

# Epidemiology of human respiratory viruses in children with acute respiratory tract infections in Parma area, northern Italy

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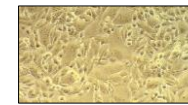
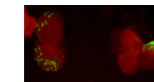
**Introduction and purpose.** Viruses are a leading cause of acute respiratory tract infections (ARTI), especially in children. Respiratory viruses are also the major cause of hospitalization and mortality in childhood worldwide. Recent epidemiological data are scanty globally and absent in Italy. The purpose of this study was to determine the prevalence of viral respiratory infections in children with ARTI in the area of Parma, northern Italy, and the distribution of viral etiological agents in four years (October 2012 – September 2015), using the data obtained from outcomes of clinical samples collected from the respiratory tract (nasopharyngeal aspirates – NPA; throat swabs – TS; nasal swabs – NS; bronchoalveolar lavages – BAL; bronchoaspirates – BAS; sputum samples – SP; pleural fluids – PF) of children and tested for respiratory viruses at the Unit of Virology of the University Hospital of Parma.

## Methods

2892 samples  
2715 patients

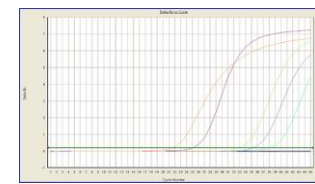
- 1 SP
- 2 PF
- 3 NS
- 3 BAL
- 8 BAS
- 703 NPA
- 2172 TS

- Respiratory Syncytial Virus (RSV) direct immunofluorescence (IF) (Argene® - bioMérieux)
- Virus antigen detection by IF in cell culture in Chamber Slide 18h after inoculation using monoclonal antibodies (mAbs) detecting Flu A, Flu B, Parainfluenza 1, 2, 3 viruses, Adenovirus, RSV (Argene® - bioMérieux).
- Conventional culture for virus isolation (till 15 days) and identification by IF with specific mAbs.



Real-time PCR for the detection of the nucleic acid of the following human viruses:

- Flu A and FluB (Influenza A/B Q-PCR Alert Kit - ELITechGroup);
- Adenovirus and Bocavirus (AdV/hBoV r-gene® - Argene®, bioMérieux);
- Respiratory Syncytial virus and metapneumovirus (RSV/hMPV r-gene® - Argene®, bioMérieux);
- Coronavirus and Parainfluenza virus (hCoV/hPIV r-gene® Argene®, bioMérieux).



**Results.** A total of **1408 samples** (48.69%), belonging to **1344 patients** (49.5%) were positive for the presence of 1 or more viruses: in 1128 samples (80.11%) of 1067 patients (19.89%) only 1 virus was revealed, in 280 samples (19.89%) of 277 patients (20.61%) a mixed viral infection was detected. In the considered period, for one-hundred thirty eight patients at least two samples were analysed in a time range comprised between 3 days and 8 months.

Figure 1. Distribution by age of 1344 patients with respiratory virus infection in comparison with that of 2715 patients suffering from acute respiratory syndrome and tested for respiratory viruses (1 October 2012 – 30 September 2015).

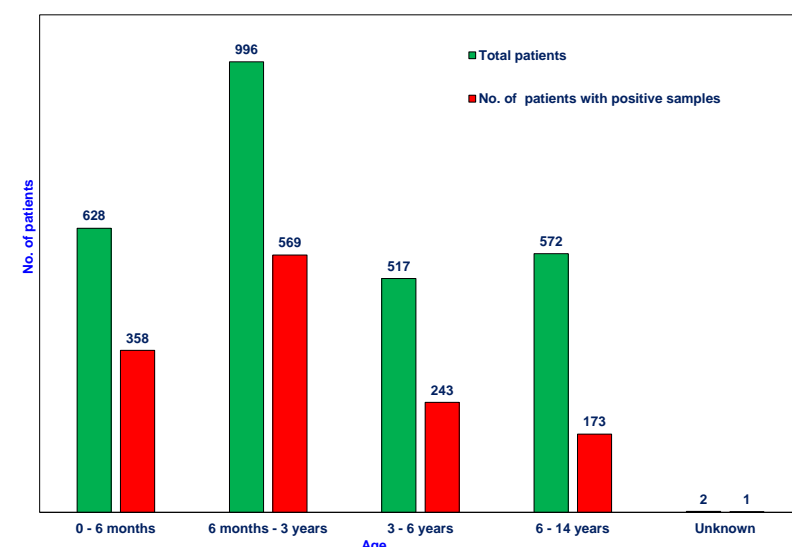


Figure 2. Monthly distribution of 1408 clinical samples positive for respiratory viruses belonging to 1344 patients in comparison with that of 2892 clinical samples belonging to 2715 patients suffering from acute respiratory syndrome and tested for respiratory viruses (1 October 2012 - 30 September 2015).

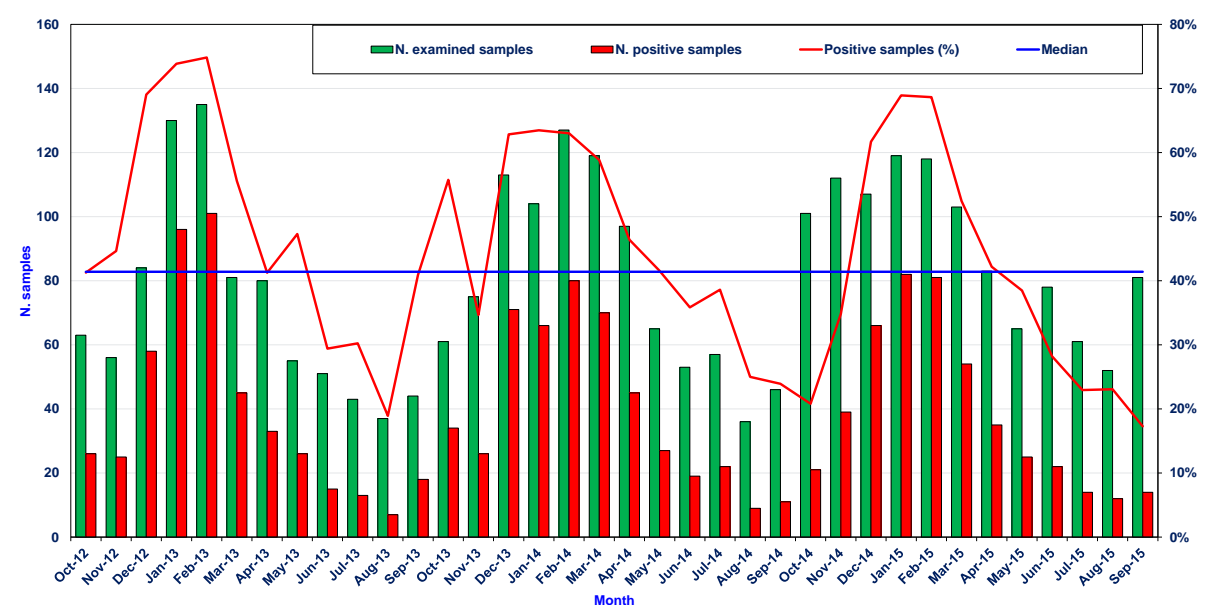
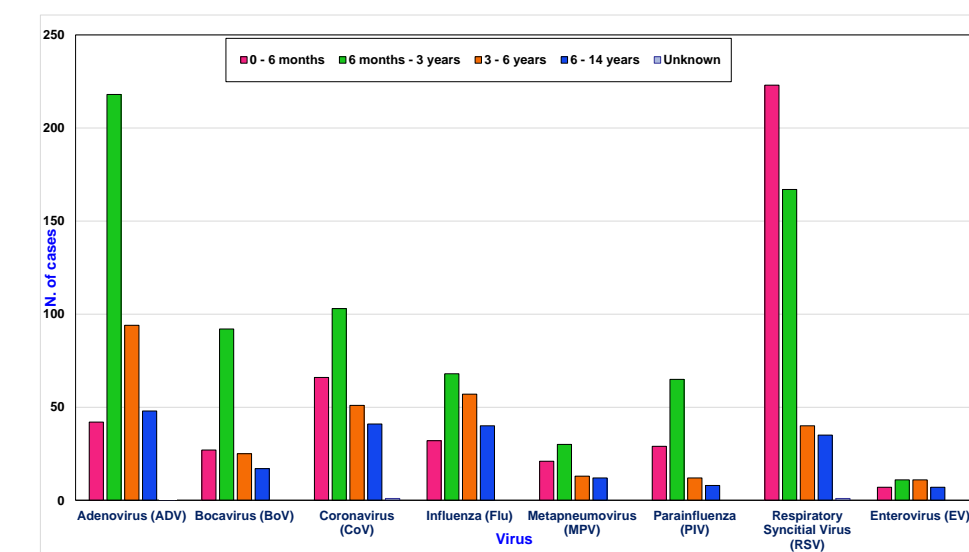


Figure 3 and Table 1. Distribution per age class of 1717 viruses detected in 1344 patients with ARTI



Age	AdV		BoV		CoV		Flu		MPV		PIV		RSV		EV		Total	
	n.	%	n.	%	n.	%	n.	%	n.	%	n.	%	n.	%	n.	%	n.	%
0 - 6 months	42	10.4%	27	16.8%	66	25.19%	32	16.2%	21	27.6%	29	25.4%	223	47.9%	7	19.4%	447	26.0%
6 months - 3 years	220	54.3%	92	57.1%	103	39.31%	68	34.5%	30	39.5%	65	57.0%	167	35.8%	11	30.6%	756	44.0%
3 - 6 years	94	23.2%	25	15.5%	51	19.47%	57	28.9%	13	17.1%	12	10.5%	40	8.6%	11	30.6%	303	17.6%
6 - 14 years	49	12.1%	17	10.6%	41	15.65%	40	20.3%	12	15.8%	8	7.0%	35	7.5%	7	19.4%	209	12.2%
Unknown	1	0.25%	1	0.25%	1	0.38%	1	0.25%	1	1.3%	1	0.8%	1	0.2%	1	2.6%	6	0.3%
<b>Total</b>	<b>405</b>		<b>161</b>		<b>262</b>		<b>197</b>		<b>76</b>		<b>114</b>		<b>466</b>		<b>36</b>		<b>1717</b>	

**Conclusions.** Epidemiological studies on viral respiratory infections spanning long periods are essential to know the temporal trends of circulating respiratory viruses, especially emerging viruses, and to monitor such infections in order to carry out preventive and therapeutic targeted strategies.

The results obtained in this study, using a variety of diagnostic methods, confirmed the high prevalence of viral infections in paediatric patients with acute respiratory syndrome and demonstrated that the most affected are children under 3 years. RSV and AdV are the most frequently detected viral agents, both alone and in mixed infections with other viruses. Furthermore, this study allowed to confirm an occurrence of the paediatric infections by Flu and RSV associated to the season and to reveal a seasonality also for other viral respiratory infections.

**References.** 1) De Conto F, Di Lonardo E, Arcangeletti MC, Chezzi C, Medici MC, Calderaro A. Highly dynamic microtubules improve the effectiveness of early stages of human influenza A/NWS/33 virus infection in LLC-MK2 cells. PLoS One. 2012; 7(7): e41207. 2) Bicer S, Giray T, Çöl D, Erdağ GÇ, Vitrinel A, Gürol Y, Çelik G, Kaspar C, Küçük Ö. Virological and clinical characterizations of respiratory infections in hospitalized children. Ital J Pediatr. 2013; 27: 39:22. 3) Dong W., Chen Q., Hu Y., He D., Liu J., Yan H., Lan K., Zhang C. Epidemiological and clinical characteristics of respiratory viral infections in children in Shanghai, China. Archives of Virology 2016; 161(7):1907-13. 4) Williams BG, Gouws E, Boschi-Pinto C, Bryce J, Dye C. Estimates of world-wide distribution of child deaths from acute respiratory infections. Lancet Infect Dis 2002; 2: 25–32.

Table 2. Viral agents revealed in 1408 clinical samples collected from children with ARTI (October 2012 - 30 September 2015)

Virus	NPA	TS	NS	BAL	BAS	SP	PF	TOT.
	N. 703	N. 2172	N. 3	N. 3	N. 8	N. 1	N. 2	N. 2892
AdV	22	240						262
BoV	27	62			1			90
CoV	33	104				1		138
Flu A	18	67		1				86
Flu B	3	47						50
MPV	16	35						51
PIV	26	56			1			83
RSV	209	130		1				340
CV (B1, B4, B5)	3	18						21
ECHO (6, 11, 21, 23, 24, 27)	2	5						7
<b>Sub Total</b>	<b>359</b>	<b>764</b>	<b>0</b>	<b>2</b>	<b>2</b>	<b>1</b>	<b>0</b>	<b>1128</b>
	(51.07%)	(35.17%)		(66.67%)	(25%)			(39%)
AdV + BoV		20						20
AdV + BoV + CoV		4						4
AdV + BoV + CoV + Flu B		1						1
AdV + BoV + Flu A		1						1
AdV + BoV + PIV		1						1
AdV + BoV + RSV		1						2
AdV + CoV	2	34						36
AdV + CoV + CV A9		1						1
AdV + CoV + FLU A		2						2
AdV + CoV + MPV		1						1
AdV + CoV + PIV		1						1
AdV + CoV + RSV	3	1						4
AdV + CV B2		1						1
AdV + CV B5		1						1
AdV + ECHO 12		1						1
AdV + ECHO 27		1						1
AdV + Flu A	1	4						5
AdV + Flu A + PIV		1						1
AdV + Flu B	2	1						3
AdV + MPV	2	6						8
AdV + PIV	1	8						9
AdV + PIV + RSV	1	1						2
AdV + RSV	15	22						37
BoV + CoV	1	6						7
BoV + CoV + Flu B		1						2
BoV + CoV + PIV + RSV		1						1
BoV + Flu A	1	6						7
BoV + Flu B + RSV	1	1						2
BoV + MPV	2	1						3
BoV + PIV	2	3						5
BoV + RSV	5	11						16
CoV + ECHO 9	2	1						3
CoV + Flu A	3	7						10
CoV + Flu A + RSV		1						1
CoV + Flu B	2	2						4
CoV + Flu B + RSV		1						1
CoV + MPV	3	5						8
CoV + MPV + RSV	1	1						2
CoV + PIV	1	2						3
CoV + RSV	22	13						35
CV B2 + RSV	1	1						2
CV B5 + RSV	1	1						2
Flu A + Flu B		1						1
Flu A + MPV	1	1						2
Flu A + PIV		2						2
Flu A + RSV	3	6		1				10
Flu B + RSV		7						7
MPV + PIV		1						1
MPV + RSV	1	1						2
PIV + RSV	1	4						5
<b>SUB TOTAL</b>	<b>79</b>	<b>200</b>	<b>1</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>280</b>
	(11.24%)	(9.21%)	(33.33%)					(9.68%)
<b>TOTAL</b>	<b>438</b>	<b>964</b>	<b>1</b>	<b>2</b>	<b>2</b>	<b>1</b>	<b>0</b>	<b>1408</b>
	(62.30%)	(35.54%)	(33.33%)	(66.67%)	(25%)			(48.69%)

Legend: AdV: Adenovirus; BoV: Bocavirus; CoV: Coronavirus; Flu: Influenza; MPV: Metapneumovirus; PIV: Parainfluenza virus; RSV: Respiratory Syncytial virus; CV: Coxsackie virus; ECHO: Echovirus