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The Distributions of HCV Genotypes in Hemodialysis Patients in Iraq

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Abstract

Background and Aims: Hepatitis C virus is a major global health problem that primarily affects the liver which lead to liver cirrhosis, liver failure and hepatocellular carcinoma. The aim of this report was to investigate the genotypes of HCV in patients on regular hemodialysis in Iraq.

Materials and Methods: A cross sectional study was conducted to investigate the genotypes of HCV in patients on regular hemodialysis in 7 centers across Iraq. A total of 255 subjects with positive anti-HCV antibodies were recruited in this study.

Results: To confirm the positivity, RT-PCR was performed. Amongst all samples, 31% (79/255) was positive by RT-PCR. Then, we genotyped all the RT-PCR positive samples, it was found that 39/79 (49.4 %) of our samples were typed as HCV genotype 1 including 26 samples (66.7%) as HCV 1a and 13 samples (33.3%) as HCV 1b. HCV genotype 4 was found in 34/79 (43%) of the samples while 6/79 (7.6%) of the samples typed as HCV 3

Conclusion: HCV genotype 1 was the most prevalent genotype followed by genotype 4. Further population-based study is required to investigate the prevalence of HCV genotypes.

Keywords: Genotypes, HCV, Hemodialysis Patients, Iraq

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Introduction

Infection with HCV is a global health issue **(1)**. Currently, more than 200 million subjects are infected with the hepatitis C virus **(2)**. Chronic infection with the virus is associated with deleterious consequences such as liver cirrhosis and hepatocellular carcinoma **(3)**. The prevalence of HCV infection has been studied thoroughly. While the prevalence of HCV positivity is 0.2% in blood donners in Iraq, around 4% of the Pakistani blood donners were positive for the virus **(4-6)**. The prevalence of HCV infection in subjects undergoing hemodialysis differs from developing countries to developed countries. The prevalence of HCV in hemodialysis subjects in Iran, Turkey and Saudi was found to be 4%, 11% and 20%, respectively **(7-9)**. In the UK, the prevalence of HCV in hemodialysis patients was 2% and around 20% in Spain and Italy **(10, 11)**. In a study conducted in Iraq recruiting patients on hemodialysis, the prevalence of HCV was 4.3% **(12)**. HCV is of six genotypes, labeled 1 through 6. The heterogeneity of the virus makes the development of vaccine insuperable **(13)**. The heterogeneity of HCV also plays an important role in determining sustained virologic response (SVR) in subjects infected with the virus. The treatment showed greater efficacy in genotype 2 and 3. Genotypes 1 and 4 are problematic to treatment with less SVR rates **(14)**.

The aim of this study was to investigate the genotype of HCV in patients on regular hemodialysis in Iraq.

Materials and Methods

During the study period between May 2017 and May 2019, 255 patients were recruited. Recruiting patients were undergoing regular hemodialysis for renal failure in seven dialysis centers in Medical City Hospital, Al-Karama Teaching Hospital, Al-Kadymia Teaching Hospital -Baghdad, Al-Basra Teaching Hospital, Duhok dialysis center and Zakho dialysis center. A 5cc syringe and needle were used to obtain five ml of blood from subjects. Then, the samples were centrifuged at 1500 rpm for 3 min to obtain serum.

ELISA

The HCV (antibody) Ab was studied using a third-generation immunoassay that allows the detection of antibodies to the NS3, NS4 and NS5 core antigens of the virus (Foresight- USA) following manufacturer's instruction. All tests were performed in duplicate.

RNA extraction and quantification

RNA was extracted by QIAamp RNA Extraction Kit (Qiagen) according to manufactures instructions and the extracted RNA concentration was confirmed by nanodrop study. Quantification of HCV RNA was performed by real-time quantative PCR-based test (Amplicor HCV test; Hoffman–La Roche, Nutley, NJ, USA). The manufacturer's instructions were followed and the internal control supplied by the manufacturer was added to each specimen, as an extraction and amplification control.

HCV genotyping

HCV genotyping was performed using a commercial line probe assay (Abbot-USA), according to the manufacturer's instructions. In this assay, after the amplification of the 5' non-translated region of the HCV genome, the product was labelled with biotin. Reverse-hybridization reaction was performed with 21 different probes. The hybridization reaction was then reacted with streptavidin–phosphatase conjugate. The reaction identified the 6 major HCV genotypes and their subtypes.

Ethics

The project was approved by the scientific and ethics committee in the college of Medicine, University of Zakho. Written consent was obtained from recruited subjects.

Results

Patients and HCV positivity

During the period from May 2017 to May 2019, 255 hemodialysis patients with positive HCV-Ab results were referred for further evaluation. HCV-Ab positivity was confirmed again by ELISA. Then, to discriminate between current infection and old resolved infection, RT-PCR was performed for all positive samples. The average age of positive

samples was 52.9±12.8 years. Amongst all samples, 31% (79/255) was positive by RT-PCR. 34.2% (27/79) of the positive samples were female.

HCV Genotype

Then, we genotyped all the RT-PCR positive samples, it was found that 39/79 (49.3%) of our samples were typed as HCV genotype 1 including 66.7% (26/39) samples as HCV 1a and 33.3% samples (13/39) as HCV 1b. HCV genotype 4 was found in 34/79 (43%) of the samples while 6/79 (7.6%) of the samples typed as HCV 3.

Discussion

In this study, it was found that 49.3% of our samples were typed as HCV genotype 1 including 26 samples as HCV 1a and 13 samples as HCV 1b. HCV genotype 4 was found in 43% of the samples while 7.6% of the samples typed as HCV 3. In a meta-analysis study conducted to investigate the prevalence of HCV in Iran the prevalence of HCV was found between 9-12% according to the technique used for the diagnosis **(9)**. In another study conducted in Turkey, 20% of the recruited subjects were positive for HCV (8). In a study conducted in Iraq, HCV positivity was found to be 4.3% **(12)**. Previously, different studies investigated HCV genotype in Iraq. In a study conducted in the southern region, 50% of the recruited samples typed as genotype 1 followed by 35% for genotype 4 **(15)**. In studies that had recruited patients with thalassemia from northern Iraq, it was found that HCV genotype 4 is the most prevalent genotype followed by genotype 1 **(16, 17)**. In another study investigating the HCV genotypes in patients with end stage kidney diseases in Iraq, HCV genotype 1a was found in all patients **(18)**. Reports from the Arab peninsula showed that genotype 4 was the most prevalent HCV genotype **(19, 20)**. Infections with HCV genotype 4 and 1 are the most difficult to treat. In Iraq, it was previously shown that, 50% of the patients infected with HCV genotypes 1 and 4 responded to the classical treatment containing interferon **(16)**. Direct acting antivirals are new potent medications but very expensive in Iraq therefore strict infection control measurement should be imposed to prevent the transmission of the virus particularly in hemodialysis patients. Studying HCV genotypes may provide a useful tool for tracking the source of HCV infection and it provides evidence for a patient to patient transmission. Additionally, studying HCV genotypes may help understanding the prognosis of the disease. It was previously found that infection with HCV 1b genotype was associated aggressive course of the disease **(21)**. Furthermore, a possible link between HCV 1b genotype and hepatocellular carcinoma has been proposed **(21)**. Therefore, studying HCV genotypes is importance particularly in vulnerable groups such as patients on hemodialysis and priority should be given to patients who are infected with virulent genotypes.

Our study has limitations. We studied HCV genotypes in few centers in Iraq. Continuous monitoring of the patients is mandated with regular check of HCV genotypes. HCV genotypes in hemodialysis patients might not reflects the genotypes in the population but certainly is important for monitoring outbreaks in such patients group A population-based project is suggested to investigate HCV in this society. However, the prevalence of HCV may be low in the population making the study of HCV genotype extremely difficult.

Conclusion

To conclude, HCV genotype 1 was the most common genotype in this study. This is in agreement with previous reports in Iraq. A population-based study is needed to determine HCV genotypes in the country.

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Conflict of Interest

The authors reported no conflict of interest.

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