

Long-term Seroprotection Rates Following Second Dose of Measles as MMR Vaccine at 15 months in Indian Children

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Objective: To find out seropositivity rates at 4-6 and 9-12 years of age; among those who received one-dose measles at 9 months and one-dose MMR at 15 months of age. **Methods:** 80 healthy children (53 males) at 4-6 or 9-12 years of age, attending outpatient department for vaccination were enrolled. Antibody titers were estimated using commercially available quantitative-IgG ELISA kits. **Results:** The seropositivity rates against measles, mumps, rubella were 80% (40/50), 86% (43/50), and 96% (48/50), respectively at 4-6 years, and 83.3% (25/30), 96.7% (29/30) and 96.7% (29/30), respectively at 9-12 years of age. **Conclusion:** Single dose of rubella vaccine seems to provide adequate long-term protection; however, measles vaccine requires more doses for similar protection.

Keywords: Antibody, Immunization, Measles-Mumps-Rubella vaccine, Seropositivity.

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Measles vaccine administered at 9-12 months of age is a part of National immunization program (NIP) of India [1]. Second dose of measles vaccine at 15-24 months became a part of this NIP in 2010. In compliance with WHO/SAGE recommendations about measles and rubella elimination, Government of India (GOI) plans to include Measles-Rubella (MR) vaccine in a two-dose schedule (9-12 and 15-24 months) [2,3].

Indian Academy of Pediatrics (IAP) has been recommending MMR vaccine since many years, initially in 2-dose schedule and now 3-dose schedule (9-12, 15-24 and 5 years) [4,5]. There is limited published literature from our country to support many of these recommendations [6]. In view of paucity of data regarding need for 2nd dose of MMR vaccine for Indian children, we planned this study to find out seropositivity rates – at 4-6 and 9-12 years of age – among those who received one-dose measles at 9 months of age and one-dose MMR at 15 months of age.

METHODS

This seroprevalence study was carried out in the outpatient department (OPD) of a tertiary-care referral hospital in Chandigarh, Northern India over a period of one year (April 2013 – March 2014). Ethical clearance was obtained from Institute ethics committee before commencement of the study. Consecutive children at either 4-6 or 9-12 years of age, attending pediatric OPD

for vaccination were screened. Only those having documentary evidence (immunization card) of having received measles vaccine at 9-12 months and MMR vaccine at 15-18 months were included. An informed written consent from their parents was obtained. Children receiving prolonged steroid therapy (>4 weeks) in past six months, those having a history of administration of blood or immunoglobulin in last three months, and those diagnosed with malignancy or immunodeficiency were excluded from the study. The primary objective was to find out the percentage of children having antibodies against measles, mumps, and rubella in seroprotective range; and secondary objective was to find out geometric mean concentration (GMC) of these IgG antibodies.

A detailed history regarding previous vaccinations and other relevant information was elicited from their parents using a pre-structured proforma, and 2-3 mL of venous blood was drawn from the enrolled subject by venipuncture. The antibody titers were estimated using ELISA IgG quantitative kits for measles (VIRO-IMMUN Labor-Diagnostika GmbH, Germany), mumps (IMMUNOLAB GmbH, Kassel, Germany) and rubella (DIA.PRO Diagnostic Biprobes SRL, Milano, Italy). Antibody levels above 0.3 IU/mL for measles, above 12 U/mL for mumps, and above 10 IU/mL for rubella were considered seropositive, as per manufacturer's recommendations [7-9]. The results of the study and their antibody titers against measles, mumps, and rubella, were informed to enrolled children and their parents. One

additional dose of MMR vaccine was advised for children whose titers were below the seroprotective range.

RESULTS

Out of total 80 children enrolled, 50 (37 boys) were in group-1 (4-6 years) and 30 (16 boys) in group-2 (9-12 years). The mean age at recruitment in group-1 was 61 months, and in group-2 was 125 months.

Majority of study children in both groups had antibodies in seroprotective range for all three disease (**Table I**). Geometric mean concentration (GMC) of IgG antibodies (IU/mL) increased from those seen at 4-6 yrs than at 9-12 yrs age for measles, mumps and rubella.

DISCUSSION

Our study showed seropositivity rates against measles, mumps, rubella to be 80%, 86%, 96% at 4-6 years and 83.3%, 96.7%, 96.7% at 9-12 years of age, respectively among studied population. In a similar study from Delhi, Gomber, *et al.* [10] reported seropositivity of 21.4%, 87.4%, 75.7%, respectively at age of 4-6 years, after receiving one dose MMR vaccine at 15 months of age. Raut, *et al.* [11] showed these titers to be 83%, 95%, and 100%, respectively, after six years of one dose of MMR in children aged 5-10 years [11]. Similar studies from other developing countries have seropositivity rates varied from 76-92%, 66-75%, 56-90%, respectively [12-15]. We did not come across studies reporting titers at the age of 10 years.

The number of susceptible subjects among population should be kept <5% to achieve and maintain measles control [9]. In our study, measles seroprevalence rates acquired by two dose measles containing vaccine (9 and 15 months) were lower than expected (80% and 83.3%). If the findings of suboptimal response remain consistent in other studies too, we may require an additional dose of measles-containing vaccine at a later age to make measles elimination possible. The current MR campaign could help in filling this immunity gap. The percentage seropositivity for Rubella in our study indicates good amount of protection offered by MMR when given at 15 months of age; the quantum of this protection during child-bearing age will decide whether there is a need for repeat MMR.

TABLE I ANTIBODIES (IgG) AGAINST MEASLES, MUMPS AND RUBELLA IN STUDY CHILDREN

| Antibody type | Children screened at age | |
|-------------------------|--------------------------|--------------------|
| | 4-6 y, n=50 | 9-12 y, n=30 |
| <i>Measles</i> | | |
| Seropositivity, no. (%) | 40 (80) | 25 (83.3) |
| GMC (IU/mL) 95% CI | 0.63 (0.46, 0.85) | 0.75 (0.49, 1.16) |
| <i>Mumps</i> | | |
| Seropositivity, no. (%) | 43 (86) | 29 (96.7) |
| GMC (IU/mL) 95% CI | 84.6 (59.0-121.4) | 114.6 (84.5-155.3) |
| <i>Rubella</i> | | |
| Seropositivity, no. (%) | 48 (96) | 29 (96.7) |
| GMC (IU/mL) 95% CI | 79.0 (59.6-104.6) | 88.4 (65.3-119.5) |

GMC: Geometric mean concentration.

The results of our study have to be viewed in context of its limitations. Our sample was small, and can be considered as a pilot to plan larger population-based studies. It was a hospital-based study, and it may not reflect the situation in communities. The results of our study are preliminary, but indicate that a single dose of MMR vaccine provide good seropositivity results against rubella till 10 years of age. However, a seropositivity rate against measles antibodies is low despite two doses of the vaccine. Similarly, immunity against mumps also may have to be boosted in older children.

Contributors: SV, HP, NS: conceptualization of study; HP collected the data; HP,SV,BB: were involved in management of cases; AR: provided the laboratory support for detailed investigation of cases; SV: monitored and reviewed the data periodically; SV, HP, BB: reviewed the literature and drafted the manuscript; All authors approved the final draft of manuscript.

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REFERENCES

1. John TJ. The role of Indian Academy of Pediatrics in the Expanded Program of Immunization. *Indian Pediatr.* 1985;22:91-5.
2. Thapa A, Khanal S, Sharapov U, Swezy V, Sedai T, Dabbagh A, *et al.* Progress towards measles elimination-South-East Asia Region 2003-2013. *MMWR Morb Mortal Wkly Rep.* 2015;64:613-7.
3. WHO. Measles Vaccine: WHO position Paper. *Wkly Epidemiol Rec.* 2009; 35: 84: 349-60.

WHAT THIS STUDY ADDS?

- Single dose of Rubella vaccine provides good long-term (over 5-10 year) protection.
- Measles vaccine requires more doses for equivalent protection.

4. Vashishtha VM, Yewale VN, Bansal CP, Mehta P. IAP perspectives on Measles and Rubella Elimination Strategies. *Indian Pediatr.* 2014;51:719-22.
 5. Vashishtha VM, Choudhury P, Kalra A, Bose A, Thacker N, Yewale VN, *et al.* Indian Academy of Pediatrics (IAP) Recommended Immunization Schedule for children aged 0 through 18 years – India, 2014 and updates on Immunization. *Indian Pediatr.* 2014; 51: 785-800.
 6. Verma S. IAP Immunization timetable 2012 clarifications. *Indian Pediatr.* 2012;49:997-8.
 7. WHO. Measles Virus Vaccine: WHO Position Paper. *Wkly Epidemiol Rec.* 2009;84:349-360.
 8. World Health Organization. The Immunological Basis for Immunization Series. Module 7, 8, 9: Measles, Mumps, Rubella updates 2009.
 9. Job JS, John TJ, Joseph A. Antibody response to measles immunization in India. *Bull World Health Organ.* 1984;62:737-41.
 10. Gomber S, Arora SK, Das S, Ramachandran VG. Immune response to second dose of MMR vaccine in Indian children. *Indian J Med Res.* 2011;134:302-6.
 11. Raut SK, Kulkarni PS, Phadke MA, Jadhav SS, Kapre SV, Dhere RM, *et al.* Persistence of antibodies induced by measles-mumps-rubella vaccine in children in India. *Clin Vaccine Immunol.* 2007;14:1370-1.
 12. Saffar MJ, Fathpour GR, Parsaei MR, Ajami A, Khalilian AR, Shojaei J, *et al.* Measles-Mumps-Rubella revaccination; 18 months vs 4-6 years of age: Potential impacts of schedule changes. *J Trop Pediatr.* 2011;57:347-51.
 13. Pebody RG, Gay NJ, Hesketh LM, Vyse A, Morgan-Capner P, Brown DW, *et al.* Immunogenicity of second dose measles-mumps-rubella (MMR) vaccine and implications for serosurveillance. *Vaccine.* 2002;20:1134-40.
 14. Rager-Zisman B, Bazarsky E, Skibin A, Chammey S, Belmaker I, Shai I, *et al.* The effect of measles-mumps-rubella (MMR) immunization on the immune response of previously immunized primary school children. *Vaccine.* 2003;21:2580-8.
 15. Johnson CE, Kumar ML, Whitwell JK, Staehle BO, Rome LP, Dinakar C, *et al.* Antibody persistence after primary measles-mumps-rubella vaccine and response to a second dose given at four to six vs. eleven to thirteen years. *Pediatr Infect Dis J.* 1996;15:687-92.
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