



Enfermedades Infecciosas y Microbiología Clínica

www.elsevier.es/eimc



Original article

Impact of the passive immunization campaign with nirsevimab in 2023–24 in Castellón. Final results



Eulalia Gregori-García^{a,b}, Juan Carlos Gascó-Laborda^b, Lledó Lluch-Bacas^b, Oscar Pérez-Olaso^c, Iris Gómez-Alfaro^c, Juan B. Bellido-Blasco^{b,d,e,*}

^a Servicio de Medicina Preventiva, Hospital General Universitario de Castellón, Castellón, Spain

^b Sección de Epidemiología, Centro de Salud Pública de Castellón, Generalitat Valenciana, Castellón, Spain

^c Servicio de Microbiología Clínica, Hospital Universitario La Plana, Vila-real, Castellón, Spain

^d Servicio de Microbiología, Hospital General Universitario de Castellón, Castellón, Spain

^e CIBER-ESP grupo 41, Spain

ARTICLE INFO

Article history:

Received 26 August 2024

Accepted 13 November 2024

Available online 6 February 2025

Keywords:

Respiratory syncytial virus

Incidence

Nirsevimab

Impact

Children

ABSTRACT

Introduction: In the 2023–2024 season, systematic immunization with the monoclonal antibody nirsevimab was recommended in Spain. The impact that this immunization program had on the target population of the program is analyzed.

Methods: Pre-post ecological study comparing 2023–24 vs 2022–23 season. The variation in incidence is described by age groups (0–5, 6–11 and 12–59 months) and hospitalization. Incidence rates were calculated and relative risks (RR) were estimated for each group.

Results: The results were very heterogeneous depending on the age group. In children 0–5 months old the RR was 0.16 (0.10–0.25); in those aged 6–11 months, RR of 0.90 (0.56–1.42); and in those aged 12–59 months, RR 1.36 (1.06–1.74). The greatest decrease in risk was in hospitalized children under 6 months, RR 0.13 (0.07–0.22).

Conclusion: The results support the positive impact that this campaign had, especially on hospitalizations.

© 2024 Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica. Published by Elsevier España, S.L.U. All rights are reserved, including those for text and data mining, AI training, and similar technologies.

Impacto de la campaña de inmunización pasiva con nirsevimab en 2023-24 en Castellón. Resultados finales

RESUMEN

Introducción: En la temporada 2023-2024 se recomendó en España la inmunización sistemática con el anticuerpo monoclonal nirsevimab. Se analiza el impacto que tuvo ese programa de inmunización en la población diana del programa.

Métodos: Estudio ecológico pre-post comparando la temporada 2023-24 vs la 2022-23. Se describe la variación en la incidencia por grupos de edad (0-5, 6-11 y 12-59 meses) y hospitalización. Se calcularon las tasas de incidencia y se estimaron los riesgos relativos (RR) para cada grupo.

Resultados: Los resultados fueron muy heterogéneos según el grupo de edad. En niños de 0-5 meses el RR fue de 0,16 (0,10-0,25); en los de 6-11 meses el RR fue de 0,90 (0,56-1,42), y en los de 12-59 meses el RR fue de 1,36 (1,06-1,74). El mayor descenso del riesgo fue en menores de 6 meses hospitalizados, con un RR de 0,13 (0,07-0,22).

Conclusión: Los resultados sustentan el impacto positivo que tuvo esa campaña, sobre todo en hospitalizaciones.

© 2024 Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica. Publicado por Elsevier España, S.L.U. Se reservan todos los derechos, incluidos los de minería de texto y datos, entrenamiento de IA y tecnologías similares.

Palabras clave:

Virus respiratorio sincitial

Incidencia

Nirsevimab

Impacto

Niños

DOI of original article: <https://doi.org/10.1016/j.eimc.2024.11.007>

* Corresponding author.

E-mail address: bellido_jua@gva.es (J.B. Bellido-Blasco).

Introduction

Worldwide, respiratory syncytial virus (RSV) is considered to be the primary cause of hospital admissions for lower respiratory tract infections in childhood, and one of the main causes of associated mortality in infants. In their first 24 months of life, a large part of the child population will have suffered an RSV infection and 14% will require medical attention.¹

Here in Spain, according to the Sistema de Vigilancia de Infección Respiratoria Aguda (SiVIRA) [Acute Respiratory Infection Surveillance System], in children under 5 years of age in the 2022–2023 season there were an estimated 259,013 cases of infection in primary care (rates of 153.6 per 1000 population) and 15,375 hospital admissions due to RSV (rate of 10.76 per 1000 population).²

As part of the preventive arsenal against RSV, the use of a new monoclonal antibody called nirsevimab was approved in October 2022. This is an antibody with proven efficacy in clinical trials^{3,4} and with an 83.3% reduction in hospital admissions attributed to RSV and the most severe forms of the disease, estimated in studies under real-life conditions.^{5,6}

In view of the above, the Spanish Ministry of Health recommended incorporating systematic passive immunisation with nirsevimab in the 2023–2024 season for all children aged under 6 months born from 1 April 2023 to 31 March 2024.⁷

The aim of this study was to analyse the potential impact of nirsevimab in the 2023–24 season in children under 5 years of age. This brings to completion the partial and provisional results previously reported, relating to the decrease in the number of cases specifically observed in children under the age of 6 months in the 2023–2024 season in Castellón.⁸

Methods

A pre-post ecological study was carried out which included all cases of RSV infection in children under 5 years of age residing in the two health departments attached to the Centro de Salud Pública de Castellón [Castellón Public Health Centre] within the 2022–23 and 2023–24 seasons. During this period there were no changes in case detection criteria or laboratory methods. Any positive detection of RSV nucleic acid included in the Red Microbiológica Valenciana

(RedMIVA) [Valencian Microbiological Network] was considered a case. Additionally, to provide a broader perspective, cases reported since the 2017–18 season have been reviewed.

A season was defined as the period of time between week 40 of one year and week 39 of the next. The season of interest was 2023–24, when the systematic immunisation programme against RSV with nirsevimab was implemented for the first time. We took the previous season, 2022–23, as reference.

To obtain the population denominators necessary for calculating the incidence, we consulted the Valencia Region Ministry of Health's Eolas application in children under 5 years of age. The population of children under 1 year of age was divided by two to obtain an approximation of the population aged 0–5 and 6–11 months.

The variables selected were gender, age, date of diagnosis and hospital admission in all cases. The data for the first three variables were obtained from RedMIVA, while those relating to hospital admission were taken from the electronic medical records. Cases were stratified by age and hospital admission. Age was categorised into three groups, corresponding to 0–5 months, 6–11 months and 12–59 months of age.

We calculated variations in incidence by age group and hospital admission in the season of interest versus the reference season. Subsequently, we estimated the incidence rates per 1000 population in each stratum, and, from them, we calculated the relative risks and their 95% confidence intervals.

The study was approved by the Independent Ethics Committee for Research in Medicines (IECm) of Castellón's Hospital General Universitario.

Results

During the time period selected for the pre-post study, a total of 489 cases of RSV were recorded in children under 5 years of age: 285 corresponding to the 2022–23 season and 204 to that of 2023–24. In these two seasons, males made up 57.7% and 54.5% ($p = 0.06$); the mean ages were 11.4 and 20.5 months ($p < 0.001$) and the hospital admission rates, 69.1% and 57.4% ($p < 0.001$) respectively.

Table 1 shows the number of cases by season, age group and sex. The percentage of females was lower than that of males, except in the 6–11-month age group of the 2023–24 season, although with-

Table 1

Recorded cases of respiratory syncytial virus infection by epidemiological season in children under 5 years of age by age group and gender in the 2022–23 and 2023–24 seasons.

Age (months)	2022–23 season				2023–24 season				$p(\chi^2)$
	Male	Female	Total	% Female	Male	Female	Total	% Female	
<6	89	48	137	35%	14	8	22	36%	0.904
6–11	25	13	38	34%	16	18	34	53%	0.112
12–59	61	49	110	45%	78	70	148	47%	0.662
Total	175	110	285	39%	108	96	204	47%	0.062

Table 2

Recorded cases of respiratory syncytial virus infection by epidemiological season in children under 5 years of age by sex and hospital admission from the seasons 2017–18 to 2023–24.

Hospital admission	Sex	Epidemiological season						
		2017–18	2018–19	2019–20	2020–21 COVID-19	2021–22	2022–23	2023–24
Not admitted	Male	7	9	7	0	17	48	39
	Female	14	3	16	0	14	40	48
	Total	21	12	23	0	31	88	87
Admitted	Male	98	109	71	0	58	127	69
	Female	63	82	73	0	50	70	48
	Total	161	191	144	0	108	197	117
All	Male	105	118	78	0	75	175	108
	Female	77	85	89	0	64	110	96
	Total	182	203	167	0	139	285	204

Table 3

Cases of RSV infection in children under 5 years of age registered during the 2022–23 and 2023–24 seasons, by season, age (3 groups), in total, admitted to hospital and not admitted.

Hospital admission	Age (months)	Epidemiological season		Population		Rate per × 1000		RR: 2024 vs 2023	95% Confidence intervals		p
		2022–23	2023–24	2023	2024	2023	2024		Lower L	Upper L	
Not admitted	<6	33	9	1726	1723	19.1	5.2	0.27	0.13	0.57	0.0002
	6–11	10	13	1726	1723	5.8	7.5	1.30	0.57	2.97	0.529
	12–59	45	65	14,793	14,651	3.0	4.4	1.46	1.00	2.13	0.050
	Total	88	87	18,245	18,097	4.8	4.8	1.00	0.74	1.34	0.983
Admitted	<6	104	13	1726	1723	60.3	7.5	0.13	0.07	0.22	<0.0001
	6–11	28	21	1726	1723	16.2	12.2	0.75	0.43	1.42	0.320
	12–59	65	83	14,793	14,651	4.4	5.7	1.29	0.93	1.78	0.124
	Total	197	117	18,245	18,097	10.8	6.5	0.60	0.48	0.76	<0.0001
All	<6	137	22	1726	1723	79.4	12.8	0.16	0.10	0.25	<0.0001
	6–11	38	34	1726	1723	22.0	19.7	0.90	0.56	1.42	0.643
	12–59	110	148	14,793	14,651	7.4	10.1	1.36	1.06	1.74	0.016
	Total	285	204	18,245	18,097	15.6	11.3	0.72	0.60	0.86	0.0003

Rates and relative risks (RR) are given with their 95% confidence intervals (lower L [limit]; upper L) and p values for statistical significance.

Calculations made with: Epidemiology/Biostatistics Tools. Wayne W. LaMorte, MD, PhD, MPH. Boston University Medical Campus. <https://www.bumc.bu.edu/medlib/files/2018/06/LaMorte.xls> visited.

out reaching statistical significance when compared to the previous season ($p = 0.112$). In children under 6 months old there was an 84% reduction in cases (from 137 to 22), in those aged 6–11 months there was hardly any change and in those aged 12–59 months there was an increase of 35% (from 110 to 148). This pattern was similar, but of a different magnitude, in patients admitted to hospital and those not admitted. The greatest reduction occurred in children aged under 6 months admitted to hospital, from 104 to 13, a reduction of 88%. Table 2 shows cases from 2017 to 18, according to sex and hospital admission.

The incidence rate of RSV in children under 5 years of age was 15.6 per 1000 in the 2022–23 season and 11.3 per 1000 in 2023–24. However, the rates were very heterogeneous by age. In children under 6 months old, for the two consecutive seasons the rates were 79.4 vs 12.8; in children aged 6–11 months, 22.0 vs 19.7, and in children aged 12–59 months, 7.4 vs 10.1. These rates are much lower than those published by SiVIRA,² which is not surprising if we look at the different estimation methods. In our study we only considered laboratory-confirmed cases, and in SiVIRA we extrapolated cases from the sentinel surveillance system.

The estimated relative risks for each age group and stratified by hospital admission are shown in Table 3. Stratification reveals large differences according to age group and hospital admission. The risk reduction in the 2023–24 season applied specifically to the group of children under 6 months old and not in the rest. It was highest in children aged under 6 months admitted to hospital, with a reduction in the risk of 87%, corresponding to an RR of 0.13 (95% CI: 0.10–0.25). We found an increase in incidence in children aged 12–59 months.

Discussion

The majority of cases recorded in both health departments of Castellón were male, with mean age 9 months older in the 2022–23 season than in the 2023–24 season. These data coincide with other studies of similar characteristics, where in the majority of cases, 58%, were male, and where in 2023–24 there was an increase in the mean age, although somewhat lower than that identified by us.^{9,10}

During 2023–24 the overall number of recorded cases decreased by 28% compared to the previous equivalent season. The decrease differed greatly according to age group; maximum in children under 6 months (84%), followed by the 6–11-month-old group (10%). However, in older children, aged 12–59 months, there was

a 36% increase in the number of cases. These findings could be attributed to the introduction of RSV immunisation with nirsevimab in children aged under 6 months during the 2023–24 season. The reduction in cases in this group was particularly notable in patients admitted to hospital (88%). The increased incidence in older children (those aged 1–4 years) could be related to the absence of RSV circulation during the pandemic, in other words, due to the so-called “immunological debt”.¹¹ These results are in line with the Spanish multicentre study by Lopez-Lacort et al.,⁶ where they found a 70%–84% reduction in hospital admission in children aged under 9 months, with the 74% in the Valencia Region reported by Estrella-Porter et al.,¹² with the 90% reported by Moline et al. in the United States,⁹ and with others similar reports.^{12–15} In our preliminary work,⁸ the 2023–24 season had not yet concluded, although the results were similar to those reported now, with an 89% reduction in the number of cases aged under 6 months admitted to hospital.

The series of RSV cases in children under 5 years of age since the 2017–18 season, which includes the period of epidemic pause during the pandemic (2020–21 season), revealed an increase in cases in 2022–23. It was also found that the decrease in the incidence of cases in children aged under 6 months occurred, very markedly, in the season analysed here in detail, 2023–24, and not in previous seasons. The predominance of cases in males seen since 2017–18, except in 2019–20, is a factor we did not thoroughly investigate in this study, but which certainly deserves further attention.

The more refined analysis presented here, that is, that of relative risks estimated from seasonal incidence taking into account population denominators, resulted in the same findings. A statistically significant reduction in the risk of hospital admission was only found in children aged under 6 months, the target population of the nirsevimab immunisation programme. Again, higher among those admitted to hospital than those not admitted.

This study had a number of limitations. First of all, these are the results of an ecological study and they therefore have to be interpreted from that perspective, avoiding the ecological fallacy. Secondly, there is no control population under 6 months of age outside the nirsevimab immunisation programme. However, the risk reduction has been detected specifically in the target population and not in older children outside the immunisation programme, with no change in screening and diagnostic criteria between the season of interest (post) and the comparison season (pre). Lastly, as there is no data on the severity of illness in the children admitted to hospital, it is not possible to distinguish between admissions as a

direct consequence of the severity of the illness and those admitted to prevent potential deterioration in their health status during the RSV infection.

In conclusion, these results support the positive impact of systematic passive immunisation with nirsevimab during the 2023–2024 season in children aged under 6 months to prevent infection, especially RSV-related hospital admission.

CRedit authorship contribution statement

EGG, JCGL and JBBB conceived the study design; EGG, JCGL and JBBB performed the epidemiological and statistical analyses; LLB, OPO and IGA performed the data search and database construction; EGG wrote the first draft of the article. All authors contributed to the writing and agree with the submitted version.

Funding

This study received no specific funding from public, private or non-profit organisations.

Declaration of competing interest

None.

Acknowledgements

Esther Silvestre-Silvestre, Noemí Meseguer-Ferrer and Viorica Rusen, Public Health nurses; Aurora Blasco-Mollá and Marina Parra-Civera, microbiologists at Hospital General Universitario de Castellón and Hospital Universitario de la Plana respectively.

References

- Francisco L, Cruz-Cañete M, Pérez C, Couceiro JA, Otheo E, Launes C, et al. Nirsevimab para la prevención de la enfermedad por virus respiratorio sincitial en niños. Posicionamiento de la Sociedad Española de Infectología Pediátrica. *An Pediatr (Barc)*. 2023;99:257–63.
- Puma Olguin TC, Mazagatos C, Galindo-Carretero S, Vega-Piris L, Lozano-Álvarez M, Pérez-Gimeno G, et al. Epidemiología y carga de enfermedad por VRS en España. SiVIRA, temporadas 2021–22 y 2022–23. *BES*. 2024;32:21–35.
- Drysdale SB, Cathie K, Flamein F, Knuf M, Collins AM, Hill HC, et al. Nirsevimab for prevention of hospitalizations due to RSV in infants. *N Engl J Med*. 2023;389:2425–35.
- Hammitt LL, Dagan R, Yuan Y, Baca Cots M, Bosheva M, Madhi SA, et al. Nirsevimab for prevention of RSV in healthy late-preterm and term infants. *N Engl J Med*. 2022;386:837–46.
- Ruiz-Galiana J, Cantón R, de Lucas Ramos P, García-Botella A, García-Lledó A, Hernández-Sampelayo T, et al. Respiratory syncytial virus: a new era. *Rev Esp Quimioter*. 2024;37:134–48. <http://dx.doi.org/10.37201/req/147.2023>.
- López-Lacort M, Muñoz-Quiles C, Mira-Iglesias A, López-Labrador FX, Mengual-Chuliá B, Fernández-García C, et al. Early estimates of nirsevimab immunoprophylaxis effectiveness against hospital admission for respiratory syncytial virus lower respiratory tract infections in infants, Spain, October 2023 to January 2024. *Euro Surveill*. 2024;29. <http://dx.doi.org/10.2807/1560-7917.ES.2024.29.6.2400046>.
- Ministerio de Sanidad, España. Recomendaciones de utilización de nirsevimab frente a virus respiratorio sincitial para la temporada 2023–2024 [Accessed 7 February 2024]. Available from: <https://www.sanidad.gob.es/areas/promocion/Prevencion/vacunaciones/comoTrabajamos/docs/Nirsevimab.pdf>.
- Gascó-Laborda JC, Lluch-Bacas L, Pérez-Olaso O, Gómez-Alfaro I, Silvestre-Silvestre E, Blasco-Mollá A, et al. Cambios en la epidemiología de la infección por virus respiratorio sincitial con la pandemia, e impacto de la campaña de inmunización pasiva con nirsevimab en 2023–24 en Castellón. Resultados preliminares. *Enf Emerg*. 2024;23:7–13.
- Moline HL, Tannis A, Toepfer AP, Williams JV, Boom JA, Englund JA, et al. Early estimate of nirsevimab effectiveness for prevention of respiratory syncytial virus-associated hospitalization among infants entering their first respiratory syncytial virus season — New Vaccine Surveillance Network, October 2023–February 2024. *MMWR Morb Mortal Wkly Rep*. 2024;73:209–14.
- Ernst C, Bejko D, Gaasch L, Hannelas E, Kahn I, Pierron C, et al. Impact of nirsevimab prophylaxis on paediatric respiratory syncytial virus (RSV)-related hospitalisations during the initial 2023/24 season in Luxembourg. *Euro Surveill*. 2024;29. <http://dx.doi.org/10.2807/1560-7917>.
- Billard MN, Bont LJ. Quantifying the RSV immunity debt following COVID-19: a public health matter. *Lancet Infect Dis*. 2023;23:3–5.
- Estrella-Porter P, Blanco-Calvo C, Lameiras-Azevedo AS, Juaneda J, Fernández-Martínez S, Gómez-Pajares F, et al. Effectiveness of nirsevimab introduction against respiratory syncytial virus in the Valencian Community: a preliminary assessment. *Vaccine*. 2024;42. <http://dx.doi.org/10.1016/j.vaccine.2024.05.078>.
- Assad Z, Romain AS, Aupiais C, Shum M, Schrimpf C, Lorrot M, et al. Nirsevimab and hospitalization for RSV bronchiolitis. *N Engl J Med*. 2024;391:144–54.
- Molina Gutiérrez MÁ, de Miguel Lavisier B, Ruiz Domínguez JA, García de Oteyza M, Velasco Molina VM, Gutiérrez Arroyo A, et al. Impact of nirsevimab immunization on RSV infections attended in the pediatric emergency department: first results in a tertiary hospital in Madrid. *Enferm Infecc Microbiol Clin (Engl Ed)*. 2024;42:367–72.
- Coma E, Martínez-Marcos M, Hermosilla E, Mendioroz J, Reñé A, Fina F, et al. Effectiveness of nirsevimab immunoprophylaxis against respiratory syncytial virus-related outcomes in hospital and primary care settings: a retrospective cohort study in infants in Catalonia (Spain). *Arch Dis Child*. 2024;109:736–41. <http://dx.doi.org/10.1136/archdischild-2024-327153>.