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Comparative analysis of immunogenicity between first-dose measles-mumps-rubella (MMR) vaccine administration and combined MMR-rotavirus vaccination

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ABSTRACT

This study compared the immunogenicity of the measles-mumps-rubella (MMR) vaccine when administered alone versus when co-administered with the rotavirus vaccine in infants aged 8–9 months. In this prospective cohort study, 1,198 infants were enrolled: 800 received combined MMR and rotavirus vaccines (experimental group), while 398 received the MMR vaccine alone (control group). A Hurdle Gamma model analyzed vaccination impact on antibody levels in both groups and the correlation between antibody responses. Geometric mean concentrations of measles, rubella, and mumps IgG antibodies increased significantly in both groups after vaccination. The experimental group demonstrated 209-fold, 25-fold, and 12-fold increases, respectively, with comparable increases in the control group. Hurdle Gamma model analysis revealed significant positive effects of vaccination on all three antibody levels, with no significant differences between MMR-rotavirus combined vaccination and MMR vaccination alone. Random effects analysis showed strong negative correlations for measles and rubella IgG antibodies (correlation coefficients: −1.00 and −0.99, respectively) and a moderate negative correlation for mumps IgG antibodies (correlation coefficient: −0.56). This study represents the first application of a Hurdle Gamma model to compare immunogenicity between standalone MMR vaccination and combined MMR-rotavirus vaccination. The results demonstrate equivalent MMR antibody responses between these two vaccination approaches.

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MMR vaccine; rotavirus vaccine; immunogenicity; separate vaccination vs. combined vaccination

Introduction

The measles-mumps-rubella (MMR) vaccine plays a crucial role in preventing three severe infectious diseases: measles, mumps, and rubella. Its global implementation has dramatically reduced disease incidence and mortality.[1] In China, healthcare providers annually administer one dose of Chinese-manufactured monovalent oral rotavirus vaccine to children aged 2 months to 3 years.[2] This schedule frequently overlaps with the 8-month MMR vaccination schedule, creating numerous opportunities for concurrent administration.[3] As vaccination programs evolve, public health priorities must focus on optimizing vaccination strategies to enhance both individual immune responses and population-level immunity.

The rotavirus vaccine effectively prevents rotavirus diarrhea and has increasingly prompted investigation into the feasibility and immune outcomes of co-administration with MMR vaccine.[4] Combining these vaccines in a single administration may offer more comprehensive protection for children and simplify the vaccination process, reducing the burden on families and the healthcare system. However, interactions between co-administered vaccines may affect the immunogenicity of individual vaccine components,[5] which can subsequently influence overall protective efficacy.[6]

Our study compares the immunogenicity between standalone MMR vaccination and concurrent MMR-rotavirus vaccination for first-dose administration. By analyzing immune responses under these two vaccination regimens, we aim to provide evidence for optimizing childhood vaccination schedules and developing more evidence-based immunization strategies.

Materials and methods

Study participants

We conducted this study across five regions in Gansu Province: Liangzhou District, Anding District, Qin'an County, Longxi County, and Lintao County. We selected healthy children aged 8–9 months based on two data sources: the three-year disease incidence data from the "China Disease Prevention and Control System" for measles, rubella, and mumps, and the rotavirus diarrhea records from county-level general hospitals' outpatient and inpatient departments. All participating children had no previous rotavirus, MMR, or measles vaccinations, and no history of confirmed rotavirus diarrhea, measles, rubella, or mumps infections. We obtained written informed consent from all participants' legal guardians in accordance with ethical principles.

Study groups

We employed a randomized approach to assign participants to study groups. We first numbered eligible participants

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according to their arrival time and then assigned random numbers to divide them into two groups. The experimental group (Rotavirus + mmR group) received concurrent administration of MMR and rotavirus vaccines, while the control group (MMR group) received the MMR vaccine alone.

Inclusion and exclusion criteria

Inclusion Criteria: (1) Children aged 8–9 months whose guardians provided informed consent; (2) Children who demonstrated good health on physical examination and met vaccination criteria; (3) Participants able to comply with study protocol requirements; (4) Children without prior administration of relevant vaccines or prophylactic products in the past month; (5) Children with axillary temperature ≤ 37°C. Exclusion Criteria: (1) Children who had any known allergies to vaccine components were excluded from the study. (2) Children who presented with active acute illness, severe chronic disease, or acute exacerbation of chronic conditions were not eligible. (3) Children who had any bleeding disorders or prolonged bleeding time could not participate. (4) Children who had a history of exanthematous disease infection within the past month were excluded. (5) Children who had received other vaccines, immunoglobulin injections, or investigational drugs within the past 4 weeks were not included. (6) Children who had immunodeficiency or were undergoing immunosuppressive therapy were excluded. (7) Children who had encephalopathy, uncontrolled epilepsy, or other progressive neurological disorders were not eligible. (8) Children who had any acute illness or infection requiring systemic antibiotic/antiviral treatment within the past 7 days were excluded. (9) Children who had experienced fever (axillary temperature ≥ 38°C) within the past 3 days could not participate. (10) Children who were participating in other clinical studies were excluded. (11) Children who had ongoing rotavirus infection or persistent watery diarrhea lasting more than 3 days were not eligible.

Sample size estimation

This study utilized a 2:1 non-inferiority design. The formula for sample size estimation is shown below:

$$n_1 = \frac{(1+k)\left(Z_{1-\alpha} + Z_{1-\beta}\right)^2 \pi(1-\pi)}{k\delta^2}$$

$$n_2 = kn_1$$

Where: n_1 represents the sample size of the control group; n_2 represents the sample size of the experimental group; k is the allocation ratio ($k = 2$, indicating twice as many subjects in the experimental group); $Z_{1-\alpha}$is the standard normal deviate at one-sided significance level $\alpha = 0.05$ ($Z_{1-\alpha} = 1.645$); $Z_{1-\beta}$ is the standard normal deviate at power 1-β, where $\beta = 0.20$ ($Z_{1-\beta} = 0.842$);δrepresents the non-inferiority margin for the difference in seroconversion rates; π is the weighted average seroconversion rate, calculated as $\pi=(2\pi_1+\pi_2)/3$,[7] where π_1 and π_2 are the expected seroconversion rates in the experimental and control groups, respectively. Based on previous literature, the seroconversion rates of serum IgG antibodies following MMR vaccination are: 99.10% for measles, 93.20% for rubella, and 89.83% for mumps.[8] Assuming that the seroconversion rate of the combined vaccination group is no lower than 90% of the single vaccination group, the control group requires approximately 396 participants, and the experimental group requires approximately 794 participants.

Study vaccines

The vaccines used in this study were Chinese produced and approved products that passed inspection by the China National Institutes for Food and Drug Control, possessing "Biological Product Batch Release Certificates." The CCID50 (Cell Culture Infectious Dose 50%) represents a 50% cell culture infection dose. The MMR vaccine was manufactured by Beijing Tiantan Biological Products Co., Ltd., formulated as a lyophilized powder, with a specification of 0.5 mL/vial. The active ingredients are: measles live virus ≥ 1000 CCID50, mumps live virus ≥ 5000 CCID50, rubella live virus ≥ 1000 CCID50, with a batch number of * 12190. The oral rotavirus vaccine was manufactured by Lanzhou Biological Products Institute Co., Ltd., formulated as an oral liquid, with a specification of 3.0 mL/vial. The dosage was 3 mL per administration, and the active ingredient was live virus content ≥ 5.5 lg CCID50/mL, with a batch number of * 04042.

Sample collection and testing methods

Blood Sample Collection: We collected blood samples from all participants through venipuncture at two time points: before vaccination and 5 weeks post-vaccination. We followed strict standard operating procedures for blood collection: controlling needle insertion depth to within 2 mm (not exceeding 2.5 mm) and ensuring the collection site showed no inflammation or edema. Using sterile techniques, we drew 3 mL of venous blood into 5 mL collection tubes.

Serum separation and storage

We processed blood samples using the following protocol: First, we allowed samples to sit at room temperature for 2–3- hours (extending this time when serum volume was insufficient, or placing samples in a 37°C water bath for 30 minutes if needed). We then centrifuged samples at 3500–4000 r/min for 3–5 minutes, repeating centrifugation when necessary to achieve adequate serum separation. We aliquoted the separated serum into two storage tubes (labeled A and B), ensuring tube numbers matched participant numbers and the randomization list. Finally, we stored all serum samples at −20°C.

Antibody Testing Method: We used enzyme-linked immunosorbent assays (ELISA) to detect specific serum antibodies: Measles IgG, Mumps IgG, and Rubella IgG antibodies. We performed all tests using quantitative assay kits from Virion-Serion Biotechnology Co., Ltd. (Germany), which included: Measles Virus IgG Antibody Test Kit (batch number: SAE.CA), Mumps Virus IgG Antibody Test Kit (batch number: SGD.DI) Rubella Virus IgG Antibody Test Kit (batch number: SHD.BN),We used all test kits within their expiration dates and strictly followed the kit instructions. We expressed all results in AU/mL.

Statistical analysis

We processed and analyzed data using R 4.4.2. We calculated the geometric mean concentration (GMC) of antibodies using the formula: GMC = exp(mean(ln(x))), where x represents antibody concentration values greater than zero.[9] We employed a Bayesian mixed-effects model for statistical inference. Due to the presence of zero values or below-detection-limit data for IgG antibody activity, we applied a hurdle gamma distribution.[10] We included a random slope term in the model to account for individual differences in vaccination response. The model construction is as follows:

For non-zero observations:

$$y_i \sim \text{Gamma}(\mu_i, \alpha)$$

$$\log(\mu_i) = \beta_0 + \beta_1 trt_i + \beta_2 time_i + \beta_3 age_i + \beta_4 gender_i + (b_{0i} + b_{1i} time_i)$$

For zero observations:

$$P(y_i = 0) = \text{logit}^{-1}(\gamma_0 + \gamma_1 trt_i + \gamma_2 time_i + \gamma_3 age_i + \gamma_4 gender_i)$$

Random effects

$$\begin{pmatrix} b_{0i} \\ b_{1i} \end{pmatrix} \sim N\left(\begin{pmatrix} 0 \\ 0 \end{pmatrix}, \begin{pmatrix} \sigma_0^2 & \rho\sigma_0\sigma_1 \\ \rho\sigma_0\sigma_1 & \sigma_1^2 \end{pmatrix} \right)$$

Where: y_i represents the IgG antibody activity of the i-th participant, μ_i is the mean parameter of the Gamma distribution, α is the shape parameter of the Gamma distribution, trt_i is the treatment variable, $time_i$ is the time variable (representing pre-vaccination/post-vaccination), age_i is the age, $gender_i$ is the gender, b_{0i} is the random intercept (representing individual baseline differences), b_{1i} is the random slope (representing individual heterogeneous response to time), $\beta_0, \beta_1, \beta_2, \beta_3, \beta_4$ are the fixed-effect coefficients for the Gamma part, $\gamma_0, \gamma_1, \gamma_2, \gamma_3, \gamma_4$ are the fixed-effect coefficients for the zero inflation part, σ_0^2 and σ_1^2 are the variances of the random intercept and the random slope, respectively, and ρ is the correlation coefficient between the random effects.

Link function: μ: uses the log link $\log(\mu_i)$, the shape parameter α: uses an identity link, and a logit link for zero-inflation probability. Bayesian statistical modeling was performed using the brms package (version [2.22.0]) in R 4.4.2.[11]

Posterior inference was based on the Markov Chain Monte Carlo (MCMC) method, generating posterior samples. To improve computational efficiency and diagnose model convergence, each model was run with four independent MCMC chains, each chain iterated 2000 times, and the first 1000 iterations were discarded as a burn-in period. The default priors of the brms package were used, and the 95% highest density interval (HDI) was calculated from the posterior samples to serve as the credible interval (CI) of parameter estimates. The practical significance of the effect was evaluated using the region of practical equivalence (ROPE) and HDI. If the 95% HDI of a parameter fell entirely outside the ROPE, the effect was considered statistically significant and practically meaningful. If the 95% HDI of a parameter fell completely within the ROPE, the effect was considered practically negligible. If the 95% HDI partially overlapped with the ROPE, the results were considered uncertain and required assessment in combination with other evidence.[12] When the Region of Practical Equivalence (ROPE) interval in Bayesian analysis could not be automatically determined using the bayestestR package, we adopted a standardized effect size of [0, 0.2] as the ROPE threshold, referencing Cohen's recommendations for effect sizes and Kruschke's research.[13,14] The ROPE intervals for measles, rubella, and mumps antibodies were calculated based on the median of their respective pre-immunization antibody titers: [0, 0.2] × Median, resulting in [0, 1.00], [0, 0.18], and [0, 2.38], respectively. Model diagnostics included: checking MCMC trace plots to evaluate chain mixing and convergence; calculating the Rhat statistic, with an Rhat value close to 1 (typically considered less than 1.1) indicating good convergence between chains[15]; and calculating the effective sample size (ESS) to assess the precision of posterior estimates. The smallest ESS value was reported, and all parameters had an ESS value that was sufficiently large (typically considered greater than 200).[16]

Quality control

We ensured all researchers completed required training and obtained necessary qualifications. Before initiating the study, we developed standard operating procedures covering informed consent, blood collection, and vaccine administration. Our dedicated monitors supervised study implementation to ensure protocol compliance. We clarified questionable data through written documentation and conducted on-site verification when necessary.

Results

Baseline characteristics of study participants

We included 800 participants in the experimental group and 398 in the control group. The experimental and control groups showed no significant differences in age and gender distribution (Table 1). Table 2 shows the GMC levels and their 95% CI of measles, rubella, and mumps antibodies before and after vaccination in both experimental and control groups. For the

Table 1. Baseline characteristics of children in the experimental and control groups (Bayesian analysis).

Group	Experimental Group ($n = 800$) %	Control Group ($n = 396$) %	95% CI	ROPE	%in ROPE
Age			−0.01 ~ .07	−0.10 ~ 0.10	100%
8 Months	357 (44.63%)	159 (40.15%)			
9 Months	443 (55.37%)	237 (59.85%)			
Gender			−0.03 ~ .12	−0.18 ~ 0.18	100%
Male	402 (20.25%)	186 (46.96%)			
Female	398 (49.75%)	210 (53.03%)			

Table 2. GMC levels and 95% CI of measles, rubella and mumps antibodies Pre- and Post-vaccination vaccination in different age groups between experimental and control groups.

			Experimental Group GMC (95% CI)		Control Group GMC (95% CI)	
IgG Antibody	Time Point	Age	Male	Female	Male	Female
Measles	Pre-Vaccination	8 Months	0.04 (0.03 ~ 0.04)	0.03 (0.02 ~ 0.04)	0.04 (0.03 ~ 0.05)	0.03 (0.03 ~ 0.04)
	Pre-Vaccination	9 Months	0.04 (0.03 ~ 0.04)	0.04 (0.03 ~ 0.05)	0.04 (0.03 ~ 0.06)	0.04 (0.03 ~ 0.05)
	Post-Vaccination	8 Months	1.44 (1.37 ~ 1.51)	1.43 (1.35 ~ 1.49)	1.41 (1.33 ~ 1.49)	1.32 (1.22 ~ 1.43)
	Post-Vaccination	9 Months	1.43 (1.32 ~ 1.55)	1.40 (1.26 ~ 1.55)	1.37 (1.19 ~ 1.58)	1.43 (1.25 ~ 1.63)
Rubella	Pre-Vaccination	8 Months	0.06 (0.05 ~ 0.08)	0.06 (0.05 ~ 0.07)	0.07 (0.06 ~ 0.09)	0.07 (0.05 ~ 0.09)
	Pre-Vaccination	9 Months	0.06 (0.05 ~ 0.07)	0.07 (0.06 ~ 0.09)	0.06 (0.05 ~ 0.08)	0.07 (0.06 ~ 0.09)
	Post-Vaccination	8 Months	1.13 (0.96 ~ 1.32)	1.07 (0.94 ~ 1.24)	0.93 (0.72 ~ 1.18)	1.02 (0.81 ~ 1.28)
	Post-Vaccination	9 Months	1.12 (0.98 ~ 1.27)	1.08(0.95 ~ 1.23)	1.04 (0.87 ~ 1.26)	1.16 (1.00 ~ 1.36)
Mumps	Pre-Vaccination	8 Months	0.02 (0.02 ~ 0.03)	0.02 (0.02 ~ 0.03)	0.02 (0.01 ~ 0.02)	0.03 (0.02 ~ 0.03)
	Pre-Vaccination	9 Months	0.02 (0.02 ~ 0.03)	0.03 (0.02 ~ 0.03)	0.02 (0.02 ~ 0.03)	0.03 (0.02 ~ 0.03)
	Post-Vaccination	8 Months	0.39 (0.34 ~ 0.46)	0.33 (0.26 ~ 0.41)	0.39 (0.30 ~ 0.48)	0.32 (0.22 ~ 0.46)
	Post-Vaccination	9 Months	0.33 (0.29 ~ 0.38)	0.35 (0.29 ~ 0.40)	0.31 (0.25 ~ 0.38)	0.40 (0.33 ~ 0.47)

8-month age group, before vaccination, the measles antibody GMC in the experimental group was 0.04 (95% CI: 0.03–0.04) for males and 0.03 (95% CI : 0.02–0.04) for females, while in the control group, it was 0.04 (95% CI: 0.03–0.05) for males and 0.03 (95% CI: 0.03–0.04) for females. After vaccination, the measles antibody GMC significantly increased to 1.44 (95% CI : 1.37–1.51) and 1.43 (95% CI: 1.35–1.49) for males and females in the experimental group, and to 1.41 (95% CI: 1.33–1.49) and 1.32 (95% CI: 1.22–1.43) for males and females in the control group, respectively. Regarding rubella antibodies in the 8-month age group, the pre-vaccination GMC in the experimental group was 0.06 (0.05–0.08) for males and 0.06 (95% CI : 0.05–0.07) for females, while the control group showed 0.07 (95% CI: 0.06–0.09) for males and 0.07 (95% CI:0.05–0.09) for females. Post-vaccination levels increased to 1.13 (95% CI: 0.96–1.32) and 1.07 (95% CI: 0.94–1.24) for males and females in the experimental group, and to 0.93 (95% CI: 0.72–1.18) and 1.02 (95% CI: 0.81–1.28) in the control group, respectively. Mumps antibody levels were generally low before vaccination in the 8-month age group, with GMC of 0.02 for both males and females in the experimental group. After vaccination, levels increased to 0.39 (95% CI: 0.34–0.46) and 0.33 (95% CI: 0.26–0.41), respectively. In the control group, pre-vaccination GMC was 0.02 (95% CI: 0.01–0.02) for males and 0.03 (95% CI: 0.02–0.03) for females, rising to 0.39 (95% CI: 0.30–0.48) and 0.32 (95% CI: 0.22–0.46) post-vaccination, respectively. The 9-month age group showed similar trends in antibody level changes as the 8-month age group.

Analysis of results in the experimental and control groups

Our analysis revealed significant increases in antibody GMCs across both groups. In the experimental group, measles IgG antibody GMC increased from 6.96 to 1457.43, rubella IgG antibody GMC rose from 1.13 to 28.11, and mumps IgG antibody GMC increased from 13.87 to 163.04. Similarly, the control group showed increases from 7.45 to 1504.75 for measles, 7.45 to 26.78 for rubella, and 13.73 to 164.25 for mumps. The Hurdle Gamma model's fixed-effect analysis demonstrated vaccination's positive impact on all three antibody levels. After adjusting for age, sex, and grouping variables, we observed the following increases in log mean antibody levels, Measles: 5.31 (95% CI: 5.15–5.47); Rubella: 3.24 (95% CI: 3.14–3.34); Mumps: 2.45 (95% CI: 2.35–2.54). Comparing the experimental and control groups, the median between-group difference in measles-specific IgG antibody levels was 0.01 (95% CI: −0.02 to 0.03), with a probability of direction of 70.75% and 71.84% of the posterior distribution falling within the ROPE (0–1.00); for rubella-specific IgG antibody levels, the median between-group difference was 0.00 (95% CI: −0.04–0.03), with a probability of direction of 56.33% and 43.34% of the posterior distribution falling within the ROPE (0–0.18); for mumps-specific IgG antibody levels, the median between-group difference was 0.00 (95% CI: −0.03–0.03), with a probability of direction of 58.79% and 40.74% of the posterior distribution falling within the ROPE (0–2.38). The 95% CI and ROPE analysis indicated no statistically significant differences between the two groups regarding measles, rubella, and mumps-specific IgG antibody levels. The median post-vaccination IgG antibody levels were 5.31 (95% CI: 5.15–5.47) for measles, 3.24 (95% CI: 3.14–3.34) for rubella, and 2.45 (95% CI: 2.35–2.54) for mumps. Analysis of the 95% CI and ROPE results demonstrated significant increases in measles and rubella antibody levels post-vaccination compared to pre-vaccination levels, with 0% and 0.00% of the posterior distribution falling within the ROPE, respectively. In contrast, mumps antibody levels showed no significant change post-vaccination, with 6.24% of the posterior distribution falling within the ROPE. These findings indicate that vaccination effectively boosted measles and rubella IgG antibody responses, while the mumps component elicited no statistically significant change in antibody levels (Table 3). Random effects analysis from the Hurdle Gamma Model revealed strong negative correlations between pre- and post-vaccination levels of measles and rubella IgG antibodies (correlation coefficients: −1.00 and −0.99, respectively), while mumps IgG antibodies exhibited a moderate negative correlation between pre- and post-vaccination levels (correlation coefficient: −0.56).

Discussion

Our study demonstrates that concurrent MMR-rotavirus vaccination achieves equivalent measles, rubella, and mumps IgG antibody responses compared to MMR vaccination alone. This finding carries significant clinical and public health implications, supporting the implementation of combined vaccination strategies without compromising individual vaccine immunogenicity. Methodologically, we

Table 3. Fixed-effect analysis results of the Hurdle Gamma model in the experimental and control groups.

IgG Antibody	Parameter	Median	95% CI	Probability of Direction	ROPE	% in ROPE	Rhat	ESS
Measles	Intercept	1.11	0.38 ~ 1.81	99.85%	0 ~ 1.00	38.87%	1.00	5294.00
	Group	0.01	−0.02 ~ 0.03	70.75%	0 ~ 1.00	71.84%	1.00	6603.00
	Vaccination	5.31	5.15 ~ 5.47	100.00%	0 ~ 1.00	0%	1.00	958.00
	Age	0.11	0.03 ~ 0.20	99.75%	0 ~ 1.00	100%	1.00	5750.00
	Gender	0.05	−0.03 ~ 0.12	88.12%	0 ~ 1.00	90.13%	1.00	5395.00
Rubella	Intercept	−0.45	−1.32 ~ 0.43	84.82%	0 ~ 0.18	8.24%	1.00	2855.00
	Group	0.00	−0.04 ~ 0.03	56.33%	0 ~ 0.18	43.34%	1.00	2654.00
	Vaccination	3.24	3.14 ~ 3.34	100.00%	0 ~ 0.18	0.00%	1.00	2314.00
	Age	0.09	−0.01 ~ 0.19	96.08%	0 ~ 0.18	95.82%	1.00	2818.00
	Gender	0.02	−0.08 ~ 0.11	63.62%	0 ~ 0.18	64.34%	1.00	2647.00
Mumps	Intercept	1.87	1.21 ~ 2.55	100.00%	0 ~ 2.38	95.59%	1.00	751.00
	Group	0.00	−0.03 ~ 0.03	58.79%	0 ~ 2.38	40.74%	1.01	584.00
	Vaccination	2.45	2.35 ~ 2.54	100.00%	0 ~ 2.38	6.24%	1.00	499.00
	Age	0.09	0.01 ~ 0.16	98.39%	0 ~ 2.38	100%	1.01	753.00
	Gender	0.07	−0.01 ~ 0.14	95.25%	0 ~ 2.38	97.63%	1.00	608.00

advanced beyond traditional antibody GMC calculations, which typically substitute zero values or below-detection-limit values with half of the lower limit of detection (LLOD). Instead, we employed a Hurdle Gamma Bayesian model to analyze the relationship between antibody activity and other variables. This approach eliminates potential data bias from variable data transformation and provides a more accurate representation of antibody level distribution, particularly for low-level antibodies .[17]

Our Hurdle Gamma model analysis demonstrates that vaccination significantly enhanced all three antibody levels, with no significant differences between groups. This finding confirms that concurrent MMR-rotavirus vaccination maintains MMR vaccine immunogenicity, providing crucial evidence for optimizing childhood immunization programs and supporting same-time-point vaccination strategies. We observed significant post-vaccination increases in all three antibodies, with measles IgG showing the most robust response ($\beta = 5.31$, 95% CI: 5.15–5.47), followed by progressively lower increases in rubella and mumps IgG levels. These findings align with Sedigheh et al.'s results.[8,9] The random effects analysis demonstrated a strong negative correlation between measles and rubella IgG antibody random effects. Mumps IgG antibodies showed a moderate negative correlation. These findings indicate that initial IgG antibody levels inversely relate to immune response intensity. Brith Christenson et al.[18] found that measles vaccine re-vaccination did not significantly boost immunity in children who had acquired natural immunity. Claire-Anne Siegrist[19] demonstrated that high maternal measles antibody levels significantly suppress infant antibody responses after immunization, resulting in lower seroconversion rates and/or geometric mean antibody titers compared to infants with low maternal antibody levels. These findings align with our study's results, which show that higher initial IgG antibody levels correlate with weaker immune responses. The mumps IgG antibody levels increased less markedly than measles and rubella IgG antibodies, consistent with Yang et al.'s[20] previous findings in Shanghai. J. Schenk et al.[21] also reported significant antibody level increases after MMR vaccination. Our results not only confirm these previous findings but also expand current knowledge by showing that rotavirus vaccine co-administration maintains MMR vaccine immunogenicity.

Despite providing significant evidence, this study has several limitations: The study was conducted only in certain regions of Gansu Province and may not fully represent the overall situation. Antibody levels were measured only 5 weeks post-vaccination, and data on long-term immune persistence are lacking. The study focused on immunogenicity, with relatively limited assessment of the safety of combined vaccination. The study did not measure rotavirus antibody levels and could not assess the impact of combined administration on the immunogenicity of the rotavirus vaccine.

Conclusion

This study pioneers the application of a Hurdle Gamma model to analyze and compare MMR vaccine immunogenicity between standalone and combined MMR-rotavirus vaccination. Our findings demonstrate comparable MMR antibody responses between these two vaccination approaches.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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Notes on contributor

Yu Tang Since 2002, I have been working at the Gansu Provincial Center for Disease Control and Prevention, focusing on vaccine research and immunization program development. Over the past decade, I have been deeply involved in the formulation and implementation of immunization policies in Gansu Province, with a specific focus on vaccine-preventable disease research. Additionally, I have participated in numerous vaccine-related research projects, accumulating substantial practical experience.

Ethical approval

The study protocol and informed consent form were approved by the Medical Ethics Committee of the Gansu Provincial Center for Disease Control and Prevention

Abbreviations

MMR	Measles-Mumps-Rubella
CCID50	Cell Culture Infectious Dose 50%
ELISA	Enzyme-linked Immunosorbent Assay
GMC	Geometric Mean Concentration
MCMC	Markov Chain Monte Carlo
HDI	Highest Density Interval
CI	Credible Interval
ROPE	Region of Practical Equivalence
ESS	Effective Sample Size
LLOD	Lower Limit of Detection

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