

Analysis of post-vaccine serum neutralizing antibody response among infants vaccinated with either RotaVac[®] or RotaSII[®]

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Background

- RV G12P[11] strain prevalent at a high frequency in neonates in NICUs in western India.
- Play role as a reservoir
- G1P[8], G2P[4], G3P[8], G4P[8] and G9P[8] - the five major RV strains. G12 strains has emerged as sixth major genotype.
- Differences in the efficacies of rotavirus vaccine in middle- and low-income countries may be related to early natural exposure of neonates before immunization.
- Unusual bovine-human-like strain G12P[11] caused outbreak in neonatal units, raising concerns about vaccine efficacy against this genotype.

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Research paper

Clinical and genetic characteristics of unusual G12P[11] rotavirus strains recovered from neonates: A study from Pune, Western India

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ARTICLE INFO ABSTRACT

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RESEARCH ARTICLE

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Complete genomic analysis of uncommon G12P[11] rotavirus causing a nosocomial outbreak of acute diarrhea in the newborns in New Delhi, India

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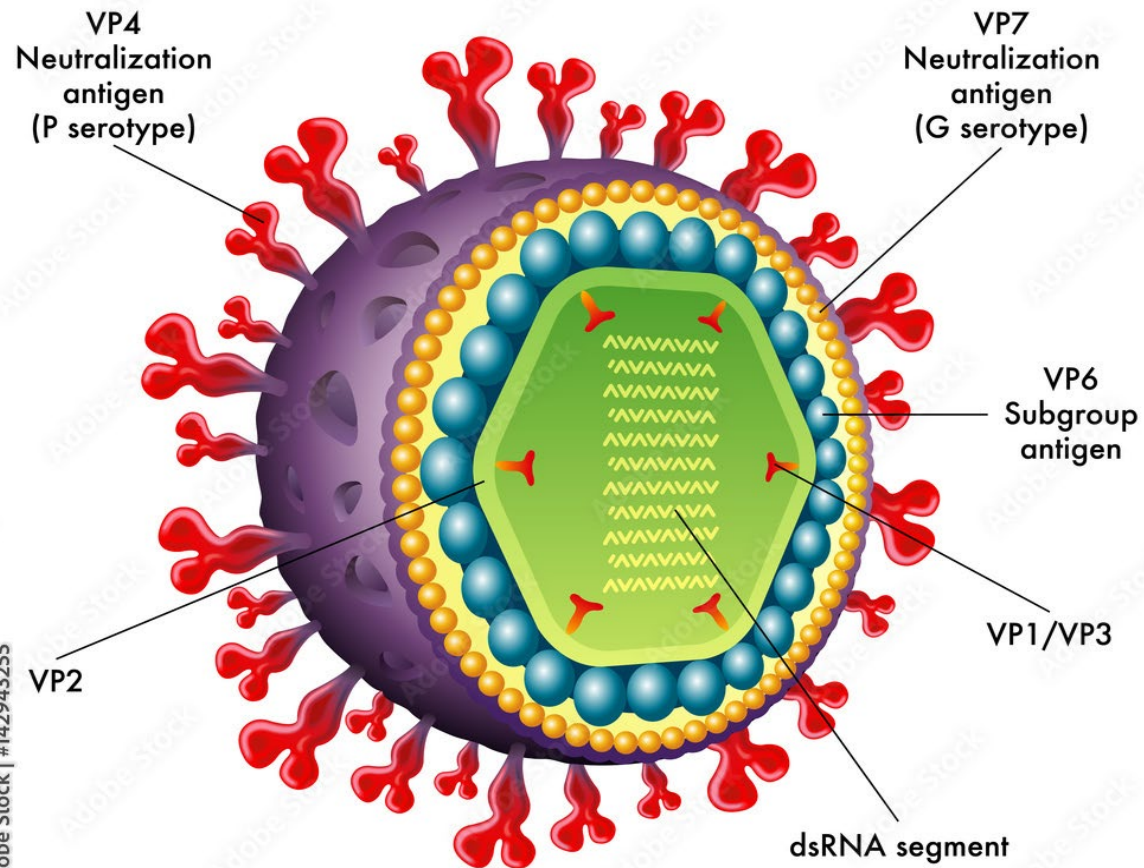
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Licensed rotavirus vaccines

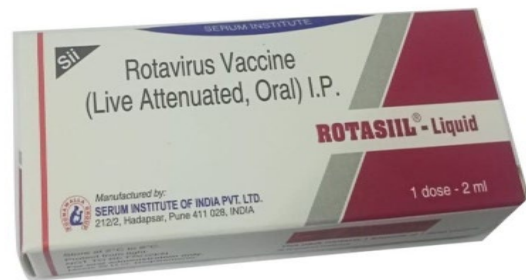
Vaccine trade name	Manufacturer	Strains	Year of Obtaining WHO Prequalification
RotaTeq	Merck Sharp & Dohme (MSD), USA	G1, G2, G3, G4, P1A[8] (Human-bovine reassortant)	2008
ROTARIX	GlaxoSmithKline Biologicals SA, Belgium	G1P[8] Human RV	2009
ROTASIIL	Serum Institute of India, India	G1, G2, G3, G4, and G9 (human-bovine reassortant)	2018
ROTASIIL-Liquid			2021
ROTASIIL Thermo			2020
ROTAVAC	Bharat Biotech International Limited, India	G9P[11] Neonatal RV	2018
Lanzhou Lamb Rotavirus (LLR)	Lanzhou Institute of Biomedical Products, China	G10P[12] Lamb RV	Nationally Licensed (2000)
Rotavin-M1	POLYVAC, Vietnam	G1P[8] Human RV	Nationally Licensed (2012)

❖ **RV strain G12 is not the component of any currently licensed or upcoming vaccine (RV3-BB; G3P[6])**

Structure of Rotavirus



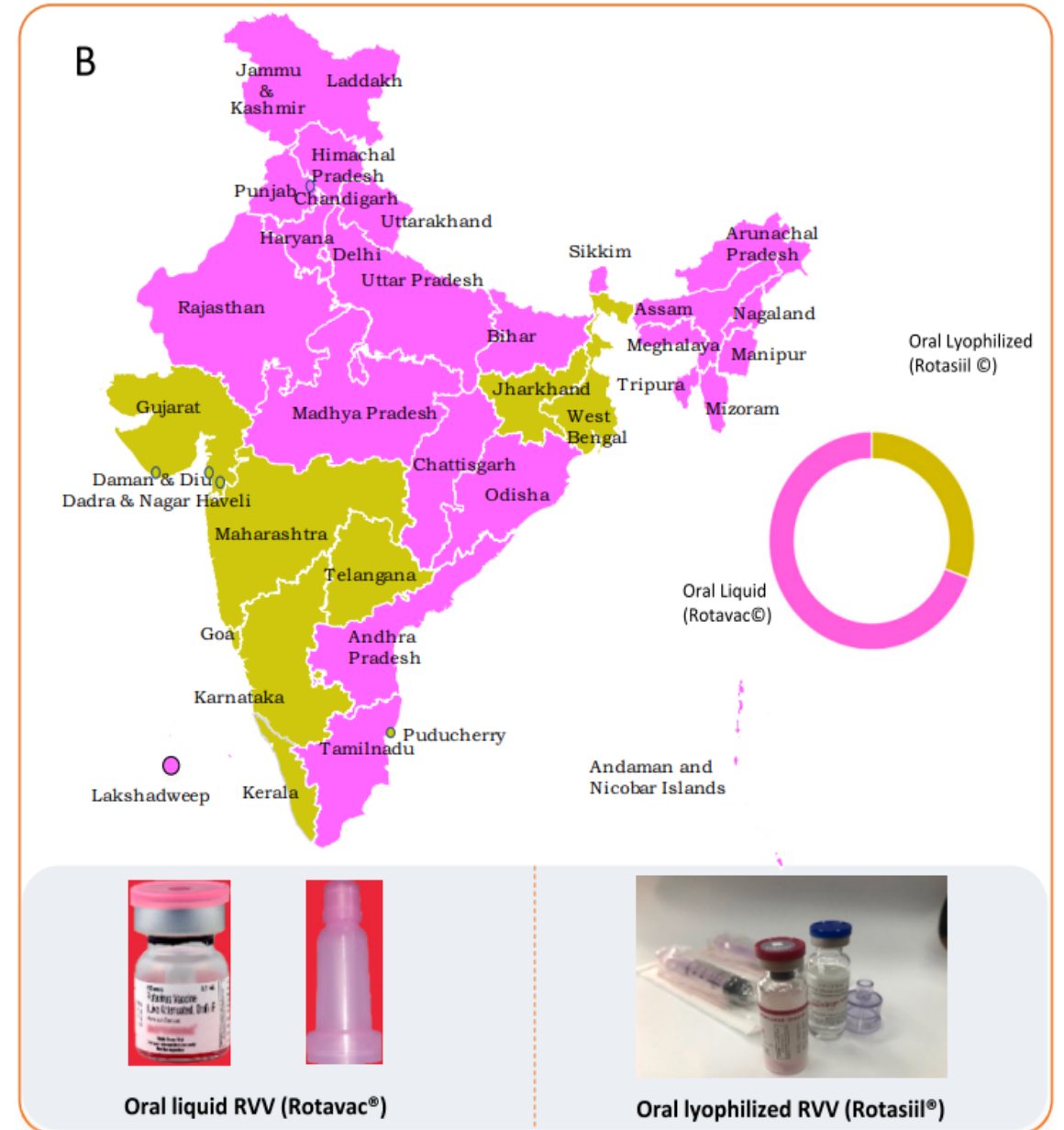
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- Neutralization of virus infectivity is believed to play a key role in immunological defense.
- Neutralizing antibodies generated against VP7 and VP4 proteins.
- Although the parameters of protection against RV disease have not been completely recognized, serum neutralizing antibody (SNA) considered correlates of protection from the disease.
- These neutralizing antibodies may act in a homotypic (genotype-specific) or heterotypic (cross-reactive) manner, forming the basis for vaccine development.

Aims

- To evaluate serum neutralizing antibody (SNA) responses to the most common RV types (G1–G4, G9, and G12) in infants vaccinated with either ROTAVAC® or ROTASIIL®.
- To compare homotypic (genotype-specific) and heterotypic (cross-reactive) immune responses elicited by the two vaccines (genotype specific effectiveness).



Study design

- The study was conducted at ICMR-National Institute of Virology (NIV), Pune, India.
- Bharati Hospital and Research Centre, Pune, India
- KEM Hospital and Research Centre, Pune, India
- Christian Medical College, Vellore, India.

Inclusion criteria

- Healthy infants aged 5-7 months who received 3 doses of vaccine.
- Written informed consents were obtained by the parents/guardians.

Sample collection

- ~ 1-2 ml blood samples, one month after the final dose and stored at -20°C until testing
- Demographic information such as including date of birth, sex and RV vaccine type were recorded in the case reporting form.



Viruses

Reference rotavirus strains

- HRV-1, G1P[8] (KU)
- HRV-2, G2P[4] (S2)
- HRV-3, G3P[8] (YO)
- HRV-4, G4P[6] (ST-3)
- HRV-9, G9P[8] (F-45) were procured from Sapporo Medical College, Sapporo, Japan
- G12P[11] (NIV-1740121) strain was isolated at NIV.

SNA titers against HRV strains using a combined cell culture and ELISA.

Immunogenicity Assessment

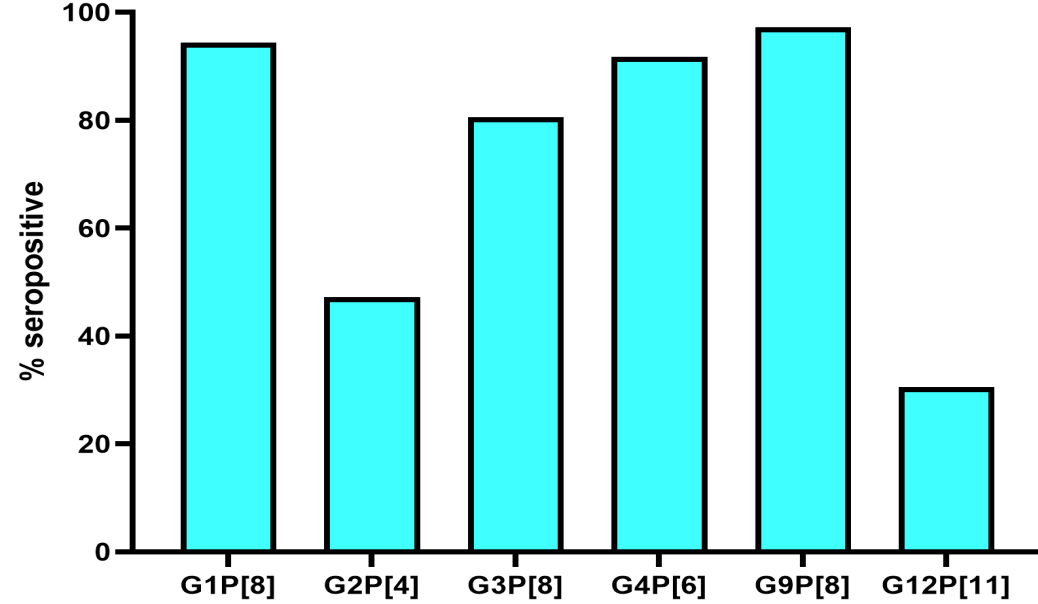
- The reciprocal of the highest dilution of a serum that reduced specific absorbency by $\geq 60\%$ was considered as its titers of SNA.
- An infant was considered seroprotective if the SNA titer against any virus was ≥ 10 .

Results

Group 1, composed of sera (n=36) from RotaSIII[®] vaccinated infants

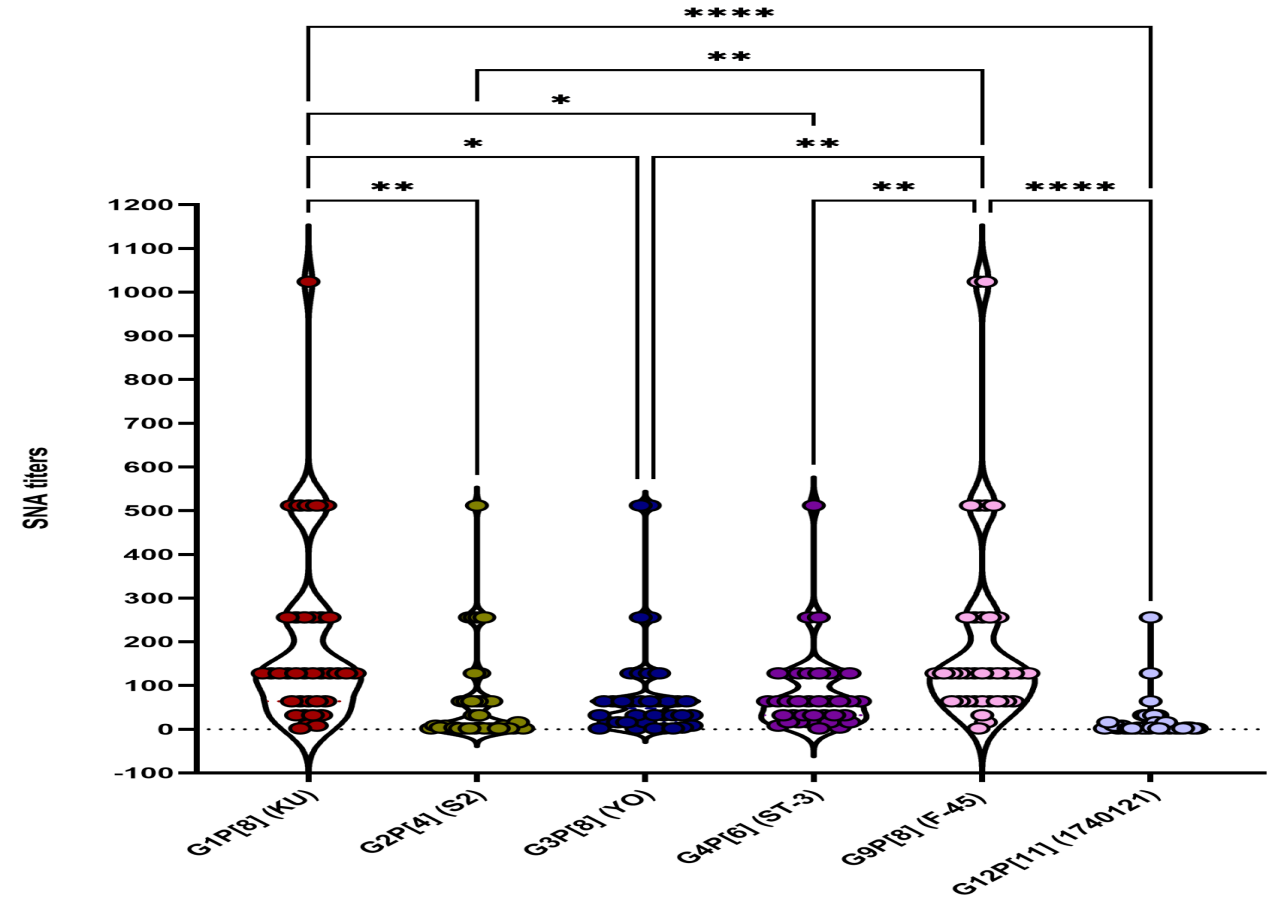
Group 2 included sera (n=31) from ROTAVAC[®] vaccinated infants.

Percentage of ROTASIL[®] vaccine recipients seroconverted to RV genotypes



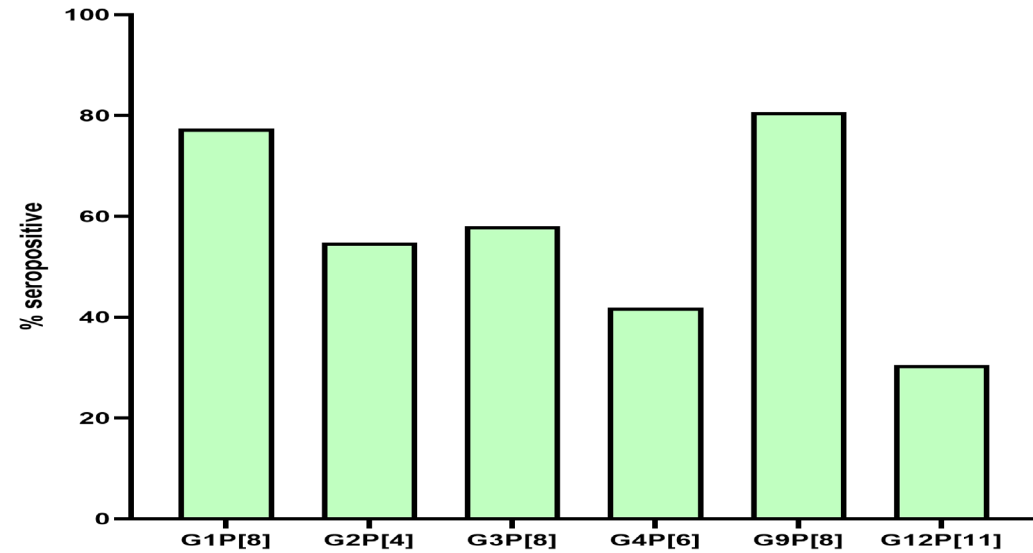
- 94.4%, 97.2%, 91.7% and 80.5% vaccine recipients were seropositive to G1, G9, G4 and G3 respectively.
- Only 47.2% of the recipients, sero-converted to the strain G2.
- The results indicate that 36.1% of the infants exhibited serum neutralization to all vaccine strains.
- Only 30.5% infants revealed cross NAs to fully heterotypic G12P[11] strain.
- 25% infants showed sero-conversion to all six RV strains with varying frequencies.

SNA titers against RV genotypes in post-vaccine sera among ROTASIL[®] vaccine recipients



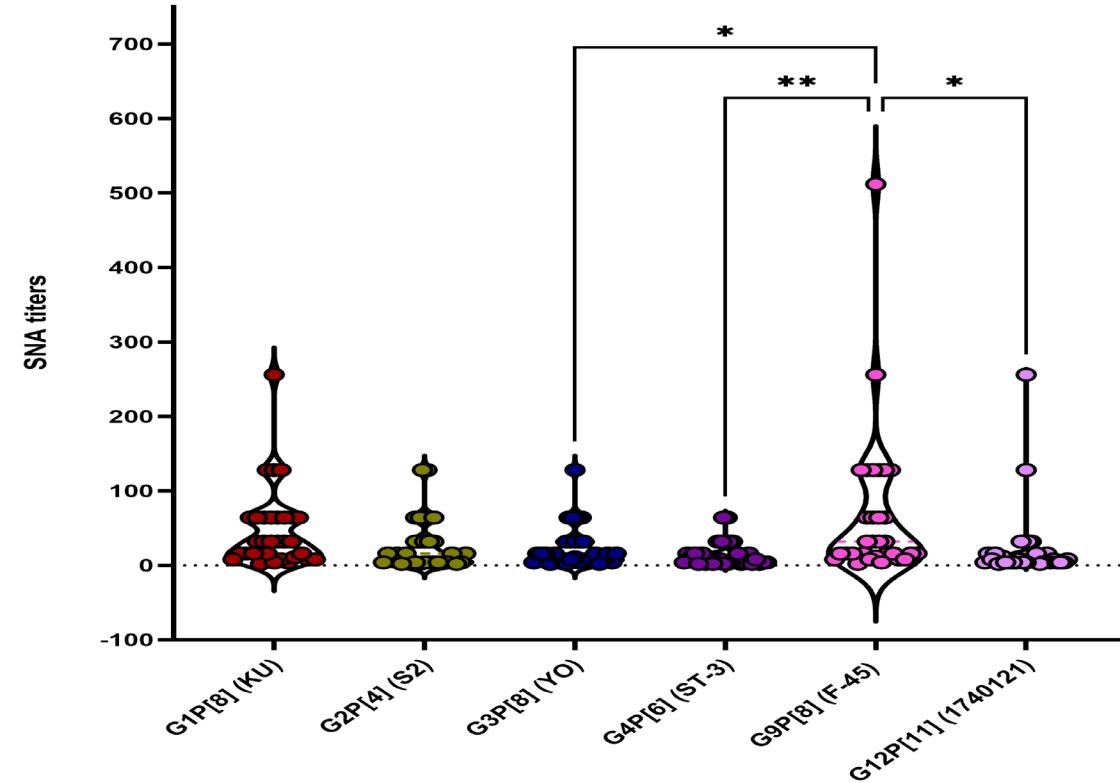
- Overall, the titers were significantly high against homotypic RV G1 and G9 strains than those against G2, G3 and G4 strains.
- G3 and G4 elicit intermediate titers
- G2 and especially G12 showed low titers

Percentage of ROTAVAC® vaccine recipients seroconverted to RV genotypes



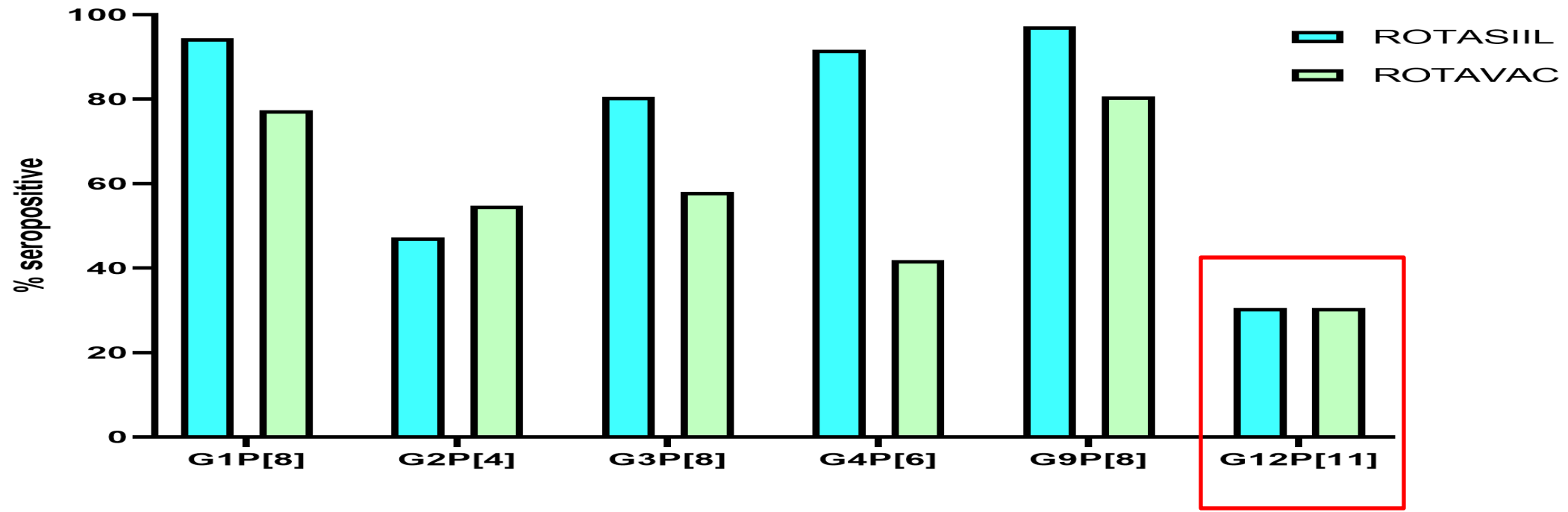
- 80.6% of recipients sero-converted to the partial homotypic RV strain, G9P[8].
- Interestingly, 77.4% of vaccine recipients were seropositive against heterotypic strain, G1P[8].
- Lower heterotypic responses to the strains; G2P[4], G3P[8] and G4P[6] were observed, with only 54.8%, 58.0%, and 41.9% of vaccine recipients, respectively, showing seroconversion.
- Only 30.48% of sera cross-neutralized partial heterotypic G12P[11] strain.

SNA titers against RV genotypes in post-vaccine sera among ROTAVAC® vaccine recipients

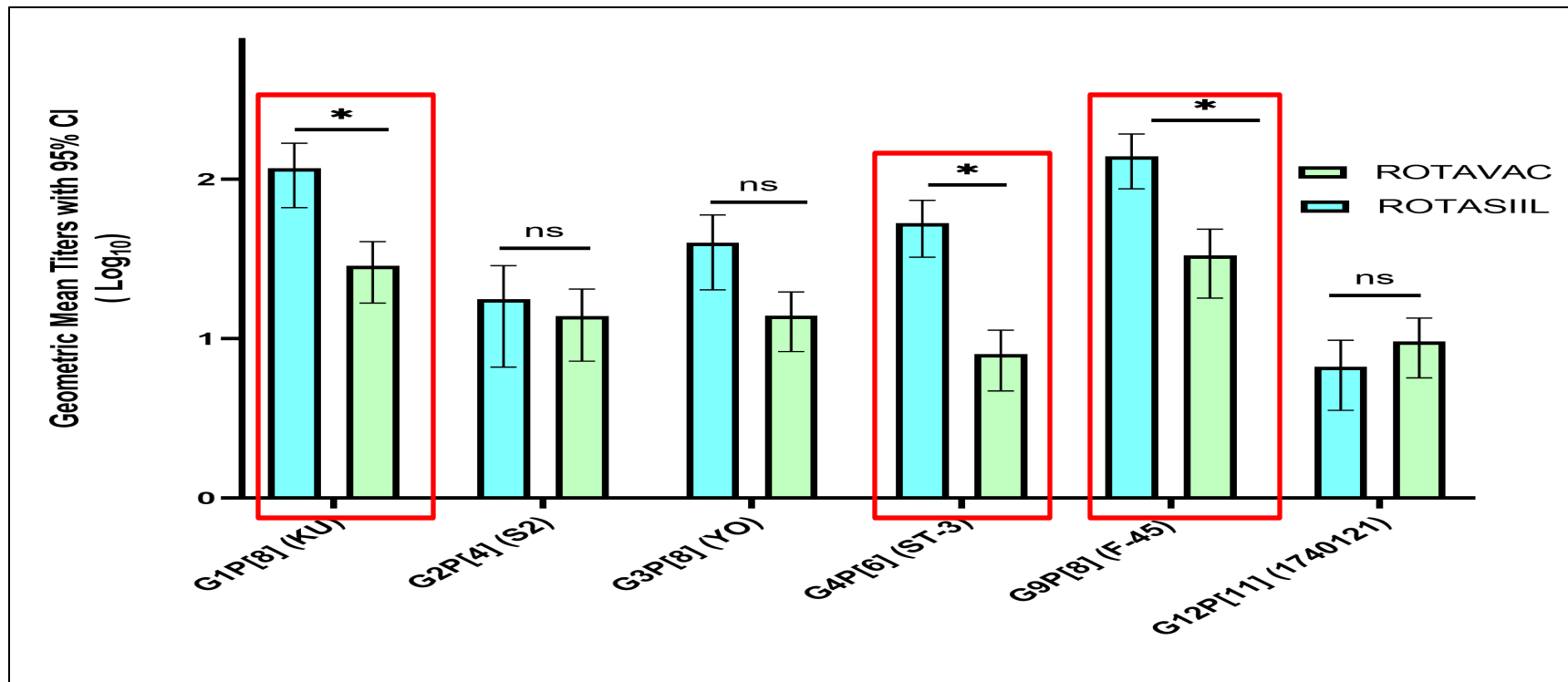


- SNA titers against strains were significantly higher G9 (p< 0.01) compared to of G3, G4 and G12.
- Only 6.45% subjects demonstrated sero-conversion against all genotypes.
- 64.51% infants revealed sero-conversion to G1P[8] and G9P[8].

Summary of vaccine recipients serconverted rates



RV genotypes	Percentage of vaccine recipients seroconverted to RV genotypes	
	RotaSIIIL [®]	ROTAVAC [®]
G1P[8]	94.4	77.4
G2P[4]	47.2	54.8
G3P[8]	80.5	58
G4P[6]	91.7	41.9
G9P[8]	97.2	80.6
G12P[11]	30.5	30.5



A comparative analysis of the log GMTs between the two groups indicated a higher proportion of SNAs against the strains G1P[8], G4P[6] and G9P[8] in subjects receiving RotaSiIL[®] vaccine compared to those receiving ROTAVAC[®]

Summary of GMTs SNA responses to RotaSiIL[®] and ROTAVAC[®] vaccine recipients

RV Genotypes	RotaSiIL [®]		ROTAVAC [®]	
	Geometric Mean	95% CI	Geometric Mean	95% CI
G1P[8] (KU)	110.10	(70.47, 172.00)	27.03	(17.64, 41.43)
G2P[4] (S2)	15.38	(7.96, 29.70)	12.79	(7.81, 20.95)
G3P[8] (YO)	36.76	(22.09, 61.17)	13.22	(8.73, 20.02)
G4P[6] (ST-3)	50.46	(33.97, 74.96)	7.56	(4.95, 11.54)
G9P[8] (F-45)	133.17	(90.82, 195.28)	31.00	(19.31, 49.77)
G12P[11] (1740121)	6.18	(3.83, 9.99)	9.06	(5.98, 13.74)

Conclusions

- RotaVac® and the polyvalent ROTASIL® were immunogenic in infants.
- A multivalent vaccine could offer broader protection against prevalent RV strains.
- Both ROTAVAC® and RotaSIL® vaccines demonstrated relatively limited cross-neutralization against RV G12P[11].
- These results highlight the need to incorporate the G12 component into the development of future rotavirus vaccines to enhance their effectiveness.

Limitation

- Only post-vaccine serum samples obtained from the infants. Serum samples could not be collected from these infants before immunization, so the presence of any SNAs prior to the vaccination could not be evaluated.

QUESTIONS?

THANK YOU