Journal of Communicable Diseases
Volume 57, Issue 4 - 2025, Pg.No.134-144
Peer Reviewed & Open Access Journal

Review Article

The Complex Interplay: Hepatitis B, HIV/AIDS and Erectile Dysfunction - A Comprehensive Review

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DOI: https://doi.org/10.24321/0019.5138.2026107

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How to cite this article:
Kesavan H, Rajappa M C, Ramaswamy S, Venkatasubramaniam N, Kumar M. The Complex Interplay: Hepatitis B, HIV/AIDS and Erectile Dysfunction - A Comprehensive Review. J Commun Dis. 2025;57(4):134-144.

Date of Submission: 2025-05-13
Date of Acceptance: 2025-12-15

A B S T R A C T

Erectile dysfunction (ED) is a prevalent clinical condition affecting male sexual health and overall quality of life. Beyond its psychosocial impact, ED is increasingly recognisedas an early marker of systemic disease. Chronic viral infections, particularly Hepatitis B virus (HBV) and Human Immunodeficiency Virus (HIV), exert profound multisystem effects that predispose affected individuals to sexual dysfunction. These effects result from intricate interactions that include hepatic impairment, immune activation, metabolic disturbances, endocrine dysregulation, medication-related adverse effects, and psychological stressors.

Patients living with HBV or HIV encounter unique sexual health challenges compounded by disease-related stigma and long-term treatment burdens. The interaction between psychological distress and organic pathophysiology further complicates clinical management. This review synthesizes current evidence on the epidemiology, pathophysiology, classification, assessment, and management of erectile dysfunction in patients with HBV and HIV, with emphasis on disease-specific mechanisms and integrated care strategies.

Keywords: Erectile dysfunction; Hepatitis B virus; Human immunodeficiency virus

Introduction

Erectile dysfunction is defined as the persistent inability to achieve or maintain an erection sufficient for satisfactory sexual performance. Although commonly associated with ageing, ED frequently occurs in younger individuals with chronic systemic illnesses. Viral infections such as HBV and HIV represent important yet under-recognised contributors to sexual dysfunction through direct biological effects and indirect psychosocial pathways.[1]

Globally, chronic HBV infection affects approximately 296 million individuals, while HIV infection affects nearly 38 million people. Coinfection is common due to shared transmission routes and is associated with accelerated liver disease progression, immune dysregulation, and increased treatment complexity. These overlapping disease processes significantly heighten the risk of erectile dysfunction and necessitate tailored clinical approaches.

Sexual health concerns are often overlooked in routine viral disease management, resulting in underdiagnosis and undertreatment of ED. Addressing erectile dysfunction in this population is clinically important not only for quality of life but also for improving treatment adherence and overall health outcomes.[2]

The association between these viral infections and erectile dysfunction stems from several factors:

1. Direct viral effects on vascular and neurological systems
2. Secondary metabolic and hormonal disruptions
3. Psychological impact of chronic disease diagnosis and management
4. Side effects of antiviral medications
5. Comorbid conditions common in affected populations

Despite the prevalence of these issues, sexual health remains inadequately addressed in the management of patients with chronic viral infections.[3] This review seeks to highlight current knowledge regarding the relationship between HBV, HIV, and erectile dysfunction, with emphasis on identifying gaps in research and clinical practice.(fig 1)

Pathophysiology of Erectile Dysfunction in HBV And HIV

Erectile dysfunction in HBV- and HIV-infected individuals arises from interrelated vascular, neurological, hormonal, metabolic, and psychological mechanisms that are directly influenced by viral pathogenesis and treatment effects.

Hepatic Dysfunction and Endocrine Disruption

Chronic HBV infection leads to progressive liver damage, impairing hepatic metabolism of sex hormones. Reduced clearance of estrogen and increased sex hormone–binding globulin levels result in decreased bioavailable testosterone. Hypogonadism is reported in up to 60% of men with chronic liver disease and is a major contributor to reduced libido and erectile impairment.[4]

Immune Activation and Vascular Dysfunction

Both HBV and HIV induce persistent immune activation characterized by elevated pro-inflammatory cytokines such as interleukin-6 and tumour necrosis factor-alpha. Chronic inflammation promotes endothelial dysfunction by reducing nitric oxide bioavailability, impairing vasodilation, and accelerating atherosclerosis. These changes compromise penile blood flow and disrupt normal erectile haemodynamics.[5]

ART-Associated Metabolic Changes

Antiretroviral therapy, particularly protease inhibitors, is strongly associated with metabolic syndrome, dyslipidaemia, insulin resistance, and lipodystrophy. These metabolic derangements exacerbate vascular dysfunction and contribute to ED. In HIV patients, prolonged ART exposure further increases cardiovascular risk, compounding erectile impairment.[6]

Neurological Involvement

HIV-associated neurotoxicity and antiviral drug effects can damage peripheral and autonomic nerves essential for erection. Sensory neuropathy reduces penile afferent signalling, while autonomic dysfunction interferes with erection initiation and maintenance.

Psychological and Neuroendocrine Pathways

Psychological stress, depression, anxiety, and stigma are highly prevalent in HBV and HIV populations. Chronic activation of the hypothalamic–pituitary–adrenal axis elevates cortisol levels, suppressing testosterone production and impairing sexual response. Fear of viral transmission and body image disturbances further intensify performance anxiety and psychogenic ED.[7]

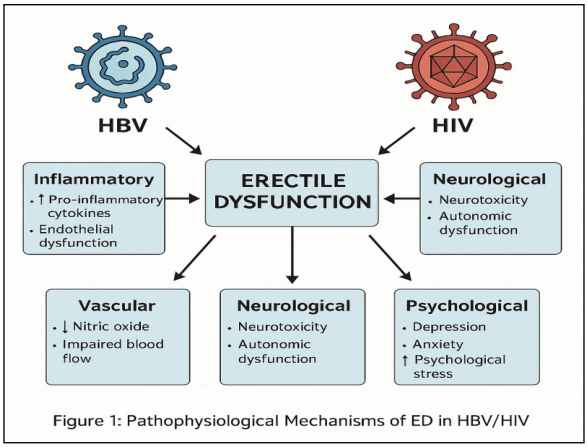

Figure 1.Pathophysiological Mechanisms of ED in HBV/HIV Infection

ISSN: 0019-5138
DOI: https://doi.org/10.24321/0019.5138.2026107

Epidemiology

The prevalence of erectile dysfunction among patients with chronic viral hepatitis varies widely across studies, ranging from 38% to 65%. This variation reflects differences in assessment methods, population characteristics, and disease severity. Among HIV-positive individuals, ED prevalence ranges from 46% to 74%, substantially higher than age-matched controls in the general population.[8]

Patients with HBV-HIV coinfection demonstrate even higher rates of sexual dysfunction, with studies reporting ED prevalence of 57-79%. This increased prevalence appears to correlate with several factors:

- Duration of viral infection
- Viral load and disease activity
- Degree of liver fibrosis (in HBV)
- CD4+ count (in HIV)[9]
- Presence of metabolic syndrome components
- Antiviral medication regimens
- Psychological comorbidities

A significant age-related pattern has been observed, with ED manifestation occurring approximately 10-15 years earlier in men with chronic viral infections compared to the general population. This accelerated presentation underscores the systemic impact of these infections on vascular and neurological health.[10](fig 2)

Demographic analyses reveal that socioeconomic factors significantly influence both the prevalence of viral infections and erectile dysfunction, with lower education levels and reduced healthcare access associated with poorer sexual health outcomes.[11] These disparities highlight the importance of addressing social determinants of health in comprehensive management approaches shown in table 1.

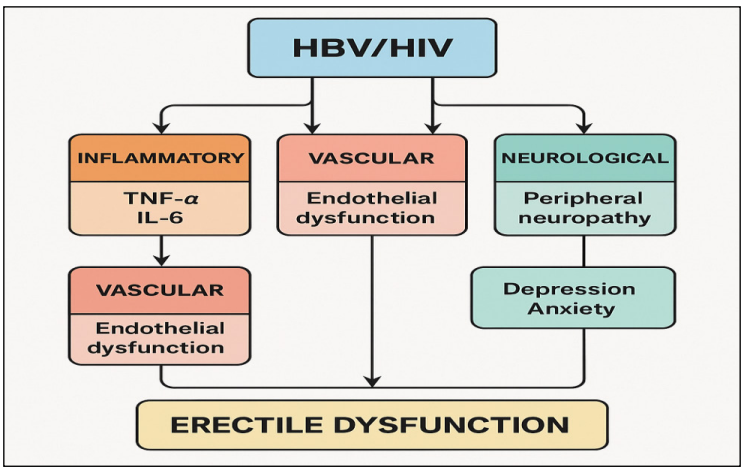

Figure 2.Prevalence of ED Among Different Patient Populations

Table 1.Prevalence of Erectile Dysfunction in Different Patient Populations

Population	ED Prevalence (%)	Key Risk Factors	Study References
General Population (40-70 years)	18-30	Age, cardiovascular disease, diabetes	Feldman et al., 1994; Thompson et al., 2023
Chronic HBV	38-65	Liver fibrosis, inflammation, treatment side effects	Chen et al., 2023; Wang et al., 2024
HIV/AIDS	46-74	CD4+ count, viral load, antiretroviral therapy	Zhang et al., 2022; Okwonkwo et al., 2023
HBV-HIV Coinfection	57-79	Disease severity, polypharmacy, psychological burden	Xiaoning et al., 2024; Hassan et al., 2023
HBV with Advanced Liver Disease	65-82	Hepatic encephalopathy, hormonal dysregulation	Wang et al., 2024
HIV with Lipodystrophy	72-88	Body image concerns, metabolic syndrome	Enderle et al., 2024

ISSN: 0019-5138
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Classification of Erectile Dysfunction

Erectile dysfunction in HBV and HIV patients is best understood as a multifactorial condition and may be classified as[12]

Organic Erectile Dysfunction

This includes vasculogenic, neurogenic, and endocrinological causes directly related to hepatic impairment, immune-mediated vascular injury, neuropathy, and hormonal imbalance.[13]

Psychogenic Erectile Dysfunction

Psychogenic ED results from depression, anxiety, stigma, fear of transmission, relationship conflict, and reduced self-esteem following chronic viral diagnosis.[14]

Mixed Erectile Dysfunction

Mixed ED is the most common presentation, involving both organic pathology and psychological distress. Bidirectional interactions between physical impairment and mental health play a central role.[15]

Medication-Induced Erectile Dysfunction

Certain antiretroviral and antiviral agents contribute to ED through mitochondrial toxicity, metabolic disruption, or drug–drug interactions affecting erectile therapies.[16]

This article presents a comprehensive narrative review of published literature addressing erectile dysfunction in patients with hepatitis B and HIV infection. We performed a systematic search of multiple electronic databases including PubMed/MEDLINE, Embase, Cochrane Library, Web of Science, and PsycINFO from inception through September 2024.[17]

Table 2.Psychological Interventions for ED in Viral Hepatitis and HIV

Intervention	Focus Areas	Efficacy	Implementation Considerations
Cognitive-Behavioral Therapy	Performance anxiety; Depression management; Catastrophic thinking	50-70% improvement in psychogenic components	Individual or couple format; 8-12 sessions typically recommended[18]
Mindfulness-Based Approaches	Body awareness; Non-judgmental acceptance; Present-moment focus	45-60% improvement in anxiety-related ED	Group or individual format; Daily practice requirements
Couples Therapy	Communication training; Sexual technique education; Intimacy rebuilding	55-65% improvement in relationship satisfaction and sexual function	Joint participation; Focus on both emotional and physical aspects
Sex Therapy	Sensate focus exercises; Gradual exposure; Performance pressure reduction	60-75% improvement in mixed ED cases	Requires motivated partners; Progressive behavioral assignments[19]
Support Groups	Stigma management; Shared experiences; Coping strategies	Adjunctive benefit, not typically sole intervention	Beneficial for addressing isolation; May improve treatment adherence

Table 3.Staging and Assessment of ED Severity in Viral Hepatitis and HIV

Severity	IIEF-5 Score	Clinical Features	Recommended Initial Approach
Mild	17-21	Occasional difficulty achieving/ maintaining erection; Usually able to complete intercourse	Lifestyle modifications; Psychoeducation; Consider PRN PDE5i[20]
Mild to Moderate	12-16	Frequent difficulty with erection quality; Sometimes unable to complete intercourse	Scheduled PDE5i; Address modifiable risk factors; Consider psychological evaluation
Moderate	8-11	Reliable difficulty with erections; Rarely able to complete intercourse	Regular PDE5i; Consider combination therapy; Psychological intervention
Severe	5-7	Almost never able to achieve functional erection	Second-line therapies (injections, VED); Comprehensive medical and psychological intervention[21]

ISSN: 0019-5138
DOI: https://doi.org/10.24321/0019.5138.2026107

Medication Effects

Pharmacological treatments used in the management of HIV and hepatitis B can adversely affect erectile function through several mechanisms.[22] Nucleoside reverse transcriptase inhibitors (NRTIs) have been associated with mitochondrial toxicity, which compromises the energy-dependent processes essential for erection. Protease inhibitors are linked to the development of metabolic syndrome and lipodystrophy, both of which can impair vascular and endocrine health. Certain medications used to treat hepatitis B may also interact with phosphodiesterase-5 inhibitors, reducing their efficacy. Moreover, the high prevalence of polypharmacy in these patients increases the risk of drug-induced sexual side effects, necessitating careful therapeutic planning.[23](table 2 & 3)

The complex interplay between these mechanisms creates a self-perpetuating cycle that can be difficult to interrupt without comprehensive management. Furthermore, the progressive nature of both viral infections means that pathophysiological impacts typically worsen over time without appropriate intervention.[24]

Principles and Management

Management of erectile dysfunction in patients with HBV and HIV requires a multidisciplinary approach addressing both underlying viral infections and specific sexual health concerns:

Assessment Principles

- Comprehensive sexual health history, including onset, progression, and situational factors[25]
- Validated assessment tools (International Index of Erectile Function, Sexual Health Inventory for Men)
- Laboratory evaluation
- Complete blood count
- Comprehensive metabolic panel
- Lipid profile
- Hormonal assays (total and free testosterone, prolactin, thyroid function)
- HBV viral load and liver function tests
- HIV viral load and CD4+ count
- Psychological screening for depression, anxiety, and relationship factors
- Medication review with particular attention to antiviral regimens[26]
- Assessment of cardiovascular risk factors(table 4)

Table 4.Pharmacological Management Options for ED in Patients with HBV/HIV

Medication Class	Examples	Efficacy in HBV/HIV Population	Considerations in Viral Infections
PDE5 Inhibitors	Sildenafil, Tadalafil, Vardenafil	60-75% success rate	Drug interactions with protease inhibitors; dose adjustment needed; contraindicated with nitrates
Intracavernosal Injections	Alprostadil, Trimix	70-85% success rate	Monitoring for injection site infections in immunocompromised patients; caution with coagulopathy in advanced liver disease
Intraurethral Suppositories	Alprostadil	40-65% success rate	Lower risk of systemic effects; option for patients with medication interactions
Testosterone Replacement	Various formulations	Variable, beneficial when hypogonadism present	Caution in patients with liver dysfunction; monitoring for hepatotoxicity; potential oncological concerns
Vacuum Erection Devices	N/A	60-80% success rate	Non-pharmacologic option; avoids drug interactions; requires manual dexterity

Table 5.Biomarkers Associated with ED in Viral Hepatitis and HIV

Biomarker	Significance in ED Pathophysiology	Values Associated with ED Risk	Monitoring Frequency
Total Testosterone	Primary male hormone; essential for libido and erectile function	<300 ng/dL (higher threshold in older men)	Every 6-12 months
Free Testosterone	Bioavailable testosterone; more accurate in liver disease where SHBG is altered	<65 pg/mL	Every 6-12 months
Viral Load (HBV DNA)	Marker of disease activity; correlates with inflammatory burden	>2000 IU/mL associated with higher ED risk	Every 3-6 months

ISSN: 0019-5138
DOI: https://doi.org/10.24321/0019.5138.2026107

HIV Viral Load	Indicates HIV control; higher levels associated with systemic inflammation	Any detectable level increases ED risk	Every 3-4 months
CD4+ Count	Immune system status; lower counts correlate with ED severity	<350 cells/mm³ significantly increases risk	Every 3-4 months
ALT/AST	Liver inflammation markers; correlate with ED in HBV	>2× upper limit of normal	Every 3-6 months
FibroScan/APRI	Liver fibrosis assessment; advanced fibrosis increases ED risk	FibroScan >9.5 kPa or APRI >1.5	Every 6-12 months
Lipid Profile	Vascular health assessment; dyslipidemia contributes to ED	LDL >130 mg/dL, HDL <40 mg/dL	Annually
HbA1c	Glycemic control; diabetes and insulin resistance increase ED risk	>5.7% associated with increased risk	Every 6 months
hs-CRP	Inflammatory marker; higher levels indicate systemic inflammation	>3.0 mg/L associated with ED	Every 6-12 months

Management Approaches

Optimisation of Viral Disease Control[27]

- Effective antiviral therapy for both HBV and HIV
- Consideration of medication adjustments to minimise sexual side effects
- Regular monitoring of disease markers and treatment response

Addressing Modifiable Risk Factors

- Smoking cessation
- Alcohol reduction, particularly important in HBV
- Weight management and metabolic syndrome control
- Physical activity promotion[28]
- Stress reduction techniques

Pharmacologic Interventions

- Phosphodiesterase-5 inhibitors (sildenafil, tadalafil, vardenafil) with consideration of drug interactions[29]
- Intracavernosal injection therapy when oral agents are ineffective
- Vacuum erection devices as non-pharmacologic options
- Testosterone replacement when hypogonadism is confirmed (with caution in liver disease)

Psychological Support[30]

- Individual and couple-focused therapy addressing disease-specific concerns
- Cognitive-behavioural approaches for performance anxiety
- Mindfulness techniques promoting sexual awareness and pleasure
- Group support addressing stigma and isolation

Patient Education

- Safe sex practices with particular attention to viral transmission risk
- Realistic expectations regarding treatment outcomes
- Communication strategies with sexual partners[31]
- Understanding of connections between viral illness and sexual function

Management success depends heavily on addressing both organic and psychological factors, with particular attention to the bidirectional relationship between viral infection control and sexual wellbeing.[32](table 5)

Treatment Practices

Current evidence supports several treatment approaches for erectile dysfunction in patients with HBV and HIV infections, though clinical practice continues to evolve:

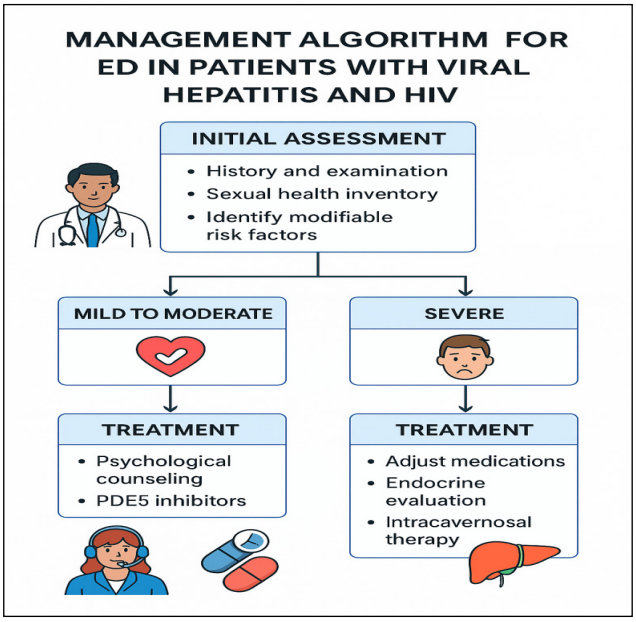

Figure 3.Management Algorithm for ED in Patients with Viral Hepatitis and HIV

ISSN: 0019-5138
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First-Line Approaches[33]

Phosphodiesterase-5 inhibitors (PDE5i) remain the cornerstone of pharmacological management:

- Sildenafil (25-100mg): Effective in 60-75% of patients with viral hepatitis/HIV
- Tadalafil (5-20mg): Longer half-life beneficial for spontaneity
- Vardenafil (5-20mg): Similar efficacy profile to sildenafil(fig 3)

Important considerations for PDE5i use in this population include:

- Drug interactions with antiretroviral protease inhibitors may require dose adjustment
- Generally well-tolerated in compensated liver disease
- Lower starting doses are recommended in patients with advanced liver disease
- Contraindicated with nitrate medications often prescribed for cardiac conditions common in this population[34]

Second-Line Approaches:

When oral medications prove ineffective or contraindicated:

Intracavernosal injection therapy (alprostadil, papaverine, phentolamine)

- Highly effective (70-85% success rate)
- Requires patient training and acceptance
- Special monitoring in coagulation disorders associated with advanced liver disease[35]

Intraurethral alprostadil suppositories

- Moderate efficacy (40-65%)
- Less invasive than injections
- Vacuum erection devices
- Non-pharmacologic option suitable for most patients
- Utility in patients with medication contraindications[36]

Psychological Interventions

Evidence supports several targeted approaches

- Cognitive-behavioural therapy demonstrating 50-70% improvement in mixed ED
- Mindfulness-based interventions showing promise for anxiety reduction
- Couples therapy addressing relationship dynamics and communication37
- Sex therapy focusing on performance pressure reduction and pleasure enhancement

Emerging Treatments[38]

Several novel approaches show promise in this population:

- Low-intensity extracorporeal shockwave therapy for vasculogenic ED
- Platelet-rich plasma injections targeting tissue regeneration
- Stem cell therapies addressing underlying endothelial dysfunction
- Neuromodulation techniques for neurogenic components39(table 6)

Table 6.Medication Interactions Between ED Treatments and Antiviral Therapies

ED Medication	Antiviral Drug Class	Interaction Effect	Clinical Management
Sildenafil	HIV Protease Inhibitors	↑ Sildenafil levels (2-11×)	Reduce sildenafil to 25mg/48h; monitor for hypotension
Tadalafil	HIV Protease Inhibitors	↑ Tadalafil levels (2-4×)	Reduce tadalafil to 5-10mg/72h; avoid daily dosing
Vardenafil	HIV Protease Inhibitors	↑ Vardenafil levels (4-16×)	Max dose 2.5mg/72h; consider alternative treatments
PDE5 Inhibitors	NNRTIs	Variable effects (↓ or ↑)	Titrate dose based on response; monitor efficacy
PDE5 Inhibitors	Tenofovir/Entecavir (HBV)	No significant interaction	Standard dosing generally appropriate
Intracavernosal injections	Most antivirals	Minimal systemic interaction	Generally safe combination; standard dosing
Testosterone	Hepatotoxic antivirals	Potential additive liver injury	Regular LFT monitoring; consider transdermal formulations

ISSN: 0019-5138
DOI: https://doi.org/10.24321/0019.5138.2026107

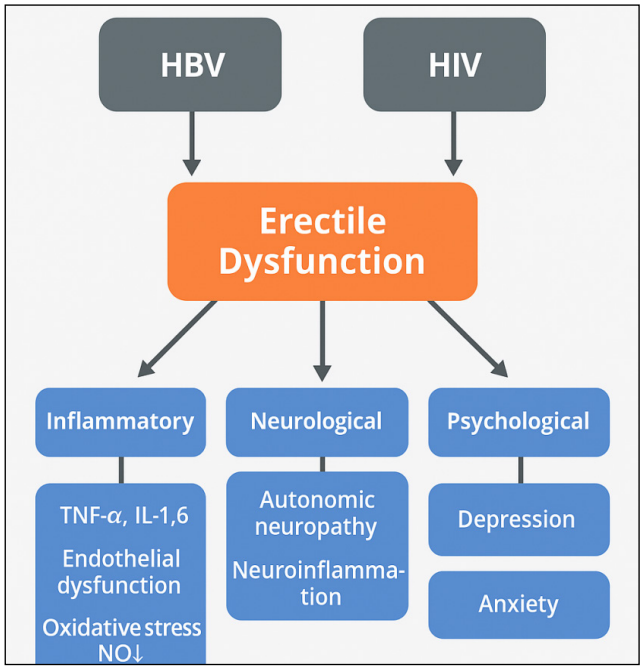

Figure 4.Mechanisms of Drug Interactions

Special Considerations

Treatment selection must account for:

- Liver function status in HBV patients[40]
- Drug interaction potential with complex medication regimens
- Cardiovascular risk assessment
- Partner concerns regarding viral transmission
- Accessibility and cost barriers affecting adherence[41]

Real-world practice data indicates that despite available effective treatments, only 22-38% of patients with HBV/HIV and ED receive appropriate therapy.[42] This treatment gap highlights the need for improved awareness, screening, and integrated care approaches.(fig 4)

Conclusion

Erectile dysfunction is a prevalent and clinically significant complication of chronic hepatitis B and HIV infection. Its development reflects a complex interplay between hepatic dysfunction, immune activation, metabolic and endocrine disturbances, medication effects, and psychological stress. Most patients exhibit mixed-aetiology ED, necessitating comprehensive assessment and individualized management.

Integrating sexual health evaluation into routine HBV and HIV care can substantially improve quality of life, relationship satisfaction, and treatment adherence. Addressing erectile dysfunction within the broader framework of chronic viral disease management represents an essential component of holistic patient-centred care.

Conflict of Interest: None

Source of Funding: None

Declaration of Generative AI and AI-Assisted Technologies in the Writing Process: None

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