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AIM AND SCOPE

Viral Hepatitis Journal (Formerly Viral Hepatit Dergisi) is the regular publishing organ of the Viral Hepatitis Society. This periodical journal covers diagnosis, treatment, epidemiology, prevention and information of hepatitis.
Viral Hepatitis Journal is an open-access journal published 3 times per year (April, August and December). In addition, the special issues are published in some periods. It is a periodic national/international journal, published in English language with abstract and title published also in Turkish language and its editorial policies are based on independent peer-review principles.
The aim of Viral Hepatitis Journal is to continuously publish original research papers of the highest scientific and clinical values specifically on hepatitis, on an international level. Additionally, reviews on basic developments in education, editorial short notes, case reports, original views, letters from a wide range of medical personal containing experiences and comments as well as social subjects are published.
For general practitioners giving first line medical service who are interested in hepatitis, specialists in internal medicine, gastroenterology, microbiology, family physician, public health and hepatology, 'things that must be known' subjects will ensure to involve in Viral Hepatitis Journal.
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INSTRUCTIONS TO AUTHORS

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Viral Hepatitis Journal (Formerly Viral Hepatit Dergisi) is an independent, peer-reviewed international journal published quarterly in April, August, December. The official language of the journal is English.

Viral Hepatitis Journal is a scientific journal that publishes retrospective, prospective or experimental research articles, review articles, case reports, editorial comment/discussion, letter to the editor, surgical technique, differential diagnosis, medical book reviews, questions-answers and also current issues of medical agenda from all fields of medicine and aims to reach all national/international institutions and individuals.

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The ORCID (Open Researcher and Contributor ID) number of the correspondence author should be provided while sending the manuscript. A free registration can be done at http://orcid.org.

In the international index and database, the name of the journal has been registered as Viral Hepatitis Journal and abbreviated as Viral Hepat J.

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Scientific and Ethics Responsibility

The author(s) undertake(s) all scientific responsibility for the manuscript. All the authors must actively participate in the study. The author(s) guarantee(s) that the manuscript itself or any substantially similar content of the manuscript has not been published or is being considered for publication elsewhere. If the manuscript had been presented in a meeting before; the name, date and the province of the meeting should be noted.

Experimental, clinical and drug studies requiring approval by an ethics committee must be submitted to the Viral Hepatitis Journal with an ethics committee approval report confirming that the study was conducted in accordance with international agreements and the Declaration of Helsinki (revised in 2013) (https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/). The approval of the ethics committee and the fact that informed consent was given by the patients should be indicated in the Materials and Methods section (including approval number). All papers reporting experiments using animals must include a statement in the Material and Methods section giving assurance that all animals have received humane care in compliance with the "Guide for the Care and Use of Laboratory Animals" (www.nap.edu/catalog/5140.html) and indicating approval by the institutional ethical review board.

The content of the submitted manuscripts should conform to the criteria stated in "Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals" published by International Committee of Medical Journal Editors and updated in 2016 (available at http://www.icmje.org/).

The authors should acknowledge and provide information on grants, contracts or other financial support of the study provided by any foundations and institutions or firms.

The articles sent to be published in the journal shouldn't have been published anywhere else previously or submitted and accepted to be published. However, a complete report that follows publication of a preliminary report, such as an abstract can be submitted. If authors intend to discard any part of the manuscript, a written application should be sent to the Editor.

In case of retraction of the text by author(s) for any reason again needs a written and signed application explaining the reasons.

The name of the institution where the authors work and the name of the institution or the department in which the study has been conducted should not be mentioned in the submitted manuscript.

The corresponding author must give the full corresponding address (including telephone, fax number and e-mail address). Contact information for corresponding author is published in the journal.

The authors should keep a copy of the submitted manuscripts and other documents.

If the whole or a part of the submitted manuscript needs to be published somewhere else, Editorial Office must be informed accordingly.

Review Process: Upon submission, all manuscripts are reviewed to check for requirements requested by the Journal. Manuscripts that do not comply with these requirements will be sent back to authors without further evaluations. All the papers are first evaluated by the editor; later the papers are sent to advisory board members. If needed, some questions can be asked to the authors to answer; or some defaults may have to be corrected by the authors.

The result can be acceptance, minor revision, major revision, rejection in the current form, or rejection. Accepted manuscripts are forwarded for publication; in this stage, all information and data are checked and controlled properly; the proof of the article to be published by the journal are forwarded to the writers for proof reading and corrections.

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The Editorial Policies and General Guidelines for manuscript preparation specified below are based on "Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals (ICMJE Recommendations)" by the International Committee of Medical Journal Editors (2016, archived at http://www.icmje.org/).

Preparation of research articles and systematic reviews meta-analyses must comply with study design guidelines: CONSORT statement for randomized controlled trials (Moher D, Schultz KF, Altman D, for the CONSORT Group. The CONSORT statement revised recommendations for improving the quality of reports of parallel group randomized trials. JAMA 2001; 285: 1987-91) (http://www.consort-statement.org/),

PRISMA for preferred reporting items for systematic reviews and meta-analyses (Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 2009; 6(7): e1000097.) (http://www.prisma-statement.org/),

STARD checklist for the reporting of studies of diagnostic accuracy (Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig LM, et al, for the STARD Group. Towards complete and accurate reporting of studies of diagnostic accuracy: the STARD initiative. Ann Intern Med 2003;138:40-4.) (http://www.stard-statement.org/),

STROBE statement—checklist of items that should be included in reports of observational studies (http://www.strobe-statement.org/),

MOOSE guidelines for meta-analysis and systemic reviews of observational studies (Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting Meta-analysis of observational Studies in Epidemiology (MOOSE) group. JAMA 2000; 283: 2008-12).

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Authors are encouraged to follow the following principles before submitting their article:

• Research articles and article collections should not exceed 15 pages including the text, figures, tables and references, while short announcements and case report presentations should not be longer than 5 pages.

Short Announcements

i. Turkish title, English title, author name and institution(s) (Turkish and English)
ii. Turkish and English Abstract (max 300 words)
iii. Turkish and English Keywords
iv. Introduction (max 300 words)
v. Materials and Methods (max 400 words)
vi. Results (max 400 words)
vii. Discussion (max 700 words)
viii. Referances (should not exceed 15), all words 2000 not exceed.

• Author number for review articles should not exceed three.

• Author number for case report presentations should not exceed four.

• Articles should be written with double line space in 10 font size and right, left, upper and lower margins should all be 2.5 cm. Writing style should be Arial.

Manuscripts should have double-line spacing, leaving sufficient margin on both sides.

Manuscripts should be written with Microsoft Word.

Abbreviations: Abbreviations should be defined at first mention and used consistently thereafter. Internationally accepted abbreviations should be used; refer to scientific writing guides as necessary.

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Title Page: Title should be concise and informative (in Turkish and English). The title page should include a list of all contributing authors and all of their affiliations. Positions of authors and names of departments and institutions to which they are attached and the province should be written. Supply full correspondence details for the corresponding author, including phone, mobile phone, fax number and e-mail address.

ARTICLE SECTIONS

The text file should include the title in Turkish, keywords, the title in English, keywords in English, the text of the article, references, tables (only one table for one page) and figure

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legends (if any), respectively. Within the text file, the names of the authors, any information about the institutions, the figures and images should be excluded.

Abstract: Turkish and English abstracts should be given together with the article title. It should be divided into four sections in the following order: Objectives, Materials and Methods, Results and Conclusion. Abstracts should not exceed 250 words. Abstracts for case reports should be unstructured and shorter (average 100-150 words; without structural divisions in Turkish and English).

Objectives: The aim of the study should be clearly stated.

Materials and Methods: **The study and standard criteria used should be defined; it should also** be indicated whether the study is randomized or not, whether it is retrospective or prospective, and the statistical methods applied should be indicated, if applicable.

Results: The detailed results of the study should be given and the statistical significance level should be indicated.

Conclusion: Should summarize the results of the study, the clinical applicability of the results should be defined, and the favorable and unfavorable aspects should be declared.

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• They should be minimally 3 and maximally 6 and should be written in Turkish and English.

• The words should be separated by semicolon (;), from each other.

• English key words should be appropriate to "Medical Subject Headings (MESH)" (www.nlm.nih.gov/mesh/MBrowser.html).

• Turkish key words should be appropriate to "Turkey Science Terms" (www.bilimterimleri.com).

Original researches should have the following sections;

Introduction: Should consist of a brief explanation of the topic and indicate the objective of the study, supported by information from the literature.

Materials and Methods: The study plan should be clearly described, indicating whether the study is randomized or not, whether it is retrospective or prospective, the number of trials, the characteristics, and the statistical methods used.

Results: The results of the study should be stated, with tables/figures given in numerical order; the results should be evaluated according to the statistical analysis methods applied. See General Guidelines for details about the preparation of visual material.

Discussion: The study results should be discussed in terms of their favorable and unfavorable aspects and they should be compared with the literature.

Study Limitations: Limitations of the study should be detailed. In addition, an evaluation of the implications of the obtained findings/results for future research should be outlined.

Conclusion: The conclusion of the study should be highlighted.

Acknowledgements: Any technical or financial support or editorial contributions (statistical analysis, English/Turkish evaluation) towards the study should appear at the end of the article. Only acknowledge persons and institutions who have made substantial contributions to the study, but was not a writer of the paper.

References: Authors are responsible for the accuracy of the references. See General Guidelines for details about the usage and formatting required.

Case Reports

Case reports should present cases which are rarely seen, feature novelty in diagnosis and treatment, and contribute to our current knowledge. The first page should include the title in Turkish and English, an unstructured summary not exceeding 150 words, and key words. The main text should consist of introduction, case report, discussion, acknowledgment, conclusion and references. The entire text should not exceed 5 pages (A4, formatted as specified above).

Review Articles

Review articles can address any aspect of viral hepatitis Review articles must provide critical analyses of contemporary evidence and provide directions of or future research. Most review articles are commissioned, but other review submissions are also welcome. Before sending a review, discussion with the editor is recommended.

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Letters to the Editor should be short commentaries related to current developments in viral hepatitis and their scientific and social aspects, or may be submitted to ask questions or offer further contributions in response to work that has been published in the Viral Hepatitis Journal. Letters do not include a title or an abstract; they should not exceed 1,000 words and can have up to 5 references.

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Follow the styles shown in examples below (please give attention to punctuation):

In reference section of the article, there should be no writing in languages other than English. The text language of the article should be indicated in parenthesis at the end of each reference.(e.g. Yoldaş O, Bulut A, Altındiş M. The Current Approach of Hepatitis A Infections. Viral Hepatitis J 2012;18:81-86. (Turkish).

Format for journal articles; initials of author's names and surnames, titles of article, journal name, date, volume, number, and inclusive pages, must be indicated.

Example: Tabak F, Ozdemir F, Tabak O, Erer B, Tahan V, Ozaras R. Autoimmune hepatitis induced by the prolonged hepatitis A virus infection. Ann Hepatol. 2008;7:177-179.

Format for books; initials of author's names and surnames, chapter title, editor's name, book title, edition, city, publisher, date and pages.

Example: Vissers RJ, Abu-Laban RB. Acute and Chronic Pancreatitis. In: Tintinalli JE, Kelen GD, Stapczynski JS (eds.), Emergency Medicine: A comprehensive Study Guide. 6 st ed. New York: McGraw-Hill Co; 2005; p. 573-577.

Format for on-line-only publications; DOI is the only acceptable on-line reference.

Figures, Pictures, Table 's and Graphics:

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Explanations about figures, pictures, tables and graphics must be placed at the end of the article.

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Conflict of interest: If any of the writers have a relationship based on self-interest, this should be explained.

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All manuscripts submitted to the Viral Hepatitis Journal are screened for plagiarism using the "Crossref Similarity Check powered by iThenticate" software. Results indicating plagiarism may result in manuscripts being returned or rejected.

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Articles must be complete. They must include the following:

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• Title Page

• Article sections

• Turkish and English titles

• Abstract (250 words) (Turkish and English)

• Keywords (minimum 3; maximum 6)

• Article divided into appropriate sections

• Complete and accurate references and citations

• List of references styled according to "journal requirements"

• All figures (with legends) and tables (with titles) cited.

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CONTENTS

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Viral Hepatitis Journal 2018;24(1):1-2

Epidemiology of Viral Hepatitis Changes in Our Country

Ülkemizde Viral Hepatitlerin Epidemiyolojisi Değişiyor

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The most important interventions in our country that significantly affect the epidemiology of viral hepatitis are the introduction of hepatitis B vaccine into the routine vaccination program for newborns since 1998 and the introduction of catch up vaccination strategies and screening for high-risk groups. In addition, the development of our surveillance system, the introduction of hepatitis A vaccine into the routine vaccination program, and the addition of studying nucleic acid testing to serological screening in blood donors are other important interventions.

When the data of the Ministry of Health for the period including 2009-2017 is reviewed, it is remarkable that there is a decrease in the cases of acute hepatitis A and this decrease is observed in all regions (1). For hepatitis B, the hepatitis B surface antigen (HBsAg) positivity varies between 3.4% and 7.8% according to the results of the field study conducted by the Viral Hepatitis Society, while it is 4% on the field study of the Turkish Liver Research Society (2,3). In addition, the fact that one out of every three people over 18 years old in our country has been exposed to hepatitis B virus (HBV), having more than 2 million HBsAg positive in the adult age group and having only 12% of these people being aware of their situation is the striking result of this study (3). A modeling study of Toy et al. (4), including 339 articles from 1999 to 2009, provided data on age-specific and region-specific hepatitis B prevalence in our country, healthcare-related groups such as blood donors and military units, pregnant women and health personnel, and high-risk groups. According to the results of this study, age and regional differences in our country are predominant and the prevalence of hepatitis B is 4.57%. This ratio numerically indicates the fact that about 3.3 million people are infected with HBV and about 330.000 cases of chronic hepatitis B are present. 70% of these cases are hepatitis B e antigen negative and 99% genotype D. Pregnant women had a predominantly 1.7% HBsAg positivity.

Şahin et al. (5) reported HBsAg positivity as 1% in pregnant women in Şırnak and Cizre cities in their study currently published in this issue of Viral Hepatitis Journal. In another study that was conducted in our eastern cities, seroprevalence was found significantly low and another good point was having anti-HBs positivity as 54.5% for pregnants under age 19 that is higher than the group above 19 years old. This is an indication that the newborn routine hepatitis B vaccination studies have reached the target.

Furuncuoğlu et al. (6) support the data of Şahin et al. (5) in the study of hepatitis B seroprevalance of 7605 pregnant women in three different periods of 1995-2015. HBsAg positivity was found to decrease from 2.6% to 0.8% between 1995 and 2001, while anti-HBs positivity increased from 9.5% to 17.5%. Since prevention of vertical transmission means to prevent new hepatitis B infections, it is very important to screen hepatitis B infection in pregnancy.

Studies in the prevention of hepatitis B infection in our country are pleasing and promising. However, much more action should be taken into account within the scope of the project focused on hepatitis elimination in 2030, which was initiated by the World Health Organization. Our national strategic plan, which aims to raise awareness, improve surveillance and screening, identify high-risk groups, and increase access to care, are crucial to take action.

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Research Article

3

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Viral Hepatitis Journal 2018;24(1):3-6

Hepatitis B and C Sero-prevalence in Patients with Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome at a Tertiary Care Hospital in Izmir

İzmir'de Üçüncü Basamak Bir Hastanede İnsan İmmün Yetmelik Virüsü/Edinsel Bağışıklık Yetmezliği Sendromu Olgularında Hepatit B ve C Sero-prevalansı

Sabri ATALAY[1], Tuba TATLI KIŞ[1], Ufuk SÖNMEZ[2], Şükran KÖSE[1]

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ABSTRACT

Objectives: Infections caused by human immunodeficiency virus (HIV), hepatitis B virus (HBV) and hepatitis C virus (HCV) represent a significant health problem. Co-infection with these viral agents is not uncommon as a result of the similar transmission routes. Our study was planned to investigate the prevalence of HBV and HCV infections in HIV/Acquired Immune Deficiency syndrome (AIDS) patients followed up at our institution.

Materials and Methods: In this study conducted in the Department of Infectious Diseases and Clinical Microbiology at Izmir Tepecik Training and Research Hospital, medical records of patients followed at the HIV/AIDS outpatient clinic between August 2002 and December 2014 were evaluated. Demographic data, main route of HIV transmission, hepatitis B surface antigen (HBsAg), anti-hepatitis B core (HBc) immunoglobulin G (IgG), anti-HBs and anti-HCV results were evaluated.

Results: A total of 157 treatment-naïve patients who were followed up at our HIV/AIDS outpatient clinic were included in this study. Four patients (2.6%), had HBsAg positivity. Anti-HBc IgG and anti-HBs positivity were detected in 34% and 28.4% of the patients, respectively. No patients had anti-HCV positivity.

Conclusion: The prevalence of HBsAg in HIV-positive individuals was found to be similar to that in other population-based studies in our country. Absence of anti-HCV positivity suggests that hepatitis C infection is not a major health problem in this population.

Keywords: Human immunodeficiency virus, hepatitis B virus, hepatitis C virus, seroprevalence

ÖZ

Amaç: İnsan immün yetmelik virüsü (HIV), hepatit B virüsü (HBV) ve hepatit C virüsünün (HCV) neden olduğu enfeksiyonlar önemli bir sağlık sorunudur. Bulaş yollarının benzerliği nedeni ile bu enfeksiyonların birlikteliği (ko-enfeksiyonu) nadir değildir. Çalışmamızda kliniğimizde HIV/Edinsel Bağışıklık Yetmezliği sendromu (AIDS) tanısı ile takip edilen hastalarda HBV ve HCV prevalansının incelenmesi amaçlanmıştır.

Gereç ve Yöntemler: İzmir Tepecik Eğitim ve Araştırma Hastanesi'nde Ağustos 2002-Aralık 2014 tarihleri arasında HIV/AIDS tanısıyla takipli hastalar retrospektif olarak incelendi. Demografik özellikler, HIV'nin en olası geçiş yolu ve hepatit B yüzey antijeni (HBsAg), anti-hepatit B çekirdeği (HBc) immünoglobülin G (IgG), anti-HBs ve anti-HCV sonuçları değerlendirildi.

Bulgular: Bu çalışmaya, polikliniğimizde takip edilen 157 naiv HIV/AIDS hastası dahil edildi. Dört hastada (%2,6) HBsAg pozitifliği saptandı. Anti-HBc IgG ve anti-HBs pozitifliği sırasıyla %34 ve %28,4 saptanmış olup, hiç bir hastada anti-HCV pozitifliği saptanmamıştır.

Sonuç: HIV pozitif kişilerde HBsAg sıklığı ülkemizde yapılmış popülasyon tabanlı diğer çalışmalar ile benzer oranda saptanmıştır. Anti-HCV pozitifliğinin olmaması, hepatit C enfeksiyonunun bu hasta grubunda önemli bir sağlık problemi olmadığını düşündürmektedir.

Anahtar Kelimeler: İnsan immün yetmezlik virüsü, hepatit B virüsü, hepatit C virüsü, seroprevalans

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Introduction

Infections caused by human immunodeficiency virus (HIV), hepatitis B virus (HBV) and hepatitis C virus (HCV) represent a significant health problem. Co-infection with these viral agents is not uncommon as a result of the similar of transmission routes. The main transmission routes of HBV infection among adults are sexual intercourse or intravenous (i.v.) drug use in low endemic countries, while horizontal and vertical transmission in high endemic countries (1). Hepatitis C is mainly transmitted through contaminated blood, as is also the case with HIV (2).

By the end of the year 2015, approximately 70 million people have been infected with HIV and 35 million deaths have occurred, with approximately 36.7 million people currently living with HIV (3). With respect to HBV, more than two billion people have been infected with this virus worldwide, and 350 to 400 million people are chronic carriers (4). The number of individuals living with chronic HCV infection exceeds 130 million (5). Among HIV-infected individuals, variable rates of HBV co-infection have been reported, ranging from 6% to 14% (6), and approximately 20-30% of HIV-positive individuals are also infected with HCV (7). The rates of HIV-HCV co-infection vary widely in different population groups depending on the geographical region, risk factors, age of infection, modes of transmission, and types of exposure (8).

The introduction of highly active antiretroviral therapy (HAART) has significantly improved the survival in patients infected with HIV (9). However, liver disease caused by HBV and HCV co-infections, chronic alcohol abuse, hepatic tuberculosis or hepatotoxicity due to antiretroviral drugs have now emerged as a major cause of mortality in these patients (10,11). In co-infected patients, these viruses have significant interaction, amplifying the pathogenicity of individual agent, leading to higher morbidity and mortality (12,13). HIV infection is associated with an acceleration of the course of liver diseases caused by hepatitis B and C, particularly in patients with more pronounced immune deficiency. Thus, co-infected patients have more severe outcomes than mono-infected patients. From a clinical viewpoint, HIV-HBV co-infection is more severe and is associated with higher rates of cirrhosis and hepatocellular carcinoma. In such cases, the risk of cirrhosis increases 4.2-fold with an associated elevation in mortality, and, in some cases, HBV can be reactivated (14,15,16). Several studies have shown that HIV-HCV co-infected patients are also at an increased risk of more rapid progression to cirrhosis, end-stage liver disease and hepatocellular carcinoma (8). Therefore, an earlier recommendation by the World Health Organization involved the commencement of HAART in HIV patients co-infected with HBV or HCV (17). This recommendation has recently been modified as to treat all patients irrespective of CD4 count. However, treatment in co-infected patients should be considered a priority, as a potential means to reduce liver-associated morbidity and mortality. Turkey is considered a low endemic country for HIV and HCV, and a low/intermediate endemic country (depending on the geographical region) for HBV infection. However, as opposed to the epidemiology of HBV and HCV, a recent rise in the number of HIV-infected individuals has been noted. On the other hand, there is a scarcity of studies examining this population in our country. Thus, this retrospective study was planned to investigate the prevalence of HBV and HCV infections in HIV/Acquired Immune Deficiency syndrome (AIDS) patients followed up at our institution.

Materials and Methods

In this study conducted at the Department of Infectious Diseases and Clinical Microbiology, Tepecik Training and Research Hospital, medical records of patients followed at the HIV/AIDS outpatient clinic between August 2002 and December 2014 were evaluated. Demographic data, potential route of HIV transmission, and hepatitis B surface antigen (HBsAg), anti-hepatitis B core (HBc) immunoglobulin G (IgG), anti-HBs and anti-HCV results based on enzyme-linked immunosorbent assay (ELISA) (Diasorin Diagnostic Specialist S.T.A., Italy) at the time of presentation were recorded. The results were classified as positive or negative using the cut-off values provided by the manufacturer. Patients with missing data or incompliance to follow-up visits were excluded. Therefore, some of the statistical procedures did not involve the whole patient population enrolled.

Results

In this study, we included a total of 157 treatment-naive patients with anti-HIV positivity based on ELISA and confirmatory Western blot test who were followed up at our HIV/AIDS outpatient clinic. The mean age was 41 years (16-79 years), and 28 patients (18%) were female. Heterosexual intercourse was the most likely mode of transmission in 64.9%. Other potential routes of transmission were as follows in the decreasing order of frequency: bisexual/homosexual intercourse, unknown, medical intervention/blood transfusion, and i.v. drug use (Table 1, 2). Four patients (2.6%), one of whom was a female, had HBsAg positivity. Anti-HBc IgG and anti-HBs positivity were detected in 34% and 28.4% of patients, respectively. No patients had anti-HCV positivity. Also, among 5554 subjects with HBV and 182 subjects with HCV followed up in our outpatient unit, none were anti-HIV-positive.

Discussion

According to the Turkish National Health Agency 2016 data, there were a total of 12.281 HIV-positive patients in Turkey, which is a low prevalence country. However, a recent and significant increase has occurred in the number of newly detected cases, with 1734 patients reported until December 2016 in the past year. Of these newly identified subjects, 84% were male and 16% were female; and 16.5% were non-nationals. Higher representation of young adults between 25 and 29 years of age was also noteworthy.

Table 1. Main transmission route for the patients

Transmission route	Number	%
Heterosexual intercourse	102	64.9
Homo/bisexual intercourse	38	24.2
Medical intervention/Blood transfusion	7	4.5
Unknown	8	5.1
i.v. drug user	2	1.3
Total	157	100

i.v.: Intravenous

There were only 529 new HIV-positive cases in 2010, and a more than 5-fold increase was found in 2015 reaching 2.130 new cases (18).

Despite the regional variation in terms of HBV seroprevalence in Turkey, a trend toward a declined prevalence was observed probably due to the impact of routine nationwide childhood immunization program initiated in 1998. In a previous review, the reported rate of HBsAg seroprevalence in the general Turkish population was 2.5 to 9% (19), which is comparable to the prevalence of HBV infection among HIV patients in our study, i.e. 2.6%. However, in another multi-center study from Turkey reported a higher rate of HBsAg positivity (6.2%) among HIV-positive individuals (20). In the same study, 0.9% of subjects were anti-HCV positive. Similar results of HBsAg positivity (4.4%) was reported in a study conducted by İnci et al. (21). In another study conducted with 70 (56 males, 14 females) HIV-infected patients, HBV and HCV co-infection rates were 14.2% and 12.8%, respectively while four (5.7%) patients were found to be infected with HBV, HCV and HIV (22). Immunity against hepatitis B infection i.e. anti-HBs and anti-HBc IgG positivity was observed in 28.4%, isolated anti-HBc IgG positivity was observed in 1.9%, isolated anti-HBs positivity was observed in 9.03% of this population. This finding is consistent with the fact that the study participants were mostly middle-aged subjects who did not benefit from the routine vaccination program initiated in 1998. On the other hand, exposure to hepatitis B (anti-HBc IgG) was found in a greater proportion (34%) of these subjects. Overall, these data underscore the high level of HBV co-infection risk in HIV-positive subjects and underlie the importance of vaccination, particularly when one considers the recent findings showing a high representation of young adults among newly diagnosed patients with HIV positivity.

HCV infection is more likely occur in specific circumstances and specific patient groups with certain risks. In a study by Freitas et al. (23), HIV-HCV co-infection was more likely to be associated with an age over 40 years, i.v. drug use, blood transfusion, and the absence of a steady partnership 8. The prevalence of HIV/HCV co-infection varies from one country to another depending on the route of HIV transmission: 10.8-42% in Brazil, 25% in the United States, 56.7% in Australia and 58.5% in Argentina.

Since i.v. drug use represents the main route of HCV transmission, HIV-HCV co-infection rates are higher among HIV/AIDS patients with i.v. drug use. High HIV-HCV co-infection rates (approximately 70%) have been reported in Eastern European countries and in Iran where i.v. drug use is the main route of HIV transmission (20). In a study of 378 HIV-positive individuals in Kenya, 1% was found to be co-infected with HCV (24). Again, in a cohort of 138 HIV-positive patients in Ghana, HCV co-infection was found in 3.6% (25). In a meta-analysis of studies reporting HCV prevalence amongst HIV patients in sub-Saharan Africa, the mean prevalence of co-infection was 7% (26). According to 2008-2012 data from the Turkish Red Crescent Blood Center, anti-HCV was found to be positive in 0.02 to 0.004% of a total of civilian donor population of 4.510.207 (27,28). The study conducted by the Turkish Association for the Study of the Liver between 2008 and 2011 found that 0.95% of 5.471 subjects were positive for HCV (29). The prevalence of anti-HCV positivity in the general Turkish population has been reported to be 1-2.2% (30). A number of factors, including anal sex, multiple partners, and co-infection with HIV and other sexually transmitted diseases, have been implicated in the increase in HCV seroconversion among HIV-positive men who have sex with men (MSM) (31,32). In this study, no anti-HCV positivity was found in this population of patients infected with HIV, possibly related to the difference in transmission routes of HIV among patients included in this study. Accordingly, heterosexual intercourse was reported to be the main route of transmission, and relatively low numbers of patients were MSM/bisexual (24.2%) and i.v. drug users (1.3%). In a previous study conducted in Turkey, the prevalence of i.v. drug use was 0.05% in the general population (33). Although heterosexual intercourse was reported to be the main route of HIV transmission, the significantly higher proportion of male participants suggests that the actual number of individuals experiencing same-sex intercourse may be higher. On the other hand, individuals may opt to conceal their sexual preferences due to a number of factors such as fear of stigmatization or disclosure. Thus, absence of anti-HCV-positive patients in our sample is most likely due to the low number of i.v. drug users and low HCV prevalence nationwide. All HIV-infected patients should be tested for HCV infection. False negative anti-HCV results may be seen in HIV-positive individuals with low CD4 (<100/mm^3) counts. If anti-HCV is negative and HCV infection is still suspected, HCV RNA should be performed (5).

Table 2. Hepatitis B virus and hepatitis C virus serology in human immunodeficiency virus patients

Serological marker	n	Total patients	%
HBsAg positive and anti-HBc IgG positive	4	155	2.6
Isolated anti-HBc IgG positive	3	155	1.9
Anti-HBc IgG positive and anti-HBs positive	44	155	28.4
Anti-HBc IgG positivity total	51	150	34
Isolated anti-HBs positive	14	155	9.03
Anti-HCV positive	0	155	0

HBsAg: Hepatitis B surface antigen, IgG: Immunoglobulin G, HBc: Hepatitis B core, HBs: Hepatitis B surface, HCV: Hepatitis C virus

Study Limitations

Certain limitations of our study should be mentioned. It was a single-center study from western Turkey with a small sample size, restricting its ability to reflect the current status in the country.

Conclusion

As a conclusion, it confirms the previous national data indicating a high prevalence of HBsAg among HIV-positive individuals and emphasizing the requirement for effective immunization in susceptible populations. Absence of anti-HCV positivity suggests that HCV infection may not represent a major health problem in our population.

Ethics

Ethics Committee Approval: Retrospective study.
Informed Consent: Retrospective study.
Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: S.A., U.S., Concept: S.A., Design: S.A., Data Collection or Processing: U.S., T.T.K., Analysis or Interpretation: S.A., U.S., T.T.K., Literature Search: S.A., Ş.K. Writing: S.A., T.T.K.

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Research Article

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Seroprevalence of Hepatitis B Surface Antigen, Anti-Hepatitis B Surface and Anti-Hepatitis C Virus Among Pregnant Women Residing in Şırnak Province

Şırnak İlinde Yaşayan Gebelerdeki Hepatit B Yüzey Antijeni, Anti-Hepatit B Yüzey ve Anti-Hepatit C Virüsü Seroprevalansı

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ABSTRACT

Objectives: The purpose of the study was to detect the rate of hepatitis B surface antigen (HBsAg), anti-HBs and anti-hepatitis C virus (HCV) seropositivity among pregnant women residing in the city of Şırnak.

Materials and Methods: Results of serological tests for HBsAg, anti-HBs and anti-HCV in 2214 pregnant women, who were admitted to the Gynecology and Obstetrics Clinics and Emergency Departments at Şırnak State Hospital and Cizre State Hospital between the dates of April 1, and October 1, 2017, were retrospectively evaluated.

Results: A total of 2214 pregnant women were included in this study. It was determined that the rate of seropositivity for HBsAg, anti-HBs and anti-HCV was 1%, 27.8%, and 0.21%, respectively. It was found that anti-HBs seropositivity rate among pregnant women younger than 19 years was 54.5%, which was higher than in those aged 19 years or older.

Conclusion: Anti-HCV positivity rate detected in pregnant women who resided in Şırnak was found to be similar to the results reported in other studies conducted in our country, however, HBsAg positivity rate was found to be lower when compared with the results of other studies. A significant increase was detected in anti-HBs seropositivity rate in Şırnak since hepatitis B vaccine was included in the national immunization schedule.

Keywords: Pregnancy, hepatitis B surface antigen, anti-hepatitis C virus, anti-hepatitis B surface, seroprevalence

ÖZ

Amaç: Bu çalışmada Şırnak ilinde yaşayan gebelerde, hepatit B yüzey antijeni (HBsAg), anti-HBs ve anti-hepatit C virüsü seropozitiflik oranlarının saptanması amaçlanmıştır.

Gereç ve Yöntemler: Şırnak Devlet Hastanesi ve Cizre Devlet Hastanesi'nin Kadın Hastalıkları ve Doğum Poliklinikleri ile Acil Servisleri'ne 1 Nisan-1 Ekim 2017 tarihleri arasında başvuran 2214 gebe kadının HBsAg, anti-HBs ve anti-HCV verileri retrospektif olarak incelendi ve sonuçlar kayıt altına alındı.

Bulgular: Çalışmaya 2214 gebe dahil edildi. HBsAg seroprevelansı %1, anti-HBs pozitiflik oranı %27,8, anti- HCV seroprevelansı %0,21 saptandı. On dokuz yaş ve altında olan gebelerde %54,5 olan anti-HBs seropozitiflik oranının, 19 yaş üstü gebelerdekine göre yüksek olması istatistiksel olarak anlamlı bulundu.

Sonuç: Şırnak ilinde yaşayan gebelerde tespit edilen anti-HCV pozitiflik oranı ülkemizde yapılan diğer çalışmalara benzer bulunurken, HBsAg pozitiflik oranı ise diğer çalışmalara göre daha düşük bulunmuştur. Hepatit B aşısının ulusal bağışıklama programına girmesi ile Şırnak ilinde anti-HBs seropozitiflik oranında belirgin bir artış olduğu tespit edilmiştir.

Anahtar Kelimeler: Gebelik, hepatit B yüzey antijeni, anti-hepatit C virüsü, anti-hepatit B yüzey, seroprevelans

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Introduction

According to the data of the World Health Organization, 1.34 million people died of viral hepatitis in 2015, being a figure which is similar to the number of deaths due to tuberculosis and more than death due to human immunodeficiency virus (HIV) infection (1).

In general, more than one third of the existing chronic hepatitis B infections occur as a result of mother-to-child transmission (2). Especially in high endemic regions where hepatitis B surface antigen (HBsAg) prevalence is ≥8%, chronic hepatitis B is mostly prevalent in early childhood, and in these regions, mother-to-child transmission is the most significant transmission route (3,4,5). It has been reported that 70-90% of children born to hepatitis B virus (HBV)-infected mothers were infected and more than 95% of them were chronic carriers. (6,7). It is known that hepatitis B vaccination and hepatitis B immunoglobulin administration in the first 12 hours of birth can reduce the risk of vertical transmission from 90% to 5-10% in children born to HBsAg-positive mothers (8,9).

The risk of mother-to-child transmission of hepatitis C virus (HCV) infection is 3-10% (6,10,11). It is estimated that 40.000 children are born to HCV-infected mothers every year, and about 4000 of them are infected with HCV (12,13).

The HBsAg seropositivity rate, which ranges from 1.9% to 8.4% in our country, is found to be 4.4% on average (6,14). The rate of HCV seroprevalence in the country is reported to be 0.3-1.7% (15,16).

Since the fertility rate is high in the Şırnak region (17), it is considered that the seroprevalence of these vertically-transmitted infections is important. For this reason, the present study aimed to determine the rate of HBsAg, anti-HBs (hepatitis B surface antibody) and anti-HCV (hepatitis C antibody) seropositivity among pregnant women living in Şırnak.

Materials and Methods

Results of serological tests for HBsAg, anti-HBs and anti-HCV in 2214 pregnant women, who were admitted to the Obstetrics and Gynecology Clinics and Emergency Departments at Şırnak State Hospital and Cizre State Hospital between April 1 and October 1, 2017, were retrospectively analyzed from the hospitals' information management system. HBsAg II (Roche, Mannheim, Germany), Elecsys anti-HBs II (Roche, Mannheim, Germany) and anti-HCV II (Roche, Mannheim, Germany) were used for these tests in the ELISA laboratory at both hospitals. In this respect, samples with a cut off index >1 were considered positive for HBsAg, and anti-HCV; and samples with a cutoff index >10 IU/mL were considered positive for anti-HBs.

Statistical Analysis

Statistical analysis was performed by using the SPSS (version 21.0, Armonk, NY, USA) program. A chi-square test was used to evaluate the data. A p value of less than 0.05 was considered statistically significant.

This study was carried out in accordance with the principles of the Helsinki Declaration.

Results

The mean age of the 2214 pregnant women was 28.3±8.26 (14-46) years. The rates of HBsAg seropositivity, anti-HBs positivity, and anti-HCV seropositivity were found to be 1%, 27.8%, and 0.21%, respectively. The seropositivity rates for HBsAg, anti-HBs and anti-HCV according to age groups are shown in Table 1. Three hundred and eighty one (27.8%) out of 1368 pregnant women were found to be anti-HBs-positive. Anti-HBs positivity rate was 54.5% in women aged ≤19 years and 26.5% in those over 19 years of age. The difference was statistically significant (p<0.001).

Discussion

Vertical transmission of hepatitis B infection to an infant can be prevented greatly by providing vaccination, and immunoglobulin within 12 hours of birth and starting antiviral treatment to the mother with high viremia in the third trimester. For this reason, routine screening for HBsAg is recommended during pregnancy in the prenatal period (2,6,8,16). Routine prenatal HCV screening is not recommended because there is no proven vaccine, intervention, or approved treatment to reduce or prevent vertical transmission of HCV infection (12,18,19). In general, screening for HCV infection is recommended for pregnant women having risk factors for hepatitis C, such as HIV infection and intravenous drug use (12,20).

It is known that approximately 5-7 million people in Turkey are active HBV carriers. Carriage rates are reported to be between 4% and 14% varying from cities to cities (21). Epidemiological studies covering the whole country in the previous years showed that the rate of HBsAg positivity was lower in the western regions of the country but was significantly higher in the regions of Central Anatolia, Eastern and Southeastern Anatolia (22). In a review published in 2011, HBsAg seroprevalence was found to be 3.47% in the Aegean and Marmara regions, 4.86% in the Central Anatolia, Mediterranean and Black Sea regions and 6.72% in the Eastern and Southeastern Anatolia regions (23,24). In their study covering Diyarbakır, Batman and Şanlıurfa provinces, Dursun et al. (25) have reported that the rate of HBsAg positivity in city centers was 7.2% in males and 5.3% in females. While the rate of HBsAg positivity in Siirt province was determined as 10% in 2011 (26), it was found to be 12.6% in a study conducted in Batman in 2012 (27). Besides,

Table 1. The rates of hepatitis B surface antigen, anti-hepatitis B surface and anti-hepatitis C virus seropositivity according to age groups

Age groups	Number of patients	Number of HBsAg-positive patients (%)	Number of anti-HCV-positive patients	Anti-HBs positivity rate (%)
≤19	117	1 (0.8)	-	36/66 (54.5)
20-25	701	3 (0.4)	1	229/439 (52.2)
26-30	637	8 (1.3)	1	57/384 (14.8)
31-35	447	3 (0.7)	1	41/280 (14.6)
36-40	256	7 (2.7)	-	17/161 (10.6)
41-45	54	0	-	1/36 (2.8)
≥46	2	0	-	0/1

HBsAg: Hepatitis B surface antigen, HCV: Hepatitis C virus, HBs: Hepatitis B surface

there has been a decline in hepatitis B seroprevalence over the years in our country. Ergunay et al. (28) found a significant decrease (from 12.3% to 5%) in the seroprevalence of hepatitis B between 2000 and 2010. An eight-year seroprevalence study performed in Diyarbakır between 2005 and 2012 reported a significant decline (from 15.9% to 9%) in HBsAg positivity over the years (29). The prevalence of HBsAg seropositivity in children examined before elective surgery in Mardin in 2011 was found to be 0.5% and the most important contribution to this result was suggested to be the vaccination program and preventive measures implemented by the Ministry of Health (30). While HBsAg positivity was found to be 9.6% in Şanlıurfa during the period of 1998-1999 (31), this rate was found to be 2.9% in blood donors in another study performed in Şanlıurfa between 2004 and 2006 (32). In Hakkari province, the HBsAg seroprevalence was detected to be 2.7% in a study conducted in 2006 and it is thought that these low carrier rates can be caused by the fact that Hakkari is a closed and isolated region in terms of both geographical and socioeconomic terms (33). In addition, when we look at the literature, the only study available on the seroprevalence of hepatitis B in Turkey was conducted by Emiroğlu et al. (34) in Şırnak. They studied the prevalence of asymptomatic HBV carriers among soldiers and civilians in Şırnak. The HBsAg positivity rate in this study was determined to be 6.8%. This study was conducted in 1998 and the group of patients was composed of soldiers who came from different regions of the country, therefore, this study cannot exactly reflect the situation in Şırnak province today.

There are also many studies on hepatitis seroprevalence in pregnant women in our country. Bakar and Dane (5) observed that the highest HBsAg seropositivity rate was 9.3% and the HBsAg seropositivity rate was not higher than 6% in the studies conducted in the last 7 years when they examined the studies conducted in Turkey over the last 20 years. In their study, they also found an HBsAg positivity rate of 2.16% in 4037 pregnant women (5). Some studies conducted in recent years on the epidemiology of hepatitis B in pregnant women in our country are reviewed in Table 2.

Table 2. Some studies on epidemiology of hepatitis B in pregnant women in Turkey

	Publication date	City	Number of pregnant women	HBsAg seropositivity rate (%)
Bakar and Dane (5)	2016	Istanbul	4037	2.16
Balık et al. (6)	2013	Rize	5894	5.7
Kasap et al. (9)	2017	Muğla	333	1.8
Kölgelier et al. (16)	2012	Adıyaman	9420	4.7
Dağ et al. (35)	2015	Kırıkkale	8442	2.34
Çiçek et al. (36)	2012	Şanlıurfa	56275	3.5
Motor et al. (37)	2010	Hatay	13065	1.6
Aynıoğlu et al. (38)	2015	Zonguldak	1084	4
Madendağ et al. (39)	2007	Ankara	90531	2.11

HBsAg: Hepatitis B surface antigen

In our study, HBsAg seropositivity rate was found to be 1%, lower than in the other studies. When the factors that may have affected this result are considered, the first thing that comes to mind is that the prevalence of hepatitis B, which declines over the years in the country as a whole, is a reflection on the region as well. In addition, Şırnak province is also a closed and isolated city in terms of geographical and socioeconomic aspects just like Hakkari, and a great change has recently been experienced in the population with the migration of local residents. Due to the social challenges experienced in the region, out-of-province referrals, follow-up and treatment of patients with chronic illnesses requiring further examinations have become difficult. Therefore, it is thought that the migration rate may have increased in the number of individuals with chronic diseases such as hepatitis B.

Hepatitis B vaccine has been included in the childhood vaccination program since 1998 in our country. According to the last application program, it is applied as 3 doses, in months 0, 1, 6. The seropositivity rate of anti-HBs in our country also increases gradually after initiation of national hepatitis B vaccination program. Dağ et al. (35) found that the rate of anti-HBs positivity was 58.51% in patients aged 18-30 years and 29.6% above in those aged 30 years and over. The decline in anti-HBs positivity rate in individuals aged 30 years and over was found to be significant. Again, Balık et al. (6) found that anti-HBs rates were significantly higher in the sub-20-year-old group when compared with other age groups. Turhanoğlu et al. (29) reported that the prevalence of anti-HBs increased from 32.9% to 52.3% in Diyarbakır in an 8-year period. Anti-HBs positivity was found to be 85% in a study conducted on 556 pediatric patients aged 0-16 years who were operated for various reasons between 2008 and 2010 in Mardin (30). In our study, similar to other studies, the seroprevalence of anti-HBs was found to be 54.5% in pregnant women born after 1998, which is the time of introduction of hepatitis B vaccine into routine vaccination program, and the rate was determined to be significantly higher than in the other age groups.

In studies on seroprevalence of anti-HCV performed in our country in 2011, Gönen (40) found an anti-HCV positivity rate of 0.6%, Kölgelier et al. (16) found 0.28%, and Madendağ et al. (39) found the rate of 0.17. In their study conducted in Kocaeli, Çakmak et al. (41) found that the rate of anti-HCV positivity was 0.3% in 3756 pregnant women. In their study, Dağ et al. (35) scanned 8120 pregnant women living in Kırıkkale in terms of anti-HCV, and calculated the anti-HCV seropositivity rate as 0.31% for those aged 18-30 years and 0.59% for those older than 30 years, however, this increase was not regarded as statistically significant (35). The frequency of anti-HCV positivity in Siirt province was determined as 0.6% (26) and in Hakkari province as 1% (33). Anti-HCV positivity was found to be 0.5% in the "Bus Project" study conducted by the VHSD (Viral Hepatitle Savaşım Derneği-Viral Hepatitis Society) between 2009 and 2011, covering all regions, primarily Eastern Anatolia and Southeastern Anatolia (22). Similar

to other studies, anti-HCV positivity rate was found to be 0.21% in our study. These results suggest that HCV infection is not a serious and widespread problem in our country except for certain risk groups.

Conclusion

As a result, it is necessary to screen all pregnant women in our country for HBsAg and to investigate, in terms of HCV, those who are especially suspected to be at risk. Applying hepatitis B vaccination program to infants as soon as they are born, and vaccinating pregnant women with negative anti-HBs results is crucial for increasing hepatitis B immunity in the country. The decline in HBsAg seropositivity over the years after the introduction of national hepatitis B vaccination in our country is also a major indicator of the importance of vaccination.

Ethics

Ethics Committee Approval: Retrospective study.
Informed Consent: Retrospective study.
Peer-review: Internally peer-reviewed.

Authorship Contributions

Concept: M.Ş., Design: M.Ş., Data Collection or Processing: M.Ş., M.Z., A.A.G., B.A.P., Analysis or Interpretation: M.Ş., M.Z., Literature Search: M.Z., M.Ş., Writing: M.Z., M.Ş.

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Research Article

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Seven-year Genotype Distribution Among Hepatitis C Patients in a City in the Central Anatolia Region of Turkey

İç Anadolu Bölgesinde Bir Şehirde Hepatit C Hastalarının Yedi Yıllık Genotip Dağılımları

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ABSTRACT

Objectives: Hepatitis C virus (HCV) is an important viral agent of hepatitis, cirrhosis and hepatocellular carcinoma. In our study, we aimed to determine the HCV genotype distribution among patients with HCV who presented to our hospital in a city in the Central Anatolia Region of Turkey.

Materials and Methods: Results of 480 patients who were positive for HCV RNA and whose serum samples were sent to our laboratory from various inpatient and outpatient clinics of the hospital with a pre-diagnosis of hepatitis C between January 2010 and May 2017 were retrospectively screened. In HCV genotype determination, a commercially available kit (Ampliquality HCV-TS, AB Analitica®, Italy) based on Reverse Line Blot was used in accordance with the manufacturer's recommendations. Genotype distributions were analyzed by years and by age. The first and only one test results of the same patients were evaluated.

Results: Of the patients whose genotyping was made, 260 (54.2%) were female and 220 (45.8%) were male. It was found that 396 (82.6%) of 480 patients were with genotype 1b, 17 (3.5%) - genotype 1a, 15 (3.1%) - genotype 3a, 14 (2.9%) - genotype 1, 9 (1.9%) - genotype 4, 8 (1.7%) - genotype 2, 6 (1.3%) - genotype 2b, 5 (1.0%) - genotype 1a/1b, 4 (0.8%) - genotype 2a/2c, 3 (0.6%) - genotype 4a, 1 (0.2%) - genotype 3, 1 (0.2%) - genotype 5a and 1 (0.2%) patient was with genotype 6.

Conclusion: In chronic HCV patients admitted to our hospital, genotype 1b, which had the highest prevalence in our country, was detected with a rate of 82.6%. In addition, the presence of rare genotypes 5a and 6 in our country has been shown.

Keywords: Hepatitis C, reverse hybridization, genotype

ÖZ

Amaç: Hepatit C virüsü (HCV), hepatit, siroz ve hepatosellüler karsinomun önemli bir viral etkenidir. Çalışmamızda, İç Anadolu Bölgesi'nde bir şehirde, hastanemize başvuran HCV ile enfekte hastaların HCV genotip dağılımlarını saptamayı hedefledik.

Gereç ve Yöntemler: Ocak 2010-Mayıs 2017 tarihleri arasında, laboratuvarımıza hastanenin çeşitli klinik ve polikliniklerinden hepatit C ön tanısı ile serum örneği gönderilen ve HCV RNA pozitifliği olan 480 hastanın sonuçları retrospektif olarak tarandı. HCV genotip tayininde, ters hibridizasyon (Reverse Line Blot) temeline dayanan ticari bir kit (Ampliquality HCV-TS; AB Analitica®, İtalya), üretici firma önerileri doğrultusunda kullanıldı. Genotip dağılımları yıllara ve yaşlara göre incelendi. Aynı hastaların ilk ve tek test sonucu değerlendirmeye alındı.

Bulgular: Genotiplemesi yapılan hastaların 260'ı (%54,2) kadın, 220'si (%45,8) erkek idi. Toplam 480 hastanın 396'sı (%82,6) genotip 1b, 17'si (%3,5) genotip 1a, 15'i (%3,1) genotip 3a, 14'ü (%2,9) genotip 1, 9'u (%1,9) genotip 4, 8'i (%1,7) genotip 2, 6'sı (%1,3) genotip 2b, 5'i (%1,0) genotip 1a/1b, 4'ü (%0,8) genotip 2a/2c, 3'ü (%0,6) genotip 4a, 1'i (%0,2) de genotip 3, genotip 5a ve genotip 6 olarak bulunmuştur.

Sonuç: Hastanemize başvuran kronik HCV hastalarında en sık; ülkemizde de en yüksek prevalansa sahip olan: genotip 1b, %82,6 oranıyla saptanmıştır. Ayrıca, ülkemizde az görülen genotip 5a ve genotip 6'nın varlığı gösterilmiştir.

Anahtar Kelimeler: Hepatit C, reverse hibridizasyon, genotip

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Introduction

Hepatitis C virus (HCV) infection is an important public health problem due to its chronicity risk up to 80% and its complications, such as cirrhosis and hepatocellular carcinoma, that may occur in advanced stages. It is estimated that more than 170 million people are infected with HCV in the world (1).

HCV is the only member of the Hepacivirus genus and belongs to the *Flaviviridae* family. The positive polarity, enveloped RNA genome of 30-60 nm in diameter; encodes 10 proteins (5'-C-E1-E2-p7-NS2-NS3-NS4A-NS4B-NS5A-NS5B-3') (2). Six major genotypes and more than 80 subtypes have been identified since HCV was first diagnosed in the late 1980s. All genomes of the genotypes are different from one another at the rate of ≥30% at the nucleotide level while the sub-types under a certain genotype typically differ at that of 15% to 25% (3,4).

In recent years, a new variant called genotype 7 has been identified in patients in Canada and Belgium (4). HCV genotypes have a worldwide distribution and each genotype is classified into several subtypes with about 20% sequence variation (5).

The RNA dependent RNA polymerase enzyme is prone to make mistakes; it causes mutations in glycoprotein and other genomes. The high mutation rate and genomic heterogeneity of the viral genome has a decisive effect on the effectiveness of treatment (5).

The gold standard of genotyping is whole-genome sequencing analysis. This method is relatively expensive, and instead the protein coding regions such as 5'UTR, NS5B, and core region are used in the new-generation tests (6).

Epidemiologic studies have suggested that HCV genotypes are differently distributed between geographical areas, however, genotype 2 is less prevalent than genotype 1 throughout the world. Genotype 3a is more prevalent in South Asia, Australia, and Iran; genotype 4 in the Middle East, and Middle and North Africa; genotype 5a in South Africa; genotype 6a in Hong Kong and Vietnam; genotype 1b in South and East Europe; genotype 1a in North America and Europe (7,8,9,10).

It has been reported in studies performed until today that genotype 1b was the most prevalent genotype in Turkey (11,12). Determining the prevalence of genotypes and their geographical variation is also important in terms of prognosis and treatment.

In our study, we aimed to determine the genotype distribution among hepatitis C patients followed up in our hospital and the potential variation of HCV transmission in our region within the years and ages.

Materials and Methods

We retrospectively analyzed medical records of 480 patients, who were diagnosed with acute hepatitis C between January 2010 and May 2017 via anti-HCV (ELISA; Abbott Laboratories, the U.S.) and HCV RNA [real-time polymerase chain reaction (PCR); COBAS® TaqMan® 48 Analyzer, Roche Diagnostics, the U.S.]. In determining HCV genotype, a commercial kit (Ampliquality HCV-TS; AB Analitica®, Italy), which is based on Reverse Line Blot and called "line prob assay" (LiPA), was used in accordance with the manufacturer's recommendations. This test is based on the fact that the 5'UTR region of HCV RNA is amplified and hybridized with the oligonucleotide primers of the nucleic acids produced. In this test, all the six major HCV genotypes and certain HCV subtypes (1, 1a, 1b, 1a/1b, 2, 2a/2c, 2b, 3, 3a, 4, 4a, 5a, 6, 6a, or 6b) can be detected. The manufacturer identifies its detection sensitivity as 98.1% and its specificity as 100%. We used bands formed in the way that the probes specific for various HCV genotypes are embedded around the nitrocellulose strips. The genotype distribution was reviewed by years. The first and only test results of the same patients were evaluated.

Statistical Analysis

For the data analysis, a software program, SAS University Edition 9.4, was utilized. In the data evaluation, analysis of variance (ANOVA) and a chi-square test were used; a p value of less than 0.05 was considered statistically significant.

Results

Of the patients whose genotyping was made, 260 (54.2%) were female and 220 (45.8%) were male (Table 1). The average age of the patients was calculated as 59.2. It was found that 396 (82.6%) of the 480 patients were with genotype 1b, 17 (3.5) - genotype 1a, 15 (3.1%) - genotype 3a, 14 (2.9%) - genotype 1, 9 (1.9%) - genotype 4, 8 (1.7%) - genotype 2, 6 (1.3%) - genotype 2b, 5 (1.0%) - genotype 1a/1b, 4 (0.8%) - genotype 2a/2c, 3 (0.6%) - genotype 4a, 1 (0.2%) - genotype 3, 1 (0.2%) - genotype 5a and 1 (0.2%) patient was with genotype 6 (Table 2).

Discussion

The HCV genotypes determine the choice of treatment and the duration of the selected treatment. For HCV genotype 1, either the rate of response to interferon treatment is lower or the risk of progression of hepatocellular carcinoma is higher compared to other genotypes. Response to treatment in infected patients with HCV genotype 1 and 4 is lower than in those with genotype 2 and 3 and treatment duration is longer (5).

Table 1. Distribution of genotypes by sex and mean age

Genotype	1a	1b	1a/1b	1	2a/2c	2b	2	3a	3	4a	4	5a	6	Total (%)
Number	17	396	5	14	4	6	8	15	1	3	9	1	1	480 (100)
Female %	7 41.2	225 56.8	4 80.0	6 42.9	3 75.0	0 0	4 50	3 20.0	1 100.0	1 33.3	5 55.6	0 0	1 100.0	260 (54.2)
Male %	10 58.8	171 43.2	1 20.0	8 57.1	1 25.0	6 100.0	4 50	12 80.0	0 0	2 66.7	4 44.4	1 100.0	0 0	220 (45.8)
Mean Age	60.8	60.4	60.0	65.3	63.3	28.5	56.1	40.7	46.0	51.7	51.1	49.0	74.0	59.2

Currently, there are many methods used for HCV genotyping. However, the gold standard of genotyping is the sequence analysis of the core, E1, NS5b and 5'-UTR regions and phylogenetic analysis made afterwards (6,30,31).

However, the methods of sequence analysis require special equipment and experienced personnel. Therefore, it can be performed only in specific labs. We can count the other methods such as genotyping performed using PCR made by targeting the core or NS5b regions with genotypic primers; genotyping performed using restriction fragment length polymorphism (RFLP) made by clipping 5'UTR region with the restriction enzymes after PCR amplification; genotyping made by targeting 5'UTR, C, E1, NS3, or NS5b; genotyping by reverse hybridization after PCR with type-specific probes; and serotyping performed using C, E2 or NS4 region peptides (30,31).

These methods used in performing HCV genotyping studies can determine major genotype groups but nonetheless, it is stated that their discriminatory power among the subtypes is not as effective as phylogenetic analysis (6).

In our study, we also used a commercial kit based on reverse line blot. In this test, based on the amplification of the 5'UTR region of HCV RNA and hybridization of the resulting nucleic acids with oligonucleotide primers, dark colored bands formed by probes specific for different HCV genotypes attached to nitrocellulose strips were evaluated.

When the four main genotypes (Turkey posthoc) were statistically compared, the average ages of patients with genotype 1 and genotype 2 (p=0.0003), genotype 1 and genotype 3 (p=0.0001) and genotype 1 and genotype 4 (p=0.0452) were found to be different from each other. The age distribution by genotypes is presented in Figure 1. When the four main genotypes were compared by gender using a chi-square test, there was a statistically significant difference among them (p=0.0491). According to our study, the average age of patients with genotype 1 was higher than 60 years (n=432) as in other countries. The highest reported HCV prevalence in the world was in Egypt, where the prevalence of infection increases steadily with age, and high rates of infection are observed among persons in all age groups (32).

In conclusion, it was found that genotype 1b, which has the highest prevalence in Turkey, is also the most prevalent genotype in our region by 82.6%. The high incidence of genotype 1b remained the same within the years, yet the ranking of other genotypes changed. In addition, the presence of genotype 5a and genotype 6, which are rare genotypes in Turkey, has been reported.

In Turkey, there are many studies conducted at various times related to HCV genotyping. These studies have been done using many different methods such as reverse hybridization, PCR, RFLP, sequence analysis, pyrosequencing and LiPA. The results of these studies are presented in Table 3. In their study investigating the distribution of HCV genotypes in 7 regions of Turkey by evaluating 7002 patients with chronic HCV infection using LiPA method, Altindis et al. (13) found that 67.7% of patients had type 1b, 7.7% had type 1, and 5.5% patients had type 1a. In their study including 422 HCV RNA-positive patients performed in Antalya, Sağlik et al. (15) determined that 63.3% of subjects had genotype 1b, 14.7% had genotype 1a and 11.1% had genotype 3a. In their study, Oztürk et al. (18), using the method of pyrosequencing of 639 samples, found genotype 1b in 86.7% and genotype 2 in 9.3% of patients in Antakya and genotype 1b in 55.2% and genotype 3 in 26% in Adana. Altuglu et al. (12) investigated serum samples collected from 535 patients with chronic HCV infection and reported that infection with subtype 1a and subtype 1b was observed in 12.9% and 80.4% of patients, respectively. In studies performed in Turkey, the incidence of genotype 1b has

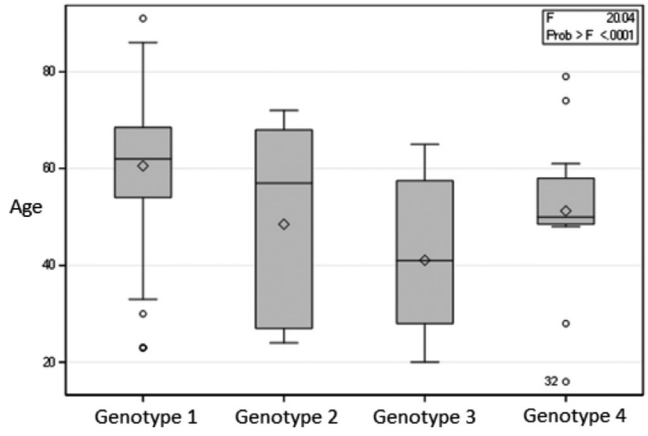

Figure 1. Age distribution by genotypes (ANOVA)

Table 2. Distribution of hepatitis C virus genotypes by years

	Genotype 1				Genotype 2			Genotype 3		Genotype 4		Genotype 5	Genotype 6
Year	**1a**	**1b**	**1a/1b**	**1**	**2a/2c**	**2b**	**2**	**3a**	**3**	**4a**	**4**	**5a**	**6**
2010	0	60	0	3	2	0	0	3	1	0	2	0	0
2011	0	76	1	1	1	1	1	1	0	0	3	0	0
2012	1	75	2	2	0	0	3	1	0	0	1	1	1
2013	1	57	1	1	0	0	3	2	0	0	0	0	0
2014	1	20	0	2	1	1	0	0	0	0	1	0	0
2015	0	23	0	0	0	0	0	1	0	0	1	0	0
2016	9	57	1	4	0	1	1	4	0	3	1	0	0
2017	5	28	0	1	0	3	0	3	0	0	0	0	0
Total	17	396	5	14	4	6	8	15	1	3	9	1	1
Percent (%)	3.5	82.6	1.0	2.9	0.8	1.3	1.7	3.1	0.2	0.6	1.9	0.2	0.2

Table 3. Hepatitis C virus genotype distributions according to studies conducted in Turkey

Location	Time	Researcher	Method	Number	1	1a	1b	1a/1b	2	2a	2b	2a/2c	3	3a	4	4a	5	6	Other
Multi-centered	2009-2014	Altindis et al.(13)	LiPA	7002	7.7%	5.5%	67.7%	0.2%	3.6%	-	0.1%	1.1%	6.7%	-	7.4%	-	0.1%	0.02%	0.13% (mix)
Istanbul	2016-2017	Oral Zeytinli et al. (14)	LİPA	554	-	22.9%	56.3%	0.5%	-	-	-	0.5%	16.9%	-	0.5%	-	-	-	0.1% (1b/4) Unknown (1.9%)
Antalya	2009-2013	Sağlik et al. (15)	LiPA	422	5.4%	14.7%	63.3%	-	2.6%	-	0.9%	-	-	11.1%	1.4%	-	-	-	0.2% (4e), 0.2% (mix)
Kayseri	2010-2011	Kayman et al. (16)	PCR	375	62.4%	-	-	-	3.2%	-	-	-	1.1%	-	32.0%	-	-	-	-
Adana	1996-2013	Kuscu et al. (17)	Different methods	369	78.3%	-	-	-	6.2%	-	-	-	14.6%	-	0.8%	-	-	-	-
Antakya	2010-2012	Oztürk et al. (18)	Pyrosequencing	324	-	0.3%	86.7%	-	9.3%	-	-	-	0.9%	-	2.8%	-	-	-	-
Adana	2010-2012	Öztürk et al. (18)	Pyrosequencing	315	-	3.5%	55.2%	-	14.6%	-	-	-	26.0%	-	0.6%	-	-	-	-
Mersin	2013	Tezcan et al. (11)	LiPA	236	3.8%	1.7%	84.7%	2.1%	0.4%	-	1.3%	0.4%	-	4.2%	0	0.8%	-	0.4%	-
Bursa	2010-2012	Agca et al. (19)	Reverse hybridization	231	92.6%	-	-	-	0.4%	-	-	-	3.9%	-	3.1%	-	-	-	-
Izmir	2005-2010	Altuglu et al. (12)	RFLP	215	-	12.9%	80.4%	-	1.5%	-	-	-	3.7%	-	1.5%	-	-	-	-
Sivas	2008-2009	Celik et al. (20)	Reverse hybridization	178	-	9.0%	88.2%	-	0	1.12%	-	-	1.7%	-	-	-	-	-	-
Nevşehir	2011-2014	Borcak et al. (21)	PCR	170	45.1%	-	37.0%	-	14.5%	-	-	-	1.2%	-	0.6%	-	-	-	-
Antalya	2011-2013	Çekın et al. (22)	RFLP- Sequence analysis	148	8.8%	12.8%	60.8%	-	4.1%	-	-	-	11.5%	-	2.0%	-	-	-	-
Kayseri	2011	Gökahmetoğlu et al. (23)	Pyrosequencing	146	5.5%	3.4%	52.7%	-	-	2.7%	-	-	-	-	21.9%	4.8%	-	-	8.9% (4d)
Eastern Anatolia Region	2011-2014	Aktas et al. (24)	Pyrosequencing	108	-	8.3%	87.0%	-	-	-	-	-	-	3.7%	-	-	-	-	1% (4d)
Kahraman-maraş	2010-2012	Kirisci et al. (25)	PCR	100	60.0%	-	-	-	-	-	-	-	40.0%	-	-	-	-	-	-
Manisa	2002-2005	Sanlidag et al. (26)	Sequence analysis	100	-	2.0%	90.0%	-	-	2.0%	-	-	-	-	-	5.0%	-	-	-
Diyarbakır	2007-2008	Ozbek et al. (27)	LiPA	74	4.1%	-	87.8%	-	2.7%	-	-	-	2.7%	2.7%	-	-	-	-	-
Adıyaman	2013-2016	Akgun et al. (28)	Sequence analysis-PCR	71	4.2%	8.4%	71.8%	-	-	-	11.3%	-	-	4.2%	-	-	-	-	-
Konya	2010-2012	Demircili et al. (29)	LIA	65	-	1.5%	90.8%	3.1%	-	-	-	1.5%	-	1.5%	1.5%	-	-	-	-
Gaziantep	2010	Karslıgil et al. (30)	Sequence analysis	51	-	9.8%	78.4%	-	-	7.8%	-	-	-	2.0%	-	-	-	-	2% (4c)

LiPA: Line prob assay, PCR: Polymerase chain reaction, RFLP: Restriction fragment length polymorphism, LIA: Line immunoassay

been reported in the range of 37-90.8% and the most commonly detected genotype was found to be genotype 1b. It is followed by genotype 1a, genotype 4, and genotype 3 respectively. Genotype 4a, genotype 5 and genotype 6, which are rare genotypes, were detected at various rates.

Conclusion

In this study, we determined the distribution of HCV genotypes in our region, which is crucial for treatment regulations and in identifying prognosis and made a contribution to the epidemiologic data in the way of evaluating its trend within the last seven-year period.

Ethics

Ethics Committee Approval: There is no ethics committee approval because the study is retrospective.

Informed Consent: Since the study was retrospective, the patient's consent was not taken.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: U.T., Design: U.T., M.B., Data Collection or Processing: B.F., Analysis or Interpretation: M.Ö., Literature Search: B.S.G., Writing: U.T.

Conflict of Interest: There is no conflict of interest between authors.

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Research Article

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Should Hepatitis C Virus Antibody Be Used for Screening Purposes?

Hepatit C Virüs Antikoru Tarama Amacıyla Kullanılmalı Mı?

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ABSTRACT

Objectives: In this study, hepatitis C virus (HCV) RNA results were retrospectively investigated in patients with reactive HCV antibodies.
Materials and Methods: HCV antibody test was performed ELISA method. Enzyme linked fluorescence assay was used as a different method. The quantitative HCV RNA test was carried out by AmpliPrep/COBAS TaqMan HCV test.
Results: HCV antibody reactivity was detected in 358 of 28081 samples, 255 samples collected from 358 anti-HCV positive-patients and were tested for HCV RNA were included in the study. The detected HCV RNA positivity rate was 5.8% in patients who had low titer reactive HCV antibody and 76.3% in patients, who had high titer reactive HCV antibody. Nine of 23980 samples, which were screened for preoperative preparation, had reactive HCV RNA. One hundred thirty seven of 4101 samples, which were obtained for diagnostic purposes in the gastroenterology and infectious diseases clinics, were HCV RNA positive.
Conclusion: Positive results should be confirmed with HCV RNA testing; if possible, testing for HCV antibodies with other methods, before HCV RNA testing, will decrease the number of tests using molecular methods; and screening for HCV antibodies is not cost-effective especially in populations with a low prevalence of HCV antibody positivity.
Keywords: Hepatitis C virus antibody, screening, cost effectiveness

ÖZ

Amaç: Bu çalışmada, reaktif hepatit C virüsü (HCV) antikorları olan hastalarda HCV RNA sonuçları retrospektif olarak incelendi.
Gereç ve Yöntemler: HCV antikor testi ELISA yöntemi ile çalışıldı. Enzim Bağlantılı Floresans testi farklı bir yöntem olarak kullanılmıştır. Kantitatif HCV RNA testi AmpliPrep/COBAS TaqMan HCV testi ile gerçekleştirildi.
Bulgular: HCV antikoru için toplam 28081 numunenin 358'inde reaktivite tespit edildi. Çalışmaya anti-HCV antikoru pozitif 358 hastadan HCV RNA çalışılan 255 hasta örneği dahil edildi. Düşük titrede reaktif HCV antikoru olan hastalarda %5,8 ve yüksek titrede reaktif HCV antikoru olan hastalarda %76,3 HCV RNA pozitifliği saptandı. Preoperatif hazırlık kapsamında test edilen 23980 örneğin 9'unda HCV RNA pozitifti. Gastroenteroloji ve enfeksiyon hastalıkları kliniklerinden tanı amaçlı olarak gelen 4101 örneğinin 137'sinde HCV RNA pozitif idi.
Sonuç: Pozitif sonuçlar HCV RNA ile doğrulanmalıdır, eğer imkan varsa HCV RNA bakılmadan önce farklı bir yöntemle HCV antikoru çalışılmasının moleküler yöntemle çalışılacak test sayısını azaltacağı ve tarama amaçlı HCV antikoru bakılmasının özellikle düşük prevalanslı toplumlarda maliyet etkin olmadığı görüşüne varılmıştır.
Anahtar Kelimeler: Hepatit C virüsü antikoru, tarama, maliyet etkinliği

Şafak B, Tombak Ö, Eren Topkaya A. Should Hepatitis C Virus Antibody Be Used for Screening Purposes? Viral Hepat J. 2018;24:18-20.

Introduction

Hepatitis C virus (HCV) can cause both acute and chronic hepatitis, ranging in severity from a mild condition lasting only a few weeks to a serious, lifelong illness. Acute HCV infection is usually asymptomatic and progresses only very rarely to a life-threatening disease. The virus is spontaneously regresses without any treatment within 6 months in approximately 15% to 45% of infected persons. The remaining 60% to 80% of infected persons will develop chronic HCV infection. 15% to 30% of these patients with chronic HCV infection are at the risk of developing liver cirrhosis within 20 years (1). The rate of mortality due to HCV-related diseases (mostly cirrhosis and hepatocellular carcinoma) shows a continuous increase (2). Central and South Asia, North

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Africa and Middle East have the highest HCV prevalence. The reported rate of the anti-HCV positivity is 1.6% worldwide and 0.4%-2.1% in our country (3). Laboratory tests play an important role in the diagnosis and follow-up of patients with chronic HCV infection. HCV antibody reactivity at the limit values is a serious problem for diagnostic laboratory practice. In the guidelines for HCV infection tests, HCV RNA analysis is recommended to confirm the HCV antibody reactivity and pseudo-reactivity (2,4).

In this retrospective study, HCV RNA results of patients with low and high reactivity of HCV antibody referred for screening and diagnostic purposes were evaluated.

Materials and Methods

The results of the samples referred for HCV antibody screening between January 2016 and July 2017 were re-evaluated with a retrospective study design. HCV RNA results of patients with low titer (≥1- <5 sample cut-off = S/CO) and high titer (≥5 S/CO) HCV antibodies for studied screening and diagnostic purposes were investigated in this study. HCV antibody test was first performed using enzyme-linked immunosorbent assay (ARCHITECT i2000 analyser; Abbott diagnostic, IL, USA). According to the manufacturer's recommendations, samples with a signal to cut-off ratio (S/CO) value of ≤ smaller than 1 were considered as non-reactive, while those with an S/CO value of ≥ greater than or equal to 1were considered reactive. Enzyme-linked fluorescence immunoassay (ELFA) (mini VIDAS; BioMérieux, Marcy l'Etoile, France) was used as a different method for samples with low reactivity. The quantitative HCV RNA assay was carried out with the COBAS AmpliPrep/COBAS TaqMan HCV Quantitative test v2.0 (Roche Molecular Systems, USA).

Results

Reactivity was detected in 358 of 28081 samples (1.27%) which were analyzed for HCV antibody in our laboratory. Two hundred and fifty-five samples collected from 358 anti-HCV antibody positive patients and were tested for HCV RNA, were included in the study. The detected HCV RNA positivity rate was 5.8% (4/69) in patients who hadlow titer reactive HCV antibody and 76.3% (142/186) in patients, who hadhigh titer reactive HCV antibody. The test was repeated by another method (ELFA) in 30 patients with low titer HCV antibody. In 12 of these patients HCV antibodies were found to be non-reactive. All patients, who were screened for HCV antibody with ELFA, were HCV RNA negative. Only 41 (0.17%) of 23980 samples, which were screened for the preoperative preparation, had reactive HCV antibody. Nine of these were HCV RNA positive. Two hundred and fourteen (5.22%) of 4101 samples, which were obtained for diagnostic purposes in the gastroenterology and infectious diseases clinics, were reactive and 137 of them were HCV RNA positive.

HCV antibody and HCV RNA results for screening and diagnostic purposes are shown in Table 1.

Discussion

Laboratory tests have important roles in the diagnosis of HCV infection and monitoring of patients. Reactive test results for HCV antibodies, with values close to borderline limits, constitute a serious problem for routine diagnostic laboratories. Most of them are observed to be false positive results (5). In populations with low seroprevalence, false positivity is observed in blood and organ donors and in individuals with positive tests for rheumatoid factor (6). The incidence of HCV infection in Turkey is low with a rate of 1% (7). Therefore, in our country, there is a high probability of false positivity. It is suggested that repeated results of reactive HCV antibodies can be associated with current HCV infections, history of HCV infections or false-positive hepatitis C antibodies. HCV RNA testing is recommended to detect any present infection (4). In our study, we also used HCV RNA test. A correlation between S/CO for HCV antibodies and HCV infections has been reported. A S/CO for determining the true HCV antibody positivity with a rate of 95% was determined to be ≥5.0 for Architect Kit (4). Another study reported a positive predictive value of 95.4% when a S/CO of 5.0 was taken for Architect Kit (8). A study conducted in our country suggested that the use of a S/CO of ≥5.0 would be more appropriate in identifying HCV infections (9). Two hundred and fifty-five samples, which have been tested for HCV RNA and with S/CO values of ≥1-<5.0 and ≥5 for HCV antibodies, have been included in our study. False positivity has been reported to be common in women and in the elderly due to their susceptibility to autoimmune diseases and infections, leading to decline HCV antibody titrations in years (5). Ecemiş et al. (9) determined HCV RNA positivity in 2 (3.8%) out of 52 patients with a S/CO value of ≤5 for HCV antibodies. Another study reported HCV RNA positivity in 3 (1.4%) out of 215 (0.9%) samples selected out of 25029 samples with S/CO values between 1 and 5 for HCV antibodies (5). In our study, HCV RNA antibody was identified in 4 (5.8%) out of 69 samples, in which low titer reactivity was detected and which were tested for viral load. On the other hand, HCV RNA positivity was identified in 142 (76.3%) out of 186 samples with high titer reactive HCV antibody. Various studies have reported HCV RNA positivity rates of 43.8-68% in patients with identified HCV antibody reactivity (10,11,12,13). In our study, out of 255 HCV antibody reactive patients 146 (57.3%) were identified with HCV RNA positivity. Given these results, it is concluded that especially samples with low titer reactive HCV antibodies may be false positives and that all positive results should be confirmed by HCV RNA testing.

Table 1. Hepatitis C virus RNA results of anti-Hepatitis C virus reactive patients

	Low titer anti-HCV positive (%)	HCV RNA positive (%)	High titer anti-HCV positive (%)	HCV RNA positive (%)	Total anti-HCV positive (%)	Total HCV RNA positive (%)
Screening anti-HCV (23980)	29 (0.12)	-	12 (0.05)	9 (0.04)	41 (0.17)	9 (0.04)
Diagnostic anti-HCV (4101)	40 (0.98)	4 (0.1)	174 (4.2)	133 (3.2)	214 (5.2)	137 (3.3)
Total (28081)	69 (0.25)	4 (0.01)	186 (0.6)	142 (0.5)	255 (0.9)	146 (0.52)

HCV: Hepatitis C virus

If distinguishing between true and false positivity is required and if multiple tests reveal positivity, it is emphasized that another type of HCV antibody test should be performed (4). In our study, 30 (all them were negative for HCV RNA) out of 69 samples with multiple HCV antibody test results with Architect i2000, and in which low titer reactivity was detected, were tested by VIDAS. Out of a total of 30 samples, 12 were detected to be non-reactive, whereas, 18 were detected to be reactive. Given these results, it is concluded that in almost half of the patients there was no need for HCV RNA testing. It is suggested that in cases with multiple test results showing reactivity, testing with another method for HCV antibodies may help reduce any unnecessary testing for HCV RNA.

A study conducted in Germany reported 0.04% positivity in patients who were screened pre-operatively. From the economic perspective, it was highlighted that routine preoperative screening should not be performed due to low rates of reactivity, and that screening only patients with risk factors would be as safe as screening all patients, and this might help reduce the costs (14). HCV screening is not recommended for preoperative preparations. However, it is recommended if exposure to HCV is in question and it is recommended in populations with high seroprevalence (2% to 5% of HCV antibody) (2,4,15). The consensus report of the Study Group for Viral Hepatitis of the Turkish Society of Clinical Microbiology and Infectious Diseases-states that routine HCV screening tests are not required in our country as the prevalence of HCV is low and that HCV should be screened only in risk groups (3). In our study, the prevalence of HCV antibody positivity was determined to be 1.27%. The incidence of HCV antibody positivity was found to be 0.9%. Of 23980 samples tested for HCV antibodies for screening, 114 (0.47%) of them were identified to be reactive for the first test. It is concluded that screening tests are unnecessary in the context of pre-operative preparations as it has been reported that they should not be performed because of being costly and, as they have not been recommended in the guidelines. In addition, in our study we also found low positivity rates.

Conclusion

We are of the following opinions that in accordance with the Centers for Disease Control and Prevention recommendations, positive results should be confirmed with HCV RNA testing; if possible, testing for HCV antibodies with other methods, before HCV RNA testing, will decrease the number of tests using molecular methods; and screening for HCV antibodies is not cost-effective especially in populations with low prevalence of HCV antibody positivity.

Ethics

Ethics Committee Approval: Retrospective study.
Informed Consent: Retrospective study.
Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Ö.T., Concept: B.Ş., Design: B.Ş., Data Collection or Processing: B.Ş., A.E.T., Analysis or Interpretation: A.E.T., Literature Search: B.Ş., Writing: B.Ş., Ö.T., A.E.T.

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Epidemiology of Hepatitis C in North Cyprus

Kuzey Kıbrıs'ta Hepatit C Epidemiyolojisi

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ABSTRACT

Hepatitis C virus (HCV) is known as the main etiological agent of chronic liver disease, cirrhosis and hepatocellular carcinoma. Studies on the Turkish Republic of North Cyprus (TRNC) population have reported that the HCV prevalence was between 0% and 1%. The low prevalence of HCV in the TRNC is a result of the small island population and the fact that HCV-positive individuals were not allowed to reside in the TRNC until 2017. However, it is likely that there will be an increase in HCV seroprevalence going forward due to relapses and cases of illegal immigration. The aim of this study was to review the HCV epidemiology in the TRNC in the light of the current data.
Keywords: Prevalence, hepatitis C virus infection, North Cyprus

ÖZ

Hepatit C virüsü (HCV), kronik karaciğer, siroz ve hepatosellüler karsinoma etkeni olduğu bilinmektedir. Kuzey Kıbrıs Türk Cumhuriyeti'nde (KKTC) yapılan çalışmalar prevelansın %0-1 arasında olduğunu göstermektedir. Ülkemizde HCV insidansının düşük olmasının nedeni nüfus olarak küçük bir ada olmamız ve HCV pozitif olgulara 2017 yılına kadar KKTC'de ikamet etme izninin verilmemesi olduğunu ve HCV için yapılan düzenlemenin sonucunda relaps olguların ve ayrıca adada illegal kesimin bulunduğu göz önüne alınırsa HCV seroprevelansında da artış olabileceğini düşünmekteyiz. Bu makalede, KKTC'deki HCV epidemiyolojinin güncel literatür ile birikte gözden geçirilmesi amaçlanmıştır.
Anahtar Kelimeler: Prevalans, hepatit C virüs enfeksiyonları, Kuzey Kıbrıs

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Introduction

Hepatitis C virus (HCV), a hepatotropic RNA virus, was discovered in 1989 (1). HCV is a small, enveloped, single-stranded, positive sense RNA virus belonging to the *Flaviviridae* genera *Pegivirus* (1,2,3). HCV infection that causes chronic liver diseases (4) as well as acute and chronic hepatitis, cirrhosis and hepatocellular carcinoma is a universal health problem (3). The World Health Organization (WHO) reported that there were 71 million people with chronic HCV infection in 2017 (5). The global prevalence of anti-HCV was estimated at 1.6% for all ages corresponding to 115 million past viraemic infections (6).

Previous studies have found that HCV seroprevalence increased to 2.8% equating to more than 185 million infections worldwide (7,8). Additionally, HCV is now considered to be pandemic and the WHO reported a world-wide prevalence of 3% (9). The WHO reported that areas with a high incidence of HCV infection included the Eastern Mediterranean Region (62.5 per 100.000) and the European Region (61.8 per 100.000) in 2017 (5).

Cyprus is a small island and is situated at the geographic crossroads of the three continents: Europe, Africa, and Asia. Furthermore, the rate of tourist and immigrant arrivals from Eastern Europe, the former Soviet Republics, Africa and Southeast Asia is relatively high (10). The majority of residents living in Cyprus belong to two ethnic groups, namely Turkish Cypriots and Greek Cypriots. The island has been divided into two regions due to the conflict between the two communities. As a result of this conflict, the Northern part of the island has since been under the control of its own government, and is called the Turkish Republic of Northern Cyprus (TRNC). The TRNC is officially recognised only by Turkey. Not only has Northern Cyprus become a destination for casino tourism and entertainment, but the country has experienced an influx of sex workers, particularly from Eastern Europe and

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the former Soviet Republics. In addition to the influx of visitors resulting from the growth in tourism, there are now 18 universities in the TRNC. The TRNC Ministry of Education has reported that there were 93.292 university students in the country in 2017, 53.135 of whom were Turkish and 27.538 were students of other nationalities.

The epidemiology and genotypes of the HCV infection in the TRNC are reviewed in this article, based on the published literature on this subject.

Prevalence and Risk Factors for Hepatitis C Virus Infection in Northern Cyprus

Cyprus is located in the Eastern Mediterranean Region and has a total population of approximately 800.000. Each year, the population is affected by the influx of immigrants, mainly due to tourism and politically displaced persons (2). The Northern Cyprus population has many similar characteristics to the population of Turkey, while there is also a close relationship with Southern Cyprus and Greece (11).

The Middle East region geographically consists of countries in Southwest Asia and parts of North Africa. In total, 17 million people are infected with chronic hepatitis C and 800.000 persons become infected with HCV each year in the Mediterranean Region (1). The epidemiology of HCV has been changed as a result of globalisation, based on the factors of modern transmission and worldwide human migration (2). The prevalence of the HCV infection varies according to different countries in the Middle East. In countries in the Middle East region such as Algeria, Egypt, Iran, Iraq, Israel, Jordan, Kuwait, Lebanon, Libya, Morocco, Oman, Palestine, Qatar, Saudi Arabia, Syria, Tunisia, Turkey, United Arab Emirates, and Yemen, the estimated prevalence of HCV in the general population is 2.7% (7). Another study indicated that the prevalence in the Middle East was between 1% and 4%, except for Egypt (3). The countries with the highest prevalence were Egypt (14.7%), Iraq (3.2%) and Yemen (2.2%). On the other hand, the lowest prevalence rates were reported to be in Qatar (0.9%) and Turkey (1.0%) (7).

The prevalence of HCV infection has been reported to be 1.6% in the Turkish population (12). Additionally, HCV prevalence has been reported to be between 1% and 1.5% in blood donors in Turkey (11). The HCV prevalence in Egypt has been reported to be approximately 14.7%, which means that globally, it has the highest known prevalence rate of HCV (3). Additionally, HCV RNA prevalence rates ranged from 0.4% in countries such as Austria, Cyprus, Denmark, France, Germany and the United Kingdom to 2.9% in Romania according to a study by Lazarus et al. (13) in 2016. Epidemiological studies in Greece have suggested that the prevalence rate ranges between 0.5% and 2% (1).

Süer et al. (14) investigated the HCV seroprevalence among 1.500 blood donors in Northern Cyprus and reported that none of the donors were anti-HCV-positive. Altındis et al. (11) reported that the prevalence of HCV in Northern Cyprus was similar to that in Turkey and Greece. A study including soldiers from Turkey, blood donors from Northern Cyprus and soldiers from North Cyprus, reported an anti-HCV prevalence of 0.46% (11). Güler et al. (15) reported that the prevalence of anti-HCV was 0.9% among 16.400 individuals in Northern Cyprus. The present research studied the prevalence of HCV in thalassemia major patients and found that there were 11 HCV-positive patients in the sample group. Tınazlı et al. (16) reported that HCV antibodies were negative in 154 patients who had been admitted to a rheumatology ward in Northern Cyprus (16). These results indicated that the prevalence rate of HCV in Northern Cyprus was similar to the rates in Turkey and Greece.

Distribution of Genotypes of Hepatitis C Virus Infection in Northern Cyprus

HCV has seven genotypes according to the sequence of the viral genome (3,7). Each genotype contains multiple subtypes, such as subtypes 1a and 1b (3). Genotype 1-3 has a worldwide circulation. On the other hand, genotypes 4-6 are restricted geographically and endemic infection is only found in specific countries (10). Additionally, only one genotype 7 infection has been reported in a Central African immigrant in Canada (7).

Worldwide, genotype 1 was identified in 46% of all infections, while the second most common was genotype 3 in 22% of infections, followed by genotypes 2 and 4 in 13% of infections each. Subtype 1b was reported for 22% of all infections (6). Subtypes 1b and genotype 2 are related with blood transfusions, specifically in older patients. Subtypes 1a and 3a are associated with transmission through injecting drug (2,10).

Although genotypes 1, 2 and 3 have been reported worldwide, genotypes 4-6 have a more restricted distribution pattern (2). It has been reported that genotype 1 was prevalent in Australasia, Europe, Latin America and North America. Genotype 3 has been identified in 40% of all infections in Asia. Furthermore, genotype 4 has been frequently reported in North Africa and the Middle East, except Egypt. In Egypt, genotype 1 accounts for 46% of infections (6). HCV genotype 5 is most commonly found in South Africa (3). Finally, HCV genotype 6 has been reported to be prevalent in Southeast Asia (17).

HCV genotype 1 is commonly found in non-Arab Middle Eastern countries, including Turkey (82%), Israel (68%), Cyprus (68%), and Iran (55%) (3). Triantos et al. (1) reported that the genotype distribution in Greece was as follows: genotype 4 (13%), genotype 2 (9%), genotype 5 (1.2%), and genotype 6 (0%) (1). In Turkey, the most common genotype was genotype 1b (67.7%), followed by genotype 1 (7.7%), genotype 4 (7.3%) and genotype 3 (6.7%) (12). Furthermore, subtype 1b was reported in Turkey, which may have been introduced to the country via virus transmission from Europe (18).

Altındis et al. (11) reported that genotype 1b (924%) was the most commonly found genotype in their Northern Cyprus study group, which included civilians, Turkish soldiers and Northern Cyprus soldiers (11). A study analyzing the genetic heterogeneity of HCV infection in Cyprus found that 5 of the 6 known HCV genotypes, which include genotypes 1 and 4, were found in intravenous drug users with the 2k/1b recombinant strain (2). The most prevalent HCV genotype strain was genotype 1 (68%), followed by genotype 3 in Cyprus, which is similar to that in the non-Arabic countries. The HCV genotype pattern may be associated with strains brought to the country by repatriated Cypriots, Cypriots who have visited other countries and tourists (3).

Treatment of Hepatitis C Virus Infection in Cyprus

Effective antivirals are used in accordance with the established guidelines in the TRNC. Until January 2017, persons who were not citizens of the TRNC were not permitted to remain in the country if anti-HCV positivity was detected. As a result of the legislative amendments implemented in 2017, HCV treatment is now permitted in the TRNC if the infected individual either pays for the treatment or seeks treatment in the country of origin. If HCV-positive cases are successfully treated in the individuals' own country and obtain an HCV RNA negative result certificate, a TRNC residency permit can be granted.

Conclusion

Various studies and reports by the WHO have stated that HCV infections would be eradicated by 2030. In the TRNC, Altındis et al. (11) found HCV seroprevalence at a moderate frequency because of the fact that the case groups investigated in the study were predominantly Turkish soldiers. However, in the study group that Güler et al. (15) investigated, HCV seroprevalence was found to be low because the case group included TRNC citizens. The authors believe that the low prevalence of HCV in the TRNC was a result of the small island population and that individuals who are HCV-positive were not allowed to reside in the TRNC until 2017. Nevertheless, it is believed that there will be an increase in HCV seroprevalence going forward as well as an increase in the seroprevalence of hepatitis B surface antigen due to changes in the regulations surrounding residency permits in the TRNC in 2009. Furthermore, it is expected that there will be an increase in HCV seroprevalence due to relapses and cases of illegal immigration.

Ethics

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.G., K.S., Concept: M.G., K.S., Design: M.G., K.S., Data Collection or Processing: M.G., K.S., Analysis or Interpretation: M.G., K.S., Literature Search: M.G., K.S., Writing: M.G., K.S.

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