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Efficacy of short-term Peg-IFN α-2b treatment in chronic hepatitis B patients with ultra-low HBsAg levels: a retrospective cohort study

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Abstract

Purpose Peginterferon alfa-2b (Peg-IFN α-2b) has demonstrated superior efficacy over nucleos(t)ide analogs (NAs) in the treatment of chronic hepatitis B (CHB), particularly among patients with low levels of hepatitis B surface antigen (HBsAg). This study aims to determine whether patients with ultra-low HBsAg levels (< 200 IU/mL) can achieve significantly higher clinical cure rates with abbreviated courses of Peg-IFN α-2b therapy.

Methods In this retrospective analysis, CHB patients with HBsAg levels below 200 IU/mL were categorized into a Peg-IFN α-2b group and a control group. The Peg-IFN α-2b group received Peg-IFN α-2b for a minimum of 24 weeks, with the possibility of early discontinuation upon achieving HBsAg clearance, and were followed through week 48. The control group remained untreated for hepatitis B virus (HBV), and was observed for 24 weeks. HBsAg clearance rates were compared between groups. Univariate and multivariate logistic regression analyses were employed to identify factors associated with HBsAg clearance .

Results By week 24, the HBsAg clearance rate in the Peg-IFN α-2b group was notably 52.1% (38/73), contrasting sharply with the mere 1.3% (1/77) observed in the control group. Within the Peg-IFN α-2b group, a substantial 97.3% (71/73) of patients noted a reduction in HBsAg levels. Besides, the decision to continue or discontinue treatment after the 24-week mark had no significant impact on the HBsAg clearance rate at week 48. Multivariable analysis pinpointed baseline HBsAg levels (OR = 0.984, $p = 0.001$) and the presence of fatty liver (OR = 5.960, $p = 0.033$) as independent predictors of HBsAg clearance.

Conclusion Our findings confirm that a 24-week course of Peg-IFN α-2b yields robust efficacy in CHB patients with ultra-low HBsAg levels. Prolonging treatment beyond the 24-week threshold is deemed unnecessary. Both baseline HBsAg level and the presence of fatty liver emerged as significant predictors for HBsAg clearance.

Keywords Chronic Hepatitis B, Peginterferon alfa-2b, Hepatitis B Surface antigen, Fatty liver, Clinical cure

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Introduction

Chronic hepatitis B virus (HBV) infection, a global health issue, affects over 296 million individuals, with a significant prevalence in the Asia-Pacific region [1]. Untreated chronic HBV infection escalates the risk of cirrhosis, liver failure and hepatocellular carcinoma (HCC) [2]. The World Health Organization reported 1.2 million new cases of chronic hepatitis B (CHB) and 1.1 million HBV-related fatalities in 2022 [2].

The presence of HBV covalently closed circular DNA (cccDNA) renders the complete eradication of HBV a formidable challenge [3]. Consequently, the primary goal of CHB treatment is to achieve a clinical cure, also known as functional cure. This is characterized by the absence of hepatitis B surface antigen (HBsAg) in serum and an undetectable HBV viral load, suggesting a reduced cccDNA presence [4, 5]. Such a cure can substantially decrease the risk of cirrhosis and HCC [5]. The therapeutic arsenal for CHB comprises two main drug classes: long-term nucleos(t)ide analogs (NAs) (including entecavir, tenofovir disoproxil fumarate, and tenofovir alafenamide) and peginterferon alfa (Peg-IFN α) therapy for more than 48 weeks [6]. Despite the strong antiviral effects of NAs, achieving HBsAg clearance is difficult, with an annual serum clearance rate ranging from 0 to 2% [7]. In contrast, Peg-IFN α-based therapy has demonstrated superior to NAs monotherapy in achieving HBsAg clearance within a limited treatment period [8]. Several studies have shown that patients with lower HBsAg levels (<1500 IU/mL) are more likely to attain a clinical cure with sequential Peg-IFN α therapy [9–11]. Moreover, an early virological response, operationalized as HBsAg levels falling below 200 IU/mL or a reduction exceeding 1 $\log_{10}$ IU/mL by the 24th week of treatment, can help predict patients who may benefit from an extended 48 to 96 weeks of Peg-IFN α treatment [8, 11]. In our clinical practice, we have observed a positive response to short-term Peg-IFN α treatment in patients with HBsAg levels below 200 IU/mL, a phenomenon not yet widely documented. This study, therefore, sought to explore the clinical outcomes of short-term Peg-IFN α treatment in CHB patients with ultra-low HBsAg levels and to identify potential influencing factors.

Methods

Patients

This single-center, retrospective, real-world clinical study was conducted at the Second Affiliated Hospital of Harbin Medical University, enrolling CHB patients aged 18–70 years from 2018 to 2024. Eligibility criteria mandated HBsAg levels below 200 IU/mL and a seropositive status for a minimum of six months. There were no restrictions on HBV DNA or HBeAg levels. Participants were also required to exhibit serum alanine aminotransferase (ALT) levels no greater than tenfold the upper limit of normal and to have abstained from immunosuppressants for at least six months prior to enrollment. The treatment history of patients must have been devoid of interferon therapy; however, other treatment histories, such as no prior anti-HBV treatment, ongoing NAs therapy, or previous NAs use, were not subject to stringent limitations.

Patients were categorized into a Peg-IFN α-2b group and a control group post-enrollment based on the treatment they received. The Peg-IFN α-2b group comprised patients administered a monotherapy regimen of Peg-IFN α-2b (180 μg subcutaneously, once weekly) for a minimum of 24 weeks, with the prerogative to discontinue prematurely upon achieving HBsAg clearance. Those who had not attained HBsAg clearance by week 24 were given the option to continue treatment at their discretion. The control group was comprised of patients who received no anti-HBV therapy.

Exclusion criteria were as follows: (1) a history of autoimmune disease; (2) co-infection with the human immunodeficiency virus, hepatitis A virus, hepatitis C virus, hepatitis D virus, or hepatitis E virus; (3) current liver decompensation or a history thereof; (4) liver cancer or suspected malignancy and other neoplastic conditions; (5) a history of severe cardiac disease, serious infections, uncontrolled diabetes, thyroid disorders, retinopathy, etc.; (6) any other contraindications for Peg-IFN α-2b treatment.

Data collection

A comprehensive review of the medical records from the Second Affiliated Hospital of Harbin Medical University was conducted to identify patients with CHB who fulfilled the established enrollment criteria. A meticulous data collection protocol was employed, capturing a spectrum of clinical parameters. Demographic details, anthropometric measurements such as height and weight, family history of CHB, and the status of fatty liver disease were meticulously documented. Laboratory assessments encompassed a complete blood count, focusing on neutrophil and platelet (PLT) counts, and a battery of liver function tests including serum ALT and aspartate aminotransferase (AST) levels. Serological profiling for HBV involved quantification of HBsAg, hepatitis B e antigen (HBeAg), hepatitis B surface antibody (HBsAb), and hepatitis B e antibody (HBeAb). The viral load, as indicated by HBV DNA concentration, was also determined. Patients were monitored for a period extending to week 24, with the Peg-IFN α-2b treatment group under extended surveillance until week 48.

HBsAg clearance was defined by a titer less than 0.05 IU/mL, and the presence of HBsAb at levels exceeding 10 mIU/mL was deemed positive. The threshold for

detectable HBV DNA was established at 30 IU/mL. Ethical considerations were rigorously adhered to, with the study receiving approval from the Ethics Committee of the Second Affiliated Hospital of Harbin Medical University (KY2024-049). Given the retrospective design of the research, the committee exempted the need for written informed consent from participants.

Outcomes

The primary outcome of this study was the assessment of HBsAg clearance in CHB patients by week 24. HBsAg clearance was defined by the absence of detectable HBsAg and undetectable HBV DNA, irrespective of whether HBsAg seroconversion had occurred. The HBsAg clearance rate was calculated as the percentage of patients achieving this outcome relative to the total number of patients in each study group.

Secondary endpoints encompassed the evaluation of HBeAg clearance and the undetectability of HBV DNA. Additionally, vigilant monitoring and documentation of adverse events were conducted among patients in the Peg-IFN α-2b group. This encompassed a spectrum of potential side effects, including but not limited to pyrexia, fatigue, anorexia, nausea, vomiting, headaches, myalgia, alopecia, rash, hepatic dysfunction, neutropenia, thrombocytopenia, and hyperthyroidism.

Statistical analysis

Statistical analysis was conducted utilizing SPSS 26.0 software. Continuous variables' measurement data were detailed employing the mean±standard deviation or median with interquartile range, contingent upon their adherence to a normal distribution. Categorical variables were articulated as frequencies and percentages. Comparative analyses between groups for continuous variables were executed via Student's t-test, Mann-Whitney U test, or analysis of variance, depending on the context. For categorical parameters, the Chi-square test or Fisher's exact test was applied, as appropriate. Univariate and multivariate logistic regression analyses were engaged to evaluate the determinants of HBsAg clearance. Statistical significance was set at a p-value threshold of less than 0.05.

Results

Baseline and clinical characteristics

Between the years 2018 and 2024, this study enrolled a total of 176 individuals diagnosed with CHB. The cohort was stratified, with 81 patients who received no treatment forming the control group, and 95 patients on Peg-IFN α-2b monotherapy constituting the treatment group. Within the control group, follow-up data for four patients was unavailable, resulting in the inclusion of 77 patients. Conversely, the Peg-IFN α-2b group experienced a loss to follow-up of six patients, eight instances of incomplete data due to missed routine examinations, and withdrawals by eight patients for personal reasons, culminating in the inclusion of 73 patients in the final analysis (Fig. 1). A comparison of baseline characteristics revealed no statistically significant differences between the control group and Peg-IFN α-2b group, as delineated in Table 1.

The HBsAg clearance rate in the Peg-IFN α-2b group was significantly higher than in the control group

In the control group, comprising 77 patients, the solitary individual attained HBsAg clearance by the 24-week mark, accompanied by seroconversion of both HBeAg and HBsAg, yielding a clearance rate of a mere 1.3% (1/77) (Fig. 2A). The remaining participants failed to achieve clearance for either HBeAg or HBsAg. Moreover, there was an absence of significant fluctuation in HBsAg levels from baseline to week 24 (Fig. 2B). Among the six patients who presented with detectable HBV DNA at the outset, all still exhibited detectable levels at week 24 (Fig. 2C).

Contrastingly, within the Peg-IFN α-2b group, a substantial 38 out of 73 CHB patients achieved HBsAg clearance by week 24, translating to a clearance rate of 52.1% (Fig. 2D). Of these 38 patients, 21 experienced HBsAg seroconversion, equating to a seroconversion rate of 28.8%. Among the 35 HBsAg-positive patients at week 24, three were initially HBeAg-positive, and by week 24, one had successfully achieved HBeAg seroconversion. Although HBsAg clearance was not accomplished by some patients in the Peg-IFN α-2b group, a notable 94.3% (33/35) demonstrated a reduction in HBsAg levels from baseline to week 24, with only two patients exhibiting an increase compared to baseline levels. Cumulatively, 97.3% (71/73) of the patients enrolled demonstrated a decrease in HBsAg levels. Furthermore, an extension of the treatment duration corresponded with a gradual decline in overall HBsAg levels (Fig. 2E). Additionally, seven patients who were initially positive for HBV DNA at baseline showed undetectable levels after 24 weeks of treatment (Fig. 2F).

Post the 24-week treatment interval, surveillance of patients in the Peg-IFN α-2b group was sustained through week 48. Out of the 35 HBsAg-positive patients, data for 31 were accessible at week 48. Driven by personal preference, 22 patients elected to proceed with Peg-IFN α-2b therapy, while nine decided to halt treatment. The outcomes revealed no significant disparities in HBsAg clearance (27.3% vs. 11.1%, $p=0.639$) or HBsAg seroconversion (9.1% vs. 11.1%, $p=0.657$) between the subgroups that continued and those that discontinued treatment (Table 2). Furthermore, with the exception of three patients lost to follow-up, none of the remaining

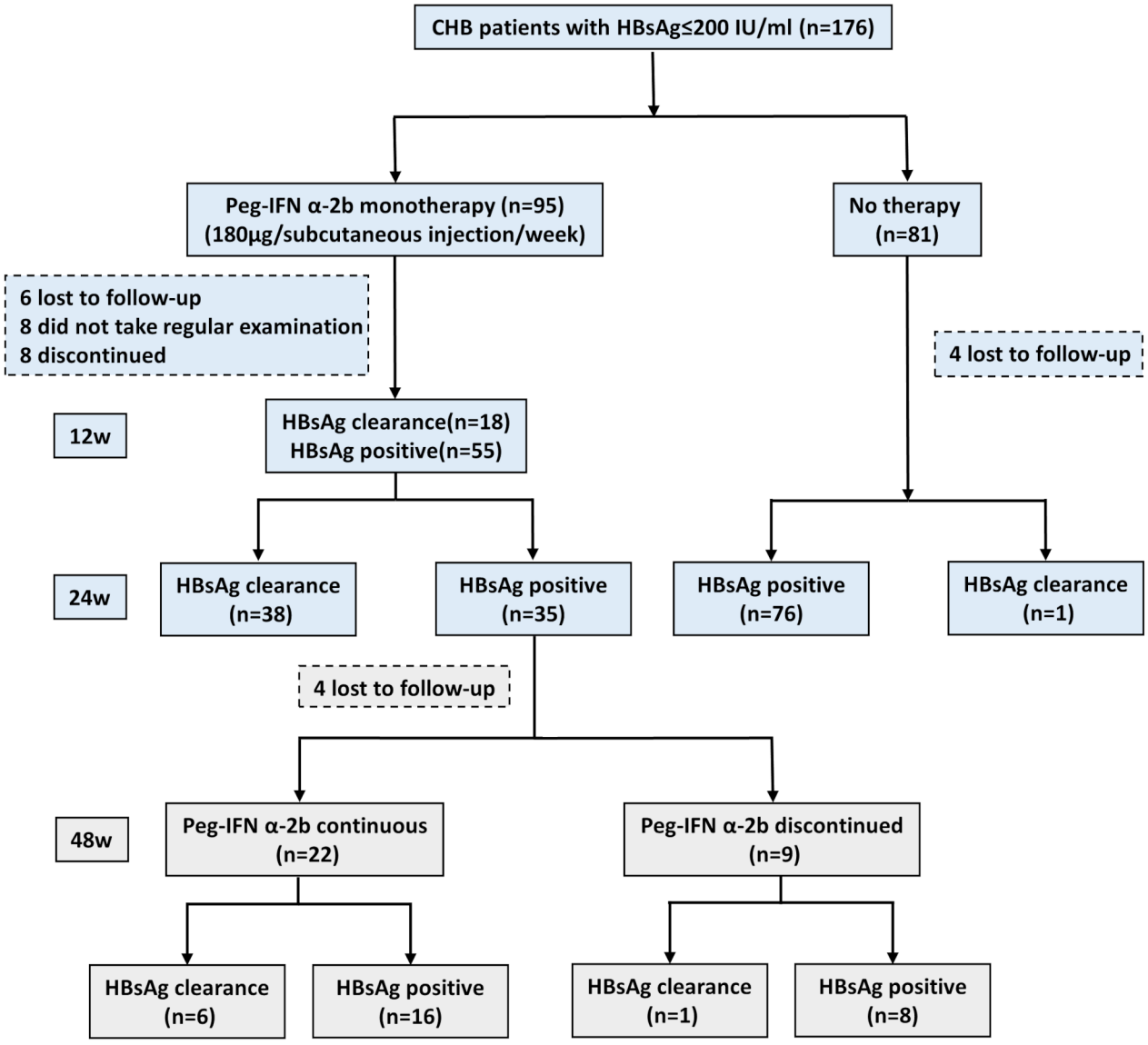

Fig. 1 Flow chart of therapy in patients

Table 1 Demographic and clinical characteristics of participants at baseline

Characteristics	Control group (*n* = 77)	Peg-IFN α-2b group (*n* = 73)	*p*
Male, *n* (%)	57 (74.0)	45 (61.6)	0.104
Age, years	38.0 (32.0–57.0)	42.0 (34.0–48.0)	0.838
CHB family history, *n* (%)	16 (20.8)	9 (12.3)	0.165
Fatty liver, *n* (%)	13 (16.9)	16 (21.9)	0.435
BMI, kg/m^2	23.8 (22.2–26.0)	22.6 (21.1–25.1)	0.081
Neutrophil, ×10^9/L	3.5 (2.6–3.9)	3.4 (2.6–3.9)	0.405
PLT, ×10^9/L	197.6 ± 80.4	179.7 ± 58.8	0.120
ALT, U/L	27.0 (20.0–44.0)	22.0 (15.5–39.0)	0.192
AST, U/L	28.0 (20.0–42.0)	22.0 (19.0–34.5)	0.277
Baseline HBsAg level, IU/ml	58.7 (11.0–121.1)	23.8 (4.1–110.4)	0.143
HBeAg-positive, *n* (%)	4 (5.2)	3 (4.1)	0.753
HBV DNA > 30 IU/mL, *n* (%)	6 (7.8)	7 (9.6)	0.696

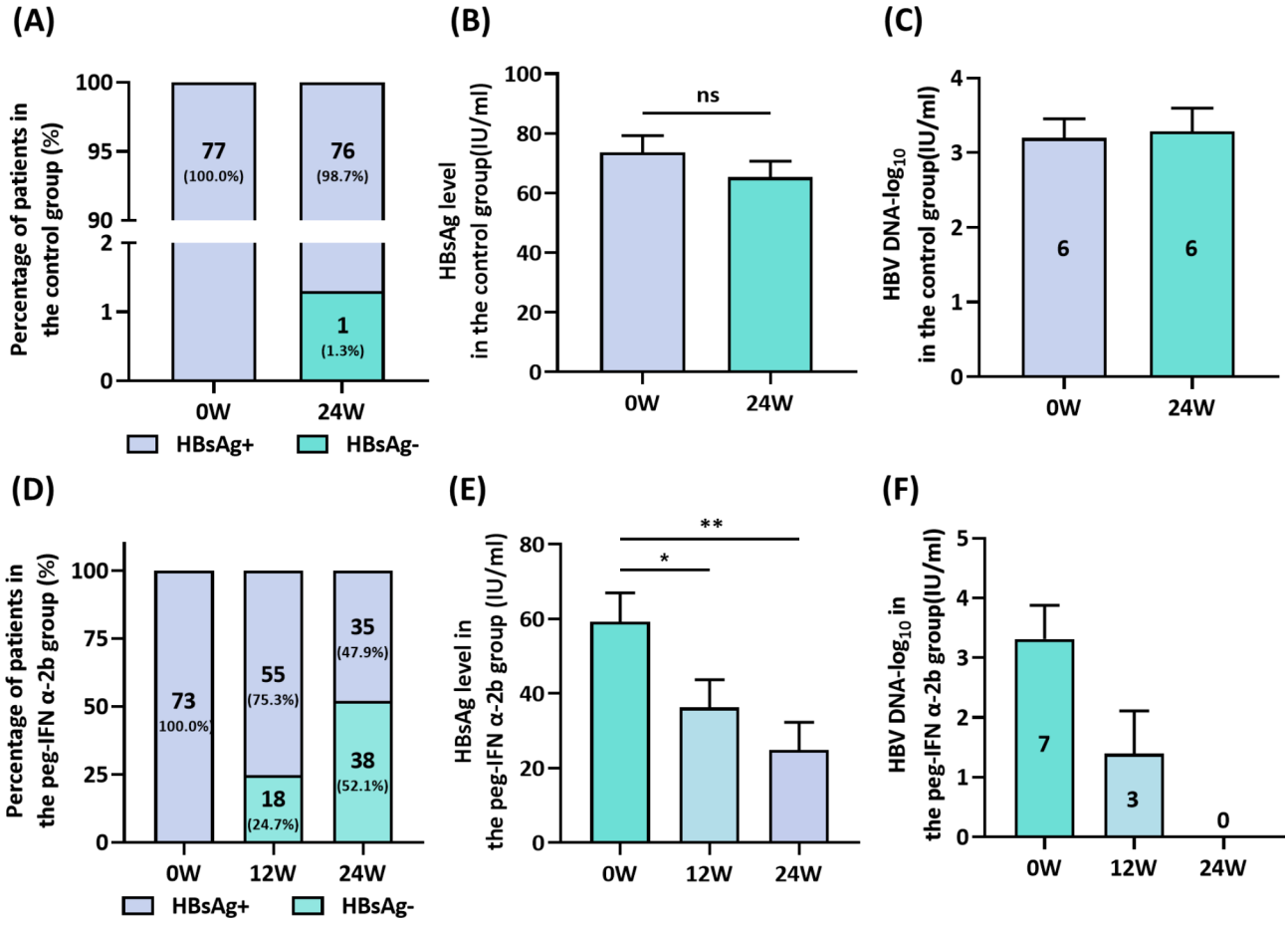

Fig. 2 The serological changes in each group. (**A**) HBsAg response at week 24 in the control group. (**B**) Dynamics of HBsAg titers in the control group. (**C**) Changes in HBV DNA levels in the six patients with baseline HBV DNA positivity in the control group. (**D**) HBsAg response at week 12 and week 24 in the Peg-IFN α-2b group. (**E**) Dynamics of HBsAg titers in the Peg-IFN α-2b group. (**F**) Changes in HBV DNA levels in the seven patients with baseline HBV DNA positivity in the Peg-IFN α-2b group

Table 2 Serological response of HBsAg at week 48

Week 24 HBsAg status	Peg-IFN α-2b	Week 48 HBsAg clearance		Week 48 HBsAg seroconversion	
		n/N (%)	*p*	*n/N* (%)	*p*
HBsAg positive (*N* = 35)	Continued (*n* = 22)	6/22 (27.3)	0.639	2/22 (9.1)	0.657
	Discontinued (*n* = 9)	1/9 (11.1)		1/9 (11.1)	
	Lost to follow-up (*n* = 4)	-	-	-	-

patients who had achieved HBsAg clearance by week 24 exhibited elevated HBsAg levels by week 48.

Baseline HBsAg level and fatty liver were independent predictors of HBsAg clearance in patients treated with Peg-IFN α-2b

The univariate regression analysis revealed that fatty liver (OR = 5.547, p = 0.014), baseline HBsAg level (OR = 0.985, p = 0.001), and the early decline in HBsAg levels from baseline to week 12 (OR = 2.419, p = 0.039) were statistically significant predictors of HBsAg clearance. In contrast, variables such as gender, age, family history of CHB, BMI, fluctuations in ALT and AST levels, as well as changes in neutrophil and PLT counts from baseline to week 12, did not achieve statistical significance. These results underscore the pivotal role of fatty liver, baseline HBsAg level, and the initial reduction in HBsAg levels in influencing HBsAg clearance. Subsequent multivariate logistic regression analysis substantiated that the presence of fatty liver (OR = 5.960, p = 0.033) and baseline HBsAg level (OR = 0.984, p = 0.001) were independent predictors of HBsAg clearance in patients administered Peg-IFN α-2b (Table 3).

Table 3 Factors related to and predictive of HBsAg clearance in patients treated with Peg-IFN α-2b at week 24

Predictors	Univariate analysis		VIF	Multivariate analysis	
	OR (95%)	*p*		OR (95%)	*p*
Gender, male	1.442 (0.559–3.719)	0.449			
Age, years	0.991 (0.940–1.044)	0.729			
CHB family history	0.706 (0.173–2.872)	0.627			
Fatty liver	5.547 (1.424–21.612)	0.014	1.089	5.960 (1.151–30.853)	0.033
BMI, kg/m^2	1.121 (0.956–1.314)	0.159			
Baseline HBsAg level, IU/ml	0.985 (0.976–0.994)	0.001	1.012	0.984 (0.975–0.994)	0.001
From baseline to week 12					
HBsAg decline, log_{10}IU/ml	2.419 (1.046–5.595)	0.039	1.096	2.023 (0.779–5.256)	0.148
ALT elevation, U/L	1.001 (0.984–1.019)	0.865			
AST elevation,U/L	1.002 (0.987–1.017)	0.816			
Neutrophil decline, $\times10^9$/L	0.834 (0.498–1.396)	0.489			
PLT decline, $\times10^9$/L	0.996 (0.987–1.004)	0.335			

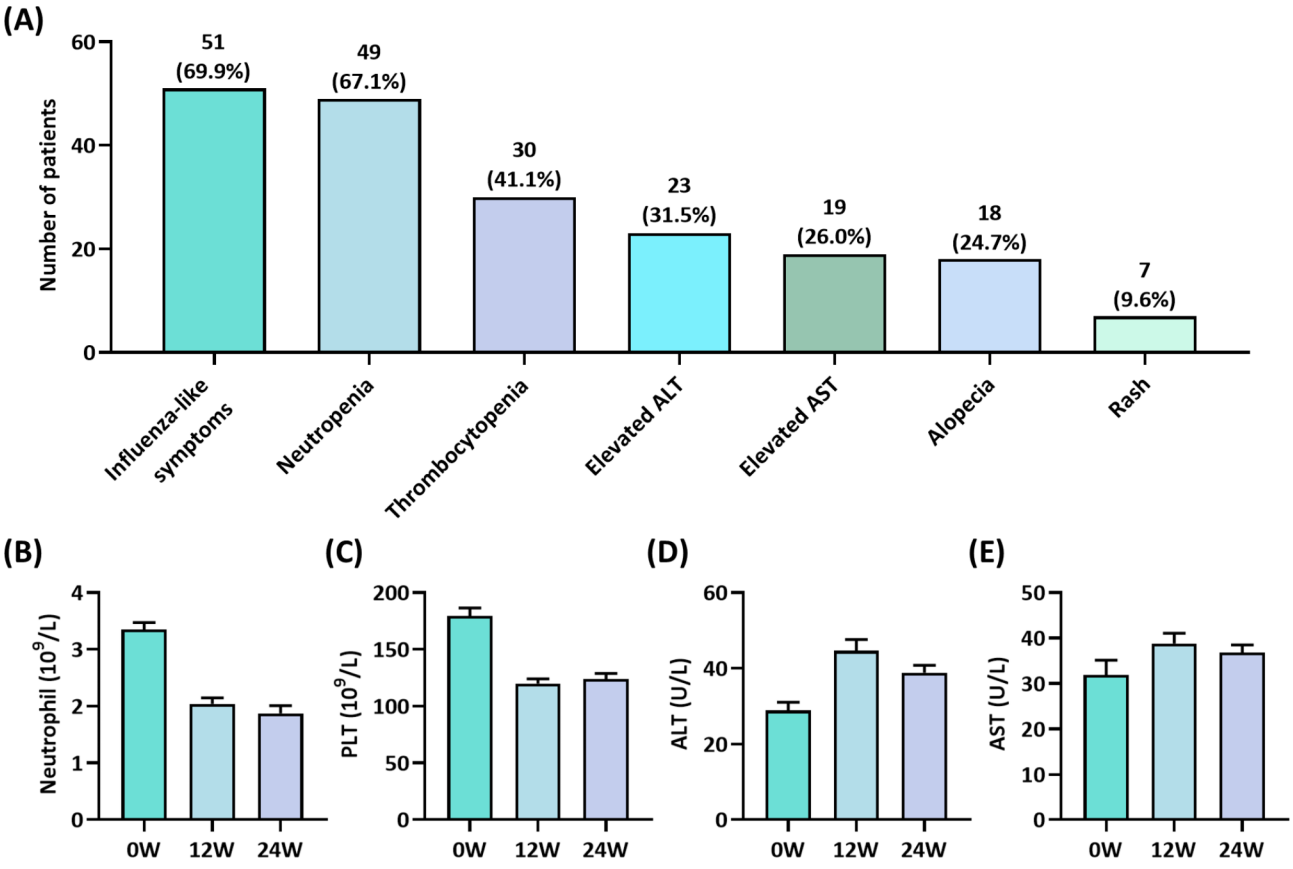

Fig. 3 Adverse events in patients receiving Peg-IFN α-2b therapy. (**A**) The number and proportion of patients who experienced adverse events. (**B-E**) Levels of neutrophils, PLT, ALT and AST, in patients at weeks 0, 12, and 24

Adverse events

The predominant adverse effect encountered during the administration of Peg-IFN α-2b was influenza-like symptoms, affecting 69.9% (51/73) of the patients. The spectrum of other adverse events included neutropenia (49/73, 67.1%), thrombocytopenia (30/73, 41.1%), elevated ALT levels (23/73, 31.5%), elevated AST levels(19/73, 26.0%), alopecia (18/73, 24.7%), and rash (7/73, 9.6%) (Fig. 3). Importantly, following symptomatic treatment, none of these adverse events led to severe outcomes.

Discussion

The advent of the hepatitis B vaccine has indeed mitigated the spread of the hepatitis B virus to a considerable extent. However, HBV infection remains a formidable

public health challenge [12]. The propensity for chronicity is high among those infected with HBV, often leading to persistent infection. Regrettably, existing therapeutic modalities have yet to achieve the complete eradication of HBV [13].

As previously highlighted, the therapeutic goal of CHB is to achieve a clinical cure, which has been demonstrated to markedly reduce the incidence of cirrhosis and even HCC [14]. The integration of the HBV genome tends to increase progressively throughout the infection, especially during the HBeAg-negative phase, thereby worsening patient outcomes [1, 15]. Consequently, the timely attainment of HBsAg clearance is crucial for improving the prognosis of patients with CHB. An array of recent studies has shown that Peg-IFN α is more effective in facilitating HBsAg clearance than NAs, with patients exhibiting low HBsAg levels being more likely to attain a clinical cure [16, 17]. Nonetheless, the complex administration, high cost, and significant adverse effects associated with Peg-IFN α have led many patients to forgo this treatment option [18]. Therefore, investigating the efficacy of short-term Peg-IFN α treatment in patients exhibiting low HBsAg levels is of considerable importance, as it could influence their decision-making towards opting for Peg-IFN α therapy. The short-term administration of Peg-IFN α holds the potential to alleviate the economic burden and shorten the duration of side effects for patients.

In this study, we analyzed a retrospective cohort of CHB patients with ultra-low HBsAg levels who received Peg-IFN α-2b under real-world conditions, with the aim of assessing the efficacy and safety of short-term treatment. Among the 73 CHB patients in the Peg-IFN α-2b group, the HBsAg clearance rate after 24 weeks of treatment reached 52.1%, with a seroconversion rate of 28.8%. This rate was significantly higher than the spontaneous HBsAg clearance rate of 1.3% observed in the control group. Dang et al. found that the combination therapy of Peg-IFN α and NAs could enhance HBsAg clearance rates compared to NAs monotherapy. In their study, a 48-week regimen of Peg-IFN α resulted in an HBsAg clearance rate of 26.4% and a seroconversion rate of 18.7% among CHB patients with HBsAg levels below 1500 IU/mL [19]. Another recent study indicated that the addition of Peg-IFN α to NAs therapy improved HBsAg clearance and seroconversion, especially in HBeAg-negative patients with lower HBsAg levels. The study reported HBsAg clearance and seroconversion rates of 38% and 25%, respectively, in patients with HBsAg levels below 1500 IU/mL after 24 weeks of Peg-IFN α-2b treatment [20]. These rates were lower than those observed in our study, possibly due to the lower baseline HBsAg levels of the patients we enrolled. Our findings revealed that 47.9% (35/73) of patients did not achieve HBsAg clearance by week 24 with standard Peg-IFN α-2b therapy, even among those with lower baseline HBsAg levels. This discrepancy could be attributed to factors such as variations in patients' immune status or the genetic characteristics of the virus [21–25]. Among these 35 patients, only two showed an increase in HBsAg levels compared to baseline. Continued follow-up to monitor subsequent changes in HBsAg levels indicated that continuing Peg-IFN α-2b treatment beyond 24 weeks did not impact HBsAg clearance by week 48. Consistent with another study's findings, our results suggest that extending the treatment duration beyond 48 weeks of Peg-IFN α-2b is not necessary [25]. However, a different real-world analysis suggested that extended treatment with Peg-IFN α could further promote HBsAg clearance, indicating that treatment duration may need to be tailored rather than uniformly limited [26]. Therefore, it is essential to individualize treatment strategies based on distinct patient profiles. Moreover, our observations indicated that none of the patients who achieved HBsAg clearance by week 24 experienced a rebound in HBsAg levels by week 48, suggesting that short-term Peg-IFN α-2b therapy can yield positive outcomes in patients with ultra-low HBsAg levels.

We did not impose restrictions on the levels of HBV DNA and HBeAg in the Peg-IFN α-2b group patients, thereby allowing us to assess the impact of Peg-IFN α-2b treatment on HBV DNA and HBeAg clearance. The results revealed that all seven patients who were positive for HBV DNA at baseline achieved undetectable HBV DNA levels by week 24. Additionally, one out of the three patients who were positive for HBeAg at baseline achieved HBeAg seroconversion by week 24, even though HBsAg remained detectable in peripheral blood. Previous studies have demonstrated that NAs effectively suppress HBV DNA levels in most patients. However, their efficacy in clearing HBeAg and HBsAg is often limited [27]. Furthermore, patients on NAs treatment often face challenges in discontinuing medication in the short term, typically requiring lifelong therapy [28]. The treatment costs for NAs are comparable to or higher than those for short-term Peg-IFN α therapy. These findings have significantly bolstered the confidence of patients with low HBsAg levels in considering Peg-IFN α treatment.

To elucidate the factors influencing HBsAg clearance, we conducted a detailed analysis of the data from the Peg-IFN α-2b group. The analysis indicated that baseline HBsAg levels and the presence of fatty liver significantly influence HBsAg clearance. It is noteworthy that our observation aligns with previous studies suggesting that CHB patients with fatty liver are more likely to achieve HBsAg clearance. Mak et al. identified that the presence of hepatic steatosis led to a three-fold increase in the HBsAg seroclearance rate [29]. Li et al. similarly found

a significant association between fatty liver and higher HBsAg seroclearance rate [30]. Furthermore, other studies have reported a correlation between fatty liver and decreased replication of HBV DNA [31–33]. Although the precise mechanism by which fatty liver facilitates HBsAg clearance remains unclear, the consistency of our results with previous studies suggests that our findings are not coincidental.

Throughout the treatment period, no patient discontinued Peg-IFN α-2b medication due to adverse events, underscoring the medication's favorable safety profile. The most prevalent adverse event was influenza-like symptoms, which typically subsided within two to three weeks following targeted symptomatic intervention. In addition to influenza-like symptoms, other adverse events that were commonly observed included neutropenia, thrombocytopenia, elevated AST and ALT levels, alopecia and rash. These side effects persisted for nearly the entire duration of treatment and were consistent with the common side effects listed on the label. Following symptomatic treatment, all patients remained stable or showed improvement without experiencing serious adverse consequences. It is noteworthy that one study indicated that the elevation of ALT levels contributed to HBsAg clearance [34]. Additionally, Chu et al. discovered that an increase in ALT level at the 12-week mark served as an independent predictor of HBsAg clearance. Their study indicated that patients with ALT elevation exceeding 27 U/L were more likely to achieve HBsAg clearance compared to those with lower ALT elevations [8]. However, these findings were not replicated in our cohort. This discrepancy could potentially be attributed to the fact that we initiated treatment with relevant medications upon the onset of ALT elevation, thereby potentially interfering with the actual ALT level. Notably, other side effects such as thyroid disorders were not observed in our cohort.

This study is not without its limitations. Its retrospective design and reliance on a small sample size may introduce certain biases. Additionally, the absence of long-term follow-up data means that the long-term therapeutic response to Peg-IFN α-2b remains to be fully elucidated. Furthermore, due to the low levels of HBV DNA in the patients included in this study, there was an absence of data regarding HBV genotype, which precluded an analysis of its potential influence on HBsAg clearance.

Conclusion

Our findings suggest that CHB patients with HBsAg levels below 200 IU/mL can attain high rates of HBsAg clearance with short-term Peg-IFN α-2b therapy. Moreover, baseline HBsAg levels and the presence of fatty liver were identified as predictive factors for HBsAg clearance during Peg-IFN α treatment. Additionally, our results indicate that extending the treatment duration is unnecessary for CHB patients with ultra-low HBsAg levels who have not achieved HBsAg clearance after 24 weeks of Peg-IFN α-2b therapy.

Abbreviations

ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
cccDNA	Covalently closed circular DNA
CHB	Chronic hepatitis B
HBeAb	Hepatitis B e antibody
HBeAg	Hepatitis B e antigen
HBsAb	Hepatitis B surface antibody
HBsAg	Hepatitis B surface antigen
HBV	Hepatitis B virus
HCC	Hepatocellular carcinoma
NAs	Nucleos(t)ide analogs
Peg-IFN α-2b	Peginterferon alfa-2b
PLT	Platelet

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Author contributions

All authors contributed to this study at various stages. The roles of each author are delineated as follows: The study concept and design were primarily undertaken by LZ, YL, SY, and CL. Data collection was carried out by YL, ZM, MZ, WZ, ZW, and HH. Statistical analysis and data interpretation were conducted by YL, SY, and CL. Manuscript drafting was primarily performed by YL, SY, and CL. Critical revisions of the manuscript for important intellectual content were conducted by LZ and WW. All authors read and approved the final manuscript.

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Data availability

The data used to support the findings of this study are available upon request from the corresponding author. Access to the data is subject to approval by the institutional review board and compliance with applicable privacy regulations.

Declarations

Ethics approval and consent to participate

This study obtained ethical approval from the Ethics Board at The Second Affiliated Hospital of Harbin Medical University (KY2024-049).

Consent for publication

All authors have approved the final version of the manuscript. Consent for the publication of data, images, or information was obtained from all participants (or their legal guardians) where applicable.

Competing interests

The authors declare no competing interests.

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