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Demographic and clinical characteristics in patients undergoing liver transplantation for hepatitis B virus: Analysis of trends over time in 1,067 cases

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Abstract

To describe the demographic and clinical profile of adult patients (≥ 18 years) who underwent liver transplantation (LT) for chronic hepatitis B (CHB) at Inonu University Liver Transplantation Institute between January 2009 and February 2025, and to analyse sixteen-year temporal trends. This was retrospective crossectional study. Patients aged 18 years and older were included in the study, and a total of 1,067 patients were analyzed. Key variables included sex, diagnostic group, MELD-Na score, transplant type, and survival status. 858 patients (80.4%) were male; mean transplant age 50.6 ± 10.5 years; predominant age bracket 50–59 years (41.1%). Diagnostic breakdown: HBV cirrhosis alone 61.7%, HCC 25.8%, HDV co-infection 15.9%. Male predominance was highest in the HCC group (90.2%) with a mean transplant age of 54.9 ± 8.9 years. The HDV group had the highest mean MELD-Na (17.2 ± 2.6). Female patients had significantly higher MELD than males (17.4 ± 2.3 vs 16.6 ± 1.6; p = 0.009). Mean transplant age increased by +0.53 years per year from 2009 to 2024 (p < 0.001). HBV-related LT is predominantly performed in middle-aged males with cirrhosis. HCC co-existence is associated with older age and marked male predominance; HDV co-infection carries the highest MELD burden. The steady rise in transplant age likely reflects disease-progression delay attributable to potent antiviral therapy.

Keywords: Hepatitis B virus, liver transplantation, carcinoma, hepatocellular, hepatitis D, end stage liver disease, Türkiye

Introduction

Liver transplantation (LT) remains the only definitively validated treatment for end-stage liver disease. According to World Health Organization (WHO) estimates, more than one million people die annually from the complications of chronic liver disease and cirrhosis, a substantial proportion of which is attributable to advanced hepatitis B virus (HBV)-related disease.

HBV Globally and in Türkiye: Burden, Carriage, and Evolution of Treatment Algorithms

HBV is a hepatotropic, partially double-stranded Deoxyribonucleic Acid (DNA) virus belonging to the family Hepadnaviridae [1]. According to the WHO 2024 Global Hepatitis Report, approximately 254–298 million individuals worldwide carry chronic HBV infection, and 1.1 million people die each year from HBV-related complications, principally cirrhosis and hepatocellular carcinoma (HCC) [2,3].

The prevalence of chronic HBV carriage varies considerably by geography. HBsAg seroprevalence exceeds 6% in sub-Saharan Africa and the Pacific Asia region, while remaining below 1% in Western Europe and North America [2]. The predominant driver of this distribution is perinatal transmission; HBV infection acquired at birth carries a chronification risk exceeding 90% [1,3].

Two fundamental transformations have occurred in the management of HBV over the past three decades. The first is the implementation of universal neonatal vaccination programmes from the 1990s onward; in countries where coverage has exceeded 90%, the incidence of new chronic HBV cases has declined

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dramatically [3]. The second is the revolution in antiviral therapy: entecavir (ETV), a high-genetic-barrier agent, entered clinical practice in 2005, followed by tenofovir disoproxil fumarate (TDF) in 2008 and tenofovir alafenamide (TAF) in 2016 [4,5]. The current EASL 2025 guidelines recommend treatment in all adults with detectable HBV DNA or those at risk of advanced fibrosis or cirrhosis [5,6]. By suppressing viral replication and thereby slowing the progression to cirrhosis, these agents defer the age at which transplant indication emerges. The rise in mean transplant age from 48.3 to 52.8 years between 2009 and 2024 in our series supports this hypothesis.

Türkiye occupies the intermediate-endemicity tier, with a national HBsAg seroprevalence of approximately 2–4%; however, regional prevalence in Eastern and South-Eastern Anatolia is known to reach 5–8% (5). In Türkiye, HBV remains the leading aetiology among liver transplant indications, and together with hepatitis C virus (HCV) accounts for the majority of patients on the national waiting list.

HBV-Related Liver Transplantation Globally, in Türkiye, and at İnönü University

The proportion of liver transplantations attributable to HBV varies markedly by region. In Asia-Pacific centres this figure ranges from 30–50%, compared with 10–20% in Europe and 5–10% in North America [6,7]. In countries where universal vaccination and potent antiviral therapies have been implemented, the proportion of HBV-indicated transplants has declined substantially over the past two decades, a trend most clearly observed in Western European and US centres [8,9].

İnönü University Liver Transplantation Institute is one of the most established and highest-volume transplant centres in Türkiye [10]. The transplant programme, initiated in 2002, has grown to rank among the foremost centres both nationally and in Europe. Drawing on extensive experience in both deceased-donor and living-donor transplantation, the centre accepts referrals from across Türkiye and from neighbouring countries. The cohort presented in this study constitutes one of the most comprehensive series of HBV-related liver transplantation published to date in Türkiye.

Routes of HBV Transmission

HBV is transmitted principally through three routes: [3].

1. **Perinatal transmission:** Transmission from an HBsAg-positive mother during or immediately after delivery; this constitutes the primary source of chronic infection in low- and middle-income countries.
2. **Sexual transmission:** Unprotected sexual intercourse is the predominant route in high-income countries.
3. **Parenteral transmission:** This category encompasses contaminated blood products, intravenous drug use, and non-sterile medical equipment.

HBV can survive on surfaces for up to seven days and is transmissible via extremely small quantities of blood [3]. Epidemiological studies conducted in Türkiye have consistently demonstrated the key role of household contact and sexual transmission in the domestic spread of HBV [5].

HDV Co-infection and HBV-Related HCC: Clinical Significance

Hepatitis D virus (HDV) is a defective Ribonucleic Acid (RNA) virus that requires HBsAg for its replication [4]. Whether encountered as a co-infection or superinfection, HDV accelerates hepatic injury far more rapidly than HBV alone; the progression to cirrhosis is expedited and the risk of HCC is markedly amplified [11]. Current estimates suggest that 15–72 million individuals worldwide carry HBV-HDV co-infection [4].

HBV-related HCC is the underlying aetiology in approximately half of all HCC cases worldwide. Male sex, the presence of cirrhosis, prolonged high viral load, and alcohol and tobacco use substantially elevate HCC risk. In our series, 90.2% of the HCC group comprised male patients, who were on average six years older at the time of transplantation than patients with HBV cirrhosis alone.

The combination of high-genetic-barrier nucleoside analogues (ETV, TDF, or TAF) with hepatitis B immunoglobulin (HBIG) for post-transplant prophylaxis against HBV recurrence represents the standard approach endorsed by current clinical guidelines [12,13].

Study Objectives

The present study aimed to characterise the demographic and clinical profile of patients aged 18 years or older who underwent liver transplantation for Chronic Hepatitis B (CHB) at our centre between 2009 and 2025; to examine the impact of HCC co-existence and HDV co-infection on this profile; and to describe sixteen-year temporal trends in transplant age and annual transplant volume.

Material and Methods

Study Design and Patient Selection

All patients aged 18 years or older who underwent liver transplantation for CHB at Inönü University Liver Transplantation Institute between January 2009 and February 2025 were enrolled This was a retrospective crossectional study. . Data were retrieved from the institutional electronic medical records system.

Inclusion criteria: Age ≥ 18 years at the time of transplantation; documented pre-transplant HBsAg positivity; CHB as the primary transplant indication; complete records of key demographic and clinical variables.

Exclusion criteria: Primary aetiology other than CHB; calculated age exceeding 70 years at transplantation; absence of essential clinical data.

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Sample size: All 1,067 patients meeting the inclusion criteria within the specified period were included; this approach is consistent with the accepted standard for retrospective cohort studies.

Data Collection and Variables

Demographic data: Age at transplantation (calculated from date of birth and transplant date), sex, body mass index (BMI), ABO blood group, and province of residence.

Clinical data: Clinical diagnosis and diagnostic group, year of transplantation, transplant type (living-donor/deceased-donor), MELD-Na score, pre-transplant HBV-DNA, HDV-RNA, AFP, HBsAg, and anti-HBs status.

Diagnostic Grouping

Patients were classified into five groups according to clinical diagnosis: HBV cirrhosis alone, HBV+HCC, HBV+HDV, HBV+HCC+HDV, and HBV+HCV. For HCC analyses, the HBV+HCC and HBV+HCC+HDV groups were merged; for HDV analyses, the HBV+HDV and HBV+HCC+HDV groups were merged (total HCC n = 275, total HDV n = 170).

Statistical Analysis

Statistical analyses were performed using SPSS v.28 (IBM Corp., Armonk, NY, USA) and Python 3.12. Continuous variables are presented as mean ± standard deviation (SD) or median (IQR) according to their distribution; categorical variables are reported as frequency and percentage. Independent-samples Student's t-test was applied for comparisons between two groups, and chi-square test for categorical variables. Linear regression was used to model temporal trends in transplant age. Statistical significance was defined at $p < 0.05$.

Ethical Approval

This study was approved by the İnönü University Scientific Research and Publication Ethics Committee (Health Sciences Scientific Research Ethics Committee) (Decision date: 10/03/2026 Decision No: 2026/9654). Given the retrospective design and anonymous analysis of data, individual patient consent was not required.

Results

Patient Flow and General Demographic Characteristics

During the study period, records were retrieved for 1,067 patients aged over 18 years who underwent liver transplantation at our centre for HBV-related end-stage liver disease. Of the 1,067 patients in the series, 858 were male (80.4%) and 209 were female (19.6%), yielding a male-to-female ratio of 4.1:1. The mean age at transplantation was 50.6 ± 10.5 years (median 52.1; IQR: 44–58; range 18–70 years). Transplant ages were comparable between male and female patients, and the difference was not statistically significant (50.5 ± 10.3 vs 50.7 ± 10.8 years; p = 0.839). Living-donor transplantation was performed in 92.6% of cases (n = 988); deceased-donor transplantation was carried out in 79 patients (7.4%)

Age Group Distribution

The 50–59 year age bracket constituted the largest group in the series (n = 439, 41.1%), followed by the 40–49 year (n = 258, 24.2%), 60–70 year (n = 196, 18.4%), 30–39 year (n = 120, 11.2%), and 18–29 year (n = 54, 5.1%) groups, respectively. In every age bracket, the number of male patients exceeded that of female patients. The cross-tabulation of age groups by diagnosis is presented in Figure 1 and Table 1.

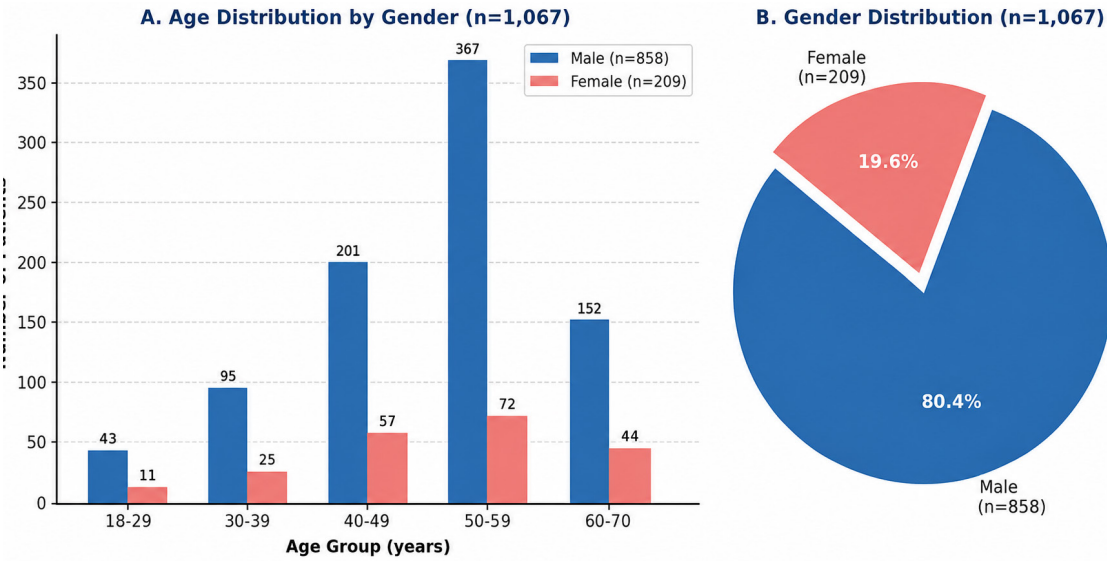

Figure 1. A) Sex distribution by age group (18–70 years); **B)** Overall sex distribution; The highest transplant frequency is observed in the 50–59 year age group (41.1%)

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Table 1. General demographic and clinical characteristics (n = 1,067; transplant age 18–70)

Variable	All (n = 1,067)	Male (n = 858)	Female (n = 209)	p value
Age at transplantation, mean ± SD (yrs)	50.6 ± 10.5	50.5 ± 10.3	50.7 ± 10.8	0.839
Median (IQR)	52.1 (44–58)	51.9 (44–57)	53.2 (44–59)	—
Range	18–70	18–70	18–70	—
BMI, mean ± SD (kg/m²)	26.1 ± 4.8	26.2 ± 4.7	25.8 ± 5.1	0.321
MELD-Na, mean ± SD	16.8 ± 1.7	16.6 ± 1.6	17.4 ± 2.3	0.009
Median (IQR)	15 (15–16)	15 (15–16)	15 (15–17)	—
Range	15–36	15–36	15–36	—
Transplant type				
Living donor (LDLT)	988 (92.6%)	793 (92.4%)	195 (93.3%)	0.821
Deceased donor (DDLT/Split)	79 (7.4%)	65 (7.6%)	14 (6.7%)	—

† Exclusion: transplant age <18; BMI: Body Mass Index, LDLT: Living Donor Liver Transplantation, DDLT: Deceased Donor Liver Transplantation, IQR: Interquartile Range

Distribution by Diagnostic Group

By diagnostic group, 658 patients (61.7%) had HBV cirrhosis alone, 234 (21.9%) HBV+HCC, 129 (12.1%) HBV+HDV, 41 (3.8%) HBV+HCC+HDV, and 5 (0.5%) HBV+HCV. When the HBV+HCC and HBV+HCC+HDV groups were combined, the overall HCC rate was 25.8% (n = 275); combining the HBV+HDV and HBV+HCC+HDV groups yielded an overall HDV co-infection rate of 15.9% (n = 170). Sex and age differences across groups are presented in Table 2 and Figure 2.

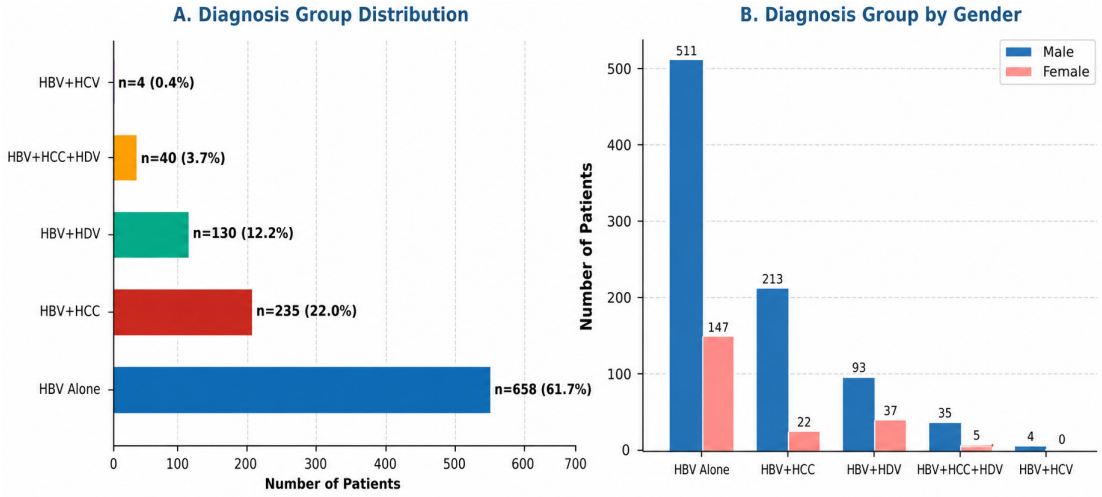

Figure 2. A) Patient distribution by diagnostic group; **B)** Cross-tabulation of diagnostic group and sex; Male predominance is most pronounced in the HBV+HCC group

Table 2. Patient Distribution by Diagnostic Group (n = 1,067)

Diagnosis group	n (%)	Male n (%)	Female n (%)	Mean age (yrs ± SD)	MELD Mean ± SD
HBV alone (cirrhosis)	658 (61.7)	517 (60.3)	141 (67.5)	48.7 ± 10.8	17.0 ± 1.9
HBV + HCC	235 (22.0)	216 (25.2)	19 (9.1)	55.2 ± 8.8	16.2 ± 0.7
HBV + HDV	130 (12.2)	94 (11.0)	36 (17.2)	49.3 ± 11.1	17.2 ± 2.6
HBV + HCC + HDV	40 (3.7)	32 (3.7)	8 (3.8)	54.2 ± 9.4	16.4 ± 1.6
HBV + HCV	5 (0.5)	5 (0.6)	0 (0.0)	52.4 ± 6.7	15.0 ± 0.0
Total	**1,067 (100)**	**858 (80.4)**	**209 (19.6)**	**50.6 ± 10.5**	**16.8 ± 3.7**

HCC: Hepatocellular Carcinoma, HDV: Hepatitis D Virus, HCV: Hepatitis C Virus; *Total HCC rate including HBV+HCC+HDV group: 25.8%; **Total HDV rate including HBV+HCC+HDV group: 15.9%

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HBV+HCC Group

HCC co-existence was identified in 275 patients (25.8%). Within this group, 90.2% were male; the mean transplant age was 54.9 ± 8.9 years, approximately six years higher than in the HBV cirrhosis-alone group ($p < 0.001$). The HCC rate in males (28.9%) significantly exceeded that in females (12.9%; $p < 0.001$). The predominant age bracket was 50–59 years (46.2%). Details are presented in Figure 3 and Table 3.

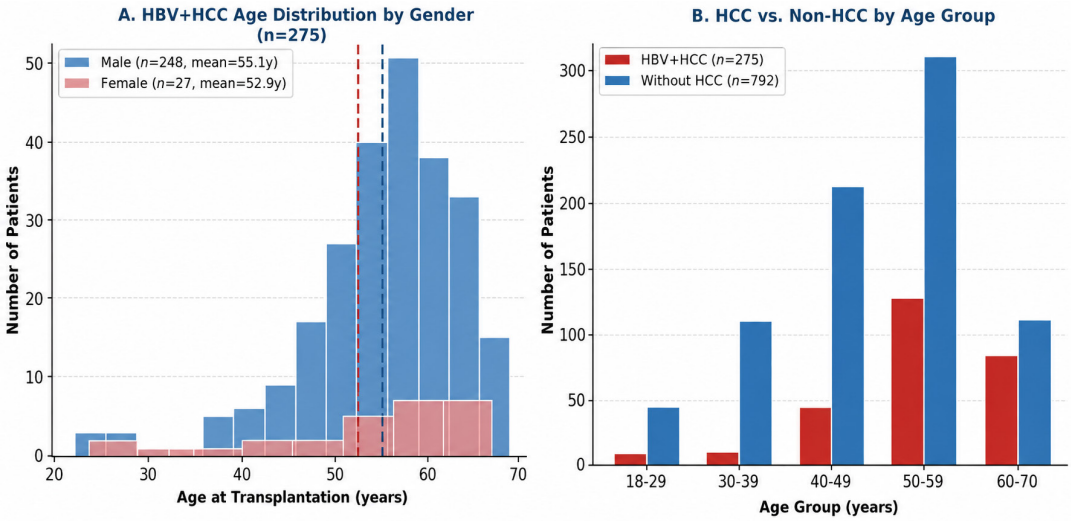

Figure 3. A) Age distribution by sex in the HBV+HCC group; **B)** Age group comparison between HCC and non-HCC patients; HCC is markedly concentrated in the 50–70 year age range and in male patients

Table 3. Annual distribution of transplants and mean transplant age (n = 1,067)

Year	n	Cumulative n	Mean age (yrs)	Dominant diagnosis	Peak age group
2009	50	50	48.3 ± 8.9	HBV Alone (58%)	40–49
2010	76	126	46.3 ± 10.4	HBV Alone (60%)	40–49
2011	65	191	47.4 ± 10.6	HBV Alone (62%)	40–49
2012	68	259	48.9 ± 10.6	HBV Alone (59%)	50–59
2013	95	354	47.7 ± 11.6	HBV Alone (55%)	50–59
2014	65	419	48.1 ± 10.3	HBV Alone (58%)	40–49
2015	49	468	50.1 ± 9.3	HBV Alone (57%)	50–59
2016	70	538	49.7 ± 11.4	HBV Alone (56%)	50–59
2017	69	607	52.3 ± 9.0	HBV+HCC (31%)	50–59
2018	66	673	53.3 ± 9.6	HBV+HCC (35%)	50–59
2019	81	754	49.7 ± 12.1	HBV Alone (52%)	50–59
2020	64	818	53.2 ± 7.9	HBV+HCC (33%)	50–59
2021	52	870	55.4 ± 7.6	HBV+HCC (37%)	50–59
2022	61	931	54.1 ± 9.4	HBV+HCC (34%)	50–59
2023	55	986	53.8 ± 12.5	HBV+HCC (31%)	50–59
2024	67	1,053	52.8 ± 8.8	HBV+HCC (30%)	50–59
2025*	14	1,067	56.4 ± 8.9	HBV+HCC (36%)	50–59
Total	**1,067**	—	**50.6 ± 10.5**	**HBV Alone (61.7%)**	**50–59**

*2025 data are partial (as of February 2025); The adverse impact of the COVID-19 pandemic on 2020–2021 transplant volumes is evident; The dominant diagnosis group refers to the most frequent diagnosis in that year

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HBV+HDV Coinfection Group

HDV co-infection was identified in 170 patients (15.9%). The mean transplant age was 49.0 ± 10.9 years, significantly lower than in the HCC group ($p < 0.001$). The proportion of female patients in this group was 24.7%, approximately three times that observed in the HCC group (9.8%; $p < 0.001$). The peak age concentration fell within the 40–49 year range. Figure 4A presents the age-sex profile for this group.

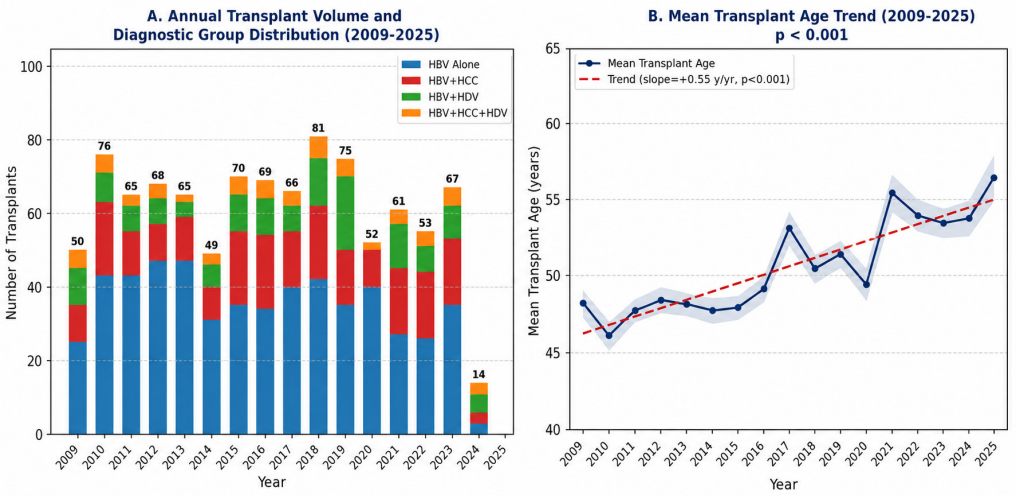

Figure 4. A) Age and sex distribution in the HBV+HDV group; **B)** Annual transplant volume, distribution by diagnostic group, and mean transplant age trend (2009–2025); A significant upward trend in transplant age is observed ($p < 0.001$)

Annual Transplant Volume and Age Trends

Annual transplant volumes followed a fluctuating course over the sixteen-year period. The highest number of HBV-related transplants was recorded in 2013 (n = 95), with 2019 ranking second (n = 81). A marked decline was observed during the COVID-19 pandemic: numbers fell to 64 in 2020 and 52 in 2021. Data for 2025 are not yet complete (n = 14, as of February 2025). The annual distribution is presented in Table 3.

Among the most striking findings in the series is the uninterrupted rise in transplant age. The mean transplant age increased from 48.3 years in 2009 to 55.4 years in 2021. Linear regression analysis indicates a mean annual increment of +0.53 years, and this trend is statistically significant ($p < 0.001$). The coincidence of this shift with the era of potent antiviral therapy reinforces the hypothesis that pharmacological treatment defers disease progression. Figure 4B illustrates the transplant age trend and the annual distribution by diagnostic group.

MELD-Na Score

MELD-Na was evaluated in all 1,067 patients. The overall mean MELD-Na was 16.8 ± 1.7 (median 15; IQR: 15–16; range 15–36). Female patients had a significantly higher mean MELD than male patients (17.4 ± 2.3 vs 16.6 ± 1.6; $p = 0.009$). Across diagnostic groups, the highest MELD was observed in the HDV group (17.2 ± 2.6), followed by HBV cirrhosis alone (17.0 ± 1.9), HBV+HCC+HDV (16.4 ± 1.6), and HBV+HCC (16.2 ± 0.7). The MELD distribution is illustrated in Figure 5.

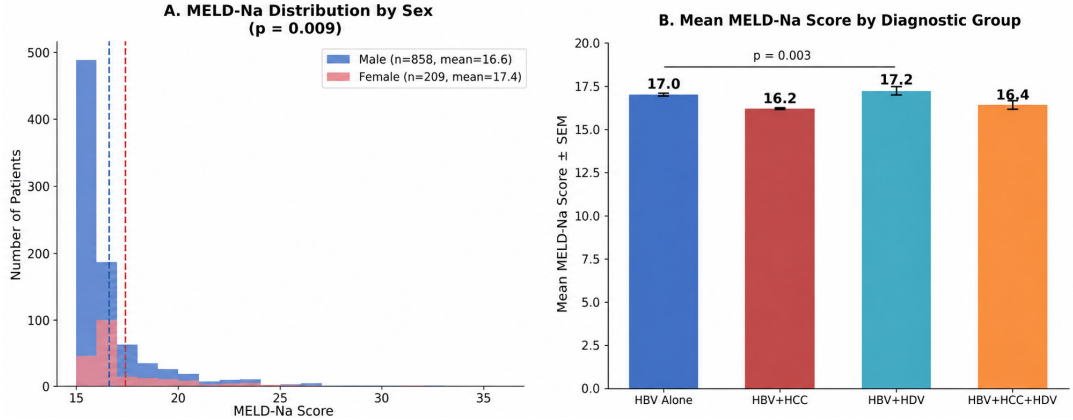

Figure 5. A) MELD-Na distribution by sex; **B)** Mean MELD-Na (± SEM) by diagnostic group; MELD-Na is markedly elevated in the HBV+HDV group; an outlier effect is observed in the HCC group

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Cross-Analysis of Age Group and Diagnosis

Examination of the age-diagnosis cross-tabulation revealed that HBV cirrhosis patients were distributed across all age brackets, while HCC became prominent above the age of 50 and HDV co-infection peaked in the 40–49 year range. The cross-tabulation is provided in Table 3.

Geographical Distribution

Although patient referrals originated from across Türkiye, the Eastern and South-Eastern Anatolian provinces of Malatya, Elazığ, Diyarbakır, and Şanlıurfa were most prominently represented. This pattern is consistent with epidemiological data demonstrating above-average HBV seroprevalence in these regions is illustrated in Figure 6.

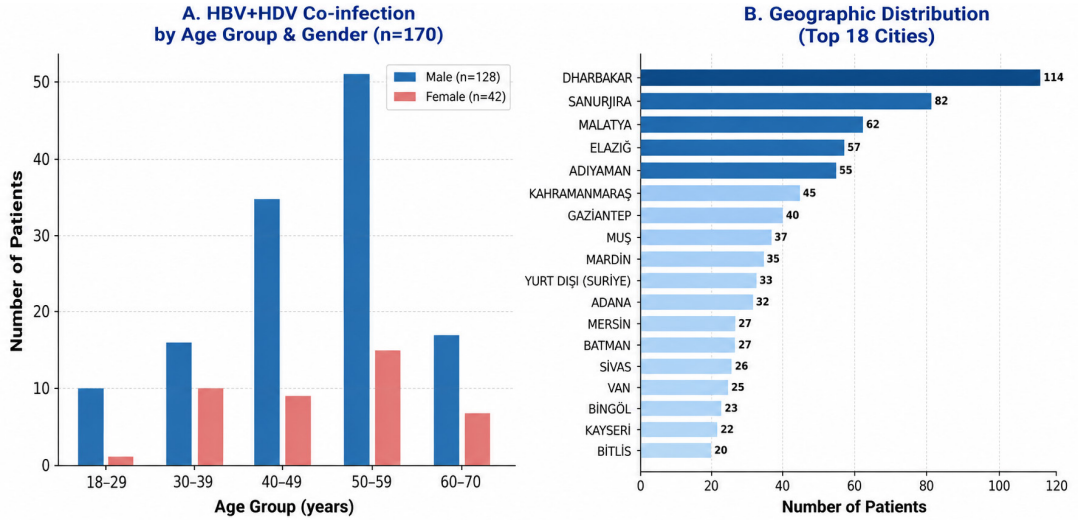

Figure 6. A) Age-sex distribution in the HBV+HDV group; **B)** Geographical distribution by province (top 18 provinces); The pronounced concentration from South-Eastern and Eastern Anatolia reflects the regional HBV burden

Discussion

Encompassing 1,067 patients aged 18 years or older followed over sixteen years, this study represents one of the most comprehensive series of CHB-related liver transplantation reported from Türkiye.

The male-to-female ratio of 4.1:1 in our series exceeds those reported by Yang et al. (74.1% male) [14]. The higher prevalence of CHB in males in Türkiye, the inherent susceptibility of male sex to fibrosis and HCC development, and the more frequent exposure of male patients to cofactors such as alcohol and tobacco partly account for this pattern. The national data reported by Vatansever et al. also reflect a comparable sex distribution [15].

Our mean transplant age of 50.6 years is consistent with the values reported by Cholongitas et al. (47.8 years) [12] and Yang et al. (51.2 years) [14]. More notably, this mean increased from 48.3 to 55.4 years over sixteen years ($p < 0.001$). The temporal coincidence of this rise with the widespread adoption of potent antiviral therapies strengthens the hypothesis that pharmacological treatment defers the onset of cirrhosis and end-stage liver disease [16,17].

Our HCC rate (25.8%) is comparable to that reported in the series of Praga et al. (22.3%) [18]. The transplant age in the HCC group exceeded that of the HBV cirrhosis group by approximately six years ($p < 0.001$), confirming that HCC evolves through decades of cumulative chronic inflammatory injury [19,20].

The marked male predominance in the HCC group (90.2%) warrants attention. The hepatoprotective effect of oestrogen, enhanced viral replication in males mediated through androgen response elements, and the tendency of male patients to present later to surveillance programmes are among the proposed explanatory mechanisms [21,22].

Our HDV co-infection rate (15.9%) exceeds those reported in Western European series. The geographical proximity of our centre to Iran and the Middle East augments patient referrals and partly accounts for the relatively high HDV prevalence [23,24]. The highest mean MELD in the HDV group (17.2 ± 2.6) indicates more severely compromised hepatic reserve in these patients, underscoring the need for close pre-transplant monitoring. The comparatively high proportion of female patients in this group (24.7%) raises the question of a sex-related susceptibility to HDV that merits prospective investigation [17,25].

At our centre, post-transplant prophylaxis consists of a combination of low-dose HBIG with a high-barrier antiviral agent (ETV, TDF, or TAF), followed by long-term antiviral monotherapy. The 2024 publication by Cholongitas et al. supports the efficacy of this protocol [12].

Conclusion

The sixteen-year data from 1,067 patients aged 18 years or older who underwent liver transplantation for CHB at our centre yield the following findings:

- HBV-related liver transplantation is characterised by pronounced male predominance (M:F 4.1:1) and concentration in the 50–59 year age group.
- HCC co-existence was present in 25.8% of cases; this group is distinguished by more advanced age (mean 54.9 years) and marked male predominance (90.2%).
- HDV co-infection (15.9%) occurs at a comparatively younger age (mean 49.0 years) and carries the highest MELD scores in the series, necessitating close pre-transplant surveillance.
- The sixteen-year upward trend in transplant age is statistically significant ($p < 0.001$) and supports the notion that potent antiviral therapies delay disease progression.
- The high referral volume from Eastern and South-Eastern Anatolia underscores the need for targeted HBV screening and vaccination programmes in these regions.

In light of these findings, the following strategies emerge as priorities: expanding HBV vaccination coverage, beginning with universal neonatal immunisation; implementing periodic ultrasonography and AFP surveillance in HBsAg carriers; ensuring continuous antiviral therapy in patients with advanced fibrosis or cirrhosis; and raising public awareness of hepatitis B. We believe our findings will provide a current reference dataset for Türkiye and facilitate comparisons with international centres.

Ethical Approval

This study was approved by the Scientific Research and Publication Ethics Committee (Health Sciences Scientific Research Ethics Committee) of İnönü University on March 10, 2026, with session number 5 and decision number 2026/9654.

Patient Consent

This study was approved by the institutional ethics committee. Given its retrospective nature and the use of fully anonymized data, the requirement for informed patient consent was waived."

Conflict of Interest

The authors confirm the absence of any conflicts associated with this work.

Funding

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