

Clinical audit of quality of care among patients with viral hepatitis in primary care in a low endemic region

Özgür M. Koc^{1,2,3,*}, Bert Vaes⁴, Geert Robaey³, Cristian F. Catalan⁵, Bert Aertgeerts^{4,6}, Frederik Nevens⁷

¹Department of Gastroenterology and Hepatology, Maastricht University Medical Centre, Maastricht, the Netherlands

²School of Nutrition and Translational Research in Metabolism (NUTRIM), University Maastricht, Maastricht, the Netherlands

³Faculty of Medicine and Life Sciences, Hasselt University, Hasselt, Belgium

⁴Department of Public Health and Primary Care, KU Leuven, Leuven, Belgium

⁵Biostatistics and Statistical Bioinformatics Centre (L-BioStat), KU Leuven, Leuven, Belgium

⁶CEBAM, Belgian Centre for Evidence Based Medicine, Leuven, Belgium

⁷Department of Gastroenterology and Hepatology, University Hospitals Leuven, Leuven, Belgium

*Corresponding author: Department of Gastroenterology and Hepatology, Maastricht University Medical Centre, Maastricht, the Netherlands.
Email: o.koc@mumc.nl

Background: The current hepatitis B (HBV) and hepatitis C virus (HCV) screening practices may fail to detect many infected patients who could benefit from new therapeutic agents to limit progression to cirrhosis and hepatocellular carcinoma.

Objectives: This study assessed the test positivity rate and cascade of care of viral hepatitis patients in primary care in a low endemic region as well as the testing policy of abnormal alanine aminotransferase (ALT) level.

Methods: This is a retrospective clinical audit among primary health care practices in Flanders, Belgium, assessing patients with an active medical file between 2019 and 2021.

Results: A total of 84/89 (94.4%) primary health care practices participated representing 621,573 patients of which 1069 patients (0.17%) were registered as having viral hepatitis, not further specified. Detailed information was available from 38 practices representing 243,723/621,573 (39.2%) patients of which 169 (0.07%) were HBsAg positive and 99 (0.04%) anti-HCV positive. A total of 96/134 (71.6%) chronic HBV-infected and 31/77 (40.3%) chronic HCV-infected patients were referred to a hepatologist. A total of 30,573/621,573 (4.9%) patients had an abnormal ALT level, and by at random selection, more detailed information was obtained on 211 patients. Information on high-risk groups was missing in up to 60%. In patients with abnormal ALT level, HBsAg and anti-HCV testing were conducted in 37/211 (17.5%) and 25/211 (11.8%), respectively.

Conclusion: In a low endemic region, the testing rate and cascade of care of HBV and HCV-infected patients can be improved in primary care, especially in high-risk groups and patients with abnormal ALT levels.

Lay summary

Infections with the hepatitis B virus (HBV) and hepatitis C virus (HCV) are a leading cause of death worldwide. Over the last decade, several new therapeutic agents have been developed and can now prevent hepatitis-related deaths. Awareness and increasing testing rates for viral hepatitis in primary care could therefore contribute to control these diseases. The findings of our clinical audit among primary health care practices in Flanders, Belgium demonstrate that screening for HBV and HCV infection can be improved in primary health care in a low endemic region, especially in high-risk groups (e.g. migrants who originate from an endemic country) and patients with abnormal ALT level. The observed suboptimal testing rate in primary health care may be due to a lack of information on risk groups. Future research should focus on interventions to enhance testing, linkage to care, and treatment initiation for HBV and HCV infection among well-defined risk groups in primary health care.

Key words: Belgium, hepatitis B, hepatitis C, liver function tests, prevalence, primary care

Introduction

Over the last decade, several new therapeutic agents have been developed for patients with chronic hepatitis B (HBV), chronic hepatitis C (HCV), and recently also for hepatitis delta virus (HDV).^{1–4} Potent nucleos(t)ide analogue with high barrier to resistance (i.e. entecavir, tenofovir disoproxil, or tenofovir alafenamide) leads to suppression of viral replication and therefore the number of liver decompensation, hepatocellular carcinoma, and liver transplantation due to chronic HBV infection has continuously declined.^{1,2} For

hepatitis C, the discovery of direct antiviral agents has almost completely eradicated the prevalence of this disease in the general population.³ Finally, Bulevirtide, a novel entry inhibitor, was approved by the EU for the treatment of chronic HDV infection.⁴ In addition to preventing disease progression, early diagnosis and antiviral treatment will reduce transmission of these viruses.^{2,5}

It is of utmost importance to screen for HBV and HCV infection. European Centre for Disease Prevention and Control identifies several risk groups for HBV and HCV, such as

Key messages

- New therapeutic agents are available for patients with HBV and HCV infection.
- Current screening practices may fail to detect many infected patients.
- This is a clinical audit among primary health care practices in Belgium.
- The prevalence of HBV and HCV infection in our study was lower than expected.
- Up to 60% of patients had no information on risk factors for HBV/HCV infection.
- Future research should focus on interventions to enhance testing.

migrants who originate from an endemic country, people who have a history of exposure or high-risk behaviours for chronic HBV or HCV infection (i.e. persons who inject drugs).⁶ Chronic viral hepatitis might manifest as abnormal alanine aminotransferase (ALT) level, lab tests which can easily be performed in daily practice. Awareness and increasing testing rates for viral hepatitis in primary care could, therefore, contribute to control these diseases.

In the past, HBV testing rate among migrants was determined to be only 2% in primary health care.⁷ An audit for HCV testing in primary health care in the United Kingdom further identified that only 10% of migrants and 40% of persons who inject drugs were tested.⁸ There was also sub-optimal testing for HBV and HCV among patients with abnormal ALT levels in primary health care: of the patients with two abnormal ALT levels over a period > 6 months, only 6% were tested for HBV and 8% for HCV. This number was 13% and 16% even among patients with more than 5 abnormal ALT levels.⁹

Electronic health records offer an important means for Audit & Feedback, a well-known health care intervention to improve the quality of care.¹⁰ The aim of the clinical audit study was to assess the registration, test positivity rate and cascade of care of chronic HBV and HCV patients in primary health care in Belgium, a low endemic region. We also determined the testing policy for abnormal ALT level. The findings from the study are intended to inform a new strategy to respond to the substantial changes in therapy options for patients with chronic HBV, HCV, and HDV infections from the general practitioner's perspective.

Methods

Study design and patients

This is a retrospective clinical audit of 89 primary health care practices with a general practice internship in Flanders, the northern portion of Belgium. The target study population consisted of patients with an active global medical file between January 2019 and December 2021. This time period was chosen since effective therapy for HBV and HCV was available at that moment.

Clinical audit

The audit consisted of two parts (Fig. 1). In the first part, the number of patients with viral hepatitis and patients with abnormal ALT levels (>40 IU/L) was retrieved. The second part consisted of a detailed analysis of patient characteristics and the cascade of care of all hepatitis B surface antigen (HBsAg) and/or antibodies against hepatitis C virus (anti-HCV)-positive patients.

For the first part, the number of registered viral hepatitis patients were listed by ICPC-2 code D72 (viral hepatitis), and a search string "hepatitis excluding vaccination" was executed on health records among patients without ICPC-2 code D72. Subsequently, we analysed the proportion of patients with a positive test for HBsAg and/or anti-HCV among patients with ICPC-2 code D72 and search string "hepatitis excluding vaccination." Only two tests were being used across the different laboratories in Belgium, i.e. Cobas Roche and Architect Abbott. Positive test was defined as mentioned on medical records or based on laboratory results.

The clinical audit was conducted with the help of Master of Medicine KU Leuven students who were following their general practice internship in the objected primary health care practices. A lecture to final year Master of Medicine KU Leuven students was given by the first and second authors regarding the details of the expected conduct of audit during the general practice internship. The medical students followed a predefined chart review and could consult their supervising general practitioner as well as the investigators for additional questions.

Data collection and definitions

Registration of HBV and HCV infection was assessed as the proportion of patients with an active global medical file between January 2019 and December 2021 and an ICPC-2 code D72 (viral hepatitis). We further analysed patients without an ICPC-2 code D72 but with a mention of "hepatitis" on medical records based on search string. In-depth analysis of (i) patients with ICPC-2 code D72 as well as (ii) patients without an ICPC-2 code D72 but with a mention of "hepatitis" assessed the proportion of patients with a positive test for HBsAg and/or anti-HCV.

Prevalence of viral hepatitis B, C and abnormal ALT level was determined by dividing the number of HBV, HCV infected patients or abnormal ALT level by the number of patients with an active global medical file between 2019 and 2021.

With regards to cascade of care for viral hepatitis B and C, chronic hepatitis B infection was defined as HBsAg positive > 6 months ago and was further classified into hepatitis B e antigen-negative chronic infection (normal ALT level, hepatitis B e antigen negative and HBV DNA < 2000 IU/mL)² which currently requires no antiviral therapy or chronic active hepatitis B (abnormal ALT level or hepatitis B e antigen-positive or HBV DNA > 2000). Chronic hepatitis C infection was defined as anti-HCV and HCV RNA positive independent of ALT levels.¹¹ Within the cascade of care, we assessed the proportion of HBV- or HCV-infected patients referred to a hepatologist and whether antiviral treatment was given.

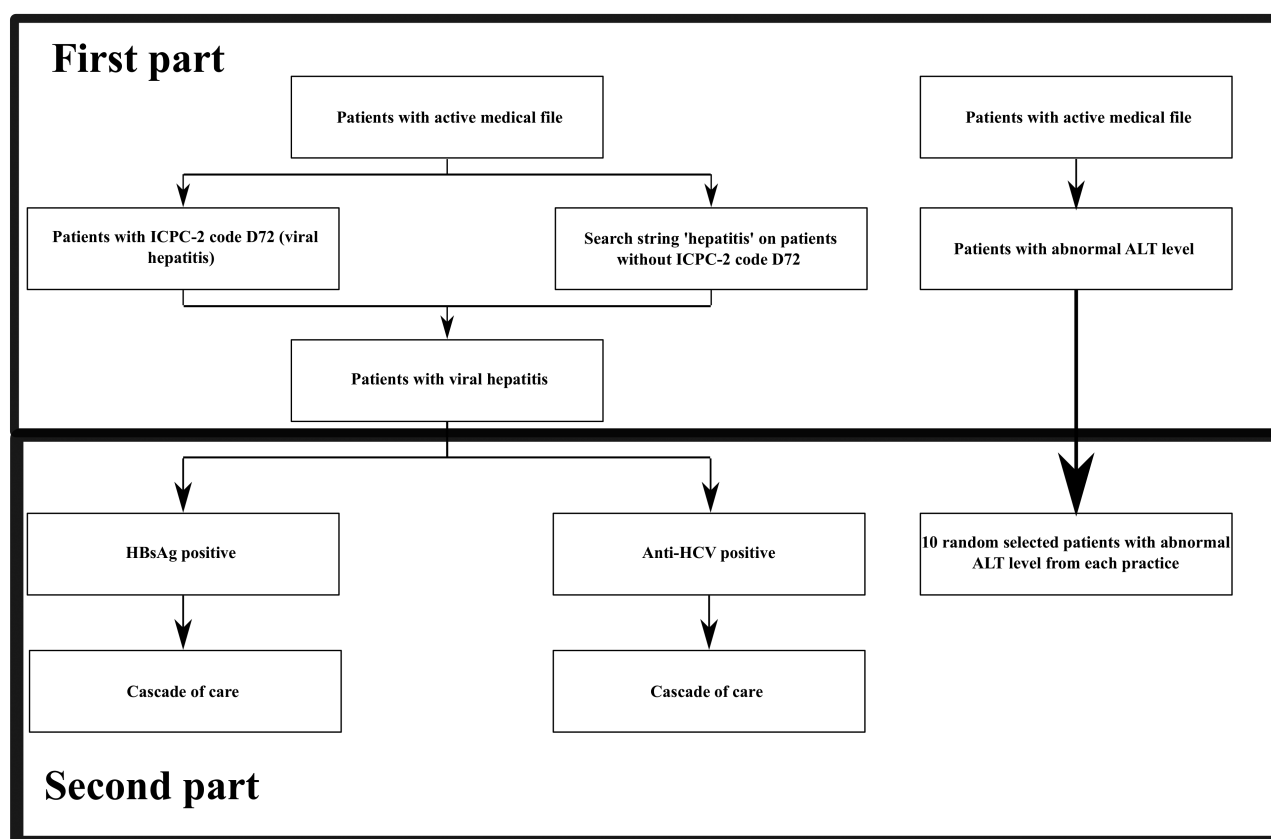


Fig. 1. Clinical audit flowchart. The clinical audit consisted of two parts. In the first part patients with viral hepatitis were extracted from the active medical file by listing patients with ICPC-2 code D72 in addition to a search string “hepatitis” among patients without ICPC-2 code D72. A list was also generated of patients with abnormal ALT levels. In the second part, patients with viral hepatitis were assessed for HBsAg and anti-HCV positive results. The cascade of care was determined for those testing positive. Moreover, ten patients with an ALT level > 40 IU/L were randomly selected for in-depth analysis from each primary health care practice. It was suggested to include every X^{th} patient where X is equal to the total number of patients with abnormal ALT level divided by 10.

Patient characteristics, and high-risk exposures for hepatitis B/C and viral hepatitis B/C risk groups were collected for HBsAg positive, anti-HCV positive patients and for patients with abnormal ALT levels. The following patient characteristics were acquired: birth cohort 1955–1974 as they represent the bulk of HCV epidemic in Europe,¹² sex, alcohol abuse (defined as > 2 units/day for females and > 3 units/day for males),¹³ components of metabolic syndrome¹⁴ and steatosis on ultrasonography.¹⁵ We collected information on high-risk exposures for viral hepatitis B/C^{16,17} such as exposure to infected blood or body fluids, needlestick injuries, non-sterile medical procedure in endemic area (HBsAg or anti-HCV prevalence > 2% in general population), tattoo, piercing, or acupuncture performed in endemic area, and, born to infected mother. Risk groups for viral hepatitis B/C^{6,16,17} were categorized as persons with an occupational risk, traveller to an endemic area, multiple unsafe sexual contacts, men who have sex with men, born in an endemic area, persons with a positive family history for chronic hepatitis/hepatocellular carcinoma and (ex-)drug user (intravenous).

Management of patients with abnormal ALT level was evaluated, such as HBsAg testing, anti-HCV testing, and the strategy to retest abnormal ALT level after 1 month and whether the patients were referred to an hepatologist.

Statistical analysis

Anonymous data analyses were performed using SPSS (IBM Corp. Released 2021. IBM SPSS Statistics for Windows, Version 28.0. Armonk, NY: IBM Corp). Results are presented as frequencies (%). The level of statistical significance was set at $P < 0.05$.

Ethical approval

General practitioners filled in a paper consent form to offer anonymous data. Following Belgian regulation, the need for informed consent from patients was waived seeing the non-interventional character of our study (reference S63674, Ethics Committee Research UZ/KU Leuven).

Results

Prevalence of viral hepatitis and patients with abnormal ALT test

A total of 84/89 (94.4%) primary health care practices responded to our appeal to participate in the study and evaluated a total of 621,573 patients with an active global medical file between 2019 and 2021. Among the study population, 1,069 (0.17%) had an ICPC-2 code of D72 (viral hepatitis). Search string “hepatitis excluding vaccination” illustrated an additional 2,393 (0.38%) with viral hepatitis. Detailed

analysis of patients with ICPC-2 code D72 as well as search string “hepatitis excluding vaccination” showed that there were a total of 696 (0.11%) patients with a positive result for HBsAg and/or anti-HCV.

Although 84/89 practices provided data on viral hepatitis registration, 38/84 (45.2%) practices provided detailed information on the cascade of care, patient characteristics, and management of patients with abnormal ALT levels. Accordingly, in the following sections of the manuscript, we only present the results from the 38 practices with additional data. Out of 38 practices representing a population of 243,723, 169 (0.07%) were HBsAg positive, and 99 (0.04%) were anti-HCV positive (Fig. 2). A total of 30,573/621,573 (4.9%) patients had an abnormal ALT level of which at random detailed information was obtained in 211 patients from 23 practices.

Cascade of care for viral hepatitis

Out of 169 HBsAg-positive patients, 133 (78.6%) were also tested for anti-HCV and 30 (17.8%) for anti-HDV. Hepatitis C co-infection was seen in 7/133 (5.3%), and hepatitis delta co-infection in 2/30 (6.7%). Out of 169 HBsAg-positive patients, 134 (79.3%) patients had chronic HBV; 113 were identified as hepatitis B e antigen-negative chronic infection and 21 as chronic active hepatitis B. A total of 96 (71.6%) were referred to a hepatologist and 12 (9.0%) patients are currently under treatment (Fig. 3).

Out of 99 anti-HCV-positive patients, 88 (88.9%) were tested for HBsAg of which 7/88 (8.0%) had hepatitis B co-infection. Of the patients with anti-HCV positive, 77/99 (77.8%) had chronic hepatitis C infection, and 31/77 (40.3%) patients were referred to a hepatologist. Eighteen (58.1%) out of 31 patients received or are currently under treatment (Fig. 4).

General characteristics of patients with viral hepatitis

Table 1 illustrates demographic characteristics of HBsAg and anti-HCV-positive patients, with an interest on the proportion of unknown information. Out of 169 HBsAg-positive

patients, alcohol abuse was not asked in 80/169 (47.3%) patients and present among 10/89 (11.2%) with known information. Information on obesity was not asked in 36/169 (21.3%) and present among 34/133 (25.6%) patients with known information. Among anti-HCV-positive patients, alcohol abuse was not asked in 33/99 (33.4%) and present in 18/66 (27.3%). These numbers were 22/99 (22.2%) and 17/77 (22.1%) for obesity.

Supplementary File S1 illustrates high-risk exposures and risk groups among HBsAg-positive patients and anti-HCV-positive patients, with a focus on the proportion of unknown information. Among HBsAg-positive patients, information among born to infected mother, multiple unsafe sexual contacts, born in endemic area, and (ex-)drug user were unknown in 125/169 (74.0%), 101/169 (59.7%), 23/169 (13.6%), and 77/169 (45.5%), respectively. These numbers were 62/99 (62.6%), 62/99 (62.6%), 13/99 (30.1%), and 31/99 (31.3%) for anti-HCV positive, respectively.

Assessment of abnormal ALT level

Among patients with abnormal ALT levels ($n = 211$), information on high-risk exposure or risk group was unknown in up to 60% of patients (Table 2).

HBsAg and anti-HCV testing were conducted among 37/211 (17.5%) and 25/211 (11.8%) of these patients with abnormal ALT levels. Abnormal ALT level was retested > 1 month later in 130/211 (61.6%) patients and remained abnormal in 54/130 (41.5%) patients. Among those with continuously abnormal ALT level > 1 month, testing rate for HBsAg and HCV Ab was 13/54 (24.1%) and 10/54 (18.5%), respectively.

Discussion

We found that in this large retrospective clinical audit, the prevalence of HBsAg and anti-HCV positivity in Flanders, the northern portion of Belgium, were only 0.07% and 0.04%. Chronic viral hepatitis may be accompanied by abnormal ALT levels. We demonstrated an abnormal ALT level rate of

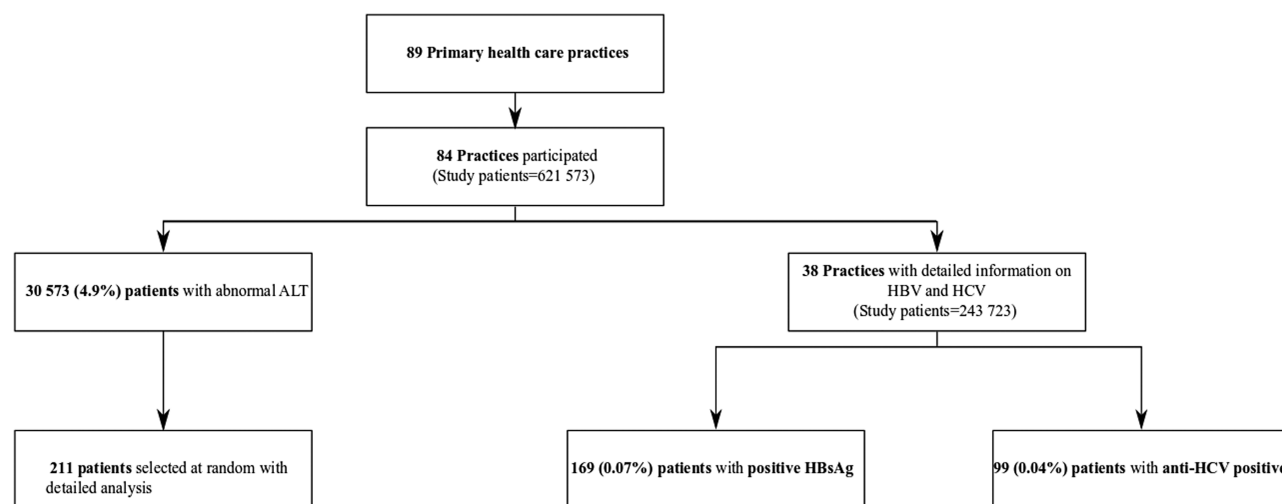


Fig. 2 Study flowchart. A total of 84/89 practices provided data on viral hepatitis registration with a total of 38 practices providing additional information on cascade of care of viral hepatitis, patient characteristics, and management of abnormal ALT level. A total of 211 patients with abnormal ALT levels were selected at random for detailed analysis. Random selection was suggested to include every X^{th} patient where X is equal to the total number of patients with abnormal ALT levels divided by 10.

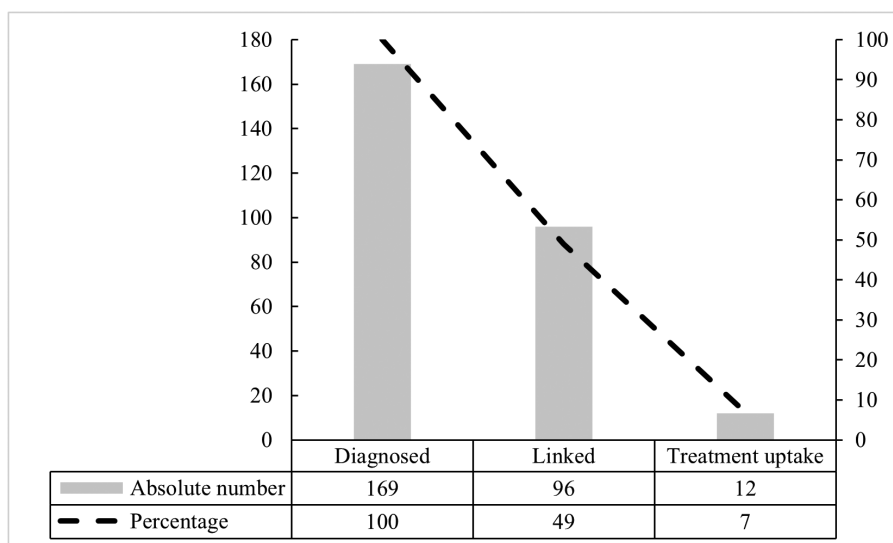


Fig. 3. Hepatitis B cascade of care in the primary health care, Flanders, Belgium.

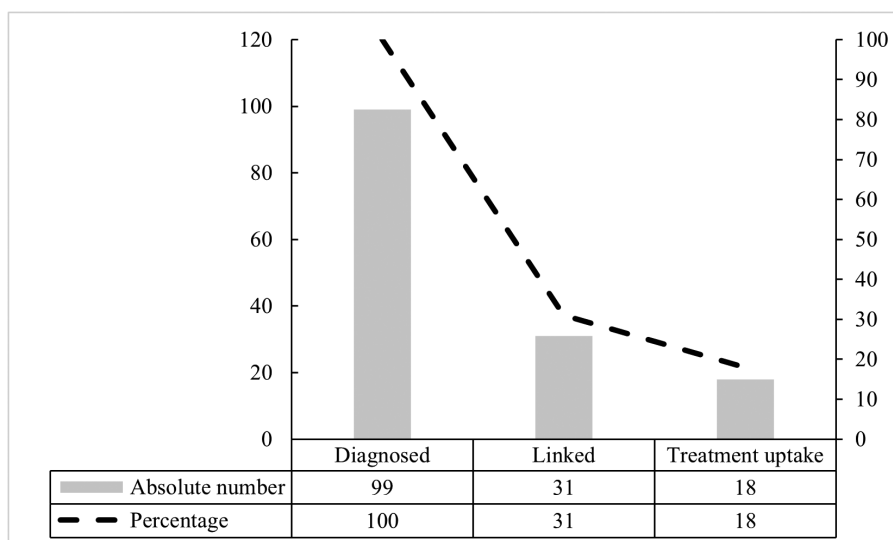


Fig. 4. Hepatitis C cascade of care in the primary health care, Flanders, Belgium.

4.9% with a lack of information on viral hepatitis high-risk exposure or risk group in up to 60% of patients. HBsAg and anti-HCV testing was conducted in respectively 17.5% and 11.8% of this group with abnormal ALT levels.

Belgium is considered a low endemic country for HBV (HBsAg prevalence < 2% in the general population) and HCV (anti-HCV < 2%) with previous studies reporting a prevalence of 0.66–0.97% for HBsAg positivity and 0.12%–1.71% for anti-HCV positivity in the general Flemish population.^{18–23} Our finding of HBsAg positivity (0.07%) is, therefore, 7–10% of the earlier observed prevalence in Belgium, and anti-HCV positivity (0.04%) is 2–33% of the expected prevalence based on previous studies.

These data suggest that current HBsAg and anti-HCV screening practices may fail to detect many infected patients who could benefit from counselling to prevent ongoing transmission and medical management to limit progression to cirrhosis and hepatocellular carcinoma. The disparity between observed and expected prevalence in our study is supported by

previous research conducted among primary care outpatients in Italy, Spain, and the United States.^{24–28} This finding might be explained by under registration and/or underdiagnosis.

Our study is unique as we minimized the impact of under registration as we identified patients without an ICPC2-code D72 (viral hepatitis) by means of search string “hepatitis.” In the collection of data regarding positive HBsAg and/or anti-HCV test, we further included patients with mention on medical records (i.e. digital data from extern) and did not only rely on patients with a positive laboratory result.

Underdiagnosis is one of the largest gaps in the cascade of care of viral hepatitis.²⁹ The World Health Organization’s global hepatitis strategy aims to increase viral hepatitis B and C diagnoses from 30% in 2020 to 90% in 2030.³⁰ Our group previously demonstrated that only 2% of the primary health care population was tested for HBsAg or anti-HCV, which is in line with testing rates of 2–16% in other countries.^{7,24,25,31–33}

The Centers for Disease Control and Prevention recommends screening all adults for HBV and HCV at least once in

Table 1. Demographic characteristics among hepatitis B surface antigen and hepatitis C virus antibody positive patients.

Characteristics	HBsAg positive (<i>n</i> = 169)	Anti-HCV positive (<i>n</i> = 99)
^a Birth cohort 1955–1974		
Yes	69 (40.8%)	50 (50.5%)
No	100 (59.2%)	49 (49.5%)
Unknown	0 (0.0%)	0 (0.0%)
Males		
Yes	92 (54.4%)	50 (50.5%)
No	77 (45.6%)	49 (49.5%)
Unknown	0 (0.0%)	0 (0.0%)
^b Alcohol abuse		
Yes	10 (5.9%)	18 (18.2%)
No	79 (46.7%)	48 (48.4%)
Unknown	80 (47.4%)	33 (33.4%)
^c Overweight		
Yes	75 (44.4%)	39 (39.4%)
No	58 (34.3%)	39 (39.4%)
Unknown	36 (21.3%)	21 (21.2%)
^d Obesity		
Yes	34 (20.1%)	17 (17.2%)
No	99 (58.6%)	60 (60.6%)
Unknown	36 (21.3%)	22 (22.2%)
Waist circumference > 94/≥80 cm for men/women		
Yes	12 (7.1%)	5 (5.1%)
No	21 (12.4%)	11 (11.1%)
Unknown	136 (80.4%)	83 (83.8%)
Arterial pressure > 130/85 mmHg or treated for hypertension		
Yes	57 (33.7%)	42 (42.4%)
No	103 (61.0%)	52 (52.5%)
Unknown	9 (5.3%)	5 (5.1%)
Fasting glucose > 100 mg/dl (5.6 mmol/L) or treated for T2DM		
Yes	40 (23.7%)	24 (24.2%)
No	107 (63.3%)	61 (61.6%)
Unknown	22 (13.0%)	14 (14.2%)
Serum triglycerides > 150 mg/dl (>1.7 mmol/L)		
Yes	28 (16.6%)	15 (15.2%)
No	86 (50.9%)	60 (60.6%)
Unknown	55 (32.5%)	24 (24.2%)
HDL cholesterol < 40/50 mg/dl for men/women (<1.0/<1.3 mmol/L)		
Yes	25 (14.8%)	17 (17.2%)
No	87 (51.5%)	59 (59.6%)
Unknown	57 (33.7%)	23 (23.2%)
Steatosis on ultrasonography		
Yes	28 (16.6%)	23 (23.2%)
No	71 (42.0%)	35 (35.4%)
Unknown	70 (41.4%)	41 (41.4%)

Results are presented as frequencies (percentage).

^aBirth cohort 1955–1974 as they represent the bulk of HCV epidemic in Europe.

^bAlcohol abuse is defined as > 2 units/day for females and > 3 units/day for males.

^cOverweight was specified as body mass index > 25 kg/m².

^dObesity was specified as body mass index > 30 kg/m².

Table 2. High-risk exposure and risk groups for hepatitis B and C among patients with abnormal ALT level.

Characteristics	Abnormal ALT level (<i>n</i> = 211)
Exposure to infected blood or body fluids	
Yes	4 (1.9%)
No	87 (41.2%)
Unknown	120 (56.9%)
Needlestick injuries	
Yes	2 (0.9%)
No	90 (42.7%)
Unknown	119 (56.4%)
^a Non-sterile medical procedure in endemic area	
Yes	0 (0.0%)
No	110 (52.1%)
Unknown	101 (47.9%)
^a Tattoo, piercing, or acupuncture performed in endemic area	
Yes	1 (0.5%)
No	90 (42.7%)
Unknown	120 (56.9%)
Born to infected mother	
Yes	0 (0.0%)
No	82 (38.9%)
Unknown	129 (61.1%)
Persons with occupational risk	
Yes	4 (1.9%)
No	131 (62.1%)
Unknown	76 (36.0%)
^a Traveler to an endemic area	
Yes	22 (10.4%)
No	57 (27.0%)
Unknown	132 (62.6%)
Multiple unsafe sexual contacts	
Yes	5 (2.4%)
No	86 (40.8%)
Unknown	120 (56.9%)
Men who have sex with men	
Yes	2 (0.9%)
No	134 (63.5%)
Unknown	75 (35.5%)
^a Born in an endemic area	
Yes	30 (14.2%)
No	143 (67.8%)
Unknown	38 (18.0%)
Persons with a positive family history for chronic hepatitis/hepatocellular carcinoma	
Yes	2 (0.9%)
No	86 (40.8%)
Unknown	123 (58.3%)
(Ex-)drug user (intravenous)	
Yes	2 (0.9%)
No	123 (58.3%)
Unknown	86 (40.8%)

Results are presented as frequencies (percentage).

^aEndemic area was defined as HBsAg or anti-HCV prevalence > 2% in general population.

their lifetime, considering the new therapeutic options as well as suboptimal results of risk-based screening.^{34,35} However, the World Health Organization advises risk-based screening in regions with a low prevalence of HBV and HCV infection.³⁶ The European Association for the Study of the Liver recommends regional or national screening approaches based on the local epidemiology.⁵ Considering the low prevalence of HBV and HCV infection in Belgium, screening of the general population is not deemed cost-effective.³⁷ Screening should, therefore, focus on well-defined risk groups for HBV and HCV infection, such as migrants and (ex-)drug users (intravenous). However, screening of HBV and HCV based on the presence of risk factors is currently unsuccessful since clinicians might lack the knowledge and/or time to question patients' risk factors. In that respect, our current study emphasized that information on high-risk exposure for HBV/HCV and risk groups was unknown in up to 60% with abnormal ALT value. Accordingly, there is increasing interest in methods for enhancing risk-based screening. Research indicates that offering general practitioners educational material and sessions would increase HBV and HCV testing.^{38,39} Electronic medical record reminders for HBV and HCV testing might further remove barriers from competing medical priorities and an outdated knowledge of testing guidelines.^{40,41} Since general practitioners are tasked with caring for a diverse range of populations in diverse settings, additional support for HBV and HCV care has the potential to improve the cascade of care.^{7,41}

Since elevated ALT levels might suggest the presence of viral hepatitis, HBV and HCV should be considered in all patients with abnormal ALT levels. Although the proposed ALT upper limit of normal varies across studies, we have chosen 40 IU/L as cut off for males and females; as a result, above this value is undisputedly considered as abnormal.⁴²⁻⁴⁵ Guidelines also disagree on the necessity of routine repeat ALT testing on the belief that test abnormalities may be transient.^{46,47} The BALLETS study demonstrated that 84% of adults still had abnormal tests when repeated one month later, and accordingly, the whole cost of repeating blood tests must be borne in mind and might only be justified where there is a high degree of certainty that the abnormality will resolve in response to an identified acute insult.⁴⁸ The prevalence of an abnormal ALT value in our study was around 5%; HBsAg and anti-HCV testing were conducted in respectively 17.5% and 11.8%. Among those with continuously abnormal ALT levels > 1 month, the testing rate for HBsAg and HCV Ab was still 24.1% and 18.5%, respectively.

This study has several limitations. First, the inclusion of only volunteer primary health care practices may represent a selection bias. Although 84/89 practices provided registration data on viral hepatitis, only 38/84 practices provided additional data on cascade of care, patient characteristics and management of abnormal ALT level. Second, the primary health care practices were all from the Flemish region, the northern portion of Belgium, and are therefore not representative of across Belgium. Third, as we only collected demographics, high-risk exposures for HBV/HCV, and risk groups from the HBsAg and/or anti-HCV positive population and not from the total study population, we could not assess risk factors for HBV or HCV infection. Nonetheless, 64% of our HBsAg population was born in the intermediate or high endemic country, a well-known risk group for HBV infection.⁴⁹ Moreover, 51% of the anti-HCV positive population consisted of the birth cohort

Table 2. Continued

1955–1974 as they represent the bulk of HCV epidemic in Europe.¹²

In conclusion, our findings demonstrate that screening for HBV and HCV infection can be improved in primary health care in a low-endemic region, especially in high-risk groups and patients with abnormal ALT levels. The observed sub-optimal testing rate in primary health care may be due to a lack of information on high-risk exposures for HBV/HCV and risk groups. Persons who are unaware of their status cannot benefit from the newly developed therapeutic agents patients with chronic HBV infection, chronic HCV infection, and for HDV. The current results should be further discussed with general practitioners with the focus on interventions (i.e. electronic medical record reminders) to enhance testing, linkage to care, and treatment initiation for HBV and HCV infection among well-defined risk groups.

Acknowledgements

We would like to acknowledge the general practitioners and the students in the masters's programme of medicine KU Leuven for collecting study data.

Supplementary material

Supplementary material is available at *Family Practice* online.

Author contributions

Ö.K., B.V., G.R., C.C., B.A., and F.N. contributed to the conception and design of the study. B.V., B.A., and F.N. supervised Ö.K. to collect data. Following statistical analysis of data by Ö.K. and C.C., Ö.K. drafted the first version of the paper, the co-authors critically revised the article and approved the final version to be submitted, including the authorship list.

Funding

This study was sponsored by Gilead Sciences. The funders had no role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Conflict of interest

Ö.K., B.V., G.R., C.C., B.A., and F.N. report no conflict of interest.

Data availability

Proposals should be directed to the corresponding author; to gain access, data requestors will need to sign a data access agreement. Only individual participant data that underlie the results reported in this article, after de-identification, will be shared.

References

1. Nguyen MH, Yang HI, Le A, Henry L, Nguyen N, Lee MH, Zhang J, Wong C, Wong C, Trinh H. Reduced incidence of hepatocellular carcinoma in cirrhotic and noncirrhotic patients with chronic hepatitis B treated with tenofovir-A propensity score-matched study. *J Infect Dis.* 2019;219(1):10–18.

2. European Association for the Study of the Liver. EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection. *J Hepatol*. 2017;67(2):370–398.
3. Asselah T, Marcellin P, Schinazi RF. Treatment of hepatitis C virus infection with direct-acting antiviral agents: 100% cure? *Liver Int*. 2018;38(Suppl 1):7–13.
4. Lampertico P, Roulot D, Wedemeyer H. Bulevirtide with or without pegIFN α for patients with compensated chronic hepatitis delta: from clinical trials to real-world studies. *J Hepatol*. 2022;77(5):1422–1430.
5. European Association for the Study of the Liver. Electronic address eee, European Association for the Study of the L. EASL Recommendations on Treatment of Hepatitis C 2018. *J Hepatol*. 2018;69(2):461–511.
6. European Centre for Disease Prevention and Control. *Public health guidance on HIV, hepatitis B and C testing in the EU/EEA – An integrated approach*. Stockholm: ECDC; 2018.
7. Flanagan S, Kunkel J, Appleby V, Eldridge SE, Ismail S, Moreea S, Griffiths C, Walton R, Pitt M, Salmon A, et al. Case finding and therapy for chronic viral hepatitis in primary care (HepFREE): a cluster-randomised controlled trial. *Lancet Gastroenterol Hepatol*. 2019;4(1):32–44.
8. Datta S, Horwood J, Hickman M, Sharp D. Case-finding for hepatitis C in primary care: a mixed-methods service evaluation. *Br J Gen Pract*. 2014;64(619):e67–e74.
9. Bielen R, Koc ÖM, Busschots D, Robaey G, Aertgeerts B, Vaes B, Mamouris P, Mathei C, Goderis G, Nevens F. Assessing testing rates for viral hepatitis B and C by general practitioners in Flanders, Belgium: a registry-based study. *BMJ Open*. 2019;9(5):e026464.
10. Van Den Bulck S, Spitaels D, Vaes B, Goderis G, Hermens R, Vankrunkelsven P. The effect of electronic audits and feedback in primary care and factors that contribute to their effectiveness: a systematic review. *Int J Qual Health Care*. 2020;32(10):708–720.
11. Isfordink CJ, van Dijk M, Brakenhoff SM, Kracht PAM, Arends JE, de Knecht RJ, van der Valk M, Drenth JPH; CELINE Study Group. Hepatitis C Elimination in the Netherlands (CELINE): how nationwide retrieval of lost to follow-up hepatitis C patients contributes to micro-elimination. *Eur J Intern Med*. 2022;101:93–97.
12. Bielen R, Kremer C, Koc Ö M, Busschots D, Hendrickx DM, Vandeloren P, Hens N, Nevens F, Robaey G. Screening for hepatitis C at the emergency department: Should babyboomers also be screened in Belgium? *Liver Int*. 2019;39(4):667–675.
13. European Association for the Study of the Liver. EASL Clinical Practice Guidelines: Management of alcohol-related liver disease. *J Hepatol*. 2018;69(1):154–181.
14. European Association for the Study of the Liver (EASL); European Association for the Study of Diabetes (EASD); European Association for the Study of Obesity (EASO). EASL-EASD-EASO Clinical Practice Guidelines for the management of non-alcoholic fatty liver disease. *J Hepatol*. 2016;64(6):1388–1402.
15. Koc O, Van Damme P, Busschots D, Bielen R, Forier A, Nevens F, Robaey G. Acute hepatitis B notification rates in Flanders, Belgium, 2009 to 2017. *Euro Surveill*. 2019;24(30):1900064.
16. World Health Organization. *Hepatitis B*. Geneva, Switzerland: World Health Organization; 2022 [accessed 2022 November 11]. <https://www.who.int/news-room/fact-sheets/detail/hepatitis-b>.
17. World Health Organization. *Hepatitis C*. Geneva, Switzerland: World Health Organization; 2022 [accessed 2022 November 11]. <https://www.who.int/news-room/fact-sheets/detail/hepatitis-b>.
18. Quoilin S, Hutse V, Vandenberghe H, Claeys F, Verhaegen E, De Cock L, Van Loock F, Top G, Van Damme P, Vranckx R, et al. A population-based prevalence study of hepatitis A, B and C virus using oral fluid in Flanders, Belgium. *Eur J Epidemiol*. 2007;22(3):195–202.
19. Koc Ö M, Kremer C, Bielen R, Buschots D, Hens N, Nevens F, et al. Prevalence and risk factors of hepatitis B virus infection in Middle-Limburg Belgium, year 2017: importance of migration. *J Med Virol*. 2019;91(8):1479–1488.
20. Beutels M, Van Damme P, Aelvoet W, Desmyter J, Dondeyne E, Goilav C, Mak R, Muylle L, Pierard D, Stroobant A, et al. Prevalence of hepatitis A, B and C in the Flemish population. *Eur J Epidemiol*. 1997;13(3):275–280.
21. Botterman R, Verhelst X, Buffel V, Derese A, Van Der Paelt T, De Volder G, Van Vlierberghe H, Boeckxstaens P. Hepatitis C in two general practices in Flanders, Belgium: is there a need to reconsider current screening recommendations? *Acta Clin Belg*. 2021;76(6):462–469.
22. Litzroth A, Suin V, Wyndham-Thomas C, Quoilin S, Muyldermans G, Vanwolleghem T, Kabamba-Mukadi B, Verburgh V, Jacques M, Van Gucht S, et al. Low hepatitis C prevalence in Belgium: implications for treatment reimbursement and scale up. *BMC public health*. 2019;19(1):39.
23. Verhelst X, Devolder G, De Wilde M, Goderis L, De Bel A, Spillebeen E, Geerts A, Derese A, Van Vlierberghe H. Screening for hepatitis C viral infection in a non-urban primary care facility in Flanders. *Acta Gastroenterol Belg*. 2019;82(1):99–100.
24. Smith BD, Yartel AK, Krauskopf K, Massoud OI, Brown KA, Fallon MB, Rein DB. Hepatitis C virus antibody positivity and predictors among previously undiagnosed adult primary care outpatients: cross-sectional analysis of a multisite retrospective cohort study. *Clin Infect Dis*. 2015;60(8):1145–1152.
25. Roblin DW, Smith BD, Weinbaum CM, Sabin ME. HCV screening practices and prevalence in an MCO, 2000–2007. *Am J Manag Care*. 2011;17(8):548–555.
26. Citarella A, Cammarota S, Bernardi FF, Coppola C, D'Antò M, Fogliasecca M, Giusto E, Masarone M, Salomone Megna A, Sellitto C, et al. Screening, linkage to care and treatment of hepatitis C infection in primary care setting in the South of Italy. *Life (Basel)*. 2020;10(12):359.
27. Andriulli A, Stroffolini T, Mariano A, Valvano MR, Grattagliano I, Ippolito AM, Grossi A, Brancaccio G, Coco C, Russello M, et al. Declining prevalence and increasing awareness of HCV infection in Italy: a population-based survey in five metropolitan areas. *Eur J Intern Med*. 2018;53:79–84.
28. Reyes-Urueña J, Celly A, Moreno S, Majó X, Colom J, Casabona J. Hepatitis C virus: testing rate and attrition at linkage to specialized care, Catalonia, Spain 2011–2016. *J Viral Hepat*. 2021;28(2):288–299.
29. Terrault NA. Hepatitis C elimination: challenges with under-diagnosis and under-treatment. *F1000Res*. 2019;8(14):54.
30. Cox AL, El-Sayed MH, Kao JH, Lazarus JV, Lemoine M, Lok AS, Zoulim F. Progress towards elimination goals for viral hepatitis. *Nat Rev Gastroenterol Hepatol*. 2020;17(9):533–542.
31. Bielen R, Koc OM, Busschots D, Robaey G, Aertgeerts B, Vaes B, Mamouris P, Mathei C, Goderis G, Nevens F. Assessing testing rates for viral hepatitis B and C by general practitioners in Flanders, Belgium: a registry-based study. *BMJ Open*. 2019;9(5):e026464.
32. Linas BP, Hu H, Barter DM, Horberg M. Hepatitis C screening trends in a large integrated health system. *Am J Med*. 2014;127(5):398–405.
33. MacLean CD, Berger C, Cangiano ML, Ziegelman D, Lidofsky SD. Impact of electronic reminder systems on hepatitis C screening in primary care. *J Viral Hepat*. 2018;25(8):939–944.
34. So S, Terrault N, Connors EE. Universal adult hepatitis B screening and vaccination as the path to elimination. *JAMA*. 2023;329(19):1639–1640.
35. Havens PL, Anderson JR. Updated CDC recommendations for universal hepatitis C virus screening among adults and pregnant women: implications for clinical practice. *JAMA*. 2020;323(22):2258–2259.
36. World Health Organization. *Guidelines on hepatitis B and C testing*. Geneva, Switzerland: World Health Organization; February 2017. <https://apps.who.int/iris/bitstream/handle/10665/254621/9789241549981-eng.pdf?sequence=1> (24 March 2021, date last accessed).
37. Hahné SJ, Veldhuijzen IK, Wiessing L, Lim TA, Salminen M, Laar M. Infection with hepatitis B and C virus in Europe: a systematic

- review of prevalence and cost-effectiveness of screening. *BMC Infect Dis.* 2013;13(18):181.
38. Helsper CW, van Essen GA, Bonten MJ, de Wit NJ. A support programme for primary care leads to substantial improvements in the effectiveness of a public hepatitis C campaign. *Fam Pract.* 2010;27(3):328–332.
 39. Richmond JA, Sasadeusz J, Temple-Smith M. The Role of Primary Health Care in Hepatitis B Testing and Management: A Case Study. *J Community Health.* 2018;43(1):38–47.
 40. Haridy J, Iyngkaran G, Nicoll A, Hebbard G, Tse E, Fazio T. eHealth technologies for screening, diagnosis, and management of viral hepatitis: a systematic review. *Clin Gastroenterol Hepatol.* 2021;19(6):1139–1150.e30.
 41. Cunningham EB, Wheeler A, Hajarizadeh B, French CE, Roche R, Marshall AD, Fontaine G, Conway A, Valencia BM, Bajis S, *et al.* Interventions to enhance testing, linkage to care, and treatment initiation for hepatitis C virus infection: a systematic review and meta-analysis. *Lancet Gastroenterol Hepatol.* 2022;7(5):426–445.
 42. Neuschwander-Tetri BA, Unalp A, Creer MH; Nonalcoholic Steatohepatitis Clinical Research Network. Influence of local reference populations on upper limits of normal for serum alanine aminotransferase levels. *Arch Intern Med.* 2008;168(6):663–666.
 43. Prati D, Taioli E, Zanella A, Della Torre E, Butelli S, Del Vecchio E, Vianello L, Zanuso F, Mozzi F, Milani S, *et al.* Updated definitions of healthy ranges for serum alanine aminotransferase levels. *Ann Intern Med.* 2002;137(1):1–10.
 44. Lee JK, Shim JH, Lee HC, Lee SH, Kim KM, Lim YS, Chung Y-H, Lee YS, Suh DJ. Estimation of the healthy upper limits for serum alanine aminotransferase in Asian populations with normal liver histology. *Hepatology.* 2010;51(5):1577–1583.
 45. Wright C, Rivera JC, Baetz JH. Liver function testing in a working population: three strategies to reduce false-positive results. *J Occup Med.* 1988;30(9):693–697.
 46. Kwo PY, Cohen SM, Lim JK. ACG Clinical Guideline: evaluation of abnormal liver chemistries. *Am J Gastroenterol.* 2017;112(1):18–35.
 47. Newsome PN, Cramb R, Davison SM, Dillon JF, Foulerton M, Godfrey EM, Hall R, Harrower U, Hudson M, Langford A, *et al.* Guidelines on the management of abnormal liver blood tests. *Gut.* 2018;67(1):6–19.
 48. Lilford RJ, Bentham L, Girling A, Litchfield I, Lancashire R, Armstrong D, Jones R, Marteau T, Neuberger J, Gill P, *et al.* Birmingham and Lambeth Liver Evaluation Testing Strategies (BALLETS): a prospective cohort study. *Health Technol Assess.* 2013;17(28):i-xiv, 1–307.
 49. Koc ÖM, Kremer C, Hens N, Bielen R, Busschots D, Van Damme P, Robaey G. Early detection of chronic hepatitis B and risk factor assessment in Turkish migrants, Middle Limburg, Belgium. *PLoS One.* 2020;15(7):e0234740.