

**Efficacy of measles vaccine in study
among primary school children during
measles outbreak in Iraq for the year 2004**

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Summary:

Background :

Progress towards the control of measles require a national capacity to measure program effectiveness. This require evaluation of the effectiveness of MMR vaccine, which is used in Iraq.

Aim:

This study aim to assess the seroconversion rate following MMR vaccination to estimate the efficacy of MMR vaccine which was given to primary school children aged 6-12 years when an out break of measles disease begun in Iraq at the beginning of the 2004.

Patients and Methods:

A total of 1692 and 1626 serum samplea were collected pre and post MMR vaccination from school children aged 6-12 years of 6 primary schools of Baghdad Al-Kerh and Al-Resafa. Sera tested to detect the level of measles IgG and Rubella IgG respectively by ELISA (Dade Behring Kits).

Results:

This study 4 fold increase of measles and Rubella IgG after MMR vaccination. The percentage of sero positive samples of measles and Rubella before receiving MMR vaccine 63% and 80% respectively and these results were increased after receiving MMR vaccine to be 85% for measles IgG and 99.5% for Rubella IgG. These results mean that the efficacy of MMR vaccine is very well and this campaign was successful. In addition to that the level of measles IgG is lower than the level of Rubella IgG and low level of measles IgG may wane by time.

Conclusions:

These finding may behind continuing measles outbreak in Iraq for two years, or it may be either due to low coverage rate of measles containing vaccine in some regions or there is a weakness in routine vaccination. Another reason may explain the reason behind that, which is the high level of measles IgG might didn't include protective antibodies to measles and because of that further studies are required to detect protective antibodies induced by MMR vaccine among this age group, especially that were is waning of measles antibodies and it may had a role in loss the protective antibodies.

*Fac Med Baghdad
2008; Vol.50, No.1
Received Dec. 2006
Accepted Aug. 2007*

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Introduction:

Measles is a highly infectious disease that causes mortality not only in developing countries but also in industrialized countries. It is estimated that in 1998 about 30 million cases of measles occurred and 875,000 of them died. Although measles is a serious disease, measles vaccine provides long-term immunity against measles adequately chosen and implemented measles vaccination strategies do not only reduce mortality and morbidity but also interrupt transmission of indigenous measles virus ⁽¹⁾.

Many live attenuated measles virus vaccines are in use worldwide. Measles antibodies develop in approximately 85% of children vaccinated at 9 months of age, 95% of children vaccinated at 12 months of age, and 98% of children vaccinated at 15 months of age. Measles vaccine provides life long immunity in most of the vaccinated people. Studies of the response to revaccination have shown that high proportion of vaccinated persons who lack detectable antibodies to measles will respond to second dose ⁽¹⁾.

Study Groups, Materials, and Methods :

The study was designed to investigate the level of measles IgG and Rubella IgG pre and post receiving MMR vaccine. The targeted group of our study is school children aged 6-12 years from 6 primary school of Baghdad AL-Kerkh and AL-Ressafa and as follows:

- 1- a total of 1692 serum samples tested for the level measles IgG, 802 samples were collected before receiving MMR vaccine and 890 samples were collected later (2 samples) from the same group plus an additional number were taken from vaccinated children. The time of collection of the post vaccination samples were after 45 days of receiving MMR vaccine.
- 2- A total 1626 serum samples tested for the level of Rubella IgG, 738 samples

were collected before receiving MMR vaccine and 888 samples were collected from the same group with an additional number were taken after 45 days of receiving MMR vaccine from vaccinated children. ELISA test was used to detect measles and Rubella IgG Antibodies as described in the leaflet of the commercial kit (Behring). & method was used to detect the level of measles and Rubella IgG in IU/ML as described in the following formula:

α method

$\text{Log}_{10} \text{ m IU/ML} = \alpha$ (from the barcode) $\times \Delta \text{ AB}$ (from barcode)

$\text{Log}_{10} \text{ m IU/ML} = 3.5373 \times \Delta \text{ A } 0,211$

For Measles IgG.

$\text{Log}_{10} \text{ m IU/ML} = 1,748 \times \Delta \text{ A } 0,4629$

For Rubella IgG .

The level of measles and Rubella IgG pre post MMR vaccination are investigated and each vaccinated child surveyed in this study is placed in one of the following groups depending upon the titer of measles IgG and Rubella IgG in his or her serum:

1. sero negative group: includes sera having level below 330 IU/ml for measles and below 7 IU/ml for Rubella.

2. low positive group: includes sera having IgG level within range ≥ 330 to 1499 IU/ml for measles and ≥ 7 IU/ml to 24 IU/ml for Rubella.

3. positive group: includes sera having IgG level range of ≥ 1499 to 7133 IU/ml for measles and ≥ 24 IU/ml to 128 IU/ml for Rubella .

4. high positive group: includes sera having higher than 7133 IU/ml and higher than 128 IU/ml for Rubella.

Lastly Z test was used for detection of statistical significant difference ⁽²⁾.

Results:

Table (1) shows that the greatest sero-conversion rate of measles IgG level were found among sero negative group, low positive and positive group (over four fold increase). Highly significant difference ($p < 0.01$) are found among those groups and no difference ($p > 0.05$) was found in high positive group when compared groups before and after receiving MMR vaccine. The percentage of sero-negative group before receiving MMR vaccine was 37% (294/802) and it's converted to be 5% (45/890) after receiving MMR vaccine and highly significant difference ($p < 0.01$) were found between them.

Table (1) Measles serum IgG level and post MMR vaccination .

| Vaccination Status | Total No. | Sero negative group | Low positive group | Positive group | High positive group |
|------------------------|-----------|---------------------|--------------------|----------------|---------------------|
| | | No. (%) | No. (%) | No. (%) | No. (%) |
| Before MMR vaccination | 802 | 294 37 | 369 46 | 114 14 | 25 3 |
| After MMR vaccination | 890 | 45 5 | 587 66 | 237 27 | 21 2 |
| Total | 1692 | 339 20 | 956 56 | 351 21 | 46 3 |

Table (2) shows high sero conversion rate of Rubella IgG when compared sera of each group pre and post receiving MMR vaccine (over four fold increase) and highly significant difference ($p < 0.01$) were found among all group pre and post receiving MMR vaccine. The percentage of sero-negative group before receiving MMR was 20% (147/738) and this percentage was converted to be 0.6% (5/888) after receiving MMR vaccine and highly significant difference ($p < 0.01$) were found between them.

Table (2) Rubella serum IgG level and post MMR vaccination .

| Vaccination Status | Total No. | Sero negative group | Low positive group | Positive group | High positive group |
|------------------------|-----------|---------------------|--------------------|----------------|---------------------|
| | | No. (%) | No. (%) | No. (%) | No. (%) |
| Before MMR vaccination | 738 | 147 20 | 151 20 | 343 47 | 97 13 |
| After MMR vaccination | 888 | 5 0.6 | 36 4.1 | 642 72.3 | 205 23.1 |
| Total | 1626 | 152 9.3 | 187 11.5 | 985 60.6 | 302 18.5 |

Immunity against both measles and Rubella were detected among the study group before receiving MMR AND Table (3) measles and rubella IgG pre and post receiving MMR vaccine, Results show that the percentage of children whom had antibodies against measles and rubella before receiving MMR vaccine is 63% (508/802) and 80% (591/738) respectively.

Table (3) : comparison of results of both measles and rubella IgG between study group pre and post MMR vaccination .

| Vaccination Status | Anti Measles IgG | | | | Anti Measles IgG | | | | Total | | |
|--------------------|------------------|----------|----|----------|------------------|---------|----------|------|-------|----------|------|
| | Ex. No. | Positive | | negative | | Ex. No. | Positive | | | negative | |
| | | No. | % | No. | % | | No. | % | | No. | % |
| Pre MMR vaccine | 802 | 508 | 63 | 294 | 37 | 738 | 591 | 80 | 147 | 20 | 1540 |
| Post MMR vaccine | 690 | 845 | 95 | 45 | 5 | 888 | 883 | 99.5 | 5 | 0.5 | 1778 |
| Total | 1962 | 1353 | 80 | 339 | 20 | 1626 | 1474 | 91 | 152 | 9 | 3318 |

These results shows that the antibodies response of those children against measles is lower than the immunization against rubella and statistic analysis shows highly significant difference ($p < 0.01$) between them .

The majority of sero-positive children of Group 1 after MMR campaign for both measles and Rubella IgG showed high antibody level representing successful vaccination.

Discussion:

The scale of routine immunization of measles in Iraq are designed to get measles vaccine in three doses: single measles vaccine are given at 9 month of age, then MMR vaccine are given again at 15 month of age and the last booster dose are given at the age of school entry. In addition to that two supplementary MMR campaign were implemented in Iraq, first one was implemented during may-2005 for children below five years to catch defaulters.

Despite implementing these entire campaign the measles outbreaks in Iraq were continuing for two years later and we need to discuss the reasons behind that in details.

The results of sero-conversion rates as shown in table(1) indicate that the sero-conversion rate among sero negative group is 85%(249/294), although high significant difference were found between sera collected pre and post vaccination for first, second, and third group immunity to measles among study subjects is slightly

lower than the results of studies done in other countries⁽³⁾.

Depending upon the schedule of the immunization of Iraq those children receive 2 doses of measles containing vaccine and just one dose of rubella, first single dose of measles at 9 month of their age and the second mixed dose (MMR) at 15 month of their age.

Table(1) and table (2)show that the level of measles IgG among study group is lower than the level of Rubella IgG and these finding is compatible with previous studies^(4,5) .vaccination against measles induce low level of measles IgG and it may wane easy and the waning of measles antibodies lead to accumulate susceptible.

As shown in table (3) on waning measles antibodies by time, these finding are consistent with the previous studies that talking about this issue . This may explain the reason behind continuing of measles outbreak when compared with Rubella. And 2 doses of measles vaccine are insufficient

to give the potential immunity against measles disease and loss of the immunity induced by vaccination to such an extent that infection becomes possible. These finding is consistent with studies which reported previously ^(6,7,8,9) .

In addition , almost all children who do not respond immunologically to the first dose of MMR vaccine will develop measles immunity after receiving a second dose. Evidence now indicates that

- a) there is intense need to ensure administering third dose of measles containing vaccine to reduce the proportion of person, who remain susceptible because of previous vaccine failure.
- b) Waning immunity is not a major cause of vaccine failure and has little influence on measles transmission.
- c) Revaccination of children who have low level of measles antibody produce only a transient rise in antibody level which will keep them a way of measles infection.

Table (3) shows that 95% of study group considered immune for measles as the result of receiving MMR vaccine in this campaign. And it's unknown why the remaining number of the children (45) is still sero-negative (5%) following MMR campaign and additional studies are needed to determine how frequently vaccine failure occurs after a second or third dose of measles vaccine in person who had no immune to a first dose.

Follow-up studies indicate that one dose of vaccine give long-term or probably

lifelong protection and greater than or equal to 95% of susceptible persons who received rubella vaccine developed serologic evidence of immunity ^(10,11,12) .

And these studies are compatible with our results which is show that Rubellaimmunity before MMR campaign (80%) and it's converted to (99%) after receiving MMR vaccine (table 3). However, recent rubella surveillance data do not indicate that increasing among vaccinated persons⁽¹³⁾ .

In conclusion these finding shows that the efficacy of MMR vaccine is very good for both measles and rubella.

Recommendations:

1-Because of that third dose of measles containing vaccine is important to prevent measles disease in Iraq MMR and the health sectors must take an additional measures needed to ensure that all school-aged children are vaccinated with two doses of MMR to be ensure that those children are immunized against measles.

2- Sustaining the elimination of measles from Iraq will need continuing to vaccinate all children with 3 doses of measles vaccine before school entry.

3- Further studies are needed to detect the level of protective antibody (Anti Hemagglutinin and Anti Fusion protein) because Hemagglutinin and Fusion protein is responsible on attaching the virus to target cell and spreading these viruses over all organs.

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