ORIGINAL ARTICLES

EVALUATION OF SEROLOGICAL STATUS AGAINST MEASLES IN 683 CHILDREN AGED 1 TO 6 IN ANKARA

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SUMMARY:

Purpose: *This serological field survey has been realized in the urban, rural and slum areas of Ankara Province in order to determine the serological status of healthy children of 1 to 6 years of age and the possible factors that might affect the serological status to measles virus.* ***Methods:*** *Stratified quota sampling method was used. Stratification criteria were age groups and settlement areas (urban, rural and slum areas). Hemagglutination Inhibition Technique was used to determine the measles immunological status.* ***Results:*** *88.3% of children included in the study were vaccinated. The highest number of unvaccinated children were living in slum areas (16.0%). Statistically, there was significant relation between the vaccination status and the settlement area ($p<0.001$). It was observed that 78.9% of all children who participated in the research were seropositive against measles. Seropositivity against measles indicated significant differences between the settlement areas ($p<0.05$). This difference arises from the slum area. Among the 603 vaccinated children, only 18.7% were found to be seronegative despite a history of one dose of measles vaccine, and seropositivity did not differ based on settlement. Stepwise logistic regression analysis indicates the age as the only factor affecting serological status. At 5-years, the risk of being seronegative is 2.33 times higher. Higher GMT levels indicate an increase in the antibody titers of the children who enter school at the age of 6 and are exposed to wild measles virus.* ***Conclusion:*** *In the light of these findings, it is important to conduct effective vaccination program and to apply a booster dose to children starting the primary school at the age of 6.*

Key Words: *Measles, Measles Vaccine, Measles Serology.*

INTRODUCTION

Measles is an important cause of childhood morbidity and mortality throughout the world. It is estimated that approximately one million child deaths occur due to measles every year (10% of all childhood deaths) (1, 2, 3, 4).

Vaccination for measles was first introduced in Turkey in 1969. According to the National Vaccination Schedule, measles vaccine is administered to infants at the age of 9 months (5, 6, 7). The measles coverage rate achieved at the national level is around 70%. Moreover,

there are major differences at the provincial level in metropolitan areas (8).

Percentage and characteristics of the population protected against measles are very important for planning, development, monitoring and evaluation of a measles control program. Determining the characteristics of high risk groups/areas and developing special strategies for these groups/areas are as important as determination of individuals seroconverted to measles.

A research was carried out in Ankara with the participation of 683 children aged between 1-6 years. The aim of the research was to obtain evidence to develop additional strategies for measles immunization policies, to collect data that will create the basis for risk approach and to select issues for further analysis. The objectives of the study are;

i) to determine seropositivity rates of children against measles virus,

ii) to determine the antibody levels (Geometric Mean Titration values) against measles virus by Hemagglutination Inhibition (HI) test,

iii) to analyze the factors (age, gender, age and site of vaccination) that might be affecting the serological status against measles,

iv) to review the measles coverage rate.

MATERIAL AND METHOD

The research was carried out in three areas of Ankara representing the urban, rural and slum settlements, where levels of vaccination rate, disease incidence, geographic and socio-economic status and the infrastructure are different. The study covered children aged between 1-6 years, who are at risk for measles, as data indicate from epidemiological studies and surveillance. Stratified quota sampling method was used due to technical and practical reasons. The criteria used during the stratification were the age groups and settlement areas (urban, rural and slum areas) (9). Vaccinated children were classified as "vaccinated" according to immunization records and/or history from mothers. Children with missing information about the vaccination status were classified as "unknown", as there were no records or reliable information gathered from the parents. This group was excluded during the statistical analysis.

Hemagglutination inhibition antibody levels against measles were determined in sera collected during the research and analyzed at Pasteur Meurix Institute in France, one of the reference laboratories of the World Health Organization. SPSS (version 6.1), Microsoft Excel and Epi-Info (version 6.0) software programs were used for the statistical analysis.

RESULTS

Of the children included in the study, 88.3% were vaccinated, 9.7% were not vaccinated and vaccination status of 2% were unknown (Table 1). When the vaccination status of the children was compared with regard to settlement areas, it was observed that the highest number of unvaccinated children were living in slum areas (16.0%), followed by rural (5.7%) and urban (3.6%) areas. Statistically, there was significant relation between the vaccination status and the settlement area ($p<0.001$).

It was determined that majority of children (85.2%) vaccinated against measles received the vaccine between the 9^{th} and 11^{th} months of age. Percentage of children who received vaccination "12 months and over" was 10.8%, and only 4% had been vaccinated before 8 months of age. No statistically significant relation was found between the vaccination age and the settlement area ($p>0.05$).

It was observed that 78.9% of all children who participated to the research were seropositive against measles (Table 2). However, 26.1% of the children living in slum areas, 18.8% living in urban areas and 15.6% rural areas were seronegative. Seropositivity against measles indicated significant difference between the settlement areas ($p<0.05$). This difference arises from the slum area.

Seropositivity of children in the study was compared with the vaccination status. 81.3% of vaccinated children and 56.1% of unvaccinated children were found to be seropositive (Table 3). There was a statistically significant difference between the immunization and the vaccination status ($p<0.05$). This difference was also observed in the slum area ($p<0.001$). The lowest seropositivity was observed among the vaccinated and unvaccinated groups in the slum area (78.0% and 52.1%, respectively). There was significant differences

Table 1 : Distribution of measles vaccination status and vaccination age, Ankara, 1994.

CHARACTERISTIC	Urban n : 192	Rural n : 192	Slum n : 299	TOTAL N : 683
		%*		
VACCINATION STATUS				
Vaccinated	95.9	90.1	82.3	88.3
Un vaccinated	3.6	5.7	16.0	9.7
Unknown**	0.5	4.2	1.7	2.0
			Chi-Square = 25.19	SD = 2 p < 0.001
AGE OF VACCINATION				
≤ 8 months	2.4	4.5	5.0	4.0
9-11 months	88.2	84.7	83.3	85.2
≥ 12 months	9.5	10.8	11.8	10.8
			Chi-Square = 2.47;	SD = 4; p < 0.05

* Column percentage
** "Unknown" groups were not included in the statistical analysis.

Table 2 :Measles serological status according to the settlement areas, Ankara, 1994.

SEROLOGICAL STATUS	Urban	Rural	Slum	TOTAL
		%*		
SEROPOSITIVE	81.2	84.4	73.9	78.9
SERONEGATIVE	18.8	15.6	26.1	21.1
TOTAL (n)	192	192	299	683
(%)	100.0	100.0	100.0	100.0
* Column percentage			Chi-Square = 8.56;	SD = 2 ; p<0.05

Table 3 : Seropositivity against measles according to the vaccination status and settlement areas, Ankara, 1994.

VACCINATION STATUS	Urban n	Urban Sero-Positive (%)	Rural n	Rural Sero-Positive (%)	Slum n	Slum Sero-Positive (%)	TOTAL N	TOTAL Sero-Positive (%)	P Value
VACCINATED	184	82.1	173	85.0	246	78.0	603	81.3	p<0.05
UNVACCINATED	7	71.4	11	63.6	48	52.1	66	56.1	p>0.05
TOTAL	191	81.7	184	83.7	294	73.8	669	78.8	
p value		p>0.05		p>0.05		p<0.001		p<0.05	

*Children, whose vaccination status are not known, were not included in the analysis.

in seropositivity between the vaccinated and unvaccinated groups according to the settlement area ($p>0.05$).

Among all children in the research, Geometric Mean Titration (GMT) value for vaccinated children was found as 32.6 IU/ml, and 40.2 IU/ml (Table 4) for unvaccinated children. GMT values of vaccinated and unvaccinated children did not show statistically significant difference ($p>0.05$).

GMT value was determined as 21.4 IU/ml for children who were vaccinated before 8^{th} months of age, and 33.5 IU/ml for those who were vaccinated between 9^{th} and 11^{th} months of age or 12^{th} months and over. There was no statistically significant difference according to the age of vaccination ($p>0.05$). In the slum areas, regarding seropositivity of children who were vaccinated before 8^{th} months, no significant difference was found when compared with those vaccinated between 9^{th} and 11^{th} months or 12^{th} month and over ($p<0.05$). No difference was observed in seropositivity related to the age of administration among the settlement areas ($p>0.05$).

When the distribution of GMT values according to the age groups were analyzed, the highest GMT value was observed in the one-year age group (47.3 IU/ml.) (Table 5, Figure 1). It was also observed that GMT value decreased with age, with an increase at the age of 6 and indicating a statistically significant difference between 4 to 6 and 1 to 2 year age groups ($p<0.05$). GMT value also indicated a difference between the 2 years old and 5 to 6 years age groups in the slum areas ($p<0.05$). However there was no difference related to the age groups in rural and urban areas ($p>0.05$).

Stepwise logistic regression analysis was completed by using the variables (settlement area, age of vaccination, place of vaccination, number of person per room and socioeconomic level of the families) that might affect the serological status of vaccinated children. As a result of the analysis, the age of child is found as the only factor effecting the serological status the. In the group of 5 years old children, risk of being seronegative is 2.33 times higher (Table 6).

DISCUSSION

Measles is a highly infectious disease and will persist in communities unless an effective vaccination program achieving high coverage rates is conducted. It was found that 78.9% of the children aged between 1-6 were seropositive. 26.1% of the children who were living in the slum areas were seronegative. Based on this evidence, children who are living in peri-urban areas are under a higher risk for measles infection.

18.7% of 603 vaccinated children were seronegative despite the fact that they received the vaccine, and seropositivity did not differ based on the place of settlement. Previous studies conducted in Turkey among vaccinated children in different age groups stated different seropositivity rates between 70.3% and 81.0 (10-15). Various international studies on seroconvertion to measles have revealed that seroconvertion after administration of measles vaccine at 9^{th} months of age can vary between 50.0% and 100.0%. Measles studies conducted worldwide indicate 85-90% prevention by vaccination at the 9^{th} months (16, 17).

However, adopting the vaccine schedule and postponing the age of vaccine administration based on serological data is not the most proper approach. The most appropriate approach is the observation and evaluation of epidemiological data as well as serological data. In Turkey, according to the routine information system, measles coverage rate is low and 10% of measles cases are found in the "0" age group (5). Besides, "0" age group has the highest age-specific measles morbidity and mortality rates. Epidemiological data support that measles cases can be prevented with 2 doses (18). By administrating a booster dose, it will be possible to seroconvert unvaccinated children, as well as to seroconvert vaccinated children who had developed primary vaccine failure. Seropositivity rates of the children surveyed did not indicate any statistical difference according to the age groups. However, it is observed that GMT values against measles show a decline with age, reach to their lowest level at the age of 5, and at the age of 6, reach to a higher level. Stepwise logistic regression analysis determines the age of the child as the only factor affecting the seropositivity

Table 4 : Geometric mean titration values (IU/ml) against measles according to the age of vaccination and settlement area, Ankara, 1994.

AGE OF VACCINATİON (month)	Urban GMT*	95% Reliance Interval Lower Limit	Upper Limit	Rural GMT*	95% Reliance Interval Lower Limit	Upper Limit	Slum GMT*	95% Reliance Interval Lower Limit	Upper Limit	TOTAL GMT*	95% Reliance Interval Lower Limit	Upper Limit
≤8	55.1	5.2	585.6	25.8	9.3	71.8	13.9	9.3	20.9	21.4	13.4	34.1
9 - 11	34.0	28.0	41.3	31.0	25.0	38.4	34.5	29.2	40.7	33.5	30.1	37.3
≥12	31.8	19.5	1.9	35.6	18.2	69.8	33.5	22.0	51.2	33.5	25.5	43.9
TOTAL	34.2	28.6	40.9	31.2	25.7	37.9	32.8	28.3	38.1	32.9	29.8	36.3

* Geometric Mean Titration Value.

Table 5 : Geometric mean titration values (IU/ml) against measles according to the age group and settlement area, Ankara, 1994.

AGE OF CHILD (year)	Urban GMT*	95% Reliance Interval Lower Limit	Upper Limit	Rural GMT*	95% Reliance Interval Lower Limit	Upper Limit	Slum GMT*	95% Reliance Interval Lower Limit	Upper Limit	TOTAL GMT*	95% Reliance Interval Lower Limit	Upper Limit
1	45.9	29.2	72.4	62.3	38.8	100.1	39.9	27.9	57.1	47.3	37.4	59.9
2	43.2	29.1	64.2	39.5	24.7	63.1	56.1	35.8	88.0	46.5	36.4	59.5
3	39.6	28.3	55.4	25.1	18.5	34.1	37.9	25.8	55.5	34.2	28.0	41.9
4	28.0	18.1	43.4	23.5	16.6	33.3	27.9	20.8	37.5	26.7	21.9	32.5
5	22.4	14.4	35.0	25.1	18.3	34.4	22.8	16.9	30.7	23.4	19.3	28.4
6	34.8	21.0	62.0	28.4	19.9	40.7	25.0	17.7	35.4	28.5	22.8	35.7
TOTAL	34.3	29.3	41.3	30.7	26.4	35.8	32.3	28.0	37.2	32.6	29.8	35.6

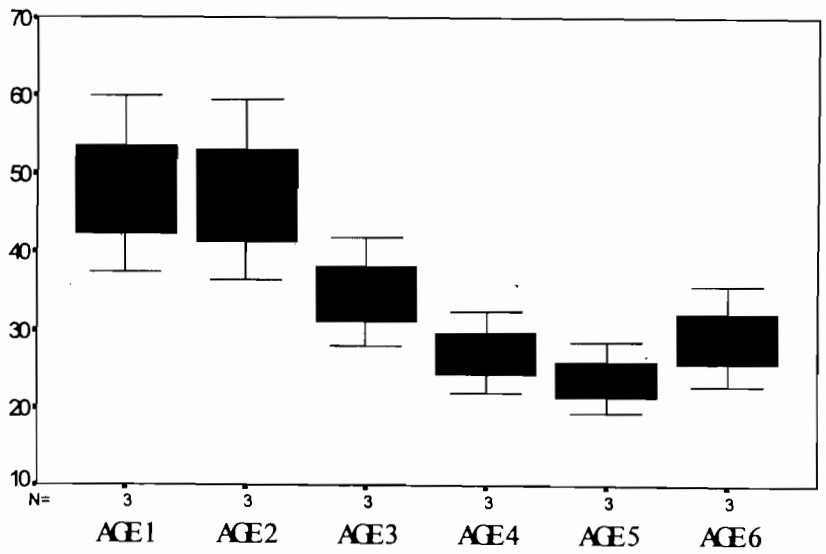
* Geometric Mean Titration Value.

Table 6 :Evaluation of the relation between various variables and serological status of vaccinated children by stepwise logistic regression analysis, Ankara, 1994.

VARIABLE	COEFFICIENT	STANDART ERROR	RELATIVE RISK	95% RELIANCE INTERVAL	IMPORTANCE
Age of Child					
1 *					
2	0.03	0.44	1.03	0.44 - 2.44	0.95
3	0.08	0.44	1.08	0.46 - 2.56	0.85
4	0.65	0.40	1.92	0.88 - 4.19	0.11
5	0.85	0.41	2.33	1.05 - 5.23	0.04
6	0.05	0.47	1.05	0.42 - 2.64	0.92

* Reference group.

Fig. 1: Geometric mean titration values (IU/ml) of vaccinated children according to the age groups, Ankara, 1994.



In the 5-year age group, the risk of being seronegative is 2.33 times higher. Higher GMT values may refer to an increase in the antibody titres of children who enter the school at the age of 6 and are infected by wild measles virus. In the light of these findings, it is important to add a booster dose to the measles schedule. In 1997, a booster measles dose applied to children attending the first grade primary school at the age of 6 was added to National Measles Vaccination Shedule.

National measles immunization program should be monitored, evaluated and directed considering the surveillance data in addition to vaccination coverage rates. Thus, research topics would be well-defined and consequently, results obtained would contribute to the management of the program. It would be useful to develop up to date measles immunization programs and strategies that are adjustable to the country by conducting periodic studies which provide valuable information to the questions defined, based on the epidemiological data from existing measles immunization program and evaluating these studies together with surveillance data.

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