



## **Sero-conversion after Second Measles' Containing Vaccine in a Selected Sample of Young Children**

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### **Authors' contributions**

*This work was carried out in collaboration among all authors. Author YGK designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors RGH and SSAW managed the analyses of the study and managed the literature searches. All authors read and approved the final manuscript.*

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### **ABSTRACT**

**Background:** This study aims to detect sero-prevalence of measles Immunoglobulin-G, antibodies, (IgG Abs) before versus after second measles containing vaccine (MCV2) among young children.

**Methodology:** This cross-sectional study was conducted in a selected primary health care centers (PHCCs), in Iraq. The study sample comprised 112 children, (66 males, & 46 females), aged 13 - < 24 months, selected at a random during their attendance for routine vaccination. The study sample subjected for estimation of measles IgG Abs titer before, and, (4-12) weeks after Measles, Mumps & Rubella (MMR) vaccination.

**Results:** Seroprevalence for specific measles IgG- Abs before MMR vaccine (41.8%) was found among those infants, when sero-conversion rate estimated after MMR vaccination it was (92.4%). The result reveals that seroconversion rate among children who had received MCV1 vaccine before was (96.8%), while it was 84.0% for those children did not have MCV1 vaccine before.

**Conclusions:** This study concluded that the two-dose schedule seems to increase the seropositivity rate, and recommended application of solid vaccination program with two doses of an effective & efficient measles vaccine, before the second year of age.

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## 1. INTRODUCTION

Measles is an acute systemic viral infection with immune system interactions that play essential roles in multiple stages of infection [1]. Despite the availability of a safe, heat-stable, effective, and inexpensive measles vaccine, and the substantial progress towards measles control, measles remains one of the leading causes of preventable death globally among children [2]. A second dose of MCV2 was added to compensate for the primary failures observed after the first vaccination, and two-dose schedules have been a key strategy for measles elimination [3,4]. In one-dose programs, vaccine effectiveness (VE) was influenced by age at vaccination [5,6]. The interference of maternal antibodies and the immaturity of the child's immune system were the alleged mechanisms that resulted in a weaker antibody response and poorer protection in younger infants [7,8,9]. The persistence of these antibodies varies in different populations, so the age at which optimal seroconversion rates are obtained also varies [10,11]. Although high level of immunity substantially reduces the likelihood, that susceptible persons within a population will be exposed to disease, but there is no level of immunity short than 100% will absolutely guarantee absence of transmission [12,13,14]. This study aims to determine sero-prevalence of specific measles IgG Abs before, and sero-conversion after MCV2, among children below two years of age.

## 2. SUBJECTS AND METHODS

This cross-sectional study, was conducted in selected primary health care centers (PHCCs) in Iraq. A random sample from children under two years aged (13 - < 24 months), undergoing routine vaccination for MCV2, (MMR) vaccine. The selected children subjected for determination of specific measles IgG Abs, before and (4-12) weeks after MMR vaccine. Total number 146, some of those children (n= 96), had measles virus live vaccine (MCV1) during their first year of life, while the others (n=50) did not have it before. The children were examined through an application of a preceded questionnaire, which was constricted and adapted by the researchers. Serum samples of a total 146 healthy children were collected and analyzed for estimation of specific measles IgG Abs titers. The standard kit

for the qualitative detection and quantitative determination of IgG Abs to measles virus in human serum and plasma, (Behring Kit / Anti measles IgG {Dade Behring , Enzygnost , Anti – Masern – Virus / IgG}, used by Enzyme immunoassay (ELISA) technique. After discussing the pattern and the aims of the study. The present study was initiated in a pilot PHC center," Data feeding followed by descriptive and analytic statistics, were carried out.

## 3. RESULTS

Table 1 demonstrated the distribution of specific measles IgG titer in the serum of children, according to their age /months, versus the serum samples results of same children after MMR vaccine .The table showed that mean IgG Abs titers was negative, for children aged 13, 14, 15, 18, 19, 21, & 23 months, (with wide variability for SD), and strong positive for children aged 17, 22 & <24 months (> 1909 mIU/ml).

In regard to the IgG titer results, when those children tested (4-12 weeks) after MMR vaccine, it was found that, the mean IgG Abs titer elevated to the upper limits of the positive value, for all children in this group , with still wide variability of SD, in addition to positive results for the median among those post- vaccinated children.

IgG, titer curve approached the normal distribution curve, although it is slightly skewed to the right. Skewness was (2 .595 mIU/mL), standard error (SE) of skewness was (0.201 mIU/mL), and kurtosis was (8.234 mIU/mL), as shown in Fig. 1. While Fig. 2, displayed IgG, titer curve approached the normal distribution curve, although it is slightly skewed to the right. Skewness (2.501 mIU/mL), was slightly less than that before MMR vaccination, but the same SE of skewness (2.501 mIU/mL). Regarding the kurtosis, it is increased (9.846 mIU/mL), that the result in pre-vaccine serum sample.

Table 2 demonstrated that, 58.2% of those children were sero-negative, and (41.8%) of them were sero-positive. When post MMR vaccination serum samples results were considered, the data showed that 7.6% of them remained sero-negative, while 92.4% of those children got positive sero-conversion.

**Table 1. Distribution of specific measles IgG Abs titers in the serum of children aged 13- < 24 months before versus, (4-12) weeks after MMR vaccination**

Age / months	IgG titer 1 mIU/mL before MMR					IgG titer 2 mIU/mL after MMR				
	Mean	SD	Minimum	Maximum	Median	Mean	SD	Minimum	Maximum	Median
13	232.6	374.0	3.21	1483.8	18.9	1000.7	1021.8	8.98	4885.1	691.1
14	148.2	268.2	6.66	737.7	21.7	742.7	629.6	17.4	2151.3	687.3
15	219.0	349.1	3.21	1385.7	23.2	905.7	602.4	145.3	2753.3	757.3
16	655.5	994.8	3.21	3511.4	148.4	1586.0	1709.9	23.2	7141.5	937.2
17	958.1	1158.9	8.98	2462.5	680.4	1702.2	1217.6	529.9	3340.2	1469.4
18	317.5	431.7	3.21	1499.2	123.6	1107.6	1050.4	6.7	5440.1	864.4
19	320.5	307.1	6.66	814.4	337.3	1140.0	715.2	8.98	2254.2	1015.3
20	497.2	325.2	10.92	885.3	457.1	1506.5	701.4	737.7	2477.3	1385.7
21	191.7	244.8	6.66	505.9	31.4	926.9	484.9	685.8	1793.7	718.4
22	1035.7	1272.5	135.89	1935.4	1035.7	1755.1	1242.8	876.3	2633.9	1755.1
23	280.7	482.0	6.66	1220.1	35.3	1855.7	787.4	811.5	3117.2	1884.6
<24	560.7	780.8	3.21	2716.7	330.2	1351.0	916.7	332.2	3369.4	1202.7

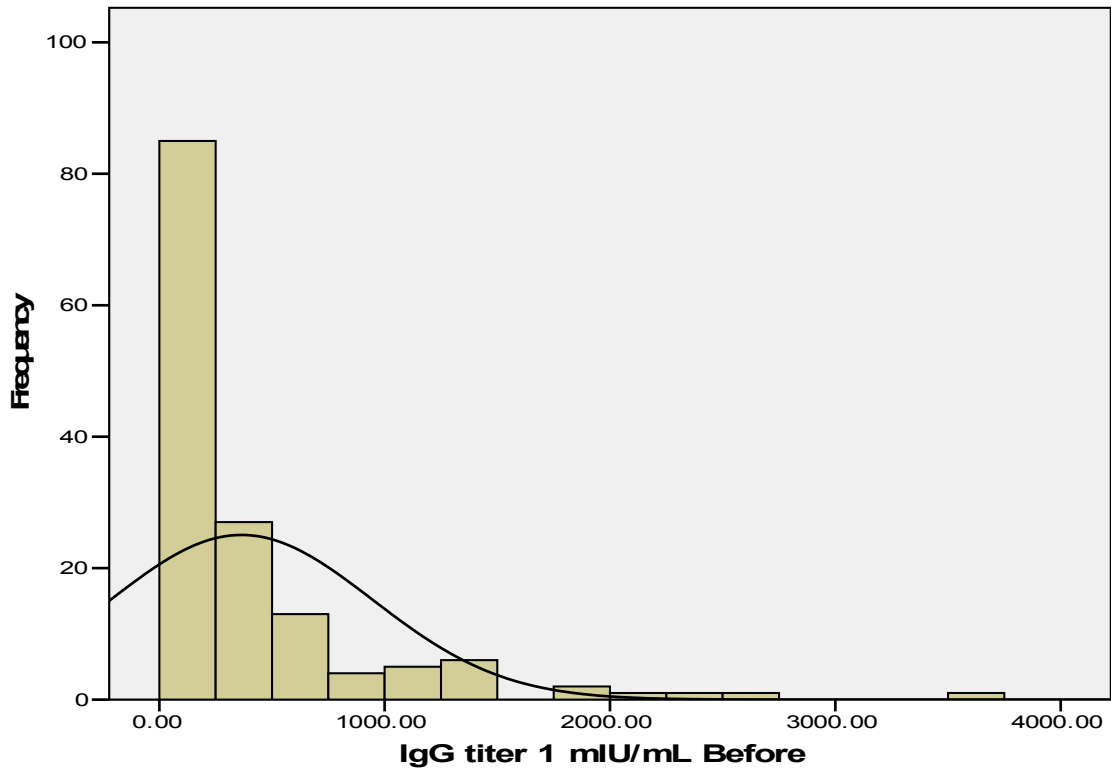


Fig. 1. Frequency of measles IgG Abs before MMR vaccine among children aged 13-< 24 months

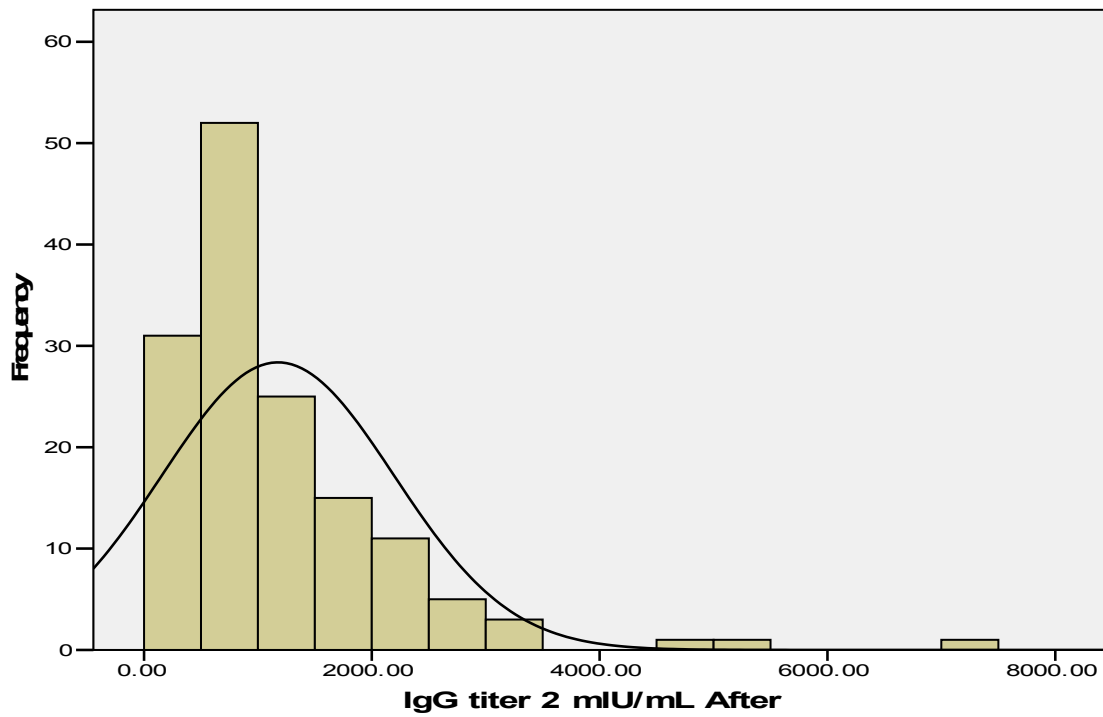


Fig. 2. Frequency of measles IgG Abs after MMR vaccine among children aged 13- < 24 months

**Table 2. Seroprevalence rate of Measles IgG antibody in the serum of children aged 13 -< 24 before and after MMR vaccine**

Group 3 (Age 13-<24 months) result (titer)		No	%
IgG titer mIU/mL before MMR (n=146)	Negative (<330)	85	58.2
	Positive (=>330)	61	41.8
IgG titer mIU/mL after MMR (n=145, missing=1)	Negative (<330)	11	7.6
	Positive (=>330)	134	92.4

**Table 3. Sero- conversion rate after MMR vaccine among children aged 13-< 24 months**

Group 3 (Age 13-<24 months) Result (titer)	IgG titer mIU/mL after MMR				
	Negative (<330) (n=11)*		Positive (=>330) (n=134)		
	No	%	No	%	
IgG titer mIU/mL before MMR	Negative (<330)	11	13.1	73	86.9
	Positive (=>330)	-	-	61	100

\*One missing readings from infants after vaccination with negative titer

**Table 4. Association between infants' characteristics and seroconversion rate after MMR vaccine among children aged 13-<24 months. (Total number146, missing=1)**

Characteristics	IgG titer mIU/mL after MMR				$\chi^2$ ; d.f.;P
	Negative (<330) (n=11)		Positive (=>330) (n=134)		
	No	%	No	%	
Gender: Male	5	6.8	68	93.2	0.114;1;0.736
Female	6	8.3	66	91.7	
Type of BF: Exclusive BF	6	8.6	64	91.4	0.187;1;0.665
Non-exclusive BF	5	6.7	70	93.3	
Duration of BF: 6 months and below	4	8.9	41	91.1	0.158;1;0.691
More than 6 months	7	7.0	93	93.0	
Childbirth order: 1 <sup>st</sup>	4	6.3	59	93.7	4.90;2;0.086
2 <sup>nd</sup>	6	15.0	34	85.0	
3 <sup>rd</sup> & >	1	4.3	22	95.7	
Measles vaccine: Yes	3	3.2	92	96.8	7.706;1;0.006*
No	8	16.0	42	84.0	

\* The Pearson Chi-square statistic is significant at the 0.05 level, with proper categorization was performed when there was a zero cell

Table 3 showed that (86.9%) of the seronegative children became seropositive (positive sero-conversion to MMR, when those children received it during their second year of life, (as first measles vaccine for them). Those who remained seronegative (13.1%) represented the Primary vaccine failure for MMR. It is worth to mention that children who were seropositive before MMR, they keep this seropositivity in 100% within the follow up period.

Concerning the association between child's characteristics and sero-conversion rate after MMR, as demonstrated in Table 4.

Table 4 demonstrated that the rate was (93.2%), for the boys, and (91.7%) for the girls. When the type of feeding considered, the rates were (91.4%, 93.3%) for exclusive and nonexclusive BF respectively. Regarding the duration of BF, the rates were, (91.1%) for duration of 6 months and below, and (93.0%), for a duration of BF more than 6 months. In the present study, the percentage of children who had measles live vaccine during their first year of life was 65.8%. Those children exhibited sero-conversion rate (96.8%), after MMR vaccine (second measles vaccine). While those children who had not receive mono-valent

measles vaccine before (34.2%), exhibited (84.0%), sero-conversion rate after MMR vaccination. High significant statistical association ( $P=0.006$ ), was found between previous measles vaccination and sero-conversion rate obtained after MMR vaccination. No statistical association was found with other child's characteristics.

#### 4. DISCUSSION

On studying measles IgG Abs titer distribution according to the age / months before MMR vaccine, who showed negative level of mean IgG Abs titers, were mostly either un-vaccinated, or because of primary vaccine failure ( PVF ) for their MCV1 [15,16,17]. While those with positive level of mean IgG Abs mostly due to response to MCV1, Table 1. Sero-positive children constituted 41.8%, and 58.25% represented those who were sero-negative. The present study found that (34%) of the study children, were un-vaccinated before and the remaining 24% were mostly due to primary vaccine failure. Table 2. The mean measles IgG Abs titer converted to positive level (and strong positive), among all children, following MMR vaccination. This result indicated an excellent sero-conversion to MMR vaccine, with the aid of previous MCV1 received during their first year of age [18,19]. This represented PVF in 7.6 percent, Tables 2 & 3. A well-managed cold chain, health education regarding vaccination, improved management skills, and community support, remain a prerequisite for any successful immunization program [20,21]. Reduced vaccine potency due to poor storage and transportation, with effect of tropical climate on the vaccine [22,23,24]. The improvements in heat stability of the vaccine increase the likelihood of providing potent vaccine [25,26]. In agreement with the present study, Karimi et al, reported that measles Abs was positive in 52.9% (14 months old children) and 89.4% (18 months old children) [27]. The longer a community goes out without circulating measles virus, and the more vigilant public health officials must maintain immunity levels in the community" [4,19,21].

Sero-conversion of 86.9% among vaccinated children aged 13-<24 months who were seronegative represented the success in response to MMR vaccine. In addition to that, those children who were already seropositive (41.8%), kept their sero-positivity, and 92.4% represented seroconversion after MMR (regardless of the past vaccination state), Table

3, while among children who had measles vaccine (during their first year), and MMR vaccine during second year of age, the rate was 96.8% Table 4. The rate reported in the present study approached that reported by WHO, where 95% of children immunized at >\_12 months were found be protected by measles vaccination (12, 15). Routine two dose schedule is recommended by WHO in countries with immunization program capable of achieving and sustaining high coverage (> 80%), coupled with a system to following up defaulters (Second opportunity for measles vaccination is required to protect those children who fail to respond to the first dose, (10,13), also a well vaccinated population, it will increase herd immunity levels above the outbreak threshold level [4,28]. No significant association was found between the majorities of child's characteristics with sero-conversion rate after triple measles vaccine (MMR) vaccination. On the other hand, excellent sero-conversion rates (96.8%), was obtained among children in response to MMR vaccination, in children received mono-valent measles vaccine during their first year of age. The association between measles vaccination and sero-conversion was high significant association ( $p= 0.006$ ). Thus, the present study concluded that the triggering factor on sero-conversion initiation is the measles vaccine.

#### 5. CONCLUSION

Positive sero-conversion was prominent among most children aged 13 – 24 months after MMR vaccine. An excellent sero-conversion rate was obtained after 2 dose of measles vaccine. High significant association was found between measles vaccine and sero-conversion among those children.

The second measles vaccine should be given at age earlier than 15-months to cover considerable susceptible after first dose and keep immunity against measles virus among the study children at high level.

It is recommended that Diyala Health Authority in collaboration with Diyala University, Collage of Medicine, to establish a mobile team of health educators to advise for health education about the role, strategies of measles vaccination.

#### CONSENT AND ETHICAL APPROVAL

Ethical clearance has been taken from scientific committee / Medical College/ University of

Diyala. An informed written consent was obtained from the parents for participation of their children in the present study.

### COMPETING INTERESTS

Authors have declared that no competing interests exist.

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