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RETROSPECTIVE ANALYSIS OF CHARACTERISTICS OF PATIENTS WITH CHRONIC HEPATITIS B

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Abstract

Introduction. Hepatitis B virus infection is widespread, progressive, and therefore presents a serious global problem. The infection can develop into a chronic form with a high risk of death from cirrhosis and liver cancer. Kazakhstan is country with high endemicity for the spread of this infection.

Objective: To determine the main demographic, clinical, laboratory, serological characteristics of chronic hepatitis B patients.

Materials and methods. This retrospective cohort study was conducted using medical records of patients with chronic hepatitis B. A total of 239 participants were enrolled. Enrolled patients had a long-term follow-up with several blood analyzed over time. Characterize of the patients was taken into account: the demographic and clinical-laboratory features, risk factors, and antiviral treatment.

Results: Chronic hepatitis B in our environment occurs mainly in married educated employed middle-aged persons. The prevalence of chronic forms of cholecystitis, pancreatitis, bronchitis was increased with age ($p<0.001$). Male patients had higher serum ALT at baseline (57.5 (31.48-95.8) U/L and during follow-up (at 6 months, 12 months, 18 months and 84 months). An HBsAg decline was observed from baseline and during follow-up. There is significant difference in HBsAg at 18 months between male and female, 3.80 (3.12-6.42) log IU/mL and 2.79 (1.76-3.28) log IU/mL, respectively ($p<0.05$). The majority of patients had dental treatment (90%), surgery operations (59,83%), in particular appendectomy and gynecological interventions. 26,8% and 23,43% of patients had beauty procedures and Hepatitis A during early *childhood, respectively.*

Conclusion: Portrait of the Chronic hepatitis B patient was formed. The management of these patients should take into consideration age, gender, comorbidities and risk factors. Characteristics of the patients can be one of the essential keys for timely diagnosis and formation of risk groups, also in patient's treatment and its adherence. This data can be vital in the development of preventive measures among the general population.

Keywords: *chronic hepatitis B, risk factors, HBsAg, antiviral treatment.*

Резюме

РЕТРОСПЕКТИВНЫЙ АНАЛИЗ ХАРАКТЕРИСТИК ПАЦИЕНТОВ С ХРОНИЧЕСКИМ ГЕПАТИТОМ В

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Актуальность. Инфекция, вызванная вирусом гепатита В, определена широко распространенной и прогрессирующей инфекцией, в связи с этим представляет собой серьезную глобальную проблему здравоохранения. Инфекция может переходить в хроническую форму с высоким риском летального исхода от цирроза и рака печени. Казахстан является страной с высокой эндемичностью по распространению данной инфекции.

Цель: Определение основных демографических, клинических, лабораторных, серологических характеристик больных хроническим гепатитом В.

Материалы и методы. Данное ретроспективное когортное исследование было проведено с использованием медицинских карт 239 пациентов с хроническим гепатитом В. Включенные в исследование пациенты проходили длительное наблюдение, имели результаты анализов в течение данного периода. Также учитывалась следующие характеристики пациентов: демографические и клинико-лабораторные особенности, факторы риска и противовирусное лечение.

Результаты. Хроническим гепатитом В болеют в основном состоящие в браке, имеющие высшее образование, работающие люди среднего возраста. Распространенность хронических форм холецистита, панкреатита, бронхита увеличивалась с возрастом (p<0,001). Пациенты мужского пола имели более высокий уровень АЛТ в сыворотке крови на исходном уровне (57,5 (31,48-95,8) Ед/л) и во время наблюдения (через 6 месяцев, 12 месяцев, 18 месяцев и 84 месяцев). Отмечается снижение уровня HBsAg, начиная с исходного уровня и во время последующего наблюдения. Существует значительная разница в показателях HBsAg через 18 месяцев между мужчинами и женщинами, 3,80 (3,12-6,42) логарифмических МЕ/мл и 2,79 (1,76-3,28) логарифмических МЕ/мл соответственно (p<0,05). Большинство пациентов в анамнезе имеют стоматологическое лечение (90%), хирургические операции (59,83%), в частности аппендэктомию и гинекологические вмешательства. 26,8% и 23,43% пациентов перенесли косметические процедуры и гепатит А в раннем детстве, соответственно.

Выводы: Был сформирован портрет пациента с хроническим гепатитом В. При ведении данных пациентов следует учитывать возраст, пол, сопутствующие заболевания и факторы риска. Характеристики пациентов могут быть одним из важнейших ключей к своевременной диагностике и формированию групп риска, а также к лечению пациента и его приверженности. Эти данные могут иметь жизненно важное значение при разработке профилактических мер среди населения в целом.

Ключевые слова: *хронический гепатит В, факторы риска, HBsAg, противовирусное лечение.*

Түйіндеме

СОЗЫЛМАЛЫ В ГЕПАТИТІ БАР НАУҚАСТАРДЫҢ СИПАТТАМАЛАРЫН РЕТРОСПЕКТИВТІ ТАЛДАУ

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Кіріспе. В гепатиті вирусынан туындаған инфекция кең таралған, дамып келеді, сондықтан жаһандық проблеманы тудырады. Инфекция цирроз мен бауыр қатерлі ісігінен өлу қаупі жоғары созылмалы түрге айналуы мүмкін. Қазақстан осы инфекцияның таралуы бойынша эндемиясы жоғары ел болып табылады.

Мақсаты: Созылмалы В гепатиті бар науқастардың негізгі демографиялық, клиникалық, зертханалық, серологиялық сипаттамаларын анықтау.

Материалдар мен әдістері. Бұл ретроспективті когорттық зерттеу созылмалы В гепатиті бар 239 науқастардың медициналық жазбаларын қолдана отырып жүргізілді. Пациенттердің келесі сипаттамасы ескерілді: демографиялық және клиникалық-зертханалық ерекшеліктері, қауіп факторлары және вирусқа қарсы емдеу.

Нәтижелері. Біздің ортамыздағы созылмалы В гепатиті негізінен некеде тұрған, білімді, орта жастағы жұмыс істейтін адамдарда кездеседі. Холециститтің, панкреатиттің, бронхиттің созылмалы түрлерінің таралуы жасына қарай өсті (p<0,001). Еркек пациенттерде бастапқы деңгейде (57,5 (31,48-95,8) бірлік/л) және бақылау кезінде (6 ай, 12 ай, 18 ай және 84 айдан кейін) қан сарысуындағы alt деңгейі жоғары болды. HBsAg деңгейінің төмендеуі бастапқы деңгейден бастап және бақылау кезінде байқалды. Ерлер мен әйелдер арасында 18 айдан кейін HBsAg-да айтарлықтай айырмашылық бар, сәйкесінше 3,80 (3,12-6,42) логарифмдік МЕ/мл және 2,79 (1,76-3,28) логарифмдік МЕ/мл (p<0,05). Пациенттердің көпшілігі стоматологиялық емдеуден (90%), хирургиялық операциялардан (59,83%), атап айтқанда аппендэктомиядан және гинекологиялық араласудан өтті. Пациенттердің 26,8% және 23,43% сәйкесінше ерте балалық шақта косметикалық процедуралар мен А гепатитін бастан өткерді.

Тұжырымдар: Созылмалы В гепатиті бар науқастың портреті қалыптасты. Бұл науқастарды басқару кезінде жасын, жынысын, қатар жүретін ауруларын және қауіп факторларын ескеру қажет. Пациенттердің сипаттамалары қауіпті топтарды уақтылы диагностикалау мен қалыптастырудың, сондай-ақ пациентті емдеу мен олардың міндеттемелерінің маңызды кілттерінің бірі болуы мүмкін. Бұл деректер жалпы халық арасында алдын алу шараларын әзірлеу кезінде маңызды болуы мүмкін.

Түйінді сөздер*: созылмалы В гепатиті, қауіп факторлары, HBsAg, вирусқа қарсы емдеу.*

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Introduction

Hepatitis virus B infection is widespread, progressive, and therefore presents a serious problem in modern medicine. The global strategy of healthcare sector on hepatitis calls for the elimination of hepatitis as a public health threat by 2030 (reduction of new infections by 90% and mortality by 65%) [20,30,36].

300-500 million patients are carriers of hepatitis B virus infection (HBV) all over the world [35]. A characteristic feature of HBV is the variety of transmission paths of sources [40]. 5-10% of all patients with acute HBV infection develop chronic hepatitis B (CHB) or become inactive carriers [36]. CHB is related to an elevated risk of progressive liver damage and the occurrence of complications such as fibrosis, cirrhosis, hepatocellular carcinoma [8,28].

Kazakhstan is located in Central Asia with multinational population of around 19 million and is one of the countries with high endemicity (more than 8%) for the spread of viral hepatitis B [37].

Study evaluating seroprevalence and risk factors for hepatitis B and hepatitis C in three large regions of Kazakhstan showed a high-intermediate level of endemicity for HBsAg in three large regions of Kazakhstan [21].

HBV-related diseases cause a substantial financial burden to patients, their families and society [42]. The medico-social significance of CHB is associated with the predominance among patients of working age, as well as the steady progression of these diseases, leading to early disability and mortality [5].

Astana city ranks first place in the numbers of cases CHB in Kazakhstan (110,4 cases per 100 thousand population, which is 3.7 times higher than the national average) [5].

In 2018 the Department of Public Health of Astana identified 16 cases with chronic hepatitis B and C viruses among employees of beauty salons and hair salons [9].

Given the relevance of this topic, we conducted a study to determine the main demographic, clinical, laboratory, serological characteristics of chronic hepatitis B patients in our environment.

Materials and Methods.

Study population

This study is a retrospective analysis of medical data from Hepatology Center serving a north region of Kazakhstan. Ethics approval of the study was obtained from the Bioethics Committee of Astana Medical University (protocol №15 dated 18.11.2021).

After reviewing patient medical records, patients with CHB who met the following criteria were enrolled in the study: age ≥ 18 years; HBsAg positive for > 6 months; eligible for antiviral treatment according to the Kazakhstan HBV Guidelines; visited from 2003 to June 30, 2021 and on antiviral treatment; no evidence of co-infection with hepatitis C virus, human immunodeficiency virus (HIV) and/or hepatitis delta virus; exclusion of other causes of chronic liver disease (alcoholism, hepatotoxic drugs, and autoimmune liver disease); and no pregnancy or lactation.

Data collection

We analyzed the medical records of each patient containing information about demographic characteristics, risk factors, laboratory data including HBV virological and serological markers (ALT and AST levels, HBsAg titer, status of HBeAg (positive or negative), HBV-DNA titer, complications, fibrosis stage, disability and antiviral treatment (type, duration).

ALT level was classified as normal (≤1× upper limit of normal; ULN) or elevated (>1× ULN), with ULN defined as 35 U/L for men and 25 U/L for women per the current AASLD guidance [33]. As a sensitivity analysis, ULN was also defined as 30 U/L for men and 19 U/L for women as per AASLD guidelines [33] and 40 U/L as per the EASL guideline [10]. Titers of HBsAg and HBV-DNA were expressed as $\log_{10}$ IU/ml.

These data were collected within all visits to the physician namely at baseline, during follow-up. All included participants underwent follow up more than 3 months with several blood analyzed over time. Treated patients have received nucleot(s) ide analogues (NA), pegylated interferon (PEG-IFN) or combination NA with PEG-IFN according to prescription of physician.

Data analysis

Descriptive statistics were reported as proportions (%) for categorical variables and as means ± standard deviations or medians with interquartile ranges in parentheses for continuous variables. The normality of quantitative variable distribution was verified using the Kolmogorov–Smirnov test. Chi-square or Fisher's exact tests for categorical variables and the Student's T-test or Mann-Whitney U test for continuous independent variables were conducted, as appropriate. The strength of correlations between two quantitative variables was determined using Spearman's or Pearson's linear correlation coefficient (r_S or r). Bivariate analysis was performed to compare differences between independent variables and HBsAg and results were reported as odds ratio (OR) and 95% confidence interval (CI).

All statistical tests were two-sided and a value of $P < 0.05$ was taken to indicate statistical significance. All analyses were performed using Statistical Package for the Social Sciences (SPSS) software, version 23.0 [14].

Results.

Baseline characteristics of the cohort

A total of 347 patients with CHB was consecutively enrolled in this study. After excluding patients less than 18 years of age and having co-infections, pregnancies, the records of 239 patients were analyzed.

The sample was composed of 118 males (49,37%) and 121 females (50,63%). The median age of the patients with CHB was 48.00 (38.00–58.00) ranging from 18 to 83 years. The majority of the patients (26.36%) were in the age group 50 – 59 years, whereas 7.95% were 18-29 and more than 70 years of age.

The majority of the patients were of Kazakh origin (91.63%), married (75.31%). For education, 58.16% were university graduates. 57,32% have work with average income (Table 1).

Table 1.

Demographic characteristics of study participants.

Characteristic		Total (n=239)
Gender (n, %)	Males	118 (49,37%)
	Female	121 (50,63%)
Age, years (median IQR)		48 (38.00-58.00)
Age category (n, %)	18-29	19 (7,95%)
	30-39	51 (21,34%)
	40-49	56 (23,43%)
	50-59	63 (26,36%)
	60-69	31 (12,97%)
	≥70	19 (7,95)
Ethnicity (n, %)	Kazakh	219 (91,63%)
	Russian	16 (6,69%)
	Other	4 (1,67%)
Marital status (n, %)	Married	180 (75,31%)
	Single/divorced	59 (24,69%)
Education level (n, %)	High school/ college	100 (41,84%)
	University	139 (58,16%)
Employment (n, %)	Employed	137 (57,32%)
	Unemployed	56 (23,43%)
	Students	6 (2,51%)
	Retired	40 (16,74%)
Income level (n, %)	High	0
	Average	95 (69,35%)
	Low	42 (30,65%)

Regarding laboratory parameters, all patients had an HBeAg test available. 94.98% had negative HBeAg. Baseline serum HBsAg and HBV DNA levels were 3.45 (2.70-3.78) log IU/mL and 5.04 (3.52-6.73) log IU/mL, respectively. In addition, the median ALT level and AST level were 46.40 (29.00-84.41) U/L and 34.80 (24.84-63.60), respectively. F2 was the most frequently recorded stage of liver fibrosis by Metavir scale (33.47%). 4.18% are disabled persons (I group of disability – 2, II group – 5, III group – 3) (Table 2).

Table 2.

Laboratory-instrumental measurements of the cohort.

	Levels at inclusion
ALT (U/L) (median IQR)	46.40 (29.00-84.41)
AST (U/L) (median IQR)	34.80 (24.84-63.60)
HBe-Ag negative (n, %)	227 (94.98%)
HBV DNA (log10 IU/mL) (median IQR)	5.04 (3.52-6.73)
HBsAg quantification (log10 UI/mL) (median IQR)	3.45 (2.70-3.78)
Fibrosis stage (Metavir) F0	47 (19.67%)
F1	35 (14.64%)
F2	80 (33.47%)
F3	43 (17.99%)
F4	34 (14.23%)

Age and Comorbidities

The prevalence of chronic bronchitis, chronic gastritis, chronic pancreatitis, chronic cholecystitis, was respectively 7.11% (17), 11.29% (27), 15.48% (37), and 30.96% (74). The prevalence of chronic cholecystitis (R = 0.213), chronic pancreatitis (R=0.245), chronic bronchitis (R=0.277) was linearly related to age ($P < 0.01$) and increased with age ($P < 0.001$) (Fig.1).

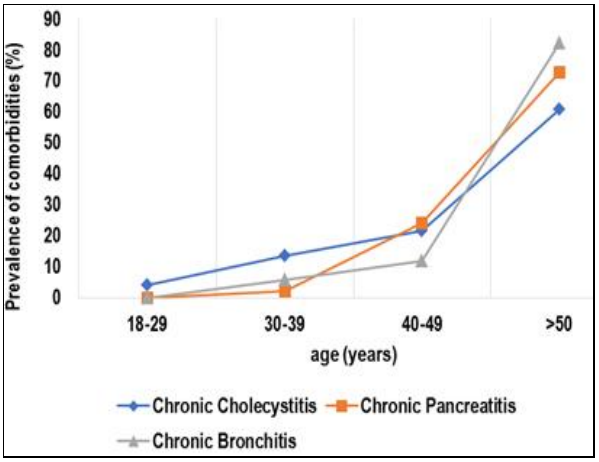

Figure 1. Comorbidities of Chronic Hepatitis B.

Antiviral treatment and laboratory measurements

The majority of the patients (77.41%) were taking NA such as tenofovir (TDF) and entecavir. 18.41% of the patients were taking PEG-IFN followed by TDF. Treatment with only PEG-IFN was administered to 10 patients (4.18%) for 24 or 48 weeks.

The median duration of antiviral treatment was 36.00 (12.00–48.00) months. 78.7% patients come to regular check-up every 6-12 months.

Compare to female, male patients had higher serum ALT at baseline (57.5 (31.48-95.8) U/L and follow-up: 6 months - 49.31 (29.3-85.15) U/L, 12 months - 37.23 (24.70-70.81) U/L, 18 months - 38.75 (24.48-65.19), and at 84 months - 38.75 (24.48-65.19) ($p<0.05$).

An HBsAg decline was observed from baseline and during follow-up. There is significant difference in HBsAg at 18 months between male and female, 3.80 (3.12-6.42) and 2.79 (1.76-3.28), respectively ($p<0.05$) (Table 3).

Table 3.

HBsAg and ALT level kinetics accordance to duration (months).

Variables	Gender category			Age category						p-value
1. ALT (U/L)	M (n=118)	F (n=121)	p-value	18-29 (n=19)	30-39 (n=51)	40-49 (n=56)	50-59 (n=63)	60-69 (n=31)	≥70 (19)	
Baseline	57.5 (31.48-95.8)	42.00 (25.75-67.65)	0.005	34.36 (19.00-69.00)	46.00 (26.16-84.08)	53.00 (33.00-90.80)	46.40 (30.00-87.00)	39.00 (22.92-59.10)	45.00 (25.5-97.60)	0.357
6 months	49.31 (29.3-85.15)	35.9 (25.00-63.87)	0.000	57.09 (43.27-99.68)	36.15 (26.29-80.68)	48.30 (27.60-76.33)	40.30 (25.03-74.94)	36.35 (25.05-53.52)	47.00 (23.90-69.82)	0.381
12 months	37.23 (24.70-70.81)	31.34 (21.89-50.19)	0.044	29.62 (23.90-50.88)	46.70 (20.10-80.33)	42.10 (24.71-68.93)	33.95 (23.73-48.30)	31.55 (23.15-51.04)	35.50 (21.57-43.70)	0.681
18 months	38.75 (24.48-65.19)	30.85 (21.33-43.47)	0.013	26.85 (23.48-58.33)	34.40 (23.86-61.30)	42.30 (21.10-73.26)	29.10 (21.56-51.22)	32.00 (21.60-42.88)	27.40 (17.80-38.00)	0.839
24 months	58.80 (24.56-95.35)	36.00 (25.66-39.82)	0.124	38.05 (25.18-50.63)	40.80 (25.20-87.35)	34.68 (24.72-44.45)	30.85 (20.76-55.00)	31.60 (16.15-64.83)	28.00 (19.10-31.25)	0.782
36 months	58.80 (33.5-64.75)	32.88 (23.72-49.30)	0.056	41.80 (23.80-52.48)	38.10 (20.25-67.83)	27.30 (21.84-35.95)	30.54 (18.63-54.25)	22.60 (14.35-44.80)	26.60 (21.50-49.40)	0.680
48 months	38.00 (17.70-52.08)	28.80 (19.22-81.56)	0.154	23.50 (18.73-49.48)	40.80 (22.08-53.13)	36.10 (19.54-57.20)	24.51 (18.95-32.60)	19.10 (15.65-29.45)	18.60 (12.00-40.40)	0.164
60 months	81.00 (17.60-92.42)	28.60 (16.15-46.81)	0.367	24.50 (16.16-28.60)	19.10 (14.80-41.45)	29.80 (19.90-46.00)	32.30 (16.70-47.30)	19.90 (17.45-25.50)	17.90 (12.65-72.90)	0.308
72 months	30.00 (19.70-50.30)	22.30 (14.13-45.36)	0.863	29.20 (21.10-41.48)	19.60 (13.83-37.16)	31.15 (25.58-44.25)	25.49 (16.76-37.08)	18.10 (17.90-35.00)	36.20 (19.18-92.72)	0.195
84 months	33.5 (19.15-57.45)	20.50 (16.35-25.30)	0.030	29.40 (23.34-36.80)	21.47 (11.45-41.35)	25.00 (20.87-30.00)	20.35 (16.12-26.15)	18.55 (14.35-22.60)	52.70 (21.28-232.48)	0.218
≥96 months	16.60 (15.25-112.67)	20.00 (16.90-36.35)	0.595	18.60 (18.00-	21.73 (10.00-	17.35 (15.63-37.23)	23.50 (13.39-204.52)	16.50 (16.30-	108.70 (20.00-	0.433
2. HBsAg log UI/mL										
0 months	3.53 (2.69-3.78)	3.33 (2.69-3.79)	0.575	3.00 (1.99-3.68)	3.28 (2.24-3.75)	3.33 (2.64-3.64)	3.62 (2.85-3.80)	3.76 (3.45-6.68)	3.63 (3.12-3.75)	0.053
6 months	3.39 (2.07-3.68)	3.15 (3.00-3.29)	0.699	-	2.90 (1.90-3.73)	3.29 (3.15-3.41)	-	-	-	0.724
12 months	4.32 (1.67-5.46)	3.63 (3.26-3.87)	0.539	-	3.71 (2.18-5.30)	3.65 (3.63-4.62)	3.64 (3.32-3.71)	3.78 (3.41-4.15)	-	0.675
18 months	3.80 (3.12-6.42)	2.79 (1.76-3.28)	0.008	7.04 (4.40-7.33)	2.23 (1.59-3.94)	3.00 (2.84-4.40)	3.40 (3.05-3.73)	3.49 (1.73-4.98)	3.01 (2.79-3.23)	0.655
24 months	3.70 (1.77-3.85)	3.29 (1.79-4.24)	0.930	-	2.30 (1.76-3.48)	1.33 (1.12-5.01)	3.85 (3.43-4.51)	3.51 (1.84-4.95)	-	0.372
36 months	2.93 (1.95-3.85)	3.00 (2.07-4.79)	0.942	2.81 (2.62-3.00)	1.73 (1.48-4.49)	2.93 (2.85-3.00)	3.60 (3.23-3.93)	-	-	0.778
48 months	3.00 (1.54-3.63)	4.05 (2.80-8.42)	0.070	3.94 (3.80-4.07)	-	3.00 (2.24-3.38)	3.11 (1.04-6.74)	6.02 (4.02-8.01)	-	0.210
60 months	3.53 (1.21-3.79)	3.67 (2.95-5.99)	0.366	-	3.67 (1.66-4.72)	-	3.46 (1.28-3.83)		-	0.500
72 months	3.60 (3.36-3.88)	3.62 (1.63-6.88)	0.806	2.30 (1.05-3.55)	3.08 (2.20-3.95)	-	3.74 (3.62-3.85)	6.78 (3.65-9.90)	-	0.388
≥96 months	2.70 (2.21-6.10)	1.44 (1.06-2.30)	0.317	-	3.24 (2.16-3.40)	-	1.77 (1.66-1.88)	-	-	0.211

Risk factors

The majority of patients had dental treatment (90%), surgery operations (59,83%), in particular appendectomy (20%) and gynecological interventions (32,17%). 26,8% and 23,43% of patients had beauty procedures and Hepatitis A during early childhood, respectively.

8.78% of CHB patients work at medical organizations as physicians, nurses. A childhood history of Hepatitis A was found in 38% among them. There was no significant difference in HBsAg according to risk factors (Table 4).

Discussion.

Data from this study provide essential insight into natural history of CHB among infected patients by describing the demographic, clinical and laboratory characteristics.

In our patients, the proportion of females was higher, and this is contrast with data from other studies [3,18]. Most of our patients were aged 50–59 years, followed by 40-49 years, and then 30–39 years. Chronic HBV in our environment occurs mainly in employed middle-aged persons. Similar studies have shown higher prevalence of chronic HBV in middle aged individuals and elders compared to youth [12,26,39]. Also, previous studies shown that the largest number of cases of HBV in Nur-Sultan city was registered in the age group of 30 and above since 2016, which is the most active, reproductive part of the population [29,32]. We can suppose this differential age distribution is likely due to the implementation of hepatitis B vaccination program started in 1998, which essentially eliminated HBV infection in patients under the age of 30 [15,24-25].

Table 4.

HBsAg level accordance to risk factors.

Factors	Variables	n=239	HBsAg (log UI/mL)	p-value
Having dental treatment	Yes	215 (90%)	3.44 (2.70-3.76)	0.571
	No	24 (10%)	3.57 (2.66-5.16)	
History of surgery	Yes	143 (59,83%)	3.50 (2.70-3.80)	0.291
	No	96 (40,17%)	3.34 (2.66-3.74)	
Beauty procedures	Yes	64 (26,8%)	3.13 (2.33-3.73)	0.342
	No	175 (73,2%)	3.53 (3.00-3.80)	
Hepatitis A during early **c**hildhood	Yes	56 (23,43%)	3.45 (3.00-3.79)	0.702
	No	183 (76,57%)	3.45 (2.62-3.78)	
History of blood transfusion	Yes	41 (17,15%)	3.63 (2.78-3.82)	0.971
	No	198 (82,85%)	3.44 (2.67-3.75)	
Having tattoo or piercing	Yes	39 (16,3%)	3.33 (2.21-3.77)	0.331
	No	200 (83,7%)	3.47 (2.81-3.80)	
Family history of HBV	Yes	38 (15,9%)	3.49 (2.09-4.43)	0.844
	No	201(84,1%)	3.42 (2.73-3.76)	
Medical workers	Yes	21 (8,78%)	3.21 (1.69-3.74)	0.196
	No	218 (91,21%)	3.50 (2.79-3.78)	
Bad habits (alcohol, smoking, drugs)	Yes	18 (7,53%)	3.29 (2.31-3.61)	0.542
	No	221 (92,47%)	3.47 (2.69-3.80)	
Blood donations	Yes	11 (4,6%)	3.24 (2.22-4.25)	0.706
	No	228 (95,4%)	3.47 (2.73-3.79)	

Most of the patients were of Kazakh origin, married and have graduated university. More than half work with average income. We can assume the absence of external manifestations of the disease does not limit the ability of patients to work. There are also medical workers (physicians and nurses) among them. In contrast, Berkinbayev et al. [6] found that the prevalence of HBsAg was higher among individuals with incomplete or secondary education in Almaty, the largest city in Kazakhstan.

We observed that the majority of the CHB population in this study had cholecystitis, gastritis and pancreatitis in chronic form. In contrast, in the USA CHB patients had high incidence and prevalence of chronic kidney disease, hypertension and diabetes mellitus [22]. Diabetes mellitus was present in enrolled population of one observation study [1], followed by hypertension, hyperlipidemia and hypothyroidism.

Our study confirms results of Hong-Kong study that CHB patients are getting older with increasing prevalence of common comorbidities [34]. Cross-sectional study in China [11] showed CHB patients are aging (due to the high coverage of hepatitis B vaccination) and have an increasing incidence of complications.

We evaluated risk factors contributed to develop of HBV. Surgical procedures are recognized as an important route of transmission for HBV infection worldwide [31]. Our findings showed the most of patients had surgery operations. The frequent operations were appendectomy and gynecological interventions. Recent study in Kazakhstan found history of surgery was not associated with HBsAg [21].

Almost all patients have visited dental clinics and beauty salons for various procedures (manicure, pedicure). Russian study [41] showed that HBV was developed during the provision of dental care, surgery operations and other medical manipulations in hospitals related to blood transfusion and its components, the provision of beauty services and when using common household items with HBV person. Yang et al. [38] investigating risk for hepatitis B and C virus transmission in nail salons and barbershops in the USA stated compliance is needed to prevent HBV/HCV transmission in these businesses.

It was observed that some patients had hepatitis A in childhood and blood transfusions. CHB patients were donors. Family history of HBV was noticed as one of the vital factors.

The percentage of HBeAg-negative CHB patients was higher than that of HBeAg-positive CHB patients, which is similar to data from recent studies from Europe, Asia, and the United States and contrast with studies from Pakistan [2,27].

HBsAg is the most important serological marker of HBV infection, and serum HBsAg level correlates with the intrahepatic amount and transcriptional activity of covalently closed circular DNA (cccDNA) [7]. Another essential factor in the decision to initiate the treatment of CHB is individual patient's ALT level [16-17,19,23].

In this study, CHB patients treated with NA or combination Peg-IFN and NA therapy resulted in a cure. TDF was used by most of the patients. Since 2018, it has been issued free of charge within the guaranteed volume of free medical care in Kazakhstan.

Seroprevalence of HBsAg was low in the young age group that similar with results of one study [21]. We demonstrated that overall, treated patients had an HBsAg and ALT decline during follow-up. There was no statistically significant difference in the level of HBsAg and ALT between different age groups. It was observed that 18 months of follow-up is key date when male and female have discrepancies in analyses.

Bao et al. [4] showed the extent of HBsAg decline from baseline in the early stages of treatment is more predictive of efficacy. On the other hand, Hui et al. [13] found that CHB patients who have persistently normal serum ALT

during follow-up are much less likely to have disease progression.

Our study has some limitations: (1) a selection bias can be identified, as all patients were selected from one center; (2) the relatively small sample size of the study population, which can be explained by our restricting criteria and conducting the study in a single-center; (3) the rate of missing records, including adverse events, which hindered drawing useful conclusions in some of the variables.

Conclusion.

To sum up, portrait of the CHB patient was formed. CHB in our environment occurs mainly in married educated employed middle-aged persons. The management of patients with CHB should take into consideration age, gender, comorbidities and risk factors. Characteristics of the patients is one of the keys for timely diagnosis and formation of risk groups, also in patient's treatment and its adherence. This data can be essential in the development of preventive measures among the general population.

Further studies are needed to better characterize the physical and psychological components of the health-related quality of life in patients with CHB.

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Abbreviations

AST: *Aspartate aminotransferase*
ALT*: Alanine aminotransferase*
CHB: *Chronic hepatitis B*
HBeAg: *Hepatitis B e-antigen*
HBsAg: *Hepatitis B surface antigen*
HBV: *Hepatitis B virus*
HBV DNA: *Hepatitis b viral load*
IQR*:* Interquartile range
NAs: *Nucleot(s)ide analogues*
PEG-IFN: *pegylated interferon alpha*
TDF: *Tenofovir*
ULN: *Upper limit of normal*

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