RESEARCH BRIEF

Long-term Seroprotection Rates Following One-dose Measles (9-month) and One-dose MMR Vaccination (15 months) in Indian Children

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ABSTRACT

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, ELISA, Immunization, Measles-Mumps-Rubella vaccine, Seropositivity*

INTRODUCTION

Measles vaccine is a part of National immunization programme (NIP) of India since 1985; administered at 9-12 months of age [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 into NIP in 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]. Recommendations may not be enough to bring changes in practice; it is important to provide local epidemiological data supporting these recommendations. 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 cross-sectional, observational study was carried out in 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, rubella in seroprotective range at 4-6 years and 9-12 years of age; 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 milliliters 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 result 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.

Forty out of 50 (80%) children at 4-6 years (group-1) and 25 out of 30 (83.3%) at 9-11 years (group-2) had antibodies in seroprotective range for measles antibodies, as per manufacturer's recommendations. For mumps, it was 43 out of 50 (86%) in group-1 and 29 out of 30 (96.7%) in group-2; and for rubella it was 48 out of 50 (96%) in group-1 and 29 out of 30 *i.e.* (96.7%) in group-2 (***Table* I**). Geometric mean concentration (GMC) of IgG antibodies (IU/mL) rose from 4-6 yrs to 9-12 yrs for measles, mumps and rubella 0.63 to 0.75, 84.6 to 114.6 and 79.0 to 88.4, respectively.

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 with other studies too; we may require an additional dose of measles-containing vaccine at a later age to make measles elimination possible. Currently undergoing 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 childbearing age group will decide whether there is a need for repeat MMR.

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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WHAT THIS STUDY ADDS?

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

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TABLE I SEROPOSITIVITY RATE AND GEOMETRIC MEAN CONCENTRATIONS (GMC) OF ANTIBODIES (IgG) AGAINST MEASLES, MUMPS RUBELLA IN STUDY CHILDREN

Antibody types	*Group I** *N=50*	*Group 2*[#] *N=30*
Measles		
Seropositivity, no. (%)	40 (80)	25 (83.3)
GMC (IU/mL) with 95% CI	0.63 (0.46, 0.85)	0.75 (0.49, 1.16)
Mumps		
Seropositivity, no. (%)	43 (86)	29 (96.7)
GMC (IU/mL) with 95% CI	84.6 (59.0-121.4)	114.6 (84.5-155.3)
Rubella		
Seropositivity, no. (%)	48 (96)	29 (96.7)
GMC (IU/mL) with 95% CI	79.0 (59.6-104.6)	88.4 (65.3-119.5)

**Group-1= Children screened at age of 4-6 years; [#]Group-2=Children screened at age of 9-12 years*