TITLE PAGE

Full-length title: Control of common viral epidemics but not of SARS-CoV-2 through the application of hygiene and distancing measures

Type of article: Article

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Abstract – 246 words

Background

Since 2003, we have systematically investigated respiratory and gastrointestinal infections of viral origin in patients who are admitted to our hospital (IHU Marseille, France) with lung or intestinal symptoms. We evaluated whether the measures implemented to fight COVID-19 had an effect on the dynamics of other viral infections.

Methods

This epidemiological surveillance (MIDaS) is carried out using a set of tests based on the recognition of specific viral sequences after polymerase chain reaction. Since 2020, a diagnosis of COVID-19 was added to the panel of tests that were already routinely used for infectious disease monitoring.

Results

In total, 100,000 analyses were carried out for respiratory infections (not including SARS-CoV-2), 500,000 for SARS-CoV-2 and 27,000 for gastrointestinal infections. In the winter of 2020–2021, when the most restrictive lockdown measures were in place in France, a disappearance of influenza and the respiratory syncytial virus was observed, demonstrating the relative effectiveness of these measures. SARS-CoV-2 did not seem to be affected by these drastic control measures. The rhinoviruses, parainfluenza 3 virus, and the NL63 coronavirus remained at levels comparable to that observed in previous years.

Conclusion

The measures taken to control COVID-19 were clearly effective against lower respiratory tract infections viruses and gastroenteritis agents, but no efficacy on the agents of the common winter cold (rhinovirus, parainfluenza 3 virus, NL63 coronavirus). These elements suggest that more specific measures to prevent COVID-19 and upper respiratory tract infections need to be discovered to limit the spread of this epidemic.

Key words: Coronavirus; respiratory infections; gastrointestinal infections; SARS-CoV-2; MIDaS

Funding

This work was supported by the French Government under the “Investments for the Future” programme managed by the National Agency for Research (ANR), Méditerranée-Infection 10-IAHU-03, and was also supported by Région Provence Alpes Côte d’Azur and European funding FEDER PRIMMI (Fonds Européen de Développement Régional - Plateformes de Recherche et d'Innovation Mutualisées Méditerranée Infection).

Competing interests

The authors have no competing interests.

Background

The SARS-CoV-2 epidemic in Europe and the United States proved to be completely unpredictable. The circulation of strains between countries and the emergence of new variants led to different epidemic profiles.

In order to reduce the spread of SARS-CoV-2, the French government decided to take several health and social measures. This initially involved repeated risk prevention messages on the use of protective measures including regularly hand washing with soap or alcohol-based hand gel, social distancing of two meters between individuals, and wearing a mask [1]. These measures had already been used in prevention campaigns for other viruses, particularly respiratory viruses such as influenza [2,3]. More restrictive measures on movement were also taken, with the implementation of a number of lockdowns and curfews (Decree No. 2020–260; Decree No. 2020–1310) [4,5]. Thus, in addition to the fight against COVID-19, these measures may also be effective at controlling other communicable respiratory and digestive diseases.

At the IHU Méditerranée Infection (IHU-MI), the work of the virology and microbiology laboratory is monitored by a collection and surveillance system known as MIDaS (for Mediterranée Infection Data Warehousing and Surveillance) [6,7]. This system enables us to monitor respiratory and digestive virus infections on a weekly basis, and has included COVID-19 since its emergence in France [8]. The objective of this paper is to analyse the epidemiological curves of respiratory and gastrointestinal viruses since the emergence of SARS-CoV-2 and to evaluate their possible epidemiological changes under the measures implemented against COVID-19 in France by comparing these results over the past five years.

Materials and methods

Surveillance system

Since 2003, the work of our clinical microbiology laboratory has involved massive and unbiased monitoring of all clinical samples received for testing bacteria, viruses, parasites and fungi (8,9). This followed recommendations one of the authors (DR) [10] made to the French government in 2003 to set up surveillance systems of any abnormal events related to infectious diseases based on our laboratory data, including through syndromic surveillance. These are the only laboratories to diagnose infections for all public university hospitals (Assistance Publique - Hôpitaux de Marseille (AP-HM)) in Marseille, which has a total of 3,288 beds with nearly 125,000 admissions and one million consultations per year. Our laboratory conducts approximately eight million tests every year.

Since 2013 when the IHU Méditerranée Infection was established, our surveillance tools have expanded further and have improved through our unique MIDaS (for Mediterranée

Infection Data Warehousing and Surveillance) collection and surveillance system, which consists of five sub-systems [6]. We systematically collect all laboratory data (samples, tests, positive diagnoses) from the Nexlab laboratory management system. All microbiological analysis results (sample identification, requesting department, date, sampling, analysis, result, antibiotic susceptibility testing, antibiotic resistance phenotype, bacterial co-identifications) and patient information (anonymised patient identification, age, sex, home postal code, anonymised hospital stay identification, date of stay within a department, death) are then deposited in a dedicated data warehouse. All samples, tests and infectious agents are monitored on a weekly basis throughout the year. MIDaS automatically detects any aberrations in the statistical signal using the CUSUM algorithm and triggers alarms [11]. These alarms are discussed during a weekly epidemiological staff meeting, which includes epidemiologists, biologists, infectiologists and pharmacists.

Respiratory and gastrointestinal samples and infectious agents are some of the items surveyed. Generally speaking, respiratory and gastrointestinal viruses are diagnosed in our laboratory using commercial or home-made real-time PCR (qPCR) tests and adopting a syndromic approach using multiplex tests or simplex tests. These include influenza A and B viruses, respiratory syncytial virus (RSV), rhinoviruses, enteroviruses, adenoviruses, metapneumovirus, endemic coronaviruses (OC43, NL63, E229 and HKU1), parainfluenza viruses 1 to 4 (HPIV1 to HPIV4) and SARS-CoV-2, over a period of time from January 2017 to February 2021. For the detection of SARS-CoV-2 RNA, we used in house RT-PCR procedures previously described [12]. To detect the other respiratory viruses, we used the FTD Respiratory pathogens 21 (Fast Track Diagnosis, Luxembourg), the Biofire FilmArray Respiratory panel 2 plus (BioMérieux, Marcy-l'Etoile, France), the Respiratory Multi-Well System r-gene (Argene, BioMérieux), or the GeneXpert Xpert Flu/RSV (Cepheid, Sunnyvale, CA) assays [13].

Data on diagnoses of influenza A and B viruses were also collected from a private clinical microbiology and virology laboratory through the PACASurvE network that extents our surveillance system to private medical biology laboratories located in the Marseille geographical area [14]. These diagnoses were reached by an immunochromatographic assay in 2017 and then switched to the GeneXpert Flu/RSV assay between 2018 and 2021.

The gastrointestinal viruses diagnosed included adenoviruses, rotaviruses, sapoviruses, noroviruses and astroviruses. The tests were performed using the FTD viral gastroenteritis pathogens assay (Fast Track Diagnosis).

Statistical analyses

In order to better understand the evolution of respiratory and gastrointestinal viruses over time, the proportion of positive results between October and the end of February were compared for each virus for the 2017–2018, 2018–2019, 2019–2020 and 2020–2021 seasons. These evolutions were analysed using the log-linear model, and the Fisher and Chi-square tests for point comparisons with a statistical significance threshold of 0.05 [15].

Government measures and policies

Measures taken by the French government in the fight against the spread of SARS-CoV-2 and dates these measures were implemented were collected from the government website (https://www.gouvernement.fr/info-coronavirus/les-actions-du-gouvernement).

Results

Total respiratory viral infections diagnoses at IHU-MI from 2017 to 2021

Over a period of five years (January 2017 to February 2021), 990,364 analyses were performed for common respiratory viruses, with 37,915 positive results. Most of these cases were due to influenza viruses (influenza A virus, 6,544; influenza B viruses, 2,459) followed by rhinoviruses (7,379), RSVs (3,846), adenovirus (1,991), metapneumoviruses (1,482), enteroviruses (790), HKU1 coronavirus (424), NL63 coronavirus (421), OC43 coronavirus (227), E229 coronavirus (87), HPIV3 (340), HPIV4 (68), HPIV2 (18) and HPIV4 (9) (Table 1).

Viruses	Tests						Positive											
	2017	2018	2019	2020	2021	**TOTAL 2017-2021**	2017		2018		2019		2020		2021		**TOTAL 2017-2021**	
	N	N	N	N	N		N	%	N	%	N	%	N	%	N	%	N	%
Adenovirus	5,656	14,881	17,636	32,237	5,283	**75,693**	160	2.8	449	3.0	652	3.7	600	1.9	130	2.5	**1,991**	**2.6**
Common coronaviruses	2,395	3,773	8,211	32,237	5,283	**51,899**	70	2.9	110	2.9	231	2.8	998	3.1	276	5.2	**1,685**	**3.2**
CoV 229E	2,395	3,773	8,211	11,739	5,283	**31,401**	0	0.0	0	0.0	0	0.0	84	0.7	3	0.1	**87**	**0.3**
CoV HKU1	2,395	3,773	8,211	11,736	5,283	**31,398**	0	0.0	0	0.0	0	0.0	423	3.6	1	0.0	**424**	**1.4**
CoV NL63	3,791	3,773	8,211	11,739	5,283	**32,797**	0	0.0	0	0.0	0	0.0	252	2.1	169	3.2	**421**	**1.3**
CoV OC43	9,007	3,773	8,211	11,740	5,283	**38,014**	0	0.0	0	0.0	0	0.0	175	1.5	102	1.9	**277**	**0.7**
Enterovirus	4,362	8,933	17,649	32,237	5,283	**68,464**	36	0.8	164	1.8	279	1.6	307	1.0	4	0.1	**790**	**1.2**
Influenza virus	12,992	14,856	17,844	32,237	5,283	**83,212**	1,737	13.4	1,708	11.5	2,427	13.6	3,119	9.7	0	0.0	**8,991**	**10.8**
Influenza A virus	12,608	14,859	17,847	32,237	5,283	**82,834**	1,525	12.1	936	6.3	2,397	13.4	1,686	5.2	0	0.0	**6,544**	**7.9**
Influenza B virus	13,088	14,858	17,847	32,237	5,283	**83,313**	222	1.7	772	5.2	30	0.2	1,435	4.5	0	0.0	**2,459**	**3.0**
Metapneumovirus	7,654	14,750	17,622	32,237	5,283	**77,546**	230	3.0	325	2.2	445	2.5	462	1.4	20	0.4	**1,482**	**1.9**
Parainfluenza	9,007	3,771	8,268	32,237	5,283	**58,566**	15	0.2	200	5.3	438	5.3	129	0.4	322	6.1	**1,104**	**1.9**
HPIV1	3,791	3,771	8,268	9,268	5,283	**30,381**	0	0.0	0	0.0	0	0.0	9	0.1	0	0.0	**9**	**0.0**
HPIV2	3,791	3,771	8,268	9,268	5,283	**30,381**	0	0.0	0	0.0	0	0.0	17	0.2	1	0.0	**18**	**0.1**
HPIV3	2,395	3,771	8,268	9,268	5,283	**28,985**	0	0.0	0	0.0	0	0.0	41	0.4	299	5.7	**340**	**1.2**
HPIV4	2,395	3,771	8,268	9,268	5,283	**28,985**	0	0.0	0	0.0	0	0.0	48	0.5	20	0.4	**68**	**0.2**
Rhinovirus	4,305	14,057	17,637	32,237	5,283	**73,519**	401	9.3	1,771	12.6	2,264	12.8	2,494	7.7	449	8.5	**7,379**	**10.0**
RSV	12,756	14,849	17,851	32,237	5,283	**82,976**	923	7.2	1,024	6.9	1,347	7.5	498	1.5	54	1.0	**3,846**	**4.6**
SARS-CoV-2	710	0	0	420,120	90,551	**511,381**	0	0,0	0	0	0	0	26,723	6.4	8,236	9.1	**34,959**	**6.8**

Table 1 – Tests performed and positive for PCR detection of respiratory viruses in 2017, 2018, 2019, 2020 and 2021 at IHU Méditerranée Infection.

Slight yearly variations were observed from 2017 to 2019 with regards to the respective prevalence of these viruses (Figure 1). In 2017, the influenza A virus was the most frequently identified respiratory viral agent (12.1%), followed by rhinovirus (9.3%) and RSV (7.2%). In the same year, 1.7% of samples tested for influenza B virus were positive for this agent. In 2018, the rhinovirus was the most commonly diagnosed (12.6%), compared to 6.9% for RSV, 6.3% for influenza A virus and 5.2% for influenza B virus. 2019 was comparable to 2017 in terms of the ranking of respiratory viruses, although the proportions of respiratory viruses' diagnoses were higher in 2019. The intensity of the epidemic peak for each of these respiratory viruses therefore changed over the years, as did the date upon which they appeared (Figure 1).

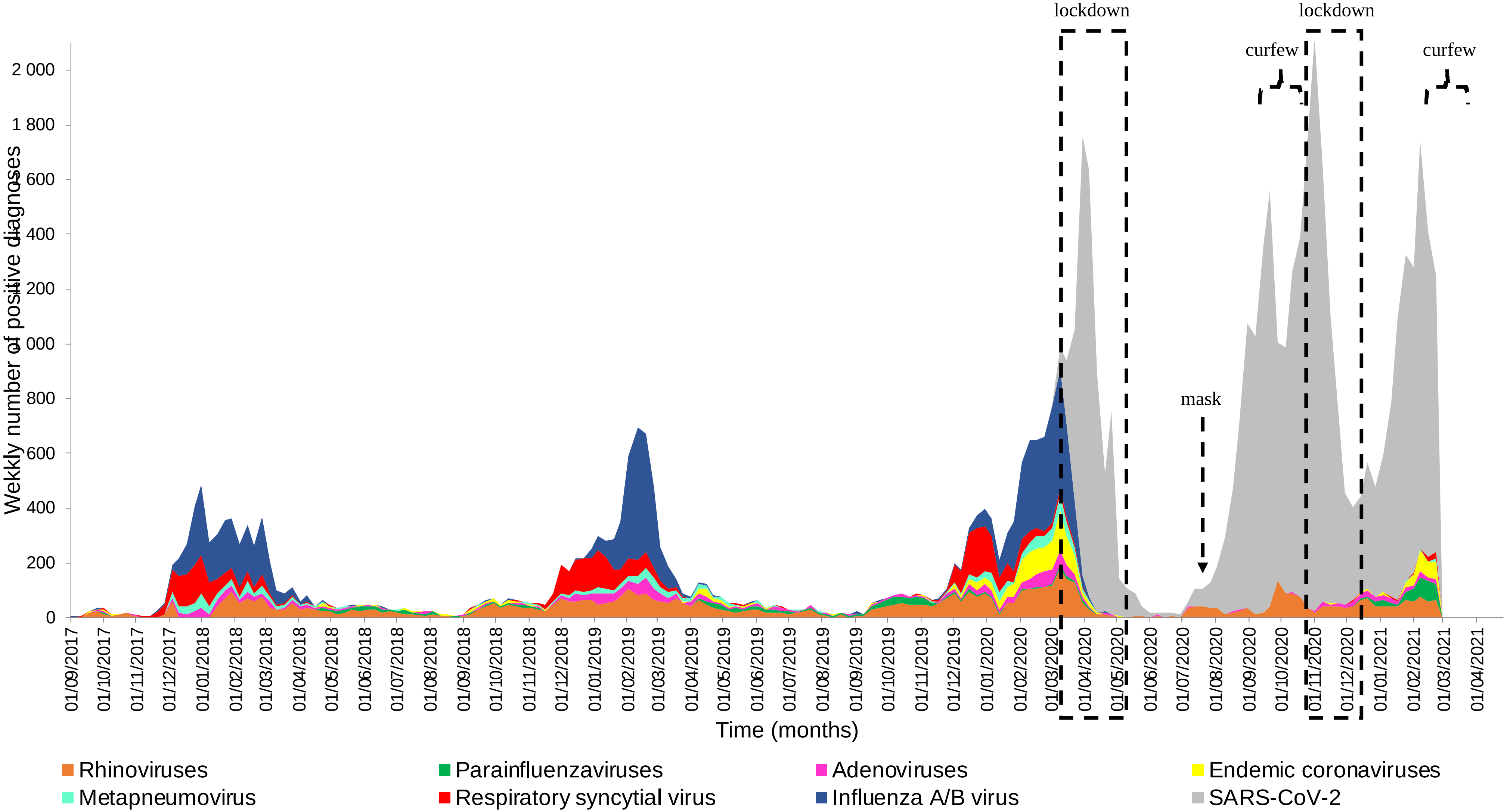

Figure 1 – Respiratory virus infections diagnosed at IHU Méditerranée Infection in 2017-2021. Actions taken by the government are indicated by a dotted square for lockdowns, an arrow for the obligation to wear a mask in enclosed spaces, and a brace symbol for curfews.

Since February 2020, 511,381 samples have been analysed for SARS-CoV-2 and 34,959 tested positive (6.8%). Of 420,120 samples tested for SARS-CoV-2 in 2020, 6.4% (N = 26,723) were positive while in 2021, out of 90,551 samples, 9.1% were positive. The government introduced several restrictive measures in an attempt to mitigate the spread of SARS-CoV-2 and to control the epidemic as effectively as possible. A first lockdown was imposed between 17 March 2020 and 11 May 2020, recommendations have been in place on wearing masks in enclosed spaces (particularly in the workplace) since 20 July 2020, a curfew was introduced between 8pm and 6am between 17 October 2020 and 28 October 2020, a second lockdown took place between 29 October 2020 and 15 December 2020, and a new curfew was introduced on 16 January 2021 from 6pm to 6am. In addition to these actions, individual preventive measures have also been recommended, including hand washing with soap or alcohol-based hand gel, a distance of 1.5 metres between individuals and the promotion of remote working. In 2020, the proportion of positive tests dramatically decreased to 7.7% for rhinovirus, 5.2% for influenza A, 4.5% for influenza B and 1.5% for RSV. This was also the case for the first two months of 2021, where no cases of influenza A or B were observed. In the first two months of 2021, the most frequently diagnosed virus was SARS-CoV-2 (9.1%), followed by rhinovirus (8.5%), parainfluenza virus (6.1%, mainly HPIV3: 5.7%) and other endemic coronaviruses (5.2%, mainly NL63: 3.2%). The same results were observed from a private clinical microbiology and virology laboratory through the PACASurvE network (Table 2).

Table 2: Results for influenza A virus and influenza B virus by year from a private clinical microbiology and virology laboratory through the PACASurvE network.

Year	**Samples**	**Influenza A virus diagnosis**	**%**	**Influenza B virus diagnosis**	**%**
2017	547	67	12.2	2	0.4
2018	1,111	63	5.7	29	2.6
2019	2,410	681	28.3	32	1.3
2020	2,625	500	19.0	357	13.6
2021	106	0	0.0	1	0.9

Comparison of winter seasons for respiratory viral infections

In order to avoid the Simpson effect [16], we compared results during cold seasons (from October to mid-February). Over the last four such seasons, the most significant variations were observed for influenza A virus, with a positivity rate of 11.3% of the 9,819 tested samples during the 2017–2018 winter season, which increased to 18.6% of the 10,973 tested samples during the 2018–2019 season, dropped to 9.6% of the 11,711 tested samples in 2019–2020 and accounted for 0% of the 8,786 tested samples in 2020–2021 (Figure 1, Table 3). As of 24 February 2021, no cases of influenza A virus had been diagnosed during the 2020–2021 winter season. Influenza B virus is also absent for the 2020–2021 winter season, although this had already been observed in 2018–2019. Respiratory syncytial virus (RSV) also showed a considerable decrease in the proportion of positive cases, reaching 0.6% (N = 56) in 2020–2021 compared to 10% on average in the other three cold periods (p-value <0.001). Metapneumovirus and enterovirus had a less marked decrease (respectively, N = 21 and 9 in 2020–2021 vs N = 339 and 375 in 2019–2020, p-value < 0.001). The adenovirus positivity rate has remained relatively constant over time, at about 3% (p-value > 0.05), as was the case for endemic coronaviruses in 2017–2018 and 2018–2019. A significant decrease was nevertheless observed in 2020–2021 (p-value < 0.001). Rhinovirus exhibited a significantly higher positivity rate in 2020–2021 (12.9%) compared to 2017–2019 and 2018–2019 (9.9% and 10.9% respectively, p-value < 0.001). The positivity rate of the HPIV3 parainfluenza virus increased from 0.1% (N = 4) in 2019–2020 to 3.7% (N = 324) in 2020–2021 (p-value < 0.001).

Table 3 - Tests performed and positive for PCR detection of respiratory viruses, during the same cold months in 2017–2018, 2018–2019, 2019‑2020 and 2020‑2021

Viruses	Tests				Positive											
	2017-2018	2018-2019	2019-2020	2020-2021	2017-2018			2018-2019			2019-2020			2020-2021	
	N	N	N	N	N	%	p-value	N	%	p-value	N	%	p-value	N	%
Adenovirus	8,876	10,831	11,687	8,786	262	3.0	0.51	416	3.8	0.006	355	3.0	0.74	274	3.1
Common coronaviruses	387	1,123	11,556	8,786	13	3.4	0.97	37	3.3	0.96	617	5.3	<0.001	292	3.3
CoV 229E	387	1,123	6,357	8,786	0	0.0	1	0	0.0	1	31	0.5	<0.001	5	0.1
CoV HKU1	387	1,123	6,357	8,786	0	0.0	1	0	0.0	1	236	3.7	<0.001	1	0.0
CoV NL63	387	1,123	6,357	8,786	0	0.0	0.006	0	0.0	<0.001	114	1.8	0.49	171	1.9
CoV OC43	657	1,123	6,357	8,786	0	0.0	0.003	0	0.0	<0.001	56	0.9	0.02	114	1.3
Enterovirus	900	10,830	11,688	8,786	13	1.4	<0.001	153	1.4	<0.001	375	3.2	<0.001	9	0.1
Influenza virus	9,819	10,973	11,711	8,786	1,839	18.7	<0.001	2,044	18.6	<0.001	1,850	15.8	<0.001	1	0.0
Influenza A virus	9,819	10,973	11,711	8,786	1,106	11.3	<0.001	2,042	18.6	<0.001	1,125	9.6	<0.001	0	0.0
Influenza B virus	9,819	10,973	11,711	8,786	743	7.6	<0.001	2	0.0	1	727	6.2	<0.001	1	0.0
Metapneumovirus	8,873	10,830	11,687	8,786	315	3.6	<0.001	258	2.4	<0.001	339	2.9	<0.001	21	0.2
Parainfluenza	657	1,127	11,605	8,786	4	0.6	<0.001	42	3.7	0.68	226	1.9	<0.001	350	4.0
HPIV1	387	1,127	6,001	8,786	0	0.0	1	0	0.0	1	2	0.0	0.16	0	0.0
HPIV2	387	1,127	6,001	8,786	0	0.0	1	0	0.0	1	4	0.1	0.17	1	0.0
HPIV3	387	1,127	6,001	8,786	0	0.0	<0.001	0	0.0	<0.001	4	0.1	<0.001	324	3.7
HPIV4	387	1,127	6,001	8,786	0	0.0	0.62	0	0.0	0.1	14	0.2	0.73	23	0.3
Rhinovirus	5,150	10,833	11,683	8,786	511	9.9	<0.001	1,194	11.0	<0.001	1,420	12.2	0.11	1,134	12.9
RSV	9,912	10,973	11,707	8,786	988	10.0	<0.001	1,196	10.9	<0.001	1,104	9.4	<0.001	56	0.6
SARS-CoV-2	183	0	5,628	244,310	0	0.0	<0.001	0	0.0	-	0	0.0	<0.001	20748	8.5

Total gastrointestinal viral infections at IHU-MI in 2017–2021

Between 2017 and 2021, 27,719 tests were performed resulting in approximately 1,098 diagnoses of gastrointestinal infections (Table 4). Rotavirus (5.6% for 6,612 samples analysed) was the most frequently diagnosed gastrointestinal virus over the study period, followed by adenovirus (5.2% for 6,227 samples analysed) and norovirus (4.2% for 7,791 samples analysed). As was previously observed for respiratory viruses, the intensity of the epidemic peak as well as the date of its onset varied over the years (Figure 2). In 2017, 2018 and 2020, adenovirus was the most frequently identified virus (5.0%, 7.6% and 4.1% respectively) while in 2019, rotavirus (8.6%) was the virus most commonly identified.

In the first two months of 2021, of the 255 samples analysed, rotavirus was again the most frequently identified virus (N = 12, 4.7%) followed by norovirus (N = 10, 3.9%) and adenovirus (N = 10, 3.9%).

Table 4 - Tests performed and positive for PCR detection of gastrointestinal viruses in 2017, 2018, 2019, 2020 and 2021 at IHU Méditerranée Infection.

Viruses	**Tests**						**Positive**											
	2017	2018	2019	2020	2021	**TOTAL 2017-2021**	2017		2018		2019		2020		2021		**TOTAL 2017-2021**	
	N	N	N	N	N	**N**	N	%	N	%	N	%	N	%	N	%	**N**	**%**
Adenovirus	1,674	1,662	1,470	1,166	255	**6,227**	83	5.0	127	7.6	56	3.8	48	4.1	10	3.9	**324**	**5.2**
Astrovirus	0	886	1,458	1,146	255	**3,745**	0	-	18	2.0	16	1.1	6	0.5	0	0.0	**40**	**1.1**
Norovirus	1,386	1,666	2,368	2,116	255	**7,791**	60	4.3	91	5.5	101	4.3	63	3.0	10	3.9	**325**	**4.2**
Rotavirus	1,640	1,662	1,471	1,184	255	**6,212**	78	4.8	88	5.3	127	8.6	45	3.8	12	4.7	**350**	**5.6**
Sapovirus	0	886	1,460	1,143	255	**3,744**	0	-	12	1.4	38	2.6	8	0.7	1	0.4	**59**	**1.6**

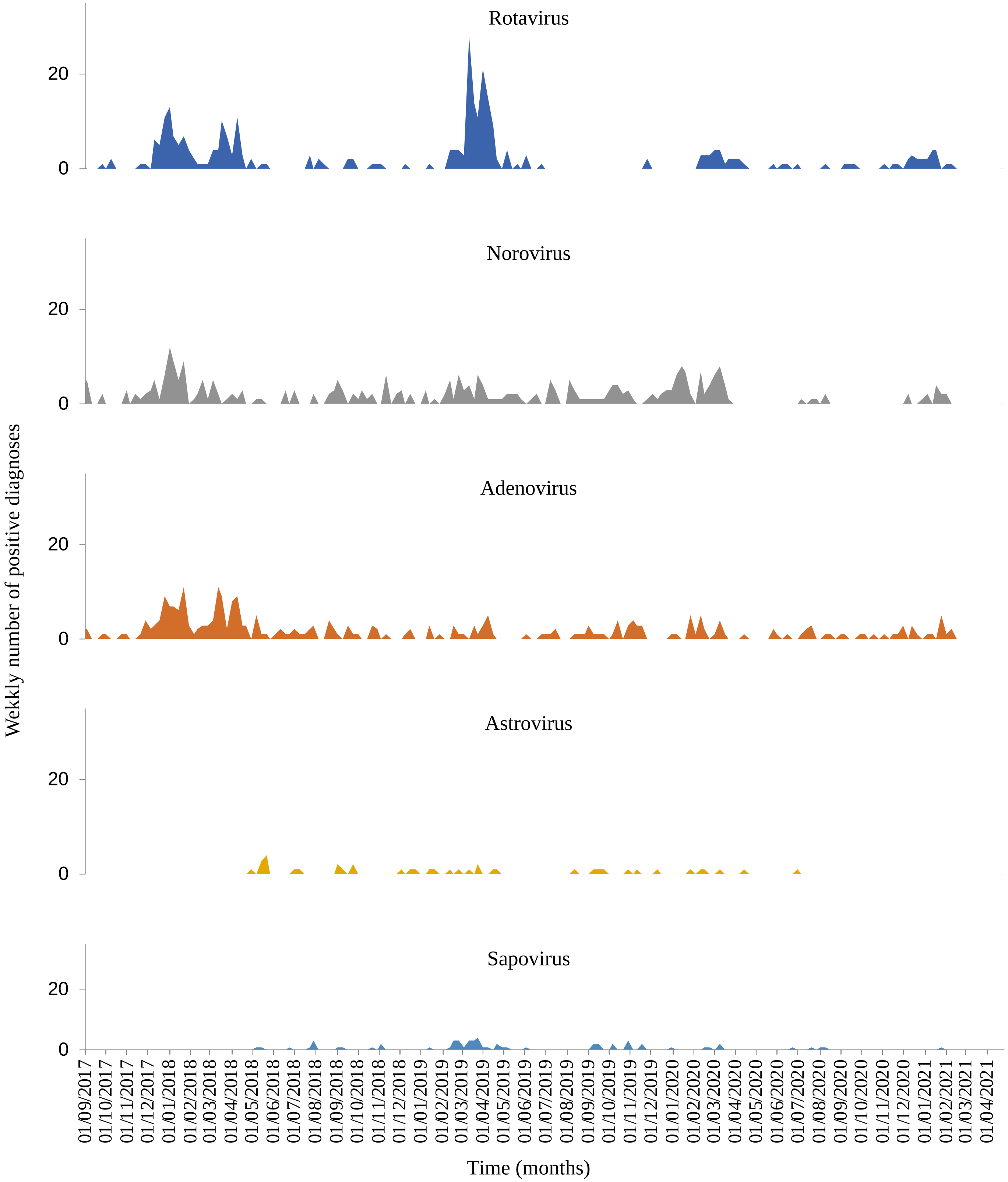

Figure 2 – Gastrointestinal viruses diagnosis between October 2017 and February 2021at IHU Méditerranée Infection.

Comparison of winter seasons for gastrointestinal viral infections

The overall positivity rate of gastrointestinal infections decreased significantly over time during the winter seasons (Table 5). Notably, the norovirus winter season positivity rates decreased continuously and significantly over time (2017–2018: 9.3%; 2018–2019: 8.4%; 2019–2020: 5.5%; 2020–2021: 2.0%).

In contrast, adenovirus and rotavirus showed stable positivity rates between 2018–2019 (3.8% and 2.4% respectively) and 2020–2021 winter seasons (3.4% and 3.6% respectively) (Figure 2).

Table 5 - Tests performed and positive for PCR detection of gastrointestinal viruses, during the same cold months in 2017‑2018, 2018‑2019, 2019‑2020 and 2020‑2021.

Viruses	**Tests**				**Positive**										
	2017-2018	2018-2019	2019-2020	2020-2021	2017-2018			2018-2019			2019-2020			2020-2021	
	N	N	N	N	N	%	p-value	N	%	p-value	N	%	p-value	N	%
Adenovirus	661	369	380	642	61	9.2	<0.001	14	3.8	0.8	31	8.2	0.001	22	3.4
Astrovirus	0	369	368	619	0	0.0	1.0	6	1.6	0.003	5	1.4	0.01	0	0.0
Norovirus	636	369	1026	664	59	9.3	<0.001	31	8.4	<0.001	56	5.5	<0.001	13	2.0
Rotavirus	661	369	380	661	64	9.7	<0.001	9	2.4	0.3	5	1.3	0.03	24	3.6
Sapovirus	0	369	369	619	0	0.0	1.0	5	1.4	0.03	8	2.2	0.002	1	0.2

Discussion

In this paper, the systematic monitoring of our microbiology and virology laboratory work has enabled us to identify changes in the epidemiology of respiratory and gastro-intestinal viral communicable diseases during the spread of a new emerging virus, SARS-CoV-2.

These data show that the epidemiology of infection with SARS-CoV-2 is not at all similar to that of other respiratory infections. As observed in other countries and in France, flu viruses have decreased dramatically [17-19]. It should be noted that the number of infections by endemic coronaviruses and rhinovirus does not seem to be particularly affected by the preventive measures taken and may have, in common with COVID-19, modes of transmission that are different from those of influenza viruses, RSV and the other respiratory viruses studied. Curiously, in our region, a higher number of parainfluenza virus 3 (HPIV3) were observed. One of the explanations for these epidemiological figures could be that the viruses experiencing a decrease in their incidence are most often involved in pneumonia, while, conversely, the agents responsible for nasal infections and for causing colds, such as endemic coronaviruses or HPIV3, remain constant. Measures to control COVID-19 would then prevent pneumonia and gastroenteritis. From this hypothesis, it would be interesting to study the nasal and pneumonic forms in COVID-19 patients and assess their evolution in time.

The impact of measures to control COVID-19 probably played a major role in these epidemiological changes [20]. These measures included both repeated recommendations on risk prevention measures such as hand washing with soap or alcohol-based hand gel, disinfecting surfaces, and social distancing, but also actions which were legally enforced, including wearing masks and the implementation of lockdown or curfews [1,21]. Hand washing and disinfection was probably the main factor having an impact upon the usual respiratory and gastrointestinal viral infections [22], and have been key elements of influenza prevention campaigns for several years [3]. It is not clear from the literature that lockdown measures and other social control measures have really had an impact on the spread of SARS-CoV-2 or on other respiratory infections [23]. For example, Sweden has issued very few social control measures while other countries such as France have implemented relatively strong measures without significantly differences in the number of cases or mortality [24].

The lack of effectiveness of these measures on the COVID-19 epidemic raises several questions. The first is the existence of infection outbreaks in animals which are distinct from outbreaks in humans. It has been demonstrated that the emergence of new variants could be encouraged by the intensive captive breeding of certain animals such as mink, which are likely to contaminate humans by being potentially more contagious or more pathogenic for humans [25-27]. Furthermore, it seems likely that a certain number of treatments, including serotherapy with hyper-human serums and antivirals such as remdesivir, can promote the appearance of mutations [28].

In conclusion, this study confirms that it is futile to try to make predictions about a disease for which the level of knowledge is limited [29]. The course of the epidemic over the past year was unpredictable and could not be integrated into any predictive models. Caution should be taken when using such models. Furthermore, this leads to the search for different modes of transmission of most respiratory diseases, as had already been mentioned in relation to SARS, where infections were retrospectively detected at a significant distance from the heart of the SARS outbreak, with no reasonable explanation [30]. In France, the issue of carriage and transmission by domestic pets has not been resolved and should be the subject of intense research to really understand the reservoirs, transmission and epidemiology of this very atypical virus.

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