Original research article

A cross sectional study to see if there's a correlation between measles antibody titres and nutritional status in children

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Abstract

Aim: to determine the association of measles antibody titres with nutritional status in paediatric population.

Methods: This was a cross-sectional study conducted in the Department of Pediatrics, Darbhanga Medical College & Hospital, Laheriasarai, Bihar, India for 1 year. on 1-10 year old children. Total 300 patients were include in this study for finding out the seroprevalence and anti-measles antibody levels, and studying their association with age, gender, as well as nutritional status of these children. Blood samples were tested for presence of measles specific IgG antibodies.

Results: Majority (66.67%) 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=0.209). 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 = 0.021). Percentage of the total subjects ≤5 years old had severe wasting (severe acute malnutrition), while 21.33% had moderate wasting. Severe and moderate stunting was observed in 5% and 24% of the total subjects. In children > 5 years, 20% had severe thinness, 12.14% had thinness and only 2 (1.43%) case was overweight. 16% of the vaccinated subjects ≤5 years old had severe wasting (severe acute malnutrition), while 21% had moderate wasting. Severe and moderate stunting was observed in 8.70% and 15.63% of the total subjects. In children > 5 years, 19% had severe thinness, 12% had thinness and only 1(1%) case was overweight. Amongst unvaccinated subjects, 16.67% children ≤5 years old had severe wasting (severe acute malnutrition), while 21.67% had moderate wasting. Severe and moderate stunting was observed in 5.88% and 30% of the total subjects. In children > 5 years, 27.50% had severe thinness, 15% had thinness and no case was overweight.

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] Measles is endemic in the DRC.[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[4], 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.[6] 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.[7,8] Children in measles-endemic regions are also at risk of exposure to measles at an earlier age, and this must be considered when determining ideal age of vaccination.[4] Determining drivers of seropositivity and low vaccine effectiveness (VE) is complex and can depend on immunization program logistical capacity[9], vaccine potency[10] and host factors, particularly immune system robustness as a function of development (age) and nutritional status.[11,12] Measles has occurred even in well-vaccinated populations, raising questions of why adequate protection is not achieved in such groups.[13-17] While vaccination induces humoral and cellular immune responses similar to those caused by natural disease, the resulting antibody levels are lower among those with vaccine - induced versus natural immunity. As measles continues to be inadequately controlled in DRC.[18,19] Population assessment of measles immunity is needed. 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.

Material and methods

This was a cross-sectional study conducted in the Department of Pediatrics, Darbhanga Medical College & Hospital, Laheriasarai, Bihar, India for 1 year, on 1-10 year old children, after taking the approval of the protocol review committee and institutional ethics committee. Total 300 patients were include in this study for finding out the seroprevalence and anti-measles antibody levels, and studying their association with age, gender, as well as nutritional status of these children. Blood samples were tested for presence of measles specific IgG antibodies.

Inclusion criteria

Children in the age group of 1 to 10 years.

Exclusion criteria

- Children were received blood or blood components within last 3 months,

- Children received corticosteroid therapy or other immunosuppressive therapy,
- HIV positive children
- Transplant recipients (bone marrow/ solid organ)
- Received of gamma globulins within last 2 months,
- Children on dialysis and are having malignancies.

Methodology

The techniques of measurement described in Cogill's (2003)[20] 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 100g 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.

Results

Children 5-18 Years: Overweight: >+1SD (equivalent to BMI 25 kg/m2 at 18 years) Obesity: >+2SD (equivalent to BMI 30 kg/m2 at 18 years). Thinness: <- 2SD. Severe thinness: <-3SD. Children 0-5 years: 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 -22 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

Table 1: Vaccination status of children against measles

Age group (years)	Vaccinated N (%)	Unvaccinated N (%)	Total	P value
1-10	200(66.67)	100(33.33)	300	0.209

Majority (66.67%) 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=0.209)

Table 2: Baseline characteristics of measles vaccinated and unvaccinated children

Characteristics	Vaccinated mean±SD	Unvaccinated mean±SD	P value
Age (years)	7.5±2.8	6.5±2.9	0.26
Weight (kg)	17.2±5.8	16.6±5.9	0.047
Height (cm)	108.4±20.5	107.8±19.1	0.212
BMI (kg/m^2)	15.7±2.7	14.7±2.3	0.231

Weight for age Z score(1-10 years)	-1.7±1.1	-2.4±1.2	0.021
Height for age Z score	-1.5±0.8	-1.9±1.1	0.0591
Weight for height Z score(1-5 years)	-1.7±1.6	-1.6±1.5	0.477
BMI Z Score	-1.7±3.2	-1.8±2.1	0.732

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 ($p = 0.021$).

Table 3: Nutritional status of subjects

Parameter of Nutritional status		Total N (%)	Vaccinated N (%)	Unvaccinated N (%)
Weight for age Z Score (age ≤10yrs)	<-3	54(18)	34(17)	20(20)
	-2 to -3	64(21.33)	40(20)	24(24)
	>-2	182(60.67)	126(63)	56(56)
	Total	300	200	100
Weight for Height Z Score (age≤5yrs)	<-3	23(14.37)	16(16)	10(16.67)
	-2 to -3	32(20)	21(21)	13(21.67)
	>-2	105(65.63)	63(63)	37(61.67)
	Total	160	100	60
Height for Age Z Score	<-3	15(5)	10(5)	5(5)
	-2 to -3	81(27)	50(25)	31(31)
	>-2	206(68.67)	140(70)	64(64)
	Total	300	200	100
BMI for age Z score (age > 5yrs;	<-3	28(20)	19(19)	11(27.50)
	-2 to -3	17(12.14)	12(12)	6(15)
	>-2 to 1	93(66.43)	68(68)	23(57.50)
	>1	2(1.43)	1(1)	0
	Total	140	100	40

% of the total subjects ≤5 years old had severe wasting (severe acute malnutrition), while 21.33% had moderate wasting. Severe and moderate stunting was observed in 5% and 24% of the total subjects. In children > 5 years, 20% had severe thinness, 12.14% had thinness and only 2 (1.43%) case was overweight.

16% of the vaccinated subjects ≤5 years old had severe wasting (severe acute malnutrition), while 21% had moderate wasting. Severe and moderate stunting was observed in 8.70% and 15.63% of the total subjects. In children > 5 years, 19% had severe thinness, 12% had thinness and only 1(1%) case was overweight.

Amongst unvaccinated subjects, 16.67% children ≤5 years old had severe wasting (severe acute malnutrition), while 21.67% had moderate wasting. Severe and moderate stunting was observed in 5.88% and 30% of the total subjects. In children > 5 years, 27.50% had severe thinness, 15% 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	24(44.44)	24(44.44)	6(11.11)	54	0.053
	-2 to-3	39(60.94)	19(29.69)	6(9.37)	64	
	>-2	245(67.68)	67(18.50)	50(13.81)	182	
Height for Age Z score	<-3	7(46.67)	6(40)	2(13.33)	15	0.017
	-2 to-3	44(54.32)	31(38.27)	6(7.40)	81	
	>-2	147(71.36)	50(24.27)	9(4.37)	206	
Weight for Height z score	<-3	12(52.17)	9(39.13)	2(8.70)	23	0.537
	-2 to-3	17(53.13)	10(31.25)	5(15.63)	32	
	>-2	54(51.43)	44(41.90)	7(6.67)	105	
BMI Z score (age≥5yrs)	<-3	16(57.14)	9(32.14)	3(10.71)	28	0.001
	-2 to-3	10(58.82)	6(35.29)	1(5.88)	17	
	>-2 to 1	80(86.02)	9(9.67)	3(3.22)	93	
	>1	2(100)	0	0	2	

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	879	0.001
	<-2SD to-3SD	677	
	<-3SD	538	
H/A z score	-2SD	1812	0.005
	-2SD to-3SD	675	
	<-3SD	377	
W/H z score	> -2SD	615	0.456
	-2SD to-3SD	577	
	<-3SD	539	

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=0.001) 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=0.017) 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 67.68%

with GMT 879mIU/ml, moderately malnourished (wasting) 68% with GMT 677 mIU/ml and in severely malnourished (severe wasting) 60.90% with GMT 538 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 54.32% with GMT 675 mIU/ml, moderately malnourished (stunting) seropositivity was 71.36% with GMT 377 mIU/ml and in severely malnourished (severe stunting) seropositivity 46.67% with GMT 351 mIU/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: 0.456)

In a study in Nigeria by Ifekwunigwe et al.[21], 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.[22], seroconversion was not associated with anthropometric indices. McMurray et al.[23] 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.[24], Halsey et al.[25], Ekunwe et al.[26] found good antibody response in children which were not severely malnourished. Similarly Lyamuya et al.[27] 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.[28,29]

Delayed antibody response to measles vaccine was seen in malnourished children.[30] Similar to our study, there was one study which demonstrated that stunting is associated with low antibody response.[31] 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.[32] found decreased antibody titre in children with Kwashiorkar. Hafez et al.[33] 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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