

Prevalence of Maternal Measles Antibody and Its Associated Factors among Infants in Coastal Karnataka, India

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Abstract

Background: The current recommendation in India to commence first dose of measles immunization is at 9 months of age. The effectiveness of measles vaccination is greatly impacted by the level of maternal measles antibody (MMA) during infancy. **Objectives:** To find the prevalence of MMA and to study the maternal and infant factors associated with persistence of MMA among the infants in a Indian rural community. **Methodology:** Dried blood spot sample was collected before vaccination among infants aged 9 months and above when they came for first dose of measles vaccine to assess measles-specific maternal IgG antibody titers by enzyme immunoassay. Maternal and child factors influencing persistence of MMA were collected by interviewing the mothers. Association between various factors affecting seropositivity was tested using univariate logistic regression analysis and strength of association is reported as risk ratio with 95% confidence interval. **Results:** Based on the qualitative estimation among all the recruited children (250) in the study, 4 (1.6%) infants showed the presence of MMA whereas 25 (10%) of children had MMA on quantitative estimation. The effect of maternal factors, child nutrition, and sociodemographic factors on the presence of MMA was not found to be statistically significant. **Conclusion:** The prevalence of persistent MMA (IgG titer ≥ 200 mIU/ml) among the infants aged 9–12 months was 10%. The choice of vaccinating infants at the end of 9 months for the first dose of measles vaccine is justified as the remaining (90%) of infants were susceptible for measles infection at this age.

Keywords: Infants, maternal antibodies, measles, persistence, prevalence, vaccine

INTRODUCTION

Measles, one of the most contagious viral diseases, affected almost every child before the widespread use of the measles vaccine. About six million measles-related deaths were estimated to occur globally each year before the use of the live attenuated measles vaccine, which was licensed in 1963.^[1] Although measles deaths in industrialized countries are rare, measles is often fatal in developing countries with increased risk of deaths for children under 5 years of age, those living in overcrowded conditions, those who are malnourished (especially with Vitamin A deficiency), and those with immunological disorders, such as advanced HIV infection.^[2,3] India introduced a second dose of measles through routine immunization as recommended by the WHO^[4] at 18 months of age in 2010 in addition to first dose which is given at the end of 9 months of age since 1985.

The effectiveness of vaccination against measles is greatly impacted by the level of maternal antibody

to measles virus (MMA) during infancy. Maternal antibodies interfere with immune response^[5-7] and antibody production.^[8] Nutritional status of pregnant mother,^[9] socioeconomic status,^[10] race and ethnicity,^[11-13] age, parity,^[14,15] and rate of decay of maternal antibody after birth^[16-18] are some of the known factors influencing MMA levels in infants. While the recommended age for the first dose of measles in developed countries is 15 months, the choice of vaccination at 9 months in India was to balance between the need for early protection and the advantage of delaying it for best vaccine efficacy.^[6,7,19]

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Therefore, estimation of MMA is important to determine the effectiveness of vaccination against measles. This study was conducted to find out the prevalence of MMA and to study the maternal and infant factors associated with persistence of MMA among the infants in a rural community in India.

METHODOLOGY

A cross-sectional study was conducted at the six Rural Maternity and Child Welfare (RMCW) homes in the study area which covers a population of 50,000 living in 8684 families spread out in 14 villages. All apparently healthy children <1 year of age coming to the RMCW homes for the first dose of measles vaccination were included in the study. Approval for the study was obtained from the Institutional Ethics Committee (IEC/60/2012-13).

Based on an Indian study^[18] which found that 5%–10% of 9–11-month-old infants had persistent MMA, the sample size was calculated using the formula $n = (Z^2pq)/d^2$; with absolute precision as 4% and allowing 15% nonresponse, the sample size was 250. Children who were appropriately immunized for age, permanent residents of the area, and consenting parents of eligible children were included. Children with mental retardation/apparent physical deformities interfering with anthropometric measurements and children of adopted parents were excluded.

Children were recruited as and when they came for immunization between January and December 2013, and personal interview was conducted with each mother with a pretested semistructured questionnaire. Variables such as name, age, sex, birth order, birth weight, blood group, antenatal and perinatal history, age at pregnancy, neonatal history, gestational age at delivery, mode of delivery, history of infection with measles, duration of breast feeding, age at weaning, and complementary foods were recorded using the questionnaire, after verifying with their antenatal and birth records. Anthropometric measurements such as length and

weight were recorded using standard weighing scales. Under sterile conditions, dried blood spot (DBS) sample was collected using Whatman 903 filter paper imprinted with a circle of diameter 12.5 mm. The dried blood spot was collected in a separate ziplock plastic bag and coded to ensure blinding of the samples [Figure 1].

The specimen was then transported in a vaccine carrier to the Department of Virus Research (DVR), Manipal Academy of Higher Education (MAHE), Manipal, on the same day, which was then stored at +2°C to +8°C. The measles-specific IgG antibody titers were assessed by an experienced lab technician in DVR using Dade Behring Enzygnost Anti-Measles Virus/IgG (measles IgG) manufactured by Siemens Healthcare Diagnostics Products GmbH, Marburg/Germany [Figure 2].

For qualitative estimation, samples registering corrected optical density (OD) value ≥ 0.2 were considered to indicate protection against measles and thus defined as “positive by ELISA.” Quantitative estimation of IgG antibody titers was done using the α -method, and geometric mean titer (GMT) was presented as mIU/ml.^[20] Thus, seropositivity was defined as samples having measles IgG level ≥ 200 mIU/ml.

Statistical analysis

Data were entered and analyzed using Statistical Package for the Social Sciences (SPSS Inc., Released 2007, SPSS for Windows, version 16.0., Chicago, IL, USA). Sociodemographic details were presented using descriptive statistics. The proportion of infants with persistent MMA were presented as percentages. Association between various factors affecting seropositivity was tested using univariate logistic regression analysis, and strength of association was reported as risk ratio (RR) with 95% confidence interval (CI).

RESULTS

Of the 250 recruited infants, 120 (48%) were male and 130 (52%) were female. The mean age (\pm standard deviation [SD]) of the infants was 9.59 (± 0.76) months with a range of

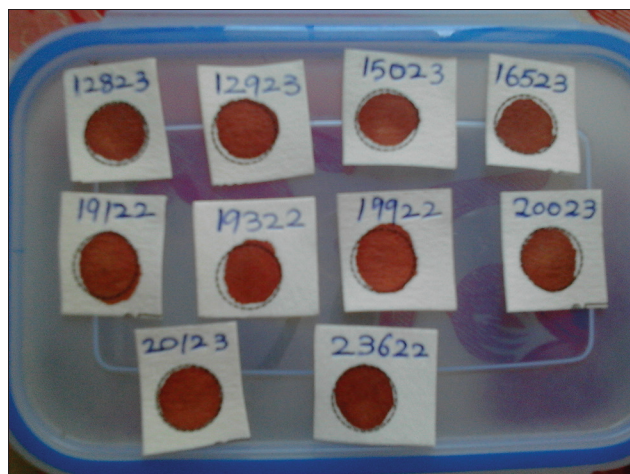


Figure 1: Drying of the blood samples collected by dried blood spot method

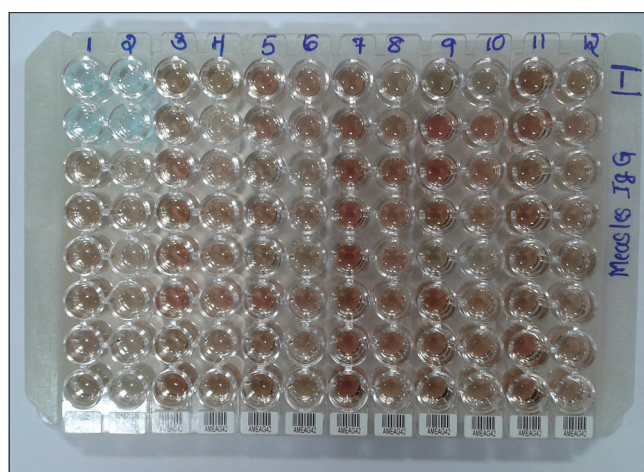


Figure 2: Dispensing the samples in the ELISA well for measles IgG estimation

9–14 months. Majority of them were Hindus (68%) followed by Muslims (29.2%) and the rest (2.8%) were Christians. Most of them (83.2%) belonged to middle socioeconomic status according to the Modified Udai Pareek Scale. It was observed in the present study that corrected OD value of 0.2 corresponds to 350 mIU/ml and corrected OD value of 0.1 corresponds to 150 mIU/ml in the quantitative estimation done for IgG antibodies. Seropositivity among the subjects based on the qualitative and quantitative estimation is shown in Table 1.

To study the effect of subject and maternal factors influencing persistent MMA using univariate logistic regression analysis, seropositivity based on quantitative estimation was considered. Among the 25 infants who showed persistent MMA levels at 9 months of age, 14 (10.8%) of them were female and 11 (9.2%) were male. It was observed that although the chance of female infants showing persistent MMA levels was higher as compared to male infants (RR = 1.20, 95% CI = 0.52–2.75); this was not statistically significant ($P = 0.673$). Children who did not cry immediately after birth had persistent maternal antibody (RR = 6.45, 95% CI = 1.02–40.52), which was statistically significant ($P = 0.047$). Furthermore, malnourished children had more chance of having maternal antibody (RR = 1.48 95% CI = 0.41–5.34), which was not statistically significant ($P = 0.554$). Initiation of supplementary feeds before 6 months, duration of exclusive breast feeding <4 months, history of fever with rash, and ≥ 3 episodes of diarrhea had more chance of having MMA levels, but these were not statistically significant. Initiating breast feeding after day 1, history of hospitalization, and neonatal jaundice had lesser chance of having MMA levels, but these were also not statistically significant [Table 2].

Among children whose mothers were ≥ 26 years of age during delivery, only 13 (8.7%) of them had persistent MMA levels at 9 months of age (RR = 0.71, 95% CI = 0.31–1.62), but this was not statistically significant ($P = 0.416$). Among 210 children born to mothers without a history of measles infection, 21 (10.0%) had persistent MMA levels whereas 5 (12.5%) out of 40 children born to mothers with a history of measles infection had persistent MMA levels at 9 months of age (RR = 1.00, 95% CI = 0.32–3.09). No significant association was found with other maternal factors such as antenatal complications, interpregnancy interval, gestational age, mode of delivery, and blood group in the present study [Table 3].

Table 1: Persistence of maternal measles antibody (IgG) among the study subjects ($n=250$)

Method of IgG estimation	<i>n</i> (%)
Qualitative estimation	
Seropositive (OD ≥ 0.2)	4 (1.6)
Seronegative (OD ≤ 0.2)	246 (98.4)
Quantitative estimation	
Seropositive (IgG titer ≥ 200 mIU/ml)	25 (10.0)
Seronegative (IgG titer <200 mIU/ml)	225 (90.0)

OD: Optical density

DISCUSSION

The present study was done among 250 rural children to find out the prevalence of MMA and the factors which determine the effectiveness of measles vaccination at the end of 9 months of age. The mean age (\pm SD) of the infants was 9.59 (± 0.76) months with a range of 9–14 months with almost equal gender distribution.

Qualitative estimation of maternal measles antibody

DBS sample was used to calculate measles-specific IgG antibodies and samples registering corrected OD value ≥ 0.2 were considered seropositive. Based on this, 4 (1.6%) infants showed the presence of MMA. An Australian study used a similar method of sample collection and cutoff value (OD value ≥ 0.2 as protective) for interpretation of results and showed an overall sensitivity of 98.4% and specificity of 97.2% compared with the results of serum testing.^[21] It was observed in the present study that corrected OD value of 0.2 corresponds to 350 mIU/ml in the quantitative estimation done for IgG antibodies as against 300 mIU/ml and 130 mIU/ml reported in other studies.^[22,23]

Quantitative estimation of maternal measles antibody

Infants with a titer ≥ 200 mIU/ml were considered protective against measles infection.^[9,24–26] Based on this, 25 (10%) children had MMA, which means the prevalence of MMA among infants in the present study was 10%, which is similar to the results reported in an Indian study.^[18] Two other studies done abroad reported passive antibody positivity rate (MMA) as 5.2% and 8.1% at 9 months of age, respectively.^[27,28]

Subject factors influencing maternal measles antibody among infants

Although female infants had persistent MMA compared to male infants, it was not statistically significant in contrast to other study done in 2009 where it was shown that girls lost maternal measles antibodies more rapidly than boys and well before 9 months of age.^[29] An Egyptian study found higher seropositive rate for MMR vaccine among infants of 1st or 2nd birth order in their family, with a significant decrease in the percentage seropositivity for infants ranked higher in the family birth order ($P < 0.001$).^[30] However, in the present study, it was observed that infants of third or more birth order were found to have persistent MMA levels (RR = 2.29, 95% CI = 0.74–7.01) compared to infants born of first and second order. Children who did not cry immediately after birth had persistent maternal antibody, which was statistically significant ($P = 0.047$). However, this might be due to very small number of children in this group. Religion and socioeconomic status were not found to have any association with persistence of MMA levels similar to other study which also found no difference in positive seroprevalence rate with respect to socioeconomic status, sibling size, and educational level of fathers.^[31]

Maternal factors influencing maternal measles antibody among infants

Increasing maternal age was found to have lower persistent MMA, but was not statistically significant. Previous studies

Table 2: Univariate logistic regression for association between subject characteristics and persistence of maternal measles antibody (n=250)

Variables affecting antibody levels	Total (n)	Seropositive n (%)	P	RR (95% CI)
Gender				
Female	130	14 (10.8)	0.673	1.20 (0.52-2.75)
Male	120	11 (9.2)		1.00
Birth order				
≥3	26	5 (19.2)	0.151	2.29 (0.74-7.01)
2	86	7 (8.1)	0.744	0.85 (0.33-2.22)
1	138	13 (9.4)		1.00
Birth weight (kg)				
<2.5	41	4 (9.8)	0.955	0.97 (0.31-2.99)
≥2.5	209	21 (10.0)		1.00
Religion				
Hindu	170	18 (10.6)	0.652	1.24 (0.49-3.09)
Others	80	7 (8.8)		1.00
Socioeconomic status				
Low	40	2 (5.0)	0.263	0.43 (0.9-1.89)
Middle and high	210	23 (11.0)		1.00
Child did not cry immediately after birth	5	2 (40.0)	0.047 [#]	6.45 (1.02-40.52)
History of Neonatal Jaundice	42	2 (4.8)	0.229	0.40 (0.91-1.78)
Breast feeding initiated after day 1 of birth	95	8 (8.4)	0.516	0.75 (0.31-1.80)
Supplementary feeds before 6 months of age	119	15 (12.6)	0.195	1.74 (0.75-4.05)
Duration of exclusive breast feeding (months)				
<4	50	6 (12.0)	0.599	1.30 (0.49-3.45)
≥4	200	19 (9.5)		1.00
Presence of malnutrition at the time of recruitment	22	3 (13.6)	0.554	1.48 (0.41-5.34)
History of hospitalization at the time of recruitment	32	2 (6.2)	0.455	0.565 (0.13-2.52)
History of fever with rash at the time of recruitment	9	2 (22.2)	0.231	2.71 (0.53-13.81)
Acute respiratory illness (episodes)				
>5	11	1 (9.1)	0.918	0.90 (0.11-7.30)
≤5	239	24 (10.0)		
Acute diarrheal illness (episodes)				
>3	6	2 (33.3)	0.079	4.80 (0.83-27.67)
≤3	244	23 (9.4)		

[#]Significant as $P < 0.05$. CI: Confidence interval, RR: Risk ratio

found a relationship between increasing age, parity of mothers, and lower GMTs.^[14,15] The present study did not find significant association with maternal history of measles infection with persistent MMA, but studies done in Europe and China concluded that infants born to mothers with a history of measles had higher antibody levels at birth and at 6 months than infants of vaccinated mothers.^[22,23,32] Children born of preterm delivery had higher persistent MMA (12.0%) compared to term infants (9.1%), but it was not statistically significant. However, other studies found that preterm infants receive significantly fewer antibodies compared to term infants.^[33,34]

Persistence of maternal measles antibody in infants

A study done in India found that the GMT of MMA in the infants blood showed a statistically significant reduction with an increase in age during the early part of the infancy and touched the lowest by 7th month and thereafter remained in the vicinity of 125 mIU/ml.^[35] In another study done in 2003, the proportion of antibody-positive infants declined from 50% at 7–9 months to 10% at 13–15 months.^[16] A similar

study done among French infants found that MMA decreases dramatically by 6 months of age and that 90% of infants are not protected against measles after 6 months of age.^[36] However, in an African study, the immune response to measles vaccine in 6-month-old infants were studied and found that out of 140 infants studied, no infant had more than 150 mIU/ml antibodies.^[37] To summarize, studies across the world have proven that only 5%–10% of infants have MMA at 9 months of age, which is concurrent with the present study findings. No clear consensus about the protective range of antibody levels or cutoff value for seropositivity might be a limitation of this study.

CONCLUSION

The prevalence of persistent MMA (IgG titer ≥ 200 mIU/ml) among the infants aged 9–12 months was 10%. The choice of vaccinating infants at the end of 9 months for the first dose of measles vaccine in India is justified as remaining 225 (90%) of infants were susceptible for measles infection at 9–12 months

Table 3: Univariate logistic regression analysis for the association between maternal factors and persistence of maternal measles antibody (n=250)

Variables affecting antibody levels	Total (n)	Seropositive, n (%)	P	RR (95% CI)
Age at 1 st pregnancy (years)				
≥26	99	9 (9.1)	0.698	0.84 (0.36-1.99)
≤25	151	16 (10.6)		1.00
Age at recent pregnancy (years)				
≥26	149	13 (8.7)	0.416	0.71 (0.31-1.62)
≤25	101	12 (11.9)		1.00
No history of measles infection	210	21 (10.0)	1.000	1.00 (0.32-3.09)
Gestational age at recent delivery				
Preterm	75	9 (12.0)	0.491	1.36 (0.57-3.23)
Term	175	16 (9.1)		1.00
Mode of delivery				
LSCS	88	12 (13.6)	0.162	1.81 (0.79-4.76)
Vaginal delivery/assisted	162	13 (8.0)		1.00
History of PIH	27	3 (11.1)	0.839	1.14 (0.32-4.10)
History of anemia	84	9 (10.7)	0.789	1.13 (0.48-2.67)
Interval between recent and previous pregnancy (years) (n=126)				
<3	48	5 (10.4)	0.789	1.18 (0.35-3.94)
≥3	78	7 (9.0)		1.00
Blood group (n=229)				
A	64	6 (9.4)	0.880	0.92 (0.31-2.73)
B	66	6 (9.1)	0.832	0.89 (0.30-2.63)
AB	10	1 (10.0)	0.991	0.99 (0.11-8.72)
O	89	9 (10.1)		1.00

LSCS: Lower segment caesarean section, PIH: Pregnancy-induced hypertension, CI: Confidence interval, RR: Risk ratio

of age. Hence, the current timing of first dose of measles vaccination at the end of 9 months is appropriate and needs to be continued. The effect of maternal factors, child nutrition, and sociodemographic factors on the presence of MMA was not found to be statistically significant.

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Conflicts of interest

There are no conflicts of interest.

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