Preliminary Results of the Micro-Elimination Project of Hepatitis C in a Disadvantaged Town in South-West of Romania-Orșova

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ABSTRACT: Despite all recent advances in the diagnosis and treatment of hepatitis C virus infection, the incidence remains high, motivating the present study to improve the prognosis of the disease through early diagnosis of asymptomatic patients with possible detectable risk factors. The aim of this study is to identify HCV infection in a disadvantaged population before the onset of symptoms and guide to specialized services for initiation of antiviral therapy, thus adhering to the WHO goal of elimination the infection. Materials and Methods: In the first two weeks after the start of the study, 320 patients with detectable risk factors for HCV were tested using rapid tests, in a southwestern city of Romania, Orșova, with the participation of four doctors, via Family Medicine Offices. Results: As a percentage, the amount of detection based on rapid tests was 2.5%, the positive results have apparently been achieved exclusively among female subjects. All patients have been informed about the result and included in the diagnostic trial, where they were fully evaluated to determine if they were eligible for therapy. Conclusions. Population screening contributes to the diagnosis and elimination of an underdiagnosed pathology, in a disadvantaged area with limited access to medical care. The positive feedback that has been received in just a few weeks after its beginning, once again has motivated to emphasis the population screening, with real considerations on the possibility of expanding this program on a large scale.

KEYWORDS: HCV elimination, disadvantaged region screening, sustained virological response.

Introduction

Hepatitis C virus is a RNA virus belonging to the family Flaviviridae, genus Hepacivirus [1].

It was discovered in 1989 and it became a real healthcare priority and a topic of strong research and clinical investigations [2].

The infection with Hepatitis C virus (HCV) is in the top of the global infectious diseases and affects around 3% of the population, according to the World Health Organization (Figure 1), having a progressive evolution to chronic liver disease, cirrhosis or hepatocellular carcinoma if the screening is not followed by treatment [3,4].

This represents a real burden on the health systems, taking into account all the costs involved in detecting the virus, as well as the costs generated by the curative treatment in order to obtain the sustained virologic response (SVR).

![Figure 1. Prevalence of HCV infection worldwide [3].](image-url)
Hepatitis C infection is a well-established cause of mortality throughout most of the world and it remains a major public health problem. Innovation in screening technology can identify the disease earlier than the appearance of signs and symptoms in order to reduce the morbidity and mortality. Once infected with HCV, some patients experience spontaneous recovery, but the majority of infections will become chronic. Long-term asymptomatic evolution of HCV infection, both in acute and chronic phase, leads almost all patients to initially be seen by family doctors.

In Romania, HCV is responsible for about 65% of the total number of viral hepatitis, with a prevalence rate of 3.23% in adults [5].

There are seven genotypes (1-7) of HCV and studies have shown genotype 1 or 1b as being more preponderant [6].

High prevalence of HCV infection is linked with decreased education and income level in disadvantaged areas [7].

Several percutaneous exposures among healthcare workers, users of injected drugs, blood recipients, persons with human immunodeficiency virus (HIV) infection, hemophilia, persons on hemodialysis, with various sexual partners, tattoos or persons with high aminotransferase (alanine and/or aspartate aminotransferase; ALT/AST) levels represent risk factor groups that have an important role in patients screening [8].

The WHO is aiming to eliminate the HCV infections by 2030, thus reducing its incidence by 80% and its mortality rate by 65% [9,10].

In order to achieve these objectives, therapies with highly effective direct-acting antivirals (DAAs) were included in the treatment of Hepatitis C infections, which also became a therapeutic standard. Real progress has been made regarding the elimination of this pathology in the last two decades, with over 95% of individuals being cured once they are identified [3].

The lack of the national screening for HCV programs, the cost of obtaining and implementing HCV screening tests, dissemination of information in different media such as television, news portals or blogs leads to a high rate of under-diagnosis.

The major impact of the COVID-19 pandemic caused one-year hiatus in Hepatitis C elimination program progress and overlapped with our screening project. The novel coronavirus (SARS-CoV-2) emerged in late 2019 has a negative influence on detection of HCV infection, treatment initiation and patient adherence. We considered the current situation an additional interest reason to start the project, which obstruct the access to medical care, attention being caught in the detriment of liver pathology.

The aim of this project is to identify the disease before the onset of the symptoms or signs, through a selective screening of individuals with high risk factors for the hepatitis C infection in a southwestern town of Romania.

### Material and Methods

The screening project was approved by Ethics Committee of University of Medicine and Pharmacy of Craiova (No. 82/16.09.2020).

A written consent form was obtained from each patient, who was interviewed about medical history and other pertinent information and they were asked to complete a survey to determine their risk factors (Figure 2).

This is a national premiere, when an university center conducts such screening project in an urban area.

The population screening is taking place in Orșova city between September and December 2020 and in the first two weeks included a number of 320 patients with an identifiable risk for Hepatitis C Infection.

**Figure 2. Survey questionnaire to determine risk factors in every patient.**
Four family doctors accepted to participate in this project, after an informative webinar about the importance of detection of HCV infection, the use of HCV rapid antibody test designed for HCV infection screening and the interpretation of results. The antibody test used for the screening is Anti-HCV TEST WB/S/P.

The inclusion criteria in this project are represented by: persons who injected drugs and shared needles or syringes in the present or in the past, persons exposed to an infected or multiple sexual partners, individuals with human immunodeficiency virus (HIV) infection, persons who have ever been on hemodialysis or who received blood, blood components, organ transplant or clotting factor concentrates, prisoners, healthcare workers after exposure to HCV-infected blood.

Preliminary results

A total of 320 patients were tested in the first two weeks in four family medicine offices, including 23 in Office 1, 107 in Office 2, 140 in Office 3, 50 in Office 4 (Figure 3).

Overall, 114 (35.6%) patients were male and 206 (64.4%) were female. The median age of all participants was 66. HCV screening was performed for 320 individuals using the Anti-HCV TEST. Eight patients (2.5%) had positive screening test and all of them were females.

Eligible patients were referred for antiviral therapy using DAAs.

Discussions

Taking into consideration the epidemiology of SARS-Cov-2 infection the authors of this screening project performed a SWOT analysis in order to correctly decide the implementation of the study.

The analysis permitted revelation of strengths and opportunities, in the same time with reduction of weaknesses and threats (Figure 4).
The main objective of this project was to identify the patients before the onset of the symptoms or signs, through a selective screening of individuals with high risk factors, and in the meantime to correctly evaluate the real prevalence of HCV infection in a southwestern town of Romania.

The epidemiological forecast has set hepatitis C infection prevalence rates between 0.5% and 3.5% in European countries \[11,12\] over the past thirty years.

In other countries outside Europe we can find values between 7% to 8% \[13\].

Romania is considered as one of the countries with high prevalence of HCV infections \[5,14\].

Although the results of our screening are preliminary, the prevalence is comparable or perhaps even higher than what is revealed in literature, most probably because it is a disadvantaged area which has a poor access to medical care.

However most of patients choose to not see their family doctors for appropriate evaluation for other reasons as well (poor social condition, lack of symptoms at first contact, reacting with fear on the simple thought that they might be infected with HCV, ethnic background).

In order for the liver damage to not turn so severe, periodically screening must become a routine for most patients.

An argument that should convince the patients to continue the investigations is the proven fact that the infection with HCV is curable.

Patients must be aware of the fact that this disease does not show quite relevant symptoms and does not always occurs in a healthy liver (non-viral hepatic pathology).

**Conclusions**

The screening project has shown a higher access to testing population at risk and is expected to have high percentage of cured patients since the availability of DAA-therapy.

Prompt actions to boost HCV screening and immediate treatment are essential to achieve the goal of the World Health Organization by 2030.

This screening project represent a step forward in early detection of Hepatitis C and also an opportunity for clinicians, researchers, general practitioners to take part in the future of HCV elimination.
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Conflict of interests
None to declare.

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