

Evaluation of humoral immunity against measles virus in Al-Najaf Governorate /Iraq.

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الملخص

أجريت هذه الدراسة لتقييم عيارات أضداد حمة الحصبة صنف (IgG) في أشخاص ملقحين وغير ملقحين ضد حمة الحصبة في محافظة النجف. أستخدم اختبار الادمصاص الكلوبوليون المناعي (الألايزا) المصلي لفحص 375 عينة مصل تم جمعها خلال فترة الدراسة (نيسان إلى تشرين الثاني 2006). تراوحت أعمار الأشخاص اللذين شملتهم الدراسة بين 1-30 سنة. كان منهم 335 ملقحين و 40 غير ملقحين. تم أخذ المعلومات المتعلقة بالعمر والجنس ومكان الإقامة وتاريخ التلقيح ضد حمة الحصبة لكل شخص. أظهرت نتائج الدراسة أن أعلى عيار لل (IgG) كان في المجموعة العمرية (A) بعمر 1-6 سنة) وهو (234.82) ولوحظ أيضاً أن العيار يتناقص مع الزيادة بالعمر وصولاً إلى أوطأ عيار لل (IgG) في المجموعة العمرية (E) (بعمر 25-30 سنة) وهو (6.6087). أظهرت النتائج عدم وجود فروقات معنوية ($p > 0.01$) لعيارات ال (IgG) بالنسبة للسكن او الجنس.

Abstract

This study was conducted to evaluate the anti-measles IgG antibody (AMAb) titers of measles vaccinated and non vaccinated normal individuals in Al-Najaf Governorate. "ELISA" test was applied to test 375 collected sera samples during April to November 2006. Individuals included with age range (1-30) years; 335 of them were vaccinated, and 40 non vaccinated (control group). Age, sex, residency and history of measles vaccination were recorded for each individual. The results revealed; that the highest IgG titer (234.82) had been seen in age group (A, age rang 1-6 year) and the titer was decreasing with increasing of age and reaching to the lowest IgG titer (6.6087) in age group (E, age range 25-30 year). The residency and sex of individuals was showed no significant differences ($p > 0.01$) in AMAb IgG titers.

Introduction

Measles, a highly contagious viral disease, is remain a major cause of worldwide infant mortality accounting for almost one million deaths every year globally (1,2,3). Measles virus (MV) is an RNA virus and generally transmitted by aerosolized secretions (4). Most children recover uneventfully from the illness, but serious complications can occur, including pneumonia and involvement of the central nervous system (5). MV has only one serotype (6), the virus is antigenically stable and vaccination with the currently used live attenuated vaccines

proved to be highly effective in preventing disease (7,8). The immunization induces both humoral and cellular immunity and the production of interferon. Laboratory evidence of immunity is most conveniently documented by use of antibody assays because test for cell-mediated immunity are not standardized. Although detectable serum IgA and IgM antibodies are transient, IgG antibodies generally persist for many years,(9). The current measles vaccines are safe and efficacious for children over the age of 9 months, but due to the less developed immune system and the presence of transplacental maternal antibody, the vaccine is less effective in infants. Another problem associated with the current attenuated measles vaccines is they do not raise as high or as long-lived, neutralizing antibody responses as wild-type MV infection (1).Recent studies about incidence of measles infection in Iraqi population indicated that there was marked increase in measles cases, and there was marked increase in the cases during the period extended from January till June 2004 and the total number of reported cases were 8253 especially in Basra and other southern governorates (10).This work aimed to assess the effectiveness of measles vaccination program , the level of specific anti-measles antibody (IgG) titer and their protective activity, and the social and residential factors and their roles in the levels of Ab specific titer .

Materials and Methods

Blood Samples

A total of (375) serum samples were collected from individuals with age range (1-30) years during the period April to November 2006. Those individuals were admitted toas mentioned in (table (1)).The vaccinated individuals were classified according to their age into five age groups (Table -2). Also, the control individuals (non vaccinated) were included (Table 3).It was too difficult to select age older than used for controls ,because of the possibility of past infection or immunization .Age, sex, residency and history of measles vaccination were recorded for each individual .Anti-measles virus IgG titer were measured in each individual using ELISA technique according to the Methods (11).

Statistical analysis

Mean, standard deviation and T-test($p>0.01$) were carried out according to (12)

Results and Discussion

The profile of AMAb titer in the studied groups is graphed in figure (1). The highest IgG titer was noted in age group A (234.82), followed by group B (48), group C (26.3178), group D (8.1951) and finally the lowest titer was in group E (6.6087). In this study it was found that the IgG titer was decreasing with increasing of age. In age group A, which is the smallest age group; the total mean of IgG titers (234.82) was the highest from the other groups, this group who had got the booster dose of MMR vaccine (Schwarz strain); this dose induces the secondary immune response (anamnestic response) characterized by greater level of antibodies due to the already present of the primarily sensitized and memory cells (13). These results were nearly the same as that of (14,15,10). Moreover; it was found that high measles antibody titers interfere with the humoral response in subjects who received a booster immunization (16). The age group (C), AMAb titer was gradually reduced when compare to the age groups A and B. This reduction may be due to the loss of antigenic stimulation. The total AMAb titer of the age groups (B, C, D, and E) were under the protective level (64) in vaccinated individuals (17), also groups D and E were showed very low IgG titer mean and they are nearly to the AMAb IgG titer mean of the control group (5.05). Therefore this study suggests that the vaccinated individuals who have been received a booster dose of measles vaccine and their AMAb (IgG) titers lower than (64) are considered to be non immune and may be susceptible to infection with measles. Another study done in Taiwan by (18) who suggested that measles neutralizing (NT) titer more than 1000 mIU/ml may prevent measles infection and NT titers more than 500 mIU/ml may prevent symptomatic infection, but vaccinees with undetectable or low NT titers may be susceptible to symptomatic infection. Likewise, a study done in Hungary by (19) found that following a period of 6 years of low measles incidence, an epidemic occurred in Hungary with more than 11,000 reported cases between September 1980 and August 1981. About 60% of the cases had a documented history of previous measles vaccination. The present study found that the total mean of AMAb (IgG) titer of control group was (5.05) because the maternal antibodies are gradually decreased at 9 to 12 months in infants, which is nearly the same as that of (20); in a study done on Turkish infants, who found that the very low passive antibody at nine months of age may suggest the measles vaccination could be carried out earlier than just before the critical age of antibody level and his results agree with (21), who suggested new measles vaccination recommendations for preterm infants.

Figure (2) reveals the distribution of AMAb IgG titers according to residency of studied measles vaccinated individuals and age groups.

In rural group, the highest IgG titer was noted in age group A (235), followed by group B (42.5714), group C (26.0426), group D (8.6667) and finally the lowest titer was in group E (6.4). Approximately, there is no significant ($p > 0.01$) differences between rural and urban groups. These results were different from (22) who found that there were differences in underlying immunologic parameters and in response to measles component of vaccine between Bedouin and Jewish children and these differences may be due to genetic or environmental including residency. According to age each group: In males, the highest AMAb IgG titer was recorded in age group A (251.0435), followed by group B (51.6757), group C (26.7077), group D (6.8889) and finally the lowest titer was in group E (6.25). On the same manner the profile of the level of humoral immune response in the females, the highest IgG titer was recorded at age group A (221) which was lower than IgG titer in age group A of males. In age groups B and C, the IgG titers (42.963) and (25.7143) respectively were also lower than IgG titer in age groups B and C of males, whereas the IgG titers in age groups D (9.2174) and E (7.4286) were higher than the IgG titers of males age groups D and E respectively (figure 3). From the above results we conclude that the immune response (AMAb IgG titer) decreases reversely with the age increase after the 6th year. Moreover, AMAb IgG titers of the vaccinated individuals in our community were lower than the protective titer (64) may predispose to measles infection. Depending on the fact that the population involved in this study, as markedly shown in this work; have titer less than the protective titer may contribute the high rate of incidence of measles infections in Iraq last years (2008-2009). Thus we recommend that the first dose of measles vaccine should be given at the 9 months of age, while more than one booster dose of measles vaccine are required at 1.5, 3, 6, and 14 years. Also any age that shows AMAb IgG titer lower than the protective level, should be included in new vaccination campaigns that could help measles eradication.

Table -1: Distribution of study samples according to sex ,age ,and vaccination status.

M = Male, F = Female, V = Vaccinated, N-V = Non-Vaccinated, y = year.

Place	No.	M	F	V	N-V	Age range (y)
Al-Zahra'a Maternity & Children Hospital	62	35	27	44	18	1-10
Al-Furat Al-Awsat General Hospital	20	11	9	12	8	1-7
Al-Nasir Health Clinic	24	16	8	10	14	1-6
Central Health Laboratory in Al-Najaf	57	32	25	57	-	14-30
Waleed Al-Ka'abah Primary School for Boys	11	11	-	11	-	7, 8
Al-Qasim Primary School for Boys	23	23	-	23	-	6-13
Zein Al-A'abdin Primary School for Girls	24	-	24	24	-	6-15
Al-Furdos Primary School for Girls	5	-	5	5	-	7, 9
Al-Jawadain Primary School for Coeducation	60	35	25	60	-	6-12, 20-29

Table-2: Distribution of vaccinated individuals according to age, sex, and residency.

Age Group (y)	Descriptive Name	Sex		Residency		Total
		M	F	R	U	
1-6	A	46	54	34	66	100
7-12	B	37	27	28	36	64
13-18	C	65	42	47	60	107
19-24	D	18	23	12	29	41
25-30	E	16	7	5	18	23
Total		182	153	126	209	335

R = Rural, U = Urban.

Table-3: Distribution of control (non-vaccinated) individuals according to age, sex, and residency

Age (y)	Sex		Residency		Total
	M	F	R	U	
1	10	6	7	9	16
2	7	5	7	5	12
3	5	7	5	7	12
Total	22	18	19	21	40

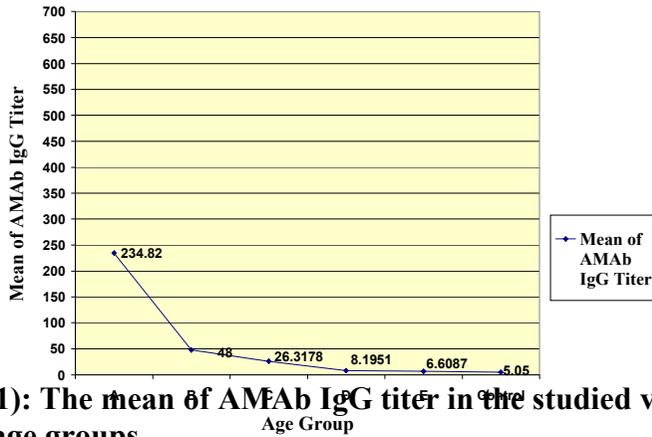
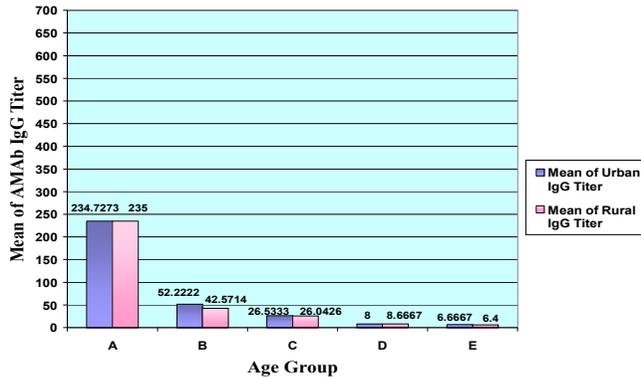


Figure (1): The mean of AMAb IgG titer in the studied vaccinated and control age groups.



Figure(2): The mean of AMAb IgG titer in rural and urban vaccinated individuals in different age groups

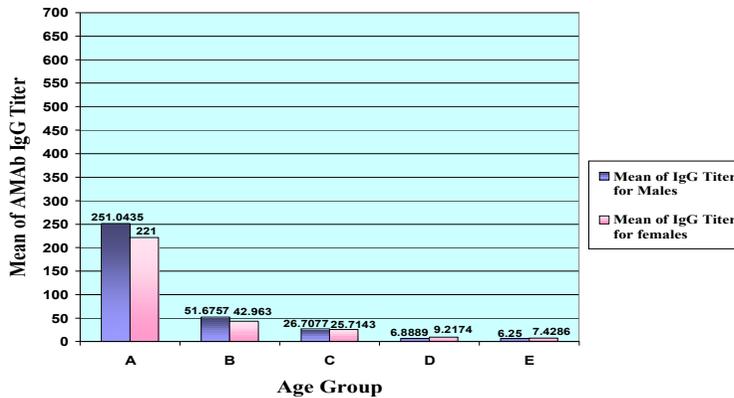


Figure (3): The mean of AMAb IgG titer in vaccinated males and females in different age groups.

References

1. Green, T. D.; Newton, B. R.; Rota, P. A.; Xu, Y.; Robinson, H. L.; and Ross, T. M. (2001). C3d enhancement of neutralizing antibodies to measles hemagglutinin. *J. Virol.* 77(6): 3505-3515.
2. WHO. (2005). Measles mortality reduction and regional elimination. Strategic plan 2001-2005. Pp: 1-33.
3. CDC. (2006b). Epidemiology and prevention of vaccine-preventable diseases. 11th ed.; Pp: 129-147.
4. Boon, N. A.; Colledge, N. R.; Walker, B. R.; and Hunter, J. A. A. (2006). Davidson's principles and practice of medicine. 20th ed.; Churchill Livingstone. Edinburg. Pp: 300-301.
5. Sips, G. J.; Chesik, D.; Glazenburg, L.; Wilschut, J.; De Keyser, J.; and Wilczak, N. (2007). Involvement of morbilliviruses in the pathogenesis of demyelinating disease. *Rev. Med. Virol., Early View*.
6. Hunt, M. (2006). Measles (Rubeola) and Mumps Viruses. In: Murray. *Microbiology*. 3rd ed.; University of South Carolina. School of Medicine. Pp: 235-245.
7. Stittelaar, K. J.; De Swart, R. L.; and Osterhaus, A. (2002). Vaccination against measles: A neverending story. *Expert Review of Vaccines*. 1(2): 151-159.
8. Permar, S. R.; Griffin, D. E.; and Letvin, N. L. (2006). Immune Containment and Consequences of Measles Virus Infection in Healthy and Immunocompromised Individuals. *Clinical and Vaccine Immunology*. 13(4): 437-443.
9. Redd, S. C.; Markowitz, L. E.; and Katz, S. L. (1999). Measles Vaccine. In: Plotkin, S. A.; and Orenstein, W. A. *Vaccines*. 3rd ed.; Philadelphia P.A.: W.B. Saunders Company. Pp: 222-266.
10. Al-Khafaji, Z. A. (2006). Isolation of measles virus and evaluation of immunological response among healthy and diabetic children. M. Sc. Thesis. College of Medicine, Al-Kufa University, Iraq.
11. Martin, B.; Carol, K. L.; Sarah, E.; and Morris, L. V. F. (1981). Comparison of enzyme-linked immunosorbent assay for acute measles with hemagglutination inhibition, complement fixation, and fluorescent-antibody Methods . *J. Clin. Microbiol.* 14(2): 147-152.
12. Bowers, D. (1997). *Statistics for health care professionals*. John Wiley and Sons. New York.
13. Parslow, T. G.; Stites, D. P.; Terr, A. I.; and Imboden, J. B. (2001). *A Lange medical book: Medical immunology*. 10th ed.; Lang medical books / McGraw-Hill medical publishing division. New York.
14. Hutchins, S. S.; Dezayas, A.; Blond, K. L.; Heath, J.; Bellini, W.; Audet, S.; Beeler, J.; Wattingney, W.; and Markowitz, L. (2001). Evaluation of an early two-dose measles vaccination schedule. *Amer. J. Epidemiol.* 154(11): 1064-1071.

15. Bautista-López, N. L.; Vaisberg, A.; Kanashiro, R.; Hernández, H.; and Ward, B. J. (2001). Immune response to measles vaccine in Peruvian children. *Bull. WHO.* 79(11).
16. Wong-Chew, R. M.; Beeler, J. A.; Audet, S.; and Santos, J. I. (2003). Cellular and humoral immune responses to measles in immune adults re-immunized with measles vaccine. *J. Med. Virol.* 70(2): 276-280.
17. Rose, N. R.; Friedman, H.; and Fahey, J. L. (1986). *Manual of clinical laboratory immunology.* 3rd ed.; American Society for Microbiology. Washington, D.C. Pp: 53-60.
18. Lee, M.; Nokes, D. J.; Hsu, H.; and Lu, C. (2000). Protective titres of measles neutralising antibody. *J. Med. Virol.* 62(4): 511-517.
19. Nagy, G.; Kósa, S.; Takátsy, S.; and Koller, M. (1984). The use of IgM tests for analysis of the causes of measles vaccine failures: Experience gained in an epidemic in Hungary in 1980 and 1981. *J. Med. Virol.* 13(1): 93-103.
20. Altintas, D. U.; Evliyaoglu, N.; Kilinc, B.; Sen'an, D. I.; and Gune S. (1996). The modification in measles vaccination age as a consequence of the earlier decline of transplacentally transferred anti-measles antibodies in Turkish infants. *Europ. J. Epidemiol.* 12(6): 647-648.
21. Linder, N.; Tallen-Gozani, E.; German, B.; Duvdevani, P.; Ferber, A.; and Sirota, L. (2004). Placental transfer of measles antibodies: Effect of gestational age and maternal vaccination status. *Vaccine.* 22(11-12): 1509-1514.
22. Rager-Zisman, B.; Bazarsky, E.; Skibin, A.; Tam, G.; Chamney, S.; Belmaker, I.; Shai, I.; Kordysh, E.; and Griffin, D. E. (2004). Differential immune response to primary measles-mumps-rubella vaccination in Israeli children. *Clin. Diagn. Lab. Immunol.* 11(5): 913-918.