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Original Research

Impact of the COVID-19 pandemic on the Italian national viral hepatitis surveillance: an interrupted time series analysis, 2006–2022

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ABSTRACT

Objectives: This study aimed to assess the impact of the COVID-19 pandemic on national surveillance of viral hepatitis in Italy.
Study design: Interrupted time series analysis.
Methods: Using an interrupted time series analysis with a customised AutoRegressive Integrated Moving Average model on hepatitis cases reported to the Integrated Epidemiological System of Acute Viral Hepatitis from 2006 to 2022, we examined trends in incidence, time to diagnosis and time to epidemiological investigations for hepatitis A, hepatitis B and hepatitis C.
Results: The quarterly incidence of hepatitis B (−0.251, $P = 0.05$) and hepatitis C (−0.243, $P = 0.003$) significantly decreased with the onset of the pandemic. Surveillance times for hepatitis B (5.496, $P < 0.001$) and hepatitis C (35.723, $P < 0.001$), measured as days lost per quarter, significantly increased 12 and 24 months after the pandemic's start. This aligns with a notable rise in quarterly incidence at 36 months for both (0.032, $P = 0.030$ for hepatitis B; 0.040, $P < 0.001$ for hepatitis C).
Conclusions: The decrease in reported cases could be due to an increase in infection prevention control and containment measures put in place in a pandemic context. However, a delay in the initiation of epidemiological investigations was observed, which could lead to a further increase in incidence in the future.
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Introduction

Viral hepatitis, which includes hepatitis A, B, C, D and E viruses, represents a substantial global health burden. According to the latest European Centre for Disease Prevention and Control (ECDC) epidemiological reports, in the countries of the European Union (EU) and the European Economic Area (EEA), hepatitis A virus (HAV) has shown an incidence of one case per 100,000 inhabitants.[1] Hepatitis B virus (HBV) and hepatitis C virus (HCV), on the other hand, had an annual crude rate of 4.7 cases (7% reported as acute, 43% as chronic, 43% as unknown and 7% could not be classified) and 3.9 cases (6% classified as acute, 35% as chronic, 53% as unknown and 5% percent could not be classified) per 100,000 inhabitants, respectively.[2,3] Hepatitis D or Delta (HDV), which requires co-infection with the hepatitis B virus for replication, is less prevalent compared with other forms of hepatitis but still demonstrates significant incidence in certain geographic areas, involving approximately 5–10% of patients with chronic HBV.[4] In contrast, the hepatitis E virus (HEV), exhibits higher incidence rates in developing regions, with a progressive increase in the number of notifications from 514 cases in 2005 to 5617 cases in 2015 across the EU/EEA countries.[5]

To counter the spread of these forms of viral hepatitis, the World Health Organization (WHO) aims to reduce new infections by 90% and deaths by 65% between 2016 and 2030.[6] These goals are particularly important especially in Italy, the European country with the highest mortality rate associated with viral hepatitis according to the latest estimates by the European Statistical Office (EUROSTAT).[7] To meet these goals, before the COVID-19 pandemic, the ECDC indicated concerted efforts were required to address viral hepatitis in Europe through enhanced surveillance, expanded screening programmes and improved access to diagnostic services.[8]

In Italy, the National Health Institute (Istituto Superiore di Sanità, ISS) established an enhanced surveillance system in 1985,

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the Integrated Epidemiological System of Acute Viral Hepatitis (SEIEVA), to support and integrate the standard Information System of Infectious and Diffusive Diseases (SIMID) managed by the Ministry of Health.[9] The SEIEVA project is based on a collaborative network of various local health authorities (LHAs), which join on a voluntary basis. The five infections caused by the major hepatitis viruses are subject to SEIEVA surveillance (HAV, HBV, HCV, HDV and HEV). Since 2011, SEIEVA has been included in the European surveillance network "Enhanced surveillance for hepatitis B and C" managed by the ECDC.[10]

The recent COVID-19 pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has had far-reaching effects on global healthcare systems, economies and societies. Beyond its direct impact, the pandemic has inadvertently disrupted various aspects of health care, including surveillance and diagnosis of viral hepatitis, a significant public health concern worldwide.[11–13] The unprecedented challenges posed by the COVID-19 pandemic have had significant implications for accurately estimating viral hepatitis burden and hampering timely interventions.[14,15]

In this article, our objective was to provide an overview of the COVID-19 pandemic's impact on acute viral hepatitis surveillance in Italy. In this study, our principal aim was to assess incidence rates and time delays for diagnosis and initiation of epidemiological investigation in relation to the COVID-19 pandemic. To achieve this, we used an interrupted time series approach, a method previously used in studies investigating temporal trends of various infectious diseases.[16] Understanding the consequences of the COVID-19 pandemic on viral hepatitis surveillance is critical for developing effective strategies to address these issues and to achieve the goals set by the WHO.[17–19]

Methods

Study design and data collection

This was a retrospective study that analysed data obtained from the SEIEVA surveillance spanning from 2006 to 2022 in Italy. The SEIEVA project operates through a collaborative network of LHAs, and participation in the network is voluntary. A digital epidemiological investigation is conducted for each reported case of hepatitis. The epidemiological investigation consists of a questionnaire that, when integrated with laboratory results, facilitates the estimation of incidence rates and identification of associated risk factors. SEIEVA differs from and complements the SIMID, where these diseases are subject to mandatory reporting but involve a less extensive level of investigation.[9]

Importantly, the questionnaire ensures full anonymity and does not solicit sensitive information from respondents. Each questionnaire is assigned a unique code, ensuring that it cannot be directly linked to the patient's sociodemographic details. Furthermore, this study only presents aggregated data; therefore, no institutional review approval was required.

Descriptive statistics

A comprehensive descriptive analysis of reported cases spanning from 2006 to 2022 was conducted. The following variables were analysed, segmented by year: count of cases categorised by hepatitis type, incidence rates and age at diagnosis. The following viruses were included: HAV, HBV and HCV. We decided to exclude HDV because the annual cases notified are very few and HEV because surveillance began in 2007 with undernotification and became fully operational with a specific epidemiological interview only in 2019.[20,21] Given the non-normal distribution observed via the Shapiro–Wilk test, age was described using medians and interquartile ranges (IQRs).

Time series analysis

To investigate the potential impact of COVID-19, an interrupted time series analysis was conducted over the period 2006–2022 with an AutoRegressive Integrated Moving Average (ARIMA) model. The time series trend was divided into quarterly intervals in accordance with McCleary et al.[22] Consequently, we calculated the quarterly incidences, the mean quarterly diagnosis time and the mean quarterly time to initiation of epidemiological investigation for the different types of hepatitis and used them as dependent variables. We have chosen to use the first quarter of 2020 as a breakpoint in the time series trend, as it was the period in which the first cases of COVID-19 were registered in Italy.[23]

We then constructed an interrupted time series model using 'time', 'level change' and 'intercept' as independent variables. The 'level change' variable represented the short-term change in the dependent variable investigated after the break. The 'intercept' variable indicated the difference in the slope of the dependent variable before and after the breakpoint.

We also strived to construct an interrupted time series model that was as optimal as possible for each dependent variable examined. The model was:

$$\text{ARIMA}\ (p, d, q) \times (P, D, Q)\ s$$

where p represents the autoregressive order, indicating the number of lag observations used in predicting the current value; d signifies the difference order, denoting the number of times differencing was applied to achieve stationarity; q stands for the moving average order, specifying the number of lagged forecast errors used in predicting the current value. P, D and Q are the seasonal equivalent, so they represent seasonal autoregressive order, seasonal difference order, and seasonal moving average order, respectively. Finally, s signifies the seasonal cycle, capturing the length of the seasonal pattern.

Visual inspection of the time series and appropriate tests were performed to verify stationarity (augmented Dickey–Fuller test and Kwiatkowski–Phillips–Schmidt–Shin test), (Autocorrelation function (ACF) and Partial autocorrelation function (pACF) plots) and seasonality (Webel and Ollech test) with the aim of choosing the optimal ARIMA model for each dependent variable analysed. We also made the choice of the model according to Akaike's information criterion, in particular choosing models with lower values of Akaike's information criterion corrected for small sample size.[24] We then corrected the trend by identifying statistically significant outliers and modelling them by applying the following effects: additive, level shifts, innovative, transients, seasonal additives, local trends, additive patches. Finally, we tested the model for lack of fit using the Box–Ljung test and model accuracy via mean absolute percentage error (MAPE).

We therefore analysed whether there were any significant changes between the prepandemic and postpandemic periods at a general level and at 3 months, 1 year, 2 years and 3 years, respectively.

Statistical analyses were performed using R (version 4.3.1) and IBM SPSS Statistics (version 28.0.1.0). The significance level was set at two-tailed $P < 0.05$.

Results

Participating regions and the relative percentages of participation among regional LHAs are summarised in Fig. 1. Twenty-one

Fig. 1. Italian regions participating in the SEIEVA surveillance system by 2022. Notable variations observed, such as 33.33% of LHAs in Sicily (3 of 9), 62.5% in Sardinia (5 of 8), 71.43% in Campania (5 of 7), and 50% in Basilicata (1 of 2). In addition, 87.5% adherence is observed in Lombardy (7 of 8). It is worth noting that in all other regions and autonomous provinces, the adherence rate is 100%.

regions/autonomous provinces actively participate in the SEIEVA surveillance system. Of these, complete coverage is achieved in 16 regions/autonomous provinces, and partial coverage at varying degrees is achieved in the remaining five regions.

Table 1 provides a summary of descriptive data disaggregated by infection type, including the number of cases, annual incidence rates, and median age at diagnosis with IQRs. With the exception of recurrent peaks of HAV cases (the last and highest in 2017, corresponding to an epidemic in men who have sex with men, which saw an annual incidence of 6.9 per 100,000 inhabitants), all trends have exhibited a progressive decline, a trend that was further accentuated during the COVID-19 pandemic. To elaborate further: HAV experienced a significant reduction in annual incidence, ranging between 66.6% and 77.4% in the three years compared with 2019; similarly, HBV demonstrated a decrease in annual incidence, falling between 47.4% and 57.9% during the same period. Conversely, HCV showed a reduction between 45.5% and 50% in the initial 2 years, but in 2022, it

Table 1
Trends in numbers of cases, annual incidence rates, and median age at diagnosis, SEIEVA surveillance, Italy 2006–2022.

Year	Hepatitis A			Hepatitis B			Hepatitis C		
	N	Incidence rate[a]	Median age (IQR)	*N*	Incidence rate[a]	Median age (IQR)	*N*	Incidence rate[a]	Median age (IQR)
2006	499	1.4	28 (11–38)	571	1.6	39 (32–48)	141	0.5	38 (26–51)
2007	734	2	28 (20–35)	562	1.5	39 (32–47)	136	0.5	40 (30–55.5)
2008	884	2.5	35 (26–43)	544	1.6	41 (34–49)	101	0.4	44 (30–53)
2009	990	2.2	34 (24–41)	478	1	44 (36–53)	106	0.2	42 (32.25–58)
2010	469	1.1	33 (16–44)	406	0.9	42 (35–52)	98	0.2	40.5 (26.25–58.75)
2011	313	0.7	30 (13–39)	422	1	42 (35–51)	111	0.3	42 (30.5–57)
2012	341	0.8	26 (9.5–43)	365	0.9	44 (36–54)	107	0.3	39.5 (27–51.5)
2013	1064	2.5	35 (21–46)	394	0.9	44.5 (37–53.75)	120	0.3	48 (34.75–60.75)
2014	394	0.9	31 (12–44)	351	0.8	45 (39–52)	104	0.2	47 (36–65.25)
2015	274	0.6	32.5 (17–46)	301	0.6	46 (39–54)	76	0.2	46 (36.75–56)
2016	386	0.8	33 (23–45)	262	0.6	47 (41–57)	90	0.2	42 (31–58.75)
2017	3376	6.9	36 (27–44)	253	0.5	49 (42–56)	64	0.1	41 (30.75–49)
2018	747	1.5	32 (14.25–46)	224	0.4	47 (39–57)	49	0.1	51 (36–59)
2019	429	0.8	28.5 (11–51)	204	0.4	50 (43–57)	45	0.1	46 (28.25–58)
2020	100	0.2	43.5 (26.75–65)	110	0.2	50 (41–59)	20	0.04	52 (35.75–63.5)
2021	130	0.3	48 (24.25–69.75)	94	0.2	50 (46–60)	26	0.05	50 (42.5–65.25)
2022	130	0.3	34 (13.25–66.5)	106	0.2	51 (43.25–60)	63	0.1	56 (49–67)

[a] Per 100,000 inhabitants.

registered an increase of 37.5% compared with the incidence observed in 2019.

The model chosen for the analysed variables of the interrupted time series and the related parameters are presented in Table 2. The most optimal models possible were chosen according to the materials and methods previously described. Almost all models showed a good level of fit according to Box–Ljung, apart from the models applied for the evaluation of HBV incidence and HCV time to initiation of epidemiological investigation. All models showed good or reasonable accuracy according to Lewis, with the only exception of the model for evaluating the diagnosis times of HCV.[25]

No significant trend was found regarding the variables analysed for HAV. The incidence of HBV and HCV showed similar patterns, with a negative level change and an increasing trend postpandemic (both statistically significant). In contrast, the time to initiation of epidemiological investigation presented opposite significant patterns: while HBV saw a positive level change with a negative postpandemic trend, HCV saw a negative level change with a positive postpandemic trend. No significant trend was found regarding the times of diagnosis of HBV and HCV.

As an illustrative example, we have reported the trend of HCV incidence in Fig. 2, with a clear trend reversal postinterruption.

Table 3 presents the trends of the variables at 3-, 12-, 24- and 36-month postinterruption. It specifically illustrates the differences in incidence rates per quarter and the average number of days lost or gained, adjusted for the number of cases per quarter, along with their corresponding *P*-values.

This subanalysis confirms that the times to diagnosis have not undergone significant changes during the pandemic, despite the relative fluctuations. However, it is important to note that the initiation times of epidemiological investigations did reveal a noteworthy deceleration. In particular, the results at specific quarterly points highlight how the start times of the epidemiological investigation for HAV also saw a significant increase in the first 24 months and how this trend, although not significant, is still positive at 36 months. The same pattern was highlighted for HBV, but with a reversal of the trend at 36 months, while HCV presented a more volatile trend with a significant collapse at 3 months, reversal of the trend at 12 months and a significant increase at 24 months. For both, HBV and HCV, a consequent significant increase in incidence was recorded, respectively at 36 and 24 months.

Discussion

This study aimed to assess the impact of the COVID-19 pandemic on national surveillance of viral hepatitis in Italy. Analysis of hepatitis cases reported from 2006 to 2022 revealed significant declines in annual incidence rates for HAV, ranging from 66.6% to 77.4%, and for HBV, with reductions between 47.4% and 57.9% postpandemic. Conversely, HCV showed an initial reduction of 45.5%–50%, followed by a notable 37.5% increase in 2022 compared with 2019. The interrupted time series model showed significant decreases in quarterly incidence rates for both HBV (−0.251, $P = 0.05$) and HCV (−0.243, $P = 0.003$) at the onset of the pandemic. At the same time, surveillance times for both HBV (5.496, $P < 0.001$) and HCV (35.723, $P < 0.001$) significantly increased 12- and 24-month postpandemic onset, respectively, indicating delays in epidemiological investigations. Notably, there was a significant rise in quarterly incidence rates at 36 months postpandemic onset for both HBV (0.032, $P = 0.030$) and HCV (0.040, $P < 0.001$). These findings could suggest complex dynamics between pandemic response measures and viral hepatitis surveillance.

Overall, the custom-built ARIMA models used in this study demonstrated robustness in capturing and analysing trends in the variables analysed in the context of the COVID-19 pandemic. Furthermore, the models showed good fit according to Box–Ljung tests and reasonable accuracy according to MAPE assessments, further strengthening confidence in their reliability.

The results of the analysis of interrupted time series deserve several considerations. The main hypothesis of the study was that the COVID-19 pandemic could have led to a general lack of attention to the surveillance system: the reallocation of resources, the reconfiguration of healthcare systems and the staffing shortages may have resulted in disruptions of routine health services, including viral hepatitis surveillance programmes, as highlighted by several international studies, which showed significant reductions in testing and diagnoses of viral hepatitis in the pandemic period.[11–15,17–19] Unfortunately, data on the number of tests are not available within our surveillance system, as it is dedicated only to the notification of acute cases already diagnosed. However, in our study, only the incidence of HBV and HCV suffered a drastic reduction at the point of interruption, and then immediately returned to non-significant values after 3 months. Even hospital access times, although with large upward fluctuations, did not highlight any statistically significant differences in the three pandemic years compared with the previous trend. This, in general, seems to be compatible with initial difficulties, but with a good performance of the National Health Service (NHS) in the 3 years postpandemic. Unfortunately, we are unable to establish causal relationships based on the nature of our data and analyses. We can only assume that, while the COVID-19 pandemic may have led to an underdiagnosis of viral hepatitis, it may also have had a somewhat

Table 2
AutoRegressive Integrated Moving Average (ARIMA) model chosen for each variable and related results.

Variable	Optimal model	AICc	Ljung–Box test's *P*-value	MAPE	Preinterruption slope (*P*-value)	Change in level (*P*-value)	Intercept with postinterruption slope (*P*-value)
Hepatitis A incidence	ARIMA(2,0,0) × (0,1,1) 4	474.74	0.255	36.56	0 (0.351)	−0.477 (0.582)	0.007 (0.635)
Hepatitis A time to diagnosis	ARIMA(0,0,0) × (2,1,0) 4	538.58	0.853	20.68	0 (0.985)	22.156 (0.100)	−0.347 (0.107)
Hepatitis A time to initiation of epidemiological investigation	ARIMA(0,0,0) × (2,1,0) 4	566.03	0.359	33.66	−0.008 (0.411)	14.711 (0.537)	−0.168 (0.661)
Hepatitis B incidence	ARIMA(1,0,1) × (0,1,1) 4 with constant	394.37	0.001	12.24	0 (0.178)	−0.251 (0.05)	0.004 (0.043)
Hepatitis B time to diagnosis	ARIMA(0,0,0) × (0,1,1) 4	534.23	0.749	18.79	−0.003 (0.260)	6.997 (0.578)	−0.109 (0.591)
Hepatitis B time to initiation of epidemiological investigation	ARIMA(0,0,0) × (0,1,1) 4	548.04	0.903	25.83	−0.003 (0.602)	73.157 (0.012)	−1.128 (0.015)
Hepatitis C incidence	ARIMA(1,0,1) × (0,1,1) 4	467.08	0.369	35.09	0 (<0.001)	−0.243 (0.003)	0.004 (0.002)
Hepatitis C time to diagnosis	ARIMA(0,0,0) × (0,1,1) 4	552.83	0.069	70.61	−0.01 (0.085)	9.815 (0.803)	−0.171 (0.786)
Hepatitis C time to initiation of epidemiological investigation	ARIMA(0,0,0) × (2,1,0) 4	566.7	0.010	41.24	−0.01 (0.638)	−477.151 (<0.001)	8.014 (<0.001)

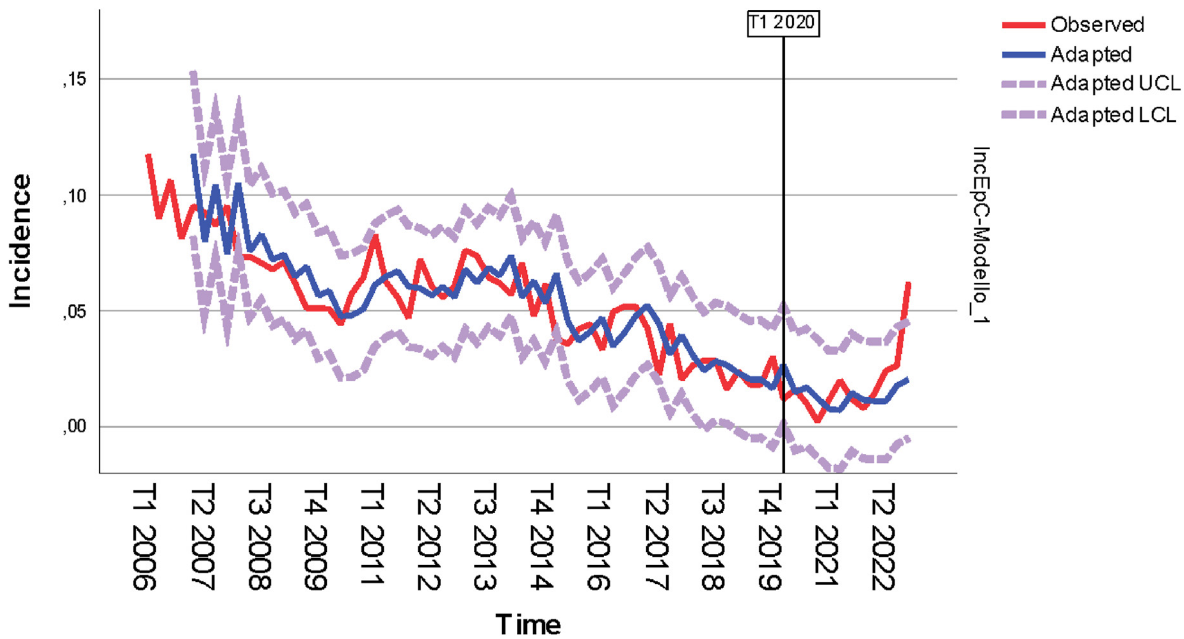

Fig. 2. Time series trend of hepatitis C incidence, 2006–2022. The x-axis represents time in quarters, ranging from T1 2006 to T4 2022. The y-axis displays the incidence of hepatitis C. The red line depicts the observed incidence trend, while the blue line represents the trendline adaptation, with its confidence interval denoted by two dashed lines. At T1 2020, a vertical line is introduced to signify the point of interruption in the time series.". (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article).

'protective' collateral effect. In this sense, the heightened focus on infection prevention and control (IPC) measures, as well as the implementation of isolation and quarantine protocols, may have contributed to a reduction in the transmission of viral hepatitis.[16,26,27]However, if hospital management seems to have withstood the strenuous tests of the COVID-19 pandemic, the same cannot be said for the SEIEVA surveillance system. The average time elapsed between the diagnosis and the start of the epidemiological investigation saw significant increases for all considered viruses, highlighting critical issues. This latency, in the case of HBV and especially HCV, seems to be associated with a subsequent gradual significant increase in incidence, which could be explained by an increase in secondary cases due to the lag in contact tracing and testing. In this sense, although the NHS appears to have succeeded in reasonably taking care of infected patients, the same attention may have been lacking in contacts due to work overload.

This study has several limitations. First of all, since SEIEVA is an epidemiological surveillance on a voluntary basis, not all LHAs have yet joined it, with more fragmented participation especially in the regions of Southern Italy: this may have resulted in incomplete data, potentially affecting the robustness of the findings. Additionally, the exclusion of LHAs not participating in the surveillance from the analysis could limit the generalizability of the results. Furthermore, the dynamic nature of the surveillance system and changes in LHA participation over the long study period may have influenced the stability and stationarity requirements of the model. Secondarily, the ARIMA models used for our interrupted time series analysis were an univariate models, so we did not include any possible covariate that could potentially impacted results: using only historical values of the target variable, without incorporating exogenous variables, can restrict the model's ability to capture causal relationships. For instance, it may be challenging to determine whether observed changes in incidence rates were directly attributable to the COVID-19 pandemic or to IPC measures implemented during the pandemic. The ARIMA model alone may not provide sufficient insight into such complex causal relationships. Furthermore, the use of ARIMA models is only one of the methodologies that can be applied to perform an interrupted time series analysis.[28] Also, the need to break down the data by quarter to have enough temporal observations even after the breakpoint resulted in a disaggregation of the data.[22] This made it impossible to carry out specific analyses for HDV and HEV, as well as not being able to estimate any regional differences. However, all this was done to ensure the implementation of a methodological approach that was as correct as possible. These model selections and their respective evaluations are critical

Table 3
Incidence difference (per quarter) and time difference (days per case per quarter) at 3, 12, 24 and 36 months (*P*-value) postinterruption (2020–2022).

Variable	3 months	12 months	24 months	36 months
Hepatitis A incidence	−0.053 (0.271)	−0.061 (0.301)	−0.035 (0.693)	−0.037 (0.785)
Hepatitis A time to diagnosis	2.408 (0.087)	1.366 (0.149)	−0.023 (0.979)	−1.412 (0.326)
Hepatitis A time to initiation of epidemiological investigation	5.174 (0.026)	4.666 (0.001)	3.989 (0.002)	3.312 (0.173)
Hepatitis B incidence	−0.14 (0.309)	−0.01 (0.897)	0.016 (0.103)	0.032 (0.030)
Hepatitis B time to diagnosis	0.744 (0.519)	0.529 (0.430)	0.056 (0.930)	−0.124 (0.924)
Hepatitis B time to initiation of epidemiological investigation	8.85 (0.001)	5.496 (<0.001)	0.968 (0.514)	−3.535 (0.228)
Hepatitis C incidence	−0.008 (0.329)	0.005 (0.381)	0.023 (0.002)	0.040 (<0.001)
Hepatitis C time to diagnosis	0.435 (0.904)	−0.207 (0.917)	−1.320 (0.446)	−1.967 (0.609)
Hepatitis C time to initiation of epidemiological investigation	−20.388 (<0.001)	3.66 (0.241)	35.723 (<0.001)	67.787 (<0.001)

components of our analysis, serving to provide insights into the temporal dynamics and trends observed in the data. Finally, as regards HBV and HCV, we are not able to estimate the long-term impact of the COVID-19 pandemic by having access only to data on acute forms and not, for example, to diagnostic screening tests for chronic forms.

Conclusion

We have shown a great reduction in the number of diagnosed cases of viral hepatitis, which could however be determined by underdiagnosis as well as by the protective effect of IPC and containment measures put in place during the pandemic. We have highlighted a general slowdown in surveillance times and hospital access times due to the COVID-19 pandemic. However, while hospital access times have returned to optimal prepandemic ranges, the surveillance system is still struggling, which could have led to an increase in diagnosed cases. It is urgent to restore previous levels of awareness and to recruit LHAs not yet active in the surveillance system to counter the spread of viral hepatitis and comply with WHO objectives.[6] In doing so, we can ensure the timely detection, management and prevention of viral hepatitis, even in the face of unprecedented global health crises such as the COVID-19 pandemic.

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References

1. European Centre for Disease Prevention and Control. Hepatitis A. In: *ECDC. Annual epidemiological report for 2022*. Stockholm: ECDC; 2024.
2. European Centre for Disease Prevention and Control. Hepatitis B. In: *ECDC. Annual epidemiological report for 2021*. Stockholm: ECDC; 2022.
3. European Centre for Disease Prevention and Control. Hepatitis C. In: *ECDC. Annual epidemiological report for 2020*. Stockholm: ECDC; 2022.
4. Demirel A, Uraz S, Deniz Z, Daglilar E, Basar O, Tahan V, et al. Epidemiology of hepatitis D virus infection in Europe: is it vanishing? *J Viral Hepat [Internet]* 2024 Feb 1;**31**(2):120–8 [cited 2024 Mar 3], https://pubmed.ncbi.nlm.nih.gov/37964693/.
5. Aspinall EJ, Couturier E, Faber M, Said B, Ijaz S, Tavoschi L, et al. Hepatitis E virus infection in Europe: surveillance and descriptive epidemiology of confirmed cases, 2005 to 2015. *Euro Surveill [Internet]* 2017 Jun 29;**22**(26):30561 [cited 2024 Mar 3], https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2017.22.26.30561.
6. World Health Organization. Hepatitis [Internet]. [cited 2023 Nov 15]. Available from: https://www.who.int/health-topics/hepatitis/#tab=tab_1.
7. European Statistical Office. About 5 500 deaths from hepatitis in the EU - Products Eurostat News - Eurostat [Internet]. [cited 2023 Nov 15]. Available from: https://ec.europa.eu/eurostat/en/web/products-eurostat-news/-/edn-20200728-1.
8. European Centre for Disease Prevention and Control. *The Sustainable Development Goals and Hepatitis B and C in the EU/EEA [Internet]* 2021 [cited 2023 Nov 15]. Available from: https://www.who.int/immunization/monitoring_surveillance/data/en.
9. Istituto Superiore di Sanità. Seieva (Sistema epidemiologico integrato dell'epatite virale acuta) [Internet]. [cited 2023 Nov 15]. Available from: https://www.epicentro.iss.it/epatite/seieva.
10. European Centre for Disease Prevention and Control. European Network for Hepatitis B and C Surveillance [Internet]. [cited 2023 Nov 15]. Available from: https://www.ecdc.europa.eu/en/about-us/who-we-work/disease-and-laboratory-networks/european-network-hepatitis-b-and-c.
11. Kaufman HW, Bull-Otterson L, Meyer WA, Huang X, Doshani M, Thompson WW, et al. Decreases in hepatitis C testing and treatment during the COVID-19 pandemic. *Am J Prev Med [Internet]* 2021 Sep 1;**61**(3):369–76 [cited 2023 Nov 15], https://pubmed.ncbi.nlm.nih.gov/34088556/.
12. Sperring H, Ruiz-Mercado G, Schechter-Perkins EM. Impact of the 2020 COVID-19 pandemic on ambulatory hepatitis C testing. *J Prim Care Community Health [Internet]* 2020;**11** [cited 2023 Nov 15], https://pubmed.ncbi.nlm.nih.gov/33225792/.
13. Mandel E, Peci A, Cronin K, Capraru CI, Shah H, Janssen HLA, et al. The impact of the first, second and third waves of covid-19 on hepatitis B and C testing in Ontario, Canada. *J Viral Hepat [Internet]* 2022 Mar 1;**29**(3):205–8 [cited 2023 Nov 15], https://pubmed.ncbi.nlm.nih.gov/34820967/.
14. Kessel B, Heinsohn T, Ott JJ, Wolff J, Hassenstein MJ, Lange B. Impact of COVID-19 pandemic and anti-pandemic measures on tuberculosis, viral hepatitis, HIV/AIDS and malaria—A systematic review [cited 2023 Nov 15] *PLOS Global Public Health [Internet]* 2023;**3**(5):e0001018. Available from:/pmc/articles/PMC10150989/.
15. Downey LE, Gadsden T, Vilas VDR, Peiris D, Jan S. The impact of COVID-19 on essential health service provision for endemic infectious diseases in the South-East Asia region: a systematic review. *The Lancet regional health Southeast Asia [Internet]* 2022;**1**:100011 [cited 2023 Nov 15]. Available from: https://pubmed.ncbi.nlm.nih.gov/35769109/.
16. Zhou Q, Hu J, Hu W, Li H, Lin G zhen. Interrupted time series analysis using the ARIMA model of the impact of COVID-19 on the incidence rate of notifiable communicable diseases in China. *BMC Infect Dis [Internet]* 2023 Dec 1;**23**(1):1–10 [cited 2023 Nov 15], https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-023-08229-5.
17. The Lancet Gastroenterology & Hepatology. Eliminating viral hepatitis in the COVID-19 era: weighing challenge and opportunity. *Lancet Gastroenterol Hepatol [Internet]* 2020 Sep 1;**5**(9):789 [cited 2023 Nov 15], https://pubmed.ncbi.nlm.nih.gov/32730787/.
18. Waheed Y. Progress on global hepatitis elimination targets. *World J Gastroenterol [Internet]* 2021 Dec 21;**27**(47):8199–200 [cited 2023 Nov 15], https://pubmed.ncbi.nlm.nih.gov/35068864/.
19. Blach S, Kondili LA, Aghemo A, Cai Z, Dugan E, Estes C, et al. Impact of COVID-19 on global HCV elimination efforts [cited 2023 Nov 15] *J Hepatol [Internet]* 2021 Jan 1;**74**(1):31. Available from:/pmc/articles/PMC7411379/.
20. Alfonsi V, Romanò L, Ciccaglione AR, La Rosa G, Bruni R, Zanetti A, et al. Hepatitis e in Italy: 5 years of national epidemiological, virological and environmental surveillance, 2012 to 2016. *Euro Surveill [Internet]* 2018 Oct 11;**23**(41):1700517 [cited 2023 Nov 15], https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2018.23.41.1700517.
21. Stroffolini T, Morisco F, Ferrigno L, Pontillo G, Iantosca G, Cossiga V, et al. Acute Delta Hepatitis in Italy spanning three decades (1991-2019): evidence for the effectiveness of the hepatitis B vaccination campaign. *J Viral Hepat [Internet]* 2022 Jan 1;**29**(1):78–86 [cited 2023 Nov 15], https://pubmed.ncbi.nlm.nih.gov/34585819/.
22. McCleary R, Hay R, Meidinger E, McDowall D. *Applied time series analysis for the social sciences* 1980:20 [cited 2023 Nov 15]; Available from: https://www.ojp.gov/ncjrs/virtual-library/abstracts/applied-time-series-analysis-social-sciences.
23. Vicentini C, Bazzolo S, Gamba D, Zotti CM. Analysis of the fatality rate in relation to testing capacity during the first 50 days of the COVID-19 epidemic in Italy. *Am J Trop Med Hyg [Internet]* 2020 Dec 1;**103**(6):2382–90 [cited 2023 Nov 15], https://pubmed.ncbi.nlm.nih.gov/33078703/.
24. Hurvich CM, Tsai C-L. A corrected akaike information criterion for vector autoregressive model selection. *J Time Ser Anal [Internet]* 1993 May 1;**14**(3):271–9 [cited 2023 Nov 15], https://onlinelibrary.wiley.com/doi/full/10.1111/j.1467-9892.1993.tb00144.x.
25. Lewis CD. *Industrial and business forecasting methods: a practical guide to exponential smoothing and curve fitting*. Oxford: Butterworth-Heinemann; 1982.
26. Wee LEI, Conceicao EP, Tan JY, Magesparan KD, Amin IBM, Ismail BBS, et al. Unintended consequences of infection prevention and control measures during COVID-19 pandemic. *Am J Infect Control [Internet]* 2021 Apr 1;**49**(4):469–77 [cited 2023 Nov 15], https://pubmed.ncbi.nlm.nih.gov/33157180/.
27. Russotto A, Rolfini E, Paladini G, Gastaldo C, Vicentini C, Zotti CM. Hand hygiene and antimicrobial resistance in the COVID-19 era: an observational study. *Antibiotics [Internet]* 2023 Mar 1;**12**(3) [cited 2024 Mar 3], https://pubmed.ncbi.nlm.nih.gov/36978450/.
28. Turner SL, Karahalios A, Forbes AB, Taljaard M, Grimshaw JM, McKenzie JE. Comparison of six statistical methods for interrupted time series studies: empirical evaluation of 190 published series. *BMC Med Res Methodol [Internet]* 2021 Jun 26;**21**(1):134 [cited 2023 Nov 15], https://bmcmedresmethodol.biomedcentral.com/articles/10.1186/s12874-021-01306-w.