

*Full Length Research Paper*

# **Evaluation of sero positivity of MMR vaccine against mumps, measles and rubella, three weeks after first inoculation (12 months after birth) and second inoculation (18 months after birth), in children referred to Abuzar's health center of Zahedan in 2009-2010.**

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Viral infections like mumps, rubella and measles have significant complications such as menengioencephalitis, adverse impact on fetal and mortality of malnourished infants. Iranian children vaccination against these three diseases (MMR vaccination) has begun since 2004 in two stages, 1 year and 4-6 years of age. Currently the vaccination program has changed to one year and 18 months of age. The aim of this study was to determine antibody titer (seropositivity) about 3 to 4 weeks after the first and second stage of MMR vaccination. In this study, that it's a descriptive - cross sectional study, antibody against mumps, rubella and measles was determined in 184 children referred to Abuzar's health center of Zahedan in 2009-2010 by using ELIZA test. In the first stage of vaccination 93 children and in the second stage 91 children were selected such as samples. Among the first customers exactly 53 people had been repeated in the second stage (during our study in the first stage and second stage had received their vaccines). In comparison between the 93 children studied in phase of one year (only once had been vaccinated) with 91 children in phase of 18 months (two had received vaccine injection) was determined that in phase of one year: rubella seropositivity was 83.9%, mumps 76.3% and measles 62.4%. But in phase of 18 months: rubella seropositivity was 93.4%, mumps 80% and measles 78%. Among 53 children studied in one year of age, almost 91% (48 cases) and 18 months of age all cases (100%) were seropositive. Mumps in 81% (43 cases) in one year of age and 84.9% (45 cases) in 18 months of age were seropositive, that difference was not significant statistically. Measles in 56.6% (30 cases) in one year and 18 months in 79.2% (42 cases) were seropositive. The results showed that there isn't any significant difference between the sexes in all level of seropositivity. In addition, two times administration of vaccine is more effective than one time vaccine administration in increasing seropositivity. The rate of seropositivity of measles and mumps is lower than rubella that need for review of interventional factors, such as malnutrition, sorts of vaccines, cold chain compliance and vaccine storage's method.

**Keywords:** seropositivity, mumps, measles, rubella, vaccination

## **INTRODUCTION**

The common sign of Mumps is fever with parotid, it's

prevalence has been reported about 0/5-5. Before vaccination this disease has been occurred primatively and epidemically every four years, among 5-9 years old children (Maldonado, 2008; Bang and BanG, 2009). In vaccinated societies, 50% of this disease occurs in

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children of 1-5 year and 90% of patients are below fourteen (Littman and Baum, 2005). In below one year old infants, the outbreak of mumps is unusual because of safety acquired from mother. Mumps virus will be spread by infected individuals and direct contact with the particles in air, objects polluted with saliva and may be urine. This virus can be separated from 6 days before until 9 days after inflammation of salivary glands. But spread of the disease continues from inflammation remission of parotid glands until 3 days later it (Maldonado, 2008). The side effect of Mumps in children is Meningoencephalitis. 20%-30% of patients may suffer from Epididymo-orchitis in adolescenc. Other side effects of the disease are: pancreatitis, diabetes, nephritis, arthrites, myocarditis and thyroid (Cherry, 2004). This disease is recognized decisively based on separation of virus and serological studies like assignment of IgM Ab against virus and PCR analysis (Littman and Baum, 2005).

Rubella or German measles or 3-day measles that was very common before but nowadays, its currency is less epidemic, is a virus infection which is recognized by fever and maculopapular skin damages and sensitivity of occipital and posterior oricular lymph glands. Rubella is from rubiviridae family and human is its only host. It spreads from saliva glands or placenta and afflicts both girls and boys equally (Malengrean, 1992; Vejtorp and Leerhoy, 2009).

Despite accomplished achievements, the epidemic of rubella and congenital rubella is still existed among unvaccinated adults (Boulianne et al., 1995). The virus is found from 7 days before manifestation of rashes until 7-8 days after they vanish in nasofarynx. The recognition is based on serological and clinical manifestations to clinic and test, and serology and virus culture are necessary to confirm the disease. Sometimes leucocytes and plaquets are reduced.

Recognition of congenital rubella is finding exclusive IgM of rubella in infant serum or rubella virus culture of nasofarynx, infant's urine, or modification of serum titer or increase of four times of IgG tittle (Moldonado, 2008). Rubella is one of fevered infectious and rashy sever diseases, that has had high death rate before public vaccination. At first this disease emerges with feebleness, weakness, fever and rashes in face and body, redness of eyes and respiratory symptoms. This disease spreads from the stage of prodermal until 5 days after rashes manifestation. One of the significant symptoms of the disease is koplik spots (which are white damages in front of the second big grinder teeth), (Rajasundari et al., 2006; Morley et al., 2009). This disease has a high death rate among children infected by malnutrition, and it's still one of the important communicable diseases of children in developing countries (Moldonado, 2008).

In our country, the vaccination against this virus has

been accomplished in nine months and 15 months of infancy, but vaccination against viruses of measles and Rubella has been accomplished since 2004. Since early 2005 vaccination of measles, mumps and rubella (MMR) is carried out in two phases, according to vaccination program of our country. The first phase is accomplished in one year old infants and the second one in 18 months of age.

At the past, the most of our studies, has been done in terms of the amount of immunization of measles. The purpose of this study is to recognize the amount of antibody against the viruses of Measles, Mumps and Rubella, three weeks after MMR vaccination of the first phase (one year old infants) and the second phase (18 months infants) by the current applied vaccine.

It's been considered that three weeks need after vaccination in order to have enough time to settle safety by infant's body against vaccine (IgG).

## MATERIALS AND METHODS

This study which is descriptive-cross sectional method, has been carried out on 90 children who had been selected by the way of easy (at hand) as random sampling. All these children were examined by physician at the time of vaccination and if they didn't have considered for acute fevered disease, background of special disease or corticothyroid usage, radiotherapy, cancer and immune system congenital diseases (totally they didn't have prevention policy for vaccination).

they came into study. So all children who refer to Abuzar Curative Health Center (both girls and boys) in 12 months of age or 18 months of age to receive the second phase of MMR at the beginning of the plan (the first six months of 2009) and they didn't have the factors for being omitted from the plan, came into the study. So the related forms and questionnaires were filled.

After receiving written satisfaction from their parents, three weeks after doing the first MMR vaccination time with MMR vaccine that was accessible for Curative Health Centers. Firstly 93 children's serums were sampled and then at the second try 91 children's serums were sampled after getting the second time of vaccine (53 children of the first try were repeated at the second phase, the remainder were not repetitive but had received two doses of MMR vaccine). Then their serums were separated and moved to laboratory of clinical researchers center and they were kept in 70 °C.

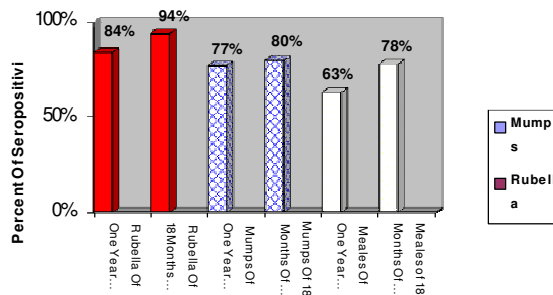
At last, in order to measure antibody against the viruses of rubella, measles and mumps and to study the samples, ELISA test was done. Statistical analysis of results was accomplished by SPSSv17 software so that at first by using square root ( $K^2$ ) the correspondence of immunization level was evaluated at the first and the second tries between the two first groups (who received

**Table 1:** The comparison of frequency distribution of rubella results in one year of age and 18 months of age

Phase	Positive		Negative		Total	
	Number	Percent	Number	Percent	Number	Percent
One Year	78	83.9	15	16.1	93	100
18 Months	85	93.4	6	6.6	91	100
Total	163	88.6	21	11.4	184	100

**Table 2:** The comparison of frequency distribution of mumps in one year of age and 18 months of age

Phase	Positive		Negative		Total	
	Number	Percent	Number	Percent	Number	Percent
One Year	71	76.3	22	23.7	93	100
18 Months	73	80.2	18	19.8	91	100
Total	144	78.3	40	21.7	184	100

**Figure 1:** The comparison of the seropositivity percent of rubella, mumps and measles after MMR vaccination based on the frequency of the first and second phases of vaccine

one time of vaccine) against the second group (who received two times of vaccine), then statistical analysis of the group that was repeated in the both phases of this study, was done by using Mac Nemar test.

## RESULTS

Among the total 184 infants during the first phase (one year old infants) and the second (18 months infants), 93 were boys and 91 were girls. At the first try, 93 infants and at the second phase 91 children were sampled. All 93 infants of the first phase received vaccine of the first phase and all 91 infants of the second phase received vaccine of the second phase. From 91 infants of the second phase 53 (56.9%) were repeated exactly. Although 38 (41.7%) were not repetitive, but had received two doses of vaccine. We start evaluation of statistical

results at two groups of one phase vaccination (93 infants) against two phases vaccination.

Statistical analysis of this group was done by test (. Then we followed the statistical results at a subgroup of these infants who were repeated in the both phases of the study (received vaccine both in the first and the second phases) under the name of repetitive group. The statistical analysis of this group has been accomplished by using Mac Nemar test.

A- The results in two groups of infants who received one phase of vaccine in comparison with infants who received two phases vaccine:

Among 93 one year old infants 78 (83.9%) were seropositive and 15 cases (16.1%) were seronegative, and in 18 months of age, 85 infants (93.4%) were seropositive and 6 infants (6.6%) were seronegative from the viewpoint of rubella (Table 1, Figure 1)

$$\chi^2 = 4.14 \quad p = 0.04 \quad df = 1$$

The results of the test ( $\chi^2$ ) demonstrated that the frequency of negative results in one year of age is more than in 18 months of age.

In the case of mumps among 93 infants, in one year of age, 71 (76.3%) were seropositive and 22, (23.7%) were seronegative and in 18 months, 73 of them (80.2%) were seropositive and 20 of them (19.8%) were seropositive (Table 2, Figure 1).

$$\chi^2 = 0.4 \quad p = 0.52 \quad df = 1$$

Results of the test ( $\chi^2$ ) didn't demonstrate significant statistical difference at the results of seropositive and seronegative in two phases.

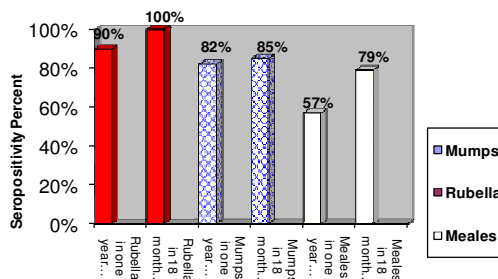
In case of measles, among 93 infants, 53 (56.9%) were seropositive and 35 (37.6%) were seronegative in one year of age. And in 18 months of age, 71 (78%) were seropositive and 20 (22%) were seronegative (Table 3 and Figure 1).

**Table 3:** The comparison of measles status in one year of age & 18 months of age

Phase	Positive		Negative		Total	
	Number	Percent	Number	Percent	Number	Percent
One Year	57	62.8	35	37.6	93	100
18 Months	71	78	20	22	91	100
Total	129	70.1	55	29.9	184	100

**Table 4:** The result of Rubella at the first & second phase, among the first & the second repetitive infants

Phase	Positive		Negative		Total	
	Number	Percent	Number	Percent	Number	Percent
One Year	48	90.5	5	9.5	53	100
18 Months	53	100	0	0	53	100



**Figure 2:** The comparison of seropositivity percent of rubella, mumps and measles after receiving one phase of vaccination in one year of age and two phases of vaccination in 18 months of age

$\chi^2 = 5/6 \quad p = 0.02 \quad df =$

Results of the test ( $\chi^2$ ) showed a significant statistical difference, it means that seronegativity in 18 months of age is less than one year of age (22% against 37.6%).

Results of the above comparison showed that the amount of seropositivity after two phases of vaccination is more than the seropositivity after one phase of vaccination.

**B. Results in the repetitive group**

Among 53 infants who were repeated after receiving vaccination at the second phase, 27 (50.9%) were boys and 26 (49.1%) were girls. Comparison of the kind of prescriptive vaccine, related antibody, and sex didn't show any significant difference. The result of above comparison showed that there's no significant difference from the viewpoint of sex and amount of seropositivity. Among 53 infants, from the viewpoint of rubella, 48 (90.6%) were seropositive and 5 (9.4%) were negative, in one year of age. Also, in 18 months of age 100% were seropositive (Table 4, Figure 2).

$P = 0.02$

The comparison of seropositivity and seronegativity of mumps was in one year of age and 18 months of age was so: 38 (88.4) were seropositive, both in one year of age and 18 months of age. But 7 (70% of the negative

cases), who were negative in one year of age, had been seropositive and this shows the effect of vaccination at the second phase. Also 5 (11.6%) seropositive cases in one year of age, have been seronegative in 18 months of age. And 3 (30%) seronegative cases were seronegative both in one year of age and in 18 months of age.  $P$  (0.77%) was not significant statistical difference (Table 5, Figure 2).

$P = 0.77$

According to the above table, seropositivity of Mumps was different after receiving two phases of vaccination, although this difference wasn't significant. In the case of Meales, among 53 understudy infants, the comparison of seropositive and seronegative demonstrates significant statistical difference, so that 23 positive cases (76.6%) have been seropositive both in 18 months of age and one year of age, while 7 seropositive cases (23.3%) in one year of age became seropositive in 18 months of age.

Also 19 negative cases (82.6%) in one year of age have been seropositive in 18 months of age, and 4 negative cases remained negative both in one year of age and 18 months of age. The significance of these results means that the vaccination in 18 months infants has effects on changing negative cases to seropositive ones. (Table 6 and figure 2),  $p$  (0.029%).

As it's shown in tables 1, 2, 3, 5, 6 and Figures 1 and 2, after receiving the 2<sup>nd</sup> phase of vaccination in cases of measles and rubella, antibody was significantly more than the 1<sup>st</sup> phase. In the case of mumps, there was also difference although it wasn't significant.

**DISCUSSION AND CONCLUSION**

The most important findings of this study is the effect of two phase vaccination in production more seropositivity in comparison with one phase vaccination. Generally it was observed that after MMR vaccination in our study, the seropositivity was increased from about 57% at the 1<sup>st</sup> phase to about 90% after receiving the 2<sup>nd</sup> phase. The

**Table 5:** The comparison of mumps vaccination status in one year of age and 18 months of age

Mumps In One Year Of Age	Result	Frequency	Mumps In 18 Months Of Age		
			Total	Negative	Positive
	Positive	Number	43	5	38
		Percent	100	11.6	88.4
	Negative	Number	10	3	7
		Percent	100	30	70
		Number	53	8	45
		Percent	100	15.9	84.9

**Table 6:** The comparison vaccination of measles in one year of age and 18 months of Age. P (0.029%)

Measles In One Year Of Age	Result	Frequency	Measles In 18 Months Of Age		
			Positive	Negative	Total
	Positive	Number	23	7	30
		Percent	76.7	23.3	100
	Negative	Number	19	4	23
		Percent	82.6	17.4	100
Total		Number	42	11	53
		Percent	79.2	20.8	100

above result demonstrated the high effect of the 2<sup>nd</sup> dose of vaccine on seropositivity raise, like previous studies (Boulianne et al., 1995). In our study, it wasn't observed significant difference in amount of seropositivity between girls and boys.

To change seronegative cases into seropositive after receiving the 2<sup>nd</sup> dose of vaccine, was the other important finding of this study. It means that at the 1<sup>st</sup> phase, in the case of rubella, seropositivity raised from 90% to about 100%. In case of measles, at the 2<sup>nd</sup> phase it raised from 57% to about 80%. And in case of mumps, at the second phase it raised from 81% to 85%. As it's observed in cases measles and rubella seropositivity change was significant, but in case of mumps it wasn't so (i.e. the second phase of mumps vaccine didn't have high effect on changing negative cases to positive).

The other point was the amount of seropositivity in each case. In case of rubella it was 100% which it was acceptable and comparable with similar studies. But about mumps and measles it was less, in other words after two phases vaccination, negative cases of measles were 21% and negative cases of mumps were 15%. (seropositivity can be reduced in future). This issue has a significant difference with the 1<sup>st</sup> point about changing seronegative to seropositive, because the vaccines has been able to change negative cases to positive ones but seropositive cases of measles and mumps were generally less than similar studies.

In order to convey the reasons of less effect of measles and mumps vaccines in producing antibody on understudy cases, we can refer to malnutrition among

understudy infants that can affect on amount of answering antibody, especially measles (Boulianne et al., 1995). We can also refer to cases like the kind of prescriptive vaccine, cold chain noncompliance or way of administration of vaccine that makes the future studies necessary in this case (it's necessary to say that with regard to the little interval between prescription of vaccine and studying serology, it was expected that the reaction of antibody in cases mumps and measles be more than current percents).

In 2003, one study has been done in this field in India in terms of measuring antibody against measles, rubella and mumps both before and after 6\_8 weeks of receiving vaccine in 120 infants of two groups (9\_10 months infants, 15\_18 months infant) (Yadar et al., 2003). According to the results, before vaccination 96(80%) of the 1<sup>st</sup> group(9\_10 months infants) were negative from the viewpoint of rubella and mumps, and 102 (85%) were negative from the viewpoint of measles. After MMR vaccination, 102 (92%) from the viewpoint of measles, 100% from the viewpoint of rubella and 100% from the viewpoint of mumps became positive.

In the 2<sup>nd</sup> group (15\_18 months infants), 67 (56%) from the viewpoint of measles, 84 (70%) from the viewpoint of mumps and 86 (71%) from the viewpoint of rubella were negative. After vaccination against MMR, from the viewpoints of measles 92%, Mumps 96% and rubella 94% were positive, The results of this study is similar to ours (Yadar et al., 2003). In a study accomplished by Soadm Jaber in Jeddah (Saudi Arabia) in 2005, the level of antibody MMR was studied in children

of preschool and school, a few years after vaccination (Soad and Jaber, 2006). From about 99% of children who had received MMR vaccine, 71% had antibody for measles, 65% had antibody for mumps, and 90% had antibody for rubella.

The amount of antibody in children who studied at public school was clearly more than the children who studied at private schools (Yalcin et al., 2006). The amount of antibody reduced with growth and in unvaccinated children seropositivity against measles increased with growth. Also two phases vaccination increases seropositivity, that is nearly similar to ours studies (Soad and Jaber, 2006).

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