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Epidemiological and Diagnostic Profile of Patients with Chronic Hepatitis B Virus from 2017 to 2021 in Parakou, Republic of Benin

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Abstract

Introduction: Viral hepatitis B is a public health problem worldwide. The objective of this study was to determine the epidemiological and diagnostic profile of chronic carriers of hepatitis B virus seen for gastroenterology consultations in Parakou, Republic of Benin. **Patients and Methods:** This was a cross-sectional and descriptive study with retrospective data collection. Patients seen for gastroenterology consultations from January 1, 2017 to June 30, 2021 at the Regional Teaching Hospital of Borgou/Alibori (CHUD-B/A) and having been diagnosed as chronic carriers of hepatitis B virus were included. A minimum initial assessment was required to be included. The minimum sample size was calculated with Schwartz formula. The variable of interest was the detection of HBsAg twice and at least 6 months apart. The other variables studied were sociodemographic, clinical and paraclinical data. The data collected were analyzed using SPSS 17 software. **Results:** A total of 2786 patients were seen for gastroenterology consultations, including 1126 (40.4%) HBsAg-positive patients. Among them, 417 patients met the inclusion criteria and were the subject of the present study. The average age of the patients was 34.8 ± 10.5 years. Two hundred and forty-seven patients (65.7%) were male, representing a sex ratio of 1.9. The discovery of positive HBsAg status was made during systematic screening in 231 patients (55.4%). Scarifications were noted in 373 patients (89.4%). Asthenia was reported in 184 patients (44.1%). Co-infections with human immunodeficiency virus, hepatitis C and D viruses were 0% (0 in 92), 2.8% (4 in 146) and 14.3% (2 in 146), respectively. During the initial assessment, 274 patients (65.7%) were se-

ro-negative for chronic HBeAg infection, 21 (5%) had clinically significant fibrosis including 16 (3.8%) at the stage of cirrhosis and 7 patients (5.4%) had hepatocellular carcinoma. **Conclusion:** In Parakou, chronic hepatitis B virus infection is common and affects young people with a male predominance. Asthenia is a non-specific symptom and the most reported by the patients. Around 5 out of 100 patients are seen for consultations at the stage of complication. Emphasis must be placed on early detection and subsidy for pre-therapeutic assessment.

Keywords

Chronic Infection, HBV, Epidemiology, Diagnosis, Parakou

1. Introduction

Viral hepatitis B is a global public health problem. According to the World Health Organization in 2019, approximately 296 million people were living with chronic hepatitis B virus (HBV) infection [1]. People with viral hepatitis B are at risk of developing complications such as cirrhosis and hepatocellular carcinoma (HCC) [2]. Viral hepatitis B is the most common cause of HCC in countries with high endemicity [3]. The number of deaths related to viral hepatitis B was 820,000 worldwide in 2019 [1]. Mortality from this disease increased by more than 33% from 1990 to 2013 [4]. Together, viral hepatitis deaths from acute infection, cirrhosis, and liver cancer were the tenth leading cause of death worldwide in 1990 and seventh (seventh to eighth) leading cause in 2013 [4]. Viral hepatitis B represents the 10th cause of death in the world and one of the three leading causes of death in Asia and Africa [5].

Chronic hepatitis B is most often asymptomatic. Its discovery was fortuitous during screening. Access to diagnosis and treatment remains a challenge, especially in countries with limited resources [1]. In 2019, 30.4 million people (10.5% of the estimated number of people living with hepatitis B) knew they were infected, while 6.6 million (22%) of those diagnosed were on treatment [1]. The main problem related to diagnosis (determination of the paraclinical profile) is the low accessibility to molecular biology (HBV DNA) due to its cost and the insufficiency of the technical platform in several emerging countries [6].

In Africa, the infection epidemiology is difficult to assess because most studies have only looked for HBs antigen (HBsAg) and most often in some groups of the population. The prevalence of HBV infection varies according to areas and populations delimiting areas of high, medium and low endemicity. Sub-Saharan Africa is an area of high endemicity with a prevalence rate between 8% and 18% [7]. Benin is located in this area with a prevalence of 9.9% among new blood donors in 2012 [6]. A study conducted in 2019 by Kpossou *et al.* [8] in the general population reported a prevalence of 6%.

In Parakou, studies carried out in some groups of the population noted a prevalence of 14.02% among pregnant women in 2017 and 16.9% in people living

with the human immunodeficiency virus (HIV) [9] [10]. As the Regional Teaching Hospital of Borgou and Alibori (CHUD-B/A) is a center for the management of viral hepatitis, it is necessary to take stock of the situation.

The objective of this study was to determine the epidemiological and diagnostic profile of chronic carriers of the hepatitis B virus in the internal medicine department of CHUD-B/A from 2017 to 2021.

2. Patients and Methods

Type and period of study

This was a cross-sectional and descriptive study with retrospective data collection from January 1, 2017 to June 30, 2021.

Study site

This study took place in the internal medicine department of CHUD-B/A, more precisely in gastroenterology unit.

Study population

The source population consisted of all patients seen and followed up in gastroenterology unit for hepatitis B virus infection during the study period.

- Inclusion criteria: All patients with chronic HBV infection (sero-positive for HBsAg twice, at least six months apart) were included in this study.

- Exclusion criteria: All patients with chronic HBV who did not perform the minimum pre-treatment assessment (HBV DNA quantification, aminotransferases, prothrombin time, blood count, HBe antigen, serum creatinine, abdominal ultrasound) were excluded from the study.

Sampling

The minimum sample size is calculated using Schwartz formula

$$n = \frac{t^2 p(1-p)}{m^2}$$

with

- n: minimum sample size
- t: confidence level (the typical value of 95% confidence level was 1.96) and $t = 1.96$
- p: prevalence of HBV infection in general practice consultations at the regional hospital of Kayes in Mali is 11.1% [11]
- m: the margin of error = 5%

$$n = \frac{(1.96)^2 * 0.111 * (1-0.111)}{(0.05)^2} = 151.63 \approx 152$$

It was predicted 5% loss and the size was increased to 152+ (5% of 152). This redefined the minimum sample size to 160 patients.

Variables

The variable of interest was chronic HBV infection defined by the presence of HBsAg in the blood by ELISA or rapid diagnostic test for at least 6 months. Independent variables were related to sociodemographic, lifestyle, associated pa-

thologies, clinical and paraclinical data.

Data collection

Information was collected from the medical records of patients using a data collection sheet designed for this purpose (in appendix).

Diagnostic Criteria

The diagnosis of cirrhosis was non-invasive based on variable associations of the following clinical and paraclinical signs: the "Aspartate aminotransferase to Platelet Ratio Index (APRI)" score greater than 2 [12]; changes in the liver on clinical examination and medical imaging (painless and hard hepatomegaly with a firm lower edge, a granular anterior surface, dysmorphia on ultrasound); signs of portal hypertension (venous collateral circulation, splenomegaly, thrombocytopenia, portal vein dilatation on ultrasound, esophago-gastric varices); signs of liver failure (white nails, palmar erythema, gynecomastia, drop in prothrombin time, hypoalbuminemia).

Performance of examinations

The clinical examination was carried out by a gastroenterologist. The quantification of HBV DNA was carried out using real-time PCR at the national virology reference laboratory in Cotonou, Benin by a medical biologist. The abdominal ultrasound was performed by radiologists.

Data processing and analysis

The information on the survey sheet was recorded in Epi Data EntryClient 3.1 software. They were analyzed with SPSS 17 software. The qualitative variables were expressed as number and percentage and the quantitative variables were expressed as mean with their standard deviation when the distribution was normal, otherwise as median with the interquartile range.

Ethical considerations

For this retrospective study, the data collected were used anonymously and confidentially.

3. Results

During the study period, 2786 subjects were seen for gastroenterology consultations, including 1126 (40.41%) HBsAg-positive patients. Among the latter, 417 were able to perform the minimum assessment and were the subject of this study.

Epidemiological data

The average age of the patients surveyed was 34.8 ± 10.5 years with the extremes of 7 years and 75 years. Two hundred and forty-seven patients (65.7%) were male, representing a sex ratio of 1.9. Among the 417 patients, 300 (71.9%) lived in urban areas. One hundred and eighty-eight (47.5%) were employees in private and public sectors, including health workers. Regarding risk factors for viral transmission, scarifications were reported by 373 patients (89.4%) and 122 (29.3%) had a family history of HBV infection. In the 417 patients, 41 (9.8%) regularly took alcoholic beverages, on average 33.4 ± 13.5 g per day with the ex-

tremes of 10 g and 60 g per day. Table 1 summarizes the epidemiological data of the patients included in the present study.

Diagnostic aspects

- *Clinical data*

The main circumstance of discovery was systematic screening (231 or 54.9%). In the 417 patients, 204 (48.9%) consulted for the first time more than a year

Table 1. Distribution of patients with chronic HBV according to epidemiological data (n = 417, CHUD-B/A, Parakou, 2017-2021).

	Size	%
Age range (years)		
<20	24	05.8
[20 - 39]	258	61.9
[40 - 59]	132	31.6
[60 - 79]	03	00.7
Sex		
Male	274	65.7
Female	143	34.3
Residence		
Urban area	300	71.9
Rural area	117	28.1
Socio-professional status		
Health worker	53	12.7
Other employees (public/private)	145	34.8
Trader/reseller	56	13.4
Pupil/Student	51	12.2
Artisan/Laborer	35	08.4
Household	33	07.9
Farmer/Breeder	27	06.5
Others (religious, herbalist, unemployed)	17	04.1
Risk factors for viral transmission		
Scarifications	373	89.4
Family history of HBV infection	122	29.3
Personal history of blood transfusion	18	04.3
Tattoo	17	04.1
Toxic habits		
Regular intake of alcoholic beverages	41	09.8
Smoking	03	00.7

after the discovery of the disease. The median duration between the date of discovery of HBV infection and the first consultation was 11 months with the extremes of 0 and 72 months. Two hundred and ninety-nine patients (71.7%) had at least one symptom on admission. Asthenia was reported by 184 patients (44.1%).

The physical examination was normal in 336 patients (80.6%). The clinical abnormalities observed were hepatomegaly and splenomegaly in 11 patients (13.6%) and 8 patients (9.9%), respectively. Table 2 shows the distribution of

Table 2. Distribution of patients with chronic HBV according to clinical data (n = 417, CHUD-B/A, Parakou, 2017-2021).

	Size	%
Complaints from patients		
None	118	28.3
Asthenia	184	44.1
Arthralgia	93	22.3
Weight loss	86	20.6
Constipation	74	17.7
Abdominal pain	70	16.8
Headache	39	09.4
Fever	20	04.8
Paresthesia	11	02.6
Nausea	07	01.7
Insomnia	06	01.4
Anorexia	05	01.2
Abdominal discomfort	04	01.0
Abdominal bloating	04	01.0
Dizziness	03	00.7
Vomiting	03	00.7
Jaundice	03	00.7
Pelvic limb edema	01	00.2
Physical examination data of patients		
Normal	336	80.6
Localized abdominal pain	54	66.6
Hepatomegaly	11	13.6
Obesity	11	13.6
Jaundice	08	09.9
Splenomegaly	08	09.9
Increased volume of the abdomen	04	04.9

A patient could have several signs at once.

patients according to clinical data.

- ***Paraclinical data***

Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were elevated in 124 (29.7%) and 95 patients (22.8%), respectively. The prothrombin time was less than 70% in 48 patients (11.5%). Thrombocytopenia was noted in 31 patients (7.4%) and serum creatinine was greater than 13 mg/L in 27 patients (6.5%). HBeAg was negative in 371 patients (89%). Among the 417 patients, 141 performed anti-HCV antibodies which were positive in 4 (2.8%), 14 did total anti-HDV antibodies which were positive in 2 (14.3%) and 92 were screened for HIV, all being negative. Table 3 shows the biological data of the patients.

HBV DNA was below 2000 IU/L in 274 patients (65.7%). Abdominal ultrasound was normal in 322 patients (77.2%) and the abnormalities reported were hepatomegaly (61 cases), homogeneous hepatic steatosis (28 cases), hepatic dysmorphia (24 cases), splenomegaly (24 cases), portal vein dilatation (7 cases), hepatic nodules (7 cases) and ascites (4 cases).

- ***Non-invasive assessment of liver fibrosis***

The APRI score was greater than or equal to 1.5 in 21 patients. Among them, 16 (3.8%) had an APRI score greater than or equal to 2.

- ***Serological and virological profile***

Among the 417 patients included, 274 (65.7%) were negative for chronic HBeAg infection (inactive carriers of HBV) and 129 patients (30.9%) had chronic active hepatitis (HBV DNA ≥ 2000 IU/ml). Among the latter, 16 patients (12.4%) were at the stage of cirrhosis and 7 (5.4%) had HCC after the initial assessment.

Table 4 shows the distribution of patients included according to the final diagnosis.

It should be pointed out that patients with HBeAg-negative or HBeAg-positive viral hepatitis B, cirrhosis, a family history of cirrhosis or liver cancer secondary to HBV, have benefited from treatment with Tenofovir. This therapeutic, evolutive ant prognostic aspect will be the subject of another study.

4. Discussion

This study made it possible to determine the epidemiological and diagnostic profile of chronic carriers of hepatitis B virus in the northern part of the Republic of Benin.

Out of 1126 patients who consulted for HBsAg positivity, 417 (37%) were able to perform the minimum assessment in order to make a decision for their management. The reason is mainly financial.

The hospital frequency of positive HBsAg in patients who were admitted for gastroenterology consultations was 40.4%. This frequency is higher than that found in the gastroenterology clinic of the National Teaching Hospital of Cotonou in the same country by Kpossou *et al.* [13] in 2019 (15.7%). Other African studies have also reported lower prevalences. Katilé *et al.* [11] in 2018 in the department of medicine of Kayes hospital in Mali found a prevalence of 11.1%.

Table 3. Distribution of patients with chronic HBV according to paraclinical and biological data (n = 417, CHUD-B/A, Parakou, 2017-2021).

	Size	%
Standard biological assessment		
ALT		
Normal	293	70.3
High (>40 UI/L)	124	29.7
AST		
Normal	322	77.2
High (>40 UI/L)	95	22.8
Prothrombin time		
Normal	369	88.5
Low (70%)	48	11.5
Platelet count		
Normal	370	88.7
Low (<150 Giga/L)	31	07.4
High (>400 Giga/L)	16	03.8
Serum creatinine		
Normal	390	93.5
High (>13 mg/L)	27	06.5
HBe status		
Negative	371	89.0
Positive	46	11.0
Co-infections and superinfections		
Anti-HCV antibodies		
Not done	271	-
Negative	142	97.2
Positive	04	02.8
Total anti-HDV antibodies		
Not done	403	-
Negative	12	85.7
Positive	02	14.3
HIV serology		
Not done	325	-
Negative	92	100.0
Positive	00	00.0

Table 4. Distribution of patients with chronic HBV according to the final diagnosis (n = 417, CHUD-B/A, Parakou, 2017-2021).

	Size	%
HBeAg-negative chronic infection	274	65.7
HBeAg-negative chronic hepatitis	97	23.2
HBeAg-positive chronic hepatitis	32	07.7
HBeAg-positive chronic infection	14	03.4
Cirrhosis	16	03.8
Hepatocellular carcinoma	07	01.7

Mongo-Okouo *et al.* [14] in Brazzaville in 2016 reported a frequency of 11.12% in a multicenter study.

This high frequency could be explained by the fact that CHUD-B/A is the public referral hospital in northern Benin and in particular one of the centers for the management of viral hepatitis. Moreover, according to WHO, Benin is located in the geographical area of high endemicity and our results clearly reflect the major public health problem posed by this infection in our country [3].

The mean age of chronic HBV carriers in our study was 34.83 ± 10.49 years. This result is similar to that found by Kodjoh *et al* [15] in Cotonou in southern Benin in 2015, Diallo *et al.* [16] in Senegal in 2018, Katilé *et al.* [11] in Mali in 2018 who reported a mean age of 36.4 ± 11.2 years, 33 years and 36.9 ± 10.8 years, respectively. Thus, in the present study, HBV infection was more prevalent in younger subjects. These findings corroborate the fact that vertical and horizontal transmission of HBV are the most frequent modes of transmission in areas of high endemicity for HBV infection [1]. Indeed, the age at the time of infection plays an important role in the transition to chronicity. In children infected in their first year of life, the risk of developing a chronic infection is 80% to 90%.

This risk is 30% - 50% in children infected before the age of six and less than 5% in healthy subjects infected in adulthood [1].

In the present study, a male predominance was noted (65.7%) with a sex ratio of 1.9. This same predominance was reported by Diallo *et al.* [16] in Senegal (68.9% with a sex ratio of 2.21), Kpossou *et al.* [13] in Cotonou in southern Benin (71.2% with a sex ratio of 2.5).

The male predominance of HBV infection is well-known in the literature [17]. It could be explained by genetic factors favoring the persistence of the virus in men. Hormonal factors may be protective in women [17]. However, the present study did not analyze a link between male sex and the transition to chronicity of HBV infection.

Scarifications were observed in 373 patients (89.4%). The same observation was made by Angounda *et al.* [18] in Congo-Brazzaville in 2014. This result could be explained by the fact that this practice is very widespread in sub-Saharan Africa and most often carried out with non-sterile equipment. The use of com-

mon sharp equipment during scarification carries a risk of direct contact with blood, promoting the transmission of HBV [18]. Family history of HBV infection was the second risk factor reported. This observation was also made by Angounda *et al.* [18] in Brazzaville in 2014. This corroborates previous studies which have shown that in countries with high endemicity for viral hepatitis B, transmission is mainly vertical and horizontal within the family during childhood and adolescence [1]. The present study did not investigate a link between the presence of scarifications, family history and HBV infection. As this is a retrospective study, the information relating to the notion of sharing of equipment used for scarification, the conditions under which it was carried out, the notion and the type of contact with an infected parent or a member of his entourage could not be documented.

HBeAg was often negative (89%). This result is similar to that reported by Kpossou *et al.* [19] in 2019 (88.2%) in southern Benin. The natural history of HBV infection in the first two phases (immunotolerance and immune clearance) is characterized by the presence of positive HBeAg, then a loss of HBeAg and the appearance of anti-HBe antibodies. Given that in Benin, as in countries with high endemicity for HBV infection, contamination occurs during childhood, HBe seroconversion already occurs in adulthood. In other words, chronic HBV infection in Parakou is often due to the pre-core mutant virus.

Among the 417 patients, 274 patients (65.7%) had HBeAg-negative chronic infection; 14 (3.4%) had HBeAg-positive chronic infection, 97 (23.2%) had HBeAg-negative chronic hepatitis and 32 (7.7%) had HBeAg-positive chronic hepatitis. Kpossou *et al.* [19] in Cotonou in the south of Benin in 2020, reported 106 patients (32.8%) with HBeAg-negative chronic infection, 10 (3.1%) with HBeAg-positive chronic infection, 68 (40%) HBeAg-negative chronic hepatitis B and 12 (7.1%) HBe Ag-positive chronic hepatitis B. In this Beninese study, approximately 31% of patients (chronic hepatitis with negative or positive HBeAg) who completed the minimal pre-therapeutic assessment required treatment against HBV.

Co-infection/superinfection with hepatitis D virus was 14.3%. This high frequency could be explained by the fact that total anti-HDV antibodies were not systematically requested in chronic carriers of HBV. The research was carried out when there was hepatic cytolysis contrasting with low viral load of HBV. This therefore constitutes a selection bias. Otherwise in the same country but in the south, the prevalence of total anti-HDV antibodies was 3.8% in adult carriers of HBsAg who were antiviral treatment-naive patients in 2016 [20].

In the present study, approximately 4 out of 100 patients were seen at the stage of cirrhosis and approximately 2 out of 100 had hepatocellular carcinoma. This demonstrates the delay experienced by the population in consultation.

The main limitation of this study is its retrospective nature. It could not provide access to all information on risk factors and co-infections.

Prospective multicenter research work is necessary not only to study the the-

rapeutic and evolutionary aspects of HBV infection but also to determine the factors influencing it. Prospective multicenter research is necessary not only to investigate the therapeutic and evolutionary aspects of HBV infection but also to determine the factors influencing it.

5. Conclusion

In Parakou, chronic infection with the hepatitis B virus is common and affects young people who are often male. Asthenia is a non-specific symptom and the most reported by these patients. More than 6 out of 10 patients have HBeAg-negative chronic infection. Around 5 out of 100 patients are seen for consultation at the stage of complication. Emphasis must be placed on screening, vaccination of sero-negative subjects as well as subsidy for pre-therapeutic assessment.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Appendix: Survey Sheet

Epidemiological and diagnostic profile of patients with chronic hepatitis B virus from 2017 to 2021 in Parakou, Republic of Benin

Identification number: ..…

I. General information

- Surname and given names:
- Sex:
- Age:
- Profession:
- Place of residence: rural area ☐ urban area ☐

II. Risk factors

- Blood transfusion: yes ☐ no ☐ If yes, specify the date: ……
- Scarification: yes ☐ no ☐
- Tattoo: yes ☐ no ☐
- Family history of HBV infection: yes ☐ no ☐
- Another health history: ……

III. Lifestyle

- Tobacco: yes ☐ no ☐ If yes, specify the number of pack-years: ……
- Alcohol: yes ☐ no ☐ If yes, specify the quantity: ……..

IV. Medical history

- Circumstances of discovery
  - Blood donation: yes ☐ no ☐
  - Prenatal consultation: yes ☐ no ☐
  - Premarital screening: yes ☐ no ☐
  - Systematic screening: yes ☐ no ☐
  - In the face of clinical symptoms: yes ☐ no ☐
- Duration between discovery and first consultation
  - Less than one week ☐
  - Less than one month ☐
  - Less than one year ☐
  - More than one year ☐
  - Duration in months: ……..
  - Date of the 1st consultation: ……..
- Symptoms
  - None: yes ☐ no ☐
  - Asthenia: yes ☐ no ☐
  - Abdominal pain: yes ☐ no ☐
  - Constipation: yes ☐ no ☐
  - Arthralgia: yes ☐ no ☐
  - Weight loss: yes ☐ no ☐
  - If other symptoms, specify: ……..

– Signs of complication: yes ☐ no ☐ If yes, specify: ……

V. Clinical examination

- Jaundice: yes ☐ no ☐
- Hepatomegaly: yes ☐ no ☐
- Signs of liver failure: yes ☐ no ☐
  - Palmar erythema: yes ☐ no ☐
  - Increase in the lunula of the nail: yes ☐ no ☐
  - Digital clubbing: yes ☐ no ☐
  - Spider angioma: yes ☐ no ☐
  - Amenorrhea: yes ☐ no ☐
  - Gynecomastia: yes ☐ no ☐
- Signs of portal hypertension
  - Venous collateral circulation: yes ☐ no ☐
  - Splenomegaly yes ☐ no ☐
- Other signs: yes ☐ no ☐ If yes, specify: ……

VI. Paraclinical data

1) Biological assessment

- Hepatic cytolysis
  - ALT:……. normal ☐ high ☐ if high, specify the value:……..
  - AST:…….. normal ☐ high ☐ if high, specify the value: ……..
- Serum creatinine:…….
- Sign of liver failure: Prothrombin Time:……. normal ☐ low ☐
- Blood count
  - Hemoglobin level: ……..
  - Mean corpuscular volume: ……..
  - White blood cell count: ……
  - platelets count: ……. normal ☐ low ☐ high ☐
- APRI score: ……..

2) Serology and virology

- HBeAg: positive ☐ negative ☐
- Anti-HBe antibodies: positive ☐ negative ☐
- Viral load: ……(UI/ml) ≥2000 UI/ml ☐ <2000 UI/ml ☐
- Anti-HCV antibodies: positive ☐ negative ☐ not done ☐
- Anti-HDV antibodies: positive ☐ negative ☐ not done ☐
- HIV serology: positive ☐ negative ☐ not done ☐

VII. Abdominal ultrasound

- Normal: yes ☐ no ☐
- Liver: heterogeneous ☐ steatosis ☐ dysmorphic ☐ hepatomegaly ☐ atrophy ☐ irregular contours ☐
- Splenomegaly: yes ☐ no ☐
- Portal vein dilatation: yes ☐ no ☐

- Ascites: yes ☐ no ☐
- Liver nodule: yes ☐ no ☐
- Recanalized umbilical vein: yes ☐ no ☐

VIII. Diagnosis

- HBeAg-negative chronic infection: yes ☐ no ☐
- HBeAg-positive chronic infection: yes ☐ no ☐
- HBeAg-negative chronic hepatitis: yes ☐ no ☐
- HBeAg-positive chronic hepatitis: yes ☐ no ☐
- Cirrhosis: yes ☐ no ☐
- Hepatocellular carcinoma: yes ☐ no ☐