

Original Research Article

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Importance of Immunoglobulin M in Detecting Cases of Measles in Children with Clinically Suspected Measles

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ABSTRACT

Measles, an acute viral illness caused by a virus belonging to the family Paramyxoviridae, is a vaccine-preventable disease. Children's between 9 months and 12 years of age are mostly affected and presents with fever and maculopapular rash. Despite the national immunization program, measles virus infection is common in India. Objectives of the study are 1. To study the suspected cases of measles virus infection with high fever and characteristic rashes, among children. 2. To detect antibody levels against measles virus by ELISA IgM and IgG. A total of 49 suspected measles cases between 9 months to 12 years of age of both sexes were included in the study and blood samples were collected after informed consent. The serum samples were screened for Measles IgM and IgG (Cal Biotech) ELISA test. The sensitivity and specificity of the test is 97%. The time taken for the test is 1 day. The test was carried out keeping in view the instructions of the manufacturer. Out of 49 cases, 25 (51%) of the patient studied were male and 24 (48.9%) were female. The samples were screened for measles virus specific IgM and IgG. 100% (49) positivity were observed in Measles virus specific IgM ELISA, whereas only 42.8% (21) positivity were observed for measles virus specific IgG in both the groups for Measles virus infection. Immediate results of IgM and IgG will help the patient in early diagnosis and also to the clinicians for patient management.

Keywords

Immunoglobulin M, Measles, IgM & IgG

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Introduction

Measles is an infectious disease caused by Morbillivirus, with a secondary attack rate in excess of 80% that usually affects children (Park, 2011). However, multiple outbreaks of the disease have even been reported among adults in heterogeneous settings (urban areas, university campuses, disaster sites, during international travel, etc.) (Centers for Disease Control and Prevention, 2013). The disease is characterized by the presence of fever, cough,

and coryza, followed by the appearance of a typical rash. The disease is generally transmitted by the airborne route, with a large proportion of cases being self-limiting; nevertheless, multiple deaths have been reported because of complications associated with disease (Patro *et al.*, 2012).

While the number of cases and deaths attributed to measles worldwide has declined substantially over the past two decades, measles remains one of the leading causes of

childhood mortality in developing countries (Centers for Disease Control and Prevention, 1997). Even countries that have achieved high levels of measles vaccination coverage have frequently witnessed large outbreaks of measles (Agocs *et al.*, 1992).

Measles-specific immunoglobulin M (IgM) serology is the standard test for the rapid laboratory diagnosis of measles, and IgM testing is now almost exclusively performed in laboratories (Performance of Indirect Immunoglobulin M (IgM) Serology Tests and IgM Capture Assays for Laboratory Diagnosis of Measles). The presence of IgG antibody to measles virus is indicative of previous exposure or vaccination. In individuals with acute measles, a significant increase in measles IgG antibody level is indicative of recent infection. IgM antibodies to measles virus are often detectable with onset of the rash and typically persist for 4 weeks. At least 80% of patients will be positive for measles IgM at 6 days and 100% at 16 days after onset of symptoms.

The assay of specific immunoglobulin M(IgM) antibodies can aid in the diagnosis of early

Infection and may obviate a paired convalescent serum sample in acute virus infections. IgG antibodies to the same antigen interfere with the assay of specific IgM antibodies by excluding the less avid IgM antibodies when the quantity of antigen is marginal (Holmgren and Svennerholm, 1973) and by providing an attachment for any IgM-rheumatoid factor (RF), thereby causing bound IgM to lose specificity (Meurman and Ziola, 1978). Thus, the removal of IgG from IgM is necessary in those systems which do not discriminate the final immunoglobulin interacting with antigen (e.g., hemagglutination inhibition assay) and vastly improves the specificity of systems which can

identify the bound immunoglobulin (Separation of Immunoglobulin M (IgM) Essentially Free of IgG from Serum for Use in Systems Requiring Assay of IgM Type Antibodies Without Interference from Rheumatoid Factor).

Y ELISA is being used. What is the rationale???

Materials and Methods

A cross-sectional study was conducted from July 2017 – Nov 2017 in Gandhi hospital where the cases with fever with rash were being admitted. A suspected case of measles was defined as the occurrence of fever for more than 3 days with maculo-papular rash and at least one of the following: cough, coryza or conjunctivitis in children as per WHO guidelines. The study protocol was approved by the Institutional ethical committee of Gandhi Medical College, Hyderabad. The cases were identified by using passive surveillance system of the hospital from both outpatient and inpatient departments. For each case, data was collected by using a pretested, pre designed, semi structured questionnaire from the parents as informants. The data collection tool has information regarding the age, sex, immunization status of the child etc. Immunization status was assessed by checking the cards if available or by extracting the history of immunization from the mothers.

Blood samples were collected by the nursing staff from the study subjects for routine examination as well as for serology. Collected clinical samples (whole blood) were processed and stored appropriately until test performed.

Laboratory investigation

Blood samples were collected from the patients who were suspected to be having

measles. The serological tests of the patients were performed at the serology dept. of microbiology laboratory Gandhi hospital. For the detection of specific measles IgM and IgG antibodies, commercial ELISA calbiotec kits were used. The sensitivity and specificity of the test is 97 %. The time taken for the test is 1 day. The assays were performed as recommended by the manufacturer and assay results on the samples were interpreted qualitatively as positive, negative or equivocal. Measles infection was confirmed when anti-measles IgM antibodies were present. If the Antibody Index Interpretation is <0.9 then no detectable antibody to measles IgM by ELISA. If it is between 0.9-1.1, then it is considered as borderline positive. If it is >1.1, then detectable antibody to measles IgM by ELISA is confirmed. Follow-up testing is recommended if clinically indicated. Measles infection was confirmed when anti-measles IgM antibodies were present. If there is any Borderline positive result, then a second serum should be requested to ascertain seroconversion. However in the present study, we did not need any second sample to ascertain seroconversion.

This procedure depends on the following: Diluted patient serum (serum diluent contains sorbent to remove Rheumatoid Factor and human IgG interference) is added to wells coated with purified measles antigen. Measles IgM specific antibody, if present, binds to the antigen.

All unbound materials are washed away and the enzyme conjugate is added to bind to the antibody-antigen complex, if present. Excess enzyme conjugate is washed off and substrate is added. The plate is incubated to allow the hydrolysis of the substrate by the enzyme.

The intensity of the color generated is proportional to the amount of IgM specific antibody in the sample.

Results and Discussion

Present study reported predominant age group between 3 – 5 years was 59.1%, whereas age between 6 – 12 years was 40.8%. The peak age for measles was observed in children under the age of 3 – 5 years.

Age wise distribution of measles cases

Out of 49 cases, 25 (51.1%) were males and 24 (48.8%) were females. A higher proportion of measles was observed in male children compared with females.

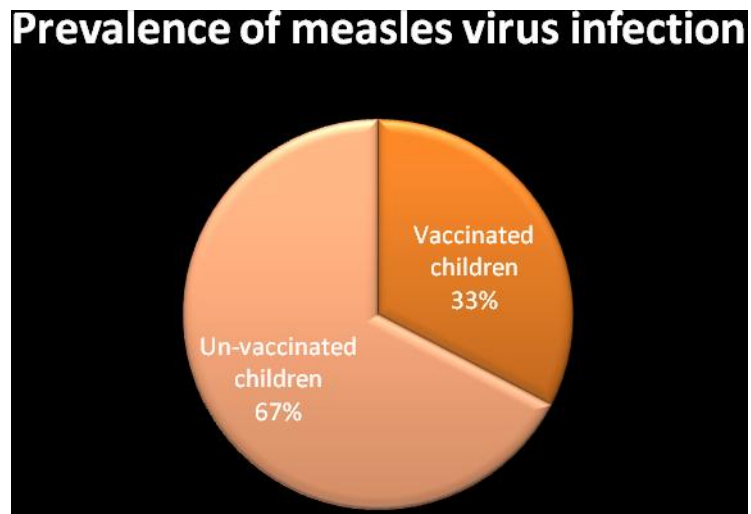
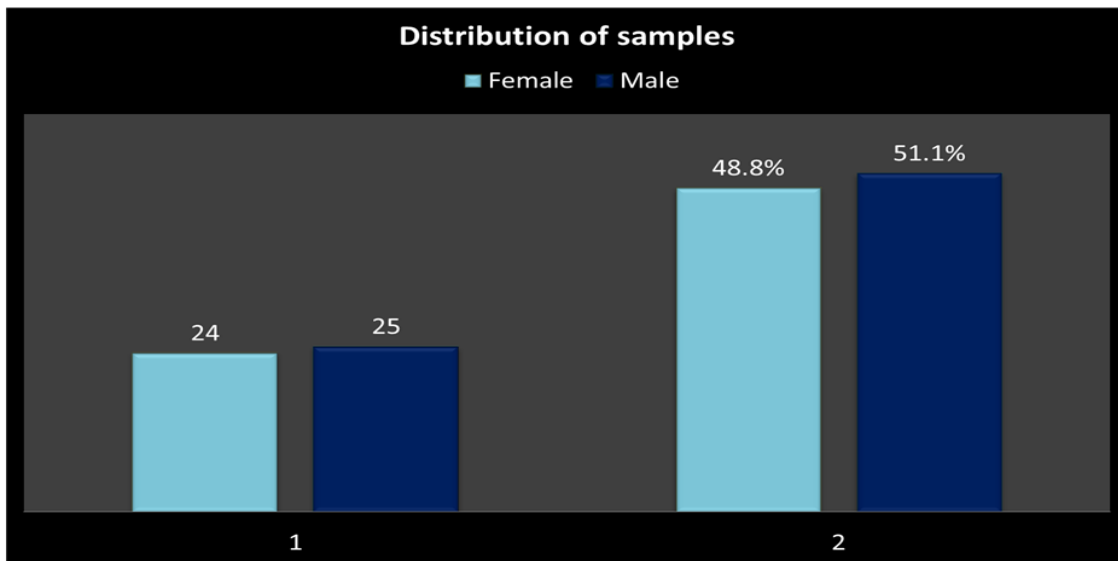
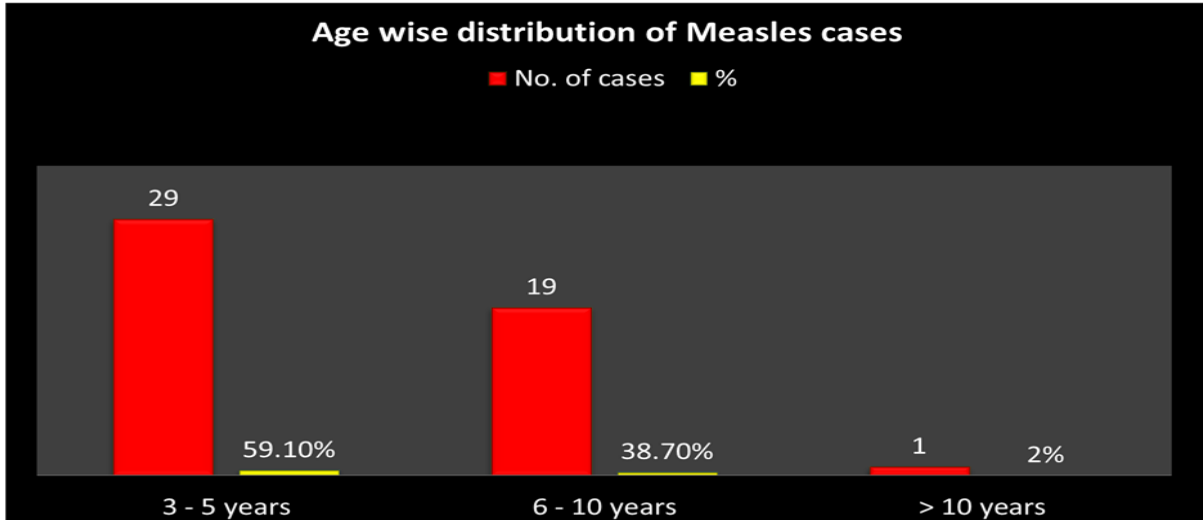
However, this difference was not found to be statistically significant. A majority of the cases (59.1%) were recorded in children under the age of 3- 5. The age wise distribution of cases is given below

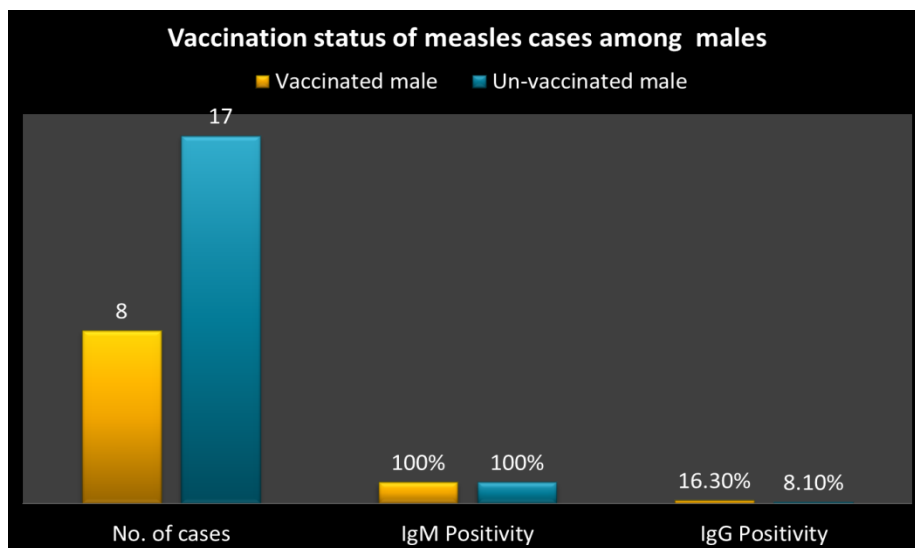
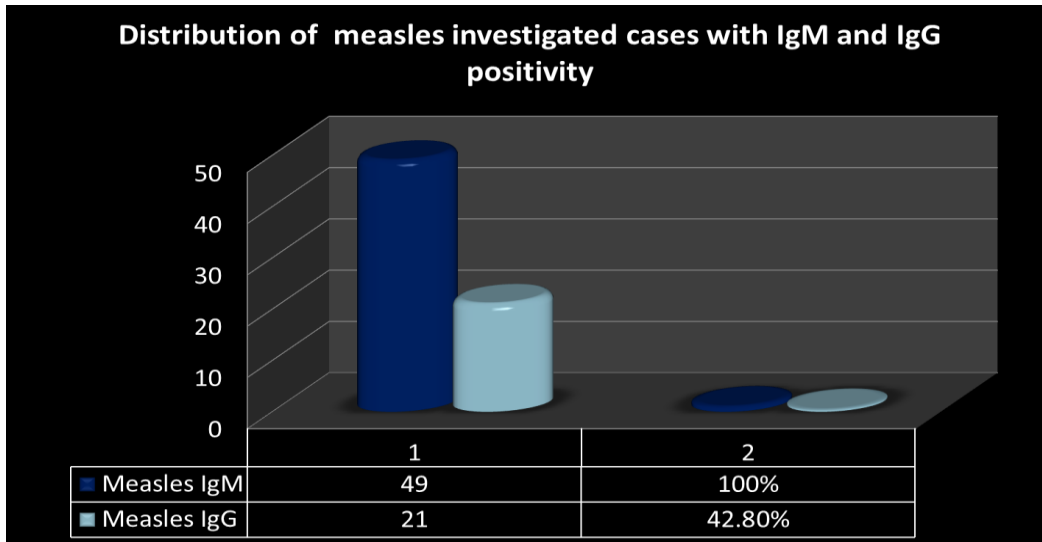
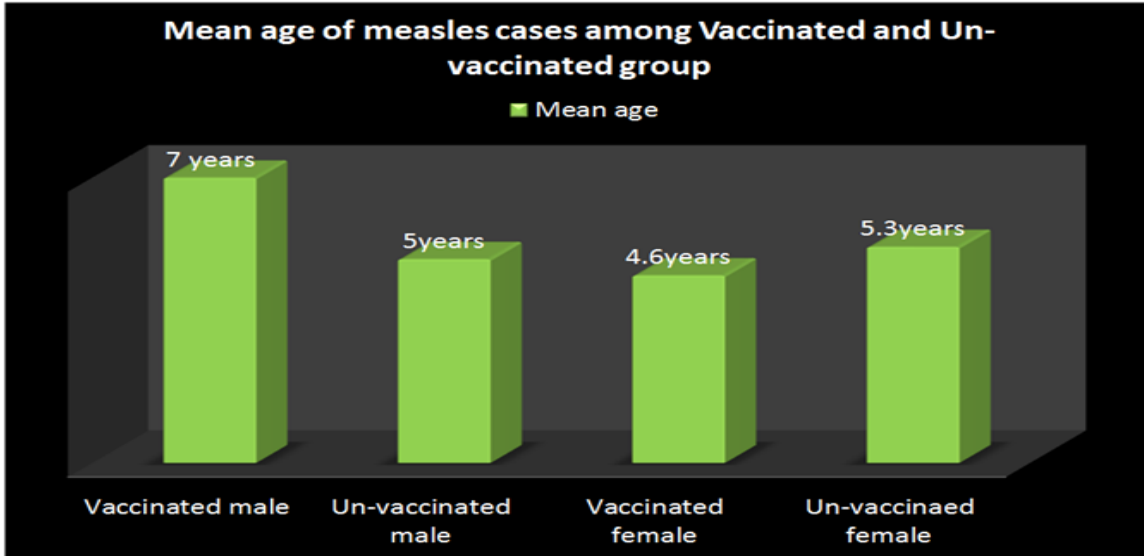
Out of 49 cases, 25 (51%) of the patient studied were male and 24 (48.9) were female. The males were found to be 51% in present study, whereas females were 48.8 %. Two peaks of age for measles were observed, the first was among 3 - 5 year olds and the second was among 6 - 10 year olds.

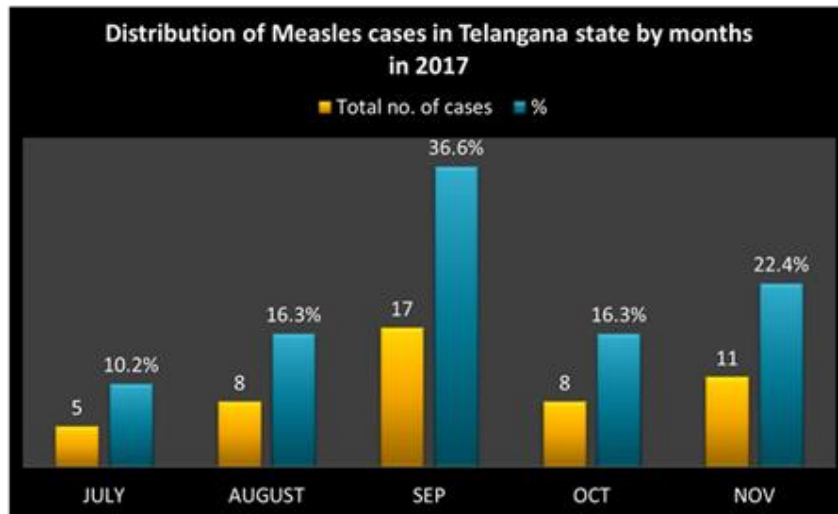
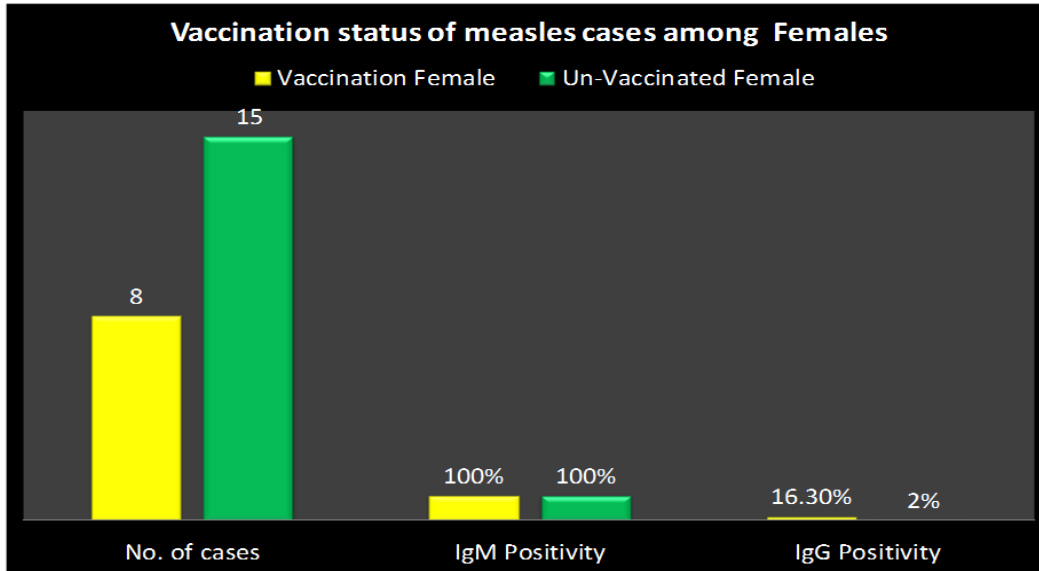
Out of total 49 patients studied, 16 (32.6%) were vaccinated and 33 (67.3%) were unvaccinated against measles. In the present study the prevalence of measles in vaccinated group was 32.6%, where as in Un-vaccinated group was 67.3%.

The mean age of the cases in the year 2017 was between 5 – 7 years for male children, whereas of females was 4 – 5 years. In total 49 measles cases, Females were contributed to disease were 24 (48.8%), Males were 25 (51.1%).

The mean age wise distribution of measles cases among vaccinated and un-vaccinated children is given below.







Studies showing the age of the study patients

Author	Place	Year	9 months – 5 years	6 - 12 years
Tony Lawrence	Kerala	2007-2008	51%	30.3%
Ashok mishra	Madhya Pradesh	May 2004	65.9%	28.4%
Adriana pistol	Atlanta, Georgia	1999-2000	41%	34%
Present study	Telangana	2017	59.1%	40.8%

Studies showing the levels of Measles IgM antibodies in different studies

Author	Place	Year	Measles IgM
Manoj V. Murhekar,	Himachal Pradesh, Uttaranchal, Tamil Nadu, and West Bengal.	2004-2006	78%
Niteen Wairagkar ¹	In 21 of 28 States and 2 of 7 Union Territories of India	2005-2010	62.8%
Adriana Pistol	Atlanta, Georgia	1999-2000	51.7%
Present study	Telangana	2017	100%

Studies showing the status of immunization among the study subjects

Author	Place	Year	Measles Vaccinated	Measles Un-Vaccinated
Tony Lawrence	Kerala	2007-2008	28.6%	54.3%
Ashok mishra	Madhya Pradesh	May 2004	18.2%	79.9%
John P.A	Sri lanka	1999-2000	40%	60%
K.Vainio	Norway	2011	46.1%	53.8%
Munesh k Sharma	Chandigarh	2003	30.7%	70.2%
Present study	Telangana	2017	32.6%	67.3%

Status of IgM and IgG

The samples were screened for measles virus specific IgM and IgG. 100% (49) positivity were observed in Measles virus specific IgM ELISA in both the groups (males and females).

Only 42.8% (21) positivity were observed in vaccinated group for Measles virus specific IgG among this male 24.4% (12) and female 18.3% (9). The IgM positivity was found to be 100% in the present study.

Vaccinated male were 8 (100 % IgM and 16.3 % IgG), whereas Un-vaccinated male were 17 (100 % IgM and 8.1 % IgG).

Vaccinated Female were 8 (100 % IgM and 16.3 % IgG), whereas Un-vaccinated Female were 15 (100 % IgM and 2 % IgG).

Seasonal distribution of measles cases

Even though measles is seen during winter and early spring (January-April). The months which had the most number of cases were

September, respectively August and October 2017. Distribution of measles cases in Telangana state by months in 2017 is given below

The ultimate goal of this study to show the performance of direct diagnosis of measles virus infection through evaluating the immunoglobulin M against the measles virus in clinically suspected measles patients serum by an enzyme linked immunosorbent assay (ELISA) in the hospital setting. Peak age for measles were observed, first among 3 - 5 year olds (59.1%) and the second peak was observed among 6 - 10 year olds (38.7%) and > 10 year old (2%).

Cases below 3 years were not observed. The cause of this particular age distribution could be the fact that measles, mumps, and rubella vaccination at 15 months was introduced into Universal Immunization Program general vaccination in 1981, causing a decrease in the incidence of the illness in the following years as the number of the vaccinated children increased (Evaluation of Diagnostic Markers for Measles Virus Infection in the Context of an Outbreak in Spain).

Studies showing the levels of Measles IgM antibodies in different studies

The overall measles IgM-positivity rate was 100 %, and was highest among persons aged 4 - 7 years, as Table indicates. We found no significant variation of measles seropositivity across the age groups. The IgM positivity was found to be 100% in current study which is in concurrence with many other studies which are given below.

Studies showing the status of immunization among the study subjects

In the Present study the number of measles cases in vaccinated group was 32.6%, where

as in Un-vaccinated group was 67.3%. The findings of other studies are given below

In the present study, cases that were immunized but developed the disease were 16 (32.6%), whereas not immunized was 33 (67.3%). Immediate results of IgM & IgG will help the patient in early diagnosis and also to the clinicians for patient management. The current study has demonstrated the effective use of IgM and IgG ELISA methods to monitor the measles cases in hospital settings.

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