Rubella seroprevalence among first-grade primary school students in a district in Istanbul, Turkey

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Summary

Objectives Rubella vaccination is not included in the national immunization programme of Turkey. However, it is on the market and is recommended, mainly by the private sector, at the age of 12-15 months. Introduction of the rubella vaccine without achieving high coverage has the risk of shifting the mean age of rubella infection among the unvaccinated population to reproductive ages. The aim of this study was to evaluate the seroprevalence of rubella and the factors associated with seropositivity among primary school students in Umraniye, a district of Istanbul.

Methods: Blood samples were collected from 489 students in 70 primary schools of Umraniye. Parents completed a concise questionnaire assessing sociodemographic characteristics and measles, mumps and rubella vaccination status.

Results: Among the students screened, 163 (33.3%, 95% confidence intervals 29.2-37.7%) were susceptible to rubella. When sociodemographic variables were evaluated, paternal education was the only variable associated with seronegativity. As the level of paternal education increased, seronegativity rates decreased. This finding may suggest that rubella vaccination is practiced more commonly among children whose fathers are better educated.

Conclusions: Surveillance and control of rubella and congenital rubella syndrome must be set as public health priorities in Turkey, particularly given that rubella vaccination is practiced partially in the country.

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Introduction

Although rubella is a self-limited disease during childhood, its consequences when it occurs in the first 3 months of pregnancy are severe. It is estimated that more than 100 000 congenital
rubella cases occur each year worldwide. It also leads to miscarriage and fetal death. Two strategies are adopted towards the elimination of congenital rubella syndrome (CRS). The direct strategy involves the vaccination of adolescent girls and women of childbearing age, and the indirect strategy involves the vaccination of infants. Some countries adopt a combination of these two strategies.

The indirect strategy is important for the elimination of CRS, and has the additional advantage of controlling rubella infection during childhood. However, this approach should be adopted carefully because introduction of the rubella vaccine without achieving high coverage has the risk of shifting the mean age of rubella infection among the unvaccinated population to reproductive ages. This change in the epidemiological pattern can lead to an increase in the percentage of susceptible women of childbearing age and thus an increase in the incidence of CRS. Moreover, a neighbouring country, Greece, has experienced the consequences of this phenomenon. The inconsistent immunization policies adopted for 15 years in Greece caused a shift in the rubella infection age towards older age groups. The CRS epidemic that took place in 1993 was attributed to the inadequate immunization practices.

In Turkey, rubella and CRS have recently been included within the surveillance system and among the list of compulsory notifiable diseases. Although rubella vaccination is not included in the national immunization programme, the vaccine has been on the market since 1989 and (mainly) the private sector, which has been flourishing for the last two decades in Turkey, recommends and vaccinates children with the measles, mumps and rubella (MMR) vaccine at the age of 12–15 months. This vaccination practice may pose additional risks for CRS in some regions as there is no national policy concerning rubella vaccination or screening directed towards adolescents or women of reproductive age.

It is important to evaluate the seroprevalence and vaccination rates for different localities and subgroups. If some subgroups in the community have different MMR vaccination rates, the seroprevalence of rubella will vary between these subgroups. This may change the epidemiological pattern of the disease and will serve as a basis for a shift in the infection age. Hence, the objective of this study was to determine the seroprevalence of rubella among first-grade primary school students in Umranıye, a district of Istanbul. The main aim was to evaluate variations in seroprevalence for different subgroups such as parental education and socio-economic status.

Methods

Study area

Umranıye is the second most populated district among the 32 health districts of Istanbul (population of approximately 600 000) and it is located on the periphery of Istanbul. The region experiences migration from different parts of the country and is composed mainly of a socio-economically disadvantaged population. While more than 90% of its inhabitants are literate, the rate of higher education is lower than the average for both Turkey and Istanbul. The rate of unemployment is also quite high compared with Istanbul and Turkey. The rate of full immunization for compulsory vaccines in children under 1 year of age is higher compared with Turkey and Istanbul. The main characteristics of the district compared with Istanbul and Turkey are summarized in Table 1.

Umranıye was chosen as the research area as it is a good example of a district located in a metropolitan area with a higher proportion of socio-economically disadvantaged inhabitants than the city’s average. The Health Directorate of this administrative region is under the supervision of the Public Health Department, School of Medicine, Marmara University, and serves as the research and training area. Fifteen primary care centres, two maternal and child health and family planning clinics and one public hospital provide primary care.

| Table 1 Main characteristics of Umranıye compared with Istanbul and Turkey. |
|---------------------------------|-----------------|-----------------|-----------------|
| Total populationa | 67 million | 10 million | 605,855 |
| Literatea | 80.6% | 93.4% | 92.8% |
| Higher education ratea,b | 7.8% | 11.2% | 6.0% |
| Unemployment ratea | 7.2% | 12.7% | 16.4% |
| Fully immunized under 1 year of agec,d | 48% | 62.3% | 79.5% |

a Census of Population.3
b The higher education graduates include college, university, Masters and PhD graduates.
c Hacettepe University Institute of Population Studies.4
d Topuzoglu et al.5
and secondary level services in the area. There are also four private hospitals, 22 private outpatient clinics (group practice) and 55 private surgeries.

Subjects and sampling

There are 70 public primary schools with approximately 10,000 first-grade students in the district. The sample size of the study was calculated as 544 based on the 60% estimate of rubella immunity, with a margin of error of 0.04 and a confidence interval (CI) of 95%. The list of students was obtained from the District Directorate of the Ministry of Education, and systematic sampling was carried out among the first-grade students of 70 public primary schools. Public primary schools constitute 97% of this age group in Umraniye.6

Data collection

Written consent was obtained from the parents of the students. This survey was carried out within the routine health examination of first-grade students in collaboration with the District Health Directorate, District National Education Directorate and Department of Health Affairs of Istanbul Metropolitan Municipality. Students’ blood samples were collected at schools by a team of doctors and trained nurses during the first week of June 2003. Parents completed a concise questionnaire assessing sociodemographic characteristics and MMR vaccination status. For students who did not return the questionnaires, the school was contacted twice and the president or the vice president of the school was asked to send a reminder to the parents. In total, 489 students participated in the survey (89.9%) and provided blood samples. Of these, 475 returned their questionnaires (97.1%).

Blood samples were collected via vacutainers and transported to the laboratory of the district health centre on the same day. Cold chain principles were maintained while transporting the blood samples. In the laboratory, serum was extracted and the samples were sent to the National Measles/Rubella Laboratory, Refik Saydam National Hygiene Centre in Ankara. In the laboratory, immunoglobulin G (IgG) avidity values were obtained using the RADIM (RADIM Diagnostics, Rome, Italy) commercial enzyme immuno-assay kit. Sera were tested at a dilution of 1:300 and according to the manufacturer’s instructions. The results were expressed as net absorbance (A450) and calculated according to the formula given in the instructions.

Definitions

An IgG avidity percentage lower than 49% indicates seropositivity that has been acquired recently (up to 6 weeks), and an IgG avidity percentage above 60% indicates seropositivity acquired more than 3 months previously. Values in between were accepted as borderline values.7

When assessing the educational status of the parents, those who did not graduate from primary school (5 years), whether literate or illiterate, were grouped together with primary school graduates. Socio-economic status was evaluated by a scoring system composed of the profession of the father, the profession of the mother and the land value of the living area adapted from Kalaycioglu et al.8 MMR vaccination status was assessed by parental self report.

Statistical analysis

Data were analysed using SPSS Version 11.0. Chi-square and linear Chi-square tests were used in the univariate analysis. The strength of association was described by odds ratios (ORs) and 95% CIs. To assess the effects of independent variables by controlling the confounders, the multiple logistic regression procedure was used. The enter method was used for logistic regression analysis. Two-sided significance tests were used and P<0.05 was accepted as the level of statistical significance.

Results

The study group contained 489 students. Basic characteristics of the students are presented in Table 2. Two hundred and forty-two students (49.5%) were female and 247 (50.5%) were male. The age of the students ranged from 5.3 to 10.4 years, and the mean age was 6.7 ± 0.5 years. Among the participants, 55.1% were less than 7 years old, 41.0% were 7 years old and 3.9% were 8 years old or more.

One hundred and forty-one (29.7%) parents declared that their children had received the MMR vaccine, 122 (25.7%) were not vaccinated and the vaccination status was unknown for 212 (44.6%) students.

Among the students screened, 163 (33.3%, 95%CI 29.2-37.7%) were susceptible to rubella. Among the 326 seropositive students, 298 (91.4%) showed IgG concentrations indicating that immunity had been acquired more than 3 months previously, 22 (6.8%) showed IgG concentrations indicating that
immunity had been acquired in the previous 6 weeks, and six (1.8%) had borderline values.

Seronegativity of students was also assessed by the reported vaccination status. Among the students who were reported as vaccinated, unvaccinated and unknown, seronegativity rates were 31.2, 34 and 38.2%, respectively ($P<0.05$).

When sociodemographic variables were evaluated, paternal education was the only variable associated with seronegativity (Table 3). As the level of paternal education increased, seronegativity rates decreased in a linear trend. In the logistic regression analysis, when high school education or more was taken as the reference category, the OR for secondary school education was 1.85 (95%CI 0.85–4.06), compared with 2.40 (95%CI 1.21–4.77) for primary school education or less.

Although younger students had a higher rate of seronegativity compared with those aged 8 years or more, the difference was not statistically significant.

Discussion

This survey was limited to one district in Istanbul. Nevertheless, the study area is similar to localities that are situated on the borders of Istanbul, so the results of this study can provide an understanding of the epidemiology of rubella for comparable regions. This study revealed that the rubella seronegativity rate was 33.3% among first-grade primary school students living in Umraniye. The seronegativity rate determined in this study is similar to rates determined among unvaccinated populations, and is higher than rates observed among vaccinated populations for the corresponding age group.

Seroprevalence rates among vaccinated and unvaccinated students were similar in the present study. This may be due to recall bias because MMR vaccination status was evaluated by parental self-report. As children are vaccinated with MMR at the age of 12–15 months, there may be recall problems among the parents. A study of seroprevalence of tetanus vaccine in Turkey determined that vaccination history obtained from the parents was not reliable. Also, in Turkey, MMR is provided through pharmacies or private facilities. The vaccines, which are not included in the Expanded Program on Immunization, are mainly purchased from a pharmacy and transferred to the service level by the user. Cold chain principles may be interrupted during this transport, as cold boxes are not used and MMR is one of the most heat-sensitive vaccines.
A study conducted in one of the provinces of Turkey revealed that the temperature of 68.7% of pharmacy refrigerators was not within the recommended temperature interval.\textsuperscript{16}

When seroprevalence of rubella was investigated among different subgroups, an association was only found with parental education. As the level of paternal education improved, the seronegativity of rubella decreased with a linear trend. This finding may be a sign that MMR vaccination is practiced more commonly among the children with better-educated fathers.

Before conducting the study, the researchers hypothesized that rubella seronegativity rates would be lower for students with a higher socio-economic status as MMR was only provided in the private sector and it was not free of charge. Such an association was not detected. However, a previous study, conducted in the same region, determined an association between socio-economic status and history of receiving at least one private vaccine.\textsuperscript{5} This finding is not totally in contrast with the present study because, in the abovementioned study, the index used for socio-economic status also included paternal education. However, in the present study, parental occupations and land value of the living area for the economic status were used, and paternal education was evaluated as a separate independent variable.

In Turkey, studies show that paternal education is an important predictor for different childhood health conditions.\textsuperscript{15,17–19} A study assessing the variables associated with tetanus immunity among children in Turkey determined a significant relationship with paternal education, but not with socio-economic status. When illiterate fathers were taken as the reference category, the OR for seropositivity of tetanus was 2.1\textsuperscript{15} among children who had literate fathers. The association between paternal education and different child health conditions has been determined in various other studies performed in Turkey.\textsuperscript{17–19}

Some studies have determined an association between maternal education and child health status.\textsuperscript{20,21} However, the present study found no association between maternal education and rubella seroprevalence. This may be related to male dominance in decision-making, thus possibly determining the use of private health services.

This study found that students aged 8 years or more had lower rates of seronegativity compared with younger children. However, the difference was not statistically significant and this may be related to the small sample size. Also, a drawback of this study was related to the age group studied. As this study was only conducted among first-grade

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Seronegativity by the characteristics of students (univariate and multivariate analysis).</th>
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<tbody>
<tr>
<td>Characteristics of the students</td>
<td>% Seronegative</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>33.5</td>
</tr>
<tr>
<td>Male</td>
<td>33.2</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
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<tr>
<td>&lt;7</td>
<td>33.6</td>
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<tr>
<td>7</td>
<td>36.6</td>
</tr>
<tr>
<td>≥ 8</td>
<td>11.1</td>
</tr>
<tr>
<td>Maternal education</td>
<td></td>
</tr>
<tr>
<td>Primary school or less</td>
<td>33.0</td>
</tr>
<tr>
<td>Secondary school</td>
<td>41.5</td>
</tr>
<tr>
<td>High school or more</td>
<td>33.3</td>
</tr>
<tr>
<td>Paternal education</td>
<td></td>
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<tr>
<td>Primary school or less</td>
<td>37.1</td>
</tr>
<tr>
<td>Secondary school</td>
<td>30.8</td>
</tr>
<tr>
<td>High school or more</td>
<td>23.9</td>
</tr>
<tr>
<td>Economic status\textsuperscript{b}</td>
<td></td>
</tr>
<tr>
<td>Low economic status</td>
<td>36.8</td>
</tr>
<tr>
<td>Middle economic status</td>
<td>31.4</td>
</tr>
<tr>
<td>High economic status</td>
<td>30.7</td>
</tr>
</tbody>
</table>

\textsuperscript{a} \chi^2 for trend.
\textsuperscript{b} By working status of parents and land value of living area.
students, the researchers could not evaluate the seroprevalence rates for a wide range of age groups.

Live-attenuated rubella vaccine is provided by the private sector in Turkey. However, there is no national ongoing programme directed towards adolescent girls or women of reproductive age. Previous models have indicated that MMR vaccination in the private sector is expected to increase the rate of CRS for the first 20 years after starting vaccination. The highest increase is expected to occur in regions where at least 50% of the population use the private sector. The present study found a significant increase in seropositivity as the level of paternal education increased. This suggests differences in the use of MMR vaccines. At this point in time, a rubella vaccination policy is needed in order to avoid additional risks for increasing the number of CRS cases.

Surveillance and control of rubella and CRS must be set as public health priorities in Turkey, particularly given that rubella vaccination is practiced partially in the country. As rubella and CRS have recently been included in the list of notifiable infectious diseases, the burden of the disease is not known. Also, vaccine coverage is not monitored. In order to highlight the risks of partial coverage, research is needed to detect the epidemiological pattern differences for rubula and CRS between the areas with and without MMR vaccination. Subsequently, a cost-effective rubella and CRS control programme should be adopted.

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