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**Original Research Article**

# A Retrospective Study to Establish the Association of Measles Antibody Titers with Nutritional Status in Children 1 to 12 Years of Age

**Rishika Verma[1], Prashant Kumar[2], Nigam Prakash Narain[3]**

[1]**Junior Resident, Upgraded Department of Pediatrics, Patna Medical College and Hospital, Patna, Bihar, India**

[2]**Junior Resident, Upgraded Department of Pediatrics, Patna Medical College and Hospital, Patna, Bihar, India**

[3]**Professor (Unit Head) Upgraded Department of Pediatrics, Patna Medical College and Hospital, Patna, Bihar, India**

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**Corresponding Author: Dr. Prashant Kumar**
**Conflict of interest: Nil**

**Abstract**

**Aim:** The aim of the present study was to find out any association of measles antibody titers with nutritional status in children 1 to 12 years.

**Methods:** A retrospective study was conducted in the duration of January 2014 to December 2014 on 1-12 year old children attending the Upgraded Department Of Pediatrics, Patna Medical College and Hospital, Patna, Bihar, India 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. Duration of study for one year.

**Results:** Majority (66.66%) of the total subjects had been vaccinated against measles. However, the relationship between age and vaccination status was not found to be statistically significant (p=0.160). 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. 38.34% of the total subjects ≤5 years old had severe wasting (severe acute malnutrition), while 35% had moderate wasting. In children > 5 years, 23.34% had severe thinness, 13.33% had thinness and only 2 (0.6%) case was overweight. 43% of the vaccinated subjects ≤5 years old had severe wasting (severe acute malnutrition), while 35% had moderate wasting. A highly statistically significant relationship 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 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

Measles is a highly infectious disease common in children. It is caused by a virus belonging to the mycoviruses group. [1] Worldwide, measles is the most common vaccine preventable disease accounting for 38% of disease burden. [2,3] Though safe and cost effective vaccine is available, measles is one of the common causes of death among young children especially in developing countries2. According to WHO, 145700 measles death have been documented in the year 2014, 400 children die every day and 16 die every hour. [3,4] Vaccination for measles has led to a 75% drop in measles mortality from 2000 to 2013 globally. [5]

Through routine immunization, globally 84% of children at 1 year had received at least a single dose of measles vaccine. In spite of above measures, measles continues to be a leading cause of morbidity and mortality in developing countries due to underlying malnutrition and overcrowding. In India, measles is a major cause of morbidity and a significant contributor to childhood mortality. [6] During the year 2011 in India, 33,634 children had measles which included 56 deaths. Measles accounts for 3% of under 5 mortality in our country. [7] India contributes 47% of global measles death due to population density and poor immunization coverage. [8] Only 71% of children receive measles vaccination between 9 to 12 months. With a seroconversion rate of 85% during vaccination at 9 months, only 60% children are protected at 9 months. Remaining 40% children remain susceptible to measles which leads to epidemics. [9]

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 trans placentally to their infants, resulting in longer lasting protection than would occur in expectant mothers with vaccine-induced antibody. [10,11] 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.

Hence the aim of study was to find out any association of measles antibody titers with nutritional status in children 1 to 12 years.

**Material & Methods**

A retrospective study was conducted in the duration of January 2014 to December 2014 on 1-12 year old children attending the Upgraded Department Of Pediatrics, Patna Medical College and Hospital, Patna, Bihar, India 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 430 patients were evaluated initially. Out of these, 300 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 Criteria**

- Children in the age group of 1 to 12 years.

**Exclusion Criteria**

- 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.

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 centimeters to a precision of 0.1cm by a wall mounted tape measuring up to 2 meters. An infant meter 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 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.

**Results**

**Table 1: Vaccination status of children against measles**

| Age group (years) | Vaccinated N (%) | Unvaccinated N (%) | Total | P value |
|---|---|---|---|---|
| 1-12 | 200 (66.66) | 100 (33.34) | 300 | 0.160 |

Majority (66.66%) of the total subjects had been vaccinated against measles. However, the relationship between age and vaccination status was not found to be statistically significant (p=0.160).

**Table 2: Baseline characteristics of measles vaccinated and unvaccinated children**

| Characteristics | Vaccinated mean±SD | Unvaccinatedmean±SD | P value |
|---|---|---|---|
| Age (years) | 6.4±3.0 | 5.6±3.4 | 0.518 |
| Weight (kg) | 16.4±7.3 | 16.2±6.1 | 0.248 |
| Height (cm) | 104.6±20.2 | 108.2±20.5 | 0.652 |
| BMI (kg/m$^2$) | 14.4±2.6 | 14.6±1.7 | 0.119 |
| Weight for age Z score (1-10 years) | -1.4±1.2 | -2.6±1.6 | 0.024 |
| Height for age Z core | -1.6±0.4 | -1.7±1.4 | 0.0752 |
| Weight for height Z score(1-5 years) | -1.6±1.6 | -1.6±1.8 | 0.422 |
| BMI Z Score | -1.6±2.4 | -1.6±1.8 | 0.645 |

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.

**Table 3: Nutritional status of subjects**

| Parameter of Nutritional status | | Total | (%) | Vaccinated | (%) | ccinated N | (%) |
|---|---|---|---|---|---|---|---|
| Weight for ageZ Score (age ≤10yrs) | < -3 | 60 | 20 | 44 | 22 | 16 | 16 |
| | -2 to-3 | 100 | 33.34 | 70 | 35 | 30 | 30 |
| | >-2 | 140 | 46.66 | 86 | 43 | 54 | 54 |
| | Total | 300 | 100 | 200 | 100 | 100 | 100 |
| Weight forHeight Z Score (age≤5yrs ) | <-3 | 80 | 26.66 | 60 | 30 | 20 | 20 |
| | -2 to-3 | 105 | 35 | 70 | 35 | 35 | 35 |
| | >-2 | 115 | 38.34 | 70 | 35 | 45 | 45 |
| | Total | 300 | 100 | 200 | 100 | 100 | 100 |
| Height for Age ZScore | <-3 | 18 | 6 | 10 | 5 | 8 | 8 |
| | -2 to-3 | 60 | 20 | 40 | 20 | 20 | 20 |
| | >-2 | 222 | 74 | 150 | 75 | 72 | 72 |
| | Total | 300 | 100 | 200 | 100 | 100 | 100 |
| BMI for age Zscore (age > 5yrs; | <-3 | 70 | 23.34 | 40 | 20 | 30 | 30 |
| | -2 to-3 | 40 | 13.33 | 20 | 10 | 20 | 20 |
| | >-2 to 1 | 188 | 62.66 | 138 | 69 | 50 | 50 |
| | >1 | 2 | 0.6 | 2 | 1 | 0 | 0 |
| | Total | 300 | 100 | 200 | 100 | 100 | 100 |

38.34% of the total subjects ≤5 years old had severe wasting (severe acute malnutrition), while 35% had moderate wasting. In children > 5 years, 23.34% had severe thinness, 13.33% had thinness and only 2 (0.6%) case was overweight. 43% of the vaccinated subjects ≤5 years old had severe wasting (severe acute malnutrition), while 35% had moderate wasting.

**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 Agez score (age ≤10yrs) | <-3 | 40 | 66.6 | 15 | 25 | 5 | 8.33 | 60 | 0.052 |
| | -2 to-3 | 72 | 72 | 20 | 20 | 8 | 8 | 100 | |
| | >-2 | 98 | 70 | 20 | 14.28 | 22 | 15.72 | 140 | |
| Height forAge Z Score | <-3 | 3 | 50 | 2 | 33.33 | 1 | 16.66 | 6 | 0.026 |
| | -2 to-3 | 9 | 45 | 8 | 40 | 3 | 15 | 20 | |
| | >-2 | 50 | 67.56 | 17 | 22.97 | 7 | 9.45 | 74 | |
| Weight for Height z Score (age <5years) | <-3 | 45 | 56.25 | 24 | 30 | 11 | 13.75 | 80 | 0.634 |
| | -2 to-3 | 65 | 61.90 | 25 | 23.80 | 15 | 14.28 | 105 | |
| | >-2 | 65 | 56.52 | 40 | 34.78 | 10 | 8.69 | 115 | |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| BMI Z score(age≥5yrs) | <-3 | 39 | 54.28 | 26 | 37.14 | 5 | 7.14 | 70 | 0.001 |
| | -2 to-3 | 24 | 60 | 12 | 30 | 4 | 10 | 40 | |
| | >-2 to 1 | 150 | 79.78 | 28 | 14.89 | 10 | 5.31 | 188 | |
| | >1 | 2 | 100 | 0 | 0 | 0 | 0 | 2 | |

A highly statistically significant relationship 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 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 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 | 932 | 0.001 |
| | <-2SD to-3SD | 669 | |
| | <-3SD | 549 | |
| H/A z score | -2SD | 1790 | 0.005 |
| | -2SD to-3SD | 680 | |
| | <-3SD | 382 | |
| W/H z score | > -2SD | 579 | 0.555 |
| | -2SD to-3SD | 569 | |
| | <-3SD | 558 | |

It was not found statistically significant with p value 0.05 for seropositivity but significant with p value 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.

## Discussion

Measles is a highly infectious disease common in children. It is caused by a virus belonging to the mycoviruses group. [13] Worldwide, measles is the most common vaccine preventable disease accounting for 38% of disease burden. [14] Though safe and cost effective vaccine is available, measles is one of the common causes of death among young children especially in developing countries. [15] According to WHO, 145700 measles death have been documented in the year 2014, 400 children die every day and 16 die every hour. [16,17] Through routine immunization, globally 84% of children at 1 year had received at least a single dose of measles vaccine. Insite of above measures, measles continues to be a leading cause of morbidity and mortality in developing countries due to underlying malnutrition and overcrowding. [18]

Majority (66.66%) of the total subjects had been vaccinated against measles. However, the relationship between age and vaccination status was not found to be statistically significant (p=0.160). 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. 38.34% of the total subjects ≤5 years old had severe wasting (severe acute malnutrition), while 35% had moderate wasting. In children > 5 years, 23.34% had severe thinness, 13.33% had thinness and only 2 (0.6%) case was overweight. 43% of the vaccinated subjects ≤5 years old had severe wasting (severe acute malnutrition), while 35% had moderate wasting. McMurray et al [19] 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 titers are slightly reduced in all nutritional groups 12 months after vaccination. Smedman et al [20], Halsey et al [21], Ekunwe et al. [22] found good antibody response in children which were not severely malnourished. Similarly, Lyamuya et al [23] 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. [24,25] Similar to our study, there was one study which demonstrated that stunting is associated with low antibody response. [26] 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 [27] found decreased antibody titre in children with Kwashiorkar. Hafez et al [28] found decrease humoral response to measles vaccine.

A highly statistically significant relationship 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 was observed between height for age Z scores and

seropositivity, with higher seropositivity being noted in children with higher height for age z scores. 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 titers as well GMT of measles specific IgG antibody, with those with better nutritional status having higher measles antibody titers.

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