Age-specific rubella seroprevalence in unvaccinated adolescents in Ankara, Turkey

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معدل الانتشار المصلي الخاص بعمر معيَّن للحصبة الألمانية لدى المراهقين غير الملقَّحين في أنقرة، تـركيا

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الخلاصـة: كان الهدف من هذه الدراسة التعرُّف على معدَّل الانتشار المصلي الخاص بعمر معيَّن للحصبة الألمانيـة مع عوامل الاختطار المرافقة للإيجابية المصلية للحصبة الألمانية بين المـراهقين غـير الملقحـين في أنقـرة، تـركيا، وهـي دراسة مستعرضة شملت 229 تلميذاً انتقاهم الباحثون بطُرُق جمع العينات المتطبَّقة في مدرستين ابتدائيتين ومدرستين ثانويتين، من حالة اجتماعية واقتصادية بين المنخفضة والمتوسطة. وقد بلغ معدَّل الانتشار المصلي الإجمالي 92.6٪، وكان هناك تـرابط يُعتَد به إحصائياً بين الإيجابية المصليَّة للحصبة الألمانيـة مـع العمـر ومـع سـوابق مـرض طفحـي. ووضع الباحثون توصيات بتلقيح جميع الأطفال في عمر سنة واحدة مع إرفاق ذلك بحملـة لمـرة واحـدة مـن تلقـيح المراهقات وصغار النسوة؛ لتقديم وقاية مستقبلية لمن يوشك الدخول في عمر الإنجاب.

ABSTRACT The purpose of this study was to determine the age-specific rubella seroprevalence and factors associated with rubella seropositivity in unvaccinated adolescents in Ankara, Turkey. In this cross-sectional study 229 students were selected with stratified sampling methods in 2 primary and 2 high schools of low to medium socioeconomic status. Overall rubella seroprevalence was 92.6%. There was a significant association of rubella seropositivity with age and history of exanthema disease. Recommendations are made for vaccination of all children at age 1 year, combined with a one-time campaign of vaccination of adolescent girls and young women to provide future protection for those who are about to enter the child-bearing age.

Séroprévalence par âge de la rubéole chez des adolescents non vaccinés d'Ankara (Turquie)
RÉSUMÉ L'objectif de cette étude était de déterminer la séroprévalence par âge de la rubéole et les facteurs associés à la séropositivité à la rubéole chez des adolescents non vaccinés d'Ankara (Turquie). Dans cette étude transversale, 229 élèves ont été sélectionnés, par des méthodes d'échantillonnage stratifié, dans deux écoles primaires et deux établissements d'enseignement secondaire d'un niveau socioéconomique faible à moyen. La séroprévalence globale de la rubéole était de 92,6 %. Il existait une association significative entre, d'une part, la séropositivité à la rubéole et d'autre part, l'âge et les antécédents d'exanthème. Des recommandations ont été faites en faveur de la vaccination de tous les enfants à l'âge d'un an, combinée à une campagne exceptionnelle de vaccination des adolescentes et des jeunes femmes destinée à protéger celles qui vont bientôt être en âge de procréer.

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Introduction

Rubella is a mild viral infection of childhood. However, if it is acquired during pregnancy it can cause abortion, stillbirth, premature delivery, low birth weight and a number of congenital anomalies such as cataract, heart disease, deafness, developmental disorders and microcephaly [1,2]. Since the beginning of rubella vaccination in 1969, the number of reported cases of rubella and congenital rubella syndrome (CRS) has decreased by over 99% in the United States [3]. After 30 years of rubella vaccination, particularly in the United States, Canada, the United Kingdom, the Nordic countries, Australia and Cuba, rubella and CRS were successfully eliminated [4]. But the global picture is very different, with only 28% of developing countries having routine vaccination against rubella [5–8]. Mathematical modelling has yielded global CRS burden estimates ranging from 110 000 to 308 000 cases per year [8].

In 1996, World Health Organization (WHO) recommendations encouraged all countries not routinely immunizing against rubella to consider universal rubella vaccination of children and ensure immunity of women of childbearing age. WHO reported that 78 out of 214 countries surveyed had a national rubella vaccination programme. Between 1996 and 1999, another 27 countries added rubella to their vaccination schedule [9,10]. In Turkey, since rubella is not a notifiable disease, there are no national data from routine surveillance systems, only limited regional data from epidemiological surveys about rubella and CRS. According to published studies in Turkey the age-specific rubella seroprevalence rate varies from 86.0% to 92.7% [11–15]. Many of these studies were conducted on selected hospital patients. Rubella vaccine is not included in the Turkish national immunization programme. However, in the private sector, the measles–mumps–rubella (MMR) vaccine has been used for 15-month-old children for about 15 years [16]. There are some concerns about rubella immunization of infants, since immunization interrupts the circulation of the virus in the community; hence rubella infection might shift to women of childbearing age and lead to CRS [1–4].

In countries such as Turkey where rubella vaccination is not applied routinely, it is important to know the seroprevalence in adolescents so that the need for vaccination can be evaluated. We therefore aimed to establish the age-specific rubella seroprevalence in adolescents in a semi-urban area.

Methods

The study was undertaken from January to September 2002.

Study population

In order to determine the rubella seroprevalence in an easily accessible population of unvaccinated adolescents, students were selected from primary and high schools. Schools were selected in a health directorate area that provides health services to a district in Ankara, the capital city of Turkey. This district is a semi-urban region of low or middle socioeconomic status. There were 23 primary health care centres in this region. The region's registered population in 2001 was 412 476 and 36.2% of the population was aged between 0 and 19 years. A total of 24.8% of the people had no access to health services provided by the government and 59.2% of the houses were shanty houses. A sample of 2 primary schools (years 6, 7 and 8) and 2 high schools were selected randomly from among 95 primary and 19 high schools [17]. These schools were from areas with different socioeconomic levels, containing both apartments and shanty houses.

Sample

The sample size was calculated from the expected rubella seroprevalence in this population; the numbers of pupils was 2249, the expected minimum rubella seroprevalence was taken as 80%, with a confidence level of 95%, giving an estimated minimum sample size of 240 pupils. To represent each school, students were selected by stratified sampling according to the classes and sex. The participation rate was 95.4% (229 students), with drop-outs due to illness, absenteeism and inadequate blood samples for laboratory examination.

The necessary permissions were taken from the University of Ankara School of Medicine ethics committee, the local authority, Ankara district national education managers and the health directorate prior to the start of the study.

Study design

This cross-sectional study was undertaken in 3 steps. The first step was inviting parents to schools through their class teachers. After receiving information about the study, parents signed informed consent forms for their child to participate in the study.

The second step was completion of the questionnaire forms by the research staff during the interview with parents at schools. The questionnaire collected data about some independent variables associated with rubella seroprevalence: age, sex, school, parent's education and work status, income, type of housing, number of persons per room, total number of brothers/sisters, number of household members, attendance at kindergarten, number of children who went to kindergarten or primary school and whether they had suffered an exanthema disease or rubella. After receiving informa-

tion about rubella symptoms, students were asked again if they had a history of rubella.

In the third step, a 5 mL sample of venous blood was collected from each student and sent to the University of Ankara Faculty of Medicine central laboratory within 2 hours where serological analysis was performed on the same day. The rubella-specific IgG antibody levels were determined by an enzyme-linked immunosorbent assay (ELISA) method (Biokit SA, Barcelona, Spain). Rubella-specific IgG antibody levels of 15 IU/mL or greater were considered positive (immune) [18,19].

After the serological analyses, students, parents and class teachers were informed about the results. Students susceptible to rubella were provided with the necessary information about rubella and vaccinated against the virus. During our study, it was observed that none of the study participants (students, parents, school managers or teachers) had prior knowledge about rubella and CRS. For this reason, a 20-minute seminar about rubella and CRS was delivered.

Statistical analysis

The dependent variable of the study was rubella seropositivity status. The interaction of dependent and independent variables was determined by uni- and multivariate analysis. Chi-squared and Fisher exact chi-squared tests were used in the univariate analysis. After univariate analysis, any statistically significant independent variables were included in the multivariate logistic regression analysis. Also, rubella-specific IgG antibody levels in 8 age groups were compared using 1-way ANOVA. A P-value < 0.05 was considered statistically significant.

Results

The overall rubella seroprevalence was 92.6% in this unvaccinated group of adolescents. There was no statistically significant difference between rubella immunity status and sex. The age-specific seroprevalence was 87.5% in the 10–11 years age group, 89.0% in the 12–14 years age group and 92.7% in the 15–17 years age groups. The rate of seropositivity increased with age, so that seropositivity rates in high-school students were statistically higher than in primary-school students.

The rubella immunity status of students according to exanthema disease and rubella history of children in their families is shown in Table 1. There were 75.5% of students who had a history of an exanthema disease and 89.0% a history of rubella. Of the students with no history of exanthema disease 83.9% had immunity to rubella. The rubella immunity level increased to 95.4% for students with a history of exanthema disease ($P < 0.01$). But no statistically association was found between rubella seroprevalence and history of rubella ($P > 0.05$).

Table 1 **Rubella immunity status of a sample of primary- and high-school students in Ankara, Turkey, by selected personal characteristics**

| Characteristic | Rubella immunity status | | | |
	Seropositive (immune) %	Seronegative (susceptible) %	Total No.	%[a]
Sex				
Male	93.8	6.2	113	49.3
Female	91.4	8.6	116	50.7
*Age group (years)**				
10–11	87.5	12.5	40	17.5
12–14	89.0	11.0	82	35.8
15–17	97.2	2.8	107	46.7
*School level**				
Primary	88.5	11.5	122	53.3
High	97.2	2.8	107	46.7
*Exanthema disease history***				
Present	95.4	4.6	173	75.5
Absent	83.9	16.1	56	24.5
Rubella history				
Present	96.1	3.9	154	89.0
Absent	89.5	10.5	19	11.0
*Sibling's exanthema disease history***				
Present	100.0	0.0	8	3.6
Absent	92.1	7.9	214	96.4
Total	92.6	7.4	229	100.0

*P < 0.05, **P < 0.01.
[a]Column percentage.

There was no significant association of rubella immunity status with some of the independent variables: parent's education and work status, income, type of housing, number of persons per room, total number of brothers/sisters, number of household members, attendance at kindergarten before primary school or number of children who attended kindergarten or primary school (Table 2) ($P > 0.05$).

As shown in Table 3, no statistical differences were found in student's rubella-specific IgG antibody levels by age.

Logistic regression analyses were performed after 1-way analysis. In this multivariate analysis, only age and exanthema disease history were taken as associated factors with rubella seropositivity. When the age group 15+ years was compared with the 10–12 age group, the rubella seropositivity rate was found to be 4 times higher (OR = 4.04; 95% CI: 0.89–18.24). In students who had a history of exanthema disease, rubella seropositivity was 3.8 times higher than the group who had no history of exanthema disease (OR = 3.80; 95% CI: 1.34–10.72). However, the same association was not observed for students who had a history of rubella.

Discussion

Rubella seroprevalence in this sample of 229 Ankara students aged 10–17 years was 92.6%, ranging from 87.5% in 10–12-year-olds to 97.2% in 15–17-year-olds. There was a statistically significant difference between age and the rate of seroprevalence. In logistic regression analysis, when the 15+ years group was compared to the 10–12 years age group, the rubella seropositivity was 4 times higher. In our country, previous studies have shown different results for rubella seroprevalence because of different study populations, age of participants, labo-

ratory methods, etc. In other studies the age-specific rubella seropositivity prevalence was 86.0% for the 15–29 years age group, 89.8% for 17–40 years, 92.5% for 12–18 years, and 92.7% for 17–40 years and 9–16 years age groups [11–15].

Therefore in this study a small proportion of students (7.4%) was found to be susceptible to rubella. Other studies conducted in rural areas of developing countries have estimated the prevalence to be 20% and above [6–8,11,20]. This is mainly due to the ease of circulation of the rubella virus in crowded urban populations compared with rural areas. This is an important finding for the susceptible group, especially susceptible women who might acquire rubella infection during pregnancy leading to CRS in their babies. Serological studies before rubella vaccination have shown that about 80%–90% of the adult population had immunity against rubella due to the natural pattern of infection worldwide [1,2]. However, seroprevalence was different in each country. In Brazil, seroprevalence was 80% in pregnant women [21] whereas seroprevalence at ages 18–20 years was 81% in France [22]. In Australia, seroprevalence was 82% before the vaccination campaign and 96% after vaccination [23].

For our students who had a history of exanthema disease, rubella seropositivity was 3.8 times higher than the group who had no history of exanthema disease. However the same association was not found for those who had a history of rubella. This could be due to the difficulty of diagnosing rubella, as approximately two-thirds of rubella infections are sub-clinical and non-specific and diagnosis is often unreliable [1,2]. Therefore, laboratory diagnosis of rubella is the most reliable method [24]. In one study of 288 pregnant women who had no rubella history, 88.6% of them were seropositive [25]. This problem with

Table 2 **Rubella immunity status of a sample of primary- and high-school students in Ankara, Turkey, by selected demographic characteristics**

Characteristic	Rubella immunity status				χ^2	*P*-value
	Seropositive (immune) %[a]	Seronegative (susceptible) %[a]	Total No.	%		
Father's education level					0.63	> 0.05
Primary school	92.7	7.3	109	47.6		
Secondary school	88.6	11.4	44	19.2		
High school	93.8	6.2	48	21.0		
University	96.4	3.6	28	12.2		
Father's job					6.08	> 0.05
Qualified civil servant	97.8	2.2	45	19.6		
Unqualified civil servant	96.2	3.8	26	11.4		
Skilled worker	94.0	6.0	67	29.3		
Tradesman	90.5	9.5	42	18.3		
Unemployed/unskilled worker	85.7	14.3	49	21.4		
Mother's education level					3.22	> 0.05
Illiterate	91.3	8.7	23	10.0		
Primary school	90.8	9.2	141	61.6		
Secondary school	100.0	0.0	29	12.7		
High school and university	94.4	5.6	36	15.7		
Mother's job					1.00	> 0.05
Housewife	91.9	8.1	197	86.0		
Working outside home	96.9	3.1	32	14.0		
Type of house					0.31	> 0.05
Shanty house	91.3	7.4	80	34.9		
Apartment	93.3	8.4	149	65.1		
Income					3.44	> 0.05
Low	86.5	13.5	37	16.2		
Middle	91.8	8.2	98	42.8		
High	95.7	4.3	94	41.0		
No. of household members					0.004	> 0.05
≤ 4	92.5	7.5	106	46.3		
> 4	92.7	7.3	123	53.7		
No. of persons per room					2.08	> 0.05
≤ 1	96.7	3.3	61	26.6		
> 1	91.1	8.9	168	73.4		
History of kindergarten before starting primary school					0.09	0.05
Yes	93.6	7.7	47	20.5		
No	92.3	6.4	182	79.5		
No. of children who went to kindergarten or primary school					0.002	> 0.05[b]
1+	92.5	7.5	120	52.4		
0	92.7	7.3	109	47.6		
Total	92.6	7.4	229	100.0		

[a]Row percentage.
[b]Fisher exact chi-squared test.

Table 3 **Distribution of rubella-specific immunoglobulin G (IgG) antibody levels in a sample of primary- and high-school students in Ankara, Turkey**

Age (years)	No. tested	Mean (SD) IgG levels (IU/mL)	95% CI
10	20	354.8 (214.8)	254.3–455.3
11	15	255.9 (199.8)	145.3–366.6
12	25	289.1 (179.7)	214.9–363.3
13	22	321.4 (179.6)	241.8–401.0
14	26	306.0 (179.0)	233.7–378.3
15	39	300.2 (217.7)	229.6–370.8
16	31	277.3 (209.4)	200.5–354.1
17	34	288.0 (222.7)	210.3–365.7
Total	212	298.5 (201.5)	271.2–325.8

$F = 0.43$; $P > 0.05$.
SD = standard deviation; CI = confidence interval.

establishing the history of rubella means that is it difficult to obtain reliable information about personal immunity status. In countries where routine rubella vaccination has not yet been introduced, rubella cases occur mainly in the 5–15 years age group. Primary rubella infection induces lifelong immunity [1,2]. In our study no significant difference was found in IgG antibody levels of students aged 10–17 years. Thus most of the rubella cases were observed before the age of 10 years. When these children are infected with rubella their mothers are at risk because many of them are still of reproductive age and may become pregnant.

WHO advises countries with greater than 80% measles immunization coverage among children to consider setting a rubella elimination goal together with measles elimination. Turkey has not yet incorporated rubella vaccine into the national immunization programme. In order to control both rubella and CRS, a combination strategy could be the most effective way in Turkey. Vaccination of all children at age 1 year, combined with a one-time campaign of vaccination of adolescent girls at approximately 11 to 14 years old and young women up to age 20 years to reduce rubella transmission and provide future protection for those who are about to enter childbearing age. Pregnant women should be excluded from rubella vaccination and women should avoid conception 3 months after vaccination [1,2,4]. By a combination of routine childhood vaccination and vaccination of adolescent girls and all susceptible women of childbearing age, cases of rubella and CRS could be minimized in Turkey.

Acknowledgements

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