European Review for Medical and Pharmacological Sciences 2023; 27: 12121-12133

National trends in the prevalence of hepatitis B and C in South Korea, before and during the COVID-19 pandemic (2007-2021) – a nationwide representative study

J.-J. PARK[1], M. LEE[1,2], H. KIM[1,3], J.-Y. PARK[1,2], H. LEE[1,2], H.J. KIM[1,2], A. KOYANAGI[4], L. SMITH[5], M.S. KIM[6], M. RAHMATI[7,8], S.Y. RHEE[1,9], Y. HA[10], K. LEE[10], D.K. YON[1,2,11]

[1]Center for Digital Health, Medical Science Research Institute, Kyung Hee University College of Medicine, Seoul, South Korea
[2]Department of Regulatory Science, Kyung Hee University, Seoul, South Korea
[3]Department of Applied Information Engineering, Yonsei University, Seoul, South Korea
[4]Research and Development Unit, Parc Sanitari Sant Joan de Deu, Barcelona, Spain
[5]Centre for Health, Performance and Wellbeing, Anglia Ruskin University, Cambridge, UK
[6]Cardiovascular Disease Initiative, Broad Institute of MIT and Harvard, Cambridge, MA, USA
[7]Department of Physical Education and Sport Sciences, Faculty of Literature and Humanities, Vali-E-Asr University of Rafsanjan, Rafsanjan, Iran
[8]Department of Physical Education and Sport Sciences, Faculty of Literature and Human Sciences, Lorestan University, Khoramabad, Iran
[9]Department of Endocrinology and Metabolism, Kyung Hee University School of Medicine, Seoul, South Korea
[10]Digestive Disease Center, CHA Bundang Medical Center, CHA University School of Medicine, Seongnam, South Korea
[11]Department of Pediatrics, Kyung Hee University College of Medicine, Seoul, South Korea

J.-J. Park, M. Lee, H. Kim, and J.-Y. Park contributed equally to this study

Abstract. – OBJECTIVE: Due to the various changes caused by the COVID-19 pandemic, some infectious diseases showed different epidemiology and prevalence during the pandemic. However, there is a lack of comprehensive studies on trends in the prevalence of hepatitis B and C related to the pandemic. Thus, we compared the prevalence of hepatitis B and C before and during the COVID-19 pandemic in South Korea.

SUBJECTS AND METHODS: We conducted a comprehensive trend analysis with a nationwide serial cross-sectional survey from 2007 to 2021 (n=86,931) using the Korea National Health and Nutrition Examination Survey (KNHANES). The changes in the prevalence of hepatitis B and C were evaluated using a weighted regression model to assess the impact of the COVID-19 pandemic.

RESULTS: From 2007 to 2021, 86,931 Korean adults aged 19 or older were included in the KNHANES data. The prevalence of hepatitis B showed a declining trend until the onset of the pandemic (1.80% in 2007-2009; 1.08% in 2016-2019; and 1.01% in 2020), at which point this trend reversed (1.39% in 2021). The prevalence of hepatitis C remained stable (0.14% in 2007-2009 and 0.18% in 2016-2019), with no particular surge related to the COVID-19 pandemic (βdiff, -0.002; 95% CI, -0.761 to 0.756). For hepatitis B, old age was identified as a pandemic-related vulnerable factor (ratio of odds ratio, 1.68; 95% CI, 1.05-2.70).

CONCLUSIONS: In this study, unlike other infectious diseases, hepatitis B and C did not show a decreasing trend during the pandemic. In particular, hepatitis B showed a rebound trend during the pandemic, which was noticeable in those aged 60 or older. Further studies are needed to support these findings.

Key Words:
Hepatitis B, Hepatitis C, Prevalence, COVID-19, SARS-CoV-2.

Introduction

The global pandemic triggered by the severe acute respiratory syndrome coronavirus 2 (SARS-

Corresponding Authors: Kwanjoo Lee, MD; e-mail: jdp1988@chamc.co.kr;
Dong Keon Yon, MD, Ph.D, FAAAAI, FACAAI; e-mail: yonkkang@gmail.com

CoV-2), commonly known as the COVID-19 pandemic, has profoundly reshaped public health policies worldwide[1-4]. Due to these profound changes, the dynamics of multiple infectious diseases have been perturbed[5-7].

Hepatitis B and C are chronic infectious diseases of the liver that cause liver cirrhosis or hepatocellular carcinoma and are a significant contributor to global morbidity and mortality[8,9]. Therefore, it is crucial to know the changes in disease prevalence and identify their underlying causes, especially in the context of informing public health practices and establishing policies for those in need. Unlike SARS-CoV-2, a predominantly airborne transmitted disease[1], hepatitis B and C have a common feature of bloodborne transmission with potential spread through other body fluids[10]. Yet, to date, no studies have examined the trends of hepatitis B and C prevalence in the context of the COVID-19 pandemic[11]. In addition, South Korea is recognized as an intermediate endemic region for the hepatitis B virus (HBV), whereas the prevalence of the hepatitis C virus (HCV) remains low[12]. The country also manages hepatitis B and C patients through its national cancer screening project. Tests for HBV surface antigen, HBV antibodies, and HCV antibodies are included in the screening items[13].

Considering the unique characteristics of South Korea's health policy, we calculated the national prevalence using data from national institutions and decided to compare the prevalence of hepatitis B and C in South Korea before and after the COVID-19 pandemic, observing any changes. Furthermore, we endeavored to elucidate the underlying determinants of these changes by identifying factors that exhibited significant differences.

Subjects and Methods

Study Design and Data Collection

In our research, we harness data from the Korea National Health and Nutrition Examination Survey (KNHANES) to perform a longitudinal examination of hepatitis B and C prevalence trends and associated factors in the adult Korean population before and during the COVID-19 pandemic, including data from 2007 to 2021[14,15]. The KNHANES is a nationwide, longitudinal, repeated serial, cross-sectional study based on a stratified, multistage probability sampling design conducted by the Korea Disease Control and Prevention Agency (KDCA) in the interest of public health[16]. The data collection process involved health interviews and examinations over a three-day across 192 primary sampling units nationwide, utilizing two dedicated mobile examination center trucks. All participants provided written informed consent, and their data were kept anonymous. Both the KDCA and Kyung Hee University (KHUH 2022-06-042) institutional review boards approved all procedures involving human subjects.

The research population encompassed adults who were 19 years or older. The collected data incorporated a variety of factors such as sex, region of residence, body mass index (BMI), educational level, income level, alcohol consumption, and smoking status, along with records of hepatitis B and C. To evaluate the prevalence of hepatitis B and C before and during the COVID-19 pandemic, we utilized a sufficient representative sample.

Ascertainment of Hepatitis B and C

The primary aim of our study was to ascertain the prevalence of hepatitis B and C. To achieve this objective, we conducted an extensive survey involving a substantial sample size. Participants were specifically asked the following targeted question regarding their hepatitis B or C diagnosis: "Have you ever received a clinical diagnosis of hepatitis B or C from a physician?"

Covariate Definitions

Participants' characteristics were classified in terms of age (19-29, 30-39, 40-49, 50-59, ≥60 years), sex (male and female), region of residence (urban and rural)[17], household income (lowest, second, third, and highest quartile), educational level (elementary school or below, middle school, high school, and college or above), alcohol consumption (non-drinker, 1-5 days/month, and 6-30 days/month), and smoking status (non-smoker, ex-smoker, and current smoker). BMI was categorized as per the Asia-Pacific guidelines into underweight (<18.5 kg/m^2), normal (18.5-22.9 kg/m^2), overweight (23.0-25.0 kg/m^2), or obese (≥25.0 kg/m^2)[18]. The pre-pandemic phase was segmented into four intervals (2007-2009, 2010-2012, 2013-2015, and 2016-2019) and juxtaposed with the durations corresponding to the pandemic (2020 and 2021)[19,20].

Statistical Analysis

The results of our study were presented with qualitative data in the form of proportions or percentages. The statistical analyses were performed using weighted multivariate regression models.

These models were employed to systematically compare and assess the prevalence of hepatitis B and hepatitis C pre-pandemic and during the COVID-19 pandemic. The estimates were presented as weighted odds ratios (wORs) or β-coefficients with 95% confidence intervals (CIs)[21,22]. The prevalence of hepatitis B and C was determined by examining data derived from the KNHANES, covering from 2007 to 2021, and grouping the data by distinct year groups. A weighted complex sampling analysis was carried out to ensure precise estimation. For statistical analysis, weighted binomial or linear logistic regression models were utilized to compute wORs or β-coefficients with 95% CIs. Moreover, the β difference was computed to assess the shift in the prevalence of hepatitis B and C prior to and during the COVID-19 pandemic. To enhance the reliability of the findings, stratification analysis was carried out, accounting for variables such as age, sex, level of education, region of residence, and income in all regression models. This approach aimed to provide a comprehensive and robust assessment of the association between the prevalence of hepatitis B and C and the investigated factors. The SAS software (version 9.4; SAS Institute, Cary, NC, USA) was employed for all statistical analyses, applying a two-sided test, with a p-value <0.05 deemed statistically significant[23].

Results

From the KNHANES, data were obtained for 120,181 participants spanning the years 2007 to 2021. After preliminary screening, 33,250 participants were excluded owing to incomplete data or being under the age of 18, yielding a final analytical sample comprising 86,931 adults (**Supplementary Figure 1**). The number of participants fluctuated annually, with distinct cohorts each year. The distribution of participants across each cohort is delineated as follows: 16,768 for the years 2007-2009; 17,773 for 2010-2012; 16,396 for 2013-2015; 24,640 for 2016-2019; 5,801 for 2020; and 5,553 for 2021.

Overall prevalence trends of hepatitis B and C from 2007 to 2021 are illustrated in Figure 1. No discernible spike was observed specifically associated with the COVID-19 pandemic. Sociodemographic characteristics of the study population in terms of crude and weighted rate are outlined in Table I. The prevalence of hepatitis B, classified by socio-demographic factors, is presented in Table II . Table II delineates the prevalence of hepatitis B stratified by socio-demographic determinants, concurrently drawing the associated trends and relative measures using wORs and the regression slope coefficient β. Before the pandemic, hepatitis B prevalence consistently waned across all evaluated subgroups. On the other hand, during the pandemic, this trend appeared to reverse, suggesting a potential rebound in prevalence rates. Specifically, prevalence rates declined from 1.80% (95% CI, 1.54-2.07) in 2007-2009 to 1.01% (95% CI, 0.66-1.35) in 2020. Notably, there was a surge to 1.39% (95% CI, 1.07-1.72) in 2021, marking a statistically significant upswing during the pandemic, as indicated by a trend difference in β, 3.956 (95% CI, 1.940-5.971).

Since the prevalence of hepatitis B shifted between pre-pandemic and during the pandem-

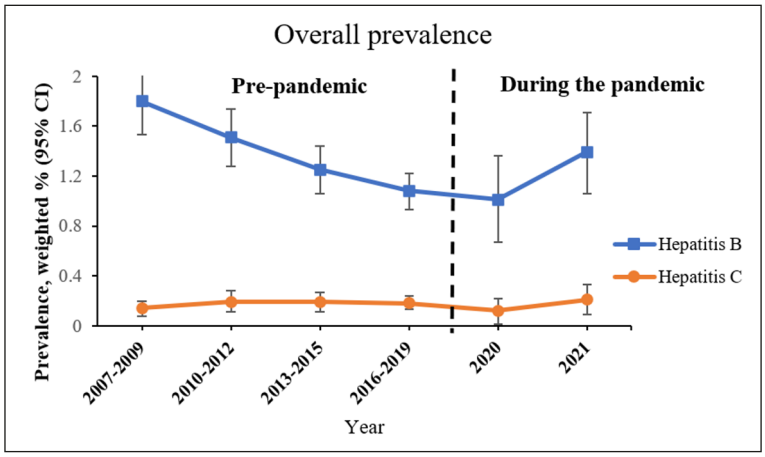

Figure 1. Graphical figure. Error bard indicates 95% CI. CI: confidence interval.

Table I. General characteristics of Korean adults, in the data obtained from the KNHANES from 2007 to 2021 (n=86,931).

		Pre-pandemic				During the pandemic	
	Total	2007-2009	2010-2012	2013-2015	2016-2019	2020	2021
Participants, n	86,931	16,768	17,773	16,396	24,640	5,801	5,553
Crude value							
Age, years, n (%)							
19-29	10,653 (12.25)	2,221 (13.25)	2,059 (11.59)	1,988 (12.12)	2,924 (11.87)	795 (13.70)	666 (11.99)
30-39	14,550 (16.74)	3,416 (20.37)	3,276 (18.43)	2,627 (16.02)	3,828 (15.54)	761 (13.12)	642 (11.56)
40-49	15,871 (18.26)	3,315 (19.77)	3,161 (17.79)	2,967 (18.10)	4,514 (18.32)	964 (16.62)	950 (17.11)
50-59	16,191 (18.63)	2,816 (16.79)	3,399 (19.12)	3,219 (19.63)	4,684 (19.01)	1,058 (18.24)	1,015 (18.28)
≥60	29,666 (34.13)	5,000 (29.82)	5,878 (33.07)	5,595 (34.12)	8,690 (35.27)	2,223 (38.32)	2,280 (41.06)
Sex, n (%)							
Male	37,454 (43.08)	7,118 (42.45)	7,504 (42.22)	6,939 (42.32)	10,838 (43.99)	2,611 (45.01)	2,444 (44.01)
Female	49,477 (56.92)	9,650 (57.55)	10,269 (57.78)	9,457 (57.68)	13,802 (56.01)	3,190 (54.99)	3,109 (55.99)
Region of residence, n (%)							
Urban	68,474 (78.77)	14,058 (79.10)	13,195 (80.48)	19,972 (81.06)	19,972 (81.06)	4,315 (77.71)	5,168 (78.53)
Rural	18,457 (21.23)	3,715 (20.90)	3,201 (19.52)	4,668 (18.94)	1,184 (18.94)	1,238 (22.29)	1,413 (21.47)
BMI groupa, n (%)							
Underweight	3,712 (4.27)	773 (4.61)	811 (4.56)	706 (4.31)	941 (3.82)	240 (4.14)	241 (4.34)
Normal	33,814 (38.90)	6,648 (39.65)	7,181 (40.40)	6,453 (39.36)	9,494 (38.53)	2,033 (35.05)	2,005 (36.11)
Overweight	20,248 (23.29)	4,013 (23.93)	4,133 (23.25)	3,852 (23.49)	5,644 (22.91)	1,326 (22.86)	1,280 (23.05)
Obese	29,157 (33.54)	5,334 (31.81)	5,648 (31.78)	5,385 (32.84)	8,561 (34.74)	2,202 (37.96)	2,027 (36.50)
Educational level, n (%)							
Elementary school or below	17,542 (20.18)	4,486 (26.75)	4,150 (23.35)	3,214 (19.60)	4,103 (16.65)	734 (12.65)	855 (15.40)
Middle school	9,259 (10.65)	1,966 (11.72)	2,035 (11.45)	1,740 (10.61)	2,448 (9.94)	543 (9.36)	527 (9.49)
High school	23,321 (26.83)	4,823 (28.76)	4,937 (27.78)	4,312 (26.30)	6,305 (25.59)	1,487 (25.63)	1,457 (26.24)
College or above	33,444 (38.47)	5,450 (32.50)	6,477 (36.44)	6,076 (37.06)	10,497 (42.60)	2,559 (44.11)	2,385 (42.95)
Unknown	3,365 (3.87)	43 (0.26)	174 (0.98)	1,054 (6.43)	1,287 (5.22)	478 (8.24)	329 (5.92)
Smoking status, n (%)							
Smoker	16,586 (19.08)	3,708 (22.11)	3,609 (20.31)	3,008 (18.35)	4,413 (17.91)	966 (16.65)	882 (15.88)
Former smoker	17,996 (20.70)	3,238 (19.31)	3,581 (20.15)	3,194 (19.48)	5,332 (21.64)	1,333 (22.98)	1,318 (23.73)
Non-smoker	52,349 (60.22)	9,822 (58.58)	10,583 (59.55)	10,194 (62.17)	14,895 (60.45)	3,502 (60.37)	3,353 (60.38)
Alcohol consumption, days/month, n (%)							
0	12,241 (14.08)	2,513 (14.99)	2,696 (15.17)	2,583 (15.75)	3,022 (12.26)	721 (12.43)	706 (12.71)
1-5	56,544 (65.04)	10,652 (63.53)	11,415 (64.23)	10,484 (63.94)	16,254 (65.97)	3,914 (67.47)	3,825 (68.88)
6-30	18,146 (20.87)	3,603 (21.49)	3,662 (20.60)	3,329 (20.30)	5,364 (21.77)	1,166 (20.10)	1,022 (18.40)
Income level, n (%)							
Lowest quartile	17,394 (20.01)	3,578 (21.34)	3,523 (19.82)	3,285 (20.04)	4,823 (19.57)	1,078 (18.58)	1,107 (19.94)
Second quartile	21,673 (24.93)	4,189 (24.98)	4,575 (25.74)	4,137 (25.23)	6,088 (24.71)	1,373 (23.67)	1,311 (23.61)
Third quartile	23,393 (26.91)	4,467 (26.64)	4,814 (27.09)	4,425 (26.99)	6,584 (26.72)	1,602 (27.62)	1,501 (27.03)
Highest quartile	24,471 (28.15)	4,534 (27.04)	4,861 (27.35)	4,549 (27.74)	7,145 (29.00)	1,748 (30.13)	1,634 (29.43)

Table continued

Table I *(Continued)*. General characteristics of Korean adults, in the data obtained from the KNHANES from 2007 to 2021 (n=86,931).

	Total	Pre-pandemic				During the pandemic	
		2007-2009	2010-2012	2013-2015	2016-2019	2020	2021
Weighted value							
Age, y, weighted % (95% CI)							
19-29	18.55 (18.09 to 19.01)	20.35 (19.19 to 21.52)	19.30 (18.21 to 20.39)	18.64 (17.64 to 19.63)	17.63 (16.81 to 18.46)	17.46 (15.86 to 19.07)	17.00 (15.18 to 18.82)
30-39	19.15 (18.65 to 19.64)	22.43 (21.18 to 23.68)	20.71 (19.63 to 21.80)	18.96 (17.86 to 20.07)	17.75 (16.82 to 18.68)	16.62 (14.70 to 18.55)	16.21 (14.52 to 17.91)
40-49	20.82 (20.39 to 21.24)	22.42 (21.38 to 23.46)	21.80 (20.78 to 22.82)	20.82 (19.91 to 21.72)	20.13 (19.34 to 20.92)	19.23 (17.50 to 20.97)	18.92 (17.23 to 20.61)
50-59	18.92 (18.55 to 19.28)	16.43 (15.63 to 17.22)	18.18 (17.37 to 18.99)	19.54 (18.71 to 20.37)	19.92 (19.24 to 20.61)	19.94 (18.53 to 21.34)	19.64 (18.12 to 21.15)
≥60	22.57 (22.08 to 23.06)	18.37 (17.42 to 19.32)	20.01 (19.03 to 20.99)	22.04 (21.01 to 23.07)	24.56 (23.53 to 25.60)	26.74 (24.33 to 29.16)	28.23 (25.84 to 30.61)
Sex, weighted % (95% CI)							
Male	49.48 (49.15 to 49.80)	49.63 (48.90 to 50.36)	49.11 (48.35 to 49.86)	48.93 (48.19 to 49.67)	49.80 (49.19 to 50.42)	49.94 (48.87 to 51.02)	49.89 (48.58 to 51.20)
Female	50.52 (50.20 to 50.85)	50.37 (49.64 to 51.10)	50.89 (50.14 to 51.65)	51.07 (50.33 to 51.81)	50.20 (49.58 to 50.81)	50.06 (48.98 to 51.13)	50.11 (48.80 to 51.42)
Region of residence, weighted % (95% CI)							
Urban	82.82 (81.51 to 84.13)	81.57 (78.52 to 84.63)	80.08 (76.83 to 83.33)	82.65 (79.76 to 85.53)	84.67 (82.22 to 87.12)	84.75 (79.65 to 89.84)	84.06 (79.06 to 89.05)
Rural	17.18 (15.87 to 18.49)	18.43 (15.37 to 21.48)	19.92 (16.67 to 23.17)	17.35 (14.47 to 20.24)	15.33 (12.88 to 17.78)	15.25 (10.16 to 20.35)	15.94 (10.95 to 20.94)
BMI group[a], weighted % (95% CI)							
Underweight	4.52 (4.34 to 4.70)	4.77 (4.35 to 5.18)	4.86 (4.46 to 5.27)	4.78 (4.37 to 5.20)	4.04 (3.73 to 4.36)	4.33 (3.60 to 5.06)	4.40 (3.76 to 5.04)
Normal	38.85 (38.44 to 39.25)	39.73 (38.87 to 40.59)	40.22 (39.25 to 41.20)	39.82 (38.93 to 40.72)	38.52 (37.77 to 39.26)	34.05 (32.51 to 35.60)	36.62 (34.99 to 38.26)
Overweight	22.82 (22.48 to 23.15)	23.78 (23.03 to 24.54)	22.70 (21.95 to 23.46)	22.87 (22.09 to 23.65)	22.49 (21.88 to 23.10)	23.15 (21.97 to 24.34)	21.76 (20.37 to 23.15)
Obese	33.82 (33.41 to 34.23)	31.72 (30.82 to 32.62)	32.21 (31.26 to 33.16)	32.52 (31.64 to 33.41)	34.95 (34.17 to 35.73)	38.47 (36.90 to 40.03)	37.22 (35.43 to 39.00)
Educational level, weighted % (95% CI)							
Elementary school or below	13.64 (13.25 to 14.02)	17.98 (17.00 to 18.96)	16.73 (15.75 to 17.70)	13.64 (12.78 to 14.49)	11.52 (10.81 to 12.22)	8.33 (6.98 to 9.68)	9.48 (7.98 to 10.98)
Middle school	8.82 (8.56 to 9.07)	10.55 (9.91 to 11.18)	10.13 (9.52 to 10.73)	8.59 (8.05 to 9.12)	8.03 (7.56 to 8.51)	7.05 (6.09 to 8.02)	7.03 (6.09 to 7.98)
High school	27.93 (27.46 to 28.40)	31.05 (29.93 to 32.16)	29.97 (28.88 to 31.07)	27.06 (26.03 to 28.10)	25.93 (25.09 to 26.78)	26.57 (24.76 to 28.38)	27.31 (25.48 to 29.13)
College or above	45.42 (44.72 to 46.12)	40.22 (38.62 to 41.82)	42.01 (40.50 to 43.51)	43.72 (42.28 to 45.15)	49.10 (47.68 to 50.51)	50.63 (47.40 to 53.85)	50.96 (47.94 to 53.98)
Unknown	4.20 (3.97 to 4.43)	0.21 (0.13 to 0.29)	1.16 (0.93 to 1.40)	6.99 (6.29 to 7.70)	5.42 (4.95 to 5.90)	7.41 (6.16 to 8.67)	5.22 (4.25 to 6.19)
Smoking status, weighted % (95% CI)							
Smoker	22.97 (22.58 to 23.37)	27.01 (26.14 to 27.87)	26.18 (25.27 to 27.09)	22.26 (21.39 to 23.14)	21.14 (20.38 to 21.89)	19.23 (17.74 to 20.72)	18.41 (16.99 to 19.83)
Former smoker	20.87 (20.56 to 21.19)	19.88 (19.19 to 20.57)	19.57 (18.85 to 20.28)	19.37 (18.66 to 20.08)	21.68 (21.10 to 22.26)	23.65 (22.51 to 24.79)	24.84 (23.52 to 26.16)
Non-smoker	56.16 (55.76 to 56.55)	53.11 (52.26 to 53.96)	54.25 (53.39 to 55.12)	58.37 (57.49 to 59.25)	57.18 (56.43 to 57.93)	57.12 (55.65 to 58.58)	56.75 (55.11 to 58.38)
Alcohol consumption, days/month, weighted % (95% CI)							
0	11.19 (10.90 to 11.48)	11.65 (11.04 to 12.27)	11.86 (11.19 to 12.54)	13.19 (12.45 to 13.92)	9.97 (9.46 to 10.47)	9.39 (8.28 to 10.50)	9.46 (8.38 to 10.55)
1-5	65.99 (65.58 to 66.41)	64.63 (63.67 to 65.59)	64.88 (63.88 to 65.87)	64.53 (63.54 to 65.51)	66.78 (66.03 to 67.52)	68.46 (66.93 to 69.99)	70.62 (69.15 to 72.08)
6-30	22.82 (22.46 to 23.18)	23.72 (22.87 to 24.57)	23.26 (22.42 to 24.09)	22.29 (21.45 to 23.12)	23.26 (22.60 to 23.92)	22.15 (20.81 to 23.49)	19.92 (18.62 to 21.22)
Income level, weighted % (95% CI)							
Lowest quartile	15.71 (15.23 to 16.19)	16.11 (15.03 to 17.18)	16.20 (15.15 to 17.24)	15.85 (14.77 to 16.92)	15.80 (14.84 to 16.76)	14.61 (12.47 to 16.75)	13.88 (11.89 to 15.86)
Second quartile	24.74 (24.18 to 25.29)	24.94 (23.65 to 26.24)	27.23 (25.91 to 28.54)	24.70 (23.44 to 25.97)	24.16 (23.16 to 25.17)	22.10 (19.95 to 24.26)	22.66 (20.57 to 24.75)
Third quartile	29.04 (28.49 to 29.60)	28.76 (27.48 to 30.04)	29.03 (27.82 to 30.24)	29.35 (28.03 to 30.68)	28.67 (27.65 to 29.69)	29.32 (27.20 to 31.43)	30.10 (27.93 to 32.26)
Highest quartile	30.51 (29.74 to 31.28)	30.19 (28.34 to 32.04)	27.54 (26.10 to 28.99)	30.10 (28.38 to 31.81)	31.37 (29.90 to 32.84)	33.97 (30.49 to 37.44)	33.37 (29.62 to 37.12)

BMI, body mass index; CI, confidence interval; KNHANES, Korea National Health and Nutrition Examination Survey. [a]According to the Asian-Pacific guidelines, the BMI is divided into four groups: underweight (<18.5 kg/m^2), normal (18.5-22.9 kg/m^2), overweight (23.0-24.9 kg/m^2), and obese (≥25.0 kg/m^2).

Table II. National trends of the prevalence of hepatitis B and β-coefficients before and during the COVID-19 pandemic, weighted % (95% CI), in the data obtained from the KNHANES.

	Pre-pandemic, weighted % (95% CI)				During the pandemic, weighted % (95% CI)		Trend analysis, β (95% CI)		
	2007-2009	2010-2012	2013-2015	2016-2019	2020	2021	Before pandemic	During pandemic	β difference (during *vs.* before pandemic)
Overall	1.80 (1.54 to 2.07)	1.51 (1.28 to 1.74)	1.25 (1.06 to 1.44)	1.08 (0.94 to 1.23)	1.01 (0.66 to 1.35)	1.39 (1.07 to 1.72)	**-2.398 (-3.332 to -1.463)**	1.558 (-0.228 to 3.344)	**3.956 (1.940 to 5.971)**
Age									
19-29	1.09 (0.59 to 1.58)	0.46 (0.10 to 0.82)	0.31 (0.07 to 0.55)	0.19 (0.01 to 0.37)	0.21 (0.00 to 0.62)	0.38 (0.00 to 0.90)	**-2.850 (-4.483 to -1.217)**	0.935 (-1.814 to 3.684)	**3.785 (0.587 to 6.982)**
30-39	1.68 (1.14 to 2.22)	1.54 (1.02 to 2.05)	1.11 (0.67 to 1.55)	0.84 (0.51 to 1.18)	0.95 (0.04 to 1.86)	0.24 (0.00 to 0.58)	**-2.923 (-4.956 to -0.891)**	**-2.955 (-5.322 to -0.588)**	-0.032 (-3.151 to 3.088)
40-49	1.97 (1.42 to 2.51)	2.14 (1.52 to 2.76)	1.16 (0.74 to 1.57)	1.20 (0.83 to 1.57)	0.68 (0.19 to 1.17)	1.58 (0.69 to 2.46)	**-3.279 (-5.381 to -1.178)**	1.843 (-2.838 to 6.523)	5.122 (-0.009 to 10.252)
50-59	2.77 (2.09 to 3.44)	1.98 (1.42 to 2.54)	2.17 (1.61 to 2.72)	1.49 (1.09 to 1.88)	1.78 (0.81 to 2.74)	2.84 (1.66 to 4.02)	**-3.625 (-6.027 to -1.223)**	**6.766 (0.636 to 12.896)**	**10.391 (3.807 to 16.975)**
≥60	1.67 (1.20 to 2.15)	1.39 (1.06 to 1.72)	1.44 (1.03 to 1.84)	1.48 (1.19 to 1.77)	1.22 (0.66 to 1.78)	1.54 (1.02 to 2.06)	-0.432 (-2.108 to 1.245)	0.380 (-2.698 to 3.459)	0.812 (-2.693 to 4.317)
Sex									
Male	2.35 (1.92 to 2.79)	1.99 (1.59 to 2.39)	1.61 (1.29 to 1.92)	1.45 (1.20 to 1.69)	1.38 (0.87 to 1.88)	2.01 (1.40 to 2.61)	**-3.070 (-4.629 to -1.511)**	2.806 (-0.449 to 6.062)	**5.876 (2.267 to 9.486)**
Female	1.26 (1.00 to 1.52)	1.05 (0.82 to 1.28)	0.91 (0.69 to 1.13)	0.72 (0.57 to 0.88)	0.64 (0.27 to 1.01)	0.79 (0.49 to 1.08)	**-1.743 (-2.686 to -0.800)**	0.310 (-1.341 to 1.962)	**2.053 (0.152 to 3.955)**
Region of residence									
Urban	1.86 (1.56 to 2.17)	1.58 (1.32 to 1.84)	1.27 (1.06 to 1.49)	1.06 (0.90 to 1.21)	1.03 (0.64 to 1.41)	1.48 (1.10 to 1.87)	**-2.713 (-3.773 to -1.653)**	**2.131 (0.088 to 4.174)**	**4.844 (2.542 to 7.145)**
Rural	1.52 (1.05 to 1.99)	1.24 (0.76 to 1.72)	1.14 (0.70 to 1.57)	1.23 (0.87 to 1.59)	0.90 (0.22 to 1.59)	0.93 (0.43 to 1.42)	-0.979 (-2.877 to 0.918)	-1.498 (-4.541 to 1.545)	-0.519 (-4.104 to 3.067)
BMI group[a]									
Underweight	1.42 (0.37 to 2.48)	0.40 (0.06 to 0.74)	0.47 (0.01 to 0.93)	0.77 (0.24 to 1.29)	1.28 (0.00 to 2.86)	1.32 (0.00 to 2.66)	-1.901 (-5.478 to 1.676)	2.753 (-4.461 to 9.967)	4.654 (-2.560 to 11.868)
Normal	1.50 (1.16 to 1.84)	1.50 (1.15 to 1.84)	0.98 (0.72 to 1.24)	0.99 (0.77 to 1.22)	0.72 (0.12 to 1.33)	1.12 (0.59 to 1.65)	**-2.041 (-3.336 to -0.745)**	0.627 (-2.190 to 3.444)	2.668 (-0.149 to 5.485)
Overweight	2.02 (1.46 to 2.58)	1.91 (1.36 to 2.46)	1.70 (1.23 to 2.17)	1.34 (1.01 to 1.67)	1.19 (0.56 to 1.81)	1.94 (1.04 to 2.83)	**-2.247 (-4.309 to -0.185)**	2.957 (-1.836 to 7.750)	**5.204 (0.411 to 9.997)**
Obese	2.07 (1.60 to 2.54)	1.42 (1.05 to 1.79)	1.37 (1.00 to 1.75)	1.06 (0.81 to 1.31)	1.12 (0.61 to 1.63)	1.36 (0.81 to 1.90)	**-3.041 (-4.685 to -1.397)**	1.506 (-1.490 to 4.503)	**4.547 (1.551 to 7.544)**
Educational level									
Middle school or below	1.73 (1.33 to 2.14)	1.20 (0.91 to 1.50)	1.63 (1.19 to 2.07)	1.31 (1.02 to 1.61)	1.29 (0.46 to 2.13)	1.68 (0.81 to 2.56)	-0.858 (-2.473 to 0.758)	1.811 (-2.687 to 6.308)	2.669 (-2.110 to 7.447)
High school or above	1.83 (1.50 to 2.17)	1.65 (1.36 to 1.94)	1.24 (1.01 to 1.47)	1.09 (0.92 to 1.26)	1.05 (0.63 to 1.47)	1.36 (0.99 to 1.74)	**-2.620 (-3.779 to -1.460)**	1.379 (-0.705 to 3.462)	**3.998 (1.614 to 6.382)**
Income level									
Lowest and second quartile	1.61 (1.25 to 1.98)	1.14 (0.87 to 1.41)	1.23 (0.93 to 1.53)	1.09 (0.88 to 1.31)	1.24 (0.52 to 1.96)	1.40 (0.85 to 1.95)	**-1.425 (-2.734 to -0.117)**	1.549 (-1.417 to 4.514)	2.974 (-0.267 to 6.215)
Third and highest quartile	1.93 (1.59 to 2.28)	1.80 (1.46 to 2.13)	1.26 (1.01 to 1.51)	1.08 (0.88 to 1.27)	0.87 (0.49 to 1.25)	1.39 (0.96 to 1.82)	**-3.091 (-4.333 to -1.848)**	1.601 (-0.748 to 3.951)	**4.692 (2.034 to 7.349)**
Drinking status									
Drinker	1.43 (0.87 to 1.99)	0.93 (0.50 to 1.36)	1.37 (0.83 to 1.91)	1.11 (0.72 to 1.50)	1.04 (0.00 to 2.09)	0.61 (0.14 to 1.08)	-0.466 (-2.633 to 1.702)	-2.485 (-5.667 to 0.698)	-2.019 (-5.869 to 1.831)
Non-drinker	1.85 (1.56 to 2.14)	1.59 (1.34 to 1.84)	1.23 (1.02 to 1.44)	1.08 (0.93 to 1.23)	1.00 (0.65 to 1.36)	1.48 (1.11 to 1.84)	**-2.645 (-3.659 to -1.631)**	**1.986 (0.032 to 3.939)**	**4.631 (2.430 to 6.832)**
Smoking status									
Smoker	1.43 (1.13 to 1.72)	1.14 (0.91 to 1.38)	1.08 (0.85 to 1.31)	0.89 (0.72 to 1.06)	0.80 (0.39 to 1.22)	1.04 (0.65 to 1.42)	**-1.666 (-2.713 to -0.620)**	0.747 (-1.323 to 2.816)	**2.413 (0.094 to 4.732)**
Non-smoker	2.22 (1.80 to 2.64)	1.95 (1.54 to 2.35)	1.49 (1.15 to 1.82)	1.35 (1.10 to 1.59)	1.28 (0.72 to 1.84)	1.86 (1.26 to 2.46)	**-3.082 (-4.623 to -1.540)**	2.603 (-0.715 to 5.920)	**5.684 (2.026 to 9.343)**

CI, confidence interval; KNHANES, Korea National Health and Nutrition Examination Survey. Bolded data indicate significant differences in the regression model ($p<0.05$). [a]According to the Asian-Pacific guidelines, the BMI is divided into four groups: underweight (<18.5 kg/m^2), normal (18.5-22.9 kg/m^2), overweight (23.0-24.9 kg/m^2), and obese (≥ 25.0 kg/m^2).

ic, each factor displayed unique trends when assessed by β difference, stratified by factor. Notably, both sex and smoking status revealed discernible β differences regardless of their presence, while other factors delineated variations between distinct groups. When the age was divided by age group, the β difference in the 50-59 years old group was the most prominent at 10.391 (95% CI, 3.807-16.975), and the 18-29 years old group also showed a significant β difference [3.785 (95% CI, 0.587-6.982)]. Pertaining to the region of residence, the rural area showed no significant β difference, but the urban area showed a significant difference with a β difference of 4.844 (95% CI, 2.542-7.145). In addition, with respect to body mass index (BMI), the β differences for the normal and underweight groups were not significant, whereas the overweight and obese groups showed significant β differences (5.204 and 4.547, respectively). When the education level was divided into less than high school graduates and high school graduates or more, a significant β difference was shown in the group of high school graduates or higher [3.998 (95% CI, 1.614-6.382)], and similarly significant β difference was shown in the upper two quartiles of income level [4.692 (95% CI, 2.034-7.349)]. For drinking status, the drinker group did not show a significant difference, while the non-drinker group showed a significant β difference of 4.631 (95% CI, 2.430-6.832).

Unlike hepatitis B, the prevalence of hepatitis C attempts remained stable. In Table III, the exact prevalence was lowest in 2007-2009 [0.14% (95% CI, 0.08-0.20)] and highest in 2021 [0.21% (95% CI, 0.09-0.33)], but there was no significant trend difference in β, -0.002 (95% CI, -0.761 to 0.756). In contrast to hepatitis B, trend analysis showed no significant β difference in all groups, but females showed a β difference value that showed a significant decrease during the pandemic compared to before the pandemic [-0.620 95% CI, -1.233--0.008)]. Conversely, in males, the prevalence rate in 2021 was 0.36% (95% CI, 0.13-0.60), which was the highest over the entire timespan but did not show a significant β difference value [0.618, (95% CI, -0.753-1.990)].

Supplementary Table I presents a comparison of wORs to identify groups that were distinctly influenced by the COVID-19 pandemic. Age was categorized into two groups: those below 60 years and those 60 years and above. The remaining variables were bifurcated in a manner consistent with the prior analysis. When comparing the change in prevalence caused by the COVID-19 pandemic by odds ratio (OR) between groups in the age group divided by age 60, the OR of the group aged 60 years or older compared to the age group under 60 was 1.68 (95% CI, 1.05 to 2.70, $p = 0.030$), which showed a statistically significantly higher OR, which could be interpreted as being more independently affected than the comparison group. For the other factors, there were no items showing statistically significant OR. Utilizing the methodology previously applied for hepatitis B, we assessed group-specific wORs to discern significant prevalence changes in hepatitis C between the pre-pandemic and pandemic. Intriguingly, unlike the results observed for hepatitis B, all subgroups of hepatitis C, inclusive of age, yielded not statistically significant wORs.

Discussion

Findings and Explanation

This research, employing national data gathered from 86,931 Korean adults spanning from 2007 to 2021, sought to analyze the trajectory and associated determinants of the prevalence of hepatitis B and C pre- and during the COVID-19 pandemic. To our knowledge, this study represents a pioneering large-scale, long-term examination into the trends and associated factors for hepatitis B and C before and during the pandemic in South Korea. Throughout the observation, hepatitis B prevalence exhibited a sustained reduction, followed by an elevation concurrent with the advent of the pandemic. These fluctuations were more pronounced in the age group of 60 years or older. In contrast, the prevalence of hepatitis C remained stable across the entire trend, demonstrating no significant fluctuations in rates pre- and during-pandemic.

Comparison of Previous Studies

Several national prevalence studies[24-28] of hepatitis B and C have been conducted in various countries. For instance, studies were carried out in Ethiopia (n=20,622; 2014-2019)[24], Brazil[25] (n=487,180; 2001-2020), China (n=65,175; 2004-2017), Spain (n=868,523; 2000-2015)[26], India (n=30,428; 2005-2007)[27], and Taiwan (n=4,471; 1991-1999)[28]. Moreover, the Global Burden of Disease study estimated the prevalence of hepatitis B from 1990 to 2019[12]. In these studies, hepatitis B and C exhibited varying trends. While hepatitis C generally trended stable or downward, hepatitis B consistently decreased in diverse subgroup eval-

Table III. National trends of the prevalence of hepatitis C and β-coefficients before and during the COVID-19 pandemic, weighted % (95% CI), in the data obtained from the KNHANES.

	Pre-pandemic, weighted % (95% CI)				During the pandemic, weighted % (95% CI)		Trend analysis, β (95% CI)		
	2007-2009	2010-2012	2013-2015	2016-2019	2020	2021	Before pandemic	During pandemic	β difference (during *vs.* before pandemic)
Overall	0.14 (0.08 to 0.20)	0.19 (0.11 to 0.28)	0.19 (0.11 to 0.27)	0.18 (0.13 to 0.24)	0.12 (0.01 to 0.22)	0.21 (0.09 to 0.33)	0.126 (-0.154 to 0.406)	0.124 (-0.581 to 0.829)	-0.002 (-0.761 to 0.756)
Age									
19-29	0.05 (0.00 to 0.16)	0.07 (0.00 to 0.22)	N/A	0.04 (0.00 to 0.11)	N/A	0.17 (0.00 to 0.51)	-0.116 (-0.526 to 0.293)	0.664 (-1.057 to 2.384)	0.780 (-0.988 to 2.549)
30-39	N/A	0.01 (0.00 to 0.03)	0.03 (0.00 to 0.08)	0.08 (0.00 to 0.15)	N/A	0.24 (0.00 to 0.71)	**0.246 (0.012 to 0.480)**	0.799 (-1.566 to 3.165)	0.553 (-1.824 to 2.930)
40-49	0.08 (0.00 to 0.16)	0.26 (0.03 to 0.50)	0.26 (0.05 to 0.47)	0.21 (0.06 to 0.35)	N/A	0.15 (0.00 to 0.45)	0.374 (-0.222 to 0.970)	-0.278 (-1.921 to 1.365)	-0.652 (-2.400 to 1.096)
50-59	0.42 (0.13 to 0.72)	0.26 (0.07 to 0.45)	0.32 (0.07 to 0.57)	0.15 (0.03 to 0.27)	0.37 (0.00 to 0.85)	0.17 (0.00 to 0.42)	-0.757 (-1.715 to 0.201)	0.109 (-1.248 to 1.465)	0.866 (-0.795 to 2.527)
≥60	0.23 (0.10 to 0.36)	0.36 (0.18 to 0.55)	0.32 (0.18 to 0.45)	0.38 (0.22 to 0.53)	0.17 (0.01 to 0.33)	0.28 (0.08 to 0.47)	0.378 (-0.293 to 1.049)	-0.465 (-1.730 to 0.800)	-0.843 (-2.275 to 0.589)
Sex									
Male	0.09 (0.01 to 0.17)	0.17 (0.06 to 0.28)	0.23 (0.11 to 0.35)	0.18 (0.10 to 0.26)	0.04 (0.00 to 0.11)	0.36 (0.13 to 0.60)	0.309 (-0.073 to 0.690)	0.927 (-0.391 to 2.244)	0.618 (-0.753 to 1.990)
Female	0.19 (0.09 to 0.28)	0.22 (0.11 to 0.33)	0.16 (0.07 to 0.25)	0.19 (0.12 to 0.26)	0.19 (0.00 to 0.39)	0.05 (0.00 to 0.11)	-0.054 (-0.439 to 0.332)	**-0.674 (-1.150 to -0.198)**	**-0.620 (-1.233 to -0.008)**
Region of residence									
Urban	0.15 (0.08 to 0.23)	0.18 (0.10 to 0.26)	0.17 (0.08 to 0.26)	0.19 (0.12 to 0.25)	0.14 (0.02 to 0.26)	0.22 (0.08 to 0.36)	0.090 (-0.223 to 0.404)	0.170 (-0.632 to 0.972)	0.080 (-0.781 to 0.941)
Rural	0.08 (0.01 to 0.15)	0.27 (0.00 to 0.56)	0.29 (0.07 to 0.51)	0.18 (0.04 to 0.32)	N/A	0.16 (0.00 to 0.38)	0.327 (-0.279 to 0.933)	-0.109 (-1.399 to 1.181)	-0.436 (-1.861 to 0.989)
BMI group[a]									
Underweight	0.08 (0.00 to 0.23)	0.30 (0.00 to 0.87)	N/A	0.30 (0.00 to 0.68)	N/A	N/A	0.340 (-1.024 to 1.705)	-1.464 (-3.337 to 0.408)	-1.804 (-3.677 to 0.068)
Normal	0.12 (0.03 to 0.21)	0.17 (0.07 to 0.27)	0.19 (0.09 to 0.29)	0.14 (0.07 to 0.22)	0.01 (0.00 to 0.02)	0.06 (0.00 to 0.16)	0.075 (-0.296 to 0.445)	-0.390 (-0.981 to 0.202)	-0.465 (-1.056 to 0.127)
Overweight	0.13 (0.02 to 0.25)	0.26 (0.04 to 0.48)	0.29 (0.10 to 0.49)	0.17 (0.06 to 0.28)	0.05 (0.00 to 0.12)	0.16 (0.00 to 0.34)	0.118 (-0.439 to 0.675)	-0.059 (-1.119 to 1.001)	-0.177 (-1.236 to 0.883)
Obese	0.18 (0.04 to 0.32)	0.16 (0.06 to 0.26)	0.15 (0.00 to 0.31)	0.23 (0.13 to 0.34)	0.27 (0.00 to 0.54)	0.41 (0.11 to 0.71)	0.162 (-0.381 to 0.706)	0.889 (-0.799 to 2.577)	0.727 (-0.961 to 2.415)
Educational level									
Middle school or below	0.31 (0.14 to 0.47)	0.20 (0.06 to 0.34)	0.28 (0.13 to 0.43)	0.41 (0.23 to 0.60)	0.16 (0.00 to 0.33)	0.43 (0.08 to 0.78)	0.356 (-0.413 to 1.125)	0.022 (-1.928 to 1.972)	-0.334 (-2.430 to 1.762)
High school or above	0.07 (0.01 to 0.13)	0.20 (0.09 to 0.30)	0.18 (0.08 to 0.29)	0.14 (0.08 to 0.20)	0.12 (0.00 to 0.25)	0.18 (0.04 to 0.31)	0.164 (-0.119 to 0.447)	0.193 (-0.603 to 0.988)	0.029 (-0.816 to 0.873)
Income level									
Lowest and second quartile	0.19 (0.07 to 0.30)	0.33 (0.16 to 0.51)	0.20 (0.08 to 0.31)	0.24 (0.14 to 0.34)	0.21 (0.00 to 0.47)	0.29 (0.06 to 0.51)	0.007 (-0.490 to 0.505)	0.227 (-0.983 to 1.436)	0.220 (-1.088 to 1.527)
Third and highest quartile	0.11 (0.04 to 0.18)	0.09 (0.03 to 0.15)	0.19 (0.09 to 0.29)	0.15 (0.08 to 0.22)	0.06 (0.00 to 0.14)	0.16 (0.02 to 0.31)	0.219 (-0.094 to 0.533)	0.095 (-0.769 to 0.959)	-0.124 (-1.043 to 0.795)
Drinking status									
Drinker	0.31 (0.07 to 0.54)	0.15 (0.00 to 0.30)	0.45 (0.15 to 0.76)	0.27 (0.10 to 0.44)	0.16 (0.00 to 0.40)	0.15 (0.00 to 0.37)	0.229 (-0.716 to 1.174)	-0.602 (-1.998 to 0.795)	-0.831 (-2.517 to 0.855)
Non-drinker	0.12 (0.05 to 0.18)	0.20 (0.10 to 0.30)	0.15 (0.08 to 0.22)	0.18 (0.12 to 0.24)	0.11 (0.00 to 0.23)	0.22 (0.08 to 0.35)	0.120 (-0.167 to 0.407)	0.203 (-0.561 to 0.967)	0.083 (-0.733 to 0.899)
Smoking status									
Smoker	0.15 (0.07 to 0.24)	0.18 (0.09 to 0.28)	0.17 (0.08 to 0.26)	0.15 (0.09 to 0.21)	0.14 (0.00 to 0.30)	0.12 (0.00 to 0.23)	-0.032 (-0.368 to 0.305)	-0.177 (-0.848 to 0.494)	-0.146 (-0.896 to 0.605)
Non-smoker	0.12 (0.03 to 0.22)	0.21 (0.06 to 0.35)	0.22 (0.10 to 0.35)	0.23 (0.13 to 0.33)	0.09 (0.00 to 0.20)	0.33 (0.09 to 0.57)	0.332 (-0.118 to 0.782)	0.518 (-0.868 to 1.905)	0.186 (-1.219 to 1.591)

CI, confidence interval; KNHANES, Korea National Health and Nutrition Examination Survey. Bolded data indicate significant differences in the regression model ($p<0.05$). [a]According to the Asian-Pacific guidelines, the BMI is divided into four groups: underweight (<18.5 kg/m^2), normal (18.5-22.9 kg/m^2), overweight (23.0-24.9 kg/m^2), and obese (≥25.0 kg/m^2).

uations. Notwithstanding, none of these studies illustrated the trend comparison between before and during the COVID-19 pandemic. Mainly, our research is the first study investigating the long-term trend of hepatitis B and C, including the pandemic. Besides, the data used in previous domestic studies may have demonstrated insufficient results attributable to restricted follow-up durations, limited sample sizes, and potentially flawed study designs, such as the selection of non-representative participants (convenience, purposive, and volunteer samplings).

Plausible Underlying Mechanisms

While the prevalence of hepatitis B found an incrementing trend coinciding with the COVID-19 pandemic, no corresponding shift was observed for hepatitis C. Although both hepatitis B and C share similar transmission routes – primarily through bodily fluids, blood, and sexual contact – their prevalence trends diverged in relation to the pandemic[29]. This is likely attributable to several intertwining factors.

Hepatitis B and C differ fundamentally from COVID-19 in their primary transmission modes, being mainly spread through bodily fluids such as blood-borne, sexual, or vertical routes[10]. Therefore, direct influences from pandemic-induced behavioral changes might be limited. Several factors could explain the resurgence in hepatitis B prevalence. The prioritization of COVID-19 vaccinations might have overshadowed hepatitis B immunization efforts, contributing to an increase in its prevalence[30]. The demands of the pandemic on healthcare systems could have resulted in delayed hepatitis diagnoses and treatments[31]. The postponement of HBV vaccinations for certain individuals could also play a role. While early-stage hepatitis often remains asymptomatic, the compromised immunity associated with SARS-CoV-2 infections might lead to more noticeable symptoms[32]. Additionally, patients seeking treatment for this respiratory infection could discover previously unrecognized early-stage hepatitis B, with a notable uptick among older populations[33]. Pinpointing the precise causes behind these observations remains challenging, and all these explanations require in-depth investigation and rigorous research.

Policy Implications

During the COVID-19 pandemic, heightened awareness of public health and hygiene worldwide led to substantial policy shifts[34]. It was initially presumed that such rigorous public health measures would result in a decline in the prevalence of viral diseases, including hepatitis B and C, in tandem with SARS-CoV-2. Contrary to this assumption, our study's findings indicate an unexpected trend. While global efforts are intensifying to eradicate hepatitis, considering its significant health implications[10,35]. It remains challenging to discern whether there's an actual surge in patient numbers or if previously undetected cases are now being identified, thus emphasizing the need for a nuanced interpretation. Although existing research indicates a decline in other infectious diseases during the pandemic[5-7], the findings of this study should not underestimate the value of the current policies. Instead, they should prompt a reflective reevaluation but rather serve as an opportunity to develop further refinement[36].

Strengths and Limitations

This study provides an in-depth examination, the most extensive to date, of the prevalence of hepatitis B and C, comparing periods before and during the COVID-19 pandemic. Our research boasts comprehensive coverage, encompassing the entire South Korean population without any regional or demographic constraints. The advantage of using long-term prevalence surveys involving a vast number of participants bolsters the reliability of our findings. The overarching goal of this study was to deepen our understanding of disease patterns in the context of global health crises and to solidify its position in the epidemiological field. Nonetheless, certain limitations of our study deserve mention. Hepatitis B and C have a primary transmission mode of vertical transmission, which makes the prevalence in younger groups crucial[37-39]. Our research primarily focuses on adults, mainly due to the lack of sufficient data for children and adolescents. This narrows the overall scope of understanding hepatitis prevalence during the SARS-CoV-2 emergence and the effectiveness of related policies. Relying on self-reported data might introduce specific biases to our research, notably recall and social desirability biases[16]. Besides, a potential limitation is that it may not adequately account for patients who have recovered from chronic infections, possibly leading to a slight overestimation of prevalence rates[38,40]. Particularly for hepatitis C and its treatments with direct-antiviral agents[40]. Furthermore, our decision to exclude serum antigen or antibody tests when measuring prevalence might influence the outcomes. Though we account for various fac-

tors influencing prevalence rates during both before and during the pandemic, drawing definitive causative links still proves to be a complex task.

Conclusions

While the COVID-19 pandemic instigated significant alterations in many domains, no decline was observed in the prevalence of hepatitis B and C in South Korea. Instead, there was an uptick in hepatitis B prevalence. Furthermore, by analyzing the effects of each subgroup, these patterns were markedly evident in individuals aged 60 and above. Although several hypotheses emerge regarding the underlying causes, they necessitate further exploration. Our findings are poised to offer pivotal insights for upcoming health policy deliberations.

Conflict of Interest
The authors declare that they have no conflict of interests.

Ethics Approval
Both the KDCA and Kyung Hee University (KHUH 2022-06-042) institutional review boards approved all procedures involving human subjects.

Informed Consent
All participating individuals provided written informed consent, and their data was kept anonymous.

Funding
The research received funding support from several Korean organizations, including a grant from the National Research Foundation of Korea (NRF; RS-2023-00248157), the Ministry of Food and Drug Safety in 2023 (21153MFDS601), and the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (grant number: HE23C002800). The funders had no role in the study design, data collection, data analysis, data interpretation, or writing of the report.

Authors' Contribution
Dr Dong Keon Yon had full access to all of the data in the study and took responsibility for the integrity of the data and the accuracy of the data analysis. All authors approved the final version before submission. Study concept and design: Junjae Park, Myeongcheol Lee, Hyejun Kim, Jaeyu Park, and Dong Keon Yon; Acquisition, analysis, or interpretation of data: Junjae Park, Myeongcheol Lee, Hyejun Kim, Jaeyu Park, and Dong Keon Yon; Drafting of the manuscript: Junjae Park, Myeongcheol Lee, Hyejun Kim, Jaeyu Park, and Dong Keon Yon; Critical revision of the manuscript for important intellectual content: Junjae Park, Myeongcheol Lee, Hyejun Kim, Jaeyu Park, Hojae Lee, Hyeon Jin Kim, Ai Koyanagi, Lee Smith, Min Seo Kim, Masoud Rahmati, Sang Youl Rhee, Yeonjung Ha, Kwanjoo Lee, and Dong Keon Yon; Statistical analysis: Dong Keon Yon; Study supervision: Dong Keon Yon. Dong Keon Yon is guarantor for this study. Junjae Park, Myeongcheol Lee, Hyejun Kim, and Jaeyu Park contributed equally as co-first authors. Kwanjoo Lee and Dong Keon Yon contributed equally as co-corresponding authors. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Availability of Data and Materials
Data are available on reasonable request. Study protocol and statistical code: available from Prof. Dong Keon Yon (email: yonkkang@gmail.com). Data set: available from the Korean Disease Control and Prevention Agency (KDCA) through a data use agreement.

ORCID ID
Junjae Park: 0009-0001-3466-2614
Myeongcheol Lee: 0009-0006-7185-9471
Hyejun Kim: 0009-0009-1409-6123
Jaeyu Park: 0009-0005-2009-386X
Hojae Lee: 0009-0002-1737-2540
Hyeon Jin Kim: 0000-0003-1286-4669
Ai Koyanagi: 0000-0002-9565-5004
Lee Smith: 0000-0002-5340-9833
Min Seo Kim: 0000-0003-2115-7835
Masoud Rahmati: 0000-0003-4792-027X
Sang Youl Rhee: 0000-0003-0119-5818
Yeonjung Ha: 0000-0002-3594-3688
Kwanjoo Lee: 0000-0002-6178-2400
Dong Keon Yon: 0000-0003-1628-9948.

Reference

1) Kim HJ, Park H, Yon DK, Rahmati M. National trends in influenza vaccination coverage rates in South Korea between 2007-2020, including the COVID-19 pandemic: a longitudinal nationwide serial study. Life Cycle 2023; 3: e9.
2) Hale T, Angrist N, Goldszmidt R, Kira B, Petherick A, Phillips T, Webster S, Cameron-Blake E, Hallas L, Majumdar S, Tatlow H. A global panel database of pandemic policies (Oxford COVID-19 Government Response Tracker). Nat Hum Behav 2021; 5: 529-538.
3) Gok Sargin Z. Awareness of chronic hepatitis C in the Western Black Sea Region. Eur Rev Med Pharmacol Sci 2022; 26: 7827-7832.
4) Aladag H, Aladag M. Is the use of Tenofovir Dipivoxil fumarate effective and safe in preventing vertical transmission in pregnant women with chronic

HBV with high viral load? Eur Rev Med Pharmacol Sci 2023; 27: 2091-2098.

5) Hibiya K, Iwata H, Kinjo T, Shinzato A, Tateyama M, Ueda S, Fujita J. Incidence of common infectious diseases in Japan during the COVID-19 pandemic. PLoS One 2022; 17: e0261332.

6) Olsen SJ, Azziz-Baumgartner E, Budd AP, Brammer L, Sullivan S, Pineda RF, Cohen C, Fry AM. Decreased influenza activity during the COVID-19 pandemic-United States, Australia, Chile, and South Africa, 2020. Am J Transplant 2020; 20: 3681-3685.

7) Johnson KA, Burghardt NO, Tang EC, Long P, Plotzker R, Gilson D, Murphy R, Jacobson K. Measuring the Impact of the COVID-19 Pandemic on Sexually Transmitted Diseases Public Health Surveillance and Program Operations in the State of California. Sex Transm Dis 2021; 48: 606-613.

8) Sheena BS, Hiebert L, Han H, Ippolito H, Abbasi-Kangevari M, Abbasi-Kangevari Z, Abbastabar H, Abdoli A, Abubaker Ali H, Adane MM, Adegboye OA, Adnani QES, Advani SM, Afzal MS, Afzal S, Aghaie Meybodi M, Ahadinezhad B, Ahinkorah BO, Ahmad S, Ahmad T, Ahmadi S, Ahmed H, Ahmed MB, Ahmed Rashid T, Akalu GT, Aklilu A, Akram T, Al Hamad H, Alahdab F, Alem AZ, Alem DT, Alhalaiqa FAN, Alhassan RK, Ali L, Ali MA, Alimohamadi Y, Alipour V, Alkhayyat M, Almustanyir S, Al-Raddadi RM, Altawalah H, Amini S, Amu H, Ancuceanu R, Andrei CL, Andrei T, Anoushiravani A, Ansar A, Anyasodor AE, Arabloo J, Arab-Zozani M, Argaw AM, Argaw ZG, Arshad M, Artamonov AA, Ashraf T, Atlaw D, Ausloos F, Ausloos M, Azadnajafabad S, Azangou-Khyavy M, Azari Jafari A, Azarian G, Bagheri S, Bahadory S, Baig AA, Banach M, Barati N, Barrow A, Batiha A-MM, Bejarano Ramirez DF, Belgaumi UI, Berhie AY, Bhagat DS, Bhardwaj N, Bhardwaj P, Bhattacharyya K, Bhojaraja VS, Bijani A, Biondi A, Bodicha BBA, Bojia HA, Boloor A, Bosetti C, Braithwaite D, Briko NI, Butt ZA, Cámera LA, Chakinala RC, Chakraborty PA, Charan J, Chen S, Choi J-YJ, Choudhari SG, Chowdhury FR, Chu D-T, Chung S-C, Cortesi PA, Cowie BC, Culbreth GT, Dadras O, Dai X, Dandona L, Dandona R, De la Hoz FP, Debela SA, Dedefo MG, Demeke FM, Demie TGG, Demissie GD, Derbew Molla M, Desta AA, Dhamnetiya D, Dhimal ML, Dhimal M, Didehdar M, Doan LP, Dorostkar F, Drake TM, Eghbalian F, Ekholuenetale M, El Sayed I, El Sayed Zaki M, Elhadi M, Elmonem MA, Elsharkawy A, Enany S, Enyew DB, Erkhembayar R, Eskandarieh S, Esmaeilzadeh F, Ezzikouri S, Farrokhpour H, Fetensa G, Fischer F, Foroutan M, Gad MM, Gaidhane AM, Gaidhane S, Galles NC, Gallus S, Gebremeskel TG, Gebreyohannes EA, Ghadiri K, Ghaffari K, Ghafourifard M, Ghamari S-H, Ghashghaee A, Gholami A, Gholizadeh A, Gilani A, Goel A, Golechha M, Goleij P, Golinelli D, Gorini G, Goshu YA, Griswold MG, Gubari MIM, Gupta B, Gupta S, Gupta VB, Gupta VK, Haddadi R, Halwani R, Hamid SS, Hamidi S, Hanif A, Haque S, Harapan H, Hargono A, Hariri S, Hasaballah AI, Hasan SMM, Hassanipour S, Hassankhani H, Hay SI, Hayat K, Heidari G, Herteliu C, Heyi DZ, Hezam K, Holla R, Hosseini M-S, Hosseini M, Hosseinzadeh M, Hostiuc M, Househ M, Huang J, Hussein NR, Iavicoli I, Ibitoye SE, Ilesanmi OS, Ilic IM, Ilic MD, Irham LM, Islam JY, Ismail NE, Jacobsen KH, Jadidi-Niaragh F, Javadi Mamaghani A, Jayaram S, Jayawardena R, Jebai R, Jha RP, Joseph N, Joukar F, Kaambwa B, Kabir A, Kabir Z, Kalhor R, Kandel H, Kanko TKT, Kantar RS, Karaye IM, Kassa BG, Kemp Bohan PM, Keykhaei M, Khader YS, Khajuria H, Khan G, Khan IA, Khan J, Khan MAB, Khanali J, Khater AM, Khatib MN, Khodadost M, Khoja AT, Khosravizadeh O, Khubchandani J, Kim GR, Kim H, Kim MS, Kim YJ, Kocarnik JM, Kolahi AA, Koteeswaran R, Kumar GA, La Vecchia C, Lal DK, Landires I, Lasrado S, Lazarus JV, Ledda C, Lee DW, Lee S-w, Lee YY, Levi M, Li J, Lim SS, Lobo SW, Lopukhov PD, Loureiro JA, MacLachlan JH, Magdy Abd El Razek H, Magdy Abd El Razek M, Majeed A, Makki A, Malekpour M-R, Malekzadeh R, Malik AA, Mansour-Ghanaei F, Mansournia MA, Martins-Melo FR, Matthews PC, Mendoza W, Menezes RG, Meretoja TJ, Mersha AG, Mestrovic T, Miller TR, Minh LHN, Mirica A, Mirmoeeni S, Mirrakhimov EM, Misra S, Mithra P, Moazen B, Mohamadkhani A, Mohammadi M, Mohammed S, Moka N, Mokdad AH, Moludi J, Momtazmanesh S, Monasta L, Moradi G, Moradzadeh M, Moradzadeh R, Moraga P, Mostafavi E, Mubarik S, Muniyandi M, Murray CJL, Naghavi M, Naimzada MD, Narasimha Swamy S, Natto ZS, Nayak BP, Nazari J, Negoi I, Negru SM, Nejadghaderi SA, Neupane Kandel S, Nguyen HLT, Ngwa CH, Niazi RK, Nnaji CA, Noubiap JJ, Nowroozi A, Nuñez-Samudio V, Oancea B, Ochir C, Odukoya OO, Oh I-H, Olagunju AT, Olakunde BO, Omar Bali A, Omer E, Otstavnov SS, Oumer B, Padubidri JR, Pana A, Pandey A, Park E-C, Pashazadeh Kan F, Patel UK, Paudel U, Petcu I-R, Piracha ZZ, Pollok RCG, Postma MJ, Pourshams A, Poustchi H, Rabiee M, Rabiee N, Rafiei A, Rafiei S, Raghuram PM, Rahman M, Rahmani AM, Rahmawaty S, Rajesh A, Ranasinghe P, Rao CR, Rao SJ, Rashidi M, Rashidi M-M, Rawaf DL, Rawaf S, Rawassizadeh R, Rezaei N, Rezapour A, Rezazadeh-Khadem S, Rodriguez JAB, Rwegerera GM, Sabour S, Saddik B, Saeb MR, Saeed U, Sahebkar A, Saif-Ur-Rahman KM, Salahi S, Salimzadeh H, Sampath C, Samy AM, Sanabria J, Sanmarchi F, Santric-Milicevic MM, Sarveazad A, Sathian B, Sawhney M, Seidu A-A, Sepanlou SG, Seylani A, Shahabi S, Shaikh MA, Shaker E, Shakhmardanov MZ, Shannawaz M, Shenoy SM, Shetty JK, Shetty PH, Shibuya K, Shin JI, Shobeiri P, Sibhat MM, Singh AD, Singh JA, Singh S, Skryabin VY, Skryabina AA, Sohrabpour AA, Song S, Tabaeian SP, Tadesse EG, Taheri M, Tampa M, Tan K-K, Tavakoli A, Tbakhi A, Tefera BN, Tehrani-Banihashemi A, Tesfaw HM, Thapar R, Thavamani A, Tohidast SA, Tollosa DN, Tosti ME, Tovani-Palone MR, Traini E, Tran MTN, Trihandini I, Tusa BS, Ullah I, Vacante M, Valadan Tahbaz S,

Valdez PR, Varthya SB, Vo B, Waheed Y, Weldesenbet AB, Woldemariam M, Xu S, Yahyazadeh Jabbari SH, Yaseri M, Yeshaw Y, Yiğit V, Yirdaw BW, Yonemoto N, Yu C, Yunusa I, Zahir M, Zaki L, Zamani M, Zamanian M, Zastrozhin MS, Vos T, Ward JW, Dirac MA. Global, regional, and national burden of hepatitis B, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet Gastroenterol Hepatol 2022; 7: 796-829.

9) Paik JM, Golabi P, Younossi Y, Mishra A, Younossi ZM. Changes in the Global Burden of Chronic Liver Diseases From 2012 to 2017: The Growing Impact of NAFLD. Hepatology 2020; 72: 1605-1616.

10) Sinn DH, Cho EJ, Kim JH, Kim DY, Kim YJ, Choi MS. Current status and strategies for viral hepatitis control in Korea. Clin Mol Hepatol 2017; 23: 189-195.

11) Ozdemir B, Altunsoy A, Akinci E, Guner R. The impacts of the COVID-19 pandemic on patients with viral hepatitis B infection: follow-up, compliance with antiviral treatment, and vaccine preferences. Eur Rev Med Pharmacol Sci 2023; 27: 5310-5317.

12) Collaborators GBDHB. Global, regional, and national burden of hepatitis B, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet Gastroenterol Hepatol 2022; 7: 796-829.

13) Shin DW, Cho J, Park JH, Cho B. National General Health Screening Program in Korea: history, current status, and future direction. Precision and Future Medicine 2022; 6: 9-31.

14) Kweon S, Kim Y, Jang MJ, Kim Y, Kim K, Choi S, Chun C, Khang YH, Oh K. Data resource profile: the Korea National Health and Nutrition Examination Survey (KNHANES). Int J Epidemiol 2014; 43: 69-77.

15) Koh HY, Kim TH, Sheen YH, Lee SW, An J, Kim MA, Han MY, Yon DK. Serum heavy metal levels are associated with asthma, allergic rhinitis, atopic dermatitis, allergic multimorbidity, and airflow obstruction. J Allergy Clin Immunol Pract 2019; 7: 2912-2915.e2912.

16) Oh K, Kim Y, Kweon S, Kim S, Yun S, Park S, Lee YK, Kim Y, Park O, Jeong EK. Korea National Health and Nutrition Examination Survey, 20th anniversary: accomplishments and future directions. Epidemiol Health 2021; 43: e2021025.

17) Kim SY. Nationwide COVID-19 vaccination coverage and COVID-19 incidence in South Korea, January 2022: a national official report. Life Cycle 2022; 2: e2.

18) Eum S, Rhee SY. Age, ethnic, and sex disparity in body mass index and waist circumference: a bi-national large-scale study in South Korea and the United States. Life Cycle 2023; 3: e4.

19) Park S, Kim HJ, Kim S, Rhee SY, Woo HG, Lim H, Cho W, Yon DK. National Trends in Physical Activity Among Adults in South Korea Before and During the COVID-19 Pandemic, 2009-2021. JAMA Netw Open 2023; 6: e2316930.

20) Park S, Yon H, Ban CY, Shin H, Eum S, Lee SW, Shin YH, Shin JU, Koyanagi A, Jacob L, Smith L, Min C, Yeniova A, Kim SY, Lee J, Hadalin V, Kwon R, Koo MJ, Fond G, Boyer L, Kim S, Hahn JW, Kim N, Lefkir E, Bondeville V, Rhee SY, Shin JI, Yon DK, Woo HG. National trends in alcohol and substance use among adolescents from 2005 to 2021: a Korean serial cross-sectional study of one million adolescents. World J Pediatr 2023: 1-11.

21) Lee SW. Methods for testing statistical differences between groups in medical research: statistical standard and guideline of Life Cycle Committee. Life Cycle 2022; 2: e1.

22) Lee SW. Regression analysis for continuous independent variables in medical research: statistical standard and guideline of Life Cycle Committee. Life Cycle 2022; 2: e3.

23) Kim J, Kim SC, Kang D, Kim SY, Kwon R, Yon DK, Kim JG. Feature extraction of time series data on functional near-infrared spectroscopy and comparison of deep learning performance for classifying patients with Alzheimer's-related mild cognitive impairment: a post-hoc analysis of a diagnostic interventional trial. Eur Rev Med Pharmacol Sci 2023; 27: 6824-6830.

24) Legese H, Berhe B, Adhanom G, Kahsay T, Gebrewahd A, Gebremariam G, Mardu F, Tesfay K, Gebremedhin H, Negash H. Trend analysis of hepatitis B and C among patients visiting health facility of Tigrai, Ethiopia, 2014–2019. BMC Gastroenterology 2023; 23: 164.

25) Grandi G, Lopez LF, Burattini MN. Regional differences and temporal trend analysis of Hepatitis B in Brazil. BMC Public Health 2022; 22: 1931.

26) Mate-Cano I, Alvaro-Meca A, Ryan P, Resino S, Briz V. Epidemiological trend of hepatitis C-related liver events in Spain (2000-2015): A nationwide population-based study. Eur J Intern Med 2020; 75: 84-92.

27) Singh K, Bhat S, Shastry S. Trend in seroprevalence of Hepatitis B virus infection among blood donors of coastal Karnataka, India. J Infect Dev Ctries 2009; 3: 376-379.

28) Lin HH, Lin SS, Chiang YM, Wang LY, Huang LC, Huang SC, Liu TT. Trend of hepatitis B virus infection in freshmen classes at two high schools in Hualien, Taiwan from 1991 to 1999. J Med Virol 2002; 67: 472-476.

29) Baseke J, Musenero M, Mayanja-Kizza H. Prevalence of hepatitis B and C and relationship to liver damage in HIV infected patients attending Joint Clinical Research Centre Clinic (JCRC), Kampala, Uganda. Afr Health Sci 2015; 15: 322-327.

30) Yon DK, Ha EK, Lee SY, Kim WK, Park YM, Kim J, Ahn K, Hahm MI, Chae Y, Lee KJ, Kwon HJ, Han MY. Hepatitis B immunogenicity after a primary vaccination course associated with childhood asthma, allergic rhinitis, and allergen sensitization. Pediatr Allergy Immunol 2018; 29: 221-224.

31) Kang E, Yun J, Hwang SH, Lee H, Lee JY. The impact of the COVID-19 pandemic in the health-

care utilization in Korea: Analysis of a nationwide survey. J Infect Public Health 2022; 15: 915-921.

32) Peluso MJ, Donatelli J, Henrich TJ. Long-term immunologic effects of SARS-CoV-2 infection: leveraging translational research methodology to address emerging questions. Transl Res 2022; 241: 1-12.

33) Gallo Marin B, Aghagoli G, Lavine K, Yang L, Siff EJ, Chiang SS, Salazar-Mather TP, Dumenco L, Savaria MC, Aung SN, Flanigan T, Michelow IC. Predictors of COVID-19 severity: A literature review. Rev Med Virol 2021; 31: 1-10.

34) Al-Jaberi TM, Al-Nabulsi AA, Osaili TM, Olaimat AN, Mutlaq S. Food safety knowledge, attitudes, and practices among Jordanian women handling food at home during COVID-19 pandemic. PLoS One 2023; 18: e0288323.

35) Ward JW, Hinman AR. What is needed to eliminate hepatitis B virus and hepatitis C virus as global health threats. Gastroenterology 2019; 156: 297-310.

36) Erismann S, Pesantes MA, Beran D, Leuenberger A, Farnham A, Berger Gonzalez de White M, Labhardt ND, Tediosi F, Akweongo P, Kuwawenaruwa A, Zinsstag J, Brugger F, Somerville C, Wyss K, Prytherch H. How to bring research evidence into policy? Synthesizing strategies of five research projects in low-and middle-income countries. Health Res Policy Syst 2021; 19: 29.

37) El-Shabrawi MHF, Kamal NM, Mogahed EA, Elhusseini MA, Aljabri MF. Perinatal transmission of hepatitis C virus: an update. Arch Med Sci 2020; 16: 1360-1369.

38) Korean Association for the Study of the L. KASL clinical practice guidelines for management of chronic hepatitis B. Clin Mol Hepatol 2019; 25: 93-159.

39) Shen GF, Ge CH, Shen W, Liu YH, Huang XY. Association between hepatitis C infection during pregnancy with maternal and neonatal outcomes: a systematic review and meta-analysis. Eur Rev Med Pharmacol Sci 2023; 27: 3475-3488.

40) Nam JY, Jang ES, Kim YS, Lee YJ, Kim IH, Cho SB, Lee HC, Bae SH, Ki M, Choi HY, Lee EY, Jeong SH. Epidemiological and Clinical Characteristics of Hepatitis C Virus Infection in South Korea from 2007 to 2017: A Prospective Multicenter Cohort Study. Gut Liver 2020; 14: 207-217.