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ÖZGÜN ARAŞTIRMA/ORIGINAL ARTICLE

Somali'de Bulunan "Mogadişu Türkiye Recep Tayyip Erdoğan Eğitim ve Araştırma Hastanesi" Kliniklerine Başvuran Hastalarda Hepatit B ve Hepatit C Virüs Enfeksiyonu Seroprevalansının Retrospektif Olarak Değerlendirilmesi

Evaluation and Comparison of the Seroprevalence of Hepatitis B and Hepatitis C Virus Infection in Patients Admitted to Clinics at the "Mogadishu, Turkey Recep Tayyip Erdogan Training and Research Hospital" in Somalia

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Geliş Tarihi/Received: 10.06.2021
Kabul Tarihi/Accepted: 23.09.2021
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Anahtar Sözcükler:
HBV
HCV
Seroprevalans
Somali

Key Words:
HBV
HCV
Seroprevalence
Somalia

ÖZ

Amaç: Somali Mogadişu'daki Türk hastanesine başvuranların hepatit B ve hepatit C seroloji bulgularını değerlendirmeyi ve mevcut prevalansının belirlenmesi.

Gereç ve Yöntemler: Hastaların demografik bulguları ve hepatit test sonuçları (HBsAg, anti-HBs antikoru ve anti-HCV) dosyalarından geriye dönük olarak kaydedildi.

Bulgular: Çalışmamıza yaş ortalaması 34 (31/61) yıl olan 75.903 (%49,8) erkek ve 76.363 (%50,2) kadın olmak üzere toplam 152.266 hasta dahil edildi. Anti-HCV için test edilen 67.749 hastanın 1.278'i (%1,9) pozitif bulundu. 27.208 hastanın (%32,2) HBV için doğal veya aşı bağışıklığı geliştirdiği bulundu. Anti-HCV (+) olanların genel olarak 55 yaşından büyük, HBsAg (+) olanların ise genellikle 55 yaşından küçük olduğu [OR: 6,02 (5,28-6,87): %95, CI] bulundu.

Sonuç: Çalışmamızda Somali popülasyonunda HBsAg ve anti-HCV seroprevalansının (sırasıyla %8,2 ve %1,9) halen istenilen seviyelerin üzerinde olduğu söylenebilir. Anti-Hbs antikor düzeylerinin %32,2 düzeyinde olması, aşılama programlarının geliştirilmesinin ve yaygınlaştırılmasının önemini vurgulamaktadır.

ABSTRACT

Objective: To evaluate hepatitis B and hepatitis C serology findings and to determine the current prevalence of those who had applied to the Turkish hospital in Mogadishu, Somalia.

Material and Method: The demographic findings and hepatitis test results (HBsAg, anti-HBs antibody, and anti-HCV) of the patients were recorded retrospectively from their files.

Results: A total of 152,266 patients, 75,903 (49.8%) male and 76,363 (50.2%) female, with a mean age of 34 (31/61) years, were included in our study. 1,278 (1.9%) of 67,749 patients who were tested for anti-HCV were found to be positive. 27,208 patients (32.2%) were found to have developed natural or vaccine immunity for HBV. It was found that those with anti-HCV (+) were generally older than 55 years and that those with HBsAg (+) were generally younger than 55 years [OR: 6.02 (5.28-6.87): 95%, CI].

Conclusion: In our study, it can be said that HBsAg and anti-HCV seroprevalence (8.2% and 1.9%, respectively) in the Somalia population is still above desired levels. The fact that anti-Hbs antibody levels are at 32.2% underscores the importance of the development and popularization of vaccination programs.

Introduction

Acute and chronic viral hepatitis are important public health problems, especially in developing countries. According to the World Health Organization (WHO), two billion people worldwide (one third of the global population) have been infected with the hepatitis B virus (HBV), and more than 240 million are inactive carriers. However, hepatitis C virus (HCV) infection, for which a vaccine protection program has not been developed yet, has become a significant viral hepatitis factor. Sub-Saharan Africa accounts for almost a fifth of infections worldwide, and more than six million people in Latin America are thought to be infected with HCV (1).

It is expected that HBV and HCV seroprevalence will undergo a dynamic change in parallel with the development of preventive and curative services in the health system in Somalia over recent years. In this study, we there fore aimed to evaluate hepatitis B and hepatitis C serology findings and to determine the current prevalence of those, who had applied to the Turkish hospital in Mogadishu, Somalia.

Material and Method

Permission for the study was obtained from the Non-Invasive Clinical Research Ethics Committee of the The Noninvasive Clinical Research Ethics Committee of Mogadishu, Turkey Recep Tayyip Erdogan Training and Research Hospital (MSTH/813). It was aimed to evaluate the results of hepatitis markers obtained from patients admitted between January 2017 and June 2019 to the Somalia Mogadishu Turkey Recep Tayyip Erdogan Training and Research Hospital. The demographic findings of the patients, antigen and antibody test results for HBV and HCV infection (HBsAg, anti-HBs antibody, and anti-HCV), liver function test were recorded retrospectively from the patient files. Patients whose HBsAg and Anti-HCV seroprevalence were included in the prevalence calculation were classified as being either active disease or inactive carriers. The presence of the anti-HBs antibody alone was evaluated as previous hepatitis b infection or immunization with vaccine.

Serology

HBsAg II, anti-HCV II and anti-HBs II tests were performed according to the manufacturer's recommended standard procedures. The mandatory dilution algorithm of the assay is an initial measurement of a 1:100 (for the Elecsys 2010 and Cobas e411, Roche Diagnostics GmbH, Mannheim, Germany). HBsAg, anti-Hbs antibody and anti-HCV concentrations were measured by means of an electro-chemiluminescence immunoassay (ECLIA) (Cobas e411, Roche Diagnostics, Mannheim, Germany). Serum HBsAg was determined qualitatively. The signal-to-cut-off signal (S/Co) ratio was used for interpretation of the initial results. Values higher than 1.00 (≥1.00) indicated a reactive result, values between ≥0.90 and samples with nonreactive and results considered to be negative for HBsAg and Anti-HCV did not require further testing. All tests including calibrations and controls were performed and interpreted in accordance with the manufacturers' recommendations.

Statistical Analysis

The SPSS 26.0 (IBM Corporation, Armonk, New York, United States) program was used for analysis of variables. The compatibility of univariate data to normal distribution was evaluated using the Kolmogorov-Smirnov test. The Mann-Whitney U test was used together with Monte Carlo results to compare two independent groups with each other according to the quantitative data. In the comparison of categorical variables, the Pearson Chi-Square test was tested with Exact results and the column proportions were compared with each other and expressed according to the Benjamini-Hochberg corrected p-value results. The Odds ratio was used with 95% confidence intervals to show how many times those with a risk factor were higher than those without. Sensitivity, specificity, positive predictivity and negative predictivity ratios for the relationship between the classification separated by the cut-off value calculated according to the variables of the groups and the actual classification were analyzed and expressed by ROC (Receiver Operating Curve) curve analysis. Quantitative variables were expressed as median (percentile 25 / percentile 75) in the tables, while categorical variables were presented as n(%).Variables were examined at a 95% confidence level, and a p-value of less than 0.05 was considered to be significant.

Results

A total of 152,266 patients, 75,903 (49.8%) male and 76,363 (50.2%) female, with a mean age of 34 (31/61) years, were included in our study.

Out of 84,505 patients tested for HBV, 6,893 (8.2%) were found to have HBsAg (+). 1,278 (1.9%) of 67,749 patients, who were tested for anti-HCV, were found to be positive. 27,208 (32.2%) patients were found to have developed immunization through natural immunization or vaccine for HBV (Table 1).

Table 1. Demographic results of HBsAg (+) or anti-HCV (+) patients.

	Total (n=8171)	Anti-HCV (+) (n=1278)	HBsAg (+) (n=6893)	*P*
Gender	n (%)	n (%)	n (%)	
Female	3376 (41.3)	495 (38.7)	2881 (41.8)	0.041
Male	4795 (58.7)	783 (61.3)	4012 (58.2)	1.13 (1.01 - 1.28) or
	Median (Q1 / Q3)	**Median (Q1 / Q3)**	**Median (Q1 / Q3)**	
Age (year)	47 (31 / 61)	65 (51 / 73)	43 (30 / 59)	<0.001
ALT (IU/L)	23 (16 / 35)	27 (18 / 43)	22 (16 / 33)	<0.001
AST (IU/L)	27 (21 / 39)	34 (23 / 61)	26 (21 / 36)	<0.001
T. Bil. (mg/dL)	0.51 (0.36 / 0.79)	0.58 (0.4 / 0.95)	0.5 (0.35 / 0.76)	<0.001
D. Bil. (mg/dL)	0.2 (0.13 / 0.33)	0.26 (0.16 / 0.53)	0.2 (0.12 / 0.31)	<0.001

Pearson Chi Square Test (exact), Mann Whitney U test (Monte Carlo), Q1: Percentile %25, Q3: Percentile %75

A total of 1,278 anti-HCV (+) patients and 6,893 HBsAg (+) patients included in our study were compared in terms of demographic findings and LFTs. While viral serology positivity was higher in men in both groups, the incidence of Anti-HCV (+) was found to be 1.13 times higher than the frequency of HBsAg in men (p=0.041) (Table 1). Patients with anti-HCV (+) were older, and their LFT and bilirubin levels were found to be higher than those of HBsAg patients (p<0.001) (Table 1).

Patients who were tested for anti-HCV and for HBV were evaluated separately. The anti-HCV test was found to be positive in 1,278 (1.9%) of 67,749 patients, who were tested for anti-HCV. HBsAg positivity was detected in 6,893 (8.2%) of 84,505 patients who underwent a hepatitis B test. (Table 2).

In our study, when the characteristics of the patients with anti-HCV (+) and HBsAg (+) were interpreted through ROC curve analysis; it was found that those with anti-HCV (+) were generally older than 55 years and that those with HBsAg (+) were generally younger than 55 years [OR: 6.02 (5.28-6.87): 95%, CI]. In patients with anti-HCV (+) ALT >32.54 IU/mL (OR:1.92, CI: 1.7-2.18), AST >36.86 IU/mL (OR: 2.72, CI: 2.41-3.08), T. Bil >0.28 mg/dL (OR: 1.53, CI: 1.35-1.72) and D. Bil. >0.25 mg/dL (OR: 2.09, CI: 1.85-2.36) predicted anti-HCV positivity (CI; 95%) (p<0.001) (Table 3).

Discussion

In Somalia, the civil war has been on-going for decades, with insufficient numbers of qualified medical staff and limited access to modern laboratory facilities also posing significant screening and vaccination challenges for viral hepatitis (2). Therefore, HBV and HCV infections transmitted by blood, sexually and via the perinatal route are still the most important preventable and treatable causes of death for Somalian people. As a result of our study, we can conclude that due to the high prevalence of HBsAg and anti-HCV, people living in the Somalia Mogadishu region are still at a serious public health risk in this respect.

HBV infection causing liver cirrhosis and hepatocellular carcinoma (HCC) is endemic worldwide. Africa is the region with the second highest number of inactive carriers following the Western Pacific regions. Chronic HBV infection is very common, especially in Asia and sub-Saharan Africa. Approximately 15-40% of individuals with chronic HBV infection have an increased risk for the development of cirrhosis, fulminant hepatitis, and HCC (3,4). Analyzes on the global distribution of chronic HBV infection were classified according to HBsAg prevalence by low (<2%), intermediate (2%-7%) and high (≥8%) prevalence regions (5). Somalia is also a region in the world with a high rate of HBV seroprevalence (>8%) (6,7). In our study,

Table 2. Test results for hepatitis B and/or hepatitis C virus infection.

	Negative n (%)	Positive n (%)	Total n (%)
Tested for HCV infection (anti-HCV)	66471 (98.1)	1278 (1.9)	67749
Tested for HBV infection (HBsAg)	77612 (91.8)	6893 (8.2)	84505
Anti-HBsAb (+) and HBsAg (-)	57297 (67.8)	27208 (32.2)	84505

The proportions were calculated as the number of positives or the number of negatives / numbers in the total column.

Table 3. ROC Curve analysis for HBsAg and anti-HCV results.

Cut-off value		Anti-HCV (+) (n=1278)	HBsAg (+) (n=6893)	Odds Ratio (%95 CI)	(SE.)	*P*
Age	>55	902 (31.5) ^{npv} (70.6) ^{sp}	1963	6.02 (5.28 / 6.87)	0.746 (0.007)	<0.001
	≤55	376	4930 (92.9) ^{ppv} (71.5) ^{sn}			
ALT	>32.54	519 (22.3) ^{npv} (40.6) ^{sp}	1807	1.92 (1.70 / 2.18)	0.581 (0.009)	<0.001
	≤32.54	759	5086 (87.0) ^{ppv} (73.8) ^{sn}			
AST	>36.86	604 (26.1) ^{npv} (47.3) ^{sp}	1706	2.72 (2.41 / 3.08)	0.616 (0.009)	<0.001
	≤36.86	674	5187 (88.5) ^{ppv} (75.3) ^{sn}			
T. Bil.	>0.28	683 (18.7) ^{npv} (53.4) ^{sp}	2960	1.53 (1.35 / 1.72)	0.562 (0.008)	<0.001
	≤0.28	595	3933 (86.9) ^{ppv} (57.1) ^{sn}			
D. Bil.	>0.25	590 (22.7) ^{npv} (46.2) ^{sp}	2006	2.09 (1.85 / 2.36)	0.599 (0.008)	<0.001
	0.25	688	4887 (87.7) ^{ppv} (70.9) ^{sn}			

Roc Curve Analysis (Youden index J - Honley & Mc Nell), AUC: Area under the ROC curve, SE: Standard Error, npv: negative predictivity value, ppv: positive predictivity value

we found that the current HBsAg seroprevalence is still 8.2%.

Development of a vaccine for HBV makes a significant contribution to this struggle. A HBV vaccine has been available since the early 1980s, and a dramatic reduction in the frequency of chronic HBV infection has been achieved through regular HBV vaccination programs. The WHO recommends that the HBV vaccine should be integrated into national vaccination programs in all countries. However, HBV vaccines are not widely available in low-income countries.

Current studies on this subject are generally carried out with refugees in the USA, which is in receipt of significant levels of immigration from these regions. Previous reports have documented the frequency of HBsAg among US refugees as 3-15% (8-10). In a recently published study, the overall frequency of HBsAg in Somali refugees, who immigrated to the United States, was found to be 2.9%, which is equal to approximately 10 times the rate of HBV infection in the general US population (11). However, the frequency of HBsAg varies between 8.2 - 40.1% in general screening and seroprevalence studies in the population of Somalia and patients diagnosed with HCC (12). In our study, the HBsAg seroprevalence of the Somali population was found to be lower when compared to the results of previous local studies and it was found to be significantly higher than the level in refugee studies. This may be attributed to the fact that people who have the opportunity to emigrate from Somalia enjoy better socioeconomic conditions generally and have access to vaccines and early treatment.

Hepatitis B is estimated to cause 87,890 deaths annually in sub-Saharan Africa, but the incidence of cirrhosis in individuals in sub-Saharan Africa is difficult to determine. Liver biopsy is not a routine procedure and non-invasive elastography is almost impossible to access (13). However, several studies have reported that HBV infection is responsible for 80% of patients diagnosed with HCC in sub-Saharan Africa (14-16). In sub-Saharan Africa, the age-standardized incidence of HCC rises to 41-2 per 100,000 people per year (17). The reported frequency of HCC and cirrhosis may only reflect a very small percentage of the actual incidence due to the inadequacy of regular recording systems (18).

As a result of the cohort studies conducted; male gender, a family history of HCC, a cirrhosis background, a high HBsAg concentration, a high HBV DNA concentration, having HBV genotypes A and C, core-promoter mutations and aflatoxin exposure were associated with an increased risk for HCC (17). Therefore, effective intervention requires a clear understanding of the dynamics of viral outbreaks.

Many countries in sub-Saharan Africa are currently in the process of developing viral hepatitis management guidelines and strategic plans to work towards the eradication of viral hepatitis. Major challenges for HBV eradication

in sub-Saharan Africa are as follows: reduction of mother-to-child transmission (materno-fetal) with the administration of a HBV birth dose vaccine and full coverage for the HBV vaccination program; identifying individuals infected with HBV, access to affordable diagnostic assays to provide an effective link to care and treatment with nucleoside analog therapy for HBV-infected individuals; and reducing the social stigma associated with HBV diagnosis.

Despite all the scientific advances and increasing knowledge of HCV, HCV infection still remains a "hidden pandemic"(19). HCV prevalence has recently decreased to 0.1% in developed countries (20). HCV is still considered endemic in developing countries with insufficient genotype data. The largest population of individuals infected with HCV was found to be in Asia (3.6% of the global population), followed by Africa (3.2% of the global population) and Latin America (1.4% of the global population), respectively (21). Most of these regions face many structural, cultural, social and political obstacles in responding to this epidemic. Social and educational programs should be encouraged, especially in countries that still ignore and stigmatize certain behaviors that lead to HCV infection. Raising awareness of HCV infection in the general population can be beneficial in two ways: First, people who are aware request treatment. Second, encouraging appropriate behavior helps to limit the risk of disease progression. A national action plan with national guidelines for the treatment of HCV infection should be supported (22).

It is noteworthy that HCV positivity is more common in older ages and LFT levels are found to be higher. This situation can be interpreted with the increase of awareness in the society and the decrease in contagiousness as a result of the early diagnosis of HCV in recent years (23). In addition, the increase in the frequency of metabolic syndrome, DM, hepatosteatosis with age may have contributed to the elevation of LFT.

In a study based on the prevalence of serological markers for HBV and HCV in 596 children, who lived in a residential institution in Somalia in 1992, it was reported that the prevalence of HBsAg was 16% and anti-HCV was 1.5%(4, 24). In our study, we found that anti-HCV seroprevalence was 1.9% in the local population, close to the levels stated in the previous literature data. This result may be significant in terms of its indicating that increasing awareness about HCV, teaching people about transmission pathways, and highlighting the importance of the widespread use of regular screening and follow-up programs are still not sufficient.

HCV infection is a global public health problem that affects millions of people worldwide. HCV-infected individuals have a 2.4 times increase in the risk of all-cause death, a 26.5 times increase in the risk of liver-related death, and a 1.8 times increase in the risk of non-liver-related death compared to the non-infected population (25). HCV has a great heterogeneity in both the prevalence of infection and the distribution of viral genotypes. This poses a serious health burden globally in terms of morbidity and mortality. In our study, the rate of anti-HCV prevalence was particulalrly highwith HCV-related morbidity and mortality difficult to determine, since the rates of compliance of patients with follow-up systems and treatments are very low.

Our study has some important limitations. First of all, HBV and HCV seroprevalence were evaluated via HBsAg, anti-HBs antibody and anti-HCV levels. Although patients living in the same region were included in our study, seroprevalence was evaluated in separate groups due to differences in the file scanning system. This situation is attributable to social security problems in the region, identity card complexities and difficulties with respect to data retrieval from the hospital registration system. Since the HBV-DNA and HCV-RNA levels and genotyping results of the patients could not be obtained, data related to the development of active infection, chronic hepatitis, liver cirrhosis and HCC could not be obtained. This situation can be explained by the regular patient follow-up problem in the region where our hospital is located and the inadequacies of laboratory capacity. However, our study's results are important with respect to their determination of seroprevalence in the region and given the very large patient cohort and resultant size of the data used patient population.

As such, based on our study, we can say that HBsAg and anti-HCV seroprevalence (8.2% and 1.9%, respectively) in Somalia is still above desired levels. The fact that anti-HBs antibody levels are 32.2% reveals the importance of the development and popularization of vaccination programs. It is vital to ensure that Somalian people have access to adequate and regular hepatitis B vaccination programs for viral hepatitis (normal population, pregnancy and neonatal follow-up, etc.), adequate medical care, a reliable drug supply and equal access to medical follow-ups.

Yazarlık Katkısı: Fikir/Hipotez: ÖS Tasarım: ÖS Veri toplama/Veri işleme: ÖS Veri analizi: ÖS Makalenin hazırlanması: ÖS

Etik Kurul Onayı: Mogadişu Somali Türkiye Recep Tayyip Erdoğan Eğitim ve Araştırma Hastanesi Girişimsel Olmayan Klinik Araştırmalar Etik Kurulu' ndan 07.08.2019 tarihinde alınmıştır (MSTH/813). Çalışma Helsinki Deklarasyonu'na uygun olarak yürütülmüştür.

Hasta Onayı: Gerek yok.

Hakem Değerlendirmesi: İlgili alan editörü tarafından atanan iki farklı kurumda çalışan bağımsız hakemler tarafından değerlendirilmiştir.

Çıkar Çatışması: Yazarlar tarafından çıkar çatışması bildirilmemiştir.

Finansal Destek: Yazarlar tarafından finansal destek almadıkları bildirilmiştir

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