

Study of appropriate timing and short term effectiveness of measles vaccination

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Abstract

Introduction: Measles remains the leading cause of vaccine preventable childhood mortality and morbidity in developing countries. Measles vaccine contributes to the reduction of childhood mortality. The optimal age of vaccination has to be individualised for each country. **Materials and Methods:** The study was done for a period of two months in a government hospital Davangere. A total of 84 children were studied in three groups. Group 1 comprised of 29 children, of 9 months (± 10 days) of age, not vaccinated against measles. Group 2 of 28 children of 18 months (± 15 days) of age, vaccinated against measles at 9 months of age. Group 3 of 27 children of 36 months (± 15 days) of age, vaccinated against measles (EZ strain) at nine months of age. Antibody titres more than 200mIU/ml, was considered seropositive and statistical analysis was done by ANOVA and Mann Whitney test, chi square test. **Results:** In group 1, 13 (45%) of 29 children were seropositive, 55% were seronegative, and 8 (28%) had antibody level above 1000 m IU/ml. In group 2, 7(26%) were seronegative. In group 3, 5(18%) were seronegative. Antibody titres had significant statistical variation between groups 1 and 2, and groups 1 and 3. Sex, nutrition status and duration of exclusive breast feeding did not have any influence in the seropositivity in all the three age groups. **Conclusion:** Measles vaccine should be administered before 9 months, as early as 6 months and second dose at 12-15 months of age.

Key words: Measles, Antibody, Seroconversion

Introduction

Measles is a vaccine preventable cause of childhood mortality and morbidity. World has turned its attention towards measles eradication next to small pox, polio. The main reasons for this can be attributed to the decreased vaccination coverage, use of low potency vaccines and low availability of resources. Very few studies are there in world [1-6]. In India reported case of measles represents only the tip of iceberg. It requires the identification of distribution and ages of susceptibility of children. There are very few Indian studies [7-9]. This study is an attempt to evaluate the appropriateness of the current measles vaccination policy in practice in our country, by estimating quantitatively measles IgG antibodies at three different age groups on the eve, when the world is eagerly waiting for the announcement of measles eradication strategy by world health organization.

The objective of present study was to know the appropriateness of the timing of measles vaccination as practiced by universal immunization programme in India and to find out about the short term protection offered against measles by the current vaccination practice.

Material and Methods

Children attending outpatient department and the immunization clinic conducted at Women and Child Health Hospital at Davangere which is attached to JJM Medical College. Study period of 2 months.

Study design and inclusion criteria: The study was a cross sectional examination of measles IgG antibody levels in children of three age groups.

1. Group 1 of 29 children, of 9 months (± 10 days) of age, not vaccinated against measles.

Manuscript received: 4th Nov 2015
Reviewed: 15th Nov 2015
Author Corrected: 27th Nov 2015
Accepted for Publication: 12th Dec 2015

2. Group 2 of 28 children of 18 months (\pm 15 days) of age, vaccinated against measles at 9 months of age.
3. Group 3 of 27 children of 36 months (\pm 15 days) of age, vaccinated against measles at a months of age.

The age, vaccination status and age at vaccination were verified from the immunization record issued by government of India.

Exclusion criteria

1. Children Without documentation of age and immunization status.
2. Children of groups 2 and 3 who have received measles vaccination from outside a government health care centre.
3. Children of groups 2 and 3 Who have received a second measles vaccine as measles, mumps and rubella vaccine (MMR)
4. Children With history suggestive of measles in the past as per WHO definition.
5. Children With grade III and grade IV PEM as per Indian Academy of pediatrics.
6. Children With chronic illness like tuberculosis, nephrotic syndrome and HIV Positive.
7. Children on steroid therapy, immunosuppression, and those with acute illness.

Results

Total of 84 children were studied in three groups.

Group 1: 29 nine month old children, not vaccinated against measles. Out of whom 15 were males and 14 were females

Group 2: 27 eighteen month old children vaccinated against measles at nine months of age. out of whom, 11 were males and 16 females

Group 3: 28, thirty six month old children vaccinated against measles at nine months of age. whom 16 were male, 12 were female

Almost all the children of the study group belonged to low socio-economic status as per modified Prasad classification. There is no variation in the socio economic status between the study groups (Fig 1). Results of Measles IgG antibody levels are shown in Table 1.

Table 2: Shows Comparison of seropositivity between the different groups, which was done by Chi-Square test (X^2). There is significant variation in the first group compared to second and third groups, but, the difference in seropositivity observed between second and third groups (74% and 82% respectively) is not statistically significant.

Measles IgG levels observed in three different groups were compared simultaneously using one way ANOVA. Table 3. This showed statistically significant variation (p -value $<$ 0.01) between the three groups. IgG levels between two groups each compared using Mann-Whitney test showed significant difference in group 1 compared to group 2 and 3 table 4. The observed variation in IgG levels between groups 2 and 3 is not statistically significant.

Methods: Consent from parents of the children were taken and interviewed according to the proforma, the age and immunization status confirmed by verifying the immunization record and also assessing the nutritional states. Blood samples obtained by venepuncture from those children who fulfilled the criteria and sera were stored in deep freezer and quantitative estimation of measles IgG was done by ELISA test kit. This ELISA kit has the sensitivity of 96.9% and 100% specificity as compared to immunofluorescence.

Serum sample was considered positive for measles antibodies if the antibody levels obtained was greater than or equal to 200 mIU/ml, and negative if it was less than 200 mIU/ml.

Descriptive data that included mean, median, standard deviation and minimum and maximum values were calculated for each group. Continuous data were analysed by one way ANOVA for multiple groups and Mann Whitney test for two group comparisons. log transformations were used for analysis whenever necessary. Pearson's coefficient was used for calculating correlation between two variables if needed. Categorical data were analysed either by chi square test or Fischer exact test. For all statistical tests, p value of less than 0.005 was considered significant.

Comparison of measles antibody levels and seropositivity between male and female children in each group using Fisher’s exact test did not show any statically significance variation table 5.

Measles antibody level compared between children with normal nutritional status according to IAP classification with that of those with grade 1 and grade 2 protein energy malnutrition (PEM) using Chi-square test showed no statistically significant difference. Comparison of seropositivity between the same using Fisher’s exact tests also did not show significant variation as shown in table 6

Duration of exclusive breast feeding and seropositivity were compared all the three age groups using fisher’s exact test, there was no significant variation in any of the groups as shown in table 7

Fig 1: Socioeconomic status:

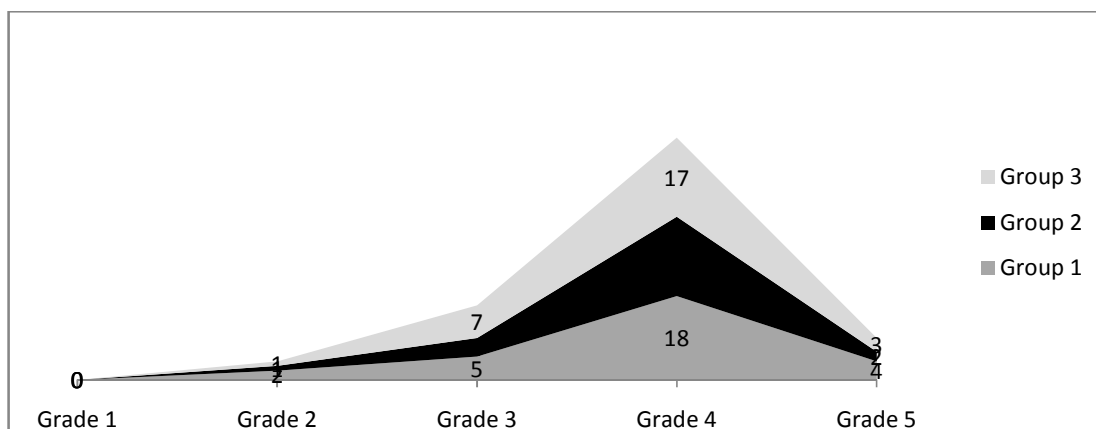


Table- 1: Showing measles IgG antibody levels

IgG antibody titer (mIU/ml)	Group 1 n (%)	Group 2 n (%)	Group 3 n (%)
<200	16(55)	7(26)	5(18)
200-350	3(10)	-	2(7)
351-1000	2(7)	4(15)	2(7)
1001-5000	5(17)	11(41)	7(25)
5001-10000	-	3(11)	9(32)
>10000	3(11)	2(7)	3(11)
Total	29(100)	27(100)	28(100)
Range	5-14701	6-13067	11-16094
Mean ±SD	1905±4307	2872±3522	4411±4229
Median	129	2115	4603

Table 2: Comparison of seropositivity across the groups

Group compared	χ^2 - value	p-value
Group 1 V/s Group 2	4.91	<0.01
Group 1 V/s Group 3	8.25	<0.01
Group 2 V/s Group 3	0.53	0.47

Table 3: Comparison of IgG levels between different age groups

Age group	IgG levels		Log levels	ANOVA results
	Mean± SD	Median	Mean± SD	
Group 1	1905± 4307	1292	2.34±0.94	f =6.62 p<.0.1
Group 2	2872±3522	2115	2.88±1.00	
Group 3	4411±4229	4603	3.22±0.84	

Table 4: Comparison of IgG levels between different age groups (Mann-Whitney test)

Age group compared	Mean difference in IgG	Mean difference in log IgG	% increased	Significance
Group 1 V/s Group 2	967	0.54	23%	p< 0.05
Group 1 V/s Group 3	2506	0.88	38%	p< 0.001
Group 2 V/s Group 3	1539	0.34	12%	p< 0.12

Table 5: Comparison of seropositivity among male and female children

		Male		Female		p-value
		n	%	n	%	
Group 1	Total	15	100	14	100	0.72
	Positive	6	40	7	50	
	Negative	9	60	7	50	
Group 2	Total	11	100	16	100	1.00
	Positive	8	73	12	75	
	Negative	3	27	4	25	
Group 3	Total	16	100	12	100	0.36
	Positive	12	75	11	92	
	Negative	4	25	1	8	

Table 6: Seropositivity in relation to nutritional status

Age	Result	Grade 1/11 PEM		Grade 1/11 PEM		p- value
		n	%	n	%	
9 months	Positive	8	44	5	45	0.30
	Negative	10	56	6	55	
18 months	Positive	5	71	15	75	0.37
	Negative	2	29	5	25	
36 months	Positive	5	84	18	82	0.45
	Negative	1	17	4	18	

Table 7: Relationship between exclusive breast-feeding (EBF) and seropositivity

		Duration of EBF		p-value
		<6 Months	≥6 Months	
Group 1	Positive	9	4	0.31
	Negative	11	5	
Group 2	Positive	13	7	0.32
	Negative	4	3	
Group 3	Positive	13	10	0.31
	Negative	2	3	

Discussion

In our study 45% of children of group 1 are seropositive. 28% of children had high antibody titres above 1000mIU/ml. This could be due to persistence of maternal antibodies or subclinical infection. Bautista-Lopez et al in a study in peruvian children considered that measles antibody levels above 200mIU/ml could protect individuals from measles infection [1].

Sharma et al study showed that 30% infections are subclinical and asymptomatic in nature [2]. Satpathy et al reported 11.5% cases of measles before 9 months of age [3].

Sehgal et al noted that passively acquired maternal antibodies for measles become undetectable at 8 months of age [4].

Sood DK et al analysed 581 infant serum samples for prevalence of maternal antibodies, and observed that 83% of the samples at the age of 3 months or below had measles antibodies, but with the increase in age there was tremendous loss with only 19-20% at age 6-7 months. After seven months of age, percentage of antibodies varied from 11-13%. [5].

In the second study group of children of 18 months, who were vaccinated at 9 months, 26% were seronegative. 19% had levels above 5000mIU/ml, which points towards subclinical infection, hence second measles vaccine should be made mandatory at a period 6 months after vaccination. Damien et al estimated the susceptibility to asymptomatic secondary immune response against measles in vaccinated and late convalescent persons to be 22.2% to 33.2% and 3.2 to 3.9% [6]. Seronegativity could also be due to vaccine failure [7,8,9,10,11].

In Group 3 children, 82% were seropositive. There was no statistical significant variation of seropositivity between 18 and 36 months old children. 18% were seronegative at 36 months, indicating less protection level, emphasizing the need for second dose of vaccination [12, 13, 14].

Conclusion

Our data suggests revision of existing measles vaccination policies from the existing single dose vaccination at 9 months to a two dose schedule, the first as early as 6 months and the second at 12-15 months of age.

Acknowledgments: Department of Biochemistry

Ethical approval: Obtained from Institutional Ethics Committee (Human Studies)

Funding: No funding sources.

Conflict of Interest: The authors declare no conflict of interest

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How to cite this article?

Vani HN, Guruprasad G, Abdul Manaf K.M. Study of appropriate timing and short term effectiveness of measles vaccination. Pediatr Rev: Int J Pediatr Res 2015;2(4):88-93.doi:10.17511/ijpr.2015.i04.10

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