






Evaluation of the effectiveness of the respiratory syncytial virus vaccine in children under 6 months of age in Córdoba, Argentina

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ABSTRACT

Introduction. The recently approved vaccine against respiratory syncytial virus (RSV) is administered to pregnant women and confers immunity to their babies; however, the evaluation of its effectiveness is limited.

Objective. To evaluate the effectiveness of the vaccine against hospitalization due to RSV in children under 6 months of age during the vaccination campaign for pregnant women.

Population and methods. Case-control study nested in a cohort of newborns whose mothers were indicated for RSV vaccination in Córdoba, Argentina. We included 180 cases with positive laboratory results for RSV and 1,069 asymptomatic controls who attended routine check-ups. Multiple logistic regression models were performed considering the presence of RSV as the primary response variable, adjusted for maternal age, gestational age, birth weight, maternal influenza vaccination, maternal education level, and multiple births. Vaccine effectiveness was calculated using the formula $EV = (1 - OR) \times 100$.

Results. The RSV vaccine reduces the likelihood of becoming ill with RSV by 74.0% (OR: 0.26; CI: 0.17-0.39); the influenza vaccine reduces it by 70% (OR: 0.30; CI: 0.21-0.43). For each completed week of gestational age, protection against the disease increases by 10% (OR: 0.90; CI: 0.81-0.99).

Conclusion. The vaccine is effective against hospitalization due to RSV in children under 6 months of age, who are the most vulnerable population, and could be an essential tool for reducing morbidity and mortality due to RSV.

Keywords: respiratory syncytial virus vaccines; effectiveness; child health; subunit vaccines.

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INTRODUCTION

Globally, respiratory syncytial virus (RSV) is one of the most reported human respiratory pathogens, especially in the post-pandemic era. It particularly affects older adults and infants, who are at higher risk of hospitalization and fatal outcomes, which are even higher in low-income countries.^{1,2}

During the SARS-CoV-2 pandemic, various preventive measures were implemented to reduce morbidity and mortality, which affected the circulation of respiratory viruses, including RSV, during 2020. Subsequently, in 2021, there was an atypical peak in incidence compared to the seasonality of the virus prior to the pandemic.³⁻⁵

In the province of Córdoba, RSV surveillance is carried out universally through the National Health Surveillance System (SNVS, by its Spanish acronym). It shows a seasonal epidemiological pattern, with an average of 960 cases per year and a peak incidence between epidemiological weeks 22 and 26, except for pandemic years (2020-2021). According to the literature, in 2021, the peak of VSR cases was recorded late (in epidemiological week 31), with an 85% increase compared to the previous week. Likewise, the cumulative incidence rate of RSV in children under 6 months of age before the SARS-CoV-2 pandemic was around 20 cases per 1000 live births, while post-pandemic rates increased to 33 cases per 1000 live births in 2023.

About the epidemiology of the virus, the risk of severe illness from RSV is associated with specific clinical characteristics of the patient, such as age younger than 3 months, genetics, history of prematurity and/or asthma in the family, overcrowding, low socioeconomic status, exposure to peers and the pathogen, the latter being more predictable due to seasonal patterns around the world, as virus activity increases during the winter.⁷⁻¹³

The recent introduction of monoclonal antibodies and vaccines has changed RSV prevention measures. In May 2023, the US Food and Drug Administration (FDA) approved the Abrysbo™ vaccine for use in older adults. Subsequently, it approved its use in pregnant women during the third trimester of pregnancy, specifically between weeks 32 and 36. In Argentina, the Disposition No. 7397 of the ANMAT (National Administration of Medicines, Food, and Medical Technology) authorized its marketing in the country.¹⁴

The vaccine incorporates a viral subunit

platform that includes immune system-stimulating components or antigens that have been shown to induce neutralizing antibodies and efficient transplacental migration of these antibodies to the fetus. In phase III clinical trials, maternal vaccination effectively reduced the risk of acute lower respiratory tract infections (ALRI) and protected infants from RSV infection during the first 6 months of life, compared to the placebo group.^{2,15,16} In addition, it proved to be a cost-effective strategy,¹⁷ considering that the estimated cost of medical care for RSV in Argentina was more than USD 25 million per year in children under 5 years of age.¹⁸

The results of the first RSV vaccination campaign in Argentina, according to data from the Directorate for the Control of Immunopreventable Diseases, indicate that RSV vaccination coverage among pregnant women was around 62%. In comparison, the province of Córdoba had coverage of 62.94%.¹⁹

Based on the above and the limited evidence available to date regarding the effectiveness of incorporating this immunization strategy at the local and global levels, the objective of this study was to evaluate the effectiveness of the vaccine against hospitalization due to RSV in the context of the vaccination campaign in the province of Córdoba, Argentina, in 2024.

POPULATION AND METHODS

A retrospective case-control study was conducted in a cohort of newborns in the province of Córdoba, Argentina. The source cohort included all children born between March 31 and October 31, 2024, a period consistent with the RSV vaccination campaign implemented between March and August 2024. Exposure (maternal vaccination between 32 and 36 weeks of gestation) was determined from the nominal vaccination registry. Cases (N = 180) were defined as those people with a positive laboratory test for RSV (by polymerase chain reaction, direct immunofluorescence test for RSV, or rapid test for RSV) and reported as hospitalized or deceased from RSV with a positive laboratory test in the SNVS. Cases were matched by age at the time of consultation with asymptomatic controls born in the same period who attended routine child health check-ups (N = 1069), who did not have an RSV test (positive or negative) during the entire study period, and who did not consult for respiratory symptoms. Children born at less than 32 weeks of gestation or weighing less than 1500 grams

were excluded from the study. *Figure 1* shows the flowchart for selecting the study population.

Maternal vaccination against RSV during pregnancy (at least 14 days before birth), outpatient medical care, hospitalization, and death, age at the time of consultation or diagnosis, birth weight, and gestational age at birth were identified in the subjects studied. In addition, variables related to the mother were identified, such as age at delivery, influenza vaccination during pregnancy, educational level, and multiple births.

The information was collected from secondary sources: the Civil Registry of the province to identify births and maternal data, the Comprehensive Health Information Management System (SIGIPSA, by its Spanish acronym) to determine the vaccinated population, the SNVS to identify cases, and the provincial Health Information System (SISalud-digital medical records) to select controls.

The variables studied were described, and an exploratory analysis was performed to identify associations. The comparison of proportions between cases and controls was performed using the difference of proportions test, supplemented with contingency tables and the chi-square test to verify the independence of variables. The Mantel-Haenszel test allowed conditional

associations to be evaluated in the presence of a third variable. Multiple logistic regression models were constructed to determine the association of covariates with the presence of RSV (primary endpoint) and mortality from RSV (secondary endpoint), adjusted for factors such as maternal age, gestational age, birth weight, previous influenza vaccine dose, maternal education level, and multiple births. Vaccine effectiveness was calculated with the formula $EV = (1 - OR) \times 100$. Stata 17.0 software was used with a confidence interval (CI) of 95%.

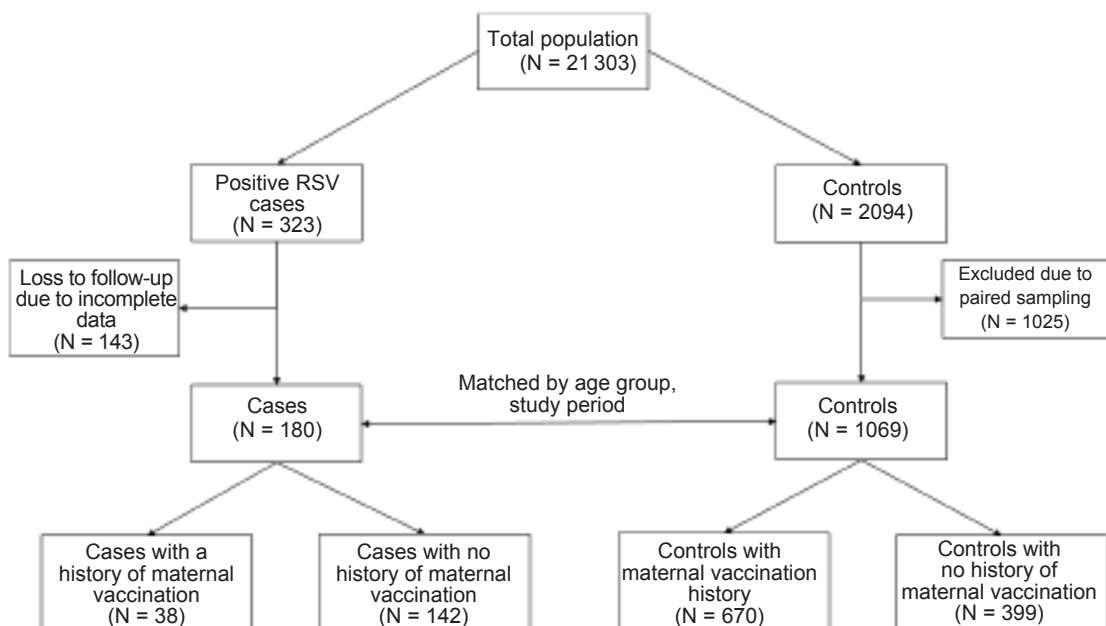
This study has been evaluated and approved by the Institutional Committee on Health Research Ethics for Children and Adults under Act No. 9 dated April 14, 2025.

RESULTS

Between March and October 2024, 180 cases and 1069 controls were included in the province. No deaths were recorded during the study period. *Table 1* shows the main characteristics of the cases and controls. In 38 (21.1%) of the cases and 670 (62.9%) of the controls, the application of the RSV vaccine at least 14 days before delivery was registered ($p < 0.01$).

There were no differences in maternal age, age at consultation, sex at birth, maternal education level, or multiple births between cases

FIGURE 1. Case and control selection process in the study population (N = 1249)



and controls. A statistically significant association was found between the presence of RSV and gestational age at birth, birth weight, and maternal vaccination against RSV and influenza. The cases were characterized by prematurity, low birth weight, and lack of vaccination against RSV and influenza.

The calculation of crude ORs showed that the chance of becoming ill was higher among those with low birth weight (OR: 2.48; CI: 1.48-4.06) or prematurity (OR: 2.61; CI: 1.60-4.15).

In contrast, the chance of becoming ill decreased in children whose mothers had received the RSV vaccine (OR: 0.16; CI: 0.11-0.23) or influenza vaccine (OR: 0.19; CI: 0.13-0.27).

The results of the multivariate analysis (*Table 2*), adjusting for variables of interest, showed that the RSV vaccine reduces the likelihood of becoming ill with RSV by 74.0% (OR: 0.26; CI: 0.17-0.39); the influenza vaccine reduced the chance of illness by 70% (OR: 0.30; CI: 0.21-0.43). For each complete week of gestational age, protection against the disease increased by 10% (OR: 0.90; CI: 0.81-0.99). In the adjusted model, no differences in low birth weight and prematurity were observed between cases and controls, which could demonstrate the protective effect of the vaccine, particularly for this population group.

TABLE 1. Variables associated with the mother and newborn, March-October 2024, Province of Córdoba, N = 1249

Variables	Cases N = 180 (%)	Control N = 1069 (%)	p-value*
Gestational age			
<37 weeks	31 (17.2)	79 (7.4)	<0.01
37 to 41 weeks	149 (82.8)	990 (92.6)	
Maternal age			
<20 years	30 (16.7)	145 (13.6)	0.145
20 to 35 years	139 (77.2)	814 (76.2)	
>35 years	11 (6.1)	110 (10.3)	
RSV vaccination			
No	142 (78.9)	399 (37.3)	<0.01
Yes	38 (21.1)	670 (62.7)	
Age at time of consultation			
<60 days	112 (62.2)	662 (61.9)	0.962
60-119 days	62 (34.4)	375 (35.1)	
>120 days	6 (3.3)	32 (3.0)	
Sex at birth			
Female	80 (44.4)	546 (51.1)	0.266
Male	100 (55.6)	523 (48.9)	
Birth weight			
1500 to 2499 g	27 (15.0)	71 (6.6)	<0.01
>2500 g	153 (85.0)	998 (93.4)	
Maternal influenza vaccination			
No	123 (68.3)	312 (29.2)	<0.01
Yes	57 (31.7)	757 (70.8)	
Mother's educational level			
Did not attend or had an incomplete primary education	3 (1.7)	5 (0.5)	0.191
Complete primary education or incomplete secondary education	97 (54.2)	584 (40.5)	
High school diploma or higher	68 (38.0)	433 (40.5)	
Complete higher education	11 (6.1)	47 (4.4)	
Multiple birth			
No	176 (97.8)	1,045 (97.8)	0.985
Yes	4 (2.2)	24	

* A p-value less than 0.05 is considered statistically significant. RSV: respiratory syncytial virus.

DISCUSSION

Argentina was the first country in Latin America to include Abrysbo™ in its vaccination schedule, so it was interesting to investigate the effectiveness of the RSV vaccine administered to pregnant women between March and October 2024 as part of the vaccination campaign in the province of Córdoba. The vaccine was effective in preventing RSV-associated hospitalizations in children under 6 months of age during the first stage of the campaign's implementation.

Age at the time of consultation was matched between cases and controls to minimize bias, with no evidence of association with RSV infection. However, most cases were under 3 months of age, which is consistent with studies identifying this group as the most susceptible to severe disease, and in which the vaccine has shown greater efficacy in phase III trials.²⁰ Regarding sex at birth, no relationship was found between cases and controls; however, the literature reports an association between male sex and the occurrence of respiratory diseases, including RSV.^{21,22} In the present study, gestational age at birth was identified as a factor significantly associated with RSV infection. This finding is consistent with previous studies, which indicate that prematurity increases the risk of both severe respiratory infection and hospitalization due to RSV, due to the immunological and pulmonary immaturity of premature infants compared to those born at term.^{23,24} Although no significant differences were observed in maternal age between cases and controls, previous studies have found that

both adolescent mothers and mothers over 35 years of age may be at increased risk of perinatal complications, such as low birth weight, preterm birth, and small for gestational age (SGA), which indirectly affect susceptibility to infections such as RSV.^{25,26} Although most of the variables addressed in this study are recognized as risk factors for RSV infection, in our study, maternal education level was not associated with RSV infection.

However, there is evidence that maternal (and parental) educational level is a predictor of disease burden and hospitalization due to RSV in infants and premature babies.²⁷⁻²⁹

Several studies have shown that influenza vaccination saves costs, increases quality-adjusted life years, improves maternal and infant outcomes, and reduces morbidity and mortality through protection against influenza-like illnesses during the first years of life,³⁰⁻³³ which is consistent with the high level of protection against RSV found in children born to mothers immunized with the influenza vaccine.

In this study, the overall effectiveness of the vaccine against hospitalization due to RSV was 74% (95% CI: 61-83), adjusted for other variables. These findings are unprecedented in the province, as there are currently no publications on the effectiveness of the vaccine in this context. The results obtained are comparable to those of previous studies. In phase III clinical trials, efficacy against severe disease was 81.8% in the first 90 days, falling to 69.4% at 180 days. A study in Buenos Aires reported an effectiveness

TABLE 2. Estimated odds ratios, confidence intervals, and p-values for risk factors for RSV disease obtained from the logistic regression model in the study population, March-October 2024, Córdoba province, N = 1249

Variables	OR	CI (95%)	p-value
Maternal RSV vaccination			
No	Reference		
Yes	0.26	0.17-0.39	<0.01
Gestational age at birth			
Week completed	0.90	0.81-0.99	0.03
Maternal influenza vaccination			
No	Reference		
Yes	0.3	0.21-0.43	<0.01
Mother's level of education			
Complete secondary education or higher	Reference		
Incomplete secondary education or less	1.02	0.72	0.89

RSV: respiratory syncytial virus; CI: confidence interval.

of 78.6% up to 3 months of age, which decreased to 71.3% up to 6 months.³⁴ These data support the robustness of our research and the effectiveness of the vaccine in the pediatric population in Argentina.

One limitation of the study was that it did not consider variables that could influence the onset of the disease, such as health insurance coverage, breastfeeding, and the parents' employment status. These variables are not available in the data sources used, which could affect the estimate of vaccine effectiveness. Furthermore, the use of asymptomatic controls instead of entirely negative controls represents another possible limitation, given that some asymptomatic controls could have been exposed to the pathogen without developing symptoms. However, previous studies in similar settings have used asymptomatic hospital controls to assess vaccine effectiveness, particularly when seeking to minimize the likelihood of coinfections or misdiagnoses, without finding significant differences with negative controls.³⁵

Another limitation was the exclusion of 44% of the positive cases due to a lack of identifying data. However, a sensitivity analysis (results not shown) was performed with the variables age and date of symptom onset, finding no significant differences between the included and excluded cases, suggesting a random loss that would not compromise the internal validity of the study.

Likewise, various strategies were implemented in both the methodological phase and the data analysis to reduce possible biases. The presence of potential confounders and/or effect modifiers was controlled through stratified analysis, calculation of crude ORs, and adjustments using statistical models.

This population-based study, being nested in a cohort of live births, minimizes selection bias and ensures better representativeness of the study population. In addition, selection bias was controlled by including as cases all children with positive RSV tests reported in the surveillance system, which reinforces the validity of the findings.

This study is relevant due to its impact on multiple sectors, including vaccine development laboratories, government agencies, vaccination centers, and public health in general. Furthermore, given the recent implementation of the vaccine in pregnant women and the limited scientific evidence published to date, it contributes to the field due to its innovative nature. Finally,

its relevance for future generations should be highlighted, given the magnitude of the impact of RSV on newborns, providing evidence for decision-making in vaccination policies at the population level.

In conclusion, our findings confirm that the vaccine implemented is effective against hospitalization due to RSV in children under 6 months of age, who are the most vulnerable population, and could be an essential tool for reducing morbidity and mortality due to RSV. ■

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