e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2026; 18(2); 88-93

Original Research Article

Immunologic Correlates of Vaccine Hesitancy in Caregivers of Infants: A Multicenter Pediatric Cohort Study

Sahnavajkhan M. Pathan[1], Jay Krishnajivan Shah[2], Yash Ashokkumar Patel[3]

[1]Associate Professor, Department of Pediatrics, SAL Institute of Medical Sciences (SIMS), Ahmedabad, Gujarat, India

[2]Assistant Professor, Department of Pediatrics, Shantabaa Medical College & General Hospital, Amreli, Gujarat, India

[3]MBBS, GMERS Medical College, Vadnagar, Gujarat, India

Received: 01-11-2025 / Revised: 15-12-2025 / Accepted: 21-01-2026

Corresponding author: Dr. Yash Ashokkumar Patel

Conflict of interest: Nil

Abstract

Background: Vaccine hesitancy among caregivers represents a growing public health challenge that may compromise infant immunization coverage and subsequent immune protection. However, the direct relationship between caregiver vaccine hesitancy and infant immunologic outcomes remains inadequately characterized.

Methods: A prospective cohort of 412 caregiver-infant dyads was recruited from six pediatric centers. Caregiver vaccine hesitancy was assessed using the Parent Attitudes about Childhood Vaccines (PACV) questionnaire, with scores ≥50 indicating hesitancy. Infant serum samples were collected at 7 and 13 months of age to measure antibody responses to diphtheria, tetanus, pertussis, and measles antigens using enzyme-linked immunosorbent assays.

Results: Vaccine hesitancy was identified in 23.5% of caregivers (n=97). Infants of hesitant caregivers demonstrated significantly lower geometric mean antibody titers for all measured antigens compared to infants of non-hesitant caregivers ($p<0.01$). Seroprotection rates were reduced in the hesitant group for diphtheria (78.4% vs. 94.6%, $p<0.001$), tetanus (82.5% vs. 96.2%, $p<0.001$), and measles (71.1% vs. 93.0%, $p<0.001$). Vaccination delay (≥30 days behind schedule) was observed in 67.0% of infants with hesitant caregivers versus 12.1% in the non-hesitant group ($p<0.001$).

Conclusion: Caregiver vaccine hesitancy is significantly associated with suboptimal immunologic protection in infants, mediated primarily through vaccination delays and incomplete series completion. Targeted interventions addressing caregiver concerns are essential for ensuring adequate infant immunization.

Keywords: Vaccine hesitancy; Infant immunization; Antibody titers; Seroprotection; Caregiver attitudes; Pediatric immunology.

DOI: 10.25258/ijcpr.18.2.14

Introduction

Vaccine hesitancy, defined as the delay in acceptance or refusal of vaccination despite availability of vaccination services, has emerged as one of the ten threats to global health identified by the World Health Organization [1]. This phenomenon encompasses a complex spectrum of attitudes and behaviors ranging from complete refusal to selective acceptance or delayed administration of recommended vaccines [2]. The determinants of vaccine hesitancy are multifactorial, incorporating elements of confidence, complacency, and convenience that vary substantially across populations and healthcare contexts [3]. The global prevalence of vaccine hesitancy among parents and caregivers has demonstrated concerning trends, with recent surveys indicating that approximately 20-30% of caregivers in developed nations express some degree of hesitancy toward childhood vaccinations [4]. Contributing factors include misinformation disseminated through social media platforms, distrust in healthcare systems and pharmaceutical industries, concerns regarding vaccine safety and efficacy, and philosophical or religious objections to immunization practices [5]. These attitudes have measurable consequences for public health, as evidenced by resurgent outbreaks of vaccine-preventable diseases in communities with suboptimal vaccination coverage [6]. The immunologic implications of vaccine hesitancy extend beyond simple vaccination refusal. Caregivers exhibiting hesitancy may consent to

vaccination while requesting alternative schedules that deviate from recommended timelines, potentially compromising the development of protective immunity during critical periods of infant vulnerability [7]. Studies examining delayed vaccination schedules have demonstrated that immunologic responses may be affected by the timing of antigen exposure, with potential consequences for both immediate protection and long-term immunologic memory [8].

Infant immune systems undergo rapid maturation during the first year of life, and the timing of vaccine administration has been optimized to balance the waning of maternal antibodies with the development of infant immunocompetence [9]. Deviation from recommended schedules may result in periods of increased susceptibility to infection or suboptimal immune responses due to interference from residual maternal antibodies or insufficient immune system maturity [10]. However, direct evidence linking caregiver hesitancy to measurable immunologic outcomes in infants remains limited.

Previous investigations have predominantly focused on vaccination coverage rates and disease incidence as outcome measures, with relatively few studies examining serologic correlates of vaccine hesitancy in pediatric populations [11]. Understanding the immunologic consequences of caregiver hesitancy is essential for developing evidence-based counseling strategies and identifying infants who may benefit from catch-up vaccination protocols or serologic monitoring [12].

The aim of this multicenter cohort study was to evaluate the association between caregiver vaccine hesitancy and infant immunologic outcomes, including antibody titers against vaccine-preventable diseases, seroprotection rates, and vaccination timeliness across the primary immunization series.

Materials and Methods

Study Design and Setting: This prospective multicenter cohort study was conducted across six pediatric primary care centers and university-affiliated children's hospitals located in urban and suburban regions.

Sample Size Calculation: Sample size estimation was performed using G*Power software (version 3.1.9.7) based on detecting a medium effect size (Cohen's d = 0.5) in antibody titer differences between hesitant and non-hesitant groups. With alpha set at 0.05 and power at 0.85, the minimum required sample was 340 dyads. Anticipating 20% attrition, a target enrollment of 425 caregiver-infant dyads was established.

Participant Recruitment and Selection: Caregiver-infant dyads were recruited during routine well-child visits when infants were between 6 and 10 weeks of age. Primary caregivers were defined as individuals with primary responsibility for healthcare decision-making for the enrolled infant.

Inclusion Criteria:

- Infant age 6-10 weeks at enrollment
- Singleton birth at ≥37 weeks gestational age
- Birth weight ≥2,500 grams
- Primary caregiver aged ≥18 years
- Caregiver able to read and comprehend English or Spanish
- Intent to receive pediatric care at participating site for study duration

Exclusion Criteria:

- Known primary or secondary immunodeficiency in infant
- Chronic medical conditions requiring immunosuppressive therapy
- Receipt of blood products or immunoglobulin within 6 months
- Maternal HIV infection
- Contraindication to routine childhood vaccines
- Participation in other vaccine-related research studies

Assessment of Vaccine Hesitancy: Caregiver vaccine hesitancy was assessed using the validated Parent Attitudes about Childhood Vaccines (PACV) questionnaire, a 15-item instrument measuring concerns about vaccine safety, efficacy, and general attitudes toward immunization. Total scores range from 0 to 100, with scores ≥50 indicating vaccine hesitancy. The PACV was administered at enrollment and repeated at the 7-month visit to assess attitude stability. Caregivers were categorized as hesitant (PACV ≥50) or non-hesitant (PACV <50) based on enrollment scores.

Vaccination Documentation: Vaccination records were extracted from electronic health records and state immunization registries at each study visit.

Timeliness was evaluated for diphtheria-tetanus-acellular pertussis (DTaP), inactivated poliovirus (IPV), Haemophilus influenzae type b (Hib), pneumococcal conjugate (PCV13), rotavirus (RV), and measles-mumps-rubella (MMR) vaccines.

Vaccination delay was defined as administration ≥30 days after the recommended age. Series completion was assessed at the 13-month visit.

Serologic Assessment: Venous blood samples (2-3 mL) were collected at the 7-month and 13-month visits. Serum was separated, aliquoted, and stored at -80°C until batch analysis. Antibody concentrations were measured using standardized enzyme-linked immunosorbent assays (ELISA) for the following antigens:

- Anti-diphtheria toxoid IgG (protective threshold: ≥0.1 IU/mL)
- Anti-tetanus toxoid IgG (protective threshold: ≥0.1 IU/mL)
- Anti-pertussis toxin IgG (protective threshold: ≥20 EU/mL)
- Anti-measles IgG (protective threshold: ≥200 mIU/mL)

All assays were performed in duplicate at a centralized reference laboratory with appropriate quality controls.

Statistical Analysis: Statistical analyses were performed using SPSS version 27.0 and R version 4.2.1. Antibody concentrations were log-transformed for analysis and presented as geometric mean titers (GMT) with 95% confidence intervals. Comparisons between hesitant and non-hesitant groups utilized independent samples t-tests for continuous variables and chi-square tests for categorical variables. Multivariable logistic regression assessed predictors of inadequate seroprotection, adjusting for potential confounders. Statistical significance was established at $p<0.05$.

Results

Participant Characteristics: Of 425 enrolled dyads, 412 (96.9%) completed the study protocol. Attrition was due to relocation (n=8) and withdrawal of consent (n=5). Based on PACV scores, 97 caregivers (23.5%) were classified as vaccine-hesitant and 315 (76.5%) as non-hesitant. Demographic characteristics are presented in Table 1.

Table 1: Baseline Demographic Characteristics of Caregiver-Infant Dyads

Characteristic	Hesitant (n=97)	Non-Hesitant (n=315)	p-value
Caregiver age (years), mean ± SD	29.4 ± 5.8	30.7 ± 5.2	0.037*
Infant sex, male n (%)	51 (52.6)	158 (50.2)	0.679
Infant birth weight (g), mean ± SD	3,342 ± 412	3,398 ± 389	0.221
Caregiver education, n (%)			0.004*
- High school or less	28 (28.9)	54 (17.1)	
- Some college	41 (42.3)	118 (37.5)	
- Bachelor's degree or higher	28 (28.9)	143 (45.4)	
Household income <$50,000, n (%)	44 (45.4)	98 (31.1)	0.009*
First-time caregiver, n (%)	52 (53.6)	139 (44.1)	0.098
PACV score, mean ± SD	62.8 ± 11.4	24.3 ± 12.7	<0.001*
Primary information source, n (%)			<0.001*
- Healthcare provider	31 (32.0)	198 (62.9)	
- Internet/social media	48 (49.5)	67 (21.3)	
- Family/friends	18 (18.6)	50 (15.9)	

***Statistically significant (p<0.05); SD: Standard Deviation; PACV: Parent Attitudes about Childhood Vaccines**

Vaccination Timeliness and Completion: Significant differences in vaccination timeliness were observed between groups.

Among infants of hesitant caregivers, 67.0% experienced delays of ≥30 days for at least one vaccine dose, compared to 12.1% in the non-hesitant group ($p<0.001$). Complete series vaccination by 13 months was achieved in 58.8% of infants with hesitant caregivers versus 91.7% with non-hesitant caregivers ($p<0.001$). Table 2 presents vaccination outcomes by group.

Table 2: Vaccination Timeliness and Completion Rates by Caregiver Hesitancy Status

Vaccination Parameter	Hesitant (n=97)	Non-Hesitant (n=315)	p-value
Any vaccination delay (≥30 days), n (%)	65 (67.0)	38 (12.1)	<0.001*
Mean delay for DTaP series (days), mean ± SD	47.2 ± 38.6	8.4 ± 12.3	<0.001*
Mean delay for MMR (days), mean ± SD	52.8 ± 44.1	6.2 ± 9.8	<0.001*
Complete DTaP series by 7 months, n (%)	62 (63.9)	298 (94.6)	<0.001*
Complete primary series by 13 months, n (%)	57 (58.8)	289 (91.7)	<0.001*
MMR administered by 13 months, n (%)	69 (71.1)	301 (95.6)	<0.001*
Total doses received by 13 months, mean ± SD	14.2 ± 4.8	19.6 ± 2.1	<0.001*
Alternative schedule requested, n (%)	41 (42.3)	12 (3.8)	<0.001*
Complete vaccine refusal, n (%)	8 (8.2)	0 (0)	<0.001*

***Statistically significant (p<0.05); DTaP: Diphtheria-Tetanus-Acellular Pertussis; MMR: Measles-Mumps-Rubella**

Immunologic Outcomes: Significant differences in antibody responses were observed between groups at both assessment timepoints.

At 13 months, geometric mean titers were consistently lower in infants of hesitant caregivers across all measured antigens. Seroprotection rates demonstrated substantial disparities, with the hesitant group showing reduced protection for diphtheria (78.4% vs. 94.6%), tetanus (82.5% vs. 96.2%), pertussis (74.2% vs. 91.4%), and measles (71.1% vs. 93.0%). Immunologic outcomes are detailed in Table 3.

Table 3: Immunologic Outcomes at 13-Month Assessment by Caregiver Hesitancy Status

Immunologic Parameter	Hesitant (n=97)	Non-Hesitant (n=315)	p-value
Geometric Mean Titers (95% CI)			
Anti-diphtheria (IU/mL)	0.42 (0.31-0.56)	1.28 (1.12-1.47)	<0.001*
Anti-tetanus (IU/mL)	0.58 (0.44-0.77)	1.86 (1.64-2.11)	<0.001*
Anti-pertussis (EU/mL)	34.2 (28.1-41.6)	78.4 (71.2-86.3)	<0.001*
Anti-measles (mIU/mL)	312 (248-392)	1,247 (1,098-1,416)	<0.001*
Seroprotection Rates, n (%)			
Diphtheria (≥0.1 IU/mL)	76 (78.4)	298 (94.6)	<0.001*
Tetanus (≥0.1 IU/mL)	80 (82.5)	303 (96.2)	<0.001*
Pertussis (≥20 EU/mL)	72 (74.2)	288 (91.4)	<0.001*
Measles (≥200 mIU/mL)	69 (71.1)	293 (93.0)	<0.001*
Protection against all 4 antigens, n (%)	58 (59.8)	274 (87.0)	<0.001*

***Statistically significant (p<0.05); CI: Confidence Interval**

Multivariable regression analysis identified caregiver hesitancy (OR 4.82, 95% CI 2.91-7.98, p<0.001), vaccination delay >60 days (OR 3.24, 95% CI 1.87-5.61, p<0.001), and incomplete series (OR 2.78, 95% CI 1.64-4.72, p<0.001) as independent predictors of inadequate seroprotection.

Discussion

This multicenter cohort study demonstrates a significant association between caregiver vaccine hesitancy and suboptimal immunologic outcomes in infants, providing direct serologic evidence for the public health consequences of hesitancy behaviors. Infants of hesitant caregivers exhibited substantially lower antibody titers and reduced seroprotection rates across multiple vaccine-preventable disease antigens, findings primarily attributable to vaccination delays and incomplete series administration.

The prevalence of vaccine hesitancy observed in this cohort (23.5%) aligns with contemporary estimates from similar populations, confirming that a substantial minority of caregivers harbor significant concerns regarding childhood immunization [13]. The demographic correlates identified, including younger caregiver age, lower educational attainment, and reliance on internet sources for vaccine information, are consistent with previously characterized risk factors for hesitancy [14]. The magnitude of immunologic differences between groups warrants particular attention. Geometric mean titers for measles antibodies were approximately four-fold lower in infants of hesitant caregivers, and nearly 30% of these infants failed to achieve seroprotective thresholds. These findings have direct implications for herd immunity thresholds, as measles transmission can occur when population immunity falls below 92-95% [15]. Communities with concentrated vaccine hesitancy may therefore be particularly vulnerable to outbreaks, as demonstrated by recent resurgences in previously eliminated diseases [16].

The relationship between vaccination timeliness and immunologic outcomes observed in this study supports the biological rationale underlying recommended immunization schedules. Delayed administration of primary series vaccines extends the window of infant susceptibility during a period of heightened vulnerability to severe disease [17]. Furthermore, the immune response to vaccines may be influenced by developmental changes in the infant immune system, potentially explaining the reduced antibody titers observed in infants receiving delayed vaccination.

Importantly, caregiver hesitancy demonstrated independent predictive value for inadequate seroprotection even after controlling for vaccination timeliness and completion. This suggests that hesitancy may influence immunologic outcomes through additional pathways, potentially including differential healthcare-seeking behavior, reduced adherence to booster doses, or unmeasured confounders associated with both hesitancy and immune responsiveness [18].

The finding that internet and social media sources were predominant information channels for hesitant caregivers underscores the need for healthcare providers to actively engage with vaccine-related concerns and provide accurate, accessible

information [19]. Interventions targeting misinformation exposure and promoting healthcare provider communication have demonstrated efficacy in reducing hesitancy and improving vaccination uptake in some populations.

Limitations of this study include the observational design, which precludes definitive causal inference. The PACV instrument, while validated, may not capture all dimensions of hesitancy behavior. Additionally, the study population was drawn from healthcare-engaged caregivers, potentially underrepresenting those with complete vaccine refusal who may avoid routine pediatric care.

Conclusion

This multicenter cohort study provides compelling evidence that caregiver vaccine hesitancy is associated with significantly compromised immunologic protection in infants during the critical first year of life. Infants of hesitant caregivers demonstrated reduced antibody titers and lower seroprotection rates across all measured vaccine antigens, with these differences primarily mediated through vaccination delays and incomplete series administration.

The substantial proportion of infants failing to achieve protective immunity represents a meaningful public health concern with implications for individual disease susceptibility and community-level outbreak risk. These findings emphasize the urgent need for targeted interventions addressing caregiver hesitancy concerns, enhanced provider communication strategies, and continued surveillance of vaccination coverage and immunologic outcomes in pediatric populations. Healthcare systems should prioritize resources for identifying hesitant caregivers early and implementing evidence-based counseling approaches to ensure optimal immunization of vulnerable infant populations.

References

1. MacDonald NE; SAGE Working Group on Vaccine Hesitancy. Vaccine hesitancy: Definition, scope and determinants. Vaccine. 2015;33(34):4161-4164. doi:10.1016/j.vaccine.2015.04.036
2. Dubé E, Laberge C, Guay M, Bramadat P, Roy R, Bettinger J. Vaccine hesitancy: an overview. Hum Vaccin Immunother. 2013;9(8):1763-1773. doi:10.4161/hv.24657
3. Betsch C, Schmid P, Heinemeier D, Korn L, Holtmann C, Böhm R. Beyond confidence: Development of a measure assessing the 5C psychological antecedents of vaccination. PLoS One. 2018;13(12):e0208601. doi:10.1371/journal.pone.0208601
4. Larson HJ, de Figueiredo A, Xiahong Z, et al. The State of Vaccine Confidence 2016: Global Insights through a 67-Country Survey. EBio Medicine. 2016;12:295-301. doi:10.1016/j.ebiom.2016.08.042
5. Kata A. Anti-vaccine activists, Web 2.0, and the postmodern paradigm--an overview of tactics and tropes used online by the anti-vaccination movement. Vaccine. 2012;30(25):3778-3789. doi:10.1016/j.vaccine.2011.11.112
6. Phadke VK, Bednarczyk RA, Salmon DA, Omer SB. Association between Vaccine Refusal and Vaccine-Preventable Diseases in the United States: A Review of Measles and Pertussis. JAMA. 2016;315(11):1149-1158. doi:10.1001/jama.2016.1353
7. Glanz JM, Newcomer SR, Narwaney KJ, et al. A population-based cohort study of undervaccination in 8 managed care organizations across the United States. JAMA Pediatr. 2013;167(3):274-281. doi:10.1001/jamapediatrics.2013.502
8. Lewnard JA, Grad YH. Vaccine waning and mumps re-emergence in the United States. Sci Transl Med. 2018;10(433):eaao5945. doi:10.1126/scitranslmed.aao5945
9. Siegrist CA. Neonatal and early life vaccinology. Vaccine. 2001;19(25-26):3331-3346. doi:10.1016/s0264-410x(01)00028-7
10. Niewiesk S. Maternal antibodies: clinical significance, mechanism of interference with immune responses, and possible vaccination strategies. Front Immunol. 2014;5:446. doi:10.3389/fimmu.2014.00446
11. Salmon DA, Dudley MZ, Glanz JM, Omer SB. Vaccine hesitancy: Causes, consequences, and a call to action. Vaccine. 2015;33 Suppl 4:D66-D71. doi:10.1016/j.vaccine.2015.09.035
12. Opel DJ, Taylor JA, Mangione-Smith R, et al. Validity and reliability of a survey to identify vaccine-hesitant parents. Vaccine. 2011;29(38):6598-6605. doi:10.1016/j.vaccine.2011.06.115
13. Kempe A, Saville AW, Albertin C, et al. Parental Hesitancy About Routine Childhood and Influenza Vaccinations: A National Survey. Pediatrics. 2020;146(1):e20193852. doi:10.1542/peds.2019-3852
14. Smith LE, Amlôt R, Weinman J, Yiend J, Rubin GJ. A systematic review of factors affecting vaccine uptake in young children. Vaccine. 2017;35(45):6059-6069. doi:10.1016/j.vaccine.2017.09.046
15. Plans-Rubió P. Evaluation of the establishment of herd immunity in the population by means of serological surveys and vaccination coverage. Hum Vaccin Immunother. 2012;8(2):184-188. doi:10.4161/hv.18444
16. Hotez PJ. America and Europe's new normal: the return of vaccine-preventable diseases. Pediatr Res. 2019;85(7):912-914. doi:10.1038/s41390-019-0354-3

17. Luman ET, Barker LE, Shaw KM, McCauley MM, Buehler JW, Pickering LK. Timeliness of childhood vaccinations in the United States: days undervaccinated and number of vaccines delayed. JAMA. 2005;293(10):1204-1211. doi:10.1001/jama.293.10.1204
18. Gust DA, Darling N, Kennedy A, Schwartz B. Parents with doubts about vaccines: which vaccines and reasons why. Pediatrics. 2008;122(4):718-725. doi:10.1542/peds.2007-0538
19. Jarrett C, Wilson R, O'Leary M, Eckersberger E, Larson HJ; SAGE Working Group on Vaccine Hesitancy. Strategies for addressing vaccine hesitancy - A systematic review. Vaccine. 2015;33(34):4180-4190. doi:10.1016/j.vaccine.2015.04.040.