Journal of Environmental and Occupational Science
www.jenvos.com
DOI: 10.5455/jeos.20170616084454

Original Research

Characteristics of rubella epidemic in Tuzla Canton

Mubidin Mujić[1], Semra Čavaljuga[2], Amer Čustović[3], Rahima Jahić[3], Sead Ahmetagić[3]

[1]Department of Hygiene and Epidemiology, Health Center Gračanica, Bosnia and Herzegovina, [2]Department of Epidemiology and Statistics, Faculty of Medicine University of Sarajevo, Bosnia and Herzegovina, [3]Department of Hygiene and Epidemiology,University Clinical Center Tuzla, Bosnia and Herzegovina

Address for correspondence: Amer Čustović, University Clinical Center Tuzla, Trnovac bb, 75000 Tuzla, Bosnia and Herzegovina. E-mail: amer.custovic@ukctuzla.ba

Received: March 20, 2016
Accepted: June 06, 2016
Published: July 01, 2017

ABSTRACT

Introduction: Rubella is an infectious disease of viral etiology. It occurs in two forms, as postnatal rubella and congenital rubella. **Objective:** The objective of this study is to assess the scope of the epidemic of rubella in Tuzla Canton (TK) in 2010, then the incidence of disease in certain segments of the population, spatial distribution, and movement in time. **Materials and Methods:** The target population of this retrospective study was people suffering from rubella in 2010 from the Tuzla Canton. **Results and Discussion:** From the topographical distribution of patients with rubella in Tuzla Canton, there is a strikingly large difference in the number of affected municipalities. Temporal distribution of patients with rubella is congruent with the epidemiological characteristics of rubella in terms of reporting the same. Gender structure of patients showed significantly higher numbers in males with 437 patients (67.33%), while for women there were 212 cases (32.67%). According to the age structure, the majority of the persons infected were aged 15-19, 470 of them which makes 72.5% of the total number of patients. When it comes to the vaccination status of patients, 3.7% was fully vaccinated (got 2 doses of vaccine), 7.6% was incompletely vaccinated (got one dose of vaccine), 66.4% was unvaccinated, and for 22.3% vaccine status is unknown. **Conclusion:** An outbreak of rubella in Tuzla Canton in 2010 and the emergence of a large number of people susceptible to rubella is a direct consequence of discontinuity of vaccination programs during the war from 1992 to 1995.

KEY WORDS: Epidemic, rubella, Tuzla Canton

INTRODUCTION

Rubella is an easy febrile rash-causing disease that medicine would not have dealt with a great deal if it did not have such a terrible teratogenic effects on the unborn child, when the mother becomes infected with rubella virus during pregnancy [1]. In 1938, Hiro and Tosaka confirmed viral etiology by causing a disease in children using the filtered nasal washings of people with acute illness. After widespread epidemic rubella in 1940, Norman Gregg, an Australian ophthalmologist, reported in 1941 on the occurrence of congenital cataracts among 78 children born to mothers who had caught rubella in early pregnancy. It was a 1st published recognition of congenital rubella syndrome (CRS) [2]. Infection of pregnant women during the 1st trimester of pregnancy can lead to infection of the embryo, its destruction or damage, i.e., embryopathy. Given the gravity of the consequences, this is a serious problem for the parents of sick children and a great burden for the community (social and medical significance of rubella) [3]. Rubella is an infectious disease of viral etiology. It occurs in two forms, as postnatal rubella, benign rash-causing infections in children and adults, and congenital rubella, a very serious disease of the fetus, which occurs as a result of primary infection in pregnant women [4]. Rubella the virus is an RNA virus and is classified as a sole member of the family Togaviridae, genus Rubivirus. It was first isolated in tissue culture in 1962 by Parkman and Weller. Under the electron microscope, it has approximately a spherical shape. It was built from the lipoprotein envelope 60 nm in diameter, which surrounds the nucleocapsid of 30 mm in diameter, which displays icosahedral symmetry and in which the protein helix and RNA are located. Structural proteins E1, E2 and C, and possibly some non-structural proteins participate in the processes of replication and transcription. E1 and E2 are transmembrane glycoproteins, and the capsid protein is C, which is surrounding the RNA [5]. Age is the most important determinant of the seriousness of rubella. Postnatally acquired rubella is usually a mild infection, as it is true for many viral diseases, children are prone to have a milder form of the disease than adults. In contrast, the fetus is at high risk for developing severe clinical symptoms of rubella, with serious consequences if infected transplacentally in early pregnancy due to maternal rubella [6,7]. The incubation period for rubella ranges from 12 to 23 days (average of 18 days). After initial viral replication in the epithelial cells of the mucosa of the upper respiratory tract, lymphatic spreading, and primary transient viremia, replication continues in lymphoreticular tissue. Secondary viremia starts 7-9 days after the onset of infection and it reaches its climax 10-17 days from the start of infection when usually clinical manifestation begins [8,9]. Transplacental infection of the fetus occurs during viremia. Fetal damage occurs due to the destruction of cells and mitotic arrest [2]. In the era before vaccination, rubella has occurred in the epidemics every 6-9 years and pandemics every 30 years. The last pandemic was in the period from 1961 to 1964. After 1964, in the countries, where it was introduced mandatory immunization against rubella, there was no large epidemic [8]. Nowadays, there are vulnerable populations with the risk of congenital rubella in underdeveloped countries and some isolated populations (e.g., some of the Island's population). CRS rates are highest in the World Health Organization African and South-East Asian regions where vaccine coverage is lowest. Vaccination against rubella is conducted in Bosnia and Herzegovina (BiH) from 1980, with the combined vaccine against measles, mumps and rubella (MMR). Before the war in the period from 1992 to 1995, coverage with MMR vaccine in BiH was 93.6%. Supply of vaccines and implementation of immunization program were difficult during the war. Age groups primarily affected were born during the war and most of them have not been vaccinated with the first dose of MMR. Schedule of two doses of MMR has been used discontinuously, and several postwar epidemics revealed gaps in immunization program during the war in BiH (1992-1995) [10]. In the postwar period, a single booster dose of vaccine against rubella was conducted in girls at the age of 14 with [11]. However, it was not carried out systematically filling the pockets of unvaccinated from the war period.

Epidemiology

The only natural reservoir and source of infection is an infected man, regardless of whether the infection is symptomatic or asymptomatic. Asymptomatic cases of rubella infection can be up to 50% [2,12]. Postnatal rubella is transmitted from an infected person to a healthy, sensitive person by aerogenic way or directly projecting droplets of an infected person's respiratory, or through contaminated objects. The infection is transmitted only in conditions of long-term and close contacts (family, preschool, and school) [8,3]. Sensitivity to rubella is general; most common in infants and preschool age. The degree of contagiousness with rubella is less than compared with measles, which is why the disease usually affects slightly older children, and the disease can occur in adults [13]. It was believed that people who have had measles or been vaccinated against rubella are protected for a lifetime from new infections. Today, it is known that reexposure may cause reinfection for such persons [14,15,16].

If re-infection occurs for the people who have had rubella, the virus replication in the epithelial cells of the upper respiratory tract is highly probable. Viremia comes but rarely, however, it is possible, and sometimes is clinically manifested by the appearance of the rash and arthritis. Re-exposure after vaccination leads to re-infection 10 times more frequently than after natural infection, some researchers reported it even in 80% of cases. In the vast majority of cases, rubella is asymptomatic and proven by serological testing. Viremia is extremely rare and even more rarely clinically manifested. Rubella usually occurs in late winter and early spring, with peak in March and April and a smaller number of cases also appeared sporadically throughout the year. Children aged 5-9 are mainly affected by it. In countries where vaccination is carried out, rubella is a rare disease. Sporadic cases occur in younger adults and fewer outbreaks in schools and military institutions where you can find a number of sensitive people together [8,4,17,18].

MATERIALS AND METHODS

The aim of the work is to assess the scope of the epidemic of rubella in the Tuzla Canton (TK) in 2010, to gain insight into the incidence of disease in certain segments of the population, spatial distribution and movement in time, and a number of other important characteristics such as age and sex of patients, immunization status with regard to rubella, and the involvement of pregnant women. This is to get to the answer to why there was a rubella epidemic in the Tuzla Canton in 2010, using the epidemiological scientific methodology, and display everything systematically to prevent similar events in the future.

Based on the objective set before us, there are following tasks to be done:

1. Collection and analysis of demographic data about the infected including the following variables: Age, sex, marital status, occupation, etc., that is to give an answer who was infected.
2. Collection and analysis of topographic data of the infected and compare infection frequency rate by municipalities; that is, to give an answer when the disease occurred.
3. Collection and analysis of chronological data considering the time the disease appeared, and how it behaves over time.
4. The collection and analysis of information on the vaccination status of patients with rubella, testing, hospital treatment, infected pregnant women, and occupation.

The Target Population and Methods

The target population of this study was the people diagnosed with rubella in 2010 from the Tuzla Canton who contacted their doctor and for which there was a written notification of an infectious disease, or for which there is a record of illness since the study was conducted retrospectively. For all registered people, a questionnaire for rubella was filled, which enabled obtaining the necessary information for processing this rubella epidemic. We were using the data of the Institute of Public Health of Tuzla Canton as a source of data on the number of people suffering from rubella, their age, sex, hospitalization, the municipality of residence, vaccination status, and other parameters.

The scientific methods used in the paper are:

1. Descriptive-epidemiological method and the case series study. This type of the study involves a group of people with a particular characteristic, which in this case is a diagnosis of rubella. Data are analyzed with respect to a person (who is sick), place (where the health disorder occurs), and time (when it happened or is happening).
2. Mathematical statistical methods (biostatistics), especially in the field of quantitative evaluation [19,20].

RESULTS

In the past decade before 2010, there has been one case of rubella registered or there were no reports of it at all. The calculated incidence rates of rubella are relatively low, with a high increase in 2010 [Figure 1].

Five municipalities with the highest number of people with rubella accounted for 85.5% of the total number of people infected, while other municipalities make up the remaining 14.5%. The largest number of people affected are registered in the area of municipality of Gradačac 159 (24.5%) and Gračanica 158 (24.4%). Tuzla, an administrative and health center of the Canton together with neighboring municipalities of Lukavac and Živinice was clearly less affected by the epidemic [Figures 2 and 3].

However, when calculating the incidence per 10,000 residents in 2010, then we see that it is the largest in the municipality of Banovići (54.3), then in Kladanj (41.4), Gradačac (34.4), while the lowest rates are in the municipalities of Tuzla (1.9), Lukavac (1.6), and Živinice (1.3) [Figure 4].

When it comes to time distribution of patients with rubella, in January, there were seven patients registered from the Municipality of Čelić. In February, there were 25 registered patients, and the largest number was in the municipality of Gradačac. The largest number of people affected was registered during March, with the largest number of patients in the municipalities of Gradačac (116) and Gračanica (94). In April, there was a slight drop in the number of patients (236). In May, there was a noticeably significant reduction in the number of patients (65), which is also expressed in the coming months ending in August [Table 1 and Figures 5 and 6].

Gender structure of patients in the epidemic of rubella in the Tuzla Canton in 2010 showed significantly higher rates in males with 437 patients (67.33%), while for female patients that number was 212 (32.67%) [Figure 7].

According to the age structure in most cases people aged between 15 and 19 were affected, 470 of them which makes 72.5% of total number of patients, of which male patients with a share of 70.6% in this age group, followed by 105 patients aged 20-29, or 16.2% of the total number, of which male patients with a share of 61.9% for this age group [Figure 8].

Table 1: Number of people infected with rubella in Tuzla Canton per months in 2010

Per months, 2010	January	February	March	April	May	June	July	August	Total
No. of infected	7	25	278	236	65	21	8	9	649
%	1,1	3,8	42,8	36,6	10,0	3,2	1,2	1,3	100%

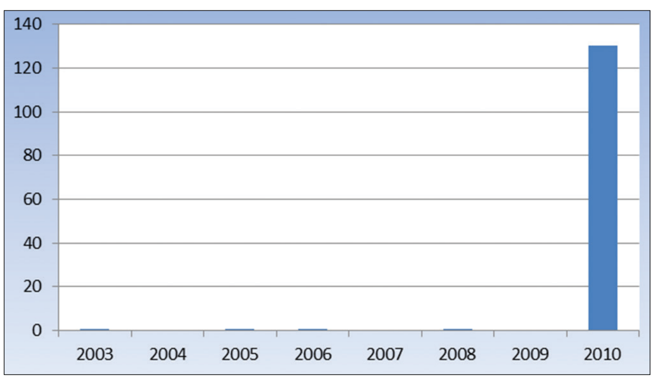

Figure 1: The incidence rates of rubella in the Tuzla Canton from 2003 to 2010 (1/100,000)

Figure 3: Dotted map of patients with rubella in the Tuzla Canton in 2010

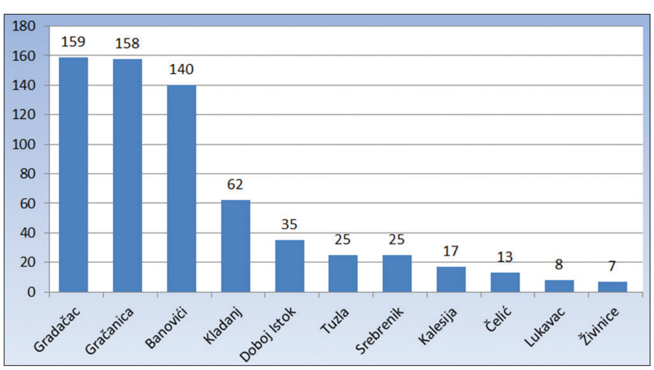

Figure 2: Number of people affected by rubella in the municipalities of Tuzla Canton in 2010

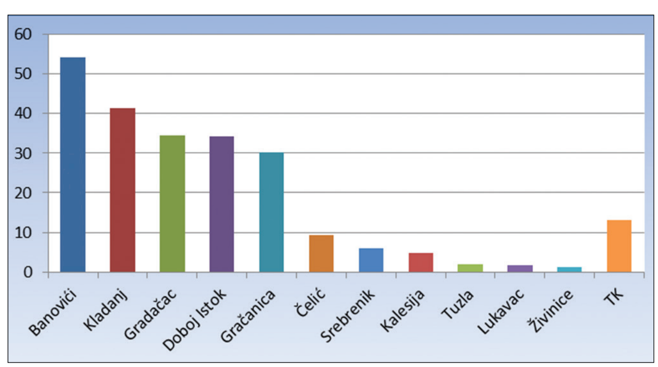

Figure 4: The incidence rates of rubella per 10,000 residents by municipalities in the Tuzla Canton in 2010

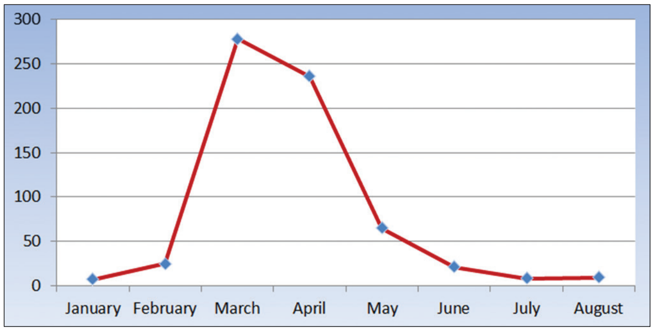

Figure 5: Time line for the number of patients with rubella in Tuzla Canton in 2010

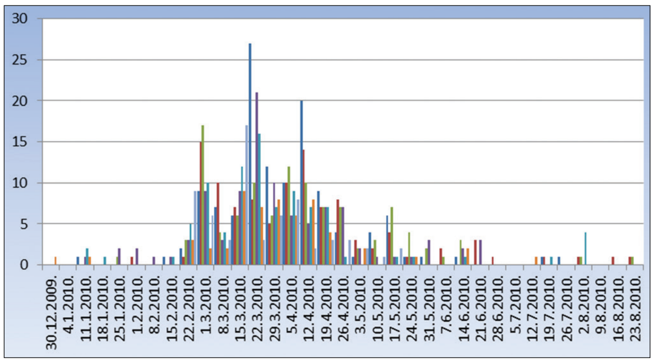

Figure 6: Epicurve of rubella outbreak, Tuzla Canton, Bosnia and Herzegovina, 2010

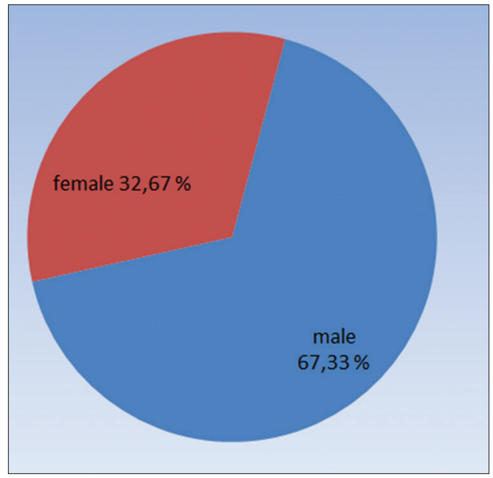

Figure 7: Gender structure of patients with rubella in Tuzla Canton in 2010

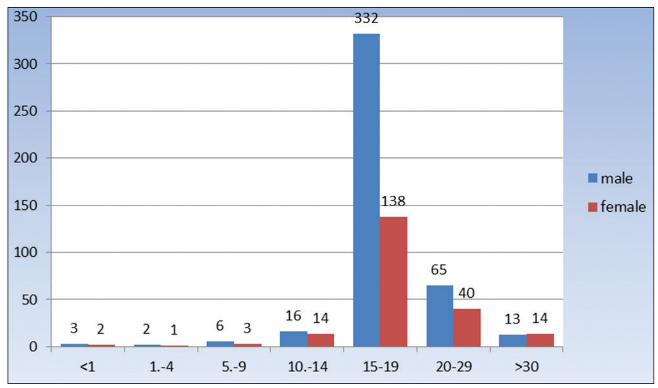

Figure 8: The gender and age structure of patients with rubella in TC in 2010

When it comes to the vaccination status of patients, 3.7% is fully vaccinated (got two doses of vaccine), 7.6% was incompletely vaccinated (got one dose of vaccine), 66.4% was unvaccinated, and for 22.3% vaccine status is unknown [Table 2].

Table 2: Vaccination status of people infected with rubella in Tuzla Canton in 2010

Vaccination status	Male	Female	Total	%
Vaccinated	11	13	24	3,7
Incompletely vaccinated	31	18	49	7,6
Unvaccinated	301	130	431	66,4
Unknown	94	51	145	22,3
Total	437	212	649	100

By serological testing, diagnosis of rubella was confirmed in 35 (5.4%) of reported patients, and for others, the diagnosis was based on clinical and epidemiological data, which indicates the insufficiency in the number of tested patients in this epidemic. According to data from the registries, 117 (18.03%) patients with rubella was sent to the hospital and 8 (1.23%) of them were hospitalized in the Clinic for Infectious Diseases in Tuzla. There were 3 pregnant women who were infected; one from the municipality of Gračanica, who continued her pregnancy, and two of them, who interrupted their pregnancies, from the municipalities of Banovići and Gradačac. These women were not vaccinated in the regular vaccination program.

DISCUSSION

This study shows how the decline in coverage of vaccination against rubella (in this case because of the destructive war) can and will lead to the emergence of the epidemic. 72.5% of patients were born during the war. Unfortunately, after the war, there were some difficulties in additional vaccination in this age group.

Considering the topographic distribution of patients with rubella in the Tuzla Canton, there can be noticed a strikingly large difference in the number of patients among municipalities. To make the data comparable incidence rates have been calculated that pointed to an even greater difference. Five marginal municipalities of the Canton account for 85.5% of cases and the highest incidence rates, while Tuzla as the administrative and health center with neighboring Lukavac and Živinice has the lowest incidence rate of rubella. These differences in the spatial distribution of patients among municipalities should be sought primarily in the dissimilar sensitivity of the population to rubella, which could be the result of unequal vaccination coverage because of the distance and the severe war conditions (1992-1995) in the peripheral municipalities of the Canton. There is a possibility that during the war some international organizations carried out the distribution of vaccines in the central municipalities, but there are no data available for this period. Time distribution of patients with rubella in the Tuzla Canton in 2010 coincides with the epidemiological characteristics of rubella in terms of season of occurrence with the largest number of people affected in March and April. By carefully observing the epidemical curve, it can be seen that the interval between the index case (30.12.2009) and the next patient was 12 days, which corresponds to the minimum incubation period for rubella. Sporadic cases are recorded up to 22.2.2010 when there is a higher frequency. Among these, three waves of illness were noticed; the first one on 3.3.2010 (17 patients), then in 19 days the second one on 22.3.2010 (27 patients), and the third wave 22 days after the second one on 12.4.2010 (20 patients), which gives the impression of an epidemic unfolding in the three major waves in March and April, each of which induced the next one. The progressive reduction in the number of patients was observed in the coming months ending with August when the last reported case was in the area of Kladanj.

In the Republic of Srpska (RS) (BiH), a year earlier, the epidemic has started on March 24 and the last case was reported on September 15, 2009, but the largest number of people affected was recorded in the springtime. In Sarajevo Canton, the epidemic lasted from February to July 2010 with the highest incidence of disease in April [21]. Studies in other countries which have not yet introduced rubella vaccine in routine immunization programs have shown widespread transmission of the virus. Studies from Nigeria, Kenya, and Ethiopia most affected were in March and April [22-24].

Gender the structure of patients in the epidemic of rubella in the Tuzla Canton in 2010 showed a significantly higher rate in males with 437 patients (67.33%), while for the female patients that number was 212 (32.67%). In a population that is partly vaccinated against rubella, such sex distribution cannot be taken as an argument for greater sensitivity of males to rubella but it is only a different immunization coverage. This difference is due to an earlier commitment to re-vaccinate female children in the age of 14 that was done by administering a single dose of vaccine against rubella [11]. In a study in Nigeria, there were no differences in morbidity between male and female; both groups had 50% of cases [23]. In Kenya, 54% of all cases were women [22]. In Ethiopia, 52.2% of confirmed cases were women [24]. In an outbreak of rubella in the Republic of Srpska (BiH) in 2009, there is a different sex ratio of patients with 55% of females and 45% of males. In three cantons in the Federation of (FBiH), males were present in slightly more than 2/3 compared to women. According to the age structure in most cases, the people affected were aged 15-19; 470 of them, which makes 72.5% of the total number of patients. The second most affected group is persons aged 20-29 years, accounting for 105 or 16.2% of all cases. There are 88.7% patients in these two age groups, whereas the remaining number is in other age groups. When analyzing what makes this age group 15-19 different from the others, we come to the realization that they were born from 1991 to 1995. This was the period of war, a struggle for survival when vaccines were of secondary importance so that the "war generation," mainly children, were not immunized against rubella. Furthermore, a significant part of the disease is those over 20 years old, accounting for 132 (20.3%) cases, which was caused because the majority of the population has been vaccinated, but not in sufficient number to prevent an epidemic, which resulted in displacements of disease in the older age group. In countries that do not implement vaccination against rubella, age involvement is different. In India, all the affected cases were under 20 years of age; attack rate was highest in the age group 11-20 years (median age 12 years) [25]. Study from Kenya recorded 32% of cases under 5 years and 80% were younger than 10 years [22]. While in Nigeria, the most patients were reported among children younger than 5 years (58.3%), followed by children aged 5-9 years (41.7%), while none were reported age ≥10 years [23]. In Ethiopia, the age of confirmed cases is from 1 month to 42 years, with a mean age of 7.3 years; Three-quarters of all confirmed cases were younger than 10 years [24]. When it comes to the vaccination status of patients, 3.7% is fully vaccinated (got two doses of vaccine), 7.6% was incompletely vaccinated (got one dose of vaccine), 66.4% is unvaccinated, and for 22.3% vaccine status is unknown. Unvaccinated and those for whom the vaccine status is unknown make the dominant group of 88.7%, which reveals the failure in the vaccination program and missed vaccinations during the war were not carried out afterward. In an outbreak in the Netherlands, there were 97% of nonvaccinated individuals of orthodox protestant denominations, with high load congenital disease [26]. The epidemic in the RS (BiH) showed that vast majority of patients were unvaccinated against rubella. The epidemic in the Sarajevo Canton showed that 98% were not vaccinated with MMR, 0.6% received one dose of MMR, and 1.2% had an unknown vaccination status. The results of the study in Brazil showed that gaps in the vaccination program can lead to CRS [27]. By serological testing, diagnosis of rubella was confirmed in 35 (5.4%) of reported patients, and for others, it was based on clinical and epidemiological data. Due to the low use of laboratory confirmation in the diagnosis, the real number of cases may be overestimated. On the other hand, some cases may remain undetected due to subclinical disease progression. A small number of laboratory confirmed cases of rubella were recorded in the RS, 8 out of 342 or 2.3%. The situation is better in the Sarajevo Canton with 16% of confirmed cases. Isolation of rubella virus genotype 2B was to be expected since the same genotype was isolated the year before (2009) in the epidemic in the RS (BiH). Since no measures were taken in the vaccination of the nonimmune, rubella was simply transferred from the RS to FBiH. Very similar genotypic sequence was isolated in 2000 in the United States, but the origin of the virus is still unclear. In BiH MMR vaccine is part of the regular immunization program for almost 40 years, there is also a surveillance system for CRS. This study pointed to the risks associated with gaps in coverage of rubella vaccine. For the elimination of rubella, it is necessary to achieve and maintain high vaccination coverage with two doses of vaccine (in BiH is used MMR vaccine) in all population groups. In the case of an outbreak, a rapid response is necessary and presented as a booster dose for children and young adults and efficient treatment of cases. High vaccination coverage is particularly evident in the case of war and natural disasters to prevent epidemics, as described in this study. Isolation and general measures have limited effects due to 50%

of asymptomatic cases of rubella and are contagious already in incubation period and easy transmission of the virus through droplets.

CONCLUSION

1. Epidemic of rubella in the Tuzla Canton in 2010 is a direct consequence of discontinuity of the vaccination program during the war from 1992 to 1995.
2. After the war, we missed opportunity to take comprehensive measures to cover gaps in the vaccination.
3. For the elimination of rubella, it is necessary to achieve and maintain high vaccination coverage with two doses of vaccine against rubella in all population groups.
4. In the case of an outbreak isolation and general measures have limited effects, and the most important measure is rapid response by booster dose of vaccine to all sensitive persons.
5. Public Health with the inevitable support of the competent authorities need to make further efforts in filling the gaps in immunization calendar, to prevent similar events in the future.
6. Programs of prevention, control and elimination of rubella and other diseases are required to contain a component that is connected to the health education of the population.

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Source of Support: Nil, Conflict of Interest: None declared.