RESEARCH LETTER

HCV point of care screening in people tested for SARS-CoV-2 in a social-housing neighbourhood of Milan, Italy

Dear Editor,

We read with interest the Editorial by Kondili et al.[1] about the potential pitfalls found in studies in which SARS-CoV-2 testing is combined with point-of-care-testing (POCT) HCV screening.[2,3] We do agree that the representativeness of the target population could be a problem in such pilot studies. In addition, it could be speculated that socioeconomically deprived people could face barriers to being engaged in HCV and SARS-CoV-2 combined screening programs.

The SARS-CoV-2 pandemic caused a significant challenge for the WHO roadmap—which aimed to achieve HCV elimination by 2030—with detrimental effects in terms of excess mortality, especially in the lower middle-income groups.[4] Italy is considered to be the country with the highest HCV seroprevalence in Western Europe, with up to 280 000 people estimated to be unaware of their HCV status and thus unlinked to care.[5] Currently, in Italy, an active free of charge HCV screening is offered to all subjects belonging to the 1969–1989 birth cohort, to intravenous drug users and convicts. Our group has previously shown the feasibility of a combined SARS-CoV-2 and HCV-Ab POCT screening in three small towns in Lombardy, finding 72 HCV-Ab positive subjects out of 2505 screened.[6] Nevertheless, we were unable to assess the proportion of HCV-RNA-positive subjects, the linkage-to-care acceptance rate, and antiviral treatment eventually received for HCV. In addition, it is still unknown whether a similar screening program would be feasible and effective in a major city neighbourhood characterized by a low socio-economic status context. Consequently, in our study, we aimed to assess the HCV-Ab status using POCT in subjects undergoing COVID-19 screening in the San Siro social-housing neighbourhood of Milan, with a multi-ethnical population and low socio-economic status, and the subsequent acceptance of linkage-to-care.

Study procedures have been described elsewhere.[7] In brief, we conducted a cross-sectional prevalence study for the detection of HCV Ab IgG performed on capillary peripheral blood via a rapid immunochromatographic test (RICT) (OraQuick HCV Test OraSure Technologies Inc.) contextually with the detection of anti-SARS-CoV-2 IgG (rapid test SARS-CoV-2 IgM-IgG gold; Technogenetics) performed on capillary peripheral blood and a rapid nasopharyngeal swab for SARS-CoV-2 (Rapid Test COVID-19 Ag; Technogenetics) between 23 December 2020 and 19 February 2021.

We set our study in the San Siro neighbourhood in north-western Milan.

The primary aim of the study was to estimate the prevalence of HCV Ab positivity through POCT. The secondary aim was to assess the proportion of linkage-to-care acceptance.

People currently living in the neighbourhood and aged >39 years at the time of the HCV Ab screening were eligible to participate in the study. A questionnaire was administered to obtain epidemiological information and clinical history. Skilled healthcare workers performed and read RICTs and a physician was always present to confirm the results and address patients' questions.

During the first 14 days of the SARS-CoV-2 screening, HCV-Ab RICTs were always readily available, whilst they were not always present during the following screening period due to supply problems.

Every subject who tested positive for HCV-Ab RICT and were unaware of their serostatus, and/or who declared to be aware of an untreated HCV infection were contacted by telephone and HCV-Ab serology and HCV-RNA quantitative PCR on peripheral blood were arranged at Luigi Sacco Hospital (Milan). Treatment and follow-up were then offered when an active HCV infection was confirmed.

Subjects who did not answer the phone call on two different occasions were considered lost to follow-up.

Out of 2394 subjects who participated in the screening for SARS-CoV-2, 1637 subjects were over 39 years of age, of whom 691 (42.2%) were screened for HCV Ab by RICTs (Table 1). During the first 14 days of the screening, when the HCV Ab RICTs were readily available, 310 out of 322 eligible subjects (96%) accepted to be screened for HCV. The median age was 64 years (inter quartile range [IQR] 54–74) and 435 subjects (62.9%) were female. Five hundred-fifty-three subjects (80%) had at least one Italian parent and 138 (20%) had no Italian parents.

Seventeen subjects (2.5%) tested positive for HCV-Ab RICTs. They were predominantly females (64.7%) with a median age of 70 years (IQR 60–80); two subjects belonged to the 1969–1989 birth-cohort and 15 to the <1969 birth-cohort. Fourteen subjects (82.4%) were born in Italy, one (5.9%) was from Egypt, one from Argentina and one from Colombia. Most subjects (82.4%) reported no risk factors for HCV infection. Two subjects (11.8%) reported a history of intravenous drug use. Five subjects (29.4%) were unaware of their serological status. Out of the 12 subjects aware of their

serological status, eight (66.7%) reported to have been successfully treated for HCV.

A graphical representation of subjects reporting a previous HCV infection in the questionnaire according to the results of HCV Ab RICTs is depicted in Figure 1. Nineteen subjects who tested negative reported a previous HCV infection in the questionnaire of whom 10 reported HCV treatment, and 9 (90%) stated that they were treated more than 5 years ago.

We contacted the five subjects who tested positive and declared themselves unaware of their serological status. During the phone call, three patients declared they were already followed/treated at other hospitals. One patient born in Egypt was

Key points

In our study, we assessed the antibody positivity for hepatitis C using point-of-care-testing in subjects undergoing COVID-19 screening in the San Siro social-housing neighbourhood of Milan which is characterized by a multi-ethnical population and low socio-economic status. Seventeen (2.5%) of 691 subjects tested positive for HCV antibodies of whom 5 (29.4%) subjects were unaware of their serological status.

TABLE 1 Characteristics of the study population according to being tested positive or not for HCV with RICTs

	Overall, n = 691 (100%)	Positive, n = 17 (2.5%)	Negative, n = 674 (97.5%)
Age, median (IQR)	64.0 (54.0–74.0)	70.0 (60.0–80.0)	63.5 (54.0–74.0)
Sex, n (%)			
Female	435 (63.0)	11 (64.7)	424 (62.0)
Male	256 (37.0)	6 (35.3)	250 (37.0)
WHO regions, n (%)			
Europe and Central Asia	564 (81.6)	14 (82.4)	550 (81.6)
America	33 (4.8)	2 (11.8)	31 (4.6)
East Asia and Pacific	10 (1.4)	0 (0.0)	10 (1.5)
Middle East and North Africa	39 (5.6)	1 (5.9)	38 (5.6)
South Asia	8 (1.2)	0 (0.0)	8 (1.2)
Sub-Saharan Africa	37 (5.4)	0 (0.0)	37 (5.5)
WHO income regions, n (%)			
High income	557 (80.6)	14 (82.4)	543 (80.6)
Low income	30 (4.3)	0 (0.0)	30 (4.5)
Lower-middle income	68 (9.8)	1 (5.9)	67 (9.9)
Upper-middle income	36 (5.2)	2 (11.8)	34 (5.0)
Citizenship, n (%)			
Italian	553 (80.0)	14 (82.4)	543 (80.6)
Not Italian	138 (20.0)	3 (17.6)	135 (20.0)
Risk factors, n (%)			
Blood transfusion	70 (10.1)	1 (5.9)	69 (10.2)
Piercings or tatoos	61 (8.8)	1 (5.9)	60 (8.9)
Risky sexual behaviour	33 (4.8)	0 (0.0)	33 (4.9)
Intravenous drug users	3 (0.4)	2 (11.8)	1 (0.1)
No one	540 (78.1)	14 (82.4)	526 (78.0)
Ever tested for HIV in life, n (%)			
Yes	219 (31.7)	7 (41.2)	212 (31.5)
Not	472 (68.3)	10 (58.8)	462 (68.5)
HIV test, n (%)			
Positive	7 (3.2)	0 (0.0)	7 (3.3)
Negative	186 (84.9)	5 (71.4)	181 (85.4)
Unknown	26 (11.9)	2 (28.6)	24 (11.3)

TABLE 1 (Continued)

	Overall, n = 691 (100%)	Positive, n = 17 (2.5%)	Negative, n = 674 (97.5%)
IgG SARS-CoV-2 results, n (%)			
Positive	77 (11.1)	2 (11.8)	75 (11.1)
Negative	610 (88.3)	15 (88.2)	595 (88.3)
Doubt	4 (0.6)	0 (0.0)	4 (0.6)
Aware of HCV status, n (%)			
Yes	31 (4.5)	12 (70.6)	19 (2.8)
Not	660 (95.5)	5 (29.4)	655 (97.2)
Previous treatment for HCV, n (%)	Of 31	Of 12	Of 19
Yes	19 (61.3)	8 (66.7)	10 (52.6)
Not	7 (22.6)	3 (25.0)	5 (26.3)
Unknown	5 (16.1)	1 (8.3)	4 (21.1)
Treatment for HCV, n (%)	Of 19	Of 8	Of 10
More than 5 years ago	12 (63.2)	3 (37.5)	9 (90.0)
Between 1 and 5 years ago	5 (26.3)	5 (62.5)	0 (0.0)
Less than 1 year ago	1 (5.3)	0 (0.0)	1 (10.0)
Unknown	1 (5.3)	0 (0.0)	0 (0.0)

Abbreviations: IQR, inter quartile range; RICT, rapid immunochromatographic test.

confirmed to be HCV-RNA positive and underwent direct-acting antivirals treatment at Luigi Sacco Hospital. One patient opposed any kind of follow-up, complaining about the location of the hospital chosen for ambulatory treatment, and consequently was extensively counselled to contact his general practitioner to proceed with the appropriate follow-up and treatment. Amongst the four patients aware of HCV-Ab positivity, who tested positive for HCV-Ab and denied having been treated in the past, three contradicted the previously administered questionnaire reporting to have been actually treated before, whereas one patient never answered the call.

Amongst the nine patients who tested negative for HCV-Ab RICT, but reported to be HCV Ab positive without a previous HCV treatment, two refused any kind of follow-up, two were confirmed to be HCV-Ab positive but HCV-RNA negative and five subjects later reported previous treatment which wasn't initially reported in the questionnaire during the screening.

In our study, a prevalence of HCV Ab positivity of 2.5% was found, which is slightly lower than the estimates made on the general population of Northern Italy about 20 years ago (3.3%),[8] with a proportion of subjects unaware of their serological status (29.4%), lower than the estimated 66% reported by a European study in 2015.[9] Nevertheless, only one subject was confirmed to be HCV RNA positive (0.14%), again a lower figure than the 0.48% which was recently estimated in the Lombardy region.[10]

In their study, D'Ambrosio et al.[2] reported a prevalence of 0.10% for HCV Ab and 0.05% for HCV-RNA, a lower proportion than the one we found. This could be expected and it is mainly explained by the demographic composition of the population selected for the screening: our study population was older (median

64 years) when compared to that of D'Ambrosio et al. (range 32–52 years).[2] In fact, we selected subjects >39 years older, as age is itself a risk factor for HCV infection, considering our limited RICTs supply.

Although the acceptance rate of HCV-Ab screening was satisfactory, our study underlines the extreme difficulty in linking to care of the subjects who tested positive (three of them refused a further clinical assessment and one subject never answered the phone call). A possible explanation for the difficulties in the follow-up could be represented by the absence of simultaneous HCV-RNA testing, not allowing to confirm an active infection and forcing the subject to attend a new medical appointment for venipuncture; this was worsened by the distance between the neighbourhood chosen for the study and Luigi Sacco Hospital, which rendered logistically difficult for patients—especially the ones with a low socio-economic status—to be followed up.

Moreover, it is possible that linguistic and cultural barriers could have rendered it difficult to explain the importance of HCV follow-up and treatment, even in the absence of any symptoms.

Our study opens several considerations related to the serological screening itself, which seems not to be effective enough in a population which is generally poorly linked to healthcare and potentially at high risk of carrying HCV infection. In particular, it could be useful to work on the creation of a path from POCT to treatment, ideally creating an efficient coordination between the general practitioner and the infectious diseases' specialist in charge of treatment, and easy-to-access "checkpoints" for screening and treatment.[11,12]

In conclusion, although the COVID-19 pandemic had negatively impacted the diagnosis, monitoring and treatment of liver disease
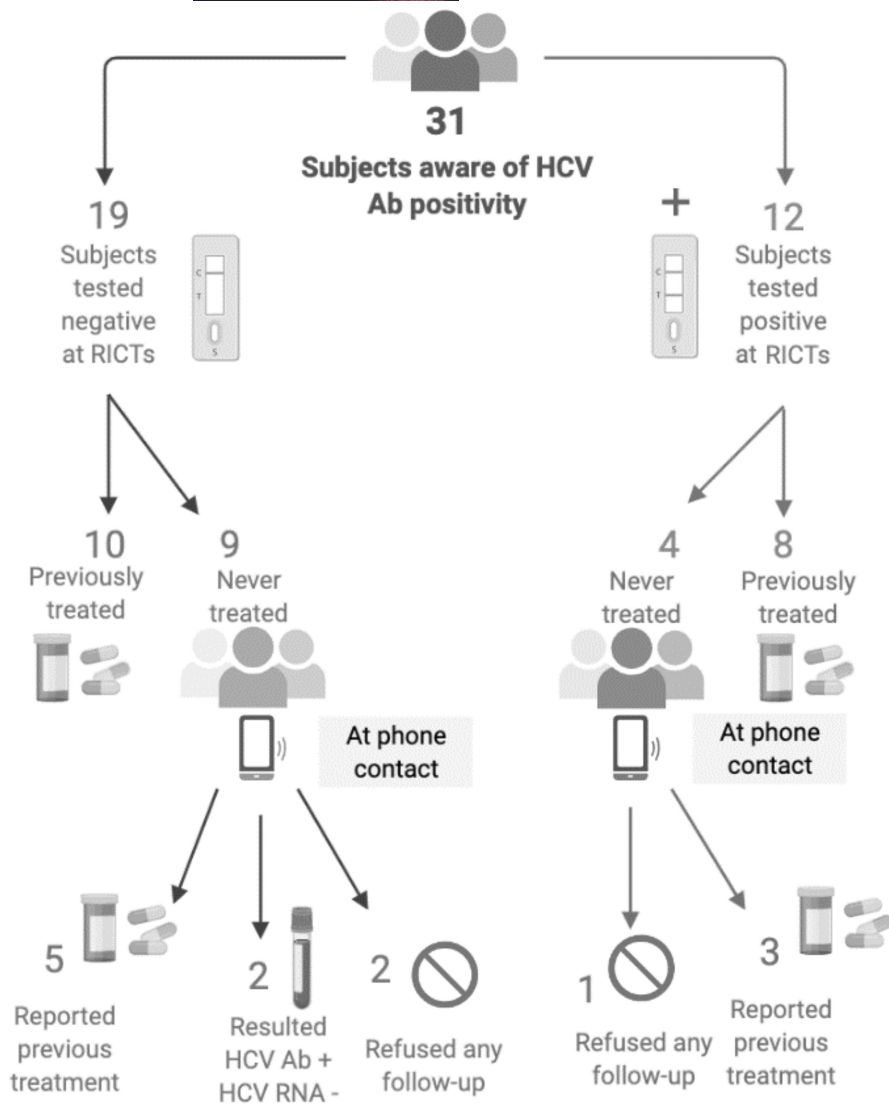
FIGURE 1 Graphical representation of subjects reporting a previous HCV infection in the questionnaire according to be tested positive or negative at HCV Ab RICTs. RICTs, rapid immunochromatographic test.

in non-COVID-19 patients, we again underline the need to turn the challenge of the pandemic into an opportunity to screen, engage and link to care for people living with HCV. The effort should be particularly focused on those who face barriers related to socioeconomic situation, cultural and linguistic barriers or stigma, to achieve the WHO's 2030 HCV elimination target.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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