

# Seroprevalence of mumps before inclusion of mumps vaccination in the Iranian Expanded Programme on Immunization

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معدّل الانتشار المصلي للنكاف قبل إدراج التلقيح ضده في البرنامج الإيراني الموسّع للتمنيع  
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**الخلاصة:** يستهدف البرنامج الموسّع للتمنيع في الوقت الراهن في إيران التلقيح ضد الحصبة والنكاف والحصبة الألمانية للأطفال في عمر 12 شهراً ثم في عمر يتراوح بين 4-6 سنوات. وقد أجرى الباحثون دراسة حول معدّل الانتشار المصلي الخاص بعمر معين لأضداد النكاف في الأطفال الذين تتراوح أعمارهم بين 3 و18 عاماً في شهر كرد، لتقرير مدى الحاجة إلى جرعات تلقيح معزّزة لتغطية الأطفال غير الممنّعين. وقد وجد الباحثون أن 19.8% من أصل 338 طفلاً كانوا سلبية المصل، وأن سلبية المصل الخاصة بعمر معين كانت 33.3% للفئة العمرية 7-11 عاماً و20.5% للفئة العمرية 12-14 عاماً و4.6% للفئة العمرية 15-18 عاماً. ويقترح الباحثون للحصول على مناعة السّرّب في السنوات الخمس القادمة أن يتم اختيار الأطفال الذين تتراوح أعمارهم بين 7 و11 عاماً، ممّن يدخلون مستوى المدارس التوجيهية، باعتبارهم المجموعة الرئيسية للتلقيح.

**ABSTRACT** The current target groups for measles, mumps and rubella vaccination in the Islamic Republic of Iran are children at 12 months and 4-6 years. A study of the age-specific seroprevalence of antibodies against mumps in children aged 3-18 years in Shahrekord aimed to establish the need for booster vaccinations to cover non-immune children. Of 338 children, 19.8% were seronegative. Age-specific seronegativity was 33.3%, 20.5% and 4.6% in age groups 7-11, 12-14 and 15-18 years respectively. To obtain herd immunity, we suggest that for the next 5 years children aged 7-11 years entering guidance school are selected as the main group for vaccination.

## Séroprévalence des oreillons avant l'intégration de la vaccination anti-ourlienne dans le programme élargi de vaccination iranien

**RÉSUMÉ** À l'heure actuelle, les groupes visés par la vaccination contre la rougeole, les oreillons et la rubéole en République islamique d'Iran sont les enfants âgés de 12 mois et ceux âgés de 4 à 6 ans. Une étude de la séroprévalence par âge des oreillons chez les enfants âgés de 3 à 18 ans a été menée à Shahrekord, dans le but de déterminer s'il y avait lieu de procéder à des vaccinations de rappel afin de protéger les enfants non immunisés. Sur 338 enfants, 19,8 % étaient séronégatifs. La séronégativité selon le critère de l'âge était respectivement de 33,3 %, 20,5 % et 4,6 % dans les groupes de sujets âgés de 7 à 11 ans, de 12 à 14 ans et de 15 à 18 ans. Pour obtenir une immunité collective, nous suggérons que pendant les 5 prochaines années, le principal groupe vacciné soit les enfants âgés de 7 à 11 ans, avant leur entrée dans le second degré.

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## Introduction

The selection of a target group for the Expanded Programme on Immunization (EPI) is important [1]. The proportion of individuals in a population with doubtful protection (unvaccinated, nonresponders and low responders after primary vaccination) affects the chances of immunity reaching the 95% threshold that is necessary for herd immunity [2]. The population with doubtful protection must be a target group for vaccination and this can only be established by seroprevalence studies. A serological prevalence survey carried out in Izmir, Turkey to determine the antibody status of a population aged 1–29 years against mumps infections reported that 20.1% were seronegative [3]. Previous studies carried out in Shiraz and Tehran in the Islamic Republic of Iran reported that 34.2% of the population of Shiraz and 82.3% of 5-year-olds and 29.4% of 10-year-olds in Tehran were seronegative [3,4]. On the basis of these results it can be seen there is a wide range of seronegativity among various age group which could affect the selection of a target group.

After March 2004, vaccination against mumps, measles and rubella (MMR) was included in the Iranian EPI. The target groups for MMR vaccination are children at 12 months and 4–6 years. There have been a limited number of studies determining the status of immunity against mumps in the Islamic Republic of Iran [4,5], and we believe that there is insufficient evidence to justify the selection of these target groups.

The main goal of this study was to establish the age-specific antibody seroprevalence against mumps in Iranian children aged 3–18 years. The other aims were to obtain a baseline level of seroprevalence for repeated surveillance of current vaccination in the years following vaccination (at least in the region of the study) and also to establish the

need for booster vaccinations to cover non-immune children. The seronegative group could be helpful to evaluate the efficacy of mumps vaccine (manufactured in the Islamic Republic of Iran) in future studies.

## Methods

This was a cross-sectional study conducted in 2004 in Shahrekord, the capital city of Chahar-Mahal and Bakhtiari province in the south-west of the Islamic Republic of Iran.

## Sample

The target group was children 3–18 years old. Based on limited previous studies [4,5], the estimated seronegativity of mumps among this population was 20%, and from this a sample size of 338 children was determined. In the Islamic Republic of Iran, about 100% of children aged 7–18 years old go to school and about 95% of those aged 3–6 years go to day care centres.

We obtained the sampling frame from a local educational organization which included 158 schools (primary schools, guidance schools and high schools) and 100 day care centres. Sampling was conducted by a 3-stage sampling method. In the first stage the total population of students was stratified according to day care centres, primary schools, guidance schools and high schools. Due to the lack of detailed previous prevalence studies on mumps, we used the probability proportional to size sampling technique, which means that samples were selected according to the proportion of children in each stratum. Each stratum included several clusters (educational units), and in the 2nd stage, clusters were randomly selected. We selected 7 schools from the primary schools, guidance schools and high schools (3 units for girls and 4 units for boys, except for guidance schools where 2 units

were selected for boys). In the last stage, in each cluster, samples were randomly selected from day care centres ( $n = 25$ , 9.2%), primary schools ( $n = 103$ , 30.5%), guidance schools ( $n = 151$ , 44.7%) and high schools ( $n = 59$ , 17.5%). There were 191 boys and 147 girls, male to female ratio 1.3:1.

### Data collection

Data collection was based on an interview questionnaire and serology testing.

The parents of selected children were given a formal invitation to attend the school where their consent to participation was obtained. We did not encounter any refusals and, with the cooperation of the manager of schools, all selected children participated in the study. The parents were interviewed by our coinvestigator (a general practitioner) to collect data such as age, sex, history of previous exposure to mumps cases, history of previous mumps involvement and vaccination against mumps (these last 3 items were recorded as self-reported). Mumps was defined as a swelling of the parotid gland which lasted for at least 5–7 days accompanied by fever and difficulty eating.

After filling in the questionnaire, 10 cm<sup>3</sup> of venous blood was taken from each child and centrifuged sera were frozen at  $-20^{\circ}\text{C}$ . At the end of blood sampling, all tests were carried out simultaneously. IgG was measured using mumps IgG (ELISA) kits and

instruments from Trinity Biotech Capita (Jamestown, United States of America). The quality control was done simultaneously with the measurement of samples. Based on the recommendation of the kit, negative and positive control numbers and the mean values were in an acceptable range. Based on the kit definition, the results were calculated as antigen–antibody ratios, and recorded as positive or negative.

Ethical approval for the study was obtained from the ethical committee of the University, and referred to the local educational organization for approval.

### Statistical analysis

Statistical analysis was performed using the chi-square test and *SPSS*, version 11.5.  $P$ -value  $< 0.05$  was considered statistically significant.

### Results

Overall seroprevalence was 80.2% and therefore 19.8% of children tested were sensitive to mumps infection (Table 1).

The sex-specific seroprevalence was 77.1% for females and 82.5% for males. Age-specific seroprevalence rose from 66.7% for age group 7–11 years (primary school) to 79.5% for age group 12–14 years (guidance school) for 95.4% at age group

Table 1 Age-specific seroprevalence of mumps IgG antibodies by sex and seropositivity

Age group (years)	Serological reaction					
	Positive		Negative		Total	
	No.	%	No.	%	No.	%
3–6	25	100.0	0	0.0	25	7.4
7–11	68	66.7	34	33.3	102	30.1
12–14	116	79.2	30	20.8	146	43.2
15–18	62	95.4	3	4.6	65	19.2
Total	271	80.2	67	19.8	338	100.0

$P < 0.05$ .

15–18 years (high school) (Table 1). The age group 3–6 years was 100% immune (Table 1). Using the chi-squared test, there was a significant difference between age and seroprevalence ( $P < 0.05$ ).

There was a past history of mumps reported in 259/338 children (76.6%). Serology confirmed this in 76.4% of these cases. There was no reported history of mumps in 79 children (23.4%). Nevertheless serology was positive in 92.4% of these cases (Table 2). Using the chi-squared test, there was a significant difference in the agreement between serology and reported past history of mumps ( $P < 0.05$ ).

There was reported past history of vaccination against mumps in 49 children (14.5%). The seroprevalence for mumps was significantly higher for vaccinated (42/49; 85.7%) than unvaccinated children (229/289; 79.2%) (Table 2). The chi-squared test showed a significant difference in the

rate of agreement between serology and reported history of vaccination ( $P < 0.05$ ).

There was reported past history of close contact with a case of mumps in 82/338 children (24.3%). Serology agreed with the past history of close contact in 86.6% of such cases for mumps. There was no such history in 256 children (75.7%). Serology was positive in 78.1% of such cases (Table 2). The chi-squared test showed no statistically significant difference in the rate of agreement between serology and reported past history of close contact with a mumps case.

## Discussion

Although MMR vaccination has been included in the Iranian EPI since March 2004, it is not clear why the present age groups (12 months and 4–6 years old) were selected for

**Table 2 Seroprevalence of mumps IgG antibodies by reported past history of mumps involvement, past history of mumps vaccination and past history of close contact with a mumps case**

Variable	Serological reaction					
	Positive		Negative		Total	
	No.	%	No.	%	No.	%
<i>Past history of mumps involvement</i>						
Positive history of mumps	198	76.4	61	23.5	259	76.6
Negative history of mumps	73	92.4	6	7.6	79	23.4
			$P < 0.05$			
<i>Past history of mumps vaccination</i>						
Vaccinated	42	85.7	7	14.3	49	14.5
Unvaccinated	229	79.2	60	20.8	289	85.5
			$P < 0.05$			
<i>Past history of close contact with mumps case</i>						
Positive history of contact	71	86.6	11	13.4	82	24.3
Negative history of contact	200	78.1	56	21.9	256	75.7
			$P < 0.05$			

mumps vaccination. One reason may be the convenience of the simultaneous administration of measles and rubella.

The method used in our study was ELISA testing, which was assumed to be suitable, specific and more sensitive than neutralization and complement-fixation [6]. A Dutch study also indicated that indirect ELISA is a reliable method for measuring mumps virus-specific antibodies in population-based studies [7].

Our study found a seronegativity rate of 19.8%, which is lower than the rates reported in previous Iranian studies (34.2% and 29.4%) [4,5], but similar to the rate reported in Izmir, Turkey (20.1%) [3]. However, wide discrepancies can occur: for example, another Turkish study reported a rate of only 10.9% [8].

The sex-specific rates in our study showed a significant difference in seronegativity between females and males (29.9% and 17.5% respectively). In a study in Shiraz, 31.4% of girls and 35.8% of boys tested seronegative for mumps antibodies [4]. The rate of seronegativity in another study was also higher in males than females [8]. Reasons for the higher rates of seronegativity in males in Shiraz are unclear, although there may be different levels of outdoor activity (e.g. boys spending more time outdoors than girls) or different levels of family crowding between the provinces.

In our study the age-specific seropositive rate rose rapidly from 66.7% at age 7–11 years to 79.2% at age 12–14 years and 95.4% at age 15–18 years.

A British study revealed that over 80% of children aged 1–2 years did not have antibodies to mumps and rubella [9]. This is in contrast to our findings that 100% of children aged 3–6 years had antibodies to mumps. This may be due to the level of public health action concerning communicable diseases. However, the seropositive rate

of 100% in day care centres may be over-reported due to local and seasonal outbreaks of mumps.

Among 8th grade students, in a Swiss study, 87% of the children tested seropositive for mumps-specific antibodies [10], similar to our findings. The prevalence of mumps IgG antibodies in a randomly selected population of children aged 1–17 years determined by ELISA showed that mumps antibodies were acquired at an early age [11]. The peak acquisition rate occurred at age 4–5 years; as in our study. In addition, the study showed that before age 15 years, 90% of children had antibodies to mumps [11], which is lower than our rate of 95.4%. A prevalence study of 333 students at Jordan University showed most of the students (93.7%) tested seropositive for mumps antibodies. Mumps occurred in all age groups in both sexes and the rate was higher in children aged 5–14 years than in adults [12]. This is in contrast to our results.

Our review of a number of previous studies carried out to detect the optimal age for vaccination showed conflicting results, suggesting that the findings depend on the age of the studied group [3,5,8,9,13,14]. For example, an Iranian study suggested that vaccination at age 1–5 years is most beneficial because 82.3% of subjects were seronegative [5]. Another study in India, indicated that, because children are at greatest risk of mumps by age 9 years, this age may be most beneficial for vaccination [13]. In addition a study carried out among infants up to 2 years of age concluded that MMR vaccination at 12 months instead of 15 months could reduce the pool of susceptible subjects in infancy [14]. A study in England on children aged 1–4 years suggested that vaccinating children early in the 2nd year of life is necessary to eliminate the 3 diseases [9]. A Turkish study in Ankara indicated the routine health supervision visit at age

11–12 years was the ideal time to immunize unvaccinated adolescents [8], whereas another study in Izmir suggested that age 1–10 years was the ideal time to immunize unvaccinated children [3].

We found a high non-immune status among children aged 7–14 years. These findings suggest that a large proportion of these children (20.5%–33.3%) are at risk in our population, and that mumps or MMR vaccination at this age may be most beneficial. We recommend that mumps immunization of these children is important until an EPI for mumps with high coverage can be sustained.

There was a reported past clinical history of mumps in 76.6% of children, confirmed serologically in 76.4%. This is similar to a previous study which suggests serology agreed with the clinical history of the subject in 82% of cases for mumps [15]. There was no clinical history of mumps in 23.4% of children, but serology was positive in 92.4% of these cases. This significant discrepancy may be due to several reasons, such as parents' poor memory, subclinical presentation of mumps or self-diagnosis and management. Similar to our study, another study showed that the frequency of seronegative subjects who were reported to have had the disease was low (< 8%) [14].

In one study, the reported rate of past history of mumps vaccination in students without antibodies was 85.0%, and in those with low-titre antibody students was 93.8% [16]. We found that the past history of mumps vaccination was reported at a rate of 14.5% and 85.7% were seropositive.

### Limitations of the study

There have been similar studies conducted in other provinces [3,4] and this is a regional study which cannot be generalized to the rest of the population of schoolchildren in

the Islamic Republic of Iran. This kind of study needs to be repeated with a larger, more extended sample size to obtain more reliable results. Another limitation of this study was determining the number of units in each stratum, so that for sampling we were obliged to use the method of probability proportional to size. If we had the prevalence rate for each stratum then it would be possible to compute the samples by stratum and this would result in a more exact sampling procedure.

### Conclusions

The Iranian EPI targets children at 12 months and 4–6 years old for MMR vaccination. However, based on the results of our study, and since a high seronegative rate may shift mumps infection to older ages, we believe mumps immunization of children aged 7–11 years entering guidance school is important and that for the next 5 years they must be selected as the main group for vaccination so that a national mumps vaccination programme with a high coverage can be sustained. The routine health supervision visit at ages 7–14 years is also an ideal time to immunize unvaccinated adolescents. This may increase the immunity to the 95% level necessary for herd immunity and elimination of the disease. After that time children less than 6 years old may be the only group needing mumps vaccination.

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