



Frequency of respiratory viruses among patients admitted to 26 intensive care units in seven consecutive winter-spring seasons (2009-2016) in Northern Italy

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Fondazione IRCCS
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Sistema Socio Sanitario



Regione
Lombardia

Severe community-acquired pneumonia

- Severe community-acquired pneumonia (CAP) is usually attributed to bacterial agents, but the introduction of broader diagnostic panels with increased sensitivity have improved the diagnosis of respiratory viruses with a relevant impact on outcomes for ICU-patients.
- Viruses account for 11-55% of the total infections in patients admitted to ICU with severe respiratory distress:

Wiemken, et al., *Eur. J. Clin. Microbiol. Infect. Dis.* 32 (2013) 705-710

Templeton et al., *Clin. Infect. Dis.* 41 (2005) 345-351

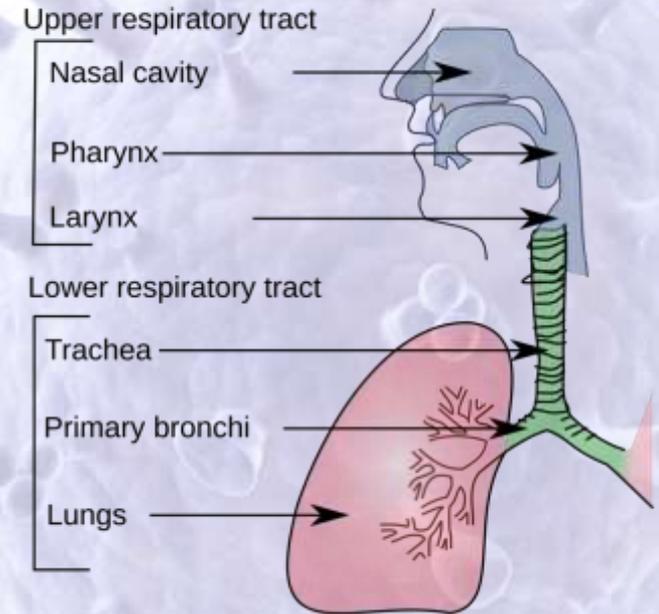
Choi et al. *Am. J. Respir. Crit. Care Med.* 186 (2012) 325-332

Wansaula et al. *Influenza Other Respir. Viruses* 10 (2015) 161-169

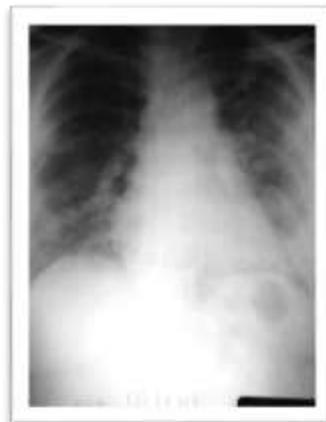
Jain et al. *N. Engl. J. Med.* 373 (2015) 415-427

Clinical syndrome – almost useless for the diagnosis

- ✓ Upper respiratory signs and symptoms (fever, fatigue, muscle aches, headache, runny or stuffy nose, sore throat, cough, wheezing)
- ✓ **dyspnea**
- ✓ **bronchopneumonia and pneumoniae**
- ✓ **Acute Severe Respiratory Syndrome (ARDS) was defined as acute onset (≤ 1 week) respiratory failure, with hypoxemia (pO_2/FiO_2 ratio < 300 mmHg while on positive end-expiratory pressure or noninvasive CPAP ≥ 5 cmH₂O) and bilateral opacities at chest imaging.**



Influenza virus A



HCoV SARS

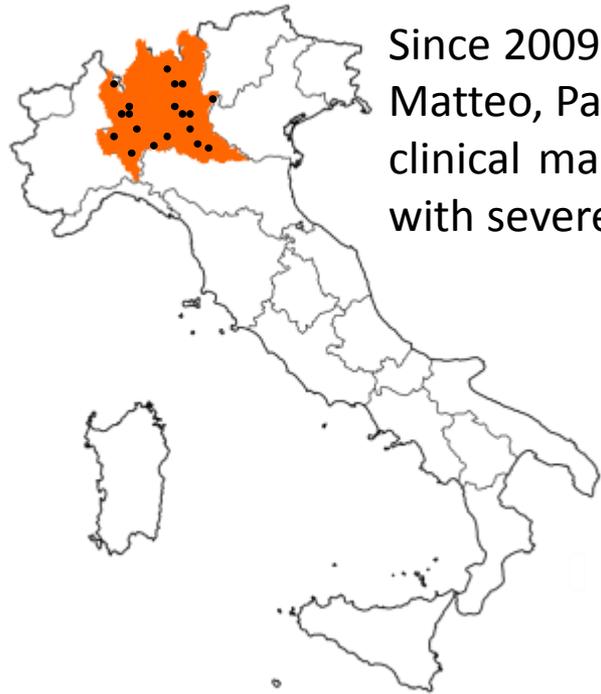


Metapneumovirus



RSV

Study design and aim



Since 2009, Molecular Virology Unit at the Fondazione IRCCS Policlinico San Matteo, Pavia has been involved as Reference Center for the diagnostic and clinical management of patients admitted to ICU in the Lombardy Region with severe influenza-like illness (ILI).

Respiratory samples collected from patients admitted to 26 ICUs in the Lombardy Region with **acute respiratory failure, severe pneumonia or ARDS assisted by non-invasive or mechanical ventilation or by extra-corporeal membrane oxygenation** were retrospectively analyzed during seven consecutive winter seasons between 1 November and 31 April (2009-2016).

Respiratory samples were tested with a panel of laboratory-developed real-time RT-PCR or real-time PCR able to detect and quantify the following viruses:

Influenza virus A (H1 or H3) and B; hRSV types A and B, hCoV types -OC43, -229E, -NL63, and -HKU1; hMPV types A and B; hPIVs (1-4), HRV, CMV (in a subset of samples).

The **aim** of this study was to investigate the prevalence of respiratory viruses in patients admitted to ICU.

Study population and samples

A total of **414** (266 male and 148 female) ICU-hospitalized patients with severe respiratory distress were analyzed.

Respiratory viruses were detected in clinical samples from:

- **225/414 (56.8%)** the upper respiratory tract (URT) (nasal swab or nasopharyngeal aspirate).
- **179/414 (43.2%)** the lower respiratory tract (LRT) (Broncho alveolar lavage or Broncho aspirate).

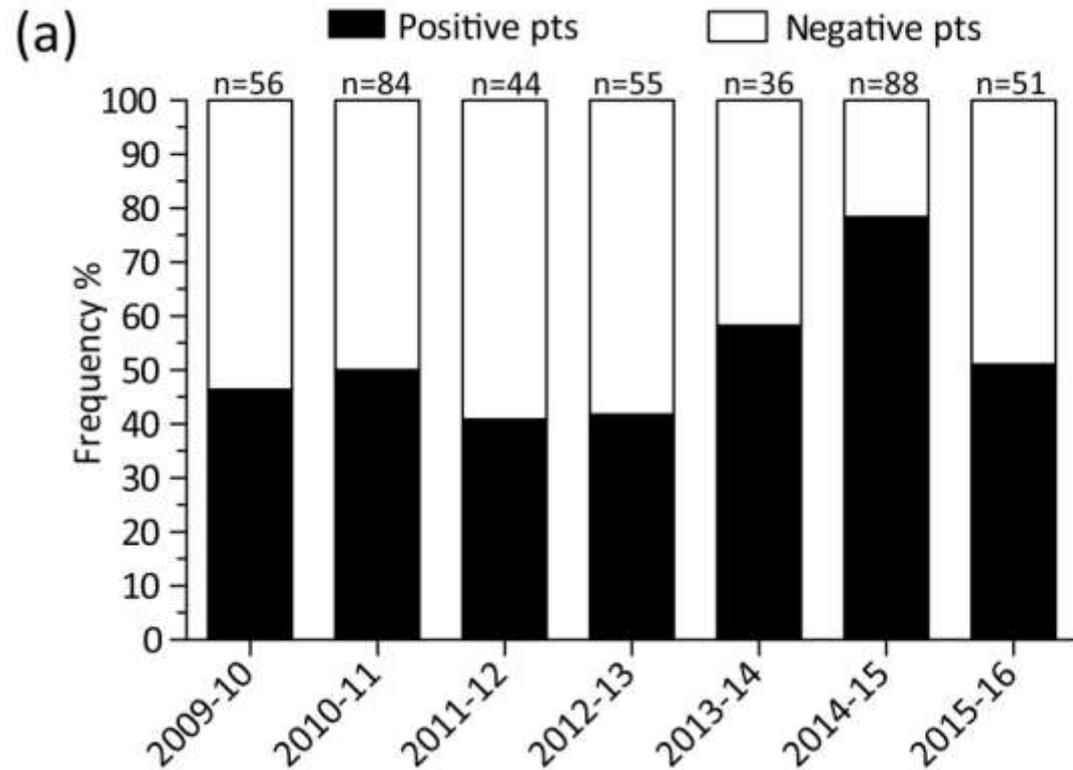
Overall, the median age was **56** years (range: 1 mos - 86 yrs).

	All seasons (n=414)	2009-10 (n=56)	2010-11 (n=84)	2011-12 (n=44)	2012-13 (n=55)	2013-14 (n=36)	2014-15 (n=88)	2015-16 (n=51)
Median age (range)	56 (1 mos-86)	52 (3-86)	52 (1 mo-84)	63 (1-83)	57 (9 mos-84)	47 (1-84)	62 (3 mos-84)	59 (1 mos-86)
Age group (%)								
<1 year	8 (1.9)	0 (0.0)	3 (3.6)	0 (0.0)	1 (1.8)	0 (0.0)	2 (2.3)	2 (3.9)
1-5 years	14 (3.4)	1 (1.8)	3 (3.6)	1 (2.3)	5 (9.1)	3 (8.3)	1 (1.1)	0 (0.0)
6-18 years	17 (4.1)	4 (7.1)	2 (2.4)	2 (4.5)	4 (7.3)	2 (5.6)	1 (1.1)	2 (3.9)
19-65 years	242 (58.2)	37 (66.1)	56 (66.7)	20 (45.5)	29 (52.7)	23 (63.9)	46 (52.3)	30 (58.8)
> 65 years	134 (32.4)	14 (25.0)	20 (23.8)	21 (47.7)	16 (29.1)	8 (22.2)	38 (43.2)	17 (33.3)

Mo, month;

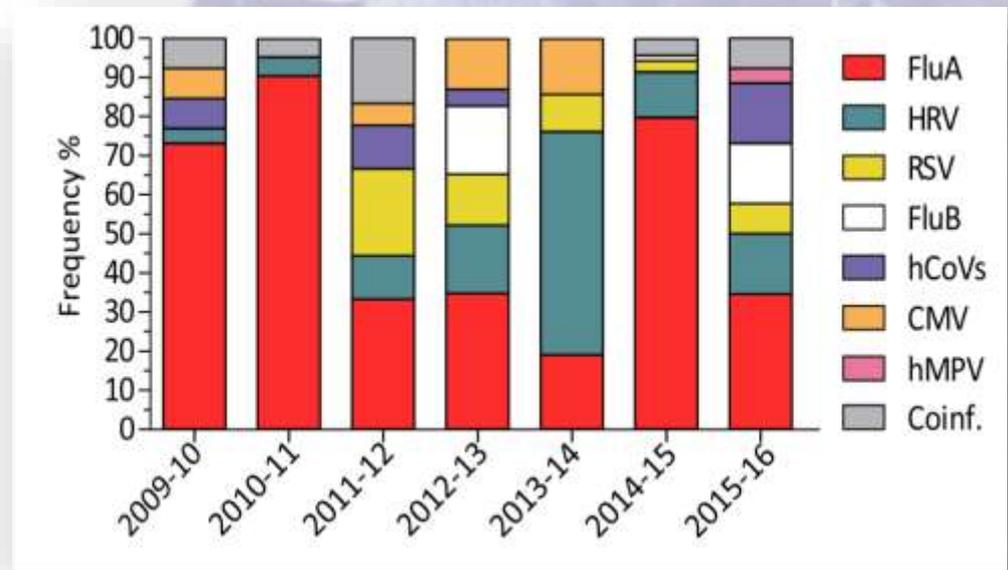
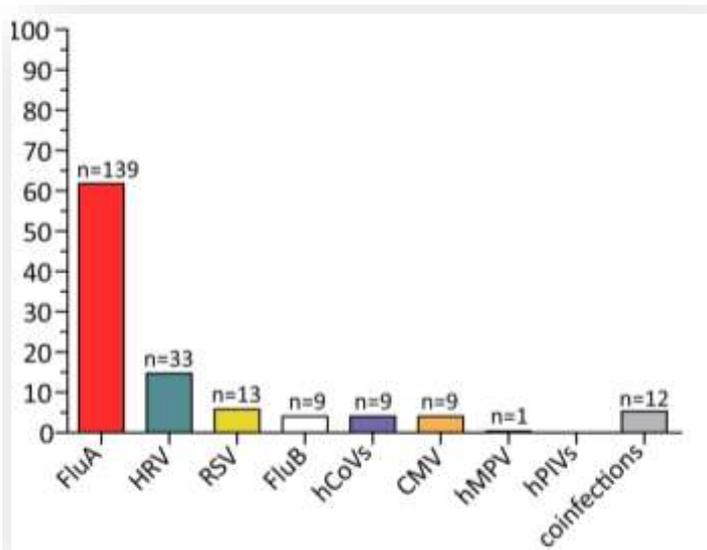
Respiratory virus positivity and distribution

In **226/414 (54.6%)** patients one or more respiratory viruses were detected, while 188/414 (45.4%) patients resulted negative.



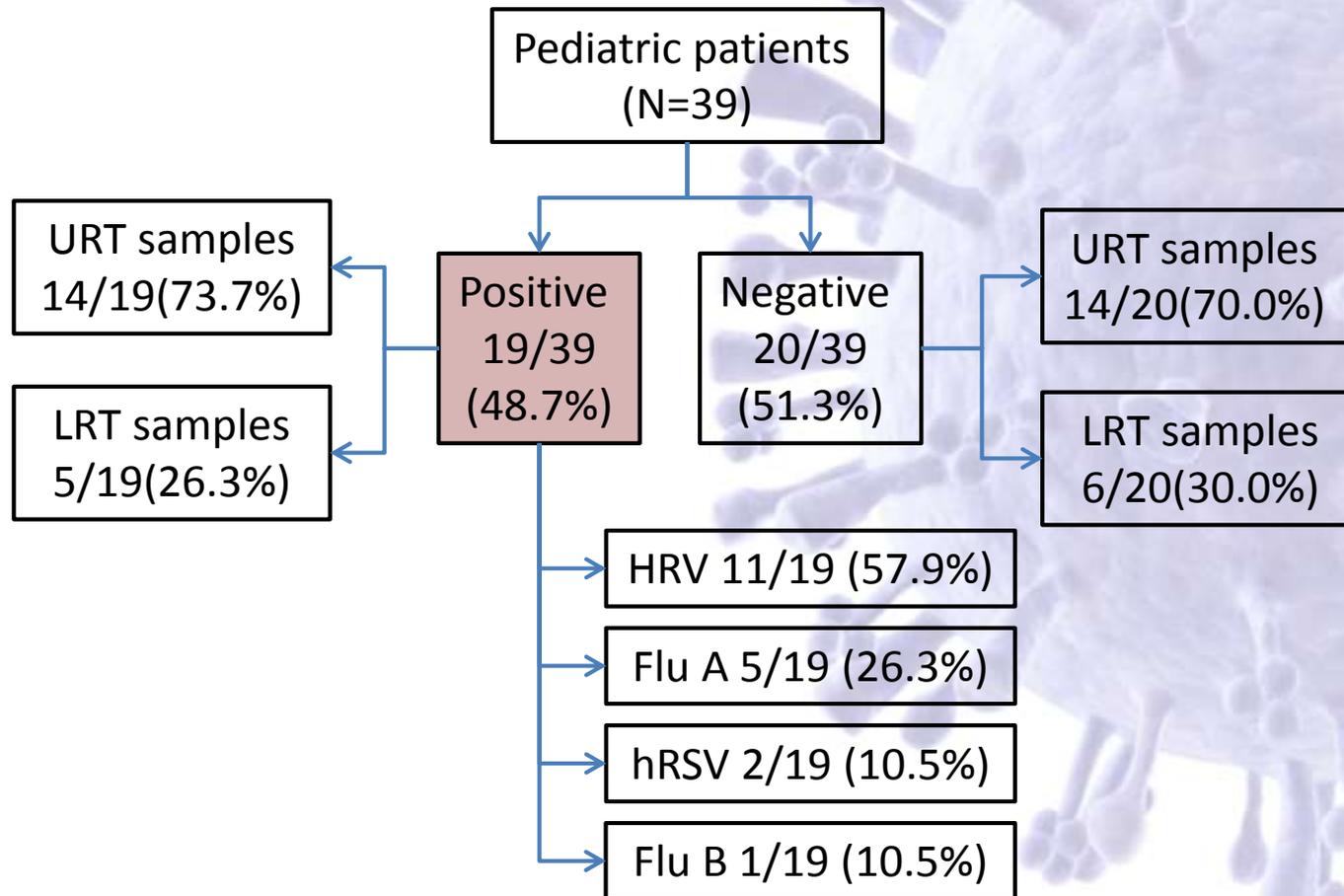
Virus distribution (type and frequency)

Overall, influenza A was the most common virus identified (139/226 patients, 61.5%) followed by HRV (33/226, 14.6%), hRSV (13/226, 5.8%), influenza B virus (9/226, 4.0%), hCoVs (9/226, 4.0%), CMV (9/226, 4.0%) and human metapneumovirus (hMPV) (1/226, 0.4%).



For 205/414 (49.5%) patients we have also retrieved data on bacteriological diagnosis. In 26/205 (12.7%) patients a virus-bacteria co-infection was observed.

Pediatric patients (n=39)



Frequency detection: URT vs LRT samples

Proportion of infections in URT as compared to LRT, for respiratory viruses with at least 10 CAP episodes (influenza A, HRV and hRSV)

Virus		All seasons	2009-10	2010-11	2011-12	2012-13	2013-14	2014-15	2015-16
Influenza A (n=139)	URT	77 (55.7)	12 (63.2)	18 (47.4)	3 (50.0)	2 (25.0)	2 (50.0)	37 (67.3)	4 (40.0)
	LRT	62 (44.3)	7 (36.8)	20 (52.6)	3 (50.0)	6 (75.0)	2 (50.0)	18 (32.7)	6 (60.0)
HRV (n=33)	URT	19 (57.6)	1 (100.0)	1 (50.0)	2 (100.0)	2 (50.0)	10 (83.3)	2 (25.0)	1 (25.0)
	LRT	14 (42.4)	0 (0.0)	1 (50.0)	0 (0.0)	2 (50.0)	2 (16.7)	6 (75.0)	3 (75.0)
hRSV (n=13)	URT	5 (38.5)	0 (0.0)	0 (0.0)	0 (0.0)	2 (66.7)	2 (100.0)	1 (50.0)	0 (0.0)
	LRT	8 (61.5)	0 (0.0)	0 (0.0)	4 (100.0)	1 (33.3)	0 (0.0)	1 (50.0)	2 (100.0)

hRSV was detected in LRT samples in 8/13 (61.5%) patients as compared to 62/139 (44.3%) for influenza A and 14/33 (42.4%) for HRV. However, due to the low number of hRSV episodes, no significant differences were observed between the observed frequency ($p > 0.05$).

Limitations

- The frequency of different respiratory viruses could be biased by the role of our center as a reference laboratory for the diagnosis and confirmation of severe influenza-like illness.
- The retrospective nature of this study limited our ability to fully collect clinical information.
- Only incomplete clinical data and diagnostic findings on bacterial co-infections were available.



Conclusions

- Viral infections were present in a large proportion of ICU-admitted patients with CAP (near 50%).
- In addition to influenza A, HRVs were shown to account for a significant number of viral CAP with a diagnosis in LRT samples for 42% of HRV-positive episodes.
- The use of LRT samples appears more informative than URT samples to correctly estimate the burden of viral infections in patients with CAP.
- We need to complete the painting of CAP with all the actors involved in the etiological role.



Acknowledgments



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