



Expanded Program on Immunization  
Government of Pakistan



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# Effectiveness of Monovalent Rotavirus Vaccine (RV1) Among Young Children in Pakistan: A Test-Negative Case-Control Evaluation

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# Conflict of Interest Disclosure

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# Rotavirus Burden in Pakistan

## Why this Study Matters



### Pakistan's Rotavirus Burden

- Top 4 countries globally for rotavirus deaths in children <5 years
- Pre-vaccine: 14,700 annual deaths; mortality rate 67.6/100,000 children



### Vaccine Introduction

- RV1 (Rotarix™) rollout: Late 2017 (nationwide by April 2018)
- Schedule: 2 doses at 6 & 10 weeks with OPV co-administration



### Knowledge Gaps

Real-world VE in high-mortality settings with challenges:

- Malnutrition (30-40%)
- OPV co-administration

# Study Objectives

## What We Aimed to Understand



### Primary Objective

Evaluate the effectiveness of 2 doses of monovalent rotavirus vaccine (RV1) in preventing hospitalizations for acute gastroenteritis among children in Pakistan.



### Effectiveness by Nutrition

Analyze VE in relation to nutritional status using weight-for-age z-score (WAZ) and height-for-age z-score (HAZ).



### Age-Specific Effectiveness

Estimate vaccine effectiveness (VE) stratified by age groups—22 weeks to 11 months, and 12 to 23 months.



### Genotype-Specific VE

Assess VE against predominant rotavirus P genotypes, especially P[4], P[6], and P[8].

# Study Design & Methodology

## How the Evaluation Was Conducted



### Design: Test-Negative Case-Control

Children hospitalized with gastroenteritis were tested for rotavirus; those testing positive were cases, and those negative served as controls.



### Enrollment Scope

Data collected from April 2018 to March 2023 across 9 hospitals in 3 provinces: Sindh, Punjab, and Khyber Pakhtunkhwa.



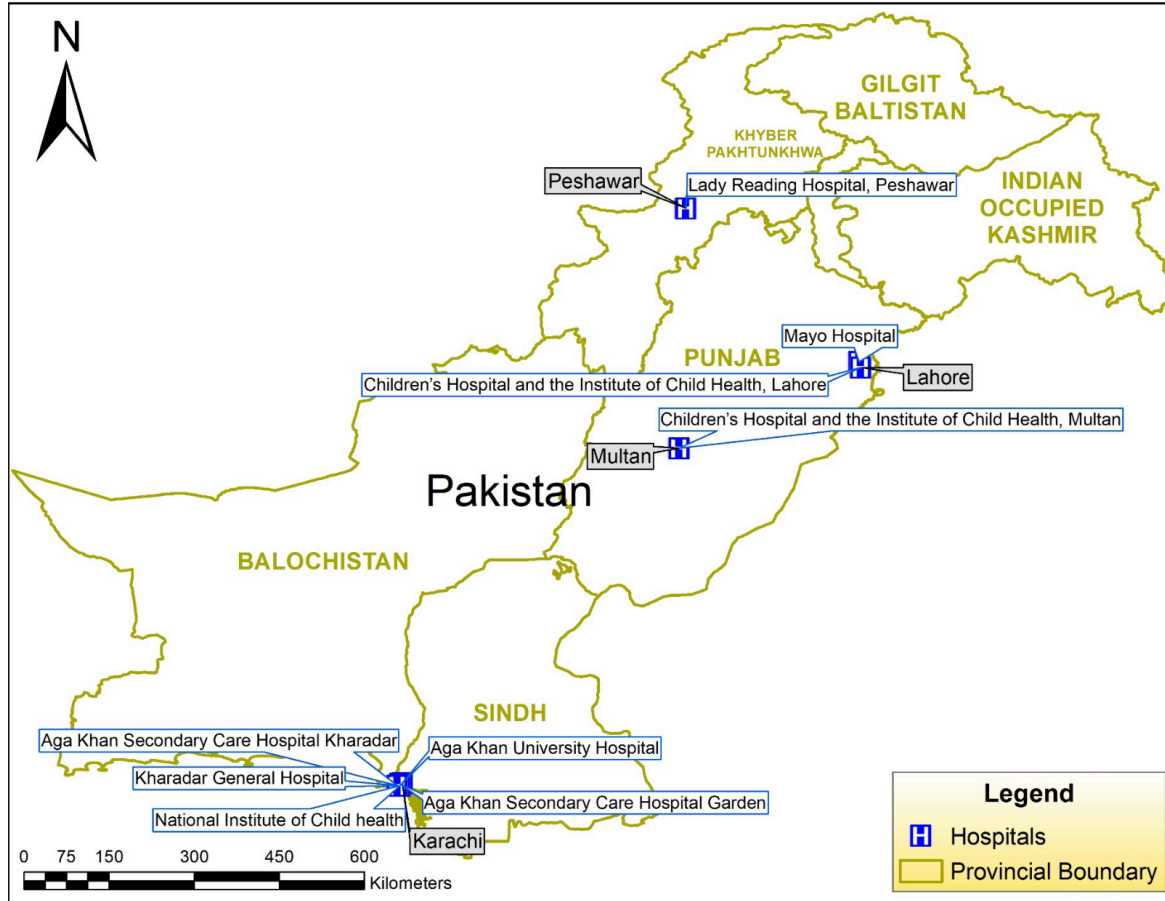
### Eligibility Criteria

Children aged  $\geq 4$  months, eligible for  $\geq 1$  RV1 dose before illness, requiring IV hydration, and without bloody diarrhea.



### Laboratory Testing

Stool samples tested via enzyme immunoassay (EIA) for rotavirus detection, followed by genotyping for positive samples.



# Study Enrollment & Participant Flow

## Capturing a Representative Sample

- **Screened Population:** 6,454 children screened between April 2018 and March 2023. Exclusions were based on age, clinical criteria, or consent.
- **Enrollment & Sampling:** 4,833 enrolled with stool samples collected; 3,774 had enzyme immunoassay (EIA) results available.
- **Analyzable Cases and Controls:** 589 rotavirus-positive cases and 1,556 rotavirusnegative controls with complete vaccination records included in final analysis.
- **Genotyping performed:** Genotyping was performed on 485 samples
- **High Data Integrity:** Strict eligibility and standardized data collection ensured robust and analyzable dataset across multiple hospitals.

# Vaccination Coverage & Demographics

## Profile of Enrolled Participants

- **RV1 Coverage:** Among children aged 22 weeks–11 months, 72% of controls and 66% of cases had received 2 RV1 doses; OPV administration exceeded 99%.
- **Geographic Spread:** Participants were enrolled from Sindh (38%), Punjab (53%), and Khyber Pakhtunkhwa (9%), ensuring wide representation.
- **Demographics:** 55% of enrolled children were male; nutritional indicators showed 40-50% of infants were underweight or stunted.
- **Data Verification:** Vaccination records were confirmed via caregiver cards, clinic registers, or mobile app for late-phase Sindh enrollees.

# Rotavirus Genotype Distribution

## P Strains Circulating in Pakistan

- **Predominant Genotypes:**
  - ✓ Among 485 typed cases, the most common P-types were P[4] (38%), P[8] (32%), and P[6] (16%).
  - ✓ The most common G and P genotype combinations were G9P[4], G12P[6], and G1P[8].
  - ✓ More than half (268/485 [56%]) contained neither G1 nor P[8].
- **Heterotypic Strains Dominated:** Only 32% of P-type strains were homotypic to the vaccine strain (P[8]); the rest were heterotypic (P[6], P[4]).
- **Seasonal and Geographic Diversity:** diversity by province and over time could not be evaluated.

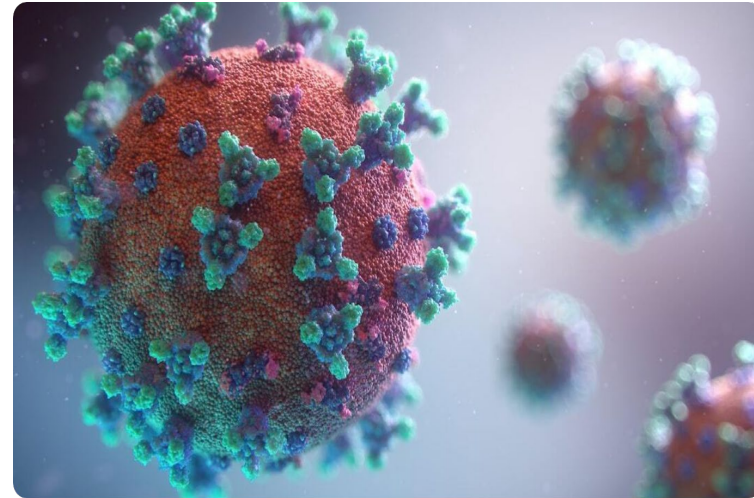


Photo by Fusion Medical Animation on Unsplash

# Vaccine Effectiveness – Overall Results

By Age Group (22w–11m & 12–23m)

AGE GROUP	VE (95% CI)	CASES/CONTROLS
22 weeks–11 mo	33% (12, 49)	517/1,310
12–23 mo	24% (-20, 52)	222/914
Overall	31% (13, 45)	

## Key Finding:

Moderate protection in infants; non -significant in 1 -year-olds

*Note: All adjusted models included birth year, birth month, admission year, admission quarter, and hospital.*

# Vaccine Effectiveness by Nutritional Status

Impact of Malnutrition on VE

NUTRITIONAL STATUS	VE (95% CI)	CASES/CONTROLS
WAZ $\geq$ -2 (Better nourished)	45% (21, 62)	313/633
WAZ < -2 (Malnourished)	23% (-13, 48)	204/676

## Critical Insight:

- VE doubled in well-nourished infants
- Malnutrition significantly blunts vaccine response

# Vaccine Effectiveness by Genotype

Strain-Specific Performance

P-TYPE DETECTED (95% CI)	CASES
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P[8]	36% (0, 59)	156
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P[6]	56% (25, 74)	79
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P[4]	21% (-21, 48)	182
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## Key Challenge:

Lowest VE against P[4] strains (heterotypic to RV1)



Photo by National Cancer Institute on Unsplash

# Discussion: Global Context & Interpretation

## Comparative Insights & Implications



### Modest VE in Pakistan

Overall VE (31%) aligns with prior observations from Bangladesh and Malawi, reflecting challenges in low resource settings.



### Comparison with Afghanistan

VE in Afghanistan was 53%, potentially higher due to better nutritional status and strain match.



### Strain Mismatch Reduces Impact

High prevalence of P[6] and P[4] strains in Pakistan may reduce efficacy of monovalent P[8] vaccine.



### Role of Malnutrition

Nutritional deficiencies may impair mucosal immunity and reduce oral vaccine uptake.

# Conclusions & Policy Implications

## What the Evidence Tells Us

### Key Findings and Implications:



Moderate Protection

RV1 provides 33% protection in high-burden Pakistan



Nutrition Matters

VE doubled (45%) in wellnourished infants



Genotype Challenge

Reduced effectiveness against P[4] strains



Age-Related Waning

Reduce VE by 12-23 months

### Program Implications:

Urgent need for improved nutrition interventions

Consider additional vaccine doses

Genotype surveillance critical for vaccine strategy

# Acknowledgments

## Expanded Contributor Recognition



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