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DOCTORAL SCHOOL OF MEDICINE AND PHARMACY

ABSTRACT OF PhD THESIS

THE DECISION-MAKING MODEL OF CHILD VACCINATION IN ROMANIA- EARLY INTERVENTIONS IN THE PRIMARY HEALTHCARE NETWORK

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BACKGROUND: In 2018, 679 million children under the age of 5 were registered globally. 5.3 million of these children lost their lives in the same year. More than 700,000 of the children died as a result of six vaccine-preventable infectious diseases (invasive infections caused by *Streptococcus pneumoniae*, *Rotavirus*, *Bordetella pertussis*, *measles virus*, *Haemophilus influenzae type B* and *influenza virus*). One child in 1000 cases dies from severe forms of whooping cough. An extremely sensitive public health problem remains the prevention of infectious diseases in pregnant women (PW).

HYPOTHESIS: applying early educational interventions in the primary healthcare network, oriented towards PW expectations and their medical informational needs, mainly, will allow to obtain an increased adherence of the PW to personal and future child vaccination. Second, lowering the impact of vaccine hesitancy and vaccine reluctance on parental vaccine acceptance decisions could raise the vaccine coverage (VC) for the studied population.

THE PURPOSE: to identify the shaping factors and the informational channels through which the vaccination decision-making model is structured, for a population with special care needs - pregnant women (PW) and infants in the age group 0-12 months.

THE OBJECTIVES were focused on: analysis of the factors that influence vaccine acceptance in pregnant women; evaluation of humoral anti-pertussis status (IgG-PT) for a group of PW; VC analysis for a total of 5,673 children aged between 0-12 months for vaccinations provided according to the National Vaccination Program (PNV); development of a medical educational program (MEP) dedicated to parents to raise awareness of the risks represented by infectious diseases.

METHODOLOGY: During 2019-2023, the studies included a total of 708 pregnant women and 5673 0-12 months old infants. Three studies, two prospective and one retrospective observational were conducted. The collected data respects the confidentiality principles, without the possibility to identify the participants. The studies complied with Romanian legislation (Law 190/2018) and the General Data Protection Regulation (GDPR) 679/2016. Clinical studies were conducted in compliance with the Declaration of Helsinki on ethical principles applicable to medical research involving human subjects. The study benefited from the approvals of the National Commission on Bioethics of Medicines and Medical Devices of the Academy of Medical Sciences.

STUDY 1: The aim of the present study was to analyze the anti-pertussis vaccination decision-shaping factors in pregnant women (PW) during two challenging epidemiological periods: the measles epidemic and the pandemic. Two groups of PW were invited to be part of a medical education program, having as the main theme the infectious diseases risk and their prevention through vaccination. Before launching the program, participants received a 12-item questionnaire. From a total number of 362 PW enrolled in the study, 182 completed the questionnaire in 2019 and 180 in 2022. Results: The socio-demographic data revealed

that the age of PW participating in medical education programs increased in 2022 by 1.7 years ($p < 0.01$). In vitro fertilization was reported in a significantly higher proportion (20% in 2022 vs 9.8% in 2019, $p < 0.01$). Participation in community-initiated educational programs almost doubled during the pandemic time, from 18.7% in 2019 to 33.9% in 2022 ($p < 0.01$). Vaccine acceptancy (VA) dropped from 85% in 2019 to 44.4% in 2022 ($p < 0.01$), with a five-fold increase in vaccine hesitancy and a three-fold increase in vaccine refusal.

Conclusions: Our data are of concern and emphasize that in a period when the degree of severity of the epidemiological context increased, the VA during pregnancy decreased. We reported in this study a fast-growing vaccine hesitancy and a severe declared vaccine reluctance. Our results draw attention to the risks of pertussis epidemic outbreaks in PW and their future infants in the first couple of months of life before initiation of vaccination.

STUDY 2: The study analyzed the determinants of VC and of parental decisions regarding immunization in children aged 0–1 year monitored during two high-risk epidemiological periods (the measles epidemic and the COVID-19 pandemic period).

A retrospective observational cohort study-data regarding vaccination of children younger than 1 year of age during the periods January 2019–June 2019 (measles epidemic) and January 2020–June 2020 (pandemic) were analyzed. 2,850 children from 2019 and 2,823 children from 2020 were enrolled. Family physicians interacted with 2,840 parents or legal guardians in 2019 and with 2,800 parents or legal guardians in 2020, during the infants' consults. Data on immunization schedules on the determinants of parents' decisions regarding vaccination were evaluated. During 2019–2020, VC has followed a declining trend for each type of vaccine included in the Romanian National Immunization Program; the most affected were infants aged 9–12 months during both periods: in 9-month aged infants, the MMR vaccine VC was 67.49% in 2019 vs. 59.04% in 2020 ($p < 0.004$). In the 12 months aged infants, the MMR VC was 64.29% in 2019 vs. 55.88% in 2020 ($p < 0.005$). For the Hexavalent vaccine administered at the age of 11 months, the VC was 71.59% in 2019 vs. 62.08% in 2020 ($p < 0.001$). The determinants of parents' decisions regarding vaccination included parental hesitance 2019—25% vs. 2020—35%, fear on side effects 2019—32% vs. 2020—45%, vaccination denial 2019—7% vs. 2020—10%. Conclusion: We found a declining trend in the VC in Romania during the epidemic and pandemic periods. The decrease in VC for MMR generated a major risk for new measles outbreaks. Permanent awareness educational campaigns regarding infectious disease risk are needed, accompanied by the empowerment of primary care and the emergence of an immunization management program based on national regulatory legislation.

STUDY 3: The aims of the present study were (1) to develop and analyze the efficacy of a medical education programme on pertussis/whooping cough and its prevention among

a cohort of PWs from Bucharest, Romania, during 2020–2022, and (2) to determine the immunity protective antibodies levels against pertussis among the enrolled cohort of PWs.

346 pregnant women were invited to join an MEP. The participants were invited to fill in a questionnaire before starting the PEM (optional). 180 of the pregnant women chose to fill in the proposed questionnaire. In the second stage of the study, pregnant women who completed the questionnaire had the opportunity to participate in the determination of the serum antibody titer (IgG-PT) in order to evaluate their immune (humoral) anti-pertussis status. The mean IgG-PT value obtained was 8.4 IU/ml (median 5.16 IU/ml).

The second part of the study focused on evaluating the IgG-PT levels in PWs in the study group. We showed that 92.9% of the study group had unprotective anti-pertussis antibody levels; 3.06% had a protective level of antibodies suggesting recent clinical pertussis infection and 4.08% of them had low antibody titers (above 50 IU/mL, suggesting clinical pertussis infection in the last 3–5 years)

The third part of the study evaluated the MEP offered to pregnant women, the research being directed at two aspects: vaccination during pregnancy (weeks 27–36), in pregnant women who adhered to the program, and vaccination of future infants in the first year of life. *Vaccination of PW:* after participating to the MEP, 92.9% of PW in the study group agreed to be vaccinated against whooping cough. One third of the initially hesitant PW in the control group decided to be vaccinated as a result of participating in the MEP. *Infant vaccination:* VC for diphtheria-tetanus-pertussis acellular- DTPa and pneumococcal vaccines was 100% for 2 and 4 months and 86% for 11 months of age, comparative values to the reported national level for DTPa3 and pneumococcal.

Conclusion: Our study showed that PWs are facing a concerning waning immunity against the *B. pertussis* infection. We also showed that awareness gaps are present among PWs regarding the role of infectious disease prevention by vaccination. Health education in pregnancy can act as a shaping factor for the informed decision of future mothers, reducing the vaccination hesitancy phenomenon and raising vaccine confidence regarding prevention against *B. pertussis* infection. Empowering childbearing-aged women with knowledge can facilitate the decision for the immunization of their future infant against severe forms of infectious disease.

The PROTECT LIFE RO medical educational project (MEP): This project was the foundation of the doctoral research, being structured around the identified educational needs of the PW. The training model applied allowed the adaptation of specific educational methods to the particularities of the epidemiological risk situations encountered: the measles epidemic and the pandemic. (PEM has moved from the "face-to-face" model to the online one, from print materials to those of electronic type); PW had easy access to education, free access to courses, facilitation of the correct understanding of the risk of infectious disease, support in understanding the vaccination process as part of the active process of maintaining personal health and that of the future child.

ORIGINALITY: The thesys represent an integrative medico-social research, focused on the study of two vulnerable population groups: PW and infants aged group 0-12 months, analysed from the perspective of the problematic fall of the VC during the two high risk epidemiological periods- the measles epidemic and the COVID 19 pandemic.

Study hypothesis: a pregnant woman who benefit from a protective titer of anti-pertussis antibodies (humoral immunity), can provide transplacental immunity to the future child, so that he can be effectively protected in the first months of life until the time when he will could be vaccinated.

The golden equation in the prevention of infectious diseases:

Communication + National Sustainable Prevention Strategy

(Legislation+

Constant vaccine flow+

MEP focused on Prevention for health (healthcare professionals+ civil society)

= "Health Education"