The Professional Medical Journal
www.theprofesional.com

ORIGINAL PROF-2401

MEASLES VACCINE;

RISK FACTORS FOR LOW ANTIBODY TITERS BEFORE AND AFTER SINGLE DOSE

Dr. Tasneem Kousar[1], Dr. Shazia Memon[2], Dr. Salma Shaikh[3], Dr. Farzana Shaikh[4]

1. Senior Registrar
   Paediatric Department
   LUMHS
2. Assistant Professor of Paediatrics
   LUMHS
3. Professor of Paediatrics
   LUMHS
4. Assistant Professor of Paediatrics
   LUMHS

Correspondence Address:
Dr. Shazia Memon
B.16 Hesco Colony
Kotri Road, Hussianabad, Hyderabad.
shazia.memon@lumhs.edu.pk

Article received on:
30/11/2013
Accepted for Publication:
24/12/2013
Received after proof reading:
21/04/2014

ABSTRACT... Objective: To determine the rate of sero-conversion after first dose of measles immunization in children less than one year of age and to find out association between sero-conversion with nutritional status, URTI, fever and diarrhea. **Methodology:** Descriptive cross sectional study of 6 month duration conducted at outpatient department, EPI center LUH Hyderabad. Total 240 children between 9 to 12 months, who came for measles immunization were enrolled. Pre-vaccination blood samples were obtained along with assessment of nutritional status, and current associated illness like pneumonia, diarrhea and fever of each child. The post vaccination samples were taken after 3 months. Measles antibodies were estimated by using ELISA technique and titers were compared with controls supplied by manufacturers. **Results:** The effectiveness of measles immunization was 87.5%. Statistical analysis proved that association sero-negativity with clinical condition was insignificant (Chi square test, P value > 0.05). Regarding the pre-vaccinated status 222 (92.5%) were found negative for anti-measles antibodies and 18 (7.5%) were found to be with persistent maternal anti-measles antibodies. **Conclusions:** Measles immunization produces adequate immunological responses even among malnourished children however a second dose is necessary to increase the efficacy more than 95%.

Key words: Measles immunization , malnutrition, sero-conversion

Article Citation: Kousar T, Memon S, Shaikh S, Shaikh F. Measles vaccine; risk factors for low antibody titers before and after single dose. Professional Med J 2014;21(2): 338-342.

INTRODUCTION

Measles is endemic in many countries and major cause of morbidity and mortality in children despite high coverage of measles vaccine[1]. It is probably due to inadequate immunization. Measles is highly contagious and serious disease, often associated with complications such as Otitis Media, Bronchopneumonia, Encephalitis and even death[2]. Epidemiological studies reveal that it occurs most often in un-immunized children younger than five years. The measles disease is unusual below the age of 4-6 months because of the presence of maternally acquired antibodies[3]. The case fatality rates are 5-25% in developing countries[4]. In 1950s, an average of 500,000 cases and 500 deaths were reported per year. With the use of live attenuated measles vaccine in 1963, a dramatic reduction of measles cases occurred. Up to 1988, the reduction rate was in excess of 80 per year and it was presumed that measles would be eradicated from the globe by year 2000;[5] However this goal has still not been achieved despite intensified efforts through appropriate vaccination[2]. Measles vaccine in United States and other developed countries is usually given to children at 12 months of age because by that time they have lost their maternally acquired immunity[5]. In developing countries, where measles transmission can be intense and risk of transmission is high in infancy, World Health Organization recommends measles vaccine at the age of 9 months[6].

Measles can occur in immunized children. This could be due to vaccine failure i.e. inactive vaccine or inadequate host response. The main risk factor

is age at time of vaccination, because persistent maternal antibodies neutralize the antibodies formed by vaccination. Malnutrition and infections may be associated with poor response; also virus might have changed genetically, rendering vaccine ineffective; which could be another possibility[7].

Measles antibody is used as an indicator of previous natural infection, vaccination and also a marker of protective immunity[8]. Therefore measurement of antibody titer is used to assess the vaccine efficacy. The vaccine efficacy was estimated to range from 73% to 90%[9].

The rationale of our study was as measles being a serious problem and recurrence of measles disease even after immunization so there is a need to look for sero-conversion of anti-measles antibodies after measles vaccine to detect the efficacy measles vaccination.

This study was to identified the risk factors responsible for low antibody titers and to estimate the persistence of measles antibodies before first dose of measles immunization and their sero-conversion rates 3 months after measles immunization.

MATERIAL AND METHODS

It was comparative analytical study approved by institutional review board of Liaquat university hospital. Our sample was 240 children, who came for first dose of measles vaccine at Expanded Program on Immunization centre, outpatient department of Liaquat University Hospital Hyderabad. The study period was of 6 month duration from 1st August 2010 to 28th Feb2011. Sampling technique was non probability purposive.

After taking informed consent from parents, following the principles of confidentiality and autonomy and giving the parents complete authority to quit at any time during study; infants between the ages of 9 to 12 months, who have not received measles vaccine before were included while the children with history of clinical measles, use of immunosuppressive drugs or history of recent blood transfusion were excluded.

Blood sample of each child was obtained by venepuncture before vaccination. The serum was separated in the laboratory, transferred to a labeled tube and stored at -20 °C until testing. Prior to administration of measles vaccine, nutritional status, any history of respiratory tract infection, diarrhea or fever of each child was recorded. The date of measles vaccine was reconfirmed from their vaccination card before taking the post vaccination samples after 3 months.

On completion of samples collection, anti measles antibodies were estimated by using ELISA technique (using commercial ELISA kit, Weisbada manufacturer Germany). The titers were compared with positive and negative controls supplied by manufacturers to test for validity.

Data was analyzed in SPSS version 18. Mean and SD were calculated for age of children. Proportion of measles antibodies was found out in pre-vaccinated and post vaccinated status. It was converted into percentage. Dependent variable was sero-conversion while independent variables were URTI, fever, diarrhea, PCM. Chi square test of significance was applied to find out association between Dependent and independent variables. P value was considered significant if found <0.05.

RESULTS

During the 6 month period 240 children were enrolled in the study. Around 222 (92.5%) were found negative for anti-measles antibodies in their pre-vaccinated samples and 18 (7.5%) were found to be with persistent anti-measles antibodies.

When their status was re-analyzed after 3 months of immunization 210 (87.5%) became sero-positive for measles antibodies, however 30 (12.5%) remained sero-negative. So measles vaccination was found to be effective in 87.5% of the children.

Regarding persistent anti- measles antibodies among pre-vaccinated subjects, their age along

with their antibody status is shown in table-I. It has been observed that number of children with persistent antibodies decreased with age.

Age in months	Anti-measles antibodies negative	Anti-measles antibodies positive	Total
9 months	180 (95.3%)	9 (4.7%)	189
10 months	30 (91%)	3 (9.0%)	33
11 months	09 (75%)	3 (25%)	12
12 months	3 (50%)	3 (50%)	06
Total	222 (92.5%)	18 (7.5%)	240

Table-I. Ages of Pre-vaccinated children in Association with persistent anti-measles antibodies (N=240)

Pre-vaccinated children with persistent antibodies when assessed regarding clinical manifestations showed that only 3 (16.6%) case presented with diarrhea and remaining 15 (83.5%) had no associated illness.

Among the post vaccinated children, 210 (87.5%) were positive for anti-measles antibodies while 30(12.5) remained sero-negative. All sero-negative cases were at the age of 12 months and they were also negative in their pre-vaccination sample (Table-II).

Age in months	Anti-measles antibodies positive	Anti-measles antibodies negative	Total
12 months	159 (84%)	30 (16%)	189
13 months	33 (100%)	-	33
14 months	12 (100%)	-	12
15 months	6 (100%)	-	06
Total	210 (87.5%)	30 (12.5%)	240

Table-II. Ages of Post vaccinated children in association with anti-measles antibodies (N=240)

Regarding the association of sero-negativity with clinical illness, of those 30 cases 6 (20%) presented with fever, 6 (20%) had history of cough, 3 (10%) presented with loose motions and remaining 15 (50%) had no illness. As far as association of seroconversion with different illnesses is concerned the statistical analysis had shown insignificant association (p-value is > 0.05). (Table-III).

Similar was the observation regarding the association of seroconversion with nutritional status as shown in Table-IV.

DISCUSSION

Status	Post vaccination +ve	Post vaccination -ve	Total	P value
URTI	48	12	60	0.453
Diarrhoea	30	03	33	1
Fever	21	-	21	1

Table-III. Association between URTI, fever, and diarrhea ith seroconversion (N=114)

	PCM I	PCM II	PCM III	Normal	Total	P value
No. of cases	102 (42.1%)	30 (12.5%)	21 (8.7%)	57 (23.7%)	240	0.8
Association of malnutrition with seronegativity N=30						
Post-vaccination -ve cases	9 (8.8%)	6 (20%)	3 (14.2%)	12 (21%)	30 (12.5%)	1

Table-IV. Nutritional status in association with vaccination status.

Measles is a major cause of mortality and morbidity mainly in developing countries. Its control is an important public health goal. The incidence of measles has decreased with introduction of measles vaccine, but measles epidemics were seen after the interval of few year due to poor immunization coverage[10].

This study was conducted to see the difference of anti-measles antibodies before and after vaccination, to see the effectiveness of measles vaccine, persistence of maternal titres and factors responsible for its failure.

This study showed that among pre-vaccinated subjects, 222 (92%) were negative for anti-measles antibodies and 210 (87.5%) were found sero-positive after 3 months of vaccination. So in our study the efficacy of single dose of measles immunization was 87.5%. A study conducted in Sirilanka has shown 99% sero-negativity before vaccination and 93.06% became sero-positive after 8 weeks of vaccination10. The effectiveness shown in Thailand study was similar to the results of our study; 93.5% infants were negative for anti-measles antibodies before vaccination at 9 months of age and 68.75% became sero-positive after 3 months of vaccination[11]. In another study in Shiraz, Islamic Republic of Iran, showed 100% sero-negative cases before vaccination[12]. A study in China showed sero conversion rate of measles IgG 91.65[13].

The prevalence of pre vaccinated subjects with persistent anti-measles antibodies in relation to age from 9 months to 12 months showed more number of children at 9 months of age as compared to 10, 11 and 12 months of age. This showed decline in number of persistence antibodies as age increases. Similar study was conducted in Shiraz, Islamic Republic of Iran. It showed that persistence of anti bodies was found at six months of age in 100 children and this number declined to 0% at nine months of age[14].

The reason of prolonged persistence of maternal transplacentaly transferred antibodies might due fact that mother immunity was due to natural infection rather then vaccine induced[15].

Regarding the status of post vaccinated children 30 (12.9%) were at 12 months of age and they all had pre vaccinated negative antibody titre. This showed the cause or risk factor for vaccine failure may be other than transplacental transfer of IgG from mother. Similar results have also been reported from India[16]. This study showed 50% post vaccinated negative cases were having clinically fever, cough and loose motion. Total number of children with clinical illness was 114 (42.5%). Among these 60 (25%) had URTI, 33(18.1%) acute diarrhoea and remaining 21 (8.7%) had fever. As far as association of seroconversion different illnesses is concerned we found p=.453 with URTI, p=1 with diarrhea, p=1 with fever and again p=1 with PCM.

Therefore no significant association was found among seroconversion and different illnesses. Statistical analysis proved that association was insignificant (Chi square test, P value > 0.05). Similar study was conducted in Spain,and showed seroconversion rates in children without URTI and with URTI at time of vaccination were similar[17]. Nutritional status may also affect the seroconversion of vaccine. Similar results were reported from India[16], and also from Pakistan[18]. But in our study no significant association was observed between seroconversion and nutritional status. Our study showed 10% vaccine failure at the age of 9 months, because these children can not develop adequate antibodies for protection of measles. Regarding the failure of vaccine further studies are needed to find out others cause of vaccine failure.

CONCLUSIONS

Measles immunization produces adequate immunological responses with no significant effect on immune function, even among children of low socioec.onomic status who suffer from poor nutrition. First dose at age less than 12 months often does not produce a significant antibody response. Therefore, infants who receive their first dose of measles immunization at 6–11 months of age need to have a repeat dose at 12 months.

RECOMMENDATIONS

Strengthening the immunization services, along with continuous outreach programs to reach pockets of unimmunized populations.

For countries that routinely give the first dose of measles immunization at less than 12 months of age, a repeat dose is recommended at 12 months with a booster at school entry.

REFERENCES

1. Sabin AB. **Treatment On Rapid Elimination And Ultimate Global Eradication Of Poliomyelitis And Measles.** Pediatrics1992;9:162-9.
2. Mason WH. Behrman RE, Kliegman RM, Janson HR, Stanton BF, **.Nelson's text book of pediatrics.** 19th ed. Philadelphia; WB Saunders, 2011: 1069-75.
3. Gold E. **Almost extinct disease;** Measles, Mumps, Rubella, Pertusis.Pediatric Rev.1996;17:120-7.
4. Adam HM. **Measles and malnutrion.** Pediatre Rev. 1998; 19: 70-1.
5. Janaszek W, Gut W, Gay NJ. **The epidemiology of measles virus antibodies in the population.** Epid inf. 2000; 125:385-92.
6. Hillerman MR. Past. **Present And Future Of Measles, Mumps, And Rubella Virus Vaccine;** Pediatrics. 1992;90:140-63.
7. Von Loveren H, Van Amsterdom JG, VAnderbriel RT, Kimman TG, RumkeHC,Streerenberg PS et al. **Vaccine induced antibody response as a parameters of the influence of endogenous and environmental factors.** Environ- perspect. 2001;190 : 757-64.
8. Saipan P, Jiwapaisarnpong T, Pattandailo CS, Loyha Y, Janggajit T. **Measles antibodies in children in Ubon Ratchathan province.** J Med Asso Thai. 2001; 84: 500- 6.
9. Murray M, Rasmussan Z. **measles outbreak in northern Pakistani village: epidemiology and vaccine effectiveness.** Am J Epid. 2000; 151:811-9.
10. Ariyasriwatanac. **Trend of measles morbidity in Thailand** J Med–asso-Thai 2003; 86:707- 18.
11. Gunawardena S, Bandaranayake V. **Seroconversion rate following measles vaccination.** Ceylon Med J. 2000. 45: 107-9.
12. Karimi IA ,Arjomandi IA, Albarzi IM, Rasoulii MR, Kadivar IB, Oboodi I etal. **Prevalence of measles antibody in children of different ages in Shiraz,** Islamic republic of Iran 2004; 10: 468-73.
13. You Wang Y, Ping W, Feng C. **Serological and epidemiological effects and influence factors of primary immunization with current live attenuated measles vaccine (Hu191) among infants aged 6-15 months.** Vaccine 2001;19 : 1998-2005.
14. Schnorr JJ, Cutts FT, Wheeler TG, Akramuzzaman SM,Alam MS, Azim T et al. **Immune modulation after measles vaccination of 6-9 months old Bangladeshi children.** Vaccine; 1999: 1503-10.
15. Sashil J,Lalitha G, George K, Abraham J. **Serological response to early measles vaccine.** J Trop paed. 2004; 3: 175-77.
16. Cilla G, Pena B, Marimon JM,Perez Te. **Serological response to measles ,mumps, rubella vaccine among children with upper respiratory tract infection.** Vaccine 1996; 14:496- 4.
17. Rafiei Tabatabaei S, Esteghamati AR, Shiva F, Fallah F, Radmanesh R, Abdinia B, Shamshiri AR, Khairkhah M, Shekari Ebrahimabad H, Karimi A. **"Detection of serum antibodies against measles, mumps and rubella after primary measles, mumps and rubella (MMR) vaccination in children"** Arch Iran Med. 2013 Jan;16(1):38-41. doi: 013161/AIM.0012.
18. Rafique Ahmad Channa, Shahzad Hussain, Nisar Ahmad Kanher, Farnaz Malik, MazharUllah Memon, Sidra Mahmood et al; **"Sero-surveillance of measles amongst vaccinated and non-vaccinated children: An age stratified population based survey in Pakistan"** African Journal of Pharmacy and Pharmacology Vol. 6(24), pp. 1713-1718, 29 June, 2012.