

浙江省湖州市新冠流行前后常见病毒性呼吸道 传染病流行特征分析

杨敏艺^{1,2▲} 刘艳^{3▲} 张素熠^{1,2} 王强² 刘光涛³ 郑波² 王鑫钰²
赵丹妮^{1,2} 沈建勇^{4△} 王伟炳^{1,2△}

(¹复旦大学上海市重大传染病和生物安全研究院 上海 200032; ²复旦大学公共卫生学院流行病学教研室-公共卫生安全教育部重点实验室 上海 200032; ³湖州市疾病预防控制中心传染病预防控制科 湖州 313000; ⁴湖州市疾病预防控制中心 湖州 313000)

【摘要】 目的 了解浙江省湖州市新型冠状病毒感染(简称“新冠”)流行前后流感样病例(influenza-like illness, ILI)和严重急性呼吸道感染(severe acute respiratory infection, SARI)病例中常见呼吸道病毒感染情况和流行特征,为制定和调整病毒性呼吸道传染病的防控策略提供依据。方法 选取2017年11月至2020年2月(新冠流行前时期)和2022年12月至2024年4月(新冠防控措施调整后阶段)在湖州市2家流感监测哨点医院就诊且采集了咽拭子标本的ILI和SARI病例作为研究对象,检测标本中甲型流感病毒H1N1和H3N2、乙型Victoria系流感病毒(FluB)、呼吸道合胞病毒(respiratory syncytial virus, RSV)、鼻病毒(human rhinovirus, HRV)、腺病毒(adenovirus, ADV)和新冠病毒(severe acute respiratory syndrome coronavirus-2, SARS-CoV-2)7种常见呼吸道病原体,比较分析ILI和SARI病例在新冠流行前后以及在不同年龄人群和不同时间的呼吸道病毒检出情况。结果 共纳入7 948份ILI样本和2 294份SARI样本。ILI样本总阳性率从33.6%上升至47.1%,主要是流感病毒和新冠感染的病例增加;SARI样本总阳性率从31.4%下降至24.8%,主要是HRV和ADV感染的病例减少。新冠防控措施调整后,ILI以新冠(22.1%)、H3N2(12.7%)和FluB(6.0%)感染为主,SARI病例以RSV(7.1%)、H3N2(5.3%)和HRV(4.5%)感染为主。新冠防控措施调整后,2023年流感病毒流行周期有所缩短。新冠流行前,RSV主要在秋冬季检出,而新冠防控措施调整后出现反季节流行,春夏季均有检出。新冠防控措施调整后,ILI阳性样本中混合感染率明显上升,主要为新冠和甲型流感病毒共感染,而SARI阳性样本中混合感染率则有所下降。结论 新冠流行前后湖州市多种呼吸道病毒流行特征发生重要变化,其中流感病毒和新冠流行强度上升,流感病毒和RSV的季节性流行模式受到影响,应根据监测数据及时调整防控策略。

【关键词】 呼吸道感染; 呼吸道病毒; 流行特征; 新冠流行

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Epidemiological characteristics of common viral respiratory infections before and after the COVID-19 pandemic in Huzhou, Zhejiang Province

YANG Min-yi^{1,2▲}, LIU Yan^{3▲}, ZHANG Su-yi^{1,2}, WANG Qiang², LIU Guang-tao³, ZHENG Bo²,
WANG Xin-yu², ZHAO Dan-ni^{1,2}, SHEN Jian-yong^{4△}, WANG Wei-bing^{1,2△}

(¹Shanghai Institute of Infectious Disease and Biosecurity, Fudan University, Shanghai 200032, China; ²Department of Epidemiology, School of Public Health, Fudan University-Key Laboratory of Public Health Safety, Ministry of

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▲YANG Min-yi and LIU Yan contributed equally to this work

△Corresponding authors E-mail: 32288746@qq.com (SHEN Jian-yong); wwb@fudan.edu.cn (WANG Wei-bing)

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Education, Shanghai 200032, China; ³Department of Infectious Disease Control and Prevention, Huzhou Center of Disease Control and Prevention, Huzhou 313000, Zhejiang Province, China; ⁴Huzhou Center of Disease Control and Prevention, Huzhou 313000, Zhejiang Province, China)

【Abstract】 Objective To investigate and compare the epidemiological characteristics of common respiratory viruses among influenza-like illness (ILI) and severe acute respiratory infection (SARI) cases in Huzhou, Zhejiang Province before and after the COVID-19 pandemic, so as to provide a basis for formulating and adjusting the prevention and control strategies for viral respiratory infectious diseases.

Methods ILI and SARI cases at two influenza surveillance sentinel hospitals in Huzhou and had throat swab samples collected during Nov 2017 to Feb 2020 (pre-COVID-19 pandemic period) and Dec 2022 to Apr 2024 (post-COVID-19 mitigation phase) were selected as the participants. Seven common viral respiratory pathogens were tested, including influenza A virus (H1N1 and H3N2 subtypes), influenza B virus (Victoria lineage, FluB), respiratory syncytial virus (RSV), rhinovirus (HRV), adenovirus (ADV), and severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). The positive rates of respiratory pathogens before and after the COVID-19 pandemic were compared across different age groups and different time.

Results A total of 7 948 ILI samples and 2 294 SARI samples were included. The overall positive rate of ILI samples increased from 33.6% to 47.1%, primarily due to the increase in influenza and COVID-19 infections; the overall positive rate of SARI samples decreased from 31.4% to 24.8%, mainly due to the reduction in HRV and ADV infections. During the post-COVID-19 mitigation phase, SARS-CoV-2 (22.1%), H3N2 (12.7%), and FluB (6.0%) were the primary pathogens in ILI samples, while RSV (7.1%), H3N2 (5.3%), and HRV (4.5%) dominated in SARI samples. During the post-COVID-19 mitigation phase, the influenza virus circulation period was shortened. Before the COVID-19 pandemic, RSV was mainly detected in autumn and winter, while during the post-COVID-19 mitigation phase, out-of-season RSV epidemics were observed in spring and summer. Co-infection rate in ILI cases increased significantly in the post-COVID-19 mitigation phase, predominantly consisting of co-infections of COVID-19 and influenza A virus, while co-infection rate in SARI cases showed a decline.

Conclusion We found important epidemiological changes in respiratory viruses in Huzhou during the post-COVID-19 mitigation phase compared to pre-COVID-19 period, including increased positive rates of influenza and COVID-19, and disruptions to the seasonal patterns of influenza and RSV. The prevention and control strategies should be adjusted in a timely manner based on the monitoring data.

【Key words】 respiratory tract infections; respiratory viruses; epidemiological characteristics; COVID-19 pandemic

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急性呼吸道感染是一类常见的感染性疾病,已成为造成全球疾病负担的主要原因之一^[1-2]。呼吸道感染多由不同的呼吸道病毒引起^[3-4],其临床症状相似,而病原学确诊依赖于病原核酸检测。持续检测常见病毒有助于了解不同病毒性呼吸道传染病的流行趋势并及时捕捉变化。自新冠流行以来,呼吸道感染的疾病负担急剧上升,新冠的流行及相关公共卫生与社会措施(public health and

social measures, PHSMs)也对其他呼吸道病毒的流行模式产生了复杂影响^[5-7]。既往已有研究对比分析了新冠流行前和流行期间不同呼吸道病原体的检出情况,发现在新冠疫情发生后,其他呼吸道病原体的流行特征发生了变化^[8-10]。上海市一项研究发现,新冠疫情发生后,急性呼吸道感染者中呼吸道病原体检出阳性率显著下降^[11]。我国从2022年12月开始逐步放宽新冠防控措施^[12],公众

社交活动逐渐恢复正常,防控措施调整前后呼吸道病毒流行情况的报道尚不多见,探究其流行特征和前后变化有助于制定和优化病毒性呼吸道传染病的防控策略。

浙江省湖州市共有2家国家级流感监测哨点医院。根据流感监测资料,2017—2024年湖州市第一人民医院流感样病例(influenza-like illness, ILI)年平均就诊例数23 545例,湖州市南浔区人民医院ILI年平均就诊例数10 291例。本研究以就诊于这2家流感监测哨点医院且采集了咽拭子标本的ILI和严重急性呼吸道感染(severe acute respiratory infection, SARI)病例为研究对象,系统分析了新冠流行前后ILI和SARI病例中7种常见呼吸道病原体的流行特征,包括甲型流感病毒H1N1和H3N2、乙型Victoria系流感病毒(Victoria lineage, FluB)、呼吸道合胞病毒(respiratory syncytial virus, RSV)、腺病毒(adenovirus, ADV)、鼻病毒(rhinovirus, HRV)及新冠病毒(SARS-CoV-2),以了解新冠防控措施调整后不同病毒性呼吸道传染病的流行特征和动态变化,为病毒性呼吸道传染病的防控工作提供科学依据。

资料和方法

研究对象和伦理审查 研究时期为2017年11月至2020年2月以及2022年12月至2024年4月,前者定义为新冠流行前时期(即新冠流行前),后者定义为新冠防控措施调整后阶段(即新冠流行后)。研究对象为研究时期内于湖州市第一人民医院或湖州市南浔区人民医院就诊且采集了咽拭子标本的ILI和SARI病例。ILI定义为门急诊患者中发热(体温 $\geq 38^{\circ}\text{C}$)伴咳嗽或咽痛之一者;SARI病例定义为住院患者中符合本次起病有发热史(体温 $\geq 38^{\circ}\text{C}$)伴有咳嗽,且发病 ≤ 10 天者^[13]。排除标准为人口学信息或临床资料缺失。

本研究通过复旦大学公共卫生学院医学研究伦理委员会的审查(审批号:IRB#2024-05-1116),符合免除知情同意要求。

标本采集和保存 咽拭子标本由哨点医院专门的工作人员采集,采集过程遵循《全国流感监测技术指南(2017年版)》^[13]。2020年2月因疫情防控原因仅采集ILI标本,未采集SARI标本。咽拭子标

本采集后置于专用的采样管中,在 4°C 条件下保存,48 h内送至湖州市疾病预防控制中心实验室,并保存在 -80°C 冰箱。

检测方法 2023年11月及之后的标本在采集后送至实验室及时进行检测,2023年11月之前的标本则于2024年3月和4月统一进行回顾性检测。使用RT-PCR方法检测标本中甲型流感病毒(influenza A virus, FluA)、乙型流感病毒(influenza B virus, FluB)、RSV、ADV、HRV的核酸,对于流感病毒检测结果呈阳性的标本进一步做亚型鉴定,采用杭州艾迪康医学检验中心有限公司的试剂盒。从2020年1月底开始采用RT-PCR法实时检测所有标本中SARS-CoV-2的核酸。以上检测均由湖州市疾病预防控制中心实验室完成,且检测标准统一。由于在新冠流行前仅有少量乙型Yamagata系流感病毒被检出,并且自2020年3月以来,全球范围内几乎未再监测到其存在^[14],因此在本研究中仅对乙型Victoria系流感病毒进行分析。

资料收集 采集标本时,利用“流感样病例标本原始登记送检表”登记病例的姓名、性别、年龄、采样日期和发病日期等信息,并通过医院信息系统进一步核实和收集病例的人口学和临床数据。

统计学分析 使用和R 4.3.1对数据进行分析。计数资料以例数和率/构成比表示,组间比较采用 χ^2 检验、校正 χ^2 检验或Fisher精确概率法。ILI样本总阳性率=(7种病原体中任一病原体检出阳性的ILI样本数/检测的ILI样本数) $\times 100\%$;SARI样本总阳性率=(7种病原体中任一病原体检出阳性的SARI样本数/检测的SARI样本数) $\times 100\%$ 。采用直接标化法,基于湖州市第七次人口普查的年龄别人口数^[15],按照0~4岁、5~14岁、15~59岁和 ≥ 60 岁进行年龄分层,计算ILI样本和SARI样本年龄标化后的总阳性率。采用双侧检验,检验水准 $\alpha=0.05$, $P<0.05$ 为差异有统计学意义。

结 果

ILI和SARI样本基本情况 共纳入7 948份ILI样本和2 294份SARI样本。ILI样本中男性占46.5%,0~4岁、5~14岁、15~59岁、 ≥ 60 岁组分别占21.1%、28.9%、43.5%、6.5%;SARI样本中男性占52.4%,0~4岁、5~14岁、15~59岁、 ≥ 60 岁组分

别占37.1%、34.5%、14.0%、14.4%。ILI和SARI样本的性别及年龄分布在新冠流行前后均有显著差异(P 均 <0.05),其中ILI样本中15~59岁组在新冠

流行后占比最高,从流行前的31.4%上升至流行后的62.6%(表1)。

表1 ILI和SARI样本的性别和年龄分布

Tab 1 Sex and age distribution of ILI and SARI samples

[n(%)]

Characteristics	ILI		χ^2	P	SARI		χ^2	P
	Pre-COVID-19 (n=4 880)	Post-COVID-19 (n=3 068)			Pre-COVID-19 (n=427)	Post-COVID-19 (n=1 867)		
Sex			10.36	0.001			5.81	0.016
Male	2 339 (47.9)	1 357 (44.2)			246 (57.6)	955 (51.2)		
Female	2 541 (52.1)	1 711 (55.8)			181 (42.4)	912 (48.8)		
Age group (y)			1 275.76	<0.001			32.27	<0.001
0-4	1 510 (30.9)	171 (5.6)			208 (48.7)	644 (34.5)		
5-14	1 663 (34.1)	636 (20.7)			110 (25.8)	682 (36.5)		
15-59	1 533 (31.4)	1 921 (62.6)			56 (13.1)	264 (14.2)		
≥ 60	174 (3.6)	340 (11.1)			53 (12.4)	277 (14.8)		

ILI: Influenza-like illness; SARI: Severe acute respiratory infection.

新冠流行前后呼吸道病原体的检出情况比较 与新冠流行前相比,新冠流行后ILI样本总阳性率从33.6%上升到47.1%($P<0.001$),年龄标化总阳性率从34.1%上升到49.0%。新冠流行前,ILI样本中阳性率最高的前3位病原体依次为HRV(10.1%)、ADV(6.8%)、H1N1(6.3%);新冠流行后,ILI样本中阳性率最高的前3位病原体变化为新冠病毒(22.1%)、H3N2(12.7%)、FluB(6.0%)。与新冠流行前相比,新冠流行后ILI样本中H3N2和FluB阳性率上升,而RSV、HRV和ADV阳性率下降(P 均 <0.001)。

与新冠流行前相比,新冠流行后SARI样本总阳性率从31.4%下降到24.8%($P=0.005$),年龄标化总阳性率从23.6%下降到19.1%。新冠流行前,HRV、RSV和ADV是SARI样本中阳性率最高的3种病原体,分别为11.7%、9.1%和6.6%;新冠流行后,SARI样本中以RSV、H3N2和HRV阳性率最高,分别为7.1%、5.3%和4.5%。与新冠流行前相比,新冠流行后SARI样本中H3N2阳性率上升,H1N1、FluB、HRV和ADV阳性率下降(P 均 <0.05)(表2)。

新冠流行前后呼吸道病原体在不同年龄组的检出情况比较 与新冠流行前相比,新冠流行后ILI在所有年龄组的总阳性率均显著上升(P 均 <0.01)。0~4岁组中大部分病原体阳性率前后差异无统计学意义,总阳性率上升主要是新冠阳性病例增加。与新冠流行前相比,新冠流行后流感病毒阳性率在 ≥ 60 岁组中显著减少,在5~14岁和15~59岁

组中则显著增加(P 均 <0.001)。新冠流行后,新冠阳性率以 ≥ 60 岁组最高(40.3%),0~4岁组次之(30.4%),不同年龄组间的阳性率差异有统计学意义($\chi^2=84.97, P<0.001$)(表3)。

新冠流行后,SARI样本中仅5~14岁组的总阳性率显著下降($P=0.028$)。新冠流行后H1N1在各年龄组中的阳性率普遍低于新冠流行前,尤其在15~59岁组差异有统计学意义($P=0.045$)。0~4岁组的ADV阳性率在新冠流行后显著降低($P<0.001$)。新冠流行后, ≥ 60 岁组的新冠阳性率(9.8%)高于其他年龄组,不同年龄组间的阳性率差异有统计学意义($\chi^2=55.55, P<0.001$)(表4)。

新冠流行前后呼吸道病原体在不同时间的检出情况比较 ILI样本的检测结果显示:2022年12月新冠暴发后,流感活动中断,随着新冠流行水平减弱,流感重新恢复流行并于2023年3月达峰,较往年推迟约1~2个月,且2023年流行周期较往年缩短。至2023—2024年度冬春季,InfA、新冠和InfB轮流暴发,流行态势更为复杂。在新冠流行后,HRV和ADV阳性率持续保持在较低水平,2024年年初呈现复苏趋势。SARI样本的检测结果显示:新冠流行前,RSV感染集中在秋冬季,新冠流行后,RSV却出现反季节流行,在2023年春夏两季均有检出(图1、图2)。

新冠流行前后呼吸道病原体混合感染情况比较 在ILI阳性样本中,新冠流行前混合感染病例共47例,占比2.9%,HRV+ADV(17例)和RSV+

表2 新冠流行前后ILI和SARI样本中呼吸道病原体检出情况比较

Tab 2 Comparison of respiratory pathogen detection in ILI and SARI samples before and after the COVID-19 pandemic [n(%)]

Pathogens	ILI				SARI			
	Before (n=4 880)	After (n=3 068)	χ^2	P	Before (n=427)	After (n=1 867)	χ^2	P
FLU	703 (14.4)	753 (24.5)	129.39	<0.001	30 (7.0)	140 (7.5)	0.11	0.737
H1N1	309 (6.3)	180 (5.9)	0.71	0.401	18 (4.2)	41 (2.2)	5.66	0.017
H3N2	197 (4.0)	388 (12.7)	204.79	<0.001	6 (1.4)	98 (5.3)	11.86	<0.001
FluB	197 (4.0)	185 (6.0)	16.36	<0.001	6 (1.4)	1 (0.1)	16.66	<0.001 ^a
RSV	156 (3.2)	29 (1.0)	42.00	<0.001	39 (9.1)	132 (7.1)	2.14	0.143
HRV	493 (10.1)	77 (2.5)	163.12	<0.001	50 (11.7)	83 (4.5)	33.57	<0.001
ADV	334 (6.8)	78 (2.5)	70.93	<0.001	28 (6.6)	65 (3.5)	8.45	0.004
SARS-CoV-2	-	679 (22.1)	-	-	-	55 (3.0)	-	-
Total	1 639 (33.6)	1 445 (47.1)	144.85	<0.001	134 (31.4)	463 (24.8)	7.82	0.005
Age-standardized positive rate (%)	34.1	49.0	-	-	23.6	19.1	-	-

^a The statistical method is Yates' s correction for continuity. ILI: Influenza-like illness; SARI: Severe acute respiratory infection; FLU: Influenza virus; H1N1: Influenza A (H1N1) virus; H3N2: Influenza A (H3N2) virus; FluB: Influenza B virus (Victoria lineage); RSV: Respiratory syncytial virus; HRV: Rhinovirus; ADV: Adenovirus; SARS-CoV-2: Severe acute respiratory syndrome coronavirus-2.

表3 新冠流行前后ILI样本中不同年龄组呼吸道病原体检出情况比较

Tab 3 Comparison of respiratory pathogen detection among different age groups in ILI samples before and after the COVID-19 pandemic [n(%)]

Pathogens	0-4 y		5-14 y				15-59 y				≥60 y					
	Before (n=1 510)	After (n=171)	χ^2	P	Before (n=1 663)	After (n=636)	χ^2	P	Before (n=1 533)	After (n=1 921)	χ^2	P	Before (n=174)	After (n=340)	χ^2	P
FLU	97 (6.4)	17 (9.9)	3.01	0.083	239 (14.4)	180 (28.3)	59.90	<0.001	333 (21.7)	533 (27.8)	16.47	<0.001	34 (19.5)	23 (6.8)	19.05	<0.001
H1N1	51 (3.4)	13 (7.6)	7.49	0.006	73 (4.4)	50 (7.9)	10.95	<0.001	165 (10.8)	106 (5.5)	32.44	<0.001	20 (11.5)	11 (3.2)	13.85	<0.001
H3N2	23 (1.5)	4 (2.3)	0.23	0.629 ^a	70 (4.2)	92 (14.5)	73.88	<0.001	93 (6.1)	281 (14.6)	64.72	<0.001	11 (6.3)	11 (3.2)	2.68	0.102
FluB	23 (1.5)	0 (0.0)	1.63	0.201 ^a	96 (5.8)	38 (6.0)	0.03	0.853	75 (4.9)	146 (7.6)	10.44	0.001	3 (1.7)	1 (0.3)	1.48	0.224 ^a
RSV	85 (5.6)	5 (2.9)	2.22	0.136	40 (2.4)	4 (0.6)	7.73	0.005	23 (1.5)	18 (0.9)	2.31	0.129	8 (4.6)	2 (0.6)	7.71	0.005 ^a
HRV	201 (13.3)	5 (2.9)	15.41	<0.001	156 (9.4)	19 (3.0)	26.74	<0.001	125 (8.2)	50 (2.6)	54.62	<0.001	11 (6.3)	3 (0.9)	10.89	<0.001 ^a
ADV	116 (7.7)	8 (4.7)	2.03	0.154	156 (9.4)	35 (5.5)	9.08	0.003	56 (3.7)	34 (1.8)	11.91	<0.001	6 (3.5)	1 (0.3)	6.34	0.012 ^a
SARS-CoV-2	-	52 (30.4)	-	-	-	123 (19.3)	-	-	-	367 (19.1)	-	-	-	137 (40.3)	-	-
Total	477 (31.6)	81 (47.37)	17.25	<0.001	575 (34.6)	318 (50.0)	46.07	<0.001	530 (34.6)	886 (46.1)	47.01	<0.001	57 (32.8)	160 (47.1)	9.65	0.002

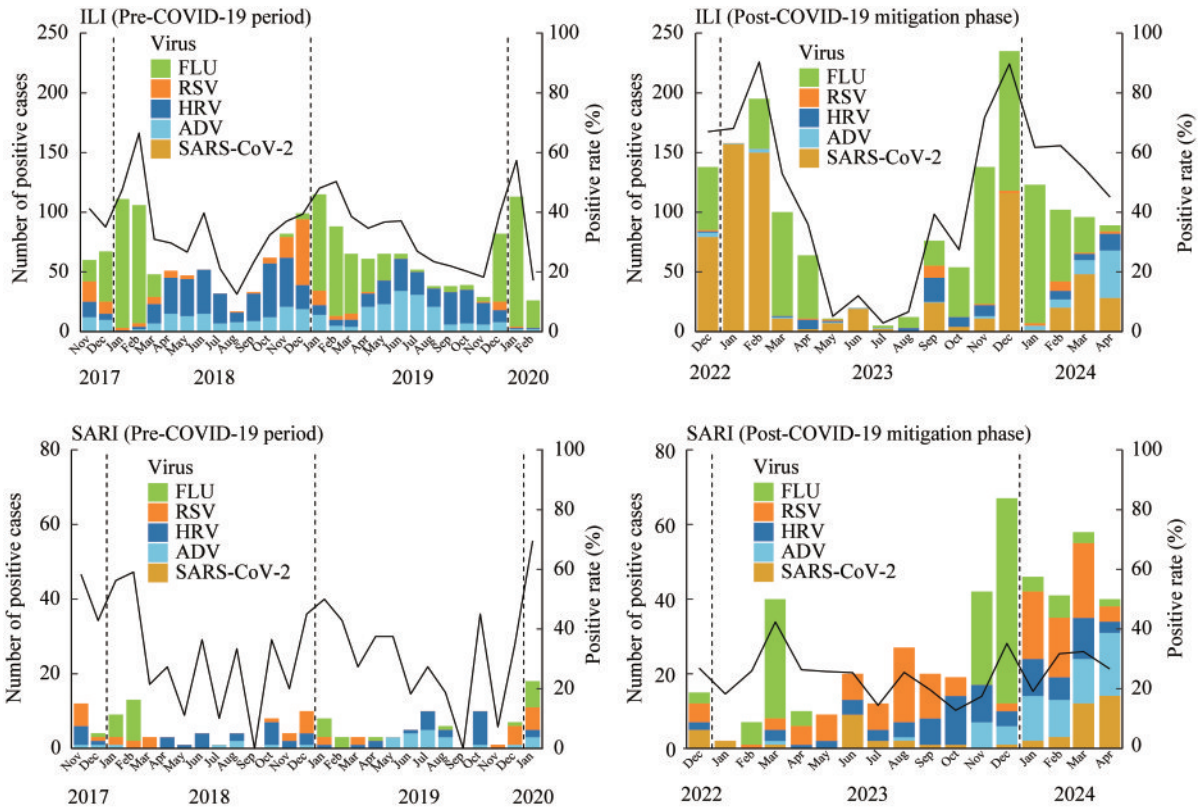
^a The statistical method is Yates' s correction for continuity. FLU: Influenza virus; H1N1: Influenza A (H1N1) virus; H3N2: Influenza A (H3N2) virus; FluB: Influenza B virus (Victoria lineage); RSV: Respiratory syncytial virus; HRV: Rhinovirus; ADV: Adenovirus; SARS-CoV-2: Severe acute respiratory syndrome coronavirus-2.

表4 新冠流行前后SARI样本中不同年龄组呼吸道病原体检出情况比较

Tab 4 Comparison of respiratory pathogen detection among different age groups in SARI samples before and after the COVID-19 pandemic

Pathogens	0-4 y		χ^2	P	5-14 y		χ^2	P	15-59 y		χ^2	P	≥ 60 y		χ^2	P
	Before (n=208)	After (n=644)			Before (n=110)	After (n=682)			Before (n=56)	After (n=264)			Before (n=53)	After (n=277)		
FLU	11 (5.3)	39 (6.1)	0.168	0.682	6 (5.5)	33 (4.8)	0.077	0.782	8 (14.3)	34 (12.9)	0.08	0.777	5 (9.4)	34 (12.3)	0.34	0.557
H1N1	7 (3.4)	17 (2.6)	0.30	0.582	2 (1.8)	8 (1.2)	0.01	0.919 ^a	6 (10.7)	9 (3.4)	4.00	0.045^a	3 (5.7)	7 (2.5)	0.61	0.434 ^a
H3N2	1 (0.5)	21 (3.3)	4.83	0.028	1 (0.9)	25 (3.7)	1.48	0.224 ^a	2 (3.6)	25 (9.5)	1.39	0.239 ^a	2 (3.8)	27 (9.8)	1.31	0.253 ^a
FluB	3 (1.4)	1 (0.16)	-	0.047^b	3 (2.7)	0 (0.0)	-	0.003^b	0 (0.0)	0 (0.0)	-	1.000 ^b	0 (0.0)	0 (0.0)	-	1.000 ^b
RSV	35 (16.8)	116 (18.0)	0.15	0.697	3 (2.7)	9 (1.3)	0.49	0.483 ^a	0 (0.0)	2 (0.8)	-	1.000 ^b	1 (1.9)	5 (1.8)	-	1.000 ^b
HRV	27 (13.0)	40 (6.2)	9.94	0.002	11 (10.0)	28 (4.1)	7.03	0.008	6 (10.7)	7 (2.7)	5.78	0.016^a	6 (11.3)	8 (2.9)	5.85	0.016^a
ADV	19 (9.1)	21 (3.3)	12.12	<0.001	7 (6.4)	25 (3.7)	1.15	0.283 ^a	1 (1.8)	14 (5.3)	0.61	0.434 ^a	1 (1.9)	5 (1.8)	-	1.000 ^b
SARS-CoV-2	-	13 (2.0)	-	-	-	7 (1.0)	-	-	-	8 (3.0)	-	-	-	27 (9.8)	-	-
Total	83 (39.9)	223 (34.6)	1.9	0.168	25 (22.7)	99 (14.5)	4.84	0.028	14 (25.0)	62 (23.5)	0.06	0.809	12 (22.6)	79 (28.5)	0.77	0.380

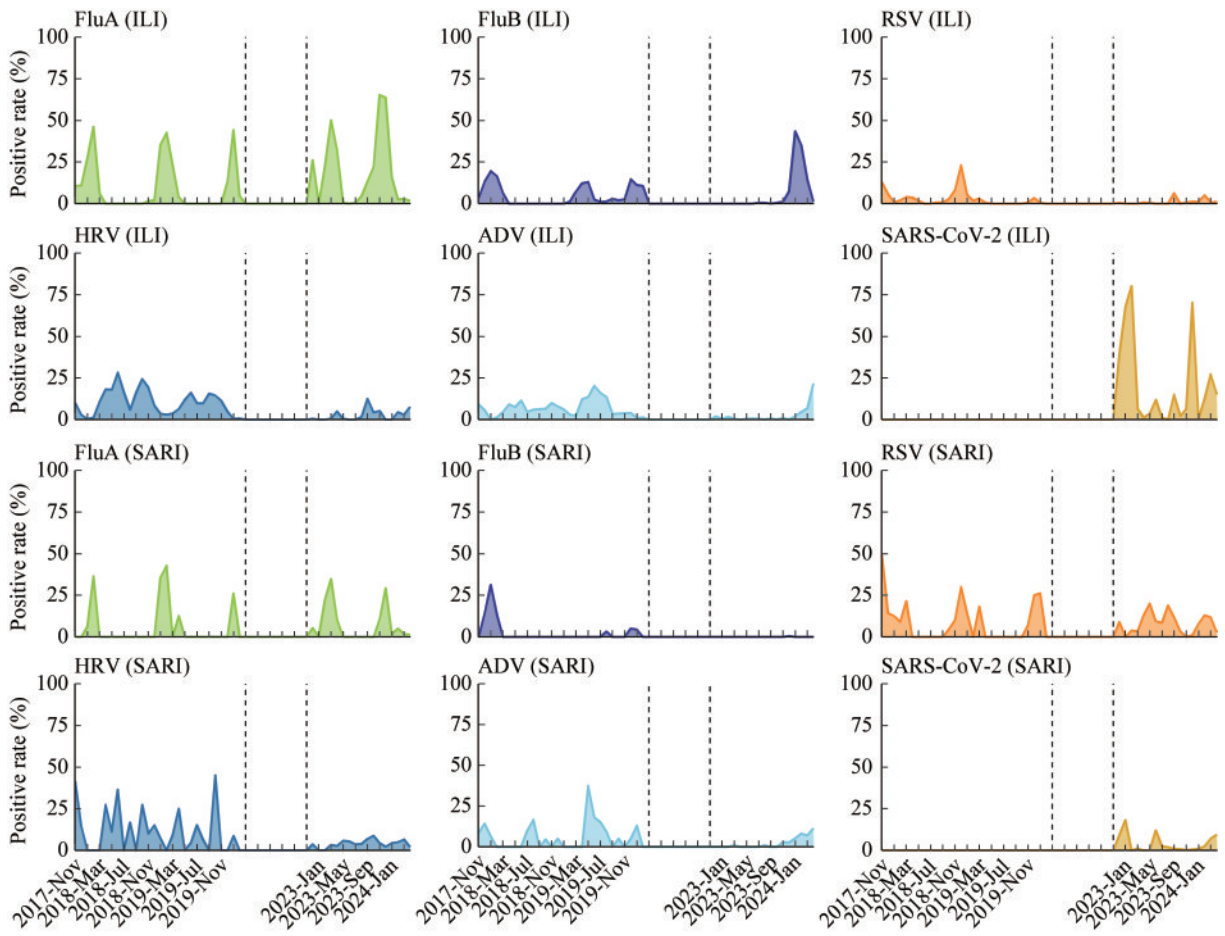
^aThe statistical method is Yates's correction for continuity; ^bThe statistical method is Fisher's exact test. FLU; Influenza virus; H1N1; Influenza A (H1N1) virus; H3N2; Influenza A (H3N2) virus; FluB; Influenza B virus (Victoria lineage); RSV; Respiratory syncytial virus; HRV; Rhinovirus; ADV; Adenovirus; SARS-CoV-2; Severe acute respiratory syndrome coronavirus-2.



ILI: Influenza-like illness; SARI: Severe acute respiratory infection; FLU: Influenza virus; RSV: Respiratory syncytial virus; HRV: Rhinovirus; ADV: Adenovirus; SARS-CoV-2: Severe acute respiratory syndrome coronavirus-2.

图1 新冠流行前后ILI和SARI样本中呼吸道病原体检出的时间分布

Fig 1 Temporal distribution of respiratory pathogen detection in ILI and SARI samples before and after the COVID-19 pandemic



ILI: Influenza-like illness; SARI: Severe acute respiratory infection; FluA: Influenza A virus; FluB: Influenza B virus (Victoria lineage); RSV: Respiratory syncytial virus; HRV: Rhinovirus; ADV: Adenovirus; SARS-CoV-2: Severe acute respiratory syndrome coronavirus-2.

图2 ILI和SARI样本中不同呼吸道病原体阳性率的时间分布

Fig 2 Temporal distribution of positive rates for different respiratory pathogens in ILI and SARI samples

HRV(11例)是最常见的混合感染组合;新冠流行后,混合感染病例共168例,占比上升至11.6%且差异有统计学意义($\chi^2=90.84, P<0.001$),最常见的混合感染组合转变为SARS-CoV-2+H3N2(89例)和SARS-CoV-2+H1N1(27例)。在SARI阳性样本中,新冠流行前混合感染病例共11例,占比8.2%,

RSV+HRV(4例)和HRV+ADV(3例)的组合较为常见;新冠流行后混合感染病例仍为11例,然而占比下降至2.4%且差异有统计学意义($\chi^2=9.96, P=0.002$),RSV+HRV(3例)和H3N2+ADV(3例)为最常见的混合感染组合(表5)。

表5 新冠流行前后呼吸道病原体混合感染情况比较

Tab 5 Comparison of respiratory pathogen co-infection before and after the COVID-19 pandemic

[n(%)]

Co-infection types	ILI		SARI	
	Before (n=47)	After (n=168)	Before (n=11)	After (n=11)
H1N1+RSV	4 (8.5)	0 (0)	0 (0)	0 (0)
H1N1+HRV	2 (4.3)	2 (1.2)	0 (0)	1 (9.1)
H1N1+ADV	3 (6.4)	1 (0.6)	0 (0)	0 (0)
H3N2+RSV	2 (4.3)	5 (3.0)	0 (0)	1 (9.1)
H3N2+HRV	1 (2.1)	14 (8.3)	0 (0)	0 (0)
H3N2+ADV	1 (2.1)	1 (0.6)	0 (0)	3 (27.3)

(续表5)

Co-infection types	ILI		SARI	
	Before (n=47)	After (n=168)	Before (n=11)	After (n=11)
FluB+RSV	2 (4.3)	2 (1.2)	0 (0)	0 (0)
FluB+HRV	3 (6.4)	0 (0)	0 (0)	0 (0)
FluB+ADV	0 (0)	2 (1.2)	1 (9.1)	0 (0)
RSV+HRV+ADV	0 (0)	0 (0)	1 (9.1)	0 (0)
RSV+HRV	11 (23.4)	4 (2.4)	4 (36.4)	3 (27.3)
RSV+ADV	1 (2.1)	0 (0)	2 (18.2)	0 (0)
HRV+ADV	17 (36.2)	4 (2.4)	3 (27.3)	2 (18.2)
SARS-CoV-2+H1N1	0 (0)	27 (16.1)	0 (0)	0 (0)
SARS-CoV-2+H3N2	0 (0)	89 (53.0)	0 (0)	0 (0)
SARS-CoV-2+FluB	0 (0)	10 (6.0)	0 (0)	0 (0)
SARS-CoV-2+RSV	0 (0)	2 (1.2)	0 (0)	1 (9.1)
SARS-CoV-2+HRV	0 (0)	1 (0.6)	0 (0)	0 (0)
SARS-CoV-2+ADV	0 (0)	4 (2.4)	0 (0)	0 (0)
Total	47 (100.0)	168 (100.0)	11 (100.0)	11 (100.0)

ILI: Influenza-like illness; SARI: Severe acute respiratory infection; H1N1: Influenza A (H1N1) virus; H3N2: Influenza A (H3N2) virus; FluB: Influenza B virus (Victoria lineage); RSV: Respiratory syncytial virus; HRV: Rhinovirus; ADV: Adenovirus; SARS-CoV-2: Severe acute respiratory syndrome coronavirus-2.

讨 论

本研究基于浙江省湖州市多重呼吸道病毒的监测数据,分析了新冠流行前后ILI和SARI病例中7种常见呼吸道病原体检出情况。结果显示,新冠防控措施调整后,ILI的总阳性率显著上升,而SARI病例的总阳性率则有所下降。同时,各呼吸道病毒的检出情况也发生明显变化。这些发现可能与新冠的流行及其防控措施密切相关。

新冠防控措施调整后,本研究检测的ILI中15~59岁人群比例扩大。湖州市哨点医院的ILI监测结果显示,就医的ILI中表现出同样的趋势,即2023年就医的ILI中15~59岁人群比例(33%)相比2017—2019年(5%~9%)显著增加。可能因为:该年龄段人群社会活动和流动性在防控措施调整后恢复更快,接触更为频繁,从而更易发生呼吸道感染^[16-17];该群体健康意识和就医意愿增强。

ILI中流感病毒的阳性率在新冠流行后显著上升至24.5%,与多项研究发现类似:在应对新冠的限制措施放宽后,流感活动的强度明显反弹,其规模超过新冠流行前水平,可能与人群对流感的易感性增加有关^[18-20]。然而,年龄分层结果显示,新冠流行后≥60岁ILI中流感病毒的阳性率不升反降,且该

群体新冠阳性率高达40%,对此可能的解释是新冠病毒和流感病毒共用宿主,而老年人群对新冠病毒易感,使得新冠病毒在两者之间的相互竞争中占据更大优势,具体原因有待进一步研究。此外,SARI病例中≥60岁老年人的新冠阳性率接近10%,明显高于其他年龄人群,提示应加强这一高危群体的新冠重症防控,可以通过加强监测、优先疫苗接种、优化医疗支持、加大健康教育与宣传等方式,降低该群体新冠重症发生率。与既往研究^[21]类似,本研究进一步支持了在新冠流行后,流感病毒和新冠病毒共同传播且呈现错峰流行的现象。同时,新冠流行后流感的流行时间与其典型的季节周期出现偏差,这可能与病毒竞争、免疫交互作用和人群易感性有关^[22-23]。未来流感的流行动态是否会回到新冠流行前的模式仍待持续观察。

在新冠流行前,RSV感染多见于秋冬季,然而新冠流行后RSV出现反季节流行,在春夏两季也有检出,但主要集中在5岁以下的SARI患者中。我国某些省市^[24-25]及欧美^[26-27]和澳大利亚^[28]等多个国家、地区在新冠限制措施放宽后也出现了儿童非典型季节的RSV流行,可能是防控措施实施期间儿童RSV免疫债的积累所致^[29]。

HRV和ADV的阳性率在新冠流行后明显降低,原因未知。研究表明,不同呼吸道病毒之间可能存在

竞争和抑制作用^[30],我们猜测新冠和流感的反复暴发可能在群体层面干扰了HRV和ADV的自由传播,导致其流行水平下降,但尚无证据表明感染新冠或流感病毒可以降低HRV或ADV感染的风险。

新冠防控措施调整后,ILI阳性患者中混合感染率大幅上升,SARS-CoV-2+H3N2和SARS-CoV-2+H1N1是最主要的混合感染组合。已有研究指出新冠和流感合并感染会增加疾病严重程度^[31-33],本研究并未在SARI病例中发现两种病毒混合感染,鉴于SARI病例中新冠阳性者多为老年人,所以推断此结果与本研究的老年SARI样本数较少有关。研究表明,先前对流感的免疫力可预防重症流感/新冠合并症^[34],提示了流感疫苗接种的必要性。

本研究存在以下局限性:(1)仅检测了部分常见呼吸道病毒,不能全面反映呼吸道病毒的流行状况。(2)新冠流行前期采集标本的SARI病例数较少,代表性可能不足;仅纳入湖州市2家哨点医院的病例,可能无法全面反映湖州市整体情况;研究样本来源可能受到医疗政策和就医行为等因素的影响,产生选择偏倚。(3)未对2020年1月前的标本进行SARS-CoV-2的回顾性检测,但鉴于湖州市2020年1—7月未检测出SARS-CoV-2阳性病例,因此2020年1月前漏检的可能性较低,对结果的影响十分有限。(4)新冠流行前后纳入的季节范围不完全一致,可能会放大季节性波动对研究结果的影响。

综上所述,本研究为了解新冠流行前后多种病毒性呼吸道传染病流行动态的变化提供了数据支持。建议积极进行多种呼吸道病毒的主动监测,以应对不同呼吸道病毒共存带来的公共卫生挑战。

作者贡献声明 杨敏艺 数据分析和作图,论文撰写。刘艳 数据整理,论文撰写。张素熠 研究设计,数据分析和作图。王强,刘光涛,郑波,王鑫钰,赵丹妮 数据整理。沈建勇,王伟炳 研究指导,论文修订,经费支持。

利益冲突声明 所有作者均声明不存在利益冲突。

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