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Original Research Article

Hospital Based Cross-Sectional Assessment of the Association of Measles Antibody Titres with Nutritional Status in Pediatric Population

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Conflict of interest: Nil

Abstract

Aim: To find out any association of measles antibody titres with nutritional status in children 1 to 12 years.

Material & Methods: This hospital based cross-sectional study was conducted over a period of two years on1-12-year-old children attending the Pediatrics & Neonatology, RIMS, Ranchi, Jharkhand with the objective of finding out the seroprevalence and anti-measles antibody levels, and studying their association with age, gender, as well as nutritional status of these children. **Results:** Majority (69.7%) of the total subjects had been vaccinated against measles. No statistically significant difference was observed in the baseline characteristics of vaccinated and unvaccinated group except for mean weight for age Z score which was significantly lower in the unvaccinated group ($p = 0.022$). A statistically significant relationship ($p=0.027$) was observed between height for age Z scores and seropositivity, with higher seropositivity being noted in children with higher height for age z scores.

Conclusion: Nutritional status of children has an association with measles antibody titres as well GMT of measles specific IgG antibody, with those with better nutritional status having higher measles antibody titres.

Keywords: Measles, Vaccine, Antibody, Vaccination, Malnourished, Anthropometry.

Introduction

In India, Measles contributes to 2.3 percent of all deaths and one tenth of all deaths in the pre-school children. [1] A review of community-based studies of published measles outbreaks, investigations found a median case fatality ratio of 3.7%, range 0 to 23.9%, primarily affecting the remote tribal populations have been reported and case fatality rates of 5-30 percent have been observed. Despite the declining trends in measles cases from a reported 162560 in 1989 to 29339 in 2011 [2], measles remains a major cause of morbidity & mortality in the children in India. Measles vaccine coverage in India is 74% (Urban-78% and rural-72%), especially 52.8% in Uttar Pradesh. [3] This is lower than the 95% coverage required to eliminate measles [4], and much of the World Health Organization (WHO) African Region, including the Democratic Republic of the Congo (DRC),

has even lower coverage than this worldwide average. [5]

Currently, DRC gives one routine dose of measles vaccine to children nine months of age, and in outbreak settings, to children as young as six months. Although the WHO states that all countries should include a second routine dose of MV, regardless of national routine coverage level of the first dose [6], this recommendation has not been implemented in the DRC. Because coverage achieved through healthcare is low in the DRC, attempts are made to reach missed children through Supplementary Immunization Activities (SIA), which Doshi et al. found to be associated with decreased measles incidence. [7] The ability of an infant to seroconvert is age dependent due to level and decay of maternal antibodies and immunological development; regional differences in seroprevalence have been observed. Expectant mothers in endemic areas may be more likely to have had natural measles infection, resulting in higher measles antibody levels, and so pass on higher levels of measles antibody transplacentally to their infants, resulting in longer lasting protection than would occur in expectant mothers with vaccine-induced antibody. [8-9]

Measles contributes to the development of malnutrition because of protein-losing enteropathy, increased metabolic demands, and decreased food intake. Children who have measles early in life have significantly lower mean weights for age than children of the same age who do not develop measles. Despite of the prevalence of malnutrition, and its fatality, scientific research in this field is lacking. Little research has been carried out in the last 10 years.

Material & Methods:

This hospital based cross-sectional study was conducted over a period of two years on 1-12 year old children attending the Pediatrics & Neonatology, RIMS, Ranchi, Jharkhand with the objective of finding out the seroprevalence and anti-measles antibody levels, and studying their association with age, gender, as well as nutritional status of these children.

Inclusion criterion was Children in the age group of 1 to 12 years. Children were excluded from the study that refuses to give parental consent, received blood or blood components within last 3 months, received corticosteroid therapy or other immunosuppressive therapy, are HIV positive, are transplant recipients (bone marrow/ solid organ), received of gamma globulins within last 2 months, are on dialysis and are having malignancies.

Methodology

A total of 400 patients were evaluated initially. Out of these, 360 patients whose parents consented for the study were enrolled in the study. The procedure of systematic random sampling was used for selection of subjects. Blood samples were tested for presence of measles specific IgG antibodies.

The techniques of measurement described in Cogill's [10]. Anthropometric Indicators Measurement Guide were followed to make the following measurements. Weight was measured using a portable electronic weighing scale with a weighing capacity from 1 kg to 150 kg in 100 g divisions, accuracy +/- 100g. Height: was measured in centimetres to a precision of 0.1cm by a wall mounted tape measuring up to 2 meters. An infantometer was used to measure the length for children less than 2 years of age.

The following indices & their z scores were calculated: Body Mass Index (BMI) = $Weight\ (Kg)/\ Height\ (m)^2$. Weight for age: for children less than 10 years of age by W.H.O standard growth chart and zscore was calculated. Height for age: for all children based on W.H.O standard growth chart and z score was calculated. Weight for height: for children less than 5 years based

on W.H.O standard growth chart and zscore was calculated.

Nutritional status of children was classified on the basis of the WHO Growth Standards, 2006 for 0-60 months; and the WHO Reference, 2007 for 5-19 years.

Children 5-19 Years:

Overweight: >+1SD (equivalent to BMI 25 kg/m2 at 19 years) Obesity: >+2SD (equivalent to BMI 30 kg/m2 at 19 years). Thinness: <- 2SD. Severe thinness: <-3SD.

Children 0-60 months:

Moderate wasting: weight-for length/ height Z -score -2 to -3 Severe wasting (severe acute malnutrition): weight-for-length/ height Z –score <-3. Overweight: BMI-for-age or weight-for-length/ height Z -score > 2. Obesity: BMI-for-age or weight for- length/ height Z -score>3. Moderate stunting: length/ height for age Z -score -2 to -3. Severe stunting: length/ height for age Z -score < -3.

Blood samples were collected, and serums were separated by centrifugation and stored at -20 degree Celsius till the time of assay. Measles specific IgG antibodies were detected by using a commercial IgG ELISA kit (Measles Virus IgG ELISA, IBL International GMBH) in accordance with the manufacturer's instructions.

Results:

Majority (69.7%) of the total subjects had been vaccinated against measles. A similar trend was observed in each of the age groups. However, the relationship between age and vaccination status was not found to be statistically significant (p=0.182) [Table 1]

No statistically significant difference was observed in the baseline characteristics of vaccinated and unvaccinated group except for mean weight for age Z score which was significantly lower in the unvaccinated group (p = 0.022). [Table 2]

58.3% of the total subjects ≤5 years old had severe wasting (severe acute malnutrition), while 23.13% had moderate wasting. Severe and moderate stunting was observed in 5.27% and 21.6% of the total subjects. In children > 5 years,

15.29% had severe thinness, 9.41% had thinness and only1 (0.58%) case was overweight. 45.29% of the vaccinated subjects ≤5 years old had severe wasting (severe acute malnutrition), while 32.9% had moderate wasting. Severe and moderate stunting was observed in 5.5% and 17.8% of the total subjects. In children >5 years, 17.4% had severe thinness, 11.1% had thinness and only1 (0.7%) case was overweight. Amongst unvaccinated subjects, 11.2% children ≤5 years old had severe wasting (severe acute malnutrition), while 27.5 % had moderate wasting. Severe and moderate stunting was observed in 26% and 54% of the total subjects. In children > 5 years, 29.5% had severe thinness, 15.9% had thinness and no case was overweight. [Table3]

A highly statistically significant relationship (p=0.002) was observed between BMI Z scores (in subjects aged ≥5yrs) and seropositivity, with higher seropositivity being noted in children with higher BMI z scores. Similarly, a statistically significant relationship (p=0.027) was observed between height for age Z scores and seropositivity, with higher seropositivity being noted in children with higher height for age z scores. [Table 4]

It was not found statistically significant with p value 0.05 for seropositivity but significant with p value 0.0001 for antibody levels. In weight for length/height both seropositivity and GMT were found insignificant in well-nourished, moderately malnourished as well as severely malnourished subject (P value: 0.652). [Table 5]

Table 1: Vaccination status of children against measles

Age group (years)	Vaccinated N (%)	Unvaccinated N (%)	Total	P value
1-12	251(69.7)	109 (30.2)	360	0.182

Table 2: Baseline characteristics of measles vaccinated and unvaccinated children

Characteristics	Vaccinated mean±SD	Unvaccinated mean±SD	P value
Age (years)	6.2±3.0	5.9±3.7	0.528
Weight (kg)	16.2±7.8	16.1±6.6	0.291
Height (cm)	103.2±21.4	10.9.1±20.8	0.619
BMI (kg/m^2)	15.2±2.3	14.3±1.6	0.119
Weight for age Z score (1-10 years)	-1.6±1.1	-2.4±1.5	0.022
Height for age Z core	-1.5±0.8	-1.8±1.3	0.0821
Weight for height Z score(1-5 years)	-1.6±1.8	-1.6±1.9	0.461
BMI Z Score	-1.6±2.7	-1.6±1.9	0.682

Table 3: Nutritional status of subjects

Parameter of Nutritional status		Total	N (%)	Vaccinated	N (%)	Unvaccinated N (%)	N (%)
Weight for age Z Score (age ≤10yrs)	< -3	58	23.2	37	21.76	9	11.25
	-2 to-3	33	13.2	56	32.94	22	27.5
	>-2	159	63.6	77	45.29	49	61.25
	Total	250	100	170	100	80	100
Weight for Height Z Score (age≤5yrs)	<-3	30	18.75	33	30	10	20
	-2 to-3	37	23.13	37	33.64	13	26
	>-2	93	58.13	40	36.36	27	54
	Total	160	100	110	100	50	100
Height for Age Z Score	<-3	19	5.278	13	5.532	8	6.4
	-2 to-3	78	21.67	42	17.87	31	24.8
	>-2	163	45.28	180	76.6	86	68.8
	Total	360	100	235	100	125	100
BMI for age Z score (age > 5yrs;	<-3	26	15.29	22	17.46	13	29.55
	-2 to-3	16	9.41	14	11.11	7	15.91
	>-2 to 1	127	74.71	89	70.63	24	54.55
	>1	1	0.58	1	0.794	0	0
	Total	170	100	126	100	44	100

Table 4: Relationship of measles antibody status with nutritional status of total subjects

Parameter of nutritional status		Antibody status						Total	P value
		Positive	N (%)	Negative	N (%)	Equivocal	N (%)		
Weight for Age z score	<-3	31	56.4	18	32.7	6	10.9	55	0.060
	-2 to-3	58	64.4	22	24.4	10	11.1	90	
	>-2	108	63.5	49	28.8	13	7.65	170	
Height for Age Z Score	<-3	9	52.9	6	35.3	2	11.8	17	0.027
	-2 to-3	42	55.3	27	35.5	7	9.21	76	
	>-2	199	74.3	54	20.1	15	5.6	268	
Weight for Height z Score	<-3	19	55.9	14	41.2	1	2.94	34	0.681
	-2 to-3	22	55	16	40	6	15	40	
	>-2	55	50	44	40	11	10	110	
BMI Z score (age≥5yrs)	<-3	27	73	10	27	7	18.9	37	0.001
	-2 to-3	18	64.3	8	28.6	2	7.14	28	
	>-2 to 1	85	78.7	18	16.7	5	4.63	108	
	>1	88	0	0	0	0	0	88	

Table 5: Nutritional status wise geometric mean titer (GMT) of measles specific igg antibody of total children

Parameters of nutritional status		GMT (mIU/mL)	P value
W/A z score	> -2SD	921	0.001
	<-2SD to-3SD	662	
	<-3SD	541	
H/A z score	-2SD	1792	0.005
	-2SD to-3SD	673	
	<-3SD	377	
W/H z score	> -2SD	574	0.652
	-2SD to-3SD	565	
	<-3SD	552	

Discussion:

In a study in Nigeria by Ifekwunigwe et al. [11], the geometric mean titer in subjects whose nutritional status was normal (>90% of median weight for age), mildly (75 to 90%), moderately (60 to 75%), or severely (<60%) malnourished were 7.5, 8.8, 7.9, and 7.9, respectively. So, malnutrition did not affect the children ability to develop adequate immune response to measles. In another study by Dao et al. [12], seroconversion was not associated with anthropometric indices. McMurray et al. [13] found that the children's nutritional status had no effect after vaccination. All the children have equal immunological response with respect to nutritional status. Mean hemagglutination-inhibition titres are slightly reduced in all nutritional groups 14 months after vaccination. Smedman et al. [14], Halsey et al. [15], Ekunwe et al. [16]

found good antibody response in children which were not severely malnourished. Similarly Lyamuya et al. [17] found there were no significant differences in measles antibody levels with regard to variations in nutritional status. Some studies reported seroconversion rates at least as high in malnourished as in well-nourished children because it is cell mediated immunity that is suppressed not the humoral immunity. [18-19]

Delayed antibody response to measles vaccine was seen in malnourished children. [20] Similar to our study, there was one study which demonstrated that stunting is associated with low antibody response. [21] In the same study, apart from severe stunting, severe wasting was also associated with lower antibody response, an observation which was not observed in our study. Idris et al [22] found decreased antibody titre in children with Kwashiorkar. Hafez et al [23] found decrease humoral response to measles vaccine.

In a study by Dao et al[24] (1992), seroconversion was not associated with anthropometric indices. McMurray et al[25] (1979) found that the children's nutritional status had no effect after vaccination. All the children have equal immunological response with respect to nutritional status. Mean hemagglutination-inhibition titres are slightly reduced in all nutritional groups 14 months after vaccination. Smedman et al[26] (1988), Halsey et al[27] (1985), Ekunwe et al[28] (1985) found good antibody response in children which were not severely malnourished. Similarly Lyamuya et al[29] found there were no significant differences in measles antibody levels with regard to variations in nutritional status. Our study is not only showing antibody response in moderately nourished children but also in severely nourished children. Some studies reported seroconversion rates at least as high in malnourished as in well-nourished children because it is cell mediated immunity that is suppressed not the humoral immunity[30-31].

Conclusion:

Nutritional status of children has an association with measles antibody titres as well GMT of measles specific IgG antibody, with those with better nutritional status having higher measles antibody titres.

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