ORIGINAL ARTICLE

Public health significance of immunization and epidemic occurrence of measles

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ABSTRACT

Aim To investigate epidemiological characteristics of the measles epidemic (risk factors and reasons for its emergence) in order to establish better control and prevention of future epidemics as well as to determine an influence of poor collective immunization of children against measles on appearance of epidemic disease.

Methods An open retrospective epidemiological study of measles infection was conducted during the epidemic in Zenica-Doboj Canton (ZDC) in the period 2014-2015. Disease reports, Disease Reporting Forms for measles and rubella cases and the Bulletin of the Institute for Health and Food Safety Zenica were used for data collection.

Results A total of 325 patients with the diagnosis of measles were registered, 262 (80.61%) in 2014 and 63 (19.39%) in 2015 resulting in overall incidence of 81.25/100.000. The majority of patients were aged 0-6 ($p < 0.05$). Of the total number of patients, only 13 (4.73%) were orderly vaccinated ($p < 0.05$). In the period 2009-2015 in ZDC 25.444 (83.34%) children ($p < 0.05$) were vaccinated with measles, mumps, rubella (MMR) vaccine.

Conclusion Results of the study show that the low level of vaccination of children continues to a risk of the emergence of epidemics of measles and other infectious diseases. Therefore, in order to prevent the disease there is a need for a better vaccination campaign.

Key words: measles, children, vaccination, Bosnia and Herzegovina

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INTRODUCTION

Despite the fact that infectious diseases are mostly under control they are still of special public health significance and their suppression is not possible without an adequate system of epidemiological surveillance. One of the most important measures for the primary prevention of infectious diseases is immunoprophylaxis (1). Massive and regular implementation of the vaccination program creates preconditions for the complete eradication of certain infectious diseases (1). In order to reach collective immunity at least 90% of children should be vaccinated (2).

Measles are a highly contagious (96%) infectious disease among all viruses. Humans are the only virus reservoir. For the maintenance of virus in the circulation, larger groups of people and intense communication among them are needed. Natural immunity to disease does not exist either in a single race or in a nation (3). Overdose of measles leaves permanent immunity, which is transmitted ba mother transmits to her baby protecting the baby for 6-9 months (1). In countries where the vaccination is regularly conducted, the incidence of the disease has dropped significantly (2). Occasional occurrence of minor epidemics is the consequence of the emergence of a sufficient number of non-vaccinated individuals, unsuccessfully vaccinated or those whose protective level of the antibody after the vaccination dropped critically. During 2001 the CDC recorded 116 cases, which mainly belong to the imported measles (4). The World Health Organization (WHO) estimates that due to non-vaccination against measles annually over one million children die worldwide due to complications (5).

Globally, there are still about 20 million cases of measles and they are the leading cause of mortality among young children (2). Although there has been a change in the occurrence of measles in Europe, epidemics could occur every 4 to 5 years in all environments that did not achieve the vaccination of children over 95% (5). As Croatia has had mandatory immunization against measles since 1968, the number of patients has been significantly reduced. In the pre-vaccination period, there used to be more than 20 000 patients per year - in 1993 only 87 cases were recorded (6).

Children younger than two years of age are more likely to be infected or their infection is complicated, especially if they are malnourished. Complications are common and caused by the action of the virus itself or associated infections. Measles belong to the diseases that create anergy, so patients are easily exposed to secondary infections, especially tuberculosis (1,2). Complications occur depending on age, body defences, type of epidemic and isolation conditions. Most commonly complications occur on the respiratory tract (2). Bacterial complications are severe and today they are less commonly seen and successfully treated with antibiotics. Neurological complications occur more often in relation to other rashes and manifest in the form of acute or chronic encephalitis (7). The virus has significant neurotropism, which does not always have to be expressed. Encephalitis (parainfectious) occurs several days after the outbreak of rash, usually between the third and the seventh day from eruption. Ethiopathogenesis is the same as in post-vaccination encephalitis and is probably an allergic genesis (7). It has a serious prognosis, mortality of about 10-30% and sequelae in about 40-55% of patients (8). Subacute sclerosing panencephalitis (SSPE) is one of the slow diseases as it develops for 10 years and more after measles in children under 2 years of age. By introducing the vaccine, the number of SSPE cases is 10 times smaller. The prognosis of the disease is poor with fatal termination within three years (9).

The WHO approved the use of vaccine in 1963, and since 1994 revaccination with a combined measles, mumps, rubella (MMR) vaccine has been carried out (10). Protective antibodies are produced with the vaccine in 85% of children at the age of 9 months, in 95% of children at the age of 12 months, and even 98% in children vaccinated at the age of 15 months (11). Post-vaccine reactions are possible after eight days and reminiscent of mitigated measles (12). Although encephalitis, encephalopathy, Guillain-Barre syndrome and cerebral ataxia are associated and described, it is difficult to determine whether these events are causally related to the vaccine (13). The occurrence of SSPE in vaccinated children is 1/1 million and in natural infection 5-10/1 million children with measles (14).

The aim of this study was to investigate epidemiological characteristics of the measles epidemic (risk factors and reasons for its emergence) in order to establish its better control and prevention of future epidemics. The second aim was to determine an influence of poor collective immu-

nization of children against measles on the appearance of the disease outbreak.

PATIENTS AND METHODS

Patients and study design

An open retrospective epidemiological study was conducted during the measles epidemic in Zenica-Doboj Canton (ZDC), Bosnia and Herzegovina (B&H), in the period 2014-2015.

All patients suffering from measles and treated as outpatients or inpatients at the Department of Infectious Diseases of the Cantonal Hospital in Zenica were involved in the study. This Department provides healthcare for 400.000 inhabitants of ZDC (including Zenica and 11 other municipalities). Inclusion criteria were: diagnosis of measles (clinical, serological or laboratory), both sexes and all age groups. Exclusion criteria were: lack of relevant information about patients or incorrect and illegible survey forms.

Methods

Cross-sectional study was used as a method of epidemiological research. The following was used for data collection: measles notification forms (as a part of official notification of infectious diseases form), official data on the number and movement of measles in ZDC in the period 2014 to 2015, i. e. Bulletins of the Institute for Health and Food Safety Zenica, Department of Epidemiology, and the forms for investigation of measles and rubella cases issued by the Federal Institute of Public Health (15). The last form is used in all cantons of the Federation of Bosnia and Herzegovina (FB&H) and is regularly delivered by Healthcare Centres to the Institute for Health and Food Safety Zenica. Except demographic data the form contains epidemiological (number of appearances, incidence, vaccination status) and clinical data (complications, death) for patients. The recommendation of the Federal Institute for Public Health at the beginning of the measles epidemic was to obtain a confirmation of the diagnosis by ELISA (IgG and IgM) for at least 5-10 cases associated with the epidemic.

Statistical analysis

Statistical significance (gender, age, complications, incidence and vaccination status) was tested with T-test and attribute characteristics with χ^2 test. The selected statistical significance level of $p<0.05$ was used.

RESULTS

The measles epidemic started in Zenica-Doboj Canton in 2014 and ended in 2015 involving 325 persons (262/80.61% in 2014 and 63/19.39% in 2015) with incidence of 81.25/100.000. The first two cases of measles were reported in March 2014 in the municipalities of Visoko (one) and Zenica (one), in April there were seven and in May 34 cases. The largest number occurred in November 2014 (57 cases). The last case was reported in November 2015 in Visoko municipality.

Majority of the involved population was aged 0-6 years, 145 (44.61%) ($p <0.05$), of whom 58 (40.00%) were females and 87 (60.00%) males ($p >0.05$) (Table 1).

Table 1. Distribution of patients involved in the 2014-2015 measles epidemic in Zenica-Doboj Canton

Age	No (%) of patients	
	Females	Males
0-6	58 (40.00)	87 (60.00)
7-14	45 (56.25)	35 (43.75)
15-24	36 (64.28)	20 (35.72)
25-49	25 (64.10)	14 (35.90)
50-64	3 (60.00)	2 (40.00)
Total	167 (51.38)	158 (48.62)

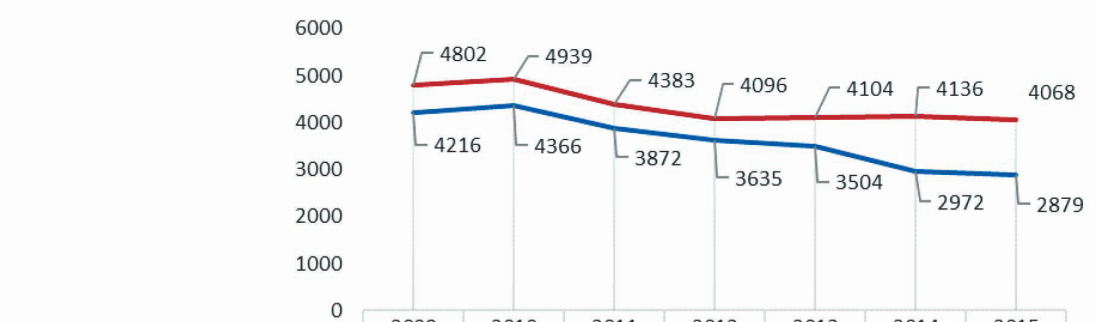
Data on vaccination of patients were obtained for 275 patients, of whom 13 (4.73%) were vaccinated ($p <0.05$), six (46.15%) females and seven (53.85%) males ($p >0.05$). Nine (3.27%) patients were incompletely vaccinated and 188 (68.36%) were not vaccinated. Data was not obtained for 65 (23.64%) patients (Table 2).

Table 2. Vaccination status of 275 measles patients in the period 2014-2015 by gender and age

	No (%) of patients			
	Vaccinated	Incompletely vaccinated	Non-vaccinated	Unknown
Age				
0-6	8 (61.54)	0	120 (63.83)	6 (9.23)
7-14	1 (7.69)	5 (55.56)	44 (23.40)	11 (16.92)
15-24	3 (23.08)	4 (44.44)	15 (7.98)	23 (35.38)
25-49	1 (7.69)	0	9 (4.79)	25 (38.47)
Total	13 (4.73)	9 (3.27)	188 (68.36)	65 (23.64)
Gender				
Males	7 (53.85)	3 (33.33)	89 (47.34)	46 (70.77)
Females	6 (46.15)	6 (66.64)	99 (52.66)	19 (29.23)
Total	13 (4.73)	9 (3.37)	188 (68.36)	65 (23.64)

The odds ratio (OR) was 76.4 between unvaccinated and vaccinated children in the age group 0-6 years.

The planned number of children to receive first measles, mumps, rubella (MMR) doses in Zenica-Doboj Canton in the period 2009-2015 was 30.528 in total, of whom 25.444 (83.34%) were vaccinated with one dose and 5.084 (16.66%) ($p <0.05$) were not vaccinated (Figure 1).



	2009	2010	2011	2012	2013	2014	2015
Vaccinated of 1 doze MMR 2009/15	4216	4366	3872	3635	3504	2972	2879
Planned to vaccinated of 1 doze MMR	4802	4939	4383	4096	4104	4136	4068

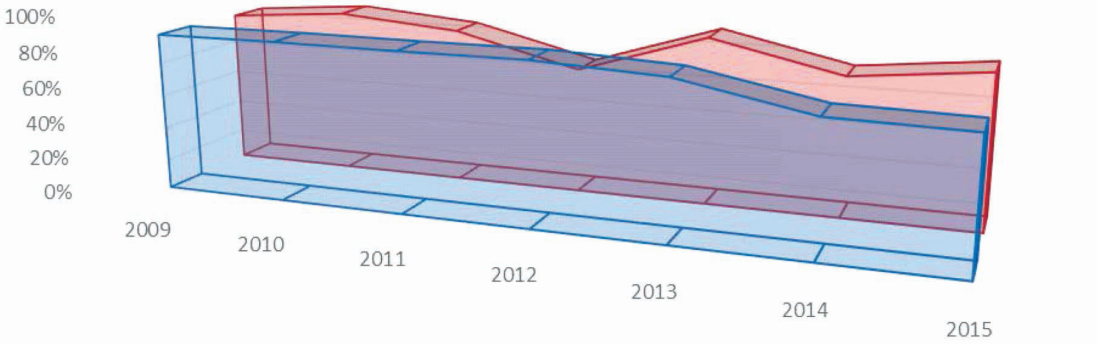
Figure 1. Number of planned and vaccinated children for the first measles, mumps, rubella (MMR) dose in Zenica-Doboj Canton in the period 2009-2015

The planned number of children for MMR re-vaccination in the period 2009-2015 was 30.982, of whom 26.926 (86.91%) were revaccinated ($p < 0.05$) (Figure 2).

The first dose and revaccination rate with MMR of the target groups (children under 6 years of age) and other age groups in Zenica-Doboj Canton in the period 2009-2015 were low (Figure 3).

	2009	2010	2011	2012	2013	2014	2015
Revaccinated of MMR 2009/15	4130	5118	3495	3577	3722	3346	3538
Planned to revaccinated of MMR 2009/15	4749	5546	4041	3998	4049	4378	4221

Figure 2. Planned and revaccinated with measles, mumps, rubella (MMR) in Zenica-Doboj Canton in the period 2009-2015



	2009	2010	2011	2012	2013	2014	2015
First doze of MMR	87,80%	88,40%	88,30%	88,70%	85,40%	71,90%	70,80%
Revaccinated of MMR	87%	92,30%	86,60%	69,50%	91,90%	76,40%	83,80%

Figure 3. First doses and revaccination rate with measles, mumps, rubella (MMR) of target (1-6 years) and other age groups in Zenica-Doboj Canton in the period 2009-2015

Complications of the disease were recorded in 66 (24.00%) patients. The most common were diarrhoea (49/17.81%) and pneumonia (14/5.10%). Complications more frequently appeared in non-vaccinated ($p > 0.05$) and at the age 0-6 years ($p > 0.05$). Neurological complications have not been recorded (data not shown).

DISCUSSION

This study has described measles epidemic during the period 2014-2015 in Zenica-Doboj Canton involving 325 patients and resulting in incidence of 81.25/100.000 population. From the beginning of 2014 until the end of 2015 a total of 5,103 (out of 103,904 infectious diseases/4.91%) patients with measles were registered in the Federation of Bosnia and Herzegovina (FB&H) resulting in incidence of 146.5/100.000 population in 2014 and 71.75/100.000 in 2015 (16). The most affected canton was Central Bosnia Canton (CBC) with incidence of 501.68/100.000 population (16). According to the definition of the World Health Organization, FB&H has become the country of endemic transmission of measles (17). Despite the significant efforts of the WHO to eradicate measles by 2015, this was not successful. In 2013 measles occurred in as many as 38 of 50 European countries with 31.520 patients (3,4). Five leading countries with the highest numbers of reported cases in 2013 inluded Georgia (7.830), Germany (1.703), Italy (2.216), the Netherlands (2.499) and Romania (1.094). The highest incidence per million inhabitants in 2013 was recorded in Georgia and the Netherlands (5).

The first cases of measles were reported in March 2014, while the most cases were noticed in November 2014 (57 cases) and in May 2015 (21 cases) resulting in incidence of 14.25/100.000 and 5.25/100.000, respectively. The highest number of patients in FB&H for the same period was recorded in May 2015 (575) with incidence of 261.36/100.000.

Highest number of infected patients during measles epidemic in the FB&H was found in Central Bosnia Canton (1.270) and the municipality of Bugojno (398) and in Tuzla Canton (1.035), with the majority of cases in the municipality of Lukavac (403) (16). In Montenegro seven cases were registered at the end of 2014, another six in January and February 2015 and four cases of suspected measles; the majority of registered patients in 2015 were in Kotor municipality (5), followed by Podgorica (2) and one in Herceg Novi and Nikšić. In the period 2010-2011 an epidemic of measles was reported in the Roma community of Brestovac (municipality of Leskovac, Republic of Serbia) (17).

During the 2014-2015 epidemic described in this study majority of patients were in the age of 0-6. Of the total number of patients, 4.73% were orderly vaccinated and the others were not. The largest number of patients in FB&H as a whole was aged 15-19 (16).

The number of children in the target group for vaccination (under 6 years of age) in ZDC in the period 2009-2015 was 30.528. In this period the rate of vaccinated children (83.34%) in ZDC was higher than non-vaccinated (16.66%) children ($p < 0.05$) with measles, mumps, rubella (MMR) vaccine, but this percentage was not sufficient to create collective immunity (2). Taking into account the fact that children aged 0-6 were the age group most involved in the epidemic as well as in this target group for vaccination, the results of this study showed that unvaccinated persons developed the disease more often and the risk of disease was about 76 times higher in children who were not vaccinated. In the Netherlands, despite the high percentage of vaccinated children with the first dose reaching up to 95% for the past 20 years, the measles epidemic in 2013 to 2014 has emerged only among the population of Protestants with a low vaccination prevalence of children (18).

In B&H children have been vaccinated against measles since 1971. Due to good coverage of vaccination, there were no major measles epidemics in this region. Only sporadic cases of the disease were reported in cases of children who missed the vaccination. During the war 1992-1995 other activities had priority in healthcare, and less attention was paid to diseases prevention. That was also largely related to the Implementation of Compulsory Immunization Program. This program was hardly implemented; sometimes it was completely interrupted due to the lack of vaccines supply and the inability of adequate maintenance of the cold chain. Due to these problems, a large number of children in B&H remained unvaccinated (18). Vaccination against measles has resulted in a decline in mor-

tality among children in the world to even 79% in the period 2000-2015. It is estimated that in this period vaccination prevented 20.3 million deaths in whole of the world (19). In 2015, about 85% of the world's population of children received one dose of vaccine against measles. Therefore, it is one of the most commonly used vaccines in public health (20). Immunization is definitely one of the greatest achievements of the 20th century, which, along with the safe drinking water supply and the discovery of antibiotics, has led to a significant reduction in the disease and deaths from infectious diseases. Therefore, in order to prevent the disease, there is a need for a better vaccination campaign (21,22).

In conclusion, the results of this study show that the low level of vaccination of children continues to pose a threat to the emergence of epidemics of measles and other infectious diseases. Therefore, in order to prevent the disease, there is a need for a better vaccination campaign. Vaccination against measles is effective, cost-effective and safe.

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TRANSPARENCY DECLARATION

Conflict of interest: None to declare.

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