ISSN (P): 2307-3748
ISSN (E): 2310 -3841

Citation:
Hamid SS, et al. Turning the Tide on Hepatitis Delta in Pakistan: An Urgent Call for Awareness, Access, and Action. Int. j. endorsing health sci. res. 2025;13(4):176-180.

Corresponding Author Email:
syedmunawarali83@gmail.com

Funding:
The authors received no external funding for this study.

Conflicts of Interests:
The authors have declared that no competing interests exist.

Data Sharing Statement:
The data that support the findings of this study are available on request from the corresponding author. The data is not publicly available due to privacy or ethical restrictions.

Received 02/06/2025
Accepted 28/10/2025
First Published 01/12/2025

Short Communication

Turning the Tide on Hepatitis Delta in Pakistan: An Urgent Call for Awareness, Access, and Action.

Saeed Sadiq Hamid[1], Syed Munawar Ali[2], Zaigham Abbas[3], Ghias Un Nabi Tayyab[4], Rao Saad Ali Khan[5], Asher Bin Feroze[6] & Saad Khalid Niaz[7]

[1]Clinical Trials Unit, Aga Khan University, Karachi, Pakistan.
[2]Clinical Operations, IQVIA Pakistan
[3]Department of Hepatogastroenterology, Dr. Ziauddin University Hospital Clifton, Karachi, Pakistan.
[4]Doctors Hospital and Medical Center, Lahore, Pakistan.
[5]Pak-Emirates Military Hospital, Rawalpindi, Pakistan.
[6]IQVIA, Karachi, Pakistan.
[7]Sindh Institute of Advanced Endoscopy and Gastroenterology/Dow University of Health Science, Karachi, Pakistan.

DOI: https://doi.org/10.29052/IJEHSR.v13.i4.2025.176-180

Abstract

Background:
Hepatitis Delta Virus (HDV) remains an under-recognized contributor to advanced liver disease in Pakistan despite the country's high burden of Hepatitis B Virus (HBV). Fragmented screening practices, inconsistent confirmatory testing, and absence of standardized national protocols limit effective disease control.

Methodology:
This short communication synthesizes previously published clinician-perspective data from major tertiary centers in Pakistan alongside international HDV guidelines and regulatory frameworks. The aim is to identify structural gaps and propose a standardized national response model.

Results:
Available data suggest that HDV co-infection among HBV patients in Pakistan is substantial, with diagnostic access constrained primarily by affordability and inconsistent RNA confirmation capacity. The absence of unified screening algorithms and dedicated programmatic inclusion has resulted in delayed detection and limited therapeutic access. Broad expert agreement supports integration of HDV into national hepatitis strategies and development of regulated early-access pathways for emerging therapies.

Conclusion:
The cumulative evidence supports the hypothesis that HDV constitutes a significant but structurally neglected public health burden in Pakistan. Establishing standardized screening protocols, improving diagnostic affordability, and incorporating HDV into national hepatitis policy frameworks are essential to reduce preventable liver-related morbidity and mortality.

Keywords:
Hepatitis Delta Virus, Hepatitis B, National Screening, Viral Hepatitis Policy, Emergency Use Authorization, Pakistan

Introduction: The HDV Crisis in Pakistan

Hepatitis Delta Virus (HDV) is a defective RNA virus that requires the hepatitis B surface antigen (HBsAg) for assembly and release; HDV RNA replicates via host RNA polymerase II and is not dependent on HBV replication per se [1]. It causes the most severe form of viral hepatitis, accelerating progression to cirrhosis, hepatocellular carcinoma (HCC), and liver failure within 5-10 years of infection.

Recent global analyses on hepatitis B disparities have underscored the importance of addressing methodological bias, missing data, and unequal healthcare access when evaluating disease burden and outcomes [2]. These factors are equally critical for HDV research in Pakistan, where variations in regional healthcare infrastructure, socioeconomic conditions, and diagnostic availability may contribute to under-recognition and inequitable disease management.

Globally, HDV affects an estimated 12 million people who have a chronic infection with HBV [2]. Mongolia had the highest anti-HDV prevalence of 60.1% of all. After controlling the sizes of the HBsAg-positive population and HDV RNA-positive rate, China had the greatest absolute number of HDV RNA-positive cases [3]. Pakistan, a country with high endemicity for HBV, bears a significant burden of HDV, with local studies suggesting co-infection rates between 20% and 35% among HBV-positive patients [4]. More recent comprehensive community-based screening revealed that 67.1% of hepatitis B surface antigen (HBsAg) positive individuals had been exposed to hepatitis D virus (HDV), with 58.1% showing active viremia [5]. The young age groups are disproportionately affected, placing a long-term burden on the nation's health and economy.

Despite this severity, HDV remains dangerously under-prioritized, lacking dedicated screening programs, treatment protocols, and policy attention, creating a silent epidemic within the already substantial viral hepatitis crisis. The limitations of current approaches are severe, first and foremost is reliance on non-standardized practices, with HDV RNA testing are largely unavailable or unaffordable. No national guidelines, leading to inconsistent care and missed diagnoses. Furthermore, no access to globally available investigational therapies, leaving patients with no options. To fully grasp the urgency of this crisis, it is essential to quantify the health and economic toll of HDV in Pakistan.

Burden of Disease and Economic Impact

Hepatitis Delta Virus (HDV) represents a severe but under-quantified contributor to liver-related morbidity and mortality in Pakistan. While reliable national surveillance data remain limited, extrapolations from available literature and current clinical expert consensus suggest that 10–20% of Hepatitis B Virus (HBV) patients in Pakistan are co-infected with HDV [7,8], translating into hundreds of thousands of affected individuals nationwide.

1. **Health Impact**

- ***Mortality:*** Patients co-infected with HDV progress to cirrhosis, liver failure, or hepatocellular carcinoma within 5–10 years, compared to decades for HBV alone. This accelerated course significantly increases premature deaths among young and middle-aged adults, the most economically productive demographic.
- ***Transplant Burden:*** Pakistan already faces limited liver transplantation capacity, concentrated in urban tertiary centers. HDV-related cirrhosis and cancer are projected to sharply increase demand for transplant services, widening inequities between rural and urban populations.

2. **Economic Impact:**

- ***Direct Costs:*** A single HDV RNA testing currently costs between PKR 12,000–18,000 (USD 40–60), unaffordable for most patients. Long-term management of cirrhosis and HCC including hospitalizations, interventions, and palliative care costs several hundred thousand rupees per patient annually, straining household and health system budgets.
- ***Indirect Costs:*** Lost productivity from premature death or chronic disability in working-age adults results in substantial economic losses. Conservative estimates suggest that HDV-related morbidity could reduce national productivity by billions of rupees annually, though precise modeling remains urgently needed.
- ***Regional Disparities:***
  - Sindh and Baluchistan report higher HBV and HDV prevalence, compounded by weaker diagnostic infrastructure.
  - Punjab and KPK have relatively better access to tertiary centers but face affordability barriers.
  - Rural populations are disproportionately affected by lack of diagnostic availability and specialist care.

3. **Policy Implication:**

Framing HDV as not only a health crisis but also an economic burden strengthens the rationale for urgent government intervention. Investment in early diagnosis, subsidized testing, and treatment access will yield cost savings by reducing downstream expenditures on transplant, hospitalization, and end-stage liver disease care.

Methods

This policy-oriented short communication draws upon previously published clinician-perspective findings from major tertiary care centers in Pakistan, combined with review of international HDV clinical practice guidelines and regulatory models for early-access therapies. The synthesized evidence was used to develop structured recommendations for screening standardization, diagnostic accessibility, and regulatory pathways for treatment access. Detailed methodology of the underlying clinician survey has been reported in prior publication.

Clinical Perspectives and System Gaps in HDV Care

Previously published clinician-perspective findings from major tertiary hepatology centers in Pakistan revealed several high-impact signals [6].

First, HDV was reported to be encountered frequently in routine hepatology practice, with experts estimating that a substantial proportion of HBV patients may have concurrent HDV infection. Given Pakistan's estimated HBV burden and reported co-infection rates in regional studies ranging from 10–35% [4,5], the potential number of affected individuals nationally may be considerable. However, the absence of standardized national surveillance limits precise quantification.

Second, diagnostic access was identified as a critical barrier. While antibody screening was commonly performed in tertiary settings, confirmatory HDV RNA testing was inconsistently accessible and frequently unaffordable [6]. This gap increases the likelihood of delayed diagnosis and progression to advanced liver disease.

Third and most notably there was unanimous expert support for the establishment of a regulated early-access pathway for HDV-specific therapies [6]. All participating specialists endorsed the need for an Emergency Use Authorization (EUA) or comparable conditional access mechanism, provided that it is supported by Phase II/III clinical evidence and appropriate safety oversight.

This 100% consensus reflects recognition of significant unmet therapeutic need. Clinicians further emphasized that HDV infection is associated with accelerated progression to cirrhosis, hepatocellular carcinoma, and liver failure compared with HBV mono-infection [1,3], underscoring the clinical urgency of integrating both screening and treatment access into national hepatitis policy.

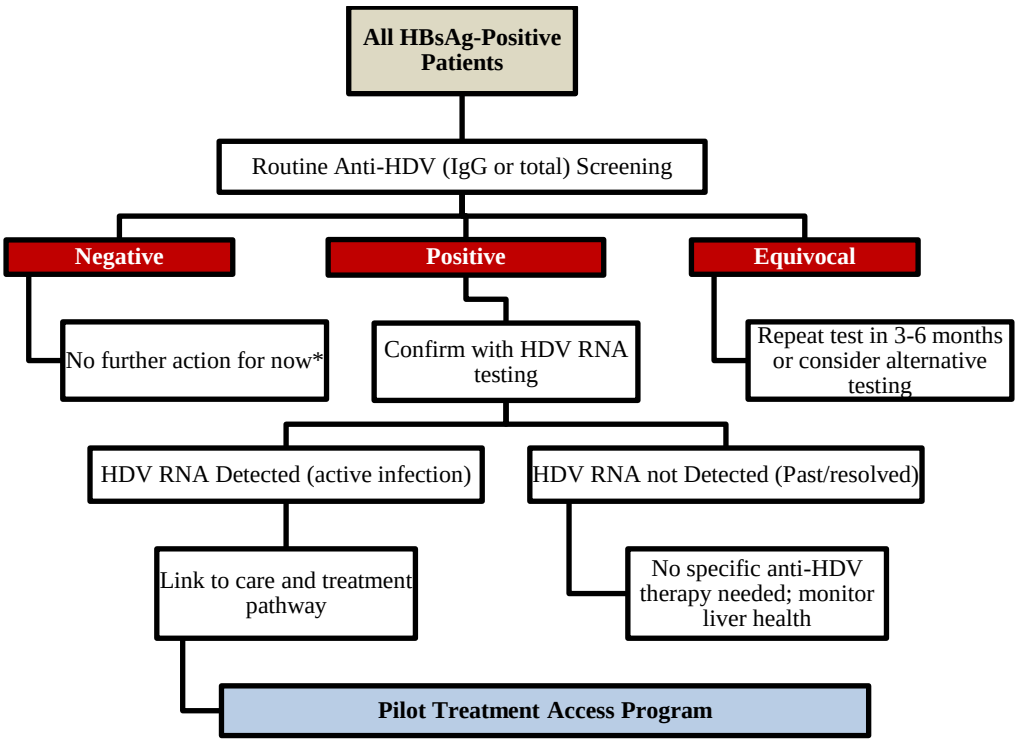

Figure 1: Proposed National Algorithm for HDV Screening and Diagnosis in HBsAg-Positive Individuals in Pakistan.

Global and Regional Lessons for Policy Adaptation

Several countries and regions with substantial HBV burdens offer useful lessons for tackling HDV, their approaches illustrate feasible policy options for surveillance, diagnostics, and early access to new therapies. Mongolia remains one of the world's highest-prevalence settings for HDV, with studies showing extremely high anti-HDV and HDV RNA rates among HBsAg-positive patients [7]. Research collaborations there have focused on mapping molecular diversity, identifying transmission hotspots, and piloting prevention strategies in rural areas. Mongolia's experience underscores the need for targeted prevalence surveys and linkages between surveillance and clinical care in high-burden regions [8].

Although Egypt's high-profile national campaigns have focused on hepatitis C, the country's mass screening and treatment program demonstrates that population-scale screening and rapid program rollout are feasible in resource-limited settings when there is strong political will, centralized coordination, and investment in rapid diagnostics and supply chains [9]. Pakistan can adapt these operational lessons, mass-case finding, task-shifting, and centralized procurement to accelerate HDV case detection and linkage to care.

Newer anti-HDV-specific therapies (notably bulevirtide) have gained conditional/market approval in some jurisdictions and are being evaluated in combination regimens globally [10]. Countries have used regulatory flexibility (conditional approvals, compassionate use / EUA-like pathways) to enable early access while collecting post-approval safety and effectiveness data. This demonstrates that Pakistan's proposed DRAP-led DRAP EUA/compassionate-use pathway is consistent with international practice for urgent unmet needs. The key transferable lessons for Pakistan include use sentinel and targeted serosurveys to identify provincial hotspots (as in Mongolia) and prioritize resources there [7]. Repurpose the mass-screening logistics and centralized procurement lessons from Egypt's HCV response to scale anti-HDV (total antibody) screening and HDV RNA test confirmation rapidly [9]. Implement a DRAP-led EUA/conditional access pathway tied to a national registry for outcomes and safety, mirroring international approaches to early access for HDV antivirals. Partner with regional research centers (as seen in Mongolia collaborations) to map genotypes/subtypes, which can inform diagnostics and therapeutic choices [7].

Based on the consensus findings, we propose a phased, integrated strategy for Pakistan that combines diagnostic standardization, treatment access, awareness, and policy integration. In the immediate term (0–1 year), physician- and community-targeted awareness campaigns must be launched. Along with that mandatory routine Anti-HDV (IgG or total) screening for all HBsAg-positive individuals. While in the short-term (1–3 years) development and publication of national HDV screening and management guidelines and establishment of pilot Emergency Use Authorization (EUA) programs in major tertiary centers under strict monitoring. In long-term (3–5 years) integration of HDV as a dedicated component within the National Hepatitis Program with separate funding. Expand equitable access to approved and investigational HDV therapies nationwide. And finally enhance global partnerships between Pakistan's DRAP and healthcare administrations of countries such as China for HBV-HDV public health initiatives. These should focus on

infrastructure, prevention, screening, early detection, treatment access, and technology transfer as pilot international programs.

The Pakistan Diagnostic Protocol for HDV

We propose a standardized national algorithm to be adopted by all public and private healthcare facilities managing HBV patients (Figure 1).

Regulated Early-Access Framework

To close the treatment gap, a DRAP-led EUA framework should be established immediately, ensuring safety and transparency.
This framework should include:

- Requirement of Phase II/III trial data and prior international approval, preferably supported by safety and efficacy data from pivotal trials involving Pakistani HDV patients.
- Oversight by an independent expert panel.
- Patient registry monitoring for safety and outcomes.

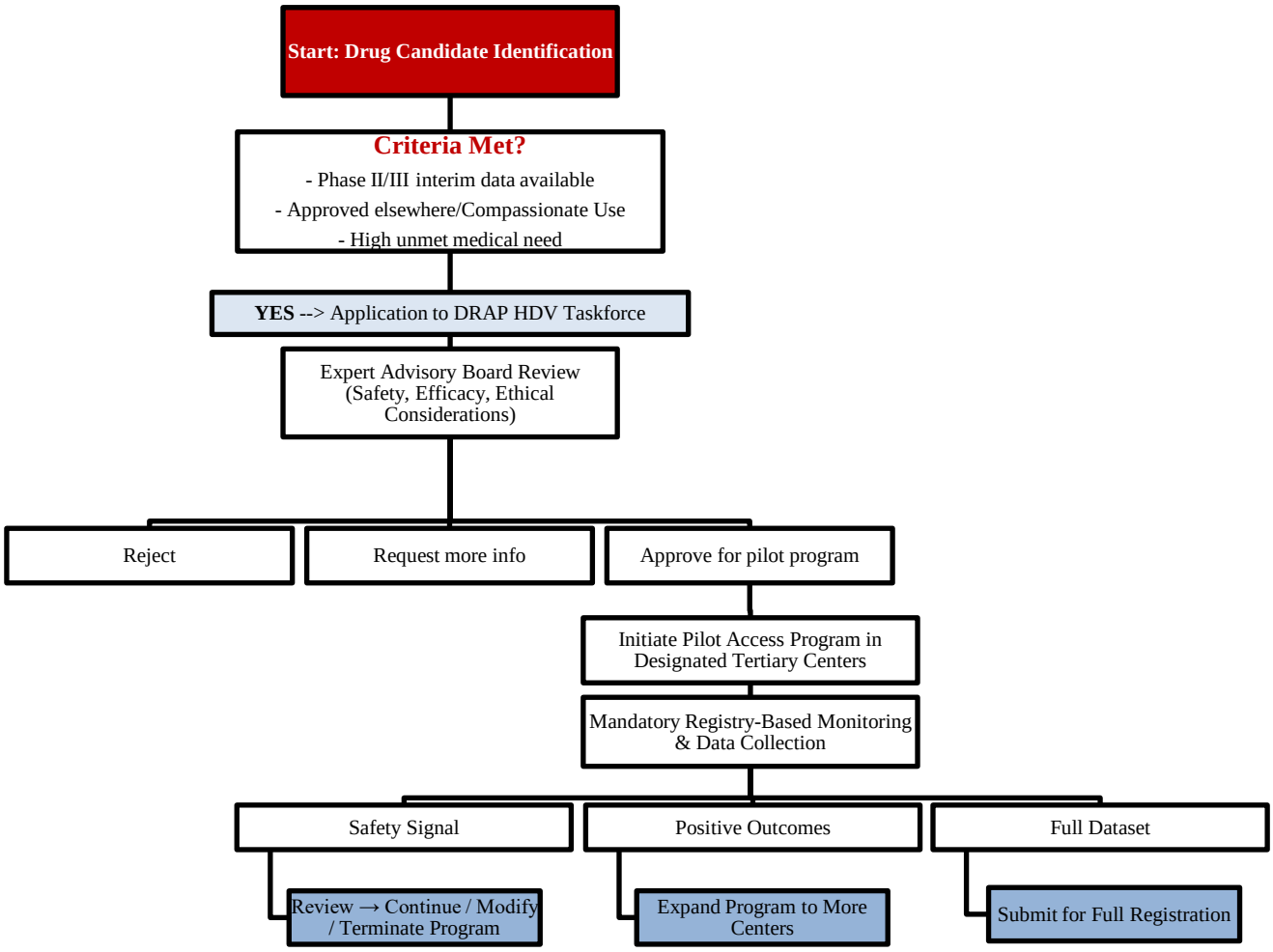

Figure 2: Proposed Framework for Emergency Use Authorization of HDV Therapies in Pakistan.

Conclusion

The findings of this consensus document are a stark warning: Hepatitis Delta is not a rare condition in Pakistan but a prevalent and devastating disease that is being systematically missed. The gaps in diagnosis, awareness, and treatment access are fueling a silent crisis with fatal consequences. The consensus from the country's leading clinicians is clear and unanimous. Urgent, coordinated, and decisive action is required. The proposed Pakistan Consensus Criteria provide a clear, actionable roadmap for the Ministry of National Health Services, Regulations and Coordination, the Drug Regulatory Authority of Pakistan (DRAP), and the National Hepatitis Program. By implementing this strategy particularly national screening, integration into the hepatitis program, and an emergency access pathway Pakistan can prevent countless deaths, reduce long-term healthcare costs, and take a monumental step towards achieving its viral hepatitis elimination goals.

Acknowledgement

The authors express their sincere gratitude to all key opinion leaders and collaborators whose insights and contributions enriched this study. Special thanks are extended to Dr. Lubna Sohail, Dr. Usman Naeem, Dr. Shahid Majid, Dr. Rizwan Aziz Qazi, Dr. Muzzian Iqbal, Dr. Syeda Faheema, Dr. Muslim Atiq, Ayesha Javed Qureshi, and Yasmeen Fazal for their valuable guidance and expert perspectives that strengthened the development of this national consensus.

References

1. Bigogno CM, Falahieh RR, Ho KM, Jeffrey-Smith A, Jones M, Usai C, Battisti A, Gill U, Kennedy P. The genetic landscape of hepatitis delta virus infection. Clinical Medicine. 2020 Mar;20(Suppl 2):s101.
2. Wang Y, Guo X, Yuan Y. Addressing bias and improving research on gender and racial disparities in hepatitis B assessment and treatment. J Hepatol. 2024 Dec;81(6):e279–e280. doi: 10.1016/j.jhep.2024.07.021.
3. Shearer DM, Cheinquer H, Razavi H, Polaris Observatory Collaborators. Adjusted estimate of the prevalence of hepatitis delta virus in 25 countries and territories. Journal of hepatology. Amsterdam. Vol. 80, no. 2 (Feb. 2024), p. 232-242. 2024.
4. Aftab M, Naz S, Aftab B, Ali A, Rafique S, Fatima Z, Inamullah, Idrees M. Characterization of hepatitis delta virus among pregnant women of Pakistan. Viral immunology. 2019 Oct 1;32(8):335-40.
5. Abbas M, Abbas Z, Sharif MY. Community-Based Double Reflex Screening Reveals Widespread Hepatitis D Viremia Among Hepatitis B Surface Antigen Carriers in Pakistan. Cureus. 2025 Jun 1;17(6):e85200.
6. Hamid S, Ali S, Abbas Z, et al. Bridging Gaps in Hepatitis Delta Virus Care: A Cross-Sectional Mixed-Methods Study of Clinician Perspectives From Major Urban Centers in Pakistan. Cureus. 2025; 17(12): e99722. doi:10.7759/cureus.99722
7. Magvan B, Kloeble AA, Ptok J, Hoffmann D, Habermann D, Gantumur A, Paluschinski M, Enebish G, Balz V, Fischer JC, Chimeddorj B, Walker A, Timm J. Sequence diversity of hepatitis D virus in Mongolia. Front Med (Lausanne). 2023 Mar 13;10:1108543. doi: 10.3389/fmed.2023.1108543. PMID: 37035318; PMCID: PMC10077969.
8. Dorj G, Baatarkhuu O, Dorj G, Lkhagvaa U, Walsh N, Choijoo A, Gurbadam U, Jargalsaikhan J, Erdenetsetseg B. Viral hepatitis elimination in Mongolia. In: Viral Hepatitis in Asia and the Pacific: Towards Elimination as a Public Health Threat. 2025. p. 155-181. doi: 10.1016/B978-0-443-23629-7.00007-3.
9. Global Hepatitis Alliance. Egypt: Country hepatitis elimination profile [Internet]. Globalhep.org. [cited 2025 Sept 10]. Available from: https://www.globalhep.org/data-profiles/countries/egypt