

Universal screening for viral hepatitis in all inpatients of a university internal medicine department

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Abstract

Background The global medical community has set a goal of reducing the prevalence of viral hepatitis by 2030, focusing on screening large segments of the population who are unaware of being infected. This study aimed to investigate the efficacy of screening hospitalized patients for viral hepatitis.

Method All patients hospitalized in an internal medicine department between January 2021 and September 2023 underwent screening for hepatitis B and C (HBV/C).

Results A total of 3914 patients were screened (mean age 69.8 ± 16.9 years). A total of 112 (2.9%) patients had positive surface antigen, and 1281 (32.8%) patients had evidence of prior HBV infection (anti-HBc+), of whom the majority (952, 74.4%) also had concurrent positive anti-HBs antibodies. HBV DNA testing was performed in 65 patients (58%), with 60 patients (92.3%) showing detectable HBV DNA levels. Of these, 13 had chronic HBV infection, and 47 had chronic HBV hepatitis. Finally, 28 patients (71.8% of eligible patients) received treatment. During screening for HCV, 102 patients (2.7%) were anti-HCV(+), and 53 patients (52%) underwent HCV RNA testing. Twenty-nine patients showed detectable HCV RNA levels (54.7%), with 13 patients eventually receiving treatment (52% of eligible patients).

Conclusions Screening for viral hepatitis can be easily and effectively performed in hospitalized patients. However, significant care should be taken to ensure that all patients undergo the entire screening process and receive treatment when eligible. Additionally, a substantial proportion of patients with previous HBV infection was recorded, which is of considerable importance in the era of immunosuppressive therapies.

Keywords Hepatitis, screening, hospitalized, viral, prevalence

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Introduction

There has been a growing interest throughout the international medical community in the elimination of viral hepatitis as a public health threat, exemplified by the goals set by the World Health Organization (WHO) to drastically reduce new infections (90% reduction) and deaths (65% reduction) from hepatitis B and C viruses (HBV/C) by 2030 [1]. However, many reports have highlighted difficulties in achieving these goals, mainly due to the inability to identify and diagnose significant parts of the infected population [2]. Furthermore, significant challenges remain concerning prevention and treatment in many parts of the world [3].

Many strategies have been proposed to screen both high- and average-risk populations. Strategies for high-risk populations have mainly focused on patients with human immunodeficiency virus, people who inject drugs, and incarcerated patients [4,5]. With regards to screening

strategies that focus on the general population, most efforts have concentrated on age-based reminders for screening to physicians and patients, as well as opportunistic screening in patients visiting healthcare facilities [6-8]. In many countries, national recommendations involve the screening of all adults at least once during their lifetime [9,10]. Although many strategies have been effectively implemented to diagnose and treat high-risk patients, there has been no implementation of screening strategies for the general population. This study aimed to explore the efficacy of universal screening for hospitalized patients with HBV/C viruses, as a potentially easy and effective screening strategy that could aid in the global effort to eradicate viral hepatitis.

Patients and methods

Study setting

This study was conducted at the First Propaedeutic University Department of Internal Medicine, Aristotle University of Thessaloniki, AHEPA University Hospital. This study was conducted from January 2021 to September 2023. The study was approved by the Institutional Review Board of the AHEPA University Hospital.

Study design

All patients admitted to the department were tested for anti-HCV, HBV surface antigen (HBsAg), and antibodies to the surface (anti-HBs) and core (anti-HBc) antigens. Further testing was left to the discretion of the attending physicians. Patients with a known history of HBV/C and those admitted because of liver disease complications were excluded from the study. Patients who had already been tested in the same hospital within the previous 5 years were excluded, to avoid including those who had already been screened and found to be negative. Patients who tested positive for HBsAg were retrospectively evaluated for treatment eligibility and were classified as having HBeAg-negative chronic infection or HBeAg-negative chronic hepatitis, according to the guidelines of the European Association for the Study of the Liver [11]. Specifically, patients with undetectable or low (<2000 IU/mL) HBV DNA and normal transaminases were classified as having chronic HBV infection. In contrast, patients with higher levels of HBV DNA or elevated transaminases were classified as having chronic HBV hepatitis.

Laboratory tests

The Alinity I assay (Abbott Laboratories, IL, USA) was used for qualitative detection of HBsAg, anti-HCV, anti-HBc,

and anti-HBs. The ELITE InGenius system was used for quantitative analysis of HCV RNA (detection sensitivity: 26 IU/mL) and HBV DNA (detection sensitivity: 9 IU/mL) by real-time polymerase chain reaction.

Statistical analysis

Statistical analysis was performed using the SPSS 29 software package (IBM Corp.). Variables are expressed as mean $\pm$ standard deviation. Chi-square tests were performed to compare frequencies between different groups, and Student's *t*-tests were used to compare normally distributed variables.

Results

A total of 3914 patients were included in this study. The majority of patients were male (56.5%), with a mean age of 69.8 ± 16.9 years. A total of 112 (2.9%) and 102 patients (2.7%) tested positive for HBsAg and anti-HCV antibodies, respectively. In addition, 1281 (32.8%) patients were positive for anti-HBc, of whom 112 (8.7%) had positive HBsAg, 952 (74.4%) had positive anti-HBs, and 217 (16.9%) had neither HBsAg nor anti-HBs positivity.

The presence of positive surface antigens was more common in patients aged 41-65 years (4.1%) than in patients over 65 years old (2.4%) and those under 40 years old (2.7%). Patients born in a foreign country accounted for 21.2% of patients with positive surface antigen, with the vast majority falling within the 41-65 age group (58.3%). In addition, the presence of prior infection (positive anti-HBc) was significantly correlated with patient age ($P < 0.001$), with patients >65 years of age having a much higher prevalence (39.9%) than patients aged 41-65 years (20.9%) or ≤ 40 years (9.5%). The presence of positive anti-HCV antibodies was more common in patients aged ≤ 40 years (9.1%) than in patients aged 41-64 years (3.5%) or >65 years (1.6%).

During hospitalization, HBV DNA testing was performed in 65 patients (58% positive for HBsAg), with 60 patients having detectable HBV DNA (92.3%). Of these, 13 had chronic HBV infection, and 47 had chronic HBV hepatitis. In addition, 23 HBsAg-positive patients died during hospitalization (20.1%), of whom 8 had chronic HBV hepatitis. No deaths were liver-related. Finally, 28 patients (71.8%) received treatment. There was a significant correlation between age and whether the patients progressed to the next level of testing or received therapy, with patients in whom further tests or treatment were not pursued being significantly older than patients who underwent all tests and received treatment when indicated (70.2 ± 14.7 vs. 61.6 ± 15.4 years, $P = 0.017$).

Among patients who tested positive for anti-HCV antibodies, 53 (52%) underwent HCV RNA testing, while 11 died during hospitalization, of whom 4 had positive HCV

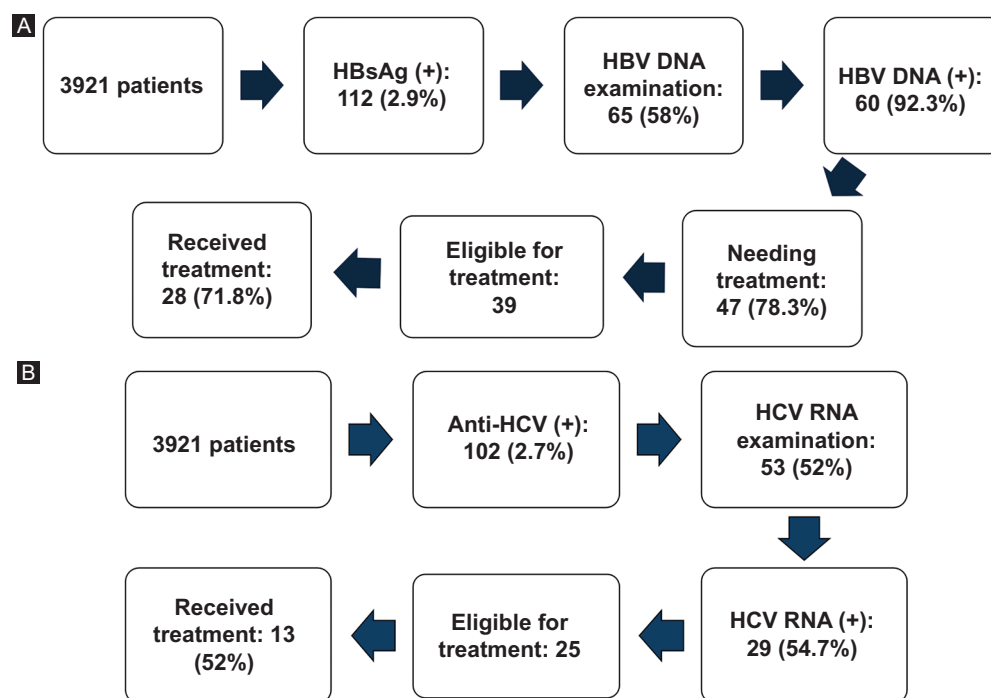


Figure 1 Cascade of care from screening to treatment for hepatitis B (A) and C (B)

RNA. No deaths were liver-related. HCV RNA was detected in 29 patients (54.7%), and 13 of 25 surviving patients ultimately received treatment (52% of the eligible patients). The process, from screening to treatment initiation, is illustrated in Fig. 1. As with HBV patients, HCV patients who did not undergo further tests or treatment were significantly older than patients who underwent all tests and received treatment when indicated (57 ± 18.1 vs. 35.8 ± 10.2 years, $P=0.007$).

Discussion

Our study demonstrated that HBV and HCV screening can be effective among inpatients in an internal medicine department of a tertiary hospital. Establishing such practices in hospitals worldwide may significantly enhance HBV and HCV elimination.

The percentages of patients positive for HBsAg and anti-HCV antibodies were consistent with those reported in previous Greek studies [12,13]. However, our results show a slightly higher prevalence for both HBV and HCV, potentially attributed to the fact that hospitalized patients may have significantly more disease risk factors than the general population. This is further explained by the fact that a significant percentage of anti-HCV-positive patients were under 40 years old (hospitalization at a young age is associated with substance abuse in many patients [14]) and that a substantial number of HBsAg-positive patients

were born in another country. Nevertheless, concomitant screening for patients from high-risk populations can be characterized as an additional benefit of this strategy, as these patients had not been identified by other screening strategies.

Regarding the percentage of patients lost during the cascade of care who did not undergo further testing or receive treatment, the characteristics of our cohort should be taken into account. Due to the severity of chronic illnesses in patients hospitalized in an internal medicine department in Greece (owing to the absence of geriatric departments), many discharged patients have a significantly shortened life expectancy, causing further diagnostic workup or treatment to be deemed irrelevant by the attending physicians. This is highlighted by the fact that patients who did not undergo further tests or were not prescribed treatment were significantly older than patients who underwent all relevant tests and were treated when indicated. Nevertheless, efforts to minimize potential deficiencies in proceeding with the appropriate diagnostic workup, or establishing contact with patients eligible for treatment, are vital. To this end, hospital policies should formalize this type of screening and ensure that specific staff are tasked with implementing the entire cascade of care for patients identified during the initial screening.

An unintended finding of our study was the significant number of individuals with a history of HBV infection, as highlighted by the very high anti-HBc positivity rate (32.8%). In the era of immunosuppressive therapies that extend to all branches of therapeutic medicine, it is essential to consider that

a significant percentage of the Greek population may require antiviral prophylaxis when initiating immunosuppressive treatment.

The overall effect of our study is reflected in the combined diagnostic rate of 5.6% among the screened patients who were positive for either anti-HCV or HBsAg. While many of these patients are not eligible for therapy, the value of maintaining follow up of patients with chronic HBV infection, and using HBV and HCV patients to screen family members, should not be overlooked. Nevertheless, even in terms of patients treated, initiating treatment in 1% (41/3921) of all patients screened is a testament to the effectiveness of this strategy.

Our study had significant limitations, especially when considering its implementation on a broader scale. As the study was conducted in a single department, the results cannot be generalized to the entire country. Moreover, the presence of patients with significant risk factors (especially substance abuse and HCV) may have led to a disproportionately high prevalence of both HBV and HCV in our cohort. The cost-effectiveness of such a strategy should also be assessed, as well as the means to avoid unnecessary testing in patients who have already been tested in another setting or have a very low life expectancy. Finally, the lack of baseline patient information, such as comorbidities, history of substance abuse, and cause for hospitalization, is a significant limitation of the study that impedes the generalization of its findings.

Mass screening of the adult population or all individuals over a certain age is becoming a common strategy in countries that have established plans for viral hepatitis elimination [8,10]. However, the effectiveness of such methods depends on their ability to perform screening. Hospitalized patients may be the most accessible population for such screening efforts, with studies in multiple countries attesting to the effectiveness of in-hospital screening [15-17]. In order to safeguard the application of such programs, individuals should be assigned to supervise the screening process and ensure that the patients complete the necessary workup and are treated accordingly. Additionally, another equally important task that must be taken into account, if such a screening program is implemented, is to ensure that family members of individuals diagnosed with the condition are also tested. Nevertheless, combined with the fact that such programs can be implemented effortlessly in many hospitals, and that a significant part of the adult population visits hospitals for emergency or scheduled examinations, this may be the first step toward mass-screening substantial parts of the adult population for HBV and HCV.

To conclude, our study shows that universal inpatient screening for HBV and HCV can be an effective strategy, and can contribute to ongoing worldwide attempts to eliminate viral hepatitis.

Summary Box

What is already known:

- The World Health Organization has set ambitious goals to significantly reduce viral hepatitis prevalence by 2030
- While significant efforts have been made in many countries, many patients with hepatitis B and C remain undiagnosed
- Screening strategies that have been implemented include nationwide screening programs, and programs focusing on screening in special populations and specific settings (hospitals and other healthcare facilities)

What the new findings are:

- Screening for viral hepatitis in inpatients is easy and effective
- Screening of inpatients should be carefully organized in order to achieve maximum efficiency
- A large percentage of hospitalized adult (~20%) and elderly patients (~40%) in Greece have a history of prior hepatitis B infection

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