PREDOMINANCE OF ON1 AND BA9 GENOTYPES AMONG CIRCULATING HUMAN RESPIRATORY SYNCYTIAL VIRUSES AT A TERTIARY CARE UNIVERSITY HOSPITAL IN CATALONIA (SPAIN) DURING THE 2013-2014 AND 2014-2015 SEASONS

Laura Gimferrer[1], Andreu Bruguera[2], Maria Gema Codina[1], Lluís Armadans[2], Juliana Esperalba[1], María del Carmen Martín[1], Francisco Fuentes[1], Magda Campins[2], Tomàs Pumarola[1], Andrés Antón[1]

[1] Virology Unit, Microbiology Department, Hospital Universitari Vall d'Hebron, Universitat Autònoma de Barcelona, Barcelona, Spain.

[2] Preventive Medicine and Epidemiology Department, Hospital Universitari Vall d'Hebron, Universitat Autònoma de Barcelona, Barcelona, Spain

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INTRODUCTION

Human respiratory syncytial virus (HRSV) is the most common respiratory pathogen and the main cause of lower respiratory tract infections among infants and young children. HRSV is also recognised as a significant respiratory pathogen among immunosuppressed and elderly patients. Antigenic and genetic differences led to classify HRSV in two different groups, HRSV-A and HRSV-B. In addition, several genotypes of each HRSV group have been described. Palivizumab, an HRSV-specific humanised monoclonal antibody that binds a highly conserved region of the HRSV fusion (F) protein, is currently used as prophylaxis for paediatric patients at high risk of severe infection. Mutations within this region might be associated with resistance. In the present study we describe the genetic diversity of circulating HRSV strains from patients attended at the Hospital Universitari Vall d'Hebron in Barcelona (Spain) during the 2013-2014 and 2014-2015 seasons.

METHODS

From October 2013 (week 40/2013) to April 2015 (week 15/2015), respiratory specimens were collected from infants, children and adults for laboratory confirmation of HRSV and other respiratory viruses infection using immunochromatography (Binax Now RSV Card, Allere Scarborough Inc., USA), immunofluorescence (D^3 Ultra 8™ DFA Respiratory Virus Screening & Identification Kit Diagnostic HYBRIDS, USA) or real-time multiplex RT-PCR (Anyplex II RV16 Detection Kit See-gene, Korea) methods. A nucleoprotein-specific real time RT-PCR assay was performed to differentiate between HRSV-A and –B groups[1]. Phylogenetic analysis and molecular characterisation from a representative sampling of laboratory-confirmed cases were carried out based on the sequences of the second hypervariable region (HVR-2) of the attachment G protein[2]. Molecular characterisation of the antigenic site A of the F protein[2] was also done from a random selection of strains belonging to different genotypes.

References:
[1]Gunson RN et al. J Clin Virol. 2005;33(4):341-4; [2]Gimferrer et al. J Clin Virol. 2015;66:27-32.

RESULTS

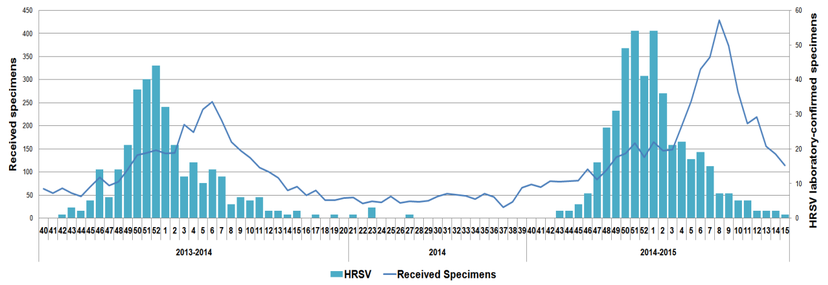
A total of 8367 respiratory specimens were studied, of which 9% were HRSV laboratory-confirmed (Table 1). Almost 70% of confirmed cases were infants aged under two years.

Table 1: Summary of detection rates, HRSV typing and molecular characterisation by season

	Specimens (patients)	HRSV specimens (n patients; %)	HRSV group (n cases; %)	HRSV genotype (n; %)
Season 2013-2014	3571 (2271)	334; 9% (320;14%)	HRSV-A (74; 23%)	ON1 (53; 98%) NA1 (1; 2%)
			HRSV-B (224; 70%)	BA9 (82; 96%) BA10 (2; 3%) BA ? (1; 1%)
			HRSV-A/B (6; 2%)	
			Untyped (16; 5%)	
Season 2014-2015	4796 (3471)	447; 9% (409; 12%)	HRSV-A (142; 35%)	ON1 (32; 97%) NA1 (1; 3%)
			HRSV-B (256; 63%)	BA9 (43; 90%) BA10 (5; 10%)
			HRSV-A/B (3; 1%)	
			Untyped (8; 1%)	

From October to April HRSV was continuously detected in both seasons, with maximum detection rates from the end of December to the beginning of January, as shown in Figure 1. As shown in Table 1 and Figure 2, the phylogenetic analyses revealed that the HRSV-A and HRSV–B strains from the two consecutive seasons mainly belonged to the ON1 and BA9 genotypes respectively, in which some phylogenetic subgroups could be differentiated (A, B, C and D). The strains detected during the 2014-2015 season showed to be slightly evolved (Figure 2) by the acquisition of some genetic and amino acid changes, and even a new genetic subgroup (ON1-D) appeared, in comparison with the genetic variants described in the previous season. As well, no 2014-2015 strains were found to belong to the undefined BA genotype reported during the 2013-2014 season. Molecular characterisation of the epitope A of the F protein from 107 strains revealed two mutations (K272M and S276N) in four strains, of which the K272M mutation was previously related to Palivizumab resistance.

Figure 1: Weekly distribution of specimens from week 40/2013 (2013-14) to week 15/2015 (2014-15)



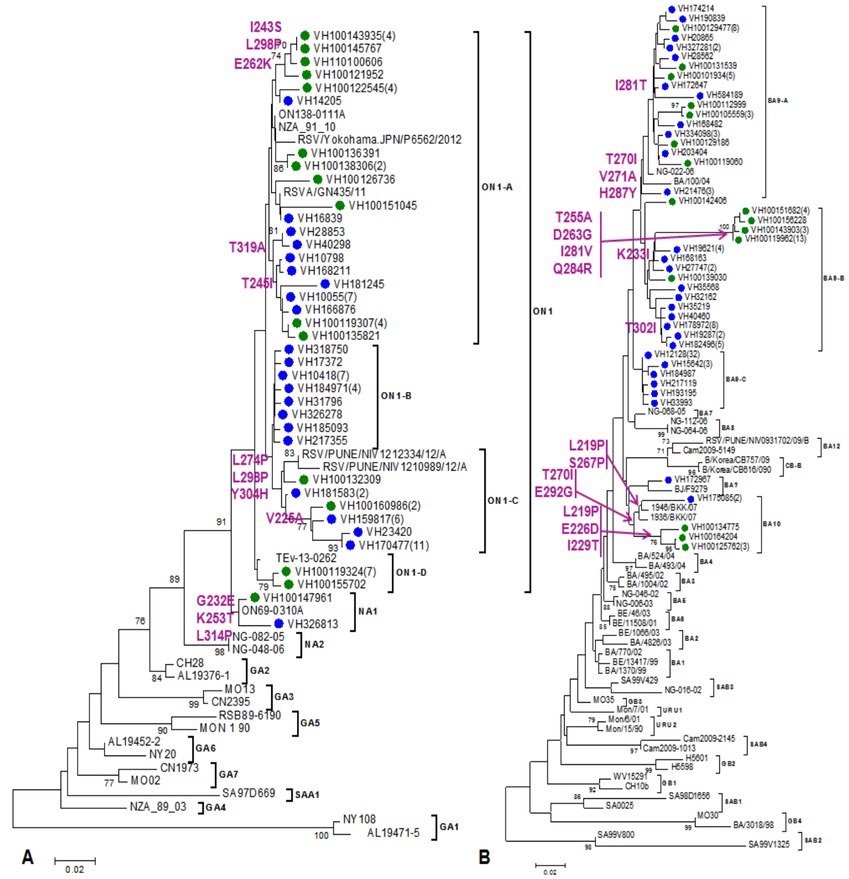


Figure 2: Phylogenetic trees of HVR-2 sequences from HRSV-A (figure 2A) and HRSV-B (figure 2B) strains. The sequences of the present study are marked with blue (2013-2014 season) and green (2014-2015 season) points. Sequences were previously collapsed to haplotypes, and the number of sequences represented is shown in brackets. Amino acid substitutions relative to first-described ON1 (HRSV-A) or BA (HRSV-B) strains that define genetic subgroups are marked in purple.

CONCLUSIONS

- The present study reports recent valuable data that describes the genetic diversity of the HRSV strains from patients attended in our hospital during the 2013-2014 and 2014-2015 seasons.
- Co-circulation of both HRSV-A and HRSV-B groups was reported, with the predominance of HRSV-B during these two consecutive seasons. Although several genotypes have been described in this study, the great predominance of ON1 (HRSV-A) and BA9 (HRSV-B) among genotypes on circulation should be noted.
- Multiple phylogenetic subgroups described within main genotypes might evolve becoming new genotypes over time.
- This report also highlights the importance of an active surveillance for the likely emergence of Palivizumab resistant strains.

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Contact: A. Antón (aanton@vhebron.net)