



POSITION PAPER

HCV/COVID-19 JOINT SCREENING



SUMMARY

- 1) The Italian journey towards the elimination of HCV infection at the end of 2019**
- 2) Impact of COVID-19 on the management of HCV-related liver diseases in Italy**
- 3) ACE's position for the development of a treatment and prevention model for infectious diseases through the activation of Covid-19 – HCV co-screening**

BACKGROUND

Strictly implementing lock-down measures has been undisputedly effective for the management of the Covid-19 pandemic, as it has contained the spread of the virus. However, at the same time it has also been the reason for the delay of services and procedures concerning other diseases, which have been deemed “non-essential” or “deferrable”. Potentially, such delays may result in increased morbidity and mortality due to many conditions, and they are therefore expected to have a severe impact on public health.

The availability of a safe and effective treatment to cure the hepatitis C virus (HCV) brought the World Health Organization (WHO) to set ambitious goals for the elimination of HCV within the year 2030⁽¹⁾. However, the Covid-19 pandemic has delayed the onset of new treatments almost anywhere in Italy, and unless specific measures are undertaken, a negative impact on the achievement of WHO goals cannot but be foreseen. It should also be reminded that the Covid emergency has entailed further delay of the epidemiologic survey for the evaluation of the spread of active HCV infection nationwide, and of the relevant initiatives aimed at the emergence of the “underground”.

1) THE ITALIAN JOURNEY TOWARDS THE ELIMINATION OF HCV AT THE END OF 2019

Hepatitis C is a global health issue with a great human, social and economic impact. According to the latest report by the World Health Organization (WHO), 71 million people are suffering from chronic liver disease due to hepatitis C virus (HCV) and, mainly because they exhibit scarce or mild symptoms, 80% of them remain undiagnosed, and 93% do not receive any treatment. Globally, more than 1,095 people die of HCV every day and 400,000 people die of HCV-related liver diseases every year ⁽²⁻⁴⁾. In 2016 the World Health Assembly has approved a resolution to eliminate hepatitis infection by 2030 and the WHO has set the global goals for the cure and management of HCV infection, known as Global Health Sector Strategy on hepatitis (GHSS) goals. Eliminating the virus means the ability to diagnose at least 90% of infected people and to treat at least 80% of them within the year 2030 ⁽¹⁾.

Forty new acute hepatitis C cases were reported in the SEIEVA register in 2019, with an incidence of 0.1 per 100,000 inhabitants, unvaried as compared to that of 2018 and halved as compared to 2009. In any case, nosocomial exposure represents the major risk factor (42,1%), followed by intravenous drug use (reported in 38.9% of the cases) and sexual exposure (30.6% of the cases). In 29.7% of the cases an exposure to aesthetic procedures (i.e. manicure, piercing and tattoos) was reported, while living together with an HCV-positive subject represents the least frequent among the analyzed risk factors (26.7%) ⁽⁵⁾.

As no universal screening program is in place allowing to diagnose HCV infection in the general population, no prevalence data is available in our country. However, the hepatitis C mortality rate in Italy is high (38 deaths per million inhabitants in 2016 versus EU average of 13 according to Eurostat), and the social burden is heavy (more than 200,000 patients treated from 2015 to today). The current estimated prevalence of HCV infection in our country is around 1%; rates up to 7% among people who were born from 1935 to 1944 were estimated in previous studies, with an increasing gradient from Northern to Southern Italy.

According to the estimates, around 281,000 patients with absent/mild to severe fibrosis and around 128,000 with cirrhosis were living in Italy and waiting to be diagnosed and treated at the end of 2019. A significant proportion of the infected is found among former users of intravenous drugs and to a lesser extent among people who underwent at-risk aesthetic procedures. Infections arising from the use of glass syringes before the introduction of disposable devices, or from blood transfusions, are found among the older population groups, with a prevalence peak in subjects of 50 years of age and 60% of asymptomatic subjects with age over 46 ⁽⁶⁾.

Early diagnosis and onset of treatment prevent disease progression, avoid the complications of the later stages of the disease (like liver cirrhosis and HCV-related extra-hepatic diseases), reduce the overall cost of treatment, and improve patients' quality of life. It is therefore essential that patients are identified and treated early.

The year 2019 has marked a decrease in the number of treatments of HCV infection as compared to those in 2017-2018, thus downgrading Italy from being on track with regard to the elimination goal. The lack of patients to treat due to underscreening is the major barrier to the elimination of HCV in several countries.

Through the implementation of HCV screening, diagnosis and cure programs that are based on effective health policies, it will be possible to achieve results that are closer to the elimination goals by the year 2030.

For this reason, sufficient funding was approved for the years 2020 and 2021 by the Parliament in order to ensure free screening for those born from 1969 to 1989, for subjects managed by public health addiction services (Servizi per tossicodipendenze, SerT), and for detainees.

LAW nr. 8 of February 28, 2020, "Conversion into Law, with changes, of the Law Decree nr. 162 of December 2019, regarding urgent provisions in matters of postponement of law terms, public administration organization, as well as technological innovation". Official Gazette nr 51 of Feb 29 2020 – Ordinary Supplement nr 10

Art. 25-sexies

National free screening for the elimination of the HCV virus

1. Free screening will be ensured in the years 2020 and 2021 with experimental purposes for those born from 1969 to 1989, for subjects managed by public health addiction services (SerT), and for subjects detained in prison, in order to prevent, eliminate and eradicate the hepatitis C virus (HCV).

2. Via Decree by the Minister for Health, along with the Minister for Economic Affairs and Finance, upon agreement within the Permanent State-Regions Autonomous Provinces Conference, to be adopted within sixty days since the coming into effect of the conversion law of the present decree, criteria and modalities for the implementation of the screening as per comma 1 are defined.

3. Burden arising from the present article, equal to 30 million euros for the year 2020 and 41.5 million euros for the year 2021, is addressed through the use of resources allocated to the achievement of specific goals of the National Health Plan, in accordance with comma 34 of Article 1 of the Law nr 662 of December 23, 1996.

2) IMPACT OF COVID-19 ON THE TREATMENT OF HCV-RELATED LIVER DISEASES IN ITALY

Since January 31, 2020 Italy too has suffered from a period of health emergency because of the COVID-19 pandemic. The overall number of cases since the beginning of the pandemic up to May 27 2020 has been 231,139, with 50,966 positive subjects, 33,072 deceased and 147,101 recovered. However, the real number of cases is much higher. The Italian Health System underwent a heavy reconversion aimed at the assistance of these patients ⁽⁷⁾, thus inevitably reducing attention and resources for the cure of common diseases.

Until recently, little was known about the impact of Covid-19 on patients with pre-existing liver diseases. According to a new study conducted by Oxford University Hospitals in UK and the North Carolina University in USA, patients with chronic liver disease or cirrhosis show elevated mortality rates due to Covid-19, up to 40% in patients with cirrhosis and 43 to 63% in those with decompensated cirrhosis as compared to 12% in patients with non-cirrhotic liver disease ⁽⁸⁾. These data suggest that the infection may directly or indirectly lead to liver function worsening.

The current spread of the COVID-19 infection on the Italian territory has caused a deep change in the health care assistance, aiming at the ultimate and worthy objective of dealing with the COVID-19 emergency. Such a context has therefore been the reason of the reallocation of bed capacities across hospital departments and the temporary interruption of specialistic clinical activities, including the hepatological ones.

A survey by EPAC on the difficulties accessing health care for patients with liver disease during the COVID-19 emergency has shown that the plan for the elimination of HCV must be totally redesigned. The emergency has forced a very high number of people to postpone follow-up visits, treatments, procedures and exams. At least 30% of these patients are affected by a severe form of disease. Continuing to postpone would expose patients to a high risk of even irreversible complications, with a negative impact on public health ⁽⁹⁾.

An exploratory survey by the Italian Association for the Study of Liver (Associazione Italiana Studio del Fegato, AISF) has highlighted a significant decrease of non-urgent outpatient activities in patients with chronic liver diseases. In detail, outpatient control visits in patients with non-cirrhotic hepatitis have declined in 12.43% of the centers, or were interrupted in 27.81%, and remotely managed via email and/or phone in 40.24%. Prescription of antiviral therapies remained unchanged only in 17.2% of the centers, was interrupted in 23.7%, and it was maintained, though with drastic reduction, in patients at the highest risk, that is, either with severe extra-hepatic HCV manifestations or compensated and decompensated liver cirrhosis ⁽¹⁰⁾.

Resumption of activities is therefore required, by rescheduling of non-deferrable activities and prioritizing based on liver disease stage, without leaving aside patient stratification by risk based on epidemiological factors, available tests and potential immunity.

In this regard, it would be necessary to use the approved HCV screening National funding to support testing as well as awareness campaigns, both across the general population and in the high-risk and high-prevalence populations, like subjects managed by addiction services and detainees. Such an approach should be comprised into the National Plan for the prevention of Viral Hepatitis (PNEV), the only document that the State-Regions Conference has acknowledged in 2015 (but never

implemented), so as to provide the Regions with instructions on how to implement specific elimination plans and protocols tailored for various types of patients with the involvement of all Health Care Operators engaged in managing HCV patients. Screening implementation should then be quickly followed by an early onset of patients' treatment.

Therefore, as of today, our National Health System should redefine its priorities redistributing the available resources and not neglecting other public health concerns like HCV infection and the elimination of it.

3) ACE'S POSITION FOR THE DEVELOPMENT OF A TREATMENT AND PREVENTION MODEL FOR INFECTIOUS DISEASES THROUGH THE ACTIVATION OF COVID-19 – HCV CO-SCREENING

Two scientific societies, namely AISF – Italian Association for the Study of Liver, and SIMIT – Italian Society of Infectious and Tropical Diseases (Società Italiana di Malattie Infettive e Tropicali), along with EpaC onlus Patient Association, gathered under the acronym “ACE” – Alliance Against Hepatitis (Alleanza Contro le Epatiti), suggest that the antibody serological screenings for both Covid-19 and HCV viruses are coupled, thus capitalizing on the following benefits:

- increasing the spread of the Covid-19 serological testing, which may help increase the screening rate of viral hepatitis
- raising public awareness of the benefits of screening in facing infectious diseases, especially those for which definitive treatments are available, like HCV
- already existing screening programs for viral hepatitis (e.g. for at-risk categories) may help spread the screening of SARS-CoV-2
- highly sensitive and specific methods for measuring antibodies available for both viruses
- quick, reliable and easy to perform serological tests available for both viruses

The chance we have to perform tests allowing Covid-19 and HCV co-screening is unprecedented in its potential to make of Italy a country free not only from Covid, but also from Hepatitis C.

Based on the “Milleproroghe” Decree (translator’s note: the annual decree extending the life of various government measures in Italy), which allocates the necessary funding to provide free HCV screening in certain categories of subjects in the years 2020 and 2021, ACE proposes that subjects born from 1969 to 1989, or managed by public health addiction services (SerT), and detainees, are also included in the serological screening program for Covid-19, through the measurement of both anti-Covid-19 and anti-HCV antibodies using the same venous blood samples.

With regard to general population, ACE proposes that the General Practitioners and Hospital Departments are involved, in order for them to be able to always make the evaluation and execute the serological measurements of anti-HCV and anti-Covid-19 antibodies.

As the population hosted in Assisted Health Residences suffered a severe impact from the Covid-19 pandemic, serological screening activities for this virus will certainly have to be performed in these subjects. As such population is composed by elderly subjects, who have been exposed to a higher risk of HCV infection in the past years (more than 140,000 HCV-positive subjects over 60 years of age are estimated in Italy), ACE proposes that the anti-Covid-19 and anti-HCV antibodies serological co-screening should be implemented also in such facilities.

Lastly, with regard to the type of testing to use in order to perform a joint Covid-19/HCV screening, the proposal is to proceed as follows:

- General population managed for Covid-19 at hospital and territory level (methodological Protocol for SARS-CoV-2 seroprevalence survey conducted by the Ministry of Health and ISTAT as per Law Decree nr 30 of May 10 2020) and specific population groups plus assisted health facilities’ patients to be included in the HCV screening: perform both tests on blood samples.

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- Special populations (subjects managed by addiction services and detainees): evaluation of potential use of Covid-19/HCV quick capillary testing (e.g. fingerstick test) in order to speed up the screening process in settings like addiction services and prisons, where the screening rate is generally low because of logistic barriers and the social and psychological context of these subjects.

The joint screening will give great impulse to such interventions and **will accelerate the journey towards the elimination of hepatitis C and the achievement of WHO objectives by 2030.**

Summarizing table of the populations who should undergo Covid-19/HCV joint screening based on the provisions of the HCV screening funding and Covid-19 serological survey

Populations at risk	Anti-HCV antibodies serological screening	Anti-Covid-19 antibodies serological screening
Subjects born from 1969 to 1989	Already in place	Specific "general population group" to be added
Subjects managed by addiction services	Already in place	To be added
Detainees	Already in place	To be added
Assisted Health Residencies patients	To be added	Already in place
General population	To be added	Already in place

REFERENCES

- 1) WHO. *Global Health Sector Strategy on Viral Hepatitis, 2016–2021 Towards Ending Viral Hepatitis*. 2016, World Health Organization. <https://www.who.int/hepatitis/strategy2016-2021/ghss-hep/en/>
- 2) Blach S, Zeuzem S, Manns M, et al. *Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study*. *Lancet Gastroenterol Hepatol*. 2016; 2: 161-76.
- 3) Shepard CW, Finelli L, Alter MJ. *Global epidemiology of hepatitis C virus infection*. *Lancet Infect Dis*. 2005; 5: 558-67.
- 4) <https://ec.europa.eu/eurostat/en/web/products-eurostat-news/-/EDN-20190726-1>.
- 5) <https://www.epicentro.iss.it/epatite/aggiornamenti>
- 6) Kondili LA, Andreoni M, Alberti A., et al. *Estimated prevalence of undiagnosed hepatitis C virus infected individuals in Italy: a mathematic model to accurately measure HCV prevalence with a route of transmission granularity*. *Hepatology*. 2019; 70 (S1) AASLD abstract (poster) N.0520 Friday 8 November 2020: p328A.
- 7) <http://www.salute.gov.it/portale/nuovocoronavirus/dettaglioContenutiNuovoCoronavirus.jsp?id=5351&area=nuovoCoronavirus&menu=vuoto>
- 8) Moon et al. *High Mortality Rates for SARS-CoV-2 Infection in Patients With Pre-existing Chronic Liver Disease and Cirrhosis: Preliminary Results From an International Registry*. *J Hepatol* 2020, doi: 10.1016/j.jhep.2020.05.013.
- 9) ACE: 1° WEB CONFERENCE - EPATITE C, UNA PATOLOGIA INVALIDANTE DA NON DIMENTICARE, Speech by Ivan Gardini (President of EpaC Association)
- 10) https://www.webaisf.org/wpcontent/uploads/2020/05/Report_Survey_110520MM.pdf

