

ONGOING RUBELLA OUTBREAK IN BOSNIA AND HERZEGOVINA, MARCH-JULY 2009 - PRELIMINARY REPORT

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Between 24 March and 31 July 2009, 342 clinically diagnosed cases of rubella were notified in five municipalities in Republika Srpska, Bosnia and Herzegovina. Eight cases were laboratory-confirmed by positive IgM against rubella virus*. Four virus isolates were obtained and identified as genotype 2B strains, with one isolate differing by a single mutation in the region of the E1 gene. This ongoing outbreak revealed gaps in the immunisation programme during the war in BiH (1992-1995) and highlights the need to revise legislation to permit immunisation of children above 14 years of age with measles, mumps, rubella (MMR) vaccine and to introduce supplemental immunisation activities.

Introduction

Rubella is a notifiable disease in Bosnia and Herzegovina (BiH; estimated population 3,9 million) and is reported on the basis of clinical symptoms. Rubella immunisation was introduced in the 1980s. In 1999-2000 a two-dose schedule with the measles, mumps, rubella (MMR) vaccine was implemented, with the first dose given at the age of 12 months (since 2008 at 11 months)

and the second dose at the age of seven years and no later than 14 years.

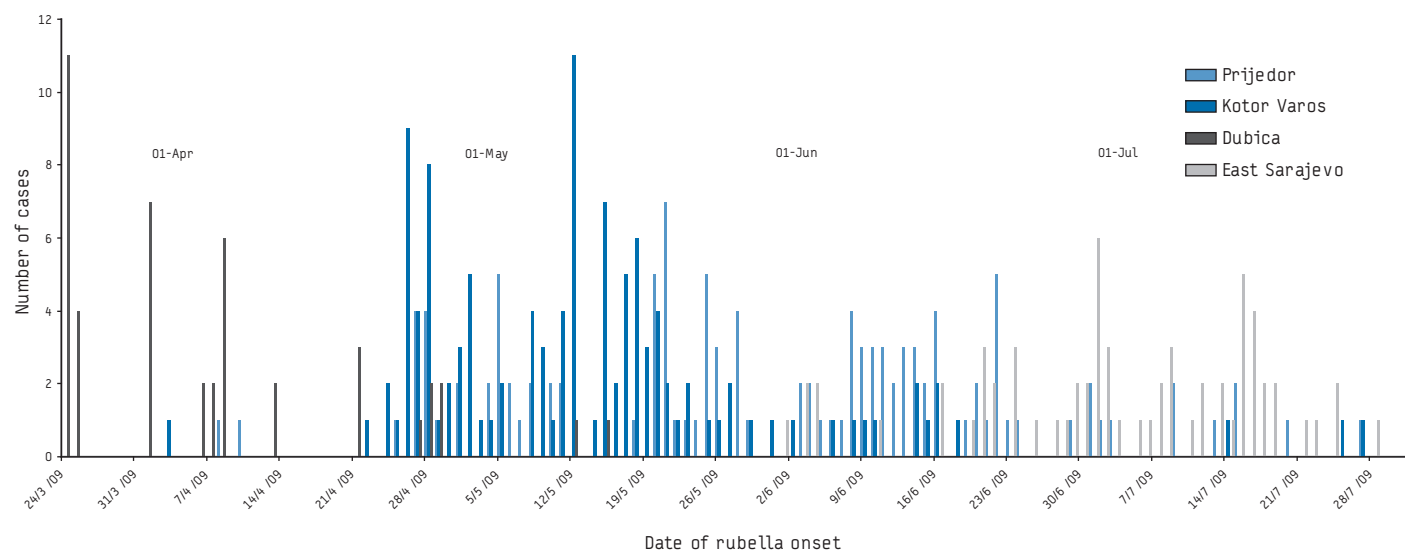
Between 24 March and 31 July 2009, 342 clinically diagnosed cases of rubella were notified in five municipalities in Republika Srpska (RS) which is one of two governing entities in BiH. At the time of publication of this report, the outbreak is ongoing, with ca. four cases per week. Epidemiological and laboratory investigation was started in early May 2009. Preliminary results are presented below.

Materials and methods

Serum samples were collected from 20 suspected rubella cases (six from Dubica, five from Kotor Varos, three from Prijedor, four from East Sarajevo-Pale and two from Trebinje). Throat swabs were obtained from the three patients from Prijedor and from two of the five patients from Kotor Varos. All sera were tested for IgM against measles and rubella and for rubella IgG (Dade Behring Enzygnost® immunoassays) at the Regional Reference Laboratory (RRL) of

FIGURE 1

Rubella cases, Bosnia and Herzegovina, 24 March - 31 July 2009 (n=342)



the World Health Organization Regional Office for Europe (WHO/Europe) in Luxembourg, and ten serum samples were also analysed for rubella IgM at the laboratory of the Public Health Institute of Republika Srpska (PHI RS). The throat swabs were used for PCR analysis as described previously [1] and for virus isolation [2]. Phylogenetic analysis based on the rubella virus E1 glycoprotein gene was done with MEGA [3] and sequences were compared to published sequences by BLAST.

Results

Outbreak profile

On 28 May 2009 the PHI RS declared a rubella outbreak in three municipalities in the Banja Luka Region: Prijedor, Dubica and Kotor Varos. Later, an outbreak occurred in the East Sarajevo region including the municipalities Pale and Sokolac. In addition, four suspected cases were reported in Banja Luka and eight in Dobojo.

In Dubica, 44 rubella cases were reported between 24 March and 15 May 2009 (Figure 1) on the basis of a clinical case definition, i.e. acute onset of generalised maculopapular rash, body temperature higher than 37.2 °C and arthralgia/arthritis, lymphadenopathy, or conjunctivitis. The outbreak in this area appears to be over. The index case was not identified.

In Kotor Varos, Prijedor and East Sarajevo, where the outbreaks are still ongoing, 117, 116 and 65 rubella cases, respectively, were reported until the end of July. The last case to date was reported on 15 September 2009 in Sokolac, East Sarajevo.

Forty-five percent of the cases were male. The age ranged from those born in 1971 to those born in 2007. Most cases (82%, n=282) were observed among teenagers born between 1990 and 1994 still attending high school (Figure 2): 66% (29/44) in Dubica, 90% (105/117) in Kotor Varos, all of them attending the same school, 87% (101/116) in Prijedor and 72% (47/65) in East Sarajevo.

In Prijedor only five of the notified rubella cases had received one dose of MMR, while all the other patients were not immunised. The vaccination status of the cases in Dubica, Kotor Varos and East Sarajevo is still under investigation.

Laboratory findings

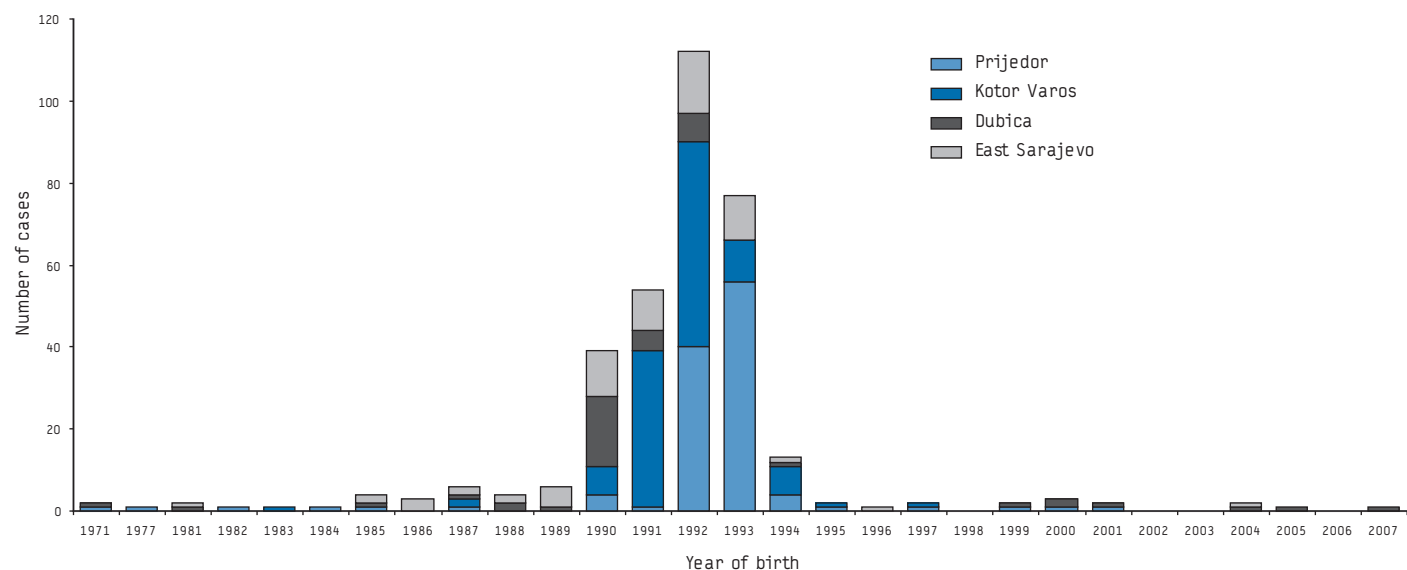
Eight samples were positive for rubella IgM, including three from Kotor Varos, one from Prijedor and four from East Sarajevo-Pale, confirming that the outbreaks in these regions were caused by rubella. Four sera were equivocal, and eight were IgM-negative for rubella (Table). There was a 100% concordance between the test results obtained at PHI RS and the Luxembourg RRL for the ten sera tested in both laboratories.

The rubella-positive samples were from seven 15-17 year-olds and from one 24 year-old. Five of them had received one dose of rubella vaccine, two were not vaccinated against rubella and for one patient no information on the vaccination status was available (Table). One rubella IgM-positive patient was negative for rubella IgG, while the other seven showed relatively low titres of rubella IgG (<77 IU/ml). In total 14 patients were positive for rubella IgG and six were negative. All 20 serum samples were negative for measles IgM.

Four of the five throat swabs were positive in the diagnostic PCR and for all four positives virus isolates were obtained. These samples were collected between one and four days after onset of rash from 16 or 17 year-olds of whom only one reported to have been vaccinated against rubella more than nine years ago. Of all four PCR-positive samples nearly complete E1 gene sequence data were obtained. Three of the sequences were identical and from Prijedor and the fourth showed one mutation at position 303 of the E1 gene and was from Kotor Varos. Phylogenetic analysis attributed the sequences to genotype 2B. According to a BLAST analysis, the most similar previously published sequence was an isolate obtained in the United States nine years ago (RVi/WA.USA/16.00, GenBank accession number AY968220) with a Kimura distance of more than 2%.

FIGURE 2

Rubella cases by year of birth, Bosnia and Herzegovina, 24 March - 31 July 2009 (n=342)



Discussion

This preliminary report describes a fairly large laboratory-confirmed outbreak of rubella affecting mainly unvaccinated or partially vaccinated 16-17 year-old school children in three contiguous municipalities and one distant region in RS. As the clinical diagnosis of rubella is unreliable, the real number of cases may be somewhat overestimated as for a few suspected cases there may have been different reasons for the symptoms observed. This may also explain why some of the sera tested negative for rubella IgM. On the other hand, several cases may have remained undetected due to a subclinical course of disease. No cases of rubella were diagnosed in BiH in 2008 nor in January and February 2009.

Due to lack of laboratory confirmation, the outbreak was recognised in the first community (Dubica) on 24 March 2009. The index case was not identified and therefore it is not clear when and from where the virus was introduced. As the most similar published sequence was found in the United States in 2000 and the genetic distance to that isolate was more than 2%, the origin of the virus remains obscure.

In early April 2009, the first cases were observed in two other municipalities, Kotor Varos and Prijedor, and in June in another two located 250-400 km away. In all of these areas, the epidemic is ongoing. Local epidemiologists speculate that the virus may have spread among teenagers during their stay in Mrakovica, Kozara mountain (56 km south from Dubica), which is a very popular place for regular school excursions in spring.

To date there is no information on occurrence of rubella in pregnant women or abortion in connection to the current rubella

outbreak. Due to the risk of congenital rubella infection during the first trimester of pregnancy, which can lead to miscarriage, stillbirth, or infants with birth defects, rubella is of high public health importance.

Before the war in 1990, coverage with MMR vaccine was 93.6% in BiH. Vaccine procurement and implementation of the immunisation programme were difficult during the war, and in the last two years of war, MMR vaccine coverage was only 56.8%. The age groups primarily affected in the current outbreak were born during the war and most of them were not even vaccinated with the first dose of MMR. Surveys done in RS in 1999 and in 2006 showed MMR vaccination coverage rates of only 54% and 79%, respectively, among 12-23 months-old children [4]. Annual statistics from PHI RS show varying vaccination coverage rates in recent years (2006: first dose 83%, second dose 83%, 2007: 92% and 93%, 2008: 78% and 52%), indicating that other age groups may also contain people at risk for infection.

As a result of the outbreaks, the Minister of Health and Social Welfare and the PHI RS have initiated immediate actions to improve the coverage with the second dose of MMR vaccine in children under the age of 14 years, and have alerted the Regional Public Health Institutes and primary health care providers of the emerging outbreak. An action plan to initiate supplementary immunisation of children and young adults with measles and rubella vaccine or rubella vaccine is presently being developed with support from WHO/Europe. The ongoing rubella outbreak also highlights the need for a revised legislation that permits MMR vaccination in children older than 14 years as well as the need to improve the surveillance of congenital rubella syndrome.

TABLE

Laboratory results, rubella outbreak in Bosnia and Herzegovina, 24 March - 31 July 2009 (n=20)

Patient	Vaccination status	Rubella virus IgM	Rubella virus IgG	PCR
1	not vaccinated	negative	negative	positive
2	not vaccinated	positive	positive	positive
3	not vaccinated	equivocal	negative	positive
4	1 dose	positive	negative	positive
5	1 dose	equivocal	negative	negative
6	1 dose	negative	negative	not done
7	1 dose	positive	positive	not done
8	1 dose	positive	positive	not done
9	1 dose	negative	positive	not done
10	no information	negative	negative	not done
11	1 dose	negative	positive	not done
12	1 dose	negative	positive	not done
13	1 dose	equivocal	positive	not done
14	1 dose	equivocal	positive	not done
15	not vaccinated	negative	positive	not done
16	not vaccinated	negative	positive	not done
17	no information	positive	positive	not done
18	1 dose	positive	positive	not done
19	not vaccinated	positive	positive	not done
20	vaccinated	positive	positive	not done

* Author's correction: On request of the authors, this sentence was corrected on 2 October 2009

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