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Original article

Effect of pertussis vaccine in pregnancy and COVID-19 pandemic in the cases of wooping cough☆

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ABSTRACT

Background: Whooping cough has had an increased incidence and severity specially in infants and maternal immunization has been implemented as a prevention strategy. COVID-19 pandemic seems to decrease the incidence of other respiratory diseases.
Methods: Retrospective study from 2012 to 2021 to assess the influence of pertussis maternal immunizations and the first year of COVID-19 pandemic in the cases of whooping cough.
Results: 960 suspected cases from primary care and hospital, with 130 cases (104 children and 26 adults) being diagnosed of whooping cough. In the post-vaccination period, a reduction in the cases and severity in infants up to 6 months old was observed as well as in the pertussis diagnosis in adult women. There were no whooping cough cases during the COVID-19 period.
Conclusions: Both the pertussis vaccination in pregnancy and the first year of the COVID-19 pandemic have decreased the number of pertussis cases.

Evolución de los casos de tosferina tras la vacunación de la embarazada y la pandemia COVID-19

Palabras clave:
Tosferina
Vacunación materna
Niños
Adultos
COVID-19

RESUMEN

Introducción: La tosferina ha aumentado su incidencia y severidad especialmente en lactantes por lo que la vacunación de la embarazada se ha introducido como estrategia preventiva. La pandemia COVID-19 parece haber disminuido la incidencia de distintas enfermedades respiratorias.
Métodos: Estudio retrospectivo entre 2012–2021, analizando la influencia de la vacunación de la embarazada y del primer año de la pandemia COVID-19 en los casos de tosferina.
Resultados: Se incluyeron 960 pacientes de Atención Primaria y Hospitalaria con sospecha de tosferina, con 130 casos diagnosticados (104 niños y 26 adultos). En el periodo postvacunal se observó una disminución de casos y de severidad de la tosferina en niños menores de 6 meses y de los diagnósticos en mujeres adultas. No se detectó ningún paciente con tosferina durante el periodo COVID-19.
Conclusión: Tanto la vacunación de la embarazada como el primer año de la pandemia COVID-19 han disminuido significativamente los casos de tosferina.

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Introduction

Whooping cough is an acute respiratory infection caused by *Bordetella pertussis* that particularly affects children, although it can affect all ages[1]. It runs in epidemic cycles every three to five years and last peaked in Spain in 2014–2015, with an increase in incidence and mortality[2]. Serious disease particularly affects children under three months, and the vaccination of pregnant women as a protection strategy began in Andalusia in January 2016, with coverage in the first year of 81.6%[3–5].

The SARS-CoV-2 coronavirus epidemic began in December 2019, with the first case of COVID-19 declared in Spain in February 2020. Since then, a decrease in the incidence of some respiratory infections has been reported[6,7].

The objective of this study was to analyse the incidence and evolution of whooping cough before and after vaccination of pregnant women and during the first year of the COVID-19 pandemic.

Methods

A retrospective study was conducted from January 2012 to January 2021 in a health district with 450,000 inhabitants, which encompasses a university hospital and 19 health centres, and with a single laboratory for conducting the polymerase chain reaction (PCR) study for *Bordetella pertussis*. All patients who underwent PCR (BORTEDELLA R-GENE®, ARGENE® and SmartCycler Bordetella pertussis/parapertussis assay, Cepheid) were included as case studies, and when the PCR was positive, they were included as cases of whooping cough. The test was requested from hospital care or primary care due to clinical suspicion. In the cases of whooping cough, the women who should have been vaccinated during pregnancy and the admitted adults were contacted by telephone to corroborate the information collected from the medical records.

Four periods were analysed during the study: the pre-vaccination period (January 2012–December 2015); the post-vaccination period (January 2016–January 2020), with a window at the start of vaccination (January–June 2016) included in the latter; and a COVID-19 period (February 2020–January 2021).

Statistical analysis was performed with the software program SPSS®, version 24.0 (IBM Corp., Armonk, NY). Measure of association was conducted with odds ratio [OR] with a 95% confidence interval (95% CI) and non-parametric tests for continuous variables. In the multivariate analysis for having whooping cough, age, the vaccination period and the COVID-19 period were analysed.

Results

960 subjects with suspected whooping cough (745 children up to 15 years old and 215 adults) aged between one month and 84 years old were included. The median age of the children was 1.5 months, while the median age of the adults was 48 years. The highest number of suspected cases (n = 192) and confirmed cases (n = 31) was in 2015 (Fig. 1), before the vaccination campaign began, with a subsequent decrease. Clinical suspicion and sample collection in adults took place mainly in primary care (56.3%) and hospital outpatient clinics (23.3%), while in children it was in hospital accident and emergency departments (44.1%) and hospitalisation (35.6%).

In total, 130 cases of whooping cough were detected; 104 in children and 26 in adults. When compared with the pre-vaccination period (Table 1), an absolute reduction in the number of cases of whooping cough in the post-vaccination period of 24.3% was observed in the total sample. During the COVID-19 period, no case of whooping cough was found among the 23 subjects (18 children and five adults) for whom the test was requested.

In children, an absolute reduction of 17.5% in the number of cases was observed in the post-vaccination period, which rose to 35.1% when excluding those diagnosed in the window period. Children with whooping cough had a median age of 4.25 months (interquartile range [IQR]: 1.89–51.58; range 0–168 months), and during the post-vaccination period there was a significant increase in age and a decrease in the disease in children under three and six months' old (Fig. 1 and Table 1). However, an increase in the number of cases was observed in the 11–15 year age group, with four cases diagnosed in the pre-vaccination period and 12 in the post-vaccination period.

When reviewing the 47 children with whooping cough in the post-vaccination period, 26 had been born before the start of the vaccination campaign for pregnant women. Upon contacting the mothers of the remaining 21, it was found that three had not been vaccinated due to the mother's wishes or vaccination campaign failure. The pregnant women had been vaccinated at a mean ± SD of 29.3 ± 2.2 weeks of gestational age (range 25.4–34.3), with a mean of 9.7 ± 2.6 weeks (range 5–15.6) from vaccination to delivery. Three children were born prematurely (one five weeks after the mother was vaccinated). A one-month-old infant, whose mother was not vaccinated during the window period, developed malignant pertussis and died after one day in the Intensive Care Unit (ICU). The other children with severe whooping cough (malignant pertussis, admission to the ICU or need for ventilation) developed the infection in the pre-vaccination period. In addition, the number of children who required admission to the ward and the length of hospital stay decreased significantly in the post-vaccination period (Table 1).

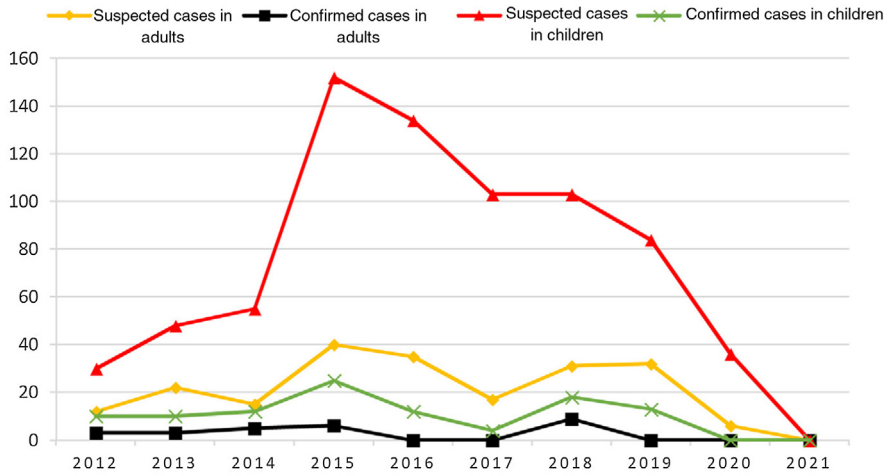
In total, 26 cases of whooping cough were diagnosed in adults (median age 45 years, IQR: 36.2–54; range 24–67), with a predominance of women (61.5%) and no cases detected between 2019 and 2021. The reduction in the post-vaccination period was 47.1% due to a decrease of 66.7% in women (from 12 to four cases), while men remained unchanged (five cases in each period). In terms of severity, in adults there were no significant complications and only two patients were admitted to the ward, with both cases occurring in the pre-vaccination period.

The vaccination period for pregnant women was a protective factor against contracting whooping cough in the multivariate analysis of the entire sample (OR = 0.46; 95% CI: 0.31–0.67; $p < 0.001$), as well as when including only children (OR = 0.44; 95% CI: 0.28–0.67; $p < 0.001$) or exclusively adults (OR = 0.38; 95% CI: 0.16–0.9; $p = 0.028$).

Discussion

This study found a reduction in the number of cases of whooping cough in children up to six months of age, as well as a reduction in its severity (hospitalisation, ICU and malignant pertussis). Other studies have also endorsed this, although some had a high risk of selection and case-control bias[8]. In our study, 18 children developed whooping cough despite maternal vaccination. One had been vaccinated at 25 weeks' gestation and three children were born prematurely. There is no absolute consensus on the best time for vaccination of pregnant women, and although it is recommended that it be administered between 27 and 36 weeks of gestation[9], protection in premature infants is possibly greater if the vaccine is received from 20 weeks[10]. In any case, the effectiveness of the vaccination of pregnant women in protecting infants from whooping cough has been estimated at 90%[11].

A significant decrease in the number of cases in adults was also observed, thanks to a reduction in the number of cases in



	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Suspected cases in adults	17	22	15	40	35	17	31	32	6	0
Confirmed cases in adults	3	3	5	6	0	0	9	0	0	0
Suspected cases in children	30	48	55	152	134	103	103	84	36	0
Confirmed cases in children	10	10	12	25	12	4	18	13	0	0

Fig. 1. Suspected and confirmed cases of whooping cough in adults and children from 2012 to 2021.

Table 1
Characteristics of whooping cough cases in children comparing the pre- (2012–2015) and post-vaccination (2016–2021) periods for pregnant women.

Characteristics	Pre-V (n = 57)	Window (n = 10)	Post-V (n = 37)	OR (95% CI)*	p*
Age in months (median; IQR)	2.87 (1.7–8.2)	3.37 (1.5–14.8)	23.3 (7.8–23.3)		<0.001
Cases <3 months; n (%)	30 (52.6%)	4 (40%)	4 (10.8%)	9.17 (2.87–29.26)	<0.001
Cases <6 months; n (%)	42 (73.7%)	8 (80%)	8 (21.6%)	10.1 (3.81–27.04)	<0.001
Severity level					
Outpatient	14 (24.6%)	0	24 (64.9%)	5.67 (2.29–14.01)	<0.001
Hospitalisation on ward	33 (57.9%)	6 (60%)	13 (35.1%)	0.39 (0.17–0.93)	0.03
ICU	10 (17.5%)	1 (10%)	0		
Non-invasive ventilation	2 (3.5%)	0	0		
Mechanical ventilation	5 (8.8%)	1 (10%)	0		
Malignant pertussis	3 (5.3%)	1 (10%)	0		
Deaths	0	1 (10%)	0		
Days of admission (median, IQR)					
Ward	11 (7–15)	7 (3–8)	6 (3.5–7)		<0.001
ICU	5 (2.75–7.25)				

* Comparison of pre-vaccination and post-vaccination period; Pre-V (pre-vaccination period); Post-V (post-vaccination period); OR: odds ratio; 95% CI: 95% confidence interval; IQR: interquartile range; ICU: Intensive Care Unit.

women. In our health district there are approximately 2,500 deliveries per year which, when estimating a vaccination coverage of 80%, equates to the vaccination of 10,000 pregnant women in five years, which could explain this decrease. According to data from the Red Nacional de Vigilancia Epidemiológica [National Epidemiological Surveillance Network], when comparing 2015 with 2018, a decrease in adult cases is also observed, it being somewhat higher in women[12,13]. To our knowledge, the impact of the vaccination of pregnant women on the adult population has not been previously evaluated in studies that include cases detected microbiologically, and not by mandatory reporting. There is a lack of consensus around the need to administer a booster dose of DTaP, which has been shown to be effective and safe, in adolescents and adults to help reduce the incidence in these groups and its transmission to young children[14].

During the COVID-19 pandemic, a decrease in respiratory symptoms has been published. In cases of viral infections, it has been speculated that this may be due to occupation of the ecological niche, while bacterial infections may be explained by a decrease in medical consultations due to fear of infection and by preventive measures such as social distancing, use of masks, hand washing and hand sanitiser[7,15].

The results of our study should be interpreted with caution, as it was a retrospective, single-centre study with few cases in adults. However, some of its strengths were that it covered both primary and hospital care, included adults, analysed all laboratory results regardless of whether or not they were reported, assessed the COVID-19 period and contacted mothers of children with whooping cough who should have been vaccinated and adults admitted with whooping cough.

In conclusion, following the vaccination of pregnant women, we saw a decrease in the number of whooping cough cases and their severity, mainly in infants up to six months' old and cases in adult women, as well as no whooping cough during the first year of the COVID-19 pandemic.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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