestation masquerading as hydatid cysts of the liver

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Abstract:
Human hepatic fascioliasis has been reported in 81 countries, some of which are endemic areas. Fascioliasis is a re-emerging food-borne parasitic zoonosis which presents with nonspecific clinical symptoms. Hepatobiliary fascioliasis is one of the rare but important parasitic infections in endemic areas such as Pakistan. Definitive diagnosis requires demonstration of parasitic ova in stool which may often be elusive. Imaging plays a crucial role in raising the possibility of this diagnosis early in the disease course. Contrast enhanced CT scan was performed in an 18 years old female with recent history of hydatid cyst excision and sub-hepatic drain placement, who now presented with increased biliary output. Endoscopic retrograde cholangiopancreatography was performed and this liver parasite was removed.

Keywords:
Fasciola Infection, ERCP, Hydatid Cyst

How to Cite this article:
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Introduction:

Over 3 million people globally suffer from the parasite illness Fasciola hepatica. In Latin America, Eastern Europe, the Far and Middle East, it occurs more commonly. It may result in pancreatitis, cholecystitis, cholangitis, and biliary blockage. There have been reports of human hepatic fascioliasis in 81 countries, including endemic ones like Bolivia, Peru, Ecuador, Iran, Egypt, Turkey, China, Vietnam, Nepal, Pakistan, and Syria. Confirmed incidences in North America are linked to immigrants or foreign workers from endemic regions. Humans may unintentionally become hosts of Fasciola hepatica by ingesting metacercarciea through contaminated food or drink.

Case Summary:

18 years old female presented with a complaint of increased drain output of about 1500ml/day. She has a past history of hydatid cyst excision from a local hospital few days back, followed by sub hepatic drain placement. Her lab workup, including liver function test, renal function test, thyroid function test, serum electrolytes, was normal. Complete blood count showed normal leukocyte count with 6% eosinophil. Her abdominal imaging showed defects involving the segment VII and VIII of the liver. There was a well-defined fluid attenuated area along resected margin, involving the sub-capsular area of segment VII having internal septations, tracking inferiorly along the peri-hepatic space and appear to be closely approximated to right intrahepatic biliary channels. There were few prominent lymph nodes at porta hepatis. Common bile duct was slightly prominent with thick walls. Another multiloculated cystic area with internal septations was noted, involving the body and tail of pancreas. Findings were consistent with hydatid cyst.

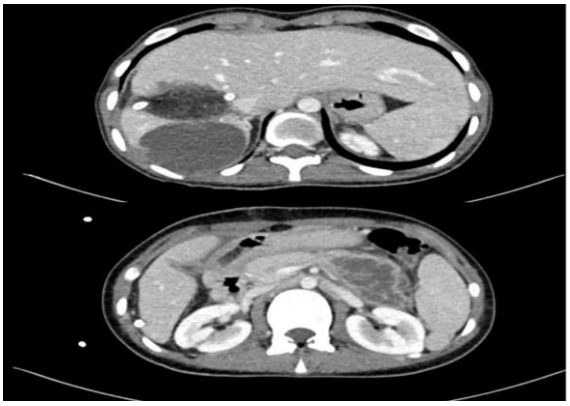

Figure I: Contrast enhanced CT showing fluid attenuated area along resected margin in segment VII.

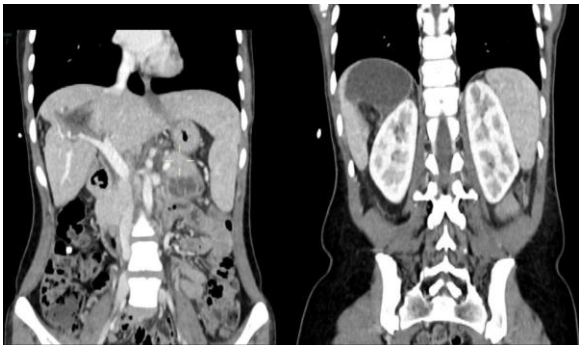

Figure II: Coronal view of CECT Abdomen showing dilated biliary channels (left) and fluid filled area in segment VII (Right).

Endoscopic retrograde cholangiopancreaticography was planned which showed deformed ampulla due to previous history of attempted ERCP from local hospital. Biliary cannulation was challenging in this patient. Contrast was injected which showed leak at common hepatic duct. Multiple balloon trawl done which showed extrusion of liver parasite. 7Fr x 12cm plastic stent was placed in CBD across leak.

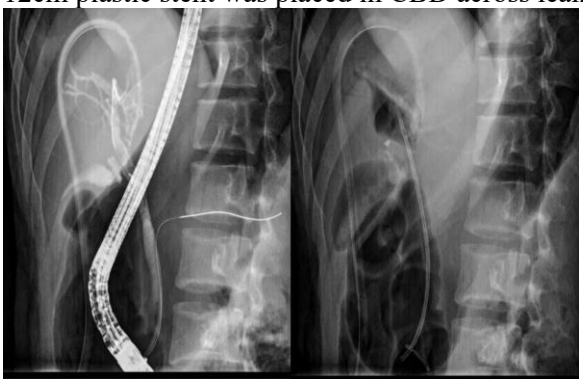

Figure III: ERCP Cholangiogram showing bile leak (left).

Parasite was retrieved by suction and sent for histopathology. Fragments of the worm confirmed Fasciola hepatica.

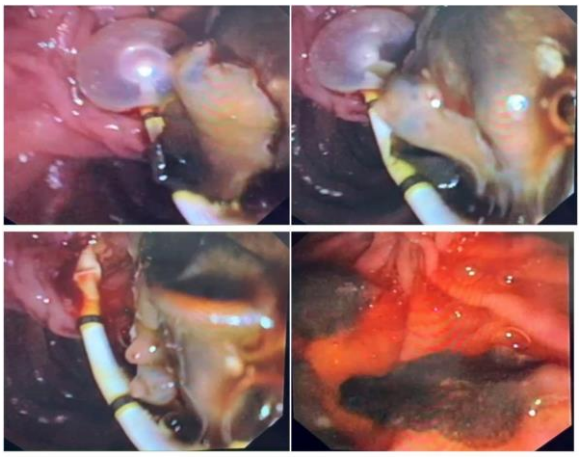

Figure IV: Endoscopic Retrograde Cholangiogram showing extrusion of liver parasite during balloon trawl.

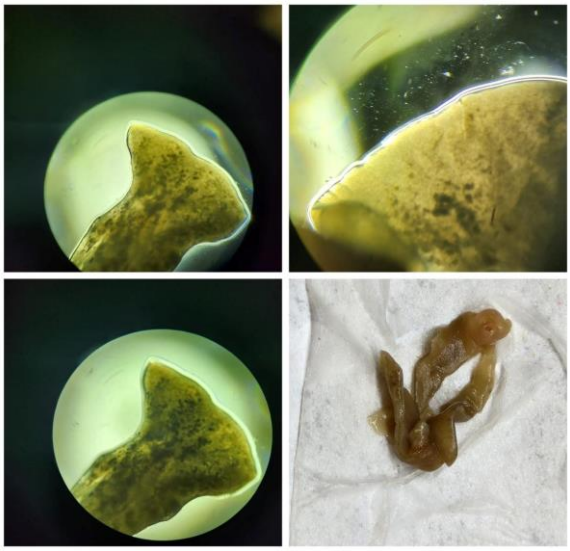

Figure V: Gross appearance of Liver fluke

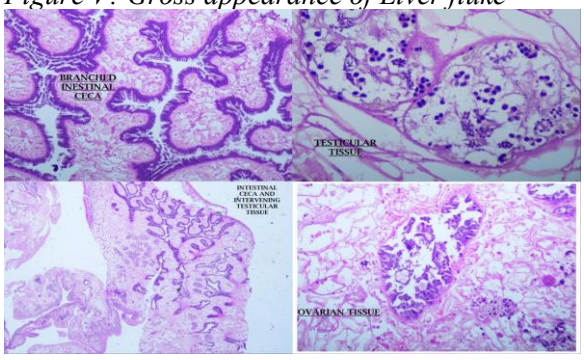

Figure VI: Histopathology slide of fragments of Fasciola Hepatica.

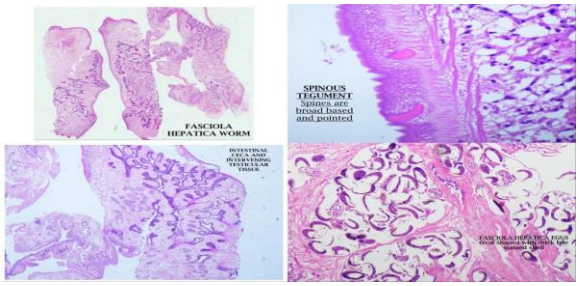

Figure VII: Histopathology slides of fragments of Fasciola Hepatica

Nitazoxanide 500mg twice daily for 7 days was started. Her drain output decreased significantly to 50ml/day.

Discussion:

In our case, we report a confirmed case of hepatic fascioliasis in a young woman, presented with increase biliary output after hydatid cyst excision and sub-hepatic drain placement. This case study emphasizes the value of cross-sectional imaging in both the diagnosis and distinction of hepatic fascioliasis from other liver illnesses that present with strikingly similar radiological and clinical features.

There have been reports of human infections caused by the liver fluke F. hepatica in various regions of the world where sheep are raised especially from Australia, China, South America, Europe, and Africa [1]. Water plants can be a cause of hepatiotic fascioliasis infection to humans with a wide range of clinical presentation, from an infection without symptoms to severe liver cirrhosis. Highly sensitive serologic tests FAST-ELISA, indirect hemagglutination, complement fixation, and indirect immunofluorescence (IIF), counter electrophoresis, as well as double diffusion are critical for the diagnosis of acute fascioliasis but may cross-react with other diseases caused by parasites, such as echinococcus relatively common in Nepal[2].

Hepatobiliary fascioliasis in humans is diagnosed using a combination of specific parasitological tests, indirect immunological testing, and cross-sectional imaging modalities including ultrasound, CT, and MRI, provided that a suitable clinical situation is present. The degree of suspicion, the disease's stage, and the availability of resources and knowledge are some of the variables that may affect the diagnostic technique. In this instance, the patient's CT scan, revealed very suggestive results for hepatic fascioliasis, which the ELISA test verified [3].

F. hepatica often manifests as a hypo dense lesion on CT scan pictures and a hypo echoic lesion on ultrasound imaging [4]. 180 million individuals are at risk and 2.4 million people worldwide have this zoonotic disease. The illness progresses in two stages: acute and chronic. The parasite's acute phase spans the hepatic invasion period, while its chronic phase is spent in the bile ducts. Because of the obstruction in the bile pathways, symptoms such as jaundice, cholangitis, pancreatitis, nausea, anorexia, and cholecystitis may manifest during the chronic phase of the parasite [5]. Because of this, the patient's history of consuming watercress and residing in an endemic location may provide diagnostic cues.

Cholangitis and hepatitis, liver abscess, brucellosis, cholecystitis, biliary tract stones, and primary and secondary liver cancers are among the conditions that fall within the category of differential diagnosis but fascioliasis hepatica is often misdiagnosed, resulting in needless surgery. Seldom is a liver biopsy for tissue diagnosis carried out; the results may necrosis, acute and/or chronic inflammatory alterations, debris, and sometimes small pieces of migratory larvae[2].

The main course of treatment is anthelminthic medication. Patients who do not respond well to treatment or who exhibit signs of acute cholangitis and bile duct obstruction may need to have their biliary system decompressed or stented, or they may need endoscopic parasite extraction. Cholecystectomy is typically required when the gallbladder is involved [6].

It is reported in the literature that ERCP is used in the diagnosis and treatment of patients in the chronic phase. In our case, we performed ERCP and the parasite was removed from the bile duct.

Conclusion:

In this case report, we emphasized that fascioliasis might manifest itself through unusual symptoms with no specific clue as to its underlying cause. They might be confused with liver abscess, malignant liver mass or complex hepatic cyst. By doing so, the problem can be diagnosed earlier, therapeutic interventions can begin sooner, and

invasive diagnostic tests can be avoided. ERCP provides important benefits both in the diagnosis and treatment of Fasciola hepatica. Fascioliasis can be prevented with public education and environmental precautions such as avoiding the consumption of contaminated water and plants.

Ethical statement:-

Consent taken from patient to report his case.

Funding Disclosure:-

None

Conflict of interest:-

None

Author's Contribution:

FA: Conceived and designed the study, involved in data collection, performed statistical analysis and writing the manuscript.

MA, ZA, MRJ, AF: Collected the data, critical review and preparation of manuscript.

All authors have read, approved the final manuscript and are responsible for the integrity of the study.

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PAKISTAN JOURNAL OF GASTROENTEROLOGY

Case Report

Pancreatic pseudocyst following enteric fever–associated acute pancreatitis in a child: successful ultrasound-guided percutaneous drainage

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Introduction:

Acute pancreatitis (AP) is an inflammatory condition of the pancreas, most often presenting with pain in the epigastric region, radiating to the back, and elevated levels of pancreatic enzymes in the blood. While AP is considered a rare condition in the pediatric population, recent studies indicate an increasing trend in its incidence over the past few years (1). This rising trend underscores the importance of understanding the clinical manifestations, causes, and potential complications of AP in pediatric patients. One of the etiologies of pancreatitis include infective agents. In a patient of fever with abdominal pain in developing countries, the availability bias keeps enteric fever as a foremost differential, Enteric fever however causes involvement of various organ systems like gastrointestinal, muscular, nervous system and has various skin manifestations as well,(2) although rare same enteric fever can be associated with gastrointestinal complications including intestinal hemorrhage, intestinal perforation, hepatic abscess, acute cholecystitis, splenic rupture, hepatitis and a rare but documented one i.e.
enteric pancreatitis that has been discussed in our case report.

One of the less common complications of AP is a pancreatic pseudocyst (PP), characterized by a fibrous-walled cavity containing necrotic tissue, pancreatic enzymes, and fluid (3). The incidence of developing a PP in children following AP is reported to be approximately 10-23% (4). The development of a PP signifies a collection of pancreatic secretions in a localized area encapsulated by fibrous and granulation tissue, lacking a true epithelial lining. The causes of AP in pediatric patients differ from those in adults, where excessive alcohol intake and gallstones are the primary risk factors (5). In children, common causes include biliary or obstructive factors, medications, and systemic diseases. Less frequent etiologies include abdominal trauma, bacterial and viral infections, and metabolic and genetic disorders (5). Notably, a significant proportion of cases, around 15-30%, are idiopathic. This case report aims to present a unique instance of PP formation in a pediatric patient following acute pancreatitis that was likely triggered by enteric fever, a rare association, and its successful management using an anterior percutaneous drainage approach.

CASE REPORT:

A 4-year-old previously healthy girl presented to the paediatric gastroenterology clinic at Lahore

General Hospital with bilious vomiting, epigastric abdominal pain radiating to the back, and recent treatment for culture-proven enteric fever. She denied trauma, drug use, or family history of pancreatitis. Examination revealed mild upper abdominal tenderness without guarding or mass.

Laboratory results showed elevated serum amylase (252 U/L) and lipase (178 U/L), along with leucocytosis and raised CRP, Liver function tests, serum triglycerides, calcium, and abdominal ultrasound showed no alternative cause of pancreatitis. Transabdominal ultrasonography demonstrated blurred pancreatic margins; CT imaging confirmed interstitial oedematous pancreatitis with peripancreatic fluid. A diagnosis of acute pancreatitis secondary to enteric fever was made.

She was managed with IV fluids, analgesics, nasogastric decompression, and antibiotics. Oral feeding was reintroduced on day six. She was discharged once clinically stable.

Two weeks later, the patient returned with early satiety and a non-tender, firm epigastric mass. CT imaging revealed a 9.2 × 8.8 × 7.4 cm thin-walled pseudocyst anterior to the pancreatic body and tail. Given the cyst's size and symptomatic nature, CT- and ultrasound-guided anterior percutaneous drainage was performed. Drainage fluid was analysed for enzyme content and infection. Culture of the drained cyst fluid grew *Salmonella Typhi*, confirming persistent enteric infection and supporting a direct infectious etiology of the pancreatitis and pseudocyst formation.

Post-procedure recovery was uneventful. The patient was monitored for complications including bleeding, infection, and fistula formation. Follow-up imaging at 8 weeks and again at 6 months confirmed complete pseudocyst resolution with no recurrence. The child remained clinically well with no evidence of pancreatic insufficiency.

DISCUSSION:

Typically, a localized *Salmonella* infection of the pancreas arises from *Salmonella choleraesuis* bacteraemia but can also result from *Salmonella typhimurium*-induced gastroenteritis or enteric fever caused by *Salmonella typhi* that can eventually lead to formation of a pancreatic abscess often occurs as a dreadful complication of pancreatitis secondary to enteric fever. (6) It has been demonstrated in studies by Hermans *et al*.,(7) and Renner *et al*.,(8) that raised amylase and lipase levels is seen in about 50, and 62% of enteric fever patients, respectively without having clinical or radiological evidence of acute pancreatitis. Baert *et al*. explained several mechanisms leading to hyperamylasemia including reduced excretion secondary to renal and hepatic dysfunctional physiology in enteric fever and immune mediated inflammation rendering increased absorption of macromolecules like amylase.(9) In this case patient not only had culture proven enteric fever but also had radiological evidence of pancreatitis that later on developed unprecedented complication of pancreatic pseudocyst necessitating aggressive and invasive management plan. Notably, cyst fluid culture in our patient yielded *Salmonella Typhi*, providing microbiological confirmation of direct pancreatic involvement rather than a coincidental association. Such confirmation is rarely documented in pediatric cases and strengthens the causal link between enteric fever and both pancreatitis and pseudocyst formation.

The most common aetiologies of paediatrics acute pancreatitis include trauma, systemic infections, drugs, gallstones, hereditary, and organic acidemias. The complications of acute pancreatitis can be divided as local or systemic according to the revision of the Atlanta classification, 2012 including two discrete morphological phenotypes delineated via abdominal contrast-enhanced CT (CECT) or contrast-enhanced MRI: acute peripancreatic fluid collection (APFC) and acute necrotic collection (ANC).

Management of paediatric pancreatic pseudocyst is controversial, ledging between conservative management and surgical management. Conservative management with measures such as total parenteral nutrition and octreotide acetate is preferred for acute paediatric pancreatic pseudocysts that measure less than 5 cm as there is an increased chance of spontaneous resolution in 6-8 weeks' time. Certain minimally invasive techniques such as laparoscopic, percutaneous, and endoscopic drainage are preferred modalities with very favourable results if expertise and logistics are available having the selection of a surgical approach for drainage or excision is contingent upon the anatomical characteristics of the pseudocyst.

Khizar *et al*. outlined in their study that both endoscopic drainage (ED) and percutaneous

drainage (PD) were associated with adverse effects but further analysis between ED and PD had comparable outcomes regarding technical success, clinical success, adverse events, recurrence, mortality, and stent migration, however, ED was associated with a shorter hospital stay and a lower rate of re-intervention compared to PD (10). Despite these advantages, both ED and PD carry inherent risks, and the selection of an appropriate drainage method must be tailored based on individual patient characteristics, clinical presentation, availability of expertise and logistics.

CONCLUSION:

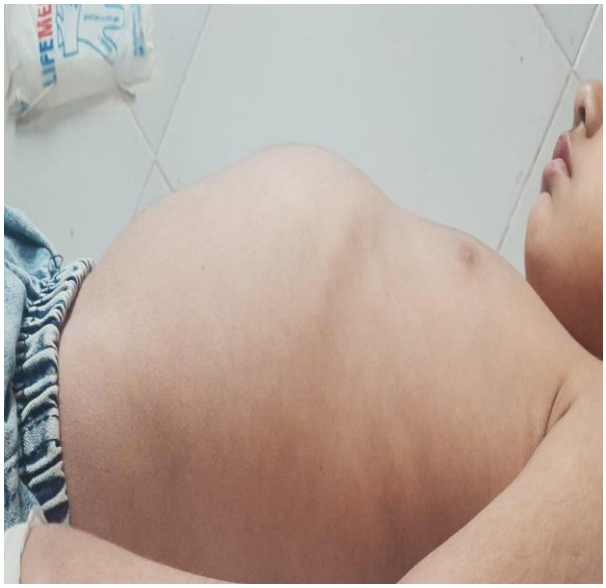
Enteric fever can occasionally lead to rare complications like pancreatitis and pancreatic pseudocyst formation. Persistent abdominal symptoms post-typhoid warrants a high index of suspicion, with early imaging and enzyme analysis being key to timely diagnosis.

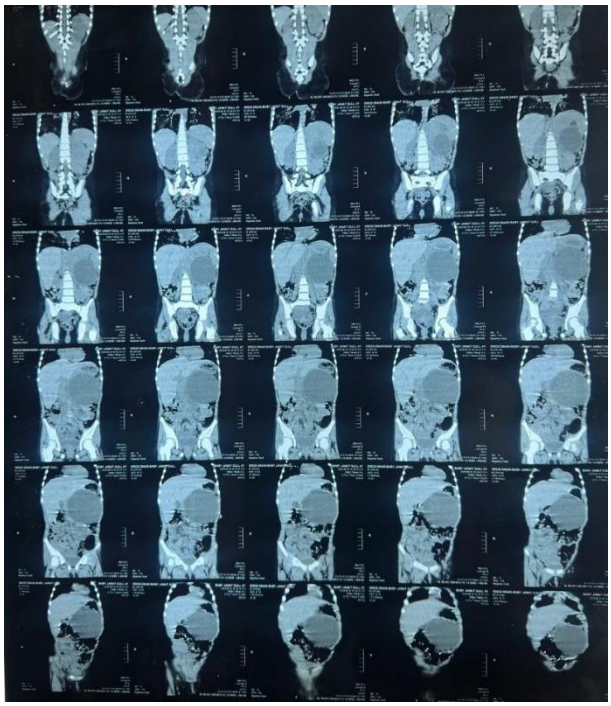
Management of pancreatic pseudocysts in children should be tailored to cyst size, symptoms, and anatomical considerations. Conservative therapy suffices for small, asymptomatic cysts, while image-guided percutaneous drainage offers a minimally invasive solution for larger, symptomatic ones.

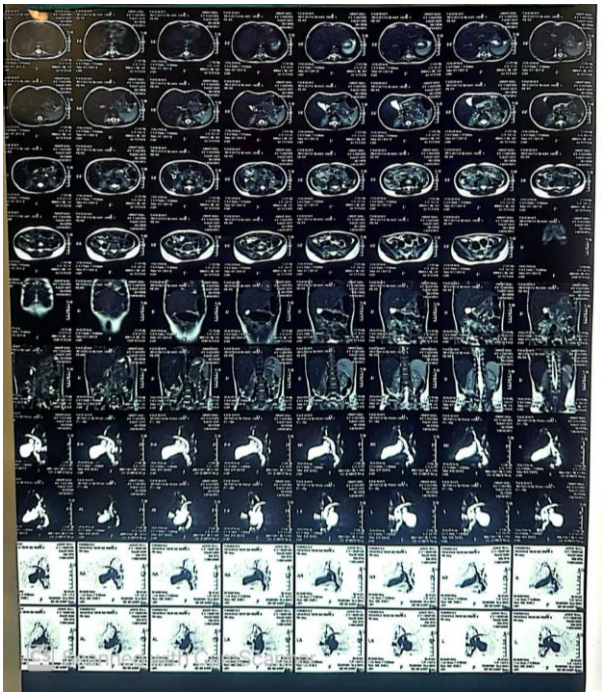
Percutaneous drainage serves as a safe, less invasive alternative to surgery, significantly reducing morbidity. However, vigilant post-procedural monitoring is critical to detect complications such as infection, fistula, or recurrence.

Typhoid-associated pancreatitis, though uncommon, underscores the importance of multidisciplinary care. Coordinated input from pediatric gastroenterology, infectious disease, and interventional radiology teams enhances outcomes. Ongoing follow-up with repeat imaging and clinical review is essential for ensuring resolution. Caregiver education on red-flag symptoms empowers early recognition and improves long-term outcomes.

FIGURES:







LEGENDS:
Figure 1. Abdominal mass with protuberant abdomen
Figure 2. Ct scan revealing pancreatic pseudocyst anterior to body and tail of pancreas
Figure 3. follow up imaging revealing resolution of Pancreatic PC.

Author's Contribution:

NA: Conceived and designed the study, involved in data collection, performed statistical analysis and writing the manuscript.
MS, HS, HR, MT: Collected the data, critical review and preparation of manuscript.

All authors have read, approved the final manuscript and are responsible for the integrity of the study.

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