

# **MMRV ANALYSIS REPORT**

**Prevalence and Titres of Measles, Mumps, Rubella and Varicella Antibodies in  
Indian Infants and Toddlers: A Pilot Study.**

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## INTRODUCTION

Measles, mumps, rubella, and varicella (chickenpox) are vaccine preventable diseases (VPDs) that cause significant morbidity (by mumps, rubella, and varicella) and mortality (mainly by measles) in infants from developing countries. These diseases are public health issues and can be controlled through an age appropriate immunization, one of the safest and cost-effective public health interventions that estimates to avert between 2 and 3 million global deaths each year (WHO: Health Topic Immunization). As per the Coverage Evaluation Survey (CES-2009), 61% of children (aged below one year) in the country were fully immunized with all vaccines - BCG 87%, OPV3 70%, DPT3 72%, and Measles 74%.

The first reported study from Delhi, India documented disappearance of maternal measles antibodies detectable by *hemagglutination inhibition* (HI) by 9 months in all the infants studied, but not for mumps or rubella (Singh J et al 1999). Importantly, evidence for subclinical infection with the three viruses was found in 19-31% infants by 15 months of age. In another study from Delhi, India, infants in the age groups of 9-10 months and toddlers in age group of 15-18 months, 85% and 56% (measles), 80% and 70% (mumps) and 80% and 71.6% (rubella) respectively were sero-negative (Yadav S et al 2003). As far as varicella is concerned, scanty data is available.

It is also known that, passive immunity of infants through the trans-placental transfer of immunoglobulin G (IgG) wane over time and vaccination at an appropriate age is the key for prevention of these diseases. The timing of primary immunization is decided on the basis of prevalence of the pathogen in a community and probable time of exposures. Unfortunately, there is very minimal data available for seroprevalence of MMRV at 6, 9, 12 and 15 months.

Thus, we propose to assess the presence and titres of antibodies against these viruses at 6, 9, 12, and 15 months of age as a primary objective. The current study will be a seroprevalence survey with less stringent inclusion and exclusion criteria (compared to Lalwani S et al 2015 study), which will be more representative of the children accessing hospital care and in turn the general pediatric population of Pune.

## OBJECTIVE

### PRIMARY

- To determine the prevalence and titres of IgG antibodies for measles, mumps, rubella and varicella in infants at 6 months of age.
- To assess IgG and IgM-anti-varicella antibody positivity at 9, 12, and 15 months

### SECONDARY

- To assess IgG antibody titres for measles mumps, and rubella in children at 9, 12 and 15 months of age

## **INCLUSION AND EXCLUSION CRITERIA**

Study participants who fulfilled all the following inclusion criteria were enrolment in the study

- Age 6 months, 9 months, 12 months, 15 months ( $\pm$  1 month for all four age groups) at the time of enrolment
- Not received any measles or MMR vaccination for infants of 9 months of age-prior to measles vaccination at 9 months
- Receipt of measles vaccination at least 4 weeks prior to enrolment for infants of 12 months and 15 months of age
- Not received any varicella vaccination for toddlers of 15 months of age
- Informed consent form signed by either of the parents

Study participants fulfilling any of the following criteria were excluded from the study

- Past (within last 6 months) or current receipt of immunoglobulins
- Known or suspected congenital or acquired immunodeficiency
- Chronic administration (defined as > 14 days) of immunosuppressant or other
- Immune modifying drugs since birth (prednisone or equivalent for >0.5mg/kg/day. Inhaled or topical steroids will be allowed)
- Acute febrile disease (axillary temperature greater than or equal to 38<sup>0</sup>C / 100.4<sup>0</sup>F) at the time of enrolment. Study participation will be delayed until the illness subsides.
- History of (H/O) natural infection of measles, mumps, rubella or varicella
- Children in care – institutions or orphanages

## **METHODOLOGY**

This hospital based cross sectional study was conducted at Bharati Hospital and Research Center, a tertiary care hospital in West India affiliated to Bharati Vidyapeeth University Medical College Pune, India. Study population included infants of 6 and 9 months and toddlers of 12 and 15 months of age ( $\pm$  1month for all ages).

Sample size based on prevalence of varicella (8.3%) and precisions values disclosed a large sample size estimate which was not feasible. So, pilot study was conducted which enrolled to 600 subjects, 150 in each subgroup. After checking inclusion and exclusion criteria written informed consent was taken.

Demographic and baseline characteristics were collected as per case record form. Blood sample was collected and serum sample was separated and stored at -20<sup>0</sup>C. All the serum samples were screened and tested (by the lab in-charge) for the presence of IgG antibodies against Measles, Mumps, Rubella and Varicella (Euroimmun, Germany) antibody titers using ELISA. Antibody titres found positive (IgG positives) for MMRV were quantitated to define the level of sero-protection.

For measles, all the IgG positives till the age of 9 were tested for IgM antibodies. Post-vaccination, samples with high antibody titres and few others were screened for IgM antibodies. For MRV, all the IgG antibody positives were tested for IgM antibodies.

Cut off for IgG antibody positivity was as follows:

- Measles > 250 IU / liter
- Mumps > 20 IU/ml
- Rubella > 10 IU/ml
- Varicella (VZV) > 100 IU/liter

All the laboratory analysis was conducted in Interactive Research School of Health Affairs (IRSHA), Research Institute of Bharati Vidyapeeth University Pune. Quantitative analysis was done using SPSS Software, Version 25 to study the sample characteristics. Mean and standard deviation were calculated for continuous data. Chi-square test was used to compare the qualitative data. Yate's correction was applied where necessary. ANNOVA was used to compare the birth weights of the participants in all cohorts.

## RESULTS

The study was planned to be conducted for nine months however it required three more months to complete due to some unavoidable delays. Total 600 participants were included in the predecided four cohorts; 150 in each of 6 months, 9 months, 12 months, and 15 months cohort. All the 600 blood samples collected from the participants and were analysed. Basic characteristics of the study population as per the cohort category are described in different tables below.

**Table 1. Cohort wise gender distribution of the study population**

Age Category	Sex		Sex Ratio
	Male n (%)	Female n (%)	Male : Female
6 months (n=150)	87 (58.0)	63 (42.0)	1:0.7
9 months (n=150)	73 (48.7)	77 (51.3)	1:1.1
12 months (n=150)	76 (50.7)	74 (49.3)	1:1
15 months (n=150)	79 (52.7)	71 (47.3)	1:0.9
<b>Total (N=600)</b>	<b>315 (52.5)</b>	<b>285 (47.5)</b>	<b>1:0.9</b>

Overall gender distribution in the study was almost equal with the male to female ratio of 1:0.9 however there was male predominance in 6 months cohort where the male to female ratio was 1:0.7. The difference in male to female ratio in all four cohorts was not statistically significant ( $p>0.05$ ).

**Table 2. Cohort wise birth and present weight distribution (N=600)**

Birth Category	Birth weight in kg Mean (SD)	Present Weight in kg Mean (SD)
6 months (n=150)	2.43 (0.7)	6.62 (1.0)
9 months (n=150)	2.55 (0.7)	7.87 (1.1)
12 months (n=150)	2.63 (0.5)	8.55 (1.0)
15 months (n=150)	2.63 (0.6)	9.26 (1.2)

Mean birth weight in the predecided cohorts varied from 2.43 ( $\pm 0.7$ ) to 2.63 ( $\pm 0.6$ ). The difference in the mean birth weight in these four cohorts was not statistically significant ( $p > 0.05$ ).

**Table 3. Cohort wise distribution of pre-term and term delivery of the participants**

Birth Category	Pre-term n (%)			Term n (%)		
	Male	Female	Total	Male	Female	Total
6 months (n=150)	26 (17.3)	18 (12.0)	44 (29.3)	61 (40.7)	45 (30.0)	106 (70.7)
9 months (n=150)	16 (10.7)	19 (12.7)	35 (23.3)	57 (38.0)	58 (38.7)	115 (76.7)
12 months (n=150)	16 (10.7)	7 (4.7)	23 (15.3)	60 (40.0)	67 (44.7)	127 (84.7)
15 months (n=150)	13 (8.7)	7 (4.7)	20 (13.3)	66 (44.0)	64 (42.7)	130 (86.7)
<b>Total (N=600)</b>	<b>71 (11.8)</b>	<b>51 (8.5)</b>	<b>122 (20.3)</b>	<b>244 (40.7)</b>	<b>234 (39.0)</b>	<b>478 (79.7)</b>

In the overall 600 participants across all the four cohorts, 122 (20.3%) were born preterm and 478 (79.7%) were born full term. Within the 4 cohorts, the proportion of participants who were born preterm varied from 13.3% in 15 months cohort to 29.3% seen in 6 months cohort. The difference in proportion of preterm versus term in all four cohorts is not statistically significant ( $p > 0.05$ ).

Overall male to female ratio in babies born full term was 1:0.95 and in preterm was 1:0.7. Male to female ratio in the babies born preterm was 1:0.7, 1:1.2, 1:0.4 and 1:0.5 in 6, 9, 12 and 15 months cohorts respectively. In term babies, the ratio varied from 1:0.7 in 6 months cohort to 1:1 in 12 months cohort. The gender difference in preterm and term babies in these four cohorts was not statistically significant ( $p > 0.05$ ).

**Table 4. Cohort wise mothers' disease status in past**

Birth Category	Measles n (%)		Mumps n (%)		Rubella n (%)		Varicella n (%)	
	Yes	No	Yes	No	Yes	No	Yes	No
6 months (n=150)	16 (10.7)	134 (89.3)	1 (0.7)	149 (99.3)	0 (0)	150 (100)	68 (45.3)	82 (54.7)
9 months (n=150)	18 (12.0)	132 (88.0)	2 (1.3)	148 (98.7)	0 (0)	150 (100)	65 (43.3)	85 (56.7)
12 months (n=150)	14 (9.3)	136 (90.7)	0 (0)	150 (100)	0 (0)	150 (100)	61 (40.7)	89 (59.3)
15 months (n=150)	12 (8.0)	138 (92.0)	2 (1.3)	148 (98.7)	0 (0)	150 (100)	62 (41.3)	88 (58.7)
<b>Total (N=600)</b>	<b>60 (10.0)</b>	<b>540 (90.0)</b>	<b>5 (0.8)</b>	<b>595 (99.2)</b>	<b>0 (0)</b>	<b>150 (100)</b>	<b>256 (42.7)</b>	<b>344 (57.3)</b>

In overall 600 participants, mothers of 60 (10%) had given history of measles disease and 256 (42.7%) gave history of varicella infection. None of the mother had reported rubella and mumps was reported only by 5 (0.8%) mothers.

History of measles disease in mother varied from 8.0% in 15 months cohort to 12.0% in 9 months cohort. This difference in various cohorts was not statistically significant ( $p>0.05$ ). For varicella, history of the disease in mothers varied from 40.7% to 45.3% in the four cohorts however the difference is not statistically significant ( $p>0.05$ ).

**Table 5. Cohort wise mothers' vaccination status**

Birth Category	Measles n (%)			Mumps n (%)			Rubella n (%)			Varicella n (%)		
	Yes	No	UK	Yes	No	UK	Yes	No	UK	Yes	No	UK
6 months (n=150)	81 (54.0)	11 (7.3)	58 (38.7)	0 (0)	150 (100)	0 (0)	2 (1.3)	148 (98.7)	0 (0)	1 (0.7)	149 (99.3)	0 (0)
9 months (n=150)	78 (52.0)	11 (7.3)	61 (40.7)	1 (0.7)	147 (98.0)	2 (1.3)	1 (0.7)	147 (98.0)	2 (1.3)	0 (0)	148 (98.7)	2 (1.3)
12 months (n=150)	73 (48.7)	20 (13.3)	57 (38.0)	0 (0)	150 (100)	0 (0)	0 (0)	150 (100)	0 (0)	1 (0.7)	149 (99.3)	0 (0)
15 months (n=150)	69 (46.0)	22 (14.7)	59 (39.3)	0 (0)	150 (100)	0 (0)	1 (0.7)	149 (99.3)	0 (0)	0 (0)	150 (100)	0 (0)
<b>Total (N=600)</b>	<b>301 (50.2)</b>	<b>64 (10.7)</b>	<b>235 (39.2)</b>	<b>1 (0.2)</b>	<b>597 (99.5)</b>	<b>2 (0.3)</b>	<b>4 (0.7)</b>	<b>594 (99.0)</b>	<b>2 (0.3)</b>	<b>2 (0.3)</b>	<b>596 (99.3)</b>	<b>2 (0.3)</b>

UK, Unknown or do not know

Overall 301 (50.2%) of mothers reported receipt of measles vaccine whereas 235 (39.2%) were unaware about their measles vaccination status. Within the cohorts, the percentage of mothers who reported receipt of measles vaccine was also almost 50%, with a variation from 46.0 % to 54.0%. The percentage of mothers who reported unknown status for their measles vaccination varied from 38.0% in 12 months cohort to 40.7% in 9 months cohort. This difference in the measles immunization status across four cohorts was not statistically significant ( $p>0.05$ ). Very few mothers had received vaccination against mumps, rubella and varicella.

**Table 6. Cohort wise children' disease status in past**

Birth Category	Measles n (%)		Mumps n (%)		Rubella n (%)		Varicella n (%)	
	Yes	No	Yes	No	Yes	No	Yes	No
6 months (n=150)	0 (0)	150 (100)	0 (0)	150 (100)	0 (0)	150 (100)	1(0.7)	149 (99.3)
9 months (n=150)	0 (0)	150 (100)	0 (0)	150 (100)	0 (0)	150 (100)	2 (1.3)	148 (98.7)
12 months (n=150)	5 (3.3)	145 (24.2)	0 (0)	150 (100)	0 (0)	150 (100)	4 (2.7)	146 (97.3)
15 months (n=150)	4 (2.7)	146 (24.3)	0 (0)	150 (100)	0 (0)	150 (100)	5 (3.3)	145 (96.7)
<b>Total (N=600)</b>	<b>9 (1.5)</b>	<b>591 (98.5)</b>	<b>0 (0)</b>	<b>600 (100)</b>	<b>0 (0)</b>	<b>600 (100)</b>	<b>12 (2.0)</b>	<b>588 (98.0)</b>

Overall measles disease was seen in 9 (1.5%) children. None of the children in 6 and 9 months cohort reported measles disease where as 5 toddlers from 12 months cohort and 4 toddlers from 15 months cohort reported the same. Mumps and rubella disease was not reported by any of the participants. Varicella disease was reported by 12 (2.0%) participants from all four cohorts. Although this is a cross sectional study, increasing trend in (measles and) varicella disease is observed from 6 months cohort to 15 months cohort.

**Table 7. Cohort wise sero-prevalence for Measles, Mumps, Rubella and Varicella**

Birth Category	Measles		Mumps		Rubella		Varicella	
	IgG+ n (%)	IgM+ n (%)	IgG+ n (%)	IgM+ n (%)	IgG+ n (%)	IgM+ n (%)	IgG+ n (%)	IgM+ n (%)
6 months (n=150)	7 (4.7)	0 (0)	4 (2.7)	0 (0)	16 (10.7)	0 (0)	8 (5.3)	1 (0.7)
9 months (n=150)	4 (2.7)	0 (0)	12 (8.0)	1 (0.7)	6 (4.0)	0 (0)	3 (2.0)	2 (1.3)
12 months (n=150)	111 (74)	2 (1.3)	12 (8.0)	4 (2.7)	13 (8.7)	2 (1.3)	6 (4.0)	3 (2.0)
15 months (n=150)	112 (74.7)	2 (1.3)	20 (13.3)	1 (0.7)	15 (10.0)	1 (0.7)	9 (6.0)	1 (0.7)
<b>Total (N=600)</b>	<b>234 (39.0)</b>	<b>4 (0.7)</b>	<b>48 (8.0)</b>	<b>6 (1.0)</b>	<b>50 (8.0)</b>	<b>3 (0.5)</b>	<b>26 (4.3)</b>	<b>7 (1.2)</b>



The IgG antibodies in 6 months and 9 months cohort were expected to be maternally transferred ones. For 12 and 15 months, as these children had received measles or MMR vaccine at least one month prior, the seropositivity reflected sero-conversion for measles or MMR vaccine rather than persistence of maternal antibodies. This might have been contributed by clinical or subclinical infections by MMRV.

In this study, only 7 of 150 infants (4.7%) in 6 months cohort had maternally transferred measles antibodies whereas it was only 2.7% in 9 months cohort. **Even though this was a cross sectional study, this indicates the decreasing trend. Similar trend was seen for rubella and varicella** however for mumps seropositivity was more in 9 months cohort than 6 months cohort.

**The sero-prevalence for Measles in 12 months and 15 months cohort was almost similar i.e. 74.0% and 74.7% respectively.**

The mumps seropositivity in both 9 and 12 months cohort was 12 (8.0%) but only 1 IgM positive was found in 9 months cohort and 4 in 12 months cohort. **There was increasing trend of mumps IgG positivity in 12 and 15 months. We do not expect all these antibodies to be maternally transmitted however none of the participant had clinical mumps, so there may be contribution of subclinical infection by mumps. Similar trend was observed for rubella infection.**

All the IgG antibody positive infants from 6 months and 9 months cohort were tested for presence of IgM antibodies to see for recent infection. None of them were positive for measles or rubella however 1 infant in 6 months group was IgM positive for varicella. In 9 months cohort, 1 was IgM positive for mumps and 2 were IgM positive for varicella. This number of IgM positivity is increased in the pooled data of 12 and 15 months cohorts as against pooled data of 6 and 9 months cohort.

All sero-positive titers for measles, mumps, rubella and varicella in all the four cohorts are seroprotective except 1 in 12 month's cohort for measles.

**Table 8. Gender wise sero-prevalence for Measles, Mumps, Rubella and Varicella**

Sex	Measles		Mumps		Rubella		Varicella	
	IgG+ n (%)	IgM+ n (%)	IgG+ n (%)	IgM+ n (%)	IgG+ n (%)	IgM+ n (%)	IgG+ n (%)	IgM+ n (%)
Male (n=315)	117 (37.1)	3 (19)	26 (8.3)	2 (0.6)	28 (8.9)	1 (0.3)	12 (3.8)	2 (0.6)
Female (n=285)	117 (41.5)	1 (0.4)	22 (7.7)	4 (1.4)	22 (7.7)	2 (0.7)	14 (4.9)	5 (1.8)
<b>Total (N=600)</b>	<b>234 (39)</b>	<b>4 (0.7)</b>	<b>48 (8.0)</b>	<b>6 (1.0)</b>	<b>50 (8.3)</b>	<b>3 (0.5)</b>	<b>26 (4.3)</b>	<b>7 (1.2)</b>

In the pooled data of all the four cohorts, there was variation in the sero-prevalence amongst males and females. For measles and varicella, sero-prevalence was more in females and for

mumps and rubella, it was more in males. This difference was not statistically significant (all  $p>0.05$ ).

## AGE COHORT WISE ANALYSIS

### 6 MONTHS

In 6 months cohort, out of 150 subjects, 106 (70.7%) babies were born full term and 44 (29.3%) were born preterm. Age at enrollment was from 5-7 months, with mean age of 6.0 (SD  $\pm$  0.7) months. Birth weight ranged from 0.70 kg to 4.30 kg with mean of 2.43 (SD  $\pm$  0.7) kg. Current weight of the participants ranged from 4.40 kg to 9.80 Kg with mean 6.62 (SD  $\pm$  1.0) Kg. As depicted in table 7, only 7 (4.7 %) babies were IgG sero-positive for measles at 6 months of age. We expect all these antibodies to be of maternal in origin.

**Table 9. Antibody response details in terms of gestational age**

Birth Category	Measles		Mumps		Rubella		Varicella	
	Sero +Ve n (%)	Sero -Ve n (%)	Sero +Ve n (%)	Sero -Ve n (%)	Sero +Ve n (%)	Sero -Ve n (%)	Sero +Ve n (%)	Sero -Ve n (%)
Preterm n = 44	1(2.3)	43(97.7)	2(4.5)	42(95.5)	2(4.5)	42(95.5)	1(2.3)	43(97.7)
Term n= 106	6(5.7)	100(94.3)	2(1.9)	104(98.0)	14(13.2)	92(86.8)	7(6.6)	99(93.4)
<b>Total N=150</b>	<b>7(4.7)</b>	<b>143(95.3)</b>	<b>4(2.7)</b>	<b>146(97.3)</b>	<b>16(10.7)</b>	<b>134(89.3)</b>	<b>8(5.3)</b>	<b>142(94.7)</b>

Sero-prevalence status for term and preterm cohort for measles, mumps, rubella and varicella is as shown in table 9. Percentage of participants who were born preterm had lower sero-prevalence rate for measles, rubella and varicella as compared to term population however for mumps, the seropositivity was higher in preterm than term babies. This difference in term versus preterm was not statistically significant ( $p>0.05$ ).

**Table 10. Gender wise Sero-prevalence for 6 months cohort**

Birth Category	Measles		Mumps		Rubella		Varicella	
	Sero +Ve n (%)	Sero -Ve n (%)	Sero +Ve n (%)	Sero -Ve n (%)	Sero +Ve n (%)	Sero -Ve n (%)	Sero +Ve n (%)	Sero -Ve n (%)
Male N= 87	5 (5.7)	82 (94.3)	4 (4.6)	83 (95.4)	10 (11.5)	77 (88.5)	6 (6.9)	81 (93.1)
Female N = 63	2 (3.2)	61 (96.8)	0	63 (100)	6 (9.5)	57 (90.5)	2 (3.2)	61 (96.8)
<b>Total N= 150</b>	<b>7 (4.7)</b>	<b>143 (95.3)</b>	<b>4 (2.7)</b>	<b>146 (97.3)</b>	<b>16 (10.7)</b>	<b>134 (89.3)</b>	<b>8 (5.3)</b>	<b>142 (94.7)</b>

Male to female ratio in this cohort was 1:0.7. Seropositivity is more in males for MMRV. The difference in the gender was not statistically significant ( $p>0.05$ ).

**Table 11. Antibody response details in terms of mothers' disease status in past**

Maternal Disease		Sero-prevalance	
Disease	Frequency (%)	Sero-positive (%)	Sero-negative (%)
Measles n = 150	Yes - 16 (10.7)	1 (6.3)	15 (93.7)
	No - 134 (89.3)	5 (3.7)	129 (96.3)
Mums n = 150	Yes - 1 (0.7)	0	1 (100)
	No - 149 (99.3)	3 (2.0)	146 (98.0)
Rubella n = 150	Yes - (0)	0	0
	No - 150 (100)	8 (5.3)	142 (94.7)
Varicella n = 150	Yes - 68 (45.3)	3 (4.4)	65 (95.6)
	No - 82 (54.7)	4 (4.9)	78 (95.1)

Seventy-eight (52.05%) mothers had history of either Measles, Mumps or Varicella disease. Sixteen (10.7 %) mothers reported history of measles disease out of which 1 (6.3%) mother showed transfer of antibodies however sero-prevalence was lower i.e. 3.7% in those who had not suffered from measles. But this difference of sero-prevalence was not statistically significant ( $p>0.05$ ).

One mother had history of mumps infection however the baby was sero-negative. Although none of the mother reported rubella disease, 8 (5.3%) babies had antibodies. Varicella disease was reported by 68 (45.3%) mothers but only 3 (4.4%) had IgG antibodies in them. One of these 3, had IgM antibodies who had varicella disease at 5 months of age. Fifty four percent of mothers had reported that they did not suffer from varicella disease. Sero-prevalence in these infants was 4.9% which was similar to those who mothers had given history of varicella disease.

**Table 12. Sero-prevalence details in terms of mothers' Measles vaccination status**

Measles Vaccination status n=150 (%)	Sero-prevalance	
	Sero-positive (%)	Sero-negative (%)
Vaccinated- 81 (54.0)	2 (2.5)	79 (97.5)
Unvaccinated- 11 (7.3)	1 (9.1)	10 (91.0)
Unknown status- 58 (38.7)	4 (6.9)	54 (93.1)

Almost half of the mothers, i.e. 81 (54.0%) were vaccinated against Measles but only 2 (2.5%) babies were sero-positive at 6 months. Sero-prevalence in infants of unvaccinated mothers was 9.1%. Fifty-eight (38.7%) mothers from this cohort were unaware of their Measles vaccination

status still 6.9% of infants were sero-positive.

Vaccination against rubella and varicella was minimal i.e [2 (1.3%)] and [1 (0.7%)] respectively. None of the mothers had received mumps vaccination. The infants whose mothers were vaccinated against rubella and varicella, were sero-negative.

There was no history of measles, mumps or rubella disease in any of the participant however 1 had reported varicella disease and had IgM antibodies for the same.

## 9 MONTHS

In 9 months' cohort, 115 (76.7%) babies were born full term and 35 (23.3%) were born preterm. Age at enrollment was from 8-10 months with mean age of 8.9 (SD  $\pm$  0.5) months. Birth weight ranged from 0.70 kg to 3.60 kg with mean of 2.55 (SD  $\pm$  0.7) kg. Current weight was ranging from 5.10 to 10.70 kg with mean of 7.87 (SD  $\pm$  1.14) kg.

Sero-prevalence at this age is depicted in table 7. Only 4 (2.7%) infants showed presence of maternally transferred antibodies against Measles whereas 12 (8.0%) were sero-positive for Mumps. Of these 12 Mumps IgG positive infants, one was positive for IgM too however there was no clinical history of mumps disease in the infant. Rubella seropositivity was 6 (4.0%) and Varicella was 3 (2.0%). Of these 3 Varicella IgG positive infants, 2 were IgM positive indicating recent infection.

**Table 13. Antibody response details in terms of gestational age**

Birth Category	Measles		Mumps		Rubella		Varicella	
	Sero +Ve n (%)	Sero -Ve n (%)	Sero +Ve n (%)	Sero -Ve n (%)	Sero +Ve n (%)	Sero -Ve n (%)	Sero +Ve n (%)	Sero -Ve n (%)
Preterm	2(5.7)	33(94.3)	3(8.6)	32(91.4)	2(5.7)	33(94.3)	0	35(100)
Term	2(1.7)	113(98.3)	9(7.8)	106(92.3)	4(3.5)	111(96.5)	3(2.6)	112(97.4)
<b>Total</b>	<b>4(2.7)</b>	<b>146(97.3)</b>	<b>12(8.0)</b>	<b>138(92)</b>	<b>6(4.0)</b>	<b>144(96.0)</b>	<b>3(2.0)</b>	<b>147(98.0)</b>

Sero-prevalence for measles and rubella was higher in preterm as against term infants whereas it was almost similar for Mumps. Seropositivity was not observed in preterms for Varicella. The difference in sero-prevalence in term versus preterm infants was not statistically significant ( $p > 0.05$ ).

**Table 14. Gender wise Sero-prevalence for 9 months cohort**

Birth Category	Measles		Mumps		Rubella		Varicella	
	Sero +Ve n (%)	Sero -Ve n (%)	Sero +Ve n (%)	Sero -Ve n (%)	Sero +Ve n (%)	Sero -Ve n (%)	Sero +Ve n (%)	Sero -Ve n (%)

Male n=73	1 (1.4%)	72 (98.6)	5 (6.8)	68 (93.2)	2 (2.7)	71 (97.3)	2 (2.7)	71 (97.3)
Female n =77	3 (3.9%)	74 (96.1)	7 (9.1)	70 (90.9)	4 (5.2)	73 (94.8)	1 (1.4)	76 (98.7)
<b>Total N= 150</b>	<b>4 (2.7%)</b>	<b>146 (97.3)</b>	<b>12 (8.0)</b>	<b>138 (92.0)</b>	<b>6 (4.0)</b>	<b>144 (96.0)</b>	<b>3 (2.0)</b>	<b>147 (98.0)</b>

The gender distribution was almost equal in this cohort with male female ratio of 1:0.9. Sero-prevalence was higher in females for measles, mumps and rubella whereas it was higher in males for varicella but this difference was not statistical significance ( $p>0.05$ ).

**Table 15. Antibody response details in terms of mothers' disease status in past**

Maternal Disease		Sero-prevalance	
Disease	Frequency (%)	Sero-positive (%)	Sero-negative (%)
Measles n=150	Yes - 18 (12.0)	0 (0)	18 (100)
	No - 132 (88.0)	4 (3.0)	128 (97.0)
Mumps n=150	Yes - 2 (1.3)	0 (0)	2 (100)
	No - 148 (98.7)	12 (8.1)	136 (91.1)
Rubella n=150	Yes - 0 (0)	0 (0)	0 (0)
	No - 150 (100)	6 (4.0)	144 (96.0)
Varicella n=150	Yes - 65 (43.3)	3 (4.6)	62 (95.4)
	No - 85 (56.7)	0 (0)	85 (100)

None of the infants with maternal infection with measles or mumps showed seropositivity. None of the mother had reported rubella infection. Sixty-five (43.3%) mothers had varicella disease, of which only three babies showed seropositivity for IgG. There is no statistically significant difference in sero-prevalence depending upon the history of any of MMRV disease in mothers and persistence of respective maternal antibodies in their infant at 9 months.

2 of these infants had history of varicella disease and were IgM positive. This is in line with the observation seen in six months cohort.

**Table 16. Sero-prevalence details in terms of mothers' Measles vaccination status**

Measles Vaccination status (%) n=150	Seroprevalence	
	Sero-positive (%)	Sero-negative (%)
Vaccinated- 78 (52.0)	1 (1.3)	77 (98.7)
Unvaccinated- 11 (7.3)	1 (9.1)	10 (91.0)
Unknown status- 61 (40.7)	2 (3.3)	59 (96.7)

Seventy-seven (51.3 %) mothers were vaccinated against measles with only 1 against MMR. Out of the 78 mothers who received measles vaccine, only 1(1.3%) infant showed seropositivity and for the one who had received MMR vaccine, the infant was sero-negative for all the three components. Almost 40% mothers were unaware of their measles vaccination status and only 3.3% of the infants were sero-positive. None was vaccinated against varicella.

None of the participants had history of Measles, Mumps and Rubella disease. Only 2 participants had history of Varicella disease who was IgM positive. One baby was IgM positive for mumps however there was no clinical history of mumps for this baby. This might be due to subclinical infection.

## 12 MONTHS

In 12 months cohort 127 (84.67%) babies were born full term and twenty-three (15.33%) were born preterm. Age at enrollment was from 11-13 months, mean age 12.01 (SD  $\pm$ 0.65) months. Birth weight ranged from 1.000 kg to 4.20 kg with mean of 2.63 (SD  $\pm$  0.58) kg Current weight was ranging from 6.2-12 kg with mean of 8.55 (SD  $\pm$  1.02) Kg. In this cohort 144 had received Measles vaccine and 6 had received MMR vaccine.

The sero-prevalence for MMRV for this cohort is shown in table 17.

**Table 17. Antibody response details in terms of gestational age**

Birth Category	Measles		Mumps		Rubella		Varicella	
	Sero +Ve n (%)	Sero -Ve n (%)	Sero +Ve n (%)	Sero -Ve n (%)	Sero +Ve n (%)	Sero -Ve n (%)	Sero +Ve n (%)	Sero -Ve n (%)
Preterm n=23	19 (82.6)	4 (17.4)	1 (4.3)	22 (95.7)	0 (0)	23 (100)	0 (0)	23 (100)
Term n=127	92 (72.4)	35 (27.6)	11 (8.7)	116 (91.3)	13 (10.2)	114 (89.8)	6 (4.7)	121 (95.3)
<b>Total N=127</b>	<b>111 (74.0)</b>	<b>39 (26.0)</b>	<b>12 (8.0)</b>	<b>13 8(92.0)</b>	<b>13 3(8.7)</b>	<b>137 (91.3)</b>	<b>6 (4.0)</b>	<b>144 (96.0)</b>

In this cohort, 23 (15.3%) subjects were born preterm where as 127 (84.7%) were born term. The sero-prevalence for measles was reflecting the seroconversion to the Measles vaccine. It was higher in preterms than the toddlers who were born at term. This difference was not statistically significant ( $p > 0.05$ ).

Sero-prevalence for mumps in toddlers who were born at term was higher than preterm but the difference was not statistically significant ( $p > 0.05$ ). None of the preterms were sero-positive for rubella and varicella.

**Table 18. Gender wise Sero-prevalence**

Gender	Measles		Mumps		Rubella		Varicella	
	Sero +Ve n (%)	Sero -Ve n (%)	Sero +Ve n (%)	Sero -Ve n (%)	Sero +Ve n (%)	Sero -Ve n (%)	Sero +Ve n (%)	Sero -Ve n (%)
Male n =76	54 (71.1)	22 (28.9)	6 (7.9)	70 (92.1)	6 (7.9)	70 (92.1)	0 (0)	76 (100)
Female n = 74	57 (77.0)	17 (23.0)	6 (8.1)	68 (91.9)	7 (9.5)	67 (90.5)	6 (8.1)	68 (91.9)
<b>Total N = 150</b>	<b>111 (74.0)</b>	<b>39 (26.0)</b>	<b>12 (8.0)</b>	<b>138 (92.0)</b>	<b>13 (8.7)</b>	<b>137 (91.3)</b>	<b>6 (4.0)</b>	<b>144 (96.0)</b>

Male to female ratio in this cohort was 1:0.9. Seroconversion after measles vaccine in female was higher than males however the difference was not statistically significant ( $p > 0.05$ ). Sero-prevalence for mumps and rubella was almost similar in both the genders however seropositivity for varicella was not seen in any male participant ( $p < 0.05$ ).

**Table 19. Antibody response details in terms of mothers' disease status in past**

Maternal Disease		Seroprevalence	
Disease	Frequency (%)	Sero-positive (%)	Sero-negative (%)
Mums n = 150	Yes -0 (0)	0	0
	No -150 (100)	7(4.7)	143(95.3)
Rubella n = 150	Yes - 0 (0)	0	0
	No - 150 (100)	7(4.7)	143(95.3)
Varicella n = 150	Yes - 61 (40.7)	3(4.9)	58(95.1)
	No - 89 (59.3)	3(3.4)	86(96.6)

In this cohort 14 mothers had history of measles disease. It is difficult to comment on presence of maternal antibodies in their children as all of them had received Measles vaccine. None of the mother gave history of mumps or rubella. Sixty-one (40.7%) mothers had given history of varicella infection of which toddlers of only 3 were sero-positive. Out of these 3 toddlers, 1 was IgM positive. In the toddlers, whose mothers had not reported varicella disease, 3 were IgG positive. Out of these, 2 also had IgM antibodies in them.

Seventy-three (48.67%) mothers were vaccinated against measles and one (0.67%) against varicella. Vaccination status of 57 (38%) mothers was unknown. Mother who gave history of varicella vaccination (n=1), her baby was sero-negative.

Nine infants had history of measles or varicella disease whereas none had history of mumps or rubella. Five (3.3%) infants had history of measles of which two infants were IgM positive and

three were IgG positive. This IgG positive status may be because of measles vaccination or the disease.

Four infants had history of varicella disease of which three were positive for IgM and IgG both. The remaining one was only IgG positive. Four infants were IgM positive for mumps but none had past history of infection. All of them might have had subclinical infection.

Two infants were rubella IgM positive. One infant had history of maculopapular rash few months prior which was reported as Measles by the mother. However, the infant was sero-negative for measles. Probably mother had misinterpreted the maculopapular rash as measles instead of rubella.

Of the 150 participants who were vaccinated against measles either as stand alone or MMR, 111 (74.0%) were seroconverted. Of these 150 participants, 6 had received MMR vaccine at least one month prior enrollment. All six were seroconverted for mumps and rubella however one was not converted for measles.

### 15 MONTHS

In 15 months cohort 130 (86.67%) babies were born full term and 20 (13.33%) were born preterm. Age at enrollment was from 14 to 16 months with mean age of 14.9 (SD  $\pm$ 0.66) months. Birth weight ranged from 0.90 kg to 3.70 kg with mean of 2.63 (SD  $\pm$  0.58) Kg. Current weight was ranging from 5.60 to 12.40 kg with mean 9.26 (SD  $\pm$  1.21) Kg.

The sero-prevalence for MMRV is shown in table 7. Of the 150 toddlers, 3 had received MMR vaccine and rest had received measles vaccine at least one month prior to enrollment.

**Table 20. Antibody response details in terms of gestational age**

Birth Category	Measles		Mumps		Rubella		Varicella	
	Sero +Ve n (%)	Sero -Ve n (%)	Sero +Ve n (%)	Sero -Ve n (%)	Sero +Ve n (%)	Sero -Ve n (%)	Sero +Ve n (%)	Sero -Ve n (%)
Preterm n = 20	18(90.0)	2(10)	2(10)	18(90)	2(10)	18(90)	1(5)	19(95)
Term n = 130	94(72.3)	36(27.7)	18(13.8)	112(86.2)	13(10)	117(90)	8(6.2)	122(93.8)
<b>Total N = 150</b>	<b>112(74.7)</b>	<b>38(25.3)</b>	<b>20(13.3)</b>	<b>130(86.7)</b>	<b>15(10)</b>	<b>135(90)</b>	<b>9(6)</b>	<b>141(94)</b>

The seroconversion for measles in preterms was higher than those born at term however this difference was not statistically significant ( $p > 0.05$ ). Sero-prevalence was similar for Mumps, Rubella and Varicella in preterms and those born at term.



**Table 21. Gender wise Sero-prevalence for 15 months cohort**

Gender	Measles		Mumps		Rubella		Varicella	
	Sero +Ve n (%)	Sero -Ve n (%)	Sero +Ve n (%)	Sero -Ve n (%)	Sero +Ve n (%)	Sero -Ve n (%)	Sero +Ve n (%)	Sero -Ve n (%)
Male n = 79	57 (72.2)	22 (27.8)	11 (13.9)	68 (86.1)	10 (12.7)	69 (87.3)	4 (5.1)	75 (94.9)
Female n = 71	55 (77.5)	16 (22.5)	9 (12.7)	62 (87.3)	5 (7.0)	66 (93.0)	5 (7.0)	66 (93.0)
<b>Total N = 150</b>	<b>112 (74.7)</b>	<b>38 (25.3)</b>	<b>20 (13.3)</b>	<b>130 (86.7)</b>	<b>15 (10.0)</b>	<b>135 (90.0)</b>	<b>9 (6.0)</b>	<b>141 (94.0)</b>

Seroconversion after measles vaccination was higher in females but this difference was not statistically significant. Sero-prevalence in males and females was almost similar for mumps and varicella however it was more in males for rubella. This difference was not statistically significant.

**Table 22. Antibody response details in terms of mothers' infection status**

Maternal Disease		Sero-prevalance	
Disease	Frequency (%)	Sero-positive (%)	Sero-negative (%)
Mumps n = 150	Yes - 2 (1.3)	1 (50.0)	1 (50.0)
	No - 148 (98.7)	13 (8.8)	135 (91.2)
Rubella n = 150	Yes - 0 (0)	0 (0)	0 (0)
	No - 150 (100)	7 (4.7)	143 (95.3)
Varicella n = 150	Yes - 62 (41.3)	5 (8.1)	57 (91.9)
	No - 88 (58.7)	4 (4.5)	84 (95.4)

Since all these participants have received measles vaccine, presence of maternal antibodies cannot be commented. Overall 67 (44.7%) mothers had history of either measles, mumps or varicella disease; 12 measles, 2 mumps and 62 varicella infection. Of 62 (41.3%) varicella infected mothers, only five toddlers had IgG antibodies. Of these 5 toddlers, 4 had history of varicella disease. None of the mothers had rubella infection.

Sixty-nine (46%) mothers were vaccinated against measles and one (0.67 %) against rubella. Vaccination status of 59 (39.33 %) mothers was unknown. Toddler of the mother who was vaccinated against rubella was sero-negative.

Four infants had history of measles infection. All of them were only IgG positive however it is difficult to attribute to infection or vaccination. Two infants were measles IgM positive but none had clinical history of measles. It may be the measles subclinical infection

Sero-prevalence of mumps was maximum in this cohort as compared to the others. Of the 20 toddlers who were IgG positive, 2 had received MMR vaccine and 1 had IgM antibodies without history of mumps disease. For rest of the 17 sero-positives, it is difficult to comment how many had maternally transmitted antibodies. None of the toddlers had history of rubella infection, but 1 was found to have IgM antibodies against it. Five toddlers had history of varicella disease of which all five had IgG antibodies and one child had IgM antibodies too.

Of the 150 toddlers who received measles vaccine, 112 (74.7%) were seroconverted. Of the three toddlers who received MMR vaccine, all sero-converted to Measles and 2 seroconverted to mumps and rubella.

## **DISCUSSION**

### Persistence of Maternal Antibodies

In our study, 4.7% of infants in 6 months cohort had maternally transferred measles antibodies whereas it was only 2.7% in 9 months' cohort. Although the 6 months and 9 months cohort are 2 independent groups, there was a decreasing trend for measles, rubella and varicella sero-prevalence. However, there was rise in sero-prevalence against mumps in 9 months cohort compared to 6 months. This may be persistence of maternal antibodies or may be subclinical infection in infants.

A cross sectional study was conducted to determine prevalence of placentally transmitted antibodies for measles in infants 3 to 11 months old in an urban slum community in Madras in 1990 by Deivanayagam N et al. 376 children were included and were tested for Hemagglutination Inhibition (HI) antibodies by standard microtitration technique. Titres greater than or equal to 1:8 was considered as protective. The proportion of children with immune level and the Geometric Mean Titres (GMT) declined to the least by 5 months. There is no significant difference in the waning pattern between different age groups, sex and nutritional status.

In the prospective longitudinal study (Sood D K et al. 1995) conducted in India, 19-20% infants of 6-7 months showed persistence of measles antibodies which decreased to 11-13% after 7 months of age.

Maternal measles antibody decay in rural Bangladeshi infants was studied in 1998 by de Francisco A et al and found that antibody levels decreased rapidly in infants with increasing age. By the age of 5 months, 67% (28/42) infants had practically no protective antibody left. Only 12% infants at 5 months of age, and 5% at 8 months had protective antibodies. In our study lower sero-prevalence was observed at 6 months and 9 months of age.

In 1999, study of decay of maternally derived antibodies to measles, mumps, and rubella viruses in Swiss infants showed that only 5 of 58 (8.6%; 95% CI, 2.9 to 19.0) infants were antibody positive for the measles virus by 9 to 12 months of age and for mumps and rubella seropositivity was 3 of 58 (5.2%; 95% CI, 1.1 to 14.4) infants.

In a study conducted by Işik N et al in 2003, 5.2% of infants were sero-positive for measles at 9 months of age.

Seroprevalence study of measles and natural rubella antibodies among children in Bangui, Central African Republic (Manirakiza A et al. 2011) reported that only 14.8% of infants aged 0-3 months had maternally derived measles IgG antibodies and antibodies were absent in all infants aged 4-8 months. This study conducted in recent years shows early decay in maternal antibodies against measles which is consistent with our study.

In a multicenter study for MMRV vaccine conducted by Lalwani S et al in India (2015) baseline seropositivity rate for measles, mumps and rubella was < 2.7% at 9 months of age. Similar rates were seen for measles in our study however sero-prevalence for mumps and rubella were higher.

### Gestational Age

Only 2.3% of preterm as against 5.7% of term babies had measles antibodies at 6 months of age in our study. Similar findings are observed in a prospective longitudinal study done by Chopra GS et al in Calcutta, India (2001) where he found that the seropositivity for measles at 5 months in preterm babies was 2%. In a study conducted by Rau ATK et al. in Delhi, India (2002), 97% of preterms versus 51 % term babies were sero-negative at 5 months.

### Maternal Infection and Vaccination

Maternally derived measles immunity in children of naturally infected and vaccinated mothers was studied by Jenks PJ et al in 1988. Lower measles antibody titres were observed in children whose mothers had been vaccinated, and these decayed to undetectable values earlier than in children whose mothers had not been vaccinated, and were assumed to have had natural measles.

Chui LW et al in 1991 studied measles virus specific antibody in infants from 2 to 12 months of age in a highly-vaccinated society and found that 93% of the infants were without detectable neutralizing antibody (NT liter  $\leq 10$ ) at 6 months of age, and by the end of the first year of life 100% had no neutralizing antibody. In our study, only 2.5 % of infants from 6 month cohort and 1.3% from 9 month cohort had antibodies whose mothers had received measles vaccination.

Passive immunity against measles during the first 8 months of life of infants born to vaccinated mothers or to mothers who sustained measles was studied by De Serres G et al in 1997. They found that all neonates had antibodies at birth and 88% at 4 months. At 8 months, 49% had antibodies in the natural measles infection group and 15% in the vaccine group ( $P < 0.001$ ). The geometric mean titers were significantly lower in the vaccine group than in the measles group.

In the prospective longitudinal study done from 36 weeks gestational age (antenatal) till 12 months of age (post natal) done by Leuridan et al in 2010 showed that at 6 months of age,

more than 99% of infants of vaccinated women and 95% of infants of naturally immune women had lost maternal antibodies. In our study seroprevalence at 6 months in infants of vaccinated mothers was 2.5% as against 6.3% whose mothers were naturally infected.

#### Seroconversion after Measles Vaccination in Infants/Toddlers

All the children from 12 months and 15 months cohort had received measles containing vaccine at least one month prior enrollment. So, the age of vaccination varied from 9 months to 15 months. Seroconversion rate at 12 months was 74% and at 15 months was 74.7% in our study.

Seroconversion rate one month after measles vaccination at 9 months of age was 77.6% in a study conducted by Isik N in Istanbul in 2003 where as it was found to be 93.06% in the study conducted by Gunawardena S from Colombo (2000).

Immune response to MMR vaccine at 9, 12 & 15 months of age was studied in India by Singh R et al (1994). Seroconversion to measles was 80% at 9 months of age as compared to > 95% at 12 or 15 months. Seroconversion to Rubella was > 92% at 9, 12 and 15 months. The seroconversion rate for mumps was also higher (92%) at 12 months than at 9 months (75%).

Seroconversion after MMR vaccination was studied in Minneapolis and St. Paul by Redd S C in 2004. They observed that seroconversion rate to measles was 87%, 95%, 98% if vaccinated at 9 months, 12 months and 15 months respectively. Immunogenicity following combined MMRV vaccine was studied in healthy Indian infants by Lalwani S et al in 2015. The seroconversion rates ranged from 87.5% to 93.2% for measles, 83.3% to 86.1% for mumps and 98.7% to 100% for rubella after dose 1 at 9 months of age.

Seroconversion rate observed in our study was lower than the rate observed in the studies mentioned above except the one conducted in Istanbul.

In studies conducted in Northern India in 2003 (Chakrawarti A et al. and Yadav S et al.), mumps susceptibility rates in 9-12 months and 15-18 months' age group were 80% and 70% respectively. However, in the current study, 92% of the children of 9 months and 12 months cohort was susceptible for mumps.

Prevalence of Anti-Varicella-Zoster Virus Antibodies in French Infants under 15 Months of Age was studied by Piquier D et al. 83% in infants between birth and 3 months had antibodies above threshold level which decreased to 29.5% and 1.1% in infants 3 to 6 months and 6- to 9-month category respectively. In the 9- to 12-month and 12- to 15-month age categories, this proportion increased slightly, to 3.5% and 2.2%, respectively. In infants, less than 6 months, antibody titers were significantly higher when the mother reported a clinical history of varicella (64.8% versus 33.3%;  $P < 0.038$ ) but no such difference was observed in infants above the age of 6 months. In our study the seroprevalence in 6 months cohort was 5.3% and that of 9 months cohort was 2.0%. Similar to this study the seroprevalence increased to 4% and 6% in 12 and 15 months cohort.

Base line seropositivity for varicella in an MMRV vaccine study by Lalwani S et al in 2015 was varying from 2.7% to 8.3% in different groups at 9 months. (7.4% in the MMRV/MMRV group,

8.3% in the MMR/MMRV group and 2.7% in the MMR/MMR+V group).

Placental transfer and decay of varicella-zoster virus antibodies in preterm infants was studied in, Israel (2000) by Linder N and observed that preterm infants of gestational age  $\leq 28$  weeks had significantly lower positive cord antibody (25%) as compared to Preterm 29 to 35 weeks (95%) and term neonates (95%) ( $P < .001$  for each). The transfer of maternal antibodies to term infants was significantly greater than to the 29- to 35-week preterm infants ( $P = .01$ ). All preterm infants were sero-negative, and the geometric mean titer in both groups declined to undetectable levels at 6 months of age.

Despite mothers having varicella disease, there is very minimal transfer of maternal antibodies which persist till 6 or 9 months of age of the infant. This is probably related to the age at which the mother had the infection.

## **SUMMARY AND CONCLUSION**

This study was conducted as a cross sectional pilot study in a tertiary care hospital attached to medical college. 150 participants were enrolled in each of the four cohorts; 6, 9, 12 and 15 months.

Baseline characteristics like gender, birth weight, gestational age, maternal infection rate and maternal vaccination rate were similar in all cohorts.

In this study, only 7 of 150 infants (4.7%) in 6 months cohort had maternally transferred measles antibodies whereas it was only 2.7% in 9 months cohort. Even though this was a cross sectional study, this indicates the decreasing trend. Similar trend was seen for rubella and varicella however for mumps seropositivity was more in 9 months cohort than 6 months cohort.

The sero-conversion for Measles in 12 months and 15 months cohort was almost similar i.e. 74.0% and 74.7% respectively.

All seropositive titers for measles, mumps, rubella and varicella in all the four cohorts are seroprotective except 1 in 12 month's cohort for measles.

There was no significant difference in seroprevalence in 6 and 9 months cohort and seroconversion in 12 and 15 months cohort for measles according to gestational age and gender.

Although percentage of mothers giving history of measles and varicella disease were similar in all the cohorts, the reliability of this history is questionable. The difference in maternally transmitted antibodies in 6 and 9 months cohort was not statistically different in allegedly diseased and non diseased mothers. Difference could not be found according to maternal vaccination status.

Mumps seroprevalence was only 2.7% in 6 months cohort. It was 8.0% in both 9 and 12 months cohorts and increased to 13.3% in 15 months cohort. There were few participants who were IgM positive without clinical history of mumps. So there may be contribution of subclinical infection by mumps.

None of the mother or participant had reported rubella disease. Although all the four cohorts studied were independent, the trend for rubella sero-prevalence was decreasing till 9 months and then showed increasing trend for the cohort of 12 and 15 months. This increase may be due to subclinical infection.

Despite high rate of natural infection by Varicella in mothers (ranging from 40.7 to 45.3%), the sero-prevalence was minimal at various ages. This may be due to natural infection at younger age of the mother. Seropositivity for varicella was not seen in any male participant in 12 months cohort ( $p < 0.05$ ).

## **LIMITATIONS AND RECOMMENDATIONS**

All these observations are from a cross sectional pilot study conducted in various age groups at only one hospital based setting, the findings may not be generalizable to other populations and settings. As vaccination and infection history (mother and child) was a self-reported the predictors reported in this study (if any) need to be taken with caution. A large multi-centric study, preferably a longitudinal one, is required to confirm the observations which might help in making policy decision regarding early vaccination against MMRV.

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