Seroprevalence of Measles, Rubella, Mumps and Varicella Specific Antibodies in Primary School Children

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Abstract

Measles, mumps, rubella and varicella are diseases that are tracked by the World Health Organization (WHO) as common and serious vaccine-preventable diseases.

Aim of the Work: To evaluate the immune status and susceptibility against measles, mumps, rubella, and varicella in primary school children and to study the effects of some sociodemographic factors on the seroprevalence.

Subjects and methods: This is a cross- sectional study conducted on 180 children. All children included in this study were subjected to thorough history taking and laboratory investigations; to measure serum levels of specific measles, rubella, mumps and varicella immunoglobulins (IgG)

Results: (88.9%) of the surveyed children were seropositive to measles, (77.8%) to mumps, (86.7%) to rubella and (38.9%) to varicella. Seropositivity was higher in males than in females for measles (57.7%), mumps (60.7%), rubella (62.2%) and varicella (68.6%) with significant difference for measles. Younger age groups were less seropositive than older age groups for measles (32.5% vs 35%), mumps (34.4 % vs 37.9%), rubella (30.8 % vs 39.7 %) and for varicella (21.4%) vs 48.6%). The highest level of seronegativity was seen with regard to varicella specific antibodies (61.1%).

Conclusion and recommendations: There is an urgent need for a planned program with different strategies to prevent and control these diseases .

Key words: Seroprevalence, measles, mumps, rubella, varicella, primary school children, Egypt

Introduction

Measles is a highly contagious viral disease. Typical symptoms are high fever, cough, coryza, conjunctivitis and maculopapular rash. Common complications include otitis media, Post-infectious encephalitis in about 0.1% of reported cases, and subacute sclerosing panencephalitis in about 1/10,000–100,000 cases.

Rubella is a viral disease presenting with fever, rash and lymphadenopathy. Its importance is caused by its teratogenic effect on the fetus causing miscarriage, fetal death and congenital rubella syndrome(2).

Mumps is a vaccine preventable viral infection. Its typical clinical manifestations are pain and swelling of the salivary glands, fever, and fatigue. Other organs are commonly affected (orchitis, oophoritis, pancreatitis, meningitis) (3).

Varicella-zoster virus (VZV) is the etiologic agent of varicella (primary infection) and herpes zoster (reactivation of latent infection). Although varicella is most often a relatively benign and self-limited childhood illness, the disease may be associated with a variety of serious and potentially lethal complications in both immunocompetent and immunocompromised persons (4).

The measles, mumps and rubella (MMR) vaccine is a mixture of measles, mumps and rubella live attenuated viruses, administered via SC injection. The shot is generally administered to children around the age of one year. The WHO recommends that in order to eliminate congenital rubella syndrome and to prevent the complications associated with mumps and measles, countries should use the measles, mumps and rubella (MMR) vaccine in a two-dose schedule for routine childhood immunization programs (5).

In 2002, Egypt established a goal of measles elimination by 2010 using the WHO/UNICEF Comprehensive Strategy for Sustainable Measles Mortality Reduction (6) and also set a goal of rubella elimination and congenital rubella syndrome (CRS) prevention by 2010. The strategy for rubella elimination included the introduction of MMR as the second dose of measles-containing vaccine(MCV) in 1999. In 2008, the immunization schedule was updated to use MMR for both doses of MCV and to administer the first dose at 12 months of age and the second dose at 18 months of age (7).

A two dose program with varicella vaccination is also likely to be required for elimination of childhood varicella and has been recently recommended in the United States(8).

The measles, mumps, rubella, and varicella (MMRV) vaccine was licensed in 2005 for use among children aged 12 months up to 12 years. It is a single shot that can be used in place of two other vaccines administered in two separate shots-the measles, mumps, rubella (MMR) vaccine and the varicella vaccine for chickenpox(9).

In Egypt, there is limited data about the serological status of school children for these infectious diseases. Monitoring school childrens' seroprevalence and understanding the immune status of children remains important to potentially identify those with higher susceptibility and guide national immunization policies to modify a routinely administered schedule or implement a new schedule.

Aim of the Work

To evaluate the immune status and susceptibility of a sample of primary school children against measles, mumps, rubella, and varicella in Egypt by conducting a seroprevalence survey utilizing an enzyme immunoassay and to study the effects of some sociodemographic factors on the seroprevalence.

Subjects and Methods

This is a cross- sectional study conducted at Meat-Mousa village school, Menoufia Governorate, Egypt in the period from June 2013 up to February 2014. Cluster sampling technique was used. One class was randomly selected from each educational grade. It was conducted on 180 children; their ages ranged from 6 to 12 years. They were 109 males and 71 females. Parents of participants were asked to fill out an especially designed questionnaire.

The studied children were subdivided into the following groups according to their ages:
- Group I 6 -8 years (n=60)
- Group II >8-10years (n=56)
- Group III >10-12 years (n=64)

Inclusion Criteria:
Apparently healthy Children aged 6-12 years.

Exclusion Criteria:
Acute illness; fever more than 38 degrees centigrade, recent administration of immunoglobulins, blood product or immunosuppressive therapy and suspected or confirmed immune suppressive conditions.

The study was conducted according to the rules of Benha Faculty of Medicine ethical committee. A written consent from all student parents was taken with explanation of the purpose of the study and ensuring privacy.

All children included in this study were subjected to the following:

1-Thorough history taking:
- ***Full medical history including:***
- Full personal and social history e.g.: age, sex, residence, order of birth.
- Nutritional history: feeding, breast fed or bottle fed.
- Developmental history: motor and mental development.
- Vaccination history especially MMR timing and number of doses.
- Contact to measles, rubella, mumps and varicella cases or catch up the diseases.

• ***Parents history including:***
- Mother and father's occupation and educational degree
- Socioeconomic status according to the following score(10) :

The total score was

Scores from 19-25	High social standard
Scores from 12-18	Moderate social standard
Scores from 6-11	Low social standard
Scores of < 6	Very low social standard

2- Thorough clinical examination:
-Anthropometric measures include: weight, height and body mass index.
- Chest, cardiac and abdominal examination.

3-Laboratory investigations:
About 3ml of peripheral blood was withdrawn from each child into a sterile vacutainer and allowed to clot. After centrifugation the obtained sera were aliquoted and kept frozen at - 20°C till further processing. The serum samples were used, according to the instructions of the manufacturers for:

1- Measurement of serum levels of specific Measles IgGusingKAPRMVG10 Measles IgG ELISA kit -DIAsource, Belgium (11).
2- Mumps, and varicella specific IgG were done for all children using ELISA kits (The KAPRMUG12 Mumps IgG ELISA kit -DIA source-Belgium and KAPRVIG20 Varicella zoster IgG ELISA kit - DIA source-Belgium (12).
3- Measurement of serum levels of specific Rubella IgG using RB025G Rubella IgG ELISA kit-Calbiotech-Spring Vally)(13).

The Cut-Off was calculated.The sample was considered:

Positive:	If the ratio was > 1.1.
Doubtful:	If +/- 10% of the Cut-Off.
Negative:	If the ratio was < 0.9.

If the result was doubtful, the test was repeated. If it was still doubtful, a new serum sample was collected.

Results

Table 1: Seroprevalence status of measles antibodies by sociodemographic factors

Measles IgG / Variable		Seropositivity		Seronegativity		
		No	%	No	%	
Gender	Female (n.=71)	68	42.5	3	15	≤ 0.05
	Male (n.=109)	92	57.5	17	85	
Age	6-8y	52	32.5	8	40	>0.05
	>8-10	52	32.5	4	20	
	>10-12	56	35	8	40	
Breast feeding	Yes	159	99.4	20	100	>0.05
	NO	1	0.6	0	0	
Social Standard	High	76	47.5	8	40	>0.05
	Middle	46	28.8	8	40	
	Low	38	23.8	4	20	
Previous Infection	No	156	97.5	20	100	>0.05
	Unknown	4	2.5	0	0	
Total		160	100	20	100	

Table 2: Seroprevalence status of mumps antibodies by sociodemographic factors

Mumps IgG / Variable		Seropositivity		Seronegativity		P value
		No	%	No	%	
Gender	Female (n.=71)	55	39.3	16	40	> 0.05
	Male (n.=109)	85	60.7	24	60	
Age	6-8y	48	34.4	12	30	≤0.05
	>8-10	39	27.9	17	42.5	
	>10-12	53	37.9	11	27.5	
Breast feeding	Yes	139	99.3	40	100	>0.05
	NO	1	0.7	0	0	
Social Standard	High	70	50	14	35	>0.05
	Middle	38	27.1	16	40	
	Low	32	22.9	10	25	
Previous Infection	Yes	11	7.9	0	0	>0.05
	No	123	87.9	39	97.5	
	Unknown	6	4.3	1	2.5	
Total		140	100	40	100	

Statistical analysis : the collected data were tabulated and analyzed using (SPSS version 16) software (SPSS Inc., Chicago, ILL Company) .

Chi-square and Fisher's exact are statistical tests used in analysis

The accepted level of significance will be (P ≤0.05)

Table 3: Seroprevalence status of rubella antibodies by sociodemographic factors

Rubella IgG / Variable		Seropositivity		Seronegativity		P value
		No	%	No	%	
Gender	Female (n.=71)	59	37.8	12	50	> 0.05
	Male (n.=109)	97	62.2	12	50	
Age	6-8y	48	30.8	12	50	≤0.05
	>8-10	46	29.5	10	41.7	
	>10-12	62	39.7	2	8.3	
Breast feeding	Yes	155	99.4	24	100	>0.05
	NO	1	0.6	0	0	
Social Standard	High	76	47.4	10	41.7	>0.05
	Middle	44	28.2	10	41.7	
	Low	38	24.4	4	16.7	
Previous Infection	No	156	97.4	24	100	>0.05
	Unknown	4	2.6	0	0	
Total		**156**	**100**	**24**	**100**	

Table 4: Seroprevalence status of varicella antibodies by sociodemographic factors

Varicella IGg / VARIABLE		Seropositivity		Seronegativity		P value
		No	%	No	%	
Gender	Female (n.=71)	22	31.4	49	44.5	> 0.05
	Male (n.=109)	48	68.6	61	55.5	
Age	6-8y	15	21.4	45	40.9	≤0.05
	>8-10	21	30	35	31.8	
	>10-12	34	48.6	30	27.3	
Breast feeding	Yes	69	98.6	110	100	>0.05
	NO	1	1.4	0	0	
Social Standard	High	36	51.4	48	43.6	>0.05
	Middle	19	27.1	35	31.8	
	Low	15	21.5	27	25.2	
Previous Infection	Yes	12	17.1	1	0.9	>0.05
	NO	58	82.9	106	96.4	
	Unknown	0	0	3	2.7	
Total		70	100	110	100	

A total of 180 children were surveyed . There were (60.6%) males and (39.4%) females. The age ranged from 6 up to 12years and distributed as 33.3% for 6-8 age group, 31.1% for > 8 -10 age group and 35.6% % for >10- 12 age group. Only 18.3% of the studied children of age group (6-8 yrs) received the MMR vaccine first dose (at 12 months) while all of the other 2 groups (>8-10 yrs and >10-12 yrs) didn't receive the first dose of the vaccine at 12 month. Regarding the second dose of the vaccine (at 18 months) all age groups received the vaccine.

There is increasing titre of measles, mumps and rubella IgG with increasing age with no statistical significant difference but there is a statistically significant decreasing varicella titre with increasing age. (Figure 1).

There is increasing titre of measles ,mumps and varicella among low social class while rubella titre reported higher figures among high social class. Figure (2)

Regarding seroprevalence of virus antibodies of the children tested 160 (88.9%) were seropositive to measles, 140 (77.8%) to mumps, 156 (86.7%) to rubella and 70 (38.9%) to varicella. Seropositivity was higher in male than in female children for measles (57.7%), mumps (60.7%), rubella (62.2%) and varicella (68.6%).

No significant difference was found between male and female with regard to seropositivity to, mumps, rubella and varicella; however, males were significantly more seropositive to measles than females

Analysis of the data according to age reveals that there were significant differences in seropositivity rates in age groups for mumps , rubella and varicella. Younger age groups were less seropositive than older age groups for measles (32.5% vs 35%), mumps (34.4% vs 37.9%), rubella (30.8% vs 39.7%) and for varicella (21.4% vs 48.6%) with statistically significant differences except for measles.

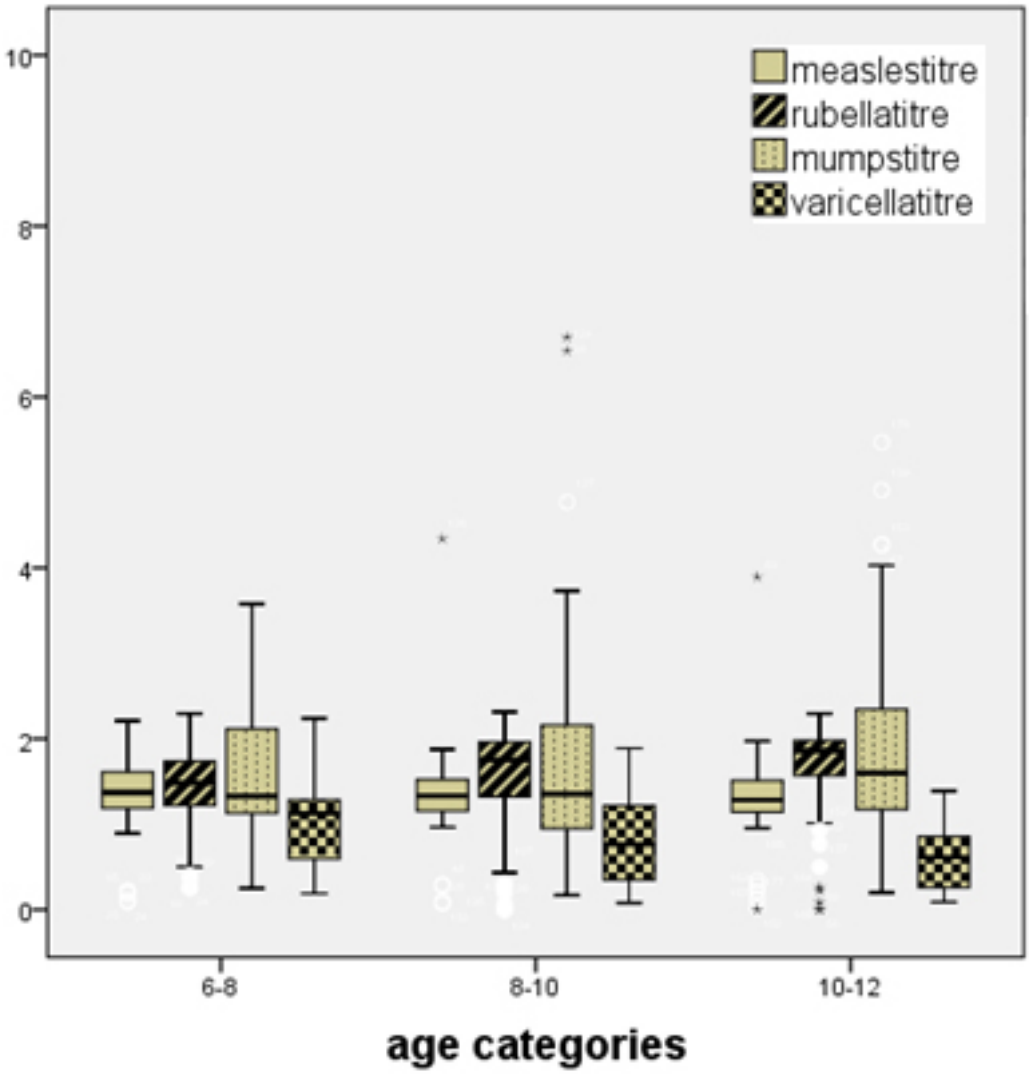


Figure 1: Distribution of titres between different age groups

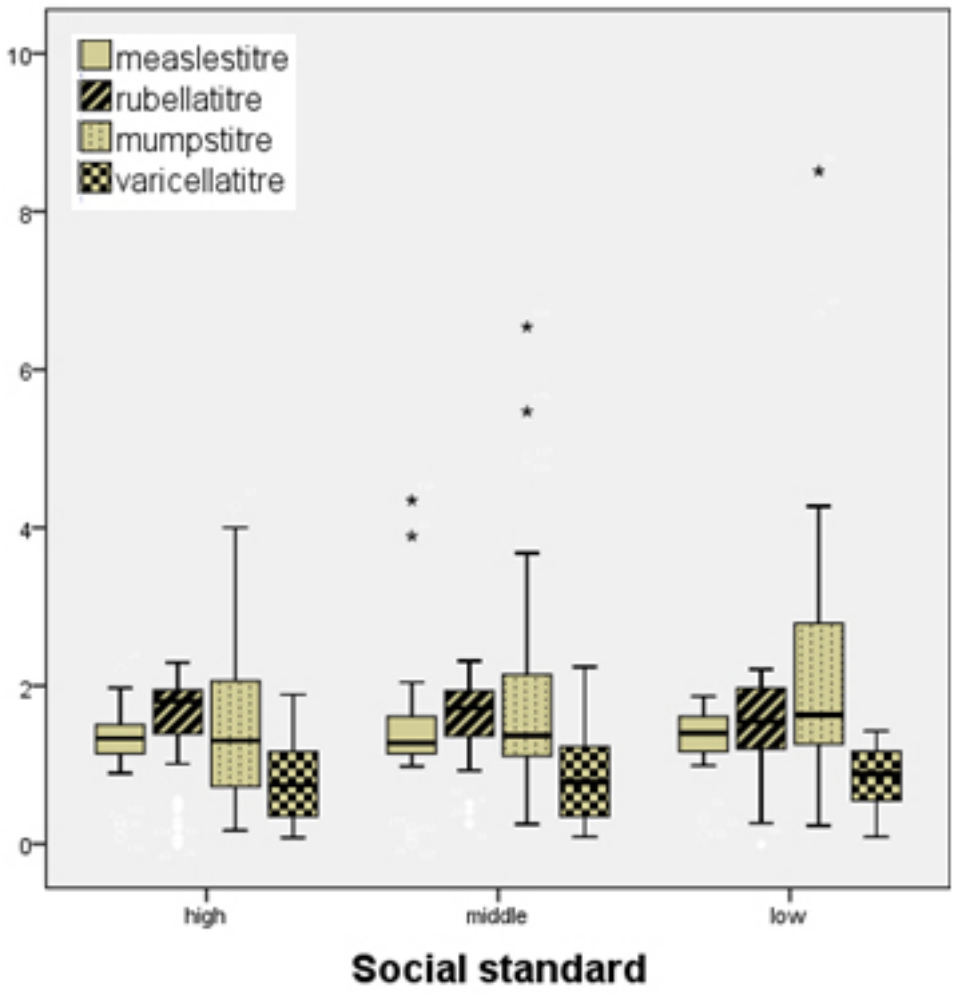


Figure 2: Distribution of titres between different social classes

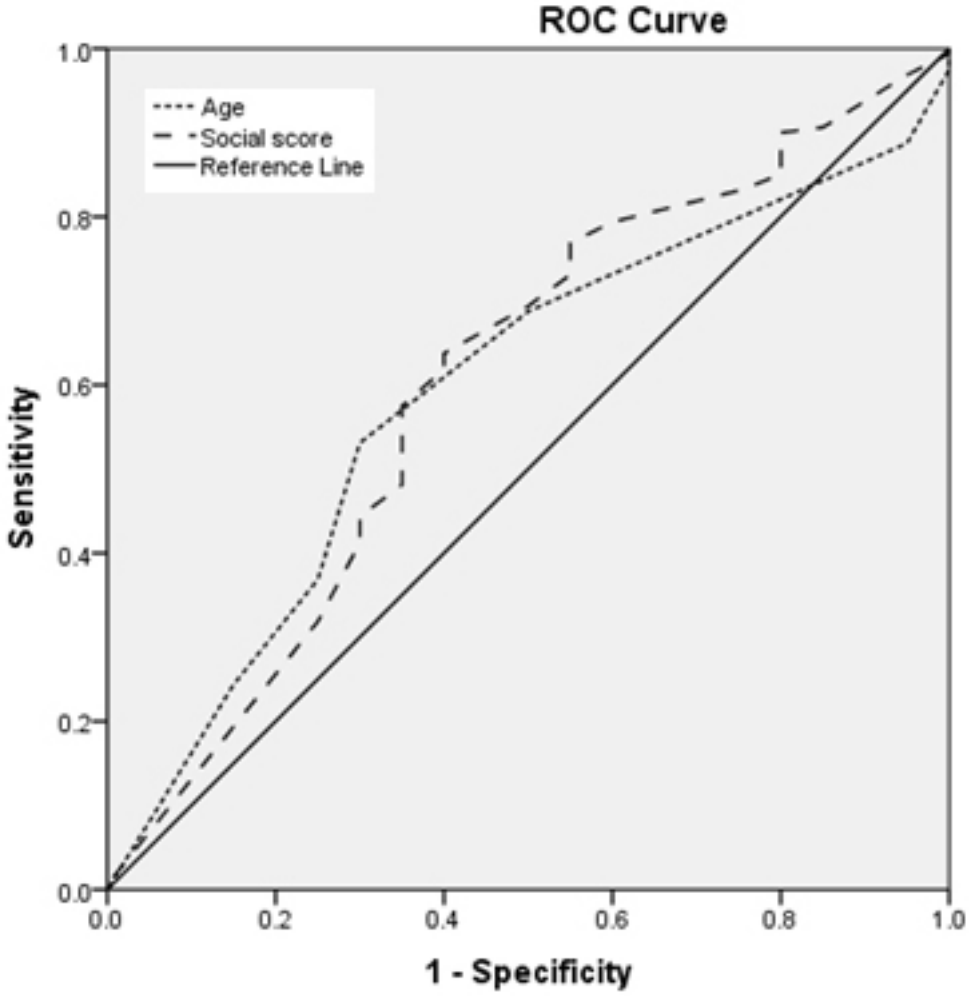
The majority of the surveyed children were normally breast fed (99.4%) with no significant higher seropositivity rates among them for measles (99.4 %), mumps (99.3%), rubella (99.4%) and varicella (98.6%).

Overall, the highest level of seronegativity was seen with regard to varicella specific antibodies (61.1%). Some differences for gender and age were seen; In general, girls had a lower rate of seronegativity for measles (15%), mumps (40%) and varicella (49%) but this pattern was not seen in rubella (50%). Generally, seronegativity was highest in the age group 6- 8 year old children for measles (40%), rubella (50%), and varicella (45%) but for mumps it is highest among 8-10 age group (42.5%).

Higher seropositivity of measles (47.5%), mumps (50%), rubella (47.4%) and varicella (51.5%) IgG were observed in high social class compared to middle and low social classes but with no statistical significant differences.

High percentage (97.5%, 87.9%, 97.4% and 82.9%) of seropositivity of the studied group was in children without past history of infection regarding measles, mumps, rubella and varicella IgG respectively with no significant statistical results.

Figure 3: Relation between measles IgG titre and age and social class



Figures (3,4,5,6,): Regarding age: Area under the curve is : less than 0.6 for rubella and mumps (i.e., age is a worthless predictor for sero- prevalence of rubella and mumps), nearly 0.6 for measles, larger than 0.6 for varicella (ie., age is a fair predictor for seroprevalence of measles and varicella) with statistically significant results for rubella and varicella.

Figures (3,4,5,6) Regarding social class : Area under the curve is: equal to 0.6 for measles (i.e., social score is a fair predictor for sero- prevalence of measles), less than 0.6 for rubella, mumps and varicella (ie., Social score is a worthless predictor for seroprevalence of rubella mumps and varicella) with non statistically significant results.

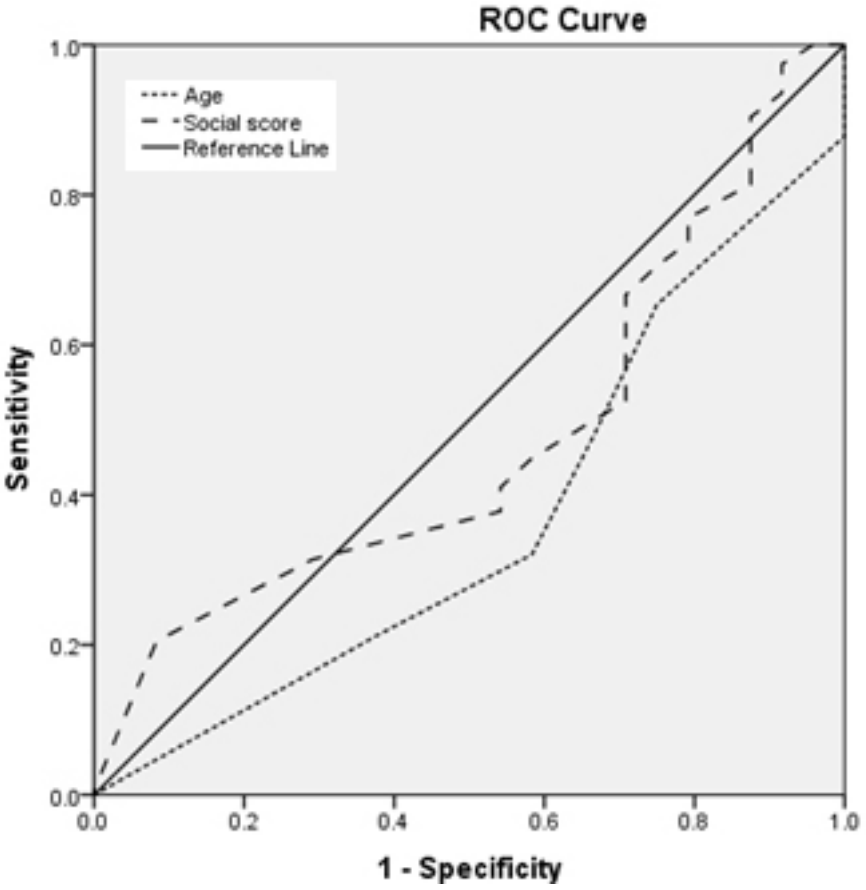


Figure 4 : Relation between rubella IgG titre and age and social class

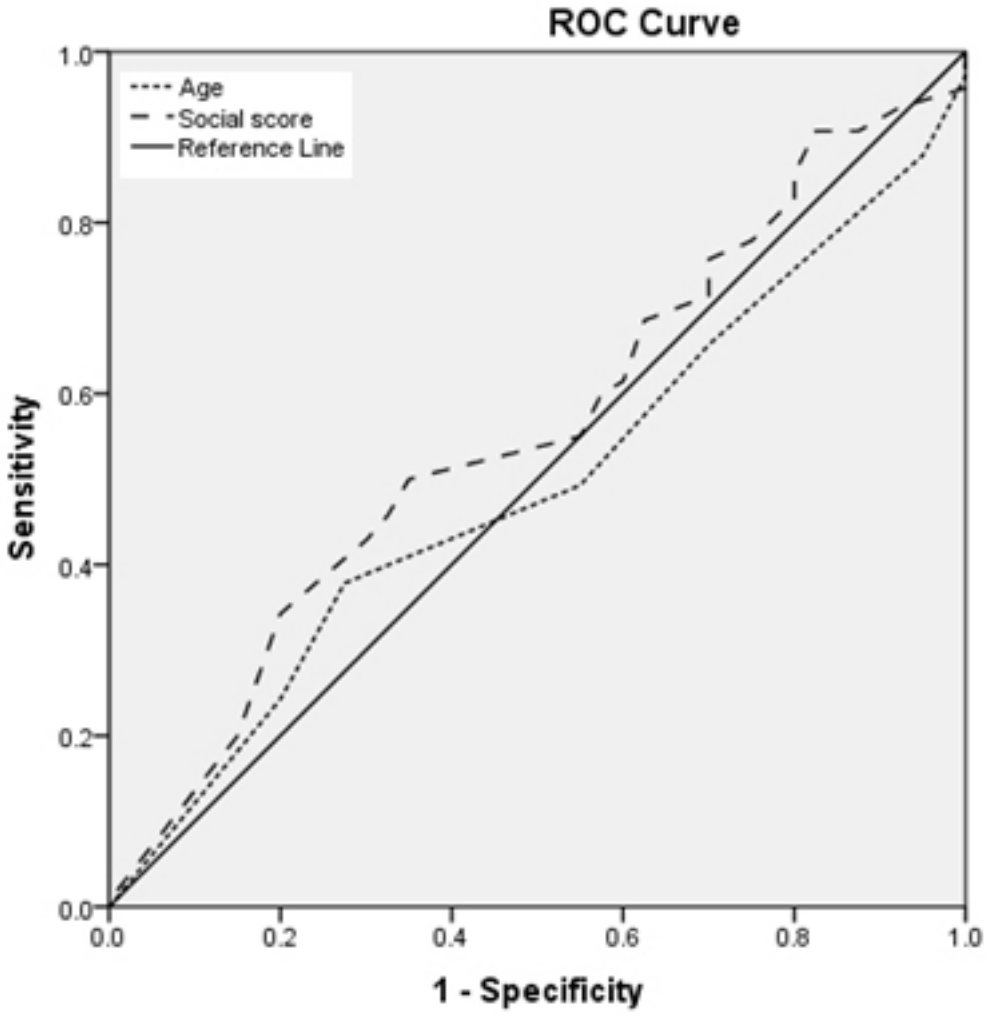
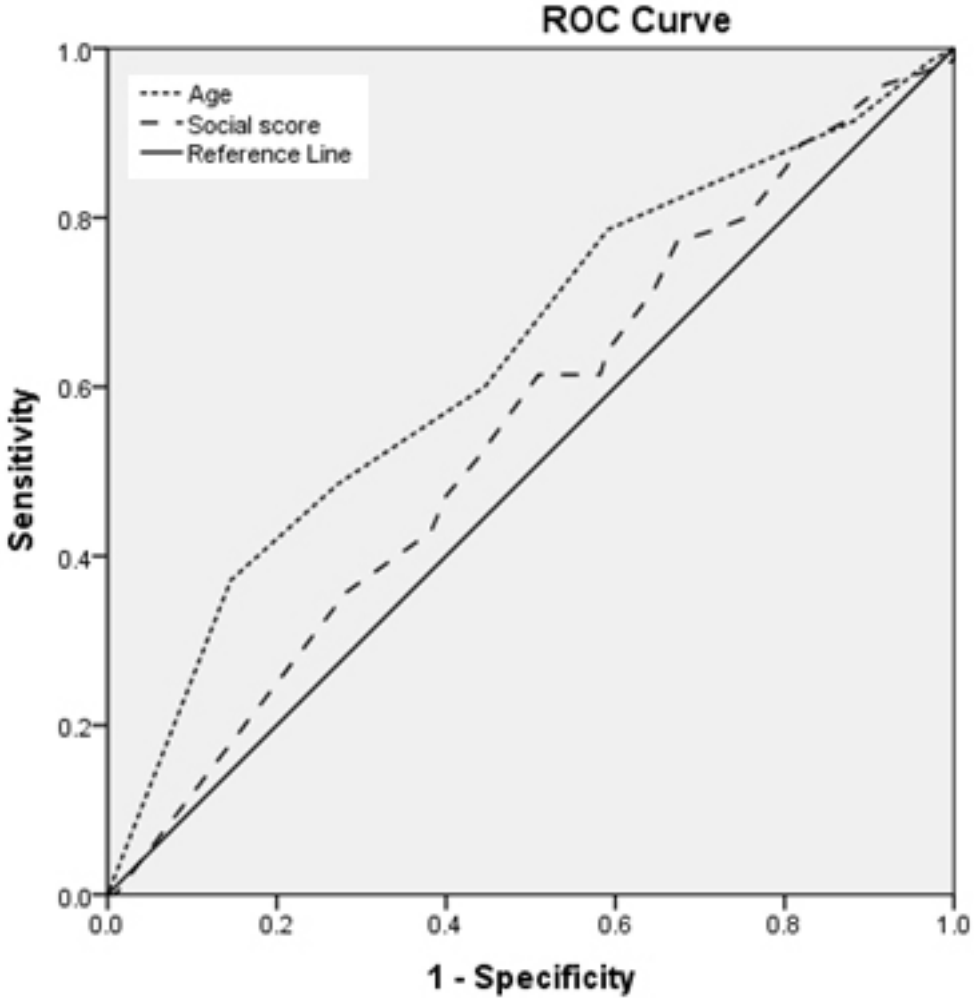


Figure 5: Relation between mumps IgG titre and age and social class

Figure 6: Relation between varicella IgG titre and age and social class



Discussion

Measles, mumps, rubella and varicella are diseases that are tracked by the World Health Organization (WHO) as common and serious vaccine-preventable diseases i.e ; licensed vaccines are available to prevent, or contribute to the prevention and control of them. Immunization is one of the safest, most cost-effective means of preventing diseases. Nowadays, all countries of the world have incorporated a broad immunization program in their public health interventions.

Our study showed that 88.8 % of the studied group was seropositive for measles IgG and 86.6% was seropositive for rubella IgG. These results were in agreement with different studies ; in Egypt and Pakistan, 86.1% and 79.9% respectively of the studied group was seropositive for measles IgG (14,15). In Germany seropositivity was 89.5% for measles and 86.25% for rubella (16) In Thailand and Iran 93.4% and 85% respectively were seropositive for rubella (17, 18).

This study revealed that 77.8%. were seropositive for mumps IgG. Different figures have been reported world wide ; in the United States 88% positivity for two doses(19,20) and overall 94% positivity were reported in another study (21) and in Bulgaria 79% were positive(3).

This study reported that the percentage of seropositivity of varicella IgG was only 38.9%. In contrary to our results a higher rate was reported in other studies; in Bangladesh seropositivity is approximately 65% (22), In Australia; 83% by the ages of 10-14 years (23) and in Turkey and Italy, levels of immunity by the ages of 10-14 years were 85% and 82 % respectively(24, 25).

Differences between countries are likely to be related to climatic conditions and mixing patterns, particularly in relation to child day care (23) or difference in vaccination program coverage. There are some differences between regional seropositivity rates which are perhaps attributable to differences in the design of early childhood immunization programmes of each country.

This study shows that seropositivity was higher in male than in female children for measles (57.7%), mumps (60.7%), rubella (62.2%) and varicella (68.6%) with no significant results except for measles.

For measles this was in agreement with many studies in Pakistan (15) and in Korea (26) but it was in contrast with others (14, 16, 27).

For rubella this was in contrast with others in Germany (16) in Japan (27) and in Colombia (28).

Regarding mumps, our results coincide with a German study which revealed that boys were more likely to be seronegative to measles, mumps and rubella than girls (16).

On the other hand a study conducted on Bulgarian children revealed a significantly higher prevalence of mumps antibodies in girls(29).

Measles was endemic in Egypt until 2008. During the 1980s, large measles epidemics occurred every 2-4 years. Similarly, outbreaks in the 1990s continued to occur every 2-4 years. Between 1996 and 2000, the majority (>80%) of measles cases were reported in persons aged >10 years (30).

Since 2000, there has been a remarkable decrease in the number of reported cases of measles. This decrease has occurred among age-groups targeted by the mass vaccination campaigns conducted during 2000-2004 as a part of the measles elimination strategy.

In 2006, however, the number of confirmed measles cases increased dramatically to 953 . In 2006, the age distribution of cases was as follows: 22% aged 1-5 years, 56% aged 6-15 years, and 10% aged 16-20 years (7).

In 2008, reported measles cases decreased to 771 with a similar age distribution . In 2008 and 2009 a 2-phase measles, rubella (MR) campaign was conducted and had a significant impact on measles cases(2).

Rubella surveillance was part of communicable diseases surveillance in Egypt and had been in place for many years (7).

In 2002 and 2003, 274 and 261 confirmed rubella cases were reported, respectively, of which many (>45%) occurred among children 5-9 years of age. In 2005 up to 2007, a nationwide epidemic began; most rubella cases were reported among persons 11-20 years old. In 2008, the epidemic waned. Following the 2008-2009 MR vaccination campaign, only a few cases of rubella were reported (2).

Also in a recent study in Egypt the overall measles antibody seropositivity was 88% and rubella antibody seropositivity was 74%. Measles antibody seropositivity averaged 87% in 1- to 4-year old children and increased to an average of 93% in children aged 10-20 years. Rubella antibody seropositivity averaged 56% (range: 43-71%) in children aged 1-4 years and gradually increased to an average of 91% in adolescents and young adults aged 15-19 years old (6).

This coincides with the results of this study which reveals that younger age groups were less seropositive than older age groups with significant differences in seropositivity rates in age groups for mumps , rubella and varicella. The increasing prevalence of antibodies in the older children may be due to either vaccination schedule or exposure to natural infection/ mature immune systems.

Regarding measles, this was in agreement with others (14, 15) but in contrast with another study in Germany (16) which reported a higher percentage in 7-10 age groups than in 11-13 years old.

Also the increasing measles antibody level by age was supported by many researchers; in Korean children (26), in Italian children (31), WHO Report (32) and in Australian children (33,15).

Regarding rubella, this was in agreement with Tharmaphornpilas (2009) study in Thailand (17), but in contrast with others (16).

In our study, age of children had a significant effect on the seropositivity of mumps titre. Age was reported as a significant factor by many studies. In a Bangladeshi population mumps antibody had shown a steep rise from age 2 to 3 years up to 14-15 years age (34). On the other hand, in another study on Finnish children there were declining mumps antibody levels and rising negativity rates (35).

In this study, varicella seronegativity decreased significantly with age of the studied children group. This coincides with a seroepidemiologic survey in Catalonia (Spain) which reported decreased susceptibility to VZV by increasing age (36) but disagrees with other studies in Canada (37) and in Sri Lanka (38). Also a study conducted in Saudi Arabia revealed a non significant difference between age groups in the prevalence of immunity to varicella (39).

Regarding the type of feeding, our study showed that breast feeding has no significant effect on measles , mumps or rubella IgG. The same results were obtained by others (40, 41).

According to the socioeconomic state, higher seropositivity of measles (47.5%), mumps (50%), rubella (47.4%) and varicella (51.5%) IgG were observed among high social class compared to middle and low social classes but with no statistical significant differences. This was in agreement with Abu Zaid study, (41) which reveals non significant differences between social levels.

Our study showed that most of the studied vaccinated children had no history of measles, rubella or mumps infections. This is also supported by the Poethko Muller and Mankertz study in Germany (16)

Conclusion

The seroprevalence survey studies had important implications for the management of vaccine programs which contributes to the prevention of disease transmission. In this study seropositivity was higher in male than in female children with a significant difference for measles. Younger age groups were less seropositive than older age groups with significant differences except for measles. The highest level of seronegativity was seen with varicella specific antibodies. Higher seropositivity was observed in high social class and in children without past history of infection with no significant statistical results.

Recommendations

Immunization programs face many challenges: to introduce new vaccines, to achieve and sustain high coverage for those already in the program. There is a need for a planned program to prevent and control these diseases with the following strategies:

• Adding a 3rd dose of MMR vaccine at age 4-6 years old to increase the protective efficiency of vaccine and to be sure of the elimination of the diseases at the adolescence period.
• Introduction of MMRV vaccine instead of MMR for all children to avoid infection and serious complications, especially in older ages of children without or of unknown history of previous infection.
• Testing older children for varicella (IgG) to determine their vulnerability to vaccine before vaccination.
• Conduction of planned health awareness activities directed towards more orientation about Immunization.
• Adopt scientific advice on vaccines that will support policy makers in their decisions regarding the national vaccination schedules.

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