Association of measles antibody titres with nutritional status in paediatric population

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Abstract

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

Material and Methods: This hospital based cross-sectional study was conducted from December 2012 to November 2014 on children between 1-12 years of age attending the Pediatric O.P.D. of Jawaharlal Nehru Medical College, A.M.U, Aligarh with the objective of finding any association of measles antibody titres with nutritional status.

Results: 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=0.024) was observed between height for age Z scores and seropositivity, with higher seropositivity being noted in children with higher height for age higher scores. However, no significant relationship was observed between serpositivity and either weight for height z scores or weight 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

Access this article online	
Quick Response Code:	Website: www.innovativepublication.com
	DOI: 10.5958/2455-6793.2016.00002.X

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]. India contributes to 47% (142000/42000 cases in 2004) of global mortality due to measles[4] and Uttar Pradesh being one of the state's accounting for more than 80% of deaths [case fatality ratio (CFR): 4.1% as compared to median national CFR of 3.8%][5].

Measles contribute 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 and Methods

This hospital based cross-sectional study was conducted from December 2012 to November 2014 on 1-12 year old children attending the Pediatric O.P.D. of Jawaharlal Nehru Medical College, A.M.U., Aligarh 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. A total of 433 patients were evaluated initially. Out of these, 400 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. 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. Clearance was sought from Institutional Ethics Committee of Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh. The techniques of measurement described in Cogill's (2003)[6] Anthropometric Indicators Measurement Guide

were followed to make the following measurements. Weigh**t** 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 z-score 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 z-score 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.

Observations and Results

Table 1: Vaccination status of children against measles

Age group (years)	Vaccinated N (%)	Unvaccinated N (%)	Total	P value
1-12	285(71.3)	115(28.8)	400	0.251

Majority (71.25%) 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=0.251)

Table 2: Baseline characteristics of measles vaccinated and unvaccinated children

Characteristics	Vaccinated mean±SD	Unvaccinated mean±SD	P value
Age (years)	6.1±3.3	5.8±3.3	0.346
Weight (kg)	17.3±7.2	15.8±6.3	0.055
Height (cm)	108.1±20.2	105.4±19.9	0.217
BMI (kg/m^2)	14.3±2.2	13.9±1.9	0.222
Weight for age Z score(1-10 years)	-1.8±1.0	-2.1±1.1	0.028
Height for age Z ccore	-1.5±0.9	-1.7±1.0	0.0701
Weight for height Z score(1-5 years)	-1.5±1.5	-1.4±1.4	0.573
BMI Z Score	-1.5±2.9	-1.6±1.7	0.679

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 = 0.028).

Table 3: Nutritional status of subjects

Parameter of Nutritional status		Total N (%)	Vaccinated N (%)	Unvaccinated N (%)
Weight for age Z Score (age ≤10yrs)	<-3	61(17.2)	39(15.4)	22(21.6)
	-2 to -3	83(23.4)	58(22.9)	25(24.5)
	>-2	211(59.4)	156(61.7)	55(53.9)
	Total	355	253	102
Weight for Height Z Score (age≤5yrs)	<-3	30(16)	20(16.1)	10(15.6)
	-2 to -3	37(19.7)	24(19.4)	13(20.3)
	>-2	121(64.4)	80(64.5)	41(64.1)
	Total	188	124	64
Height for Age Z Score	<-3	21(5.3)	15(5.3)	6(5.2)
	-2 to -3	101(25.3)	64(22.5)	37(32.2)
	>-2	278(69.5)	206(72.3)	72(62.6)
	Total	400	285	115
BMI for age Z score (age > 5yrs;	<-3	45(21.2)	29(18)	16(31.4)
	-2 to -3	28(13.2)	19(11.8)	9(17.6)
	>-2 to 1	138(65.1)	112(69.6)	26(51)
	>1	1(0.5)	1(0.6)	0
	Total	212	161	51

% of the total subjects ≤5 years old had severe wasting (severe acute malnutrition), while 19.7% had moderate wasting. Severe and moderate stunting was observed in 5.3% and 25.3% of the total subjects. In children > 5 years, 21.2% had severe thinness, 13.2% had thinness and only1 (0.5%) case was overweight.

16.1% of the vaccinated subjects ≤5 years old had severe wasting (severe acute malnutrition), while 19.4% had moderate wasting. Severe and moderate stunting was observed in 5.3% and 22.5% of the total subjects. In children > 5 years, 18% had severe thinness, 11.8% had thinness and only1 (0.6%) case was overweight.

Amongst unvaccinated subjects, 15.6% children ≤5 years old had severe wasting (severe acute malnutrition), while 20.3 % had moderate wasting. Severe and moderate stunting was observed in 5.2% and 32.2% of the total subjects. In children > 5 years, 31.4% had severe thinness, 17.6% had thinness and no case was overweight.

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	28(45.9)	28(45.9)	5(8.2)	61	0.061
	-2 to-3	49(59)	26(31.3)	8(9.6)	83	
	>-2	139(65.9)	58(27.5)	14(16.6)	211	
Height for Age Z score	<-3	10(47.6)	9(42.9)	2(9.5)	21	0.024
	-2 to-3	54(53.5)	39(38.6)	8(7.9)	101	
	>-2	193(69.4)	67(24.1)	18(6.5)	278	
Weight for Height z score	<-3	15(50)	14(46.7)	1(3.3)	30	0.583
	-2 to-3	19(51.4)	13(35.1)	5(13.5)	37	
	>-2	61(50.4)	51(42.1)	9(7.4)	121	
BMI Z score (age≥5yrs)	<-3	27(60)	13(28.9)	5(11.1)	45	0.002
	-2 to-3	16(57.1)	10(35.7)	2(7.1)	28	
	>-2 to 1	118(85.5)	14(10.1)	6(4.3)	138	
	>1	100	0	0	1	

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

Parameter of nutritional status		GMT (mIU/mL)	P value
W/A z score	> -2SD	932	0.001
	<-2SD to-3SD	657	
	<-3SD	574	
H/A z score	-2SD	1892	0.005
	-2SD to-3SD	701	
	<-3SD	365	
W/H z score	> -2SD	590	0.495
	-2SD to-3SD	574	
	<-3SD	572	

Discussion

Measles vaccination triggers both a cellular and a humoral immune response. Following the activation of T-lymphocytes, B-cells produce measles-specific antibodies. The specific level of immunoglobulin is an indicator of the immune response. Protein energy malnutrition can be a contributory factor for immunodeficiency, thereby diminishing the immunological response to the vaccine. Though many studies reported normal antibody response to measles vaccination in malnourished children, however, specific antibody response was suppressed in severe cases of PEM. Our study also gives conflicting results. We have taken four parameters to study nutritional status: weight for age, height for age, weight for height and BMI. 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=0.024) was observed between height for age Z scores and seropositivity, with higher seropositivity being noted in children with higher height for age z scores. However, no significant relationship was observed between seropositivity and either weight for height z scores or weight for age z scores. According to weight for age, in well-nourished children seropositivity was 78% with GMT 932 mIU/ml, moderately malnourished (wasting) 67% with GMT 657 mIU/ml and in severely malnourished (severe wasting) 67% with GMT 574 mIU/ml. It was not found statistically significant with p value 0.05 for seropositivity but significant with p value 0.0001 for antibody levels. According to Height for age in well-nourished children seropositivity was 79% with GMT 657 mIU/ml, moderately malnourished (stunting) seropositivity was 70% with GMT 469 mIU/ml and in severely malnourished (severe stunting) seropositivity 45% with GMT 341mIU/ml. P value noted was 0.005 which is significant. 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: 0.495).

In a study in Nigeria by Ifekwunigwe et al[7] (1980), 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[8] (1992), seroconversion was not associated with anthropometric indices. McMurray et al[9] (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[10] (1988), Halsey et al[11] (1985), Ekunwe et al[12] (1985) found good antibody response in children which were not severely malnourished. Similarly Lyamuya et al[13] 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[14,15].

Delayed antibody response to measles vaccine was seen in malnourished children[16]. Similar to our study, there was one study which demonstrated that stunting is associated with low antibody response[17]. 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[18] (1983) found decreased antibody titre in children with Kwashiorkar. Hafez et al[19] (1983) found decrease humoral response to measles vaccine.

So, it was seen that malnourished children in the community can be safely and effectively vaccinated against measles. But some studies showing good antibody response and some showing poor antibody response. The mechanisms behind the immunological response are still inadequately understood. More

researches are needed in this field to come to any conclusion.

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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