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RESEARCH ARTICLE

Antibodies to measles following vaccination with measles containing vaccine in a selected sample of an Iraqi young adults

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Abstract

Background: Despite the implementation of mass school catch-up campaigns for measles, an outbreak of measles occurred mostly affecting the adult population.

Objectives: Evaluation of measles immunity among adults by estimation of measles IgG Antibodies, and to compare the results with that following measles vaccination.

Design &subject: A sero-surveys was carried out to estimate measles IgG Abs titer before and after a national campaign with measles containing vaccine. The study sample included (155) healthy young adults aged 19-25 years, randomly selected, Serum samples were examined for measles IgG Abs in the National measles laboratory using ELISA technique.

Results: Participants with serum positive for measles IgG antibodies were found in 68%, those were considered protected or immune to measles infection. While 32% of them found with negative serum results for measles IgG Abs and considered un-protected to measles infection. Sero-positivity increased to 85 % among the study sample. Mean measles IgG Abs. titer prior to the vaccination was negative (0.294 mIU/ml), to became positive (0.449mIU/ml) after re-vaccination with measles containing vaccine (MCV).

Conclusions: Immunity among the study sample was low. While it is unclear that the susceptible population can support continuous, indigenous transmission of measles. Recommendation to health care providers to evaluate measles susceptibility of individuals born in the vaccine era and vaccinate eligible patients

Introduction

Prior to the introduction of vaccine, most people acquired immunity through infection with wild measles virus during childhood (1, 2). Measles morbidity had been reduced greatly since measles containing vaccine (MCV) was introduced in 1966 (3). The availability of measles vaccine in Australia in 1968 lead to a reduction in circulating wild measles virus, reflected in decreased measles and measles encephalitis (4). Reflecting previous disease circulation and vaccination policies, it was recognized that, by the end of the twentieth century in Australia, measles had become a disease mostly affecting young adults However, re-emergence is possible to occur several decades

after introduction of high levels of vaccination (1, 4). Time until re-emergence depends primarily on the contagiousness of vaccine-modified measles cases in comparison to classical measles. Interestingly, in a population with a high proportion of vaccinees, vaccine-modified measles and classical measles would occur essentially in the same age groups. Although waning of humeral immunity in vaccinees is widely observed. Re-emergence of measles in highly vaccinated populations depends on parameters for which better estimates are needed **(5).**A national estimate of measles immunity and an understanding of predictors of measles susceptibility are essential for assuring sustained elimination of endemic disease (4,5). Measles incidence in the United States is at a record low, and indigenous transmission has been interrupted in each year since 1996, suggesting that measles is no longer endemic (6). Though largely eradicated in the U.S. due to vaccines, the World Health Organization (WHO) estimates that there are still an estimated 10 million cases of measles worldwide, resulting in nearly 200,000 deaths. While measles outbreaks often happen in countries without strong childhood immunization programs, recent outbreaks have also appeared in Europe, South Africa, and the Philippines (7).The population immunity did not reach the presumed thresholds of measles elimination. The significant decay of antibody against measles was found since adolescences. Secondary school students can acquire sufficient immunity to measles after revaccination program which can be conducted effectively and practically (8).Some adults may not have received full protection due to changes in the MMR vaccine (9). A big barrier to eliminating measles in Canada is a group of adults too young to have been exposed to the highly contagious disease but too old to have fully benefitted from vaccination programs (10). In order to prevent measles in adults, high-risk groups must be identified and catch-up for selected groups considered. Vaccination of international travelers to endemic areas should be recommended until global elimination has been achieved. Appropriate measles control strategies in younger populations seem to be effective in preventing measles in adults (7).The current study aimed at identification of measles immunity by assessment of measles IgG Abs titer among a selected sample of young adults and to compare that titer levels following measles immunization campaign to this category.

Subjects & Methods

A cross – sectional study, was conducted in Diyala Medical College. Sero-survey was done for selected random sample of medical students, aged 19-25 years. The study sample was (155) healthy medical students, of them 57 (36.8%) were males, and 98(63.2%) were females. Serum samples were collected and analyzed from the study sample for estimation of specific measles IgG Abs titers, prior to their submission to vaccination by measles containing vaccine (MCV) during National measles, mumps & rubella campaign 2011. Second serum samples were collected four weeks following that campaign. Testing of serum samples were performed at the National reference laboratory for measles in the Central Public health Laboratory (CPHL) in Baghdad City (Capital of Iraq). This laboratory was accredited by World health Organization (WHO), as one of reference laboratories in Eastern Mediterranean region for measles. Testing was done using the Enzygnost (Dade Behring, Marburg- Germany) commercial measles IgG enzyme immunoassay (IA). Using the alpha formula provided, the manufacturer's instructions for the calculation of immunoglobulin class G (IgG) concentration based on optical density (OD), were followed and immunity was determined (positive) as an OD = + > 0.2, which is equivalent to approximately 330 – 1909 milli-International Units per milliliter (mIU/ml). Equivocal samples (< 0.2) were retested and reclassified as positive or negative, where indicated. Final equivocal results were counted as non-immune.

Results:

With respect to the subjects "Age Groups", the majority of the sample were reported at the age ranged (20 – 24) years. And they are accounted 135(87.1%) with mean value was (22.11 ± 1.64). Relative to subject of "Gender", results indicated that the highest percentage of the study sample was females, and they are accounted for 98(63.2%).

Regarding to the subjects "BMI", the greater number of them illustrated normal level, and they are accounted 78(50.3%), and whatever to that those whom had overweight and obesity were reported too highly numbers due to the selected sample's age, and they are accounted 55(35.5%).

Table (1): Distribution of the observed frequencies, percents, and summary statistics of some characteristics variables of the study sample

Parameters	Groups/ years	No.	Percent
Age (year)	19	9	5.8
	20	23	14.8
	21	30	19.4
	22	27	17.4
	23	26	16.8
	24	29	18.7
	25	11	7.1
Total		155	100
Mean ± SD		22.11 ± 1.64	
Gender	Male	57	36.8
	Female	98	63.2
Total		155	100
BMI	Under weight (<18.5)	22	14.2
	Normal weight(18.5-<25)	78	50.3
	Over weight(25-30)	39	25.2
	Obese(>30)	16	10.3
Total		155	100
Mean ± SD		23.29 ± 2.77	

Table (2): Frequency distribution of serum sample level before and after vaccination with MCV.

Quality	Levels	Frequency	Percent
Before	Neg.	54	35.1
	Low Pos.	54	35.1
	Pos.	38	24
	Strong Pos.	9	5.8
	Total	155	100
After	Neg.	16	15.4
	Low Pos.	52	50
	Pos.	28	26.9
	Strong Pos.	8	7.7
	Total	104	100

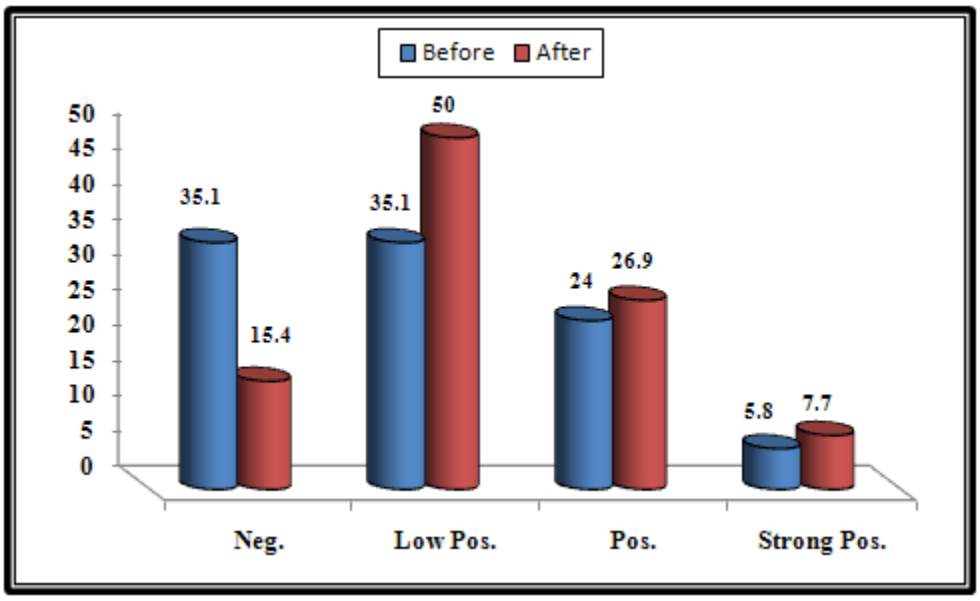

Figure (2): Cluster Bar chart of the frequencies, percent's of serum sample level before and after vaccination with MCV

Table (3): Summary statistics with comparison significant of Measles IgG titer before and after vaccination

Titer	Mean	No.	Std. Deviation	Std. Error Mean	Person's Correlation Coefficient	Paired Samples Test	P-value
Before	0.294	104	0.22	0.04	0.807 P=0.000 HS	-5.270	0.000 HS
After	0.449	104	0.25	0.05			

HS: Highly Sig. at P<0.01

Table (4) represented the distribution of different quality assessment before and after vaccination, which showed a non-significant association at P> 0.05. But the actual of calculated P-value is more informative to be reported, rather than simply the significant level was not achieved. This is indicating that we sure within not less than 88.5% (the complement value of the significant level of the contingency coefficient) that the association between the two periods (before and after) according to the diagnosis of the studied cases would be informative.

Table (5) shows the summary statistics with comparison significant of measles IgM titer, the result indicating that under the null hypothesis which says that the testing value of mean is coincidence to zero value, and the result showed that a highly significant difference are accounted at P<0.0001 which indicating that IgM titer's readings (0.090 mIU/ml) was meaningful and can't be neglected.

Table (4): Distribution of the Quality measles IgG titer at the two periods according to the levels of an ordinal scale of diagnosis

Quality	Levels	No. and Percents	Quality After				Total	C.S. P-value
			Neg.	Low Pos.	Pos.	Strong Pos.		
Quality Before	Neg.	No.	12	32	8	0	52	C.C.=0.532 P=0.115 NS
		% Quality before	23.1%	61.5%	15.4%	0.0%	100%	
		%Quality after	75.0%	61.5%	28.6%	0.0%	50%	
	Low Pos.	No.	4	12	12	0	28	
		% Quality before	14.3%	42.9%	42.9%	0.0%	100%	
		%Quality after	25.0%	23.1%	42.9%	0.0%	26.9%	
	Pos.	No.	0	8	8	8	24	
		% Quality before	0.0%	33.3%	33.3%	33.3%	100%	
		%Quality after	0.0%	15.4%	28.6%	100%	23.1%	
	Total	No.	16	52	28	8	104	
		% Quality before	15.4%	50.0%	26.9%	7.7%	100%	
		%Quality after	100%	100%	100%	100%	100%	

NS: Non Sig. at P>0.05

Table (5): Summary statistics with comparison significant of Measles IgM titer

One-Sample Statistics					Test Value = 0	
Parameter	No.	Mean	Std. Deviation	Std. Error Mean	t-test	Sig. (2-tailed)
IgM titer	155	0.090	0.20	0.016	5.523	0.000 (HS)

HS: Highly Sig. at P<0.01

Discussion:

In the recent measles outbreaks in Zhejiang Province, Hanqing He et.al. conducted a sero-prevalence survey of measles antibody among 1961 participants aged 0-60 years randomly selected by age-stratified purpose sampling, and the effect of revaccination program in secondary school was evaluate . The adjusted overall sero-positivity rate of measles was 88% (95% confidence interval [CI]: 86-89%) with geometric mean titers (GMT), 976±86 mIU/ml (2).

Measles incidence has declined significantly in the United States since the 1989–1991. Several conditions, including pockets of under-immunization, international importation, and the inability to rapidly detect and contain cases, represent potential threats to this success (3). During the 1995–1996 winter holiday season, the Minnesota Department of Health investigated an outbreak of measles among unvaccinated young adults affiliated with a religious community. A total of 26 outbreak-associated cases of measles were identified; most case patients (65%) were 20–29 years of age (range, 18 months to 35 years). Although case patients had multiple opportunities to expose the general public, no subsequent transmission was identified despite extensive surveillance efforts. This is in agreement with current study. Among young adults, 5% to 20% are susceptible to rubella and measles, and outbreaks occur where these persons congregate, while in the current study 35% susceptible to measles. Most adults are not immunized, despite recommendations for vaccines against these diseases. Vigorous efforts are needed to implement strategies to reduce disease incidence, morbidity, and death among adults.

In their study Mark M. et.al. concluded that although adults accounted for a steadily increasing proportion of measles cases during the study period, incidence rates in all age groups have decreased. Most adults who had measles were susceptible because of lack of vaccination rather than vaccine failure. This analysis supports current strategies to ensure the immunity of school/college-aged populations, and health care workers. (3).

In their study Kelly A.H. et.al., indicated no significant change in immunity of the cohort following the young adult MMR campaign (83.9% immune pre and 85.5% immune post campaign) while the Victorian component of the national sero-survey indicated a significant decline in immunity (91.0% to 84.2%; $p = 0.006$). Both surveys indicated about 15% susceptibility to measles among young Victorian adults after the campaign. Measles outbreaks in Victoria between 2000– 4 confirmed the susceptibility of young adults. Outbreaks involved a median of 2.5 cases with a median age of 24.5 years. And concluded that the young adult MMR program appears to have had no effect on residual susceptibility to measles among the 1968–82 birth cohort. Young adults in Victoria, as in other countries where past immunization policies have left a residual susceptible cohort, represent a potential problem for the maintenance of measles elimination. (1).

A measles sero- prevalence survey of 508 Minnesota blood donors aged 20–39 years was conducted; 91% had serological evidence of immunity to measles. Our findings illustrate that high levels of population immunity. (Alan et.al), Alan et.al. result is higher than what is found in the current study. The first major measles outbreak in Australia involving predominantly young adults occurred in Victoria between February and May 1999. Approximately 85% of the 75 notified cases confirmed with measles in this outbreak were born between 1968 and 1981 (aged between 18 and 31 years at the time) [2]. These young adults were most likely to be susceptible to infection because of the timing of changes to measles vaccination practices in Australia. This report published in Communicable Diseases Intelligence Volume 25, No 3, and August 2001 contains the findings of a sero-survey of 300 18-30-year-old healthy blood donors and 312 sera retrieved after diagnostic testing for a non-rash illness in patients of the same age group, with the aim of estimating the proportion of young adults in Victoria immune to measles.

Measles outbreaks in Victoria in 1999 and 2001 have suggested that a substantial proportion of young Victorian adults may be susceptible to measles infection**.** In three large measles outbreaks in Victoria between 1999 and 2002, the median age of cases has varied between 22 and 25 years [2,6,7]. Estimates of susceptibility to measles in the 1968–82 birth cohort ranged from 15–21% from two surveys with sera collected in 1999, one using blood donors and the other using residual diagnostic sera stored at the Victorian Infectious Diseases Reference Laboratory .Estimated measles susceptibility at a national level was 9% [9].

Since the immunization programme began, there has been a dramatic and complicated shift in the age pattern of measles immunity in the population, such that some young age groups are now better protected, but some older age groups less well protected, than they were before the programme. These trends are discussed with critical attention to the possibility that they may reflect biases in the available data. It is concluded that the number of susceptible over 10 years of age is increasing, and that this could have appreciable public health implications in the years to come (10).Waning vaccine immunity/secondary vaccine failure. In order to identify the high-risk age groups of measles for targeted intervention, A national estimate of measles immunity and an understanding of predictors of measles susceptibility are essential for assuring sustained elimination of disease. Although waning of humeral immunity in vaccinees is widely observed, re-emergence of measles in highly vaccinated populations depends on parameters for which better estimates are needed(13).There is an increasing susceptibility of infection with measles for infant less than one year of age and for children with poor family economic status in Diyala (14).

The study concluded that in order to prevent measles in adults, high-risk groups must be identified and catch-up for selected groups considered. Vaccination of international travelers to endemic areas should be recommended until global elimination has been achieved. Appropriate measles control strategies in younger populations seem to be effective in preventing measles in adults. The experience in Canada and the US suggests that measles transmission in adults is unlikely to be a major impediment to regional elimination or global eradication.

Regarding to the subjects of serum sample level before and after vaccination with MCV, as illustrated in table (2), the studied healthy students (volunteers), whom were tested their serum after vaccination with MCV including 104

(67.7%) individuals, while 51(32.3%) were lost to follow up. In addition to that they seem to be more effective compared with the pre vaccination period along the levels of an ordinal scale of diagnosis, and as illustrated in figure (2).

Table (3) shows the summary statistics with comparison significance of measles IgG titer before and after vaccination, the result indicating that actual difference has been occurred according to the effectiveness of IgG titer at the two periods, and that accounted a highly significant difference at $P<0.01$ with meaningful increasing of titer at the post vaccination period, as well as a meaningful correlation ship has reported at all the studied volunteers according to their IgG titer along the studied periods.

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