Original Articles

A serological survey of measles, mumps and rubella immunity among school aged children in Western Saudi Arabia

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ABSTRACT

Objectives: To evaluate the adequacy of measles, mumps and rubella (MMR) vaccination among children and to assess risk of outbreak in Jeddah, Kingdom of Saudi Arabia (KSA).

Methods: We recruited a total of 527 children from schools located at different urban regions, and preschool children from those attending the well baby clinics in Jeddah, KSA. We tested for MMR viruses' antibodies using ELISA technique.

Results: Approximately 99% of children received MMR vaccine. Overall seropositivity for measles antibodies was 71%, mumps 65% and rubella 90%, which were elevated in vaccinated versus non-vaccinated children (p<0.000). In vaccinated children, percentage of seropositivity for MMR was higher in public school children versus private (p<0.01) or those who did not attend school (p<0.01) and in Saudi versus non-Saudi children (p<0.000). In vaccinated children, percentage of seropositivity obtained according to age groups of 4-6 years for measles was 73.7%, for mumps 66.7% and for rubella 91.7%. As for 7-11 years age group, seropositivity for measles was 72.6%, for mumps 68.1% and for rubella 93%, while for the 12-14 years, seropositivity for measles was 66.4%, mumps 59.1% and for rubella 86.1%. The prevalence of seropositivity against the above-mentioned viruses decreased with progression of age.

Conclusion: An MMR mass vaccination program achieved high coverage rate among children, in Jeddah, KSA. However, there is still a high level of sera negative children among vaccinated ones for measles and mumps. Seropositivity decreased with age, which might raise possibility of outbreaks among adolescent. Additional doses of vaccine against measles and mumps are recommended and evaluation of new MMR protocol should be made.

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Acute measles is normally a mild disease in children and young adults caused by infection with a highly contagious measles virus.[1] On the basis of World Health Organization (WHO) / United Nations Children's Fund (UNICEF) estimates, global routine measles vaccination coverage rate among one- year-old infants increased from 71-77% between 1999 and 2004. In the year 2003, a total of 164 (85%) countries offered children a second measles booster dose, compared with 150 (78%) countries in 2001.[2] Endemic measles has been successfully controlled in Americas and to a lesser extent in Europe by giving 2 doses of measles-containing vaccine.[3] In some industrialized countries, where vaccine uptake is

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poor, as in Japan[3] and in developing countries[2] the disease is still a significant cause of morbidity and mortality. Vaccine response failure is primary due to host reaction, which may, in part, be genetic in origin and related to **HLA** type.[3] Therefore, a 2-dose vaccine schedule has been introduced in many countries, the aim is to improve vaccine coverage and to prevent accumulation of susceptible persons, which may prevent periodic outbreaks.[4]

Serosurveys to assess mumps immunity was conducted in a number of countries prior to introduction of vaccine. Data from England and Wales, Netherlands, Singapore[5] and St. Lucia[6] document a steep increase in mumps antibody level from age 2–3 years; 50% of children aged 4-5 years had acquired natural antibodies; and 90% of the population aged 14–15 years was seropositive. The situation in other countries is different, with a large proportion of adults remaining susceptible to infection, such as Saudi Arabia[7] and Poland.[8] Mumps virus outbreaks have not been completely eliminated, even in vaccinated populations.[9] Mumps virus infections in vaccinees are due to either infection with a wild-type of virus following primary vaccine failure[10] or inoculation with a relatively neurovirulent mumps virus vaccine.[11]

The important tool to assess risk for disease outbreaks is by knowing the prevalence of MMR susceptibility as measured, either by serologic markers of immunity or by surveys of vaccination coverage. In the present work the prevalence of anti-measles, anti-mumps and anti-rubella antibodies among school aged children in Jeddah, Saudi Arabia was investigated. The chief objective was to make an empirical evaluation of the need for mass immunization, including a third compulsory dose of measles, mumps and rubella (MMR) vaccine in order to control and eliminate MMR infection in Saudi Arabia.

Methods. We randomly recruited children from kindergarten, primary, elementary, secondary schools located at different urban regions and preschool children who attended the well baby clinic, in Jeddah, Saudi Arabia during the year 2004. Blood samples (3 ml) were obtained by venous puncture from 527 healthy school aged children (285 males and 242 females); aged 4-14 years (8.90 ± 3.34 years). The samples were centrifuged and sera were frozen at –20° until the serological analysis was performed. All subjects were in a good state of health. The study was approved by the Medical Ethics Committee of King Abdul-Aziz University, Jeddah, Saudi Arabia.

For each participant, a questionnaire was completed by the students themselves or the helpers in the school. It included demographic information including name, age, gender, and nationality, type of school and vaccination state. The immunization status of the study subjects was verified from their vaccination records. The vaccination schedule against measles employed in this study was 1st dose of measles vaccine alone at 6 months and another dose at 12 months by combined MMR vaccine.

Measles immunoglobulin G (IgG) antibodies were determined using enzyme link immunosorbent assay (ELISA) kit (series # 9Z9271G) supplied by Zeus Scientific, Inc. (New Jersey, USA). The specificity of the kit was 93.3% while sensitivity was 97.4%. An optic density (OD) ratio ≥1.1 is interpreted as positive while value ≤0.9 is interpreted as negative for IgG measles. Specimens with ratio value in the equivocal range were considered borderline for IgG to measles and were retested.

Mumps IgG antibodies were determined by ELISA kits (DSL-05-10-MuGi) supplied by Diagnostic System Laboratories, Inc. (Texas, USA). The sensitivity of the kit was 99.1% while the specificity was 94.1%. The sample would be considered positive if the odds ratio was >1.1, doubtful or equivocal if results were ±10% of the cutoff and negative if the odds ratio was ≤0.9.

Rubella IgG antibodies were determined using Bioelisa Rubella IgG kits (COD # 3000-1215) supplied by BioKit (Barcelona, Spain). The person is considered non-immune if the concentration of antibodies was <10 IU/ml and is considered immune when the concentration of antibodies was ≥10 IU/ml.

Statistical analysis. Data were analyzed using the Statistical Package for Social Sciences software, version 10. The percentages of positive, negative and equivocal sera were calculated according to age, gender, type of school and nationality. The prevalence among different groups was compared using the Chi-Square test. A $p<0.05$ was considered statistically significant.

Results. This seroepidemiological study for MMR, showed that the overall seropositive rate was 71% for measles, 65% for mumps and 90% for rubella, while seronegative rate was 28% for measles, 32% for mumps and 10% for rubella; and equivocal rate of 1% for measles, 3% for mumps and 0% for rubella. The seropositivity against MMR antibodies was significantly elevated in vaccinated children compared to non-vaccinated ones ($p<0.000$ for all) (**Table 1**).

Table 2 showed the overall prevalence of anti-measles, anti-mumps and anti-rubella antibodies in

Table1 - Prevalence of antibodies against measles, mumps and rubella in school-aged children (n=527) in Jeddah, Saudi Arabia grouped according to their vaccination status.

Variable	Seropositive		Equivocal		Seronegative	
	n	(%)	n	(%)	n	(%)
Measles						
Vaccinated (n=523), % to vaccine	373	(71)	5	(1)	145	(28)
Non-vaccinated (n=4), % to vaccine	2	(50)	0	(0)	2	(50)
p-value	p<0.000		-		p<0.000	
Total (n=527), (%)	**375**	**(71)**	**5**	**(1)**	**147**	**(28)**
Mumps						
Vaccinated (n=522), % to vaccine	341	(65)	15	(3)	166	(32)
Non-vaccinated (n=5), % to vaccine	1	(20)	0	(0)	4	(80)
p-value	p<0.000		-		p<0.000	
Total (n=527)	**342**	**(65)**	**15**	**(3)**	**170**	**(32)**
Rubella						
Vaccinated (n=522), % to vaccine	474	(91)	0	(0)	48	(9)
Non-vaccinated (n=5), % to vaccine	2	(40)	0	(0)	3	(60)
p-value	p<0.000		-		p<0.000	
Total (n=527)	**476**	**(90)**	**0**	**(0)**	**51**	**(10)**

vaccinated and non-vaccinated children grouped according to gender, nationality and type of school attended. In vaccinated children, the percentage of seropositivity for MMR antibodies was higher in public school children than in private school children or those who did not attend school (p<0.000 for all) and in Saudi compared to non-Saudi children (measles p<0.01, mumps p<0.01 and rubella p<0.000).

In the 4-6 year age group, all the recruited children were vaccinated. The overall anti-measles seropositivity rate was 737%, anti-mumps was 66.7% and anti-rubella antibodies was 91.7%; seronegativity rate for measles was 25%, mumps 30.8% and 8.3% for rubella; and equivocal rate was 1.3% for measles, 2.6% for mumps and 0% for rubella. The prevalence of seropositivity was significantly higher in males compared to females (p<0.001 for measles, p<0.01 for mumps, p<0.01 for rubella). The percentage of seropositivity for measles and rubella antibodies was higher in children who did not go to school (p<0.01) compared to those attended private and public schools (p<0.000), while the percentage of seropositivity for mumps antibodies did not show any difference regarding the type of school (**Table 3**).

In the 7-11 year age group, most of the children enrolled were vaccinated and few of them were not. In vaccinated children seropositivity for measles was 72.6%, 68.1% for mumps and for rubella 93%, seronegativity for measles was 27.4%, 29.3% for mumps, and 7% for rubella while the equivocal rate was 0% for measles, 2.6% for mumps, and 0% for rubella. The percentage of seropositivity against MMR was higher in children attending public schools compared to those who attended private schools and those who did not attend schools (p<0.000 for all). The percentage of seropositivity against measles and rubella was significantly higher in Saudi compared to non-Saudi children (p<0.05 for both) (**Table 3**).

In the 12-14 year age group, seropositivity rate for measles was 66.4%, 59.1% for mumps and 86.1% for rubella, seronegativity rate was 31.4% for measles, 37.2% for mumps, and 13.9% for rubella, and equivocal rate was 2.2% for measles, 3.6% for mumps and 0% for rubella. The percentage of seropositivity for measles, mumps and rubella was higher in Saudi compared to non-Saudi children (measles p<0.001, mumps p<0.000, rubella p<0.000). The percentage of seropositivity against measles was significantly higher in public school children compared to private school children and children who did not attend school (p<0.000) and the percentage of seropositivity against mumps was higher in females compared to males (p<0.05) (**Table 3**).

Discussion. In the establishment of the vaccination programmes, post-implementation surveillance is necessary to monitor the effectiveness of the programme.[12] The incidence rate of measles

Table 2 - Prevalence of antibodies against measles, mumps and rubella in vaccinated and non-vaccinated children (n=527) in Jeddah, Saudi Arabia grouped according to gender, type of school and nationality.

Variable	Gender		*p*-value	Schools			*p*-value	Nationality		*p*-value	Total
	Male (n=285)	Female (n=242)		Private (n=161)	Public (n=287)	No school (n =79)		Saudi (n=298)	Non-Saudi (n=229)		(n=527)
	n (%)	n (%)		n (%)	n (%)	n (%)		n (%)	n (%)		n (%)
Measles											
Vaccinated (n=523)											
Seropositive	198 (38)	175 (33)	*p*>0.05	116 (22)	199 (38)	58 (11)	*p*<0.000	213 (40.5)	160 (30.5)	*p*<0.01	**373 (71)**
Equivocal	2 (0.4)	3 (0.6)	*p*>0.05	3 (0.6)	1 (0.2)	1 (0.2)	*p*>0.05	3 (0.6)	2 (0.4)	*p*>0.05	**5 (1)**
Seronegative	82 (16)	63 (12)	*p*>0.05	40 (8)	85 (16)	20 (4)	*p*<0.000	79 (15)	66 (13)	*p*>0.05	**145 (28)**
Non-vaccinated (n=4)											
Seropositive	1 (25)	1 (25)	*p*>0.05	0 (0)	2 (50)	0 (0)	-	1 (25)	1 (25)	*p*>0.05	**2 (50)**
Equivocal	0 (0)	0 (0)	-	0 (0)	0 (0)	0 (0)	-	0 (0)	0 (0)	-	**0 (0)**
Seronegative	2 (50)	0 (0)	-	2 (50)	0 (0)	0 (0)	-	2 (50)	0 (0)	-	**2 (50)**
Mumps											
Vaccinated (n=522)											
Seropositive	176 (33)	165 (32)	*p*>0.05	115 (22)	179 (34)	47 (9)	*p*<0.000	197 (38)	144 (28)	*p*<0.01	**341 (65)**
Equivocal	6 (1)	9 (2)	*p*>0.05	6 (1.1)	7 (1.3)	2 (0.4)	*p*>0.05	7 (1.3)	8 (1.5)	*p*>0.05	**15 (3)**
Seronegative	99 (19)	67 (13)	*p*<0.05	38 (7)	98 (19)	30 (6)	*p*<0.000	91 (17)	75 (14)	*p*>0.05	**166 (32)**
Non-vaccinated (n=5)											
Seropositive	1 (20)	0 (0)	-	0 (0)	1 (20)	0 (0)	-	0 (0)	1 (20)	-	**1 (20)**
Equivocal	0 (0)	0 (0)	-	0 (0)	0 (0)	0 (0)	-	0 (0)	0 (0)	-	**0 (0)**
Seronegative	3 (60)	1 (20)	*p*>0.05	2 (40)	2 (40)	0 (0)	*p*>0.05	3 (60)	1 (20)	*p*>0.05	**4 (80)**
Rubella											
Vaccinated (n=522)											
Seropositive	252 (48)	222 (43)	*p*>0.05	147 (28)	255 (49)	72 (14)	*p*<0.000	275 (53)	199 (38)	*p*<0.000	**474 (91)**
Equivocal	0 (0)	0 (0)	-	0 (0)	0 (0)	0 (0)	-	0 (0)	0 (0)	-	**0 (0)**
Seronegative	29 (6)	19 (3)	*p*>0.05	12 (2)	29 (6)	7 (1)	*p*<0.000	20 (4)	28 (5)	*p*>0.05	**48 (9)**
Non-vaccinated (n=5)											
Seropositive	1 (20)	1 (20)	*p*>0.05	0 (0)	2 (40)	0 (0)	-	1 (20)	1 (20)	*p*>0.05	**2 (40)**
Equivocal	0 (0)	0 (0)	-	0 (0)	0 (0)	0 (0)	-	0 (0)	0 (0)	-	**0 (0)**
Seronegative	3 (60)	0 (0)	-	2 (40)	1 (20)	0 (0)	*p*>0.05	2 (40)	1 (20)	*p*>0.05	**3 (60)**

Data are represented by number (%) to vaccine.

Table 3 - Prevalence of seropositivity against measles, mumps and rubella in vaccinated children aged 4-6 (n=156), 7-11 (n=233) and 12-14 (n=138) years in Jeddah, Saudi Arabia grouped according to gender, type of school and nationality.

Variable	Gender		*p*-value	School			*p*-value	Nationality		*p*-value	Total
	Males (n=98)	Females (n=58)		Private (n=41)	Public (n=39)	No School (n=76)		Saudi (n=73)	Non-Saudi (n=83)		(n=156)
	n (%)	n (%)		n (%)	n (%)	n (%)		n (%)	n (%)		n (%)
Measles virus											
4-6 years (n=156)	76 (48.7)	39 (25)	<0.001	30 (19.2)	30 (19.2)	55 (35.5)	<0.01	55 (35.3)	60 (38.5)	>0.05	**115 (73.7)**
7-11 years (n=233)	82 (35.7)	85 (37)	>0.05	44 (19.1)	121 (52.6)	2 (0.9)	<0.000	97 (42.2)	70 (30.4)	<0.05	**167 (72.6)**
12-14 years (n=138)	40 (29.2)	51 (37.2)	>0.05	42 (30.7)	48 (35)	1 (0.7)	<0.000	61 (44.5)	30 (21.9)	<0.001	**91 (66.4)**
Mumps virus											
4-6 years (n=156)	67 (42.9)	37 (23.7)	<0.01	31 (19.9)	28 (17.9)	45 (28.8)	>0.05	51 (32.7)	53 (34)	>0.05	**104 (66.7)**
7-11 years (n=233)	78 (34.1)	78 (34.1)	>0.05	43 (18.8)	111 (48.5)	2 (0.9)	<0.000	89 (38.9)	67 (29.3)	>0.05	**156 (68.1)**
12-14 years (n=138)	31 (22.6)	50 (36.5)	<0.05	41 (29.9)	40 (29.2)	-	>0.05	57 (41.6)	24 (17.5)	<0.000	**81 (59.1)**
Rubella											
4-6 years (n=156)	88 (56.4)	55 (35.3)	<0.01	36 (23.1)	37 (23.7)	70 (44.9)	<0.000	69 (44.2)	74 (47.4)	>0.05	**143 (91.7)**
7-11 years (n=233)	106 (46.3)	107 (46.7)	>0.05	57 (24.9)	154 (67.2)	2 (0.9)	<0.000	124 (54.1)	89 (38.9)	<0.05	**213 (93)**
12-14 years (n=138)	58 (42.3)	60 (43.8)	>0.05	54 (39.4)	64 (46.7)	-	>0.05	82 (59.9)	36 (26.3)	<0.000	**118 (86.1)**

Data are represented by number (%) to total number.

in Saudi Arabia dramatically declined after the establishment of national vaccine programme from 294/100,000 in the year 1978 to 48.1/100,000 in the year 1991.[13] This study revealed that measles vaccine coverage was approximately 99% of the recruited children. However, the overall seropositivity for measles antibodies was 71%, which was significantly elevated among vaccinated versus non-vaccinated children. It decreased by increasing the age of the vaccinated children. In non-vaccinated children, seropositivity against measles increased by age. In vaccinated children, we found significant elevation of seropositivity against measles antibodies in public school students and Saudi children compared to private school students, non-school attendants and non-Saudi children. This high IgG seronegativity in vaccinated population (28%) increased the risk of future outbreaks of measles.

Hegazy et al[14] reported that in Al-Qassim region, Saudi Arabia, 26.3% of vaccinated population developed measles, among which 79% were more than 5 years of age. They compared their results with other countries including the United Kingdom (57%), [15] the USA (25.3%), [16] Canada (66%) and (61%),[17] Tunisia (16%),[18] and Hong Kong (23.6%).[19] This could be explained either by primary vaccination failure attributed to persistence of maternal antibodies, impotent vaccine, improper vaccine storage and inappropriate administration techniques,[20] limitation of the efficacy of the vaccine for more than 12 years[21] or secondary vaccination failure, which might be due to other reasons; such as, lack of continuous antigenic stimulation, because of which life long immunity is not produced.[22] In order to decrease the number of susceptible individuals in the older age groups, a catch-up vaccination campaign covering persons aged 9 months to 18 years should be conducted.[23] Alternatively, the outbreaks of measles could be due to accumulated unvaccinated cases. Studies reported that 3% of children who received MMR vaccine at 12–18 months of age were seronegative after 4 years in the United Kingdom.[24] In Canada, Boulianne et al[25] reported that 3.6% and 12% of children vaccinated by different vaccine strains at 12–15 months of age were seronegative after 5–6 years.[25]

Data obtained from this study revealed that the overall percentage of seropositivity against mumps antibodies was 65%, which was significantly higher among vaccinated older children. In vaccinated children, the seropositivity rate increased significantly among public school attendants and Saudi children compared to others. Approximately 32% of the vaccinated children were seronegative and liable to outbreaks on school campus. Furthermore, if susceptible females are not vaccinated before marriage and if infection occurs early in gestation, they will be at risk of spontaneous abortion.[26] It had been reported that countries implemented a one-dose schedule at high coverage levels reported reductions in mumps incidence of ≥88%, while those who implemented a 2-dose, reported reductions in mumps incidence of ≥97%, and several countries reached the elimination target of <1 mumps case per 100,000 population.[7]

As observed by other studies,[28] this study showed faster antibody decay of mumps than that of measles. Relatively lower sero-prevalence against mumps was also observed in other countries,[29,30] and lower vaccine-induced immunity of the Rubini strain was suspected to be the reason for the lagging increment of immunity in preschool children.[29,30]

The Advisory Committee on Immunization Practice recommended a second MMR vaccine dose at the age of 4–6 years.[31] In the USA, administration of a second dose of MMR vaccine at 4–6 years reduced incidence of mumps and risk of infertility caused by disease in boys.[32]

Rubella serosurveys are useful particularly to determine the proportion of women of childbearing age who are susceptible to rubella. Variation in the age-specific seroprevalence of rubella between countries exist.[33] Considering the age-specific profiles of rubella seropositivity in some Latin American rural populations in the pre-vaccination era, rubella is predominantly a childhood disease in Brazil, Chile and Argentina with over 60% of seropositive subjects in the younger age group (5–9 years), while in other countries, like Panama and Trinidad, only approximately 10% of the children in the same age group were seropositive.[34]

We found high prevalence of seropositivity against rubella virus (90%), which was higher among vaccinated versus non-vaccinated students and decreased by increasing age of the students. In vaccinated children, the seropositivity rate increased significantly among public schools children versus private school children and those who did not attend school, and in Saudi versus non-Saudi children. In non-vaccinated children, percentage of seropositivity increased with increasing age of children.

Data concerning persistence of antibodies after rubella vaccination are somewhat variable, but the majority of studies seem to show maintenance of antibodies for at least 20 years.[35] Nevertheless, a second dose of rubella vaccine at 4–12 years of age is routinely recommended in many developed countries, primarily to immunize the few primary vaccine failures but secondarily to provide a booster to those whose titers have fallen to low levels.[36]

Childhood immunization poses a risk of an increase in susceptibility in women of childbearing age, with the potential of an increased number of cases of congenital rubella syndrome unless at least 80% coverage is achieved.[37]

In conclusion, the results obtained from this study suggested a good coverage of vaccination programme in school aged children in Jeddah, Saudi Arabia. High prevalence of seronegativity against measles and mumps antibodies was observed by increasing age suggesting the possibility of outbreak of these diseases in the future. It has been believed that natural infection confers lifelong immunity and vaccination also gives protection against measles transmission for a long time. However, vaccine induced immunity was significantly lower than naturally acquired immunity. Therefore, to avoid accumulation of non-immune individuals against measles and mumps, we recommend vaccination of susceptible children before and at school age. Also, vaccination of adolescents is recommended since the study demonstrated that 37% of vaccinated students aged 12-14 years were seronegative. Since the strategy of MMR vaccination has been changed in 2002. A large scale population surveys after 5 and 10 years should be made in order to measure the reduction of the incidence of measles, mumps and rubella after application of the new 2 dose MMR vaccination strategy.

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