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Inherited, Versus Acquired, Measles IgG-antibodies after Measles Vaccination Among Infants in Diyala /Iraq

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Abstract:

Back-ground: In developing countries, measles is regarded as a serious problem and can only be combated by large-scale vaccination programs. The main known risk factor for primary vaccine failure is age at vaccination, due to persistence of maternal antibodies, which interferes with the success of measles immunization.

Objectives: Identification of sero-prevalence rate of inherited measles IgG- antibodies among infants aged 9-12months, before measles vaccination. And assessment of acquired sero-conversion rate after inoculation of measles vaccine among those infants.

Subjects and Methods: A cross –sectional study, was conducted in a selected primary health care centers in Diyala Province. The study sample included 117 infants (56 males & 61 females), aged 9-12 months, selected at a random during their routine vaccination, for the period extending from the 1st of February/2007 to the 31st January/2008. Anti measles IgG antibodies (Abs), were detected in the serum by Enzyme Linked Immuno-Sorbent Assay, using "Dade Behring" standard test kit.

Results: The results revealed that the mean & geometric mean measles IgG Abs titers, before measles vaccination were negative (cut off= <330 mIU/ml). After measles vaccination, the mean changed to a positive value (cut off= >330mIU/ml- <1909mIU/ml), but geometric mean titer remained in a negative level. Inherited measles IgG Abs in the serum samples of those infants was 9.4%, before measles vaccination, while sero-convertion rate was 70.3%, acquired after measles vaccination.

Conclusion: The least of infants were sero-positive at 9th months (before measles vaccination age) , and a positive sero-conversion obtained after that vaccine, with a primary vaccine failure in about quarter of them.

Key wards: Sero-prevalence of measles IgG. Maternal, passive measles IgG antibodies. Acquired measles IgG. Sero-conversion to measles vaccine. Primary vaccine failure after measles vaccination.

Introduction:

Measles an acute highly infectious disease of childhood caused by a specific virus of the group myxoviruses. It is clinically characterized by fever and catarrhal symptoms of the upper respiratory tract followed by a typical rash. Measles is associated with high morbidity and mortality in developing countries (1, 2). In the pre-vaccine period virtually all persons contracted the disease leading to an estimated 135 million cases each year. Measles is endemic virtually in all parts of the world. It tends to occur in epidemics when the proportion of susceptible children reaches about 40% (3). The mortality of measles varies greatly in different parts of the world. It is 100 to 400 times more likely to cause deaths in a preschool child of developing countries than it is in the USA and Europe (4). In developing countries, case fatality rates range from 2 to 15%, as compared to less 0.2 per 10.000 notified cases in developed countries (5). In spite of great progress made in controlling measles by vaccination, there an estimated 30-40 million cases (3, 4), and in 2006, there were estimated 242,000 measles deaths (5, 6). Thus measles is still a leading killer among malnourished children whose natural defences have been weakened by other infections and who live in

crowded urban localities (5). Infants are generally protected by maternal antibodies until 5-9 months of age that is why most of developing countries vaccinate against measles at 9th month of age (7,8). Although measles immunization is an effective strategy to prevent cases, outbreaks can continue, especially in densely populated areas such as urban slums, even with good coverage. This is because vaccine efficacy is only 85%, and because there are pockets of poorly immunized children (5). As the coverage increases, the time in between outbreaks increases, and a shift toward older age group may be seen (7). Understanding the role of primary vaccine failure and secondary vaccine failure in measles epidemics is important for the evaluation of measles control programs in developing countries (9). The main known risk factor for primary vaccine failure is age at vaccination. Because, the persistence of maternal antibodies interferes with the success of measles immunization (10).

This study was conducted for estimation of sero-prevelanc of inherited measles virus IgG Abs among infants aged 9-12 months, and to determine the sero-conversion rate, after that measles vaccination among those infant in Diyala Province.

Subjects and methods:

A ross –sectional study, was conducted in a selected primary health care centers (PHCcs) in Baquba City (center of Diyala Governorate), for the period extending from the first of February 2007 to the 31st of January/ 2008. The study sample included infants aged 9-12 months, selected randomly from routine activities for vaccination. The questionnaire used for this study. Contained questions about the socio-demographic characteristics of the infants, parents, and the vaccine. Serum samples of a total 117 (56 males & 61 females) healthy infants, were collected and analyzed for estimation of specific measles IgG Abs titer, using Enzyme Linked Immunoassay Assay (ELISA) with a standard kit (Dade Behring),for the qualitative detection and quantitative determination of IgG antibodies to measles virus in human serum and plasma. Blood samples were collected from the child by a veine-puncture. An informed written consent was obtained from the parents for participation of their children in the present study. Data feeding followed by descriptive and analytic statistics, were carried out utilizing the "Statistical Package for Social Science" (SPSS) for windows software (SPSS-16.0). The tests used in the analysis were descriptive tests, including geometric mean titer (GMT), and analytic test.

Results:

Table (1) Serological profile of infants aged 9-12 months before, versus after measles vaccination.

Serological variables		IgG titer mIU/mL before vaccine	IgG titer mIU/ mL after vaccine
Number	Valid	117	111
	Missing	0	6
Mean		73.8342	517.1440
Std. Error of Mean		18.10047	54.29644
Geometric Mean		19.1518	256.9578
Median		12.6862	382.0811
Std. Deviation		195.78652	572.04853
Range		1382.51	4665.80
Minimum		3.21	6.66
Maximum		1385.72	4672.46
Percentiles	25	6.6606	95.6103
	50	12.6862	382.0811
	75	30.0735	643.2549

Table (2) Distribution of specific measles IgG antibody titers in the serum of the study's infant, before versus after measles vaccination.

Age	IgG titer mIU/mL before vaccine					IgG titer mIU/mL after vaccine				
	Mean	SD	Minimum	Maximum	Median	Mean	SD	Minimum	Maximum	Median
9 months	**77.8**	**208.9**	**3.2**	**1385.7**	**14.3**	**458.1**	**644.0**	**6.7**	**4672.5**	**355.8**
10 months	**90.0**	**227.2**	**3.2**	**1097.5**	**10.9**	**627.0**	**515.1**	**6.7**	**1979.4**	**513.9**
11 months	**26.2**	**41.3**	**6.7**	**148.4**	**12.7**	**369.1**	**312.8**	**10.9**	**1044.9**	**363.3**
12 months	**59.17**	**125.3**	**6.7**	**443.5**	**12.7**	**735.8**	**327.1**	**352.7**	**1237.6**	**584.2**

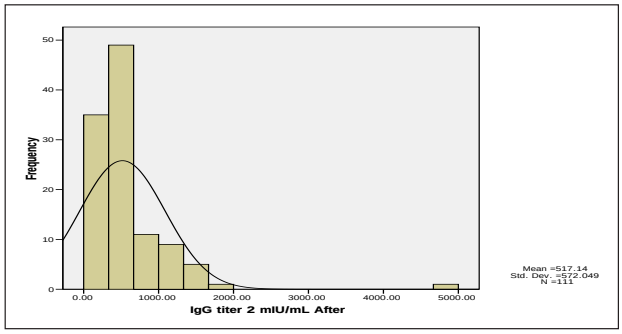

Figure (1): Frequency of inherited measles IgG antibody titer before measles vaccination among infants aged 9-12 months.

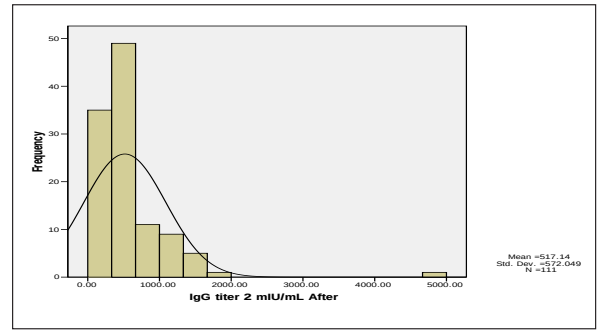

Figure (2): Frequency of measles IgG antibody titer acquired after measles vaccination among infants aged 9-12 months.

Table (3) Sero-prevalence rate for inherited Measles virus IgG Abs in the infants' serum before, versus sero-conversion rate after measles vaccination.

Group 2 (Age 9-12 months) Result (titer)		Infants aged 9--12 months	
		No	%
IgG titer mIU/mL Before (n=117)	Negative (<330)	106	90.6
	Positive (=>330)	11	9.4
IgG titer mIU/mL After (n=111)	Negative (<330)	30	27.0
	Positive (=>330)	81	73.0

Table (4) Relevance between serum samples results before & after measles vaccination for infants including in the study.

Group 2 (Age 9-12 months) Result (titer)		IgG titer mIU/mL after vaccine			
		Negative (<330) (n=30)		Positive (=>330) (n=81)	
		No	%	No	%
IgG titer mIU/mL Before vaccination	Negative (<330)#	30	29.7	71	70.3
	Positive (=>330)	-	-	10	100

 # six infants were missing from follow-up.

Discussion:

In the present study, mean measles IgG Abs titer increased sharply from negative level before measles live vaccine, to a positive value after vaccination. GMT which was, of a negative value, increased but, remained in a negative level after measles vaccination.{Table(1)}.These changes in the serological profile of the study children, attributed to successful response and positive seoconversion after measles vaccine.

Studying the distribution of measles IgG Abs according to the age/months, before vaccination {table (2)}, where mean titer was negative among infants aged 9, 10, 11 & 12 months. This is due to IgG Abs decline during first 6-months of life and afterward (6, 11). These results are a confirmation for the decline of passive maternal immunity among those age groups. Consequently those infants were susceptible to measles infection, unless they received measles live vaccine in proper time. Maximum levels of the mean in the same table were positive for infants aged 9, 10 & 12 months. This is due either to passive maternal immunity which still present among those infants, or due to a subclinical or mild infection which passed un-diagnosed. The last mentioned cause, could be expected, particularly Diyala Governorate, (during the study period), was in the most critical situation, with nearly absence of health services, care and medical personnel to diagnose such cases.

Within a period of 4-12 weeks, followed measles live virus vaccine inoculation to the infants included in the present study, a strong positive & positive mean for measles-IgG Abs titer results obtained, mostly attributed to the decline of maternal antibodies to the level that allows initiation of seroconversion among the study's infants,(13, 14). {Table (2)}.

Nicoara, reported that, by 9-12 months of age, only (8.6%), infants were sero-positive for measles virus Abs, and he found that between 9 and 15 months of age, the percentage of infants with detectable antibodies for measles virus reached a very low level (7.5%). (15). This is in agreement with the present study results, where only 9.4% of non- vaccinated infants aged 9-12 months were found to be positive for measles virus IgG Abs (table 3).

When the same sample, received measles live vaccine and were retested 4-12 weeks latter {tables (3,4)}, it is found that 70.3%, of infants responded to mono-valent measles vaccine and became sero-positive. The other (29.7%), remained sero-negative. Those who were already sero-positive remain as such (100% sero-positivity) The (70.3%) sero-conversion rate in the present study, is lower than the rate reported by WHO, which was found in 85% among infants vaccinated by measles live vaccine at age 9 months (2, 5).

Those vaccinated infants who remained sero-negative represented a primary vaccine failure (PVF), it can be attributed to either an inactive vaccine or an inadequate host response. Inactivation of the live virus in the vaccine can be caused by the lack of an effective stabilizer or improper handling. Inoculation of inactive vaccine due to vaccine spoiling because of shortage in electrical current and its direct effect on vaccine cold chain (16). The introduction (in 1979), of a good stabilizer rendered measles vaccine quite resistant to heat, and thus reduced the risk of vaccine failure caused by improper handling. Keeping in mind that even with vaccine coverage of 96% to 98% the few susceptible that were remain, are sufficient to sustain several generation of measles transmission (9,13,). The main known cause of primary vaccine failure is the age at vaccination, because of the persistence of inherited maternal antibodies which interferes with the success of measles immunization (6, 14). WHO reported that primary vaccine failure occur in 2-5% of vaccinated children despite age –appropriate first dose measles vaccination (18). This result is much less than the result of the present study when PVF constituted 29.7% of vaccinated infants. (5, 18).

This study concluded that the least rate of infants in this age group were sero-positive due to inherited maternal measles Abs. With moderate sero-conversion rate 70.3% (about 3-quarters of the study's infants), was obtained after inoculation of measles live vaccine, and approximately one quarter, remained sero-negative, which represented a primary vaccine failure to measles vaccine.

The present study recommended a mobile team

of health educators in collaboration between Diyala Directorate of Health & Diyala Medical College's academics, to advise for health education about the importance, role, strategies of measles and the proper time for vaccination. In addition to that, vitamin- A deficiency need to be considered parallel problems and its supplementation is necessary.

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التحري عن نسبة المناعة الموروثة ضد فايروس الحصبة ومقارنتها بنسبة المناعة المكتسبة في مصل الدم بعد لقاح الحصبة لدى الرضع في محافظة ديالى/ العراق

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الخلاصة:

اجريت هذة الدراسة المقطعية ٥دف تقدير نسبة انتشار الغلوبيولين المناعي)IgG(لمستضدات الحصبة في مصل الدم لدى الرضع بعمر 9-12 شهر . وكدلك ٥دف تقييم نسبة التحول في مصل الدم لهذة المستضدات المناعية)IgG(بعد لقاح الحصبة بين الرضع المشمولين بالدراسة. انجزت الدراسة خلال الفترة من الاول من شباط \2007 , لغاية الحادي والثلاثين من كانون الثاني \2008 ,في مدينة بعقوبة, مركز محافظة ديالى. شملت الدراسة 117 رضيع)56 من الذكور و61 من الاناث(. تم اختيار الرضع عينة الدراسة عشوائيا من خلال فعاليات التلقيح الروتيني في مراكز الرعاية الصحية الاولية في المحافظة. خضع هولاء الرضع الى فحص مصل الدم قبل لقاح الحصبة للتعرف على المناعة السالبة الموروثة من الام, ثم اعادة الفحص بعد فترة)4-12 اسبوع (من اللقاح لتقدير معدل الغلوبيولين المناعي)measles IgG(المكتسب من اللقاح.

اظهرت النتائج ان قيم المعدل والمعدل الهندسي للغلوبيولين المناعي IgG((السالب واالموروث من الام , في مصل الدم كانت سالبة. اما بعد اللقاح فقد اصبحت قيمة المعدل موجبة, بينما بقيت قيمة المعدل الهندسي سالبة . كما اظهرت النتائج وجود نسبة انتشار مصلي لمستضدات الحصبة) 9.4 %) قبل اللقاح. وقد لوحظ تحول مصلي موجب بعد اللقاح بنسبة)70.3 % (. نستنتج من هذة الدراسة ان نسبة الرضع اللذين يظهرون المناعة السالبة الموروثة من الام , هي نسبة قليلة جدا, مع حدوث استجابة جيدة بعد اللقاح . وتوصي الدراسة بالاهتمام بالتثقيف الصحي لبرنامج التلقيحات الفاعلة والفعالة للقاح الحصبة لغرض زيادة نسبة الرضع المحصنين وتقليل نسبة المعرضين للاصابة بالمرض.