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IMMUNIZATION OF CHILDREN USING VACCINE AGAINST MORBILE, MUMPS AND RUBELLA, IN TUZLA CANTON: FIVE YEARS REVIEW

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IMMUNIZATION OF CHILDREN USING VACCINE AGAINST MORBILE, MUMPS AND RUBELLA, IN TUZLA CANTON: FIVE YEARS REVIEW

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Introduction: Vaccines are biological preparations that allow the formation of anti-bodies in the human body, while preparing the immune system to fight infection. The goal of vaccination is to produce enough antibodies to provide long-term protection against the disease. Currently, there is a growing trend in the world of non-vaccination of children, and therefore a drop in coverage below the expected 95%. This trend is mostly related to the vaccine against measles,mumps and rubella (MMR). The decline is noticeable throughout BiH, as well as in the countries of the region and the European Union. Method: The main objective of the study is to determine the percentage coverage of the target group with two doses of MMR vaccine per year and municipalities in the Tuzla Canton (TC). The survey is retrospective in nature and covers the period from 01.01.2013. until 31.12.2017. The target group is children from 5 to 6 years of age.

Results: The overall coverage rate of the target group with two doses of MMR vaccine in the TC area by years is 82.0% (2013), 83.7% (2014), 78.8% (2015), 73.0% (2016) and 67.2% (2017). So, from the coverage of 82.0% achieved in 2013, the rate is constantly declining and reaching the value of 67.2% in 2017, which is 14.8% lower. Research shows that the coverage of MMR vaccine in the area of TC is not satisfactory, and the most critical municipalities are Lukavac, Banovici, Sapna, Tuzla, Gracanica and Kalesija.

Conclusion: The key strategic directions for prevention are maintaining a high coverage rate (≥ 95%) with two doses of MMR vaccine, then creating conditions for vaccination in unvaccinated or under-vaccinated population groups, and strengthening surveillance systems and increasing the availability of information for to the general public on the benefits of MMR immunization. The decline in the quality of the population's collective immunity against certain infectious diseases greatly threatens the recurrence of sporadic or epidemic outbreaks.

Keywords: immunization, MMR vaccine, prevention

INTRODUCTION

Immunization is the process of achieving resistance to certain diseases, and the most common means of achieving this result is through vaccination. According to the World Health Organization (WHO) definition, a vaccine is a biological preparation of attenuated or dead microorganisms; their toxins or surface proteins, which improves immunity to a particular disease, stimulating the immune system to recognize germs as a foreign body, and to destroy and "remember" them, in order to more easily identify and destroy microorganisms in the event of their subsequent appearance [1]. The views that immunization is one of the greatest medical achievements of modern civilization are widespread. Apart from the introduction of vaccination and the provision of clean water, no other intervention has had such an effective effect on reducing child mortality [2]. Immunization is a very cost-effective investment and widely available to the most vulnerable population groups, which has a significant impact in reducing costs in the healthcare system [2, 3].Mandatory immunization of certain age groups in Bosnia and Herzegovina (BiH) it implies, above all, children according to an established calendar, and at an age when they are most susceptible to infectious diseases, and when there is a greatest risk of complications or death. Delaying the immunization carries an increased risk of the child suffering from a disease against which they have not received the vaccine, which is why it is never recommended to deviate from the immunization calendar unless there are contraindications. BiH is among the countries in which the coverage of children with MMR vaccine has been steadily declining year by year, and with its decline the chances of epidemic proportions of measles, rubella and mumps increase.

Epidemiology of measles

Prior to the onset of measles vaccination in 1963, major measles outbreaks occurred in the world every 2 to 3 years, killing 2.6 million people annually [4]. Morbili had a seasonal nature, so epidemics in developed countries and temperate climates erupted in late winter and early spring, which coincided with the beginning of the school year, while in tropical climates they erupted during periods of drought, which corresponds to the annual migration of farmers in affected countries.

The epidemiology of rubella

The rubella is transmitted by droplet, or in direct contact with the secretion of the nose and throat of the infected person. Over 100,000 children with congenital rubella syndrome (KRS) are born each year worldwide, and especially in countries where women of generative age do not have good immunity. Before vaccination was introduced, the incidence rate was up to 4 per 1,000 live births. Out of 38,847 rubella patients in the European Union in 2013, 99% were in Poland, 88% of which were unvaccinated or vaccination status unknown. In 2013, 49 children were born with KRS. Poland recorded the highest number of diseased patients in 2016 as well [5]. In the United States, in 1964 and 1965, the rubella epidemic affected 12.5 million people and caused over 11,000 stillbirths, 8.000 newborns with hearing impairment, 1.800 mentally retarded and 20.000 cases of KRS [6]. Countries where vaccination is consistently performed have only sporadic cases of the disease. In the Federation of BiH, rubella is rare, and according to the data of the Institute of Public Health of the Federation of BiH (FBiH Health Insurance Institute), only 1 case was reported in 2017 [7]. Prevention is performed by an MMR vaccine containing a live attenuated RA27 / 3 strain of Rubella virus. The efficacy is extremely high, and developed immunity is assumed to be lifelong [8].

Epidemiology of mumps

Worldwide, mumps appear endemic throughout the year. Most often, children between the ages of five and ten are affected. The number of outbreaks has decreased significantly since the start of mandatory immunization. However, it is most likely that the virus is maintained in the unvaccinated person, thus re-developing the disease. In the Federation of BiH, mumps is the second most common vaccine-preventable disease with a morbidity rate of 3.90 / 100,000 and in 2016, 86 cases of parotitis were reported [9]. Disease prevention is carried out with the use of two doses of the combined MMR vaccine, in the 1st year of life and in the 1st grade of primary school [8].

METHODS AND MATERIAL

The following research objectives are defined:

1. Determine the percentage coverage of the target group with two doses of MMR vaccine per year in the TC area;
2. Determine the percentage coverage of the target group with two doses of MMR vaccine by municipalities in the area of TC;

The survey is retrospective in nature and covers the period from 01.01.2013. until 31.12.2017. The target group is children aged 5 to 6 years of age. Children of other age groups / nonimmunized according to the immunization calendar from the Tuzla Canton area, as well as measles patients from the area of TC who reported to the doctor and for whom a report of infectious diseases was written, or for which there is a record of the disease, were also analyzed in the study. As the basic medical documentation, statistical data of the Institute of Public Health of TC on planned primary vaccination and revaccination of children were used, as well as the actual number of vaccinated and revaccinated children in the period from 01.01.2013 to 31.12.2017. As a source of data on the number of people with measles and their age, sex, municipality of residence, immunization status and other parameters, data from the Public Health Institute of Tuzla Canton is used. In addition to the aforementioned, the survey used data from measles patients from the Report of a person suffering from an infectious disease in the period from 01.01.2013. until 31.12.2017. who have permanent residence in the Tuzla Canton. The reports of persons suffering from measles were recorded in the infectious diseases book of the hygienically epidemiologic services of the health centers in the municipalities and submitted to the Institute for Public Health of the Tuzla Canton. The data on the affected persons are sorted by: years of disease, age of patient, sex, place of residence and immunization status. Standard descriptive statistics procedures were used for the statistical processing of data and their presentation. The statistical hypotheses were tested using the Hi-square test and the Student T test of proportions with a significance level of 5%. Excel, IBM SPSS Statistics and Epi Info were used for this purpose.

RESULTS

Overview of MMR vaccine coverage by target group, by years and municipalities of Tuzla Canton in cohort group.

2013	Number	548	3867	4415
	% year	12,4%	87,6%	100,0%
	%MRP coverage	15,2%	22,6%	21,3%
2014	Number	490	3801	4291
	% year	11,4%	88,6%	100,0%
	% MRP coverage	13,6%	22,2%	20,7%
2015	Number	471	3538	4009
	% year	11,7%	88,3%	100,0%
	% MRP coverage	13,1%	20,6%	19,3%
2016	Number	910	3059	3969
	% year	22,9%	77,1%	100,0%
	% MRP coverage	25,3%	17,8%	19,1%

Table 1: MMR vaccine coverage in cohort group by year

			MMR coverage		TOTAL
			Difference in number of		
			planned	Vaccinated	
YEAR	2017	Number	1175	2879	4054
		% year	29,0%	71,0%	100,0%
		% MRP coverage	32,7%	16,8%	19,5%

TOTAL	Number	3594	17144	20738
	% year	17,3%	82,7%	100,0%
	% MRP coverage	100,0%	100,0%	100,0%

Table 2: Hi-square test on the association between MMR vaccination in the cohort group by year

Chi-Square Tests				
	Value	df	(2-Asymp. sided)	Sig.
	Pearson Chi-Square	737.427[a]	4	,000
	Likelihood Ratio	707,584	4	,000
	N of Valid Cases	20738		

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 687.85.

Based on the analysis of MMR coverage of the target group in the cohort group, by age, we conclude that in the cohort group the number of patients vaccinated differs significantly by year ($\chi2$ = 737,427, df = 4, p <0.001, table value $\chi2$ = 18,467) . In terms of age, the number of vaccinations in the cohort group has been declining since 2016, and there is an increasing difference from the number of planned vaccinations.

2013	Number	813	3703	4516
	% year	18,0%	82,0%	100,0%
	% MMR coverage	15,8%	21,5%	20,2%
2014	Number	737	3779	4516
	% year	16,3%	83,7%	100,0%
	% MMR coverage	14,3%	21,9%	20,2%
2015	Number	974	3619	4593
	% year	21,2%	78,8%	100,0%
	% MMR coverage	19,0%	21,0%	20,5%
2016	Number	1193	3218	4411
	% year	27,0%	73,0%	100,0%
	% MMR coverage	23,2%	18,7%	19,7%

Table 3: MMR revaccin coverage in cohort group by year

			MMR coverage		TOTAL
			Difference in number of planned	Vaccinated	
YEAR 2017	Number	1421	2910	4331	
	% year	32,8%	67,2%	100,0%	
	% MMR coverage	27,7%	16,9%	19,4%	
TOTAL	Number	5138	17229	22367	
	% year	23,0%	77,0%	100,0%	
	% MMR coverage	100,0%	100,0%	100,0%	

Table 4: Hi-square test on the association between MMR revaccination in the cohort group by year

Chi-Square Tests				
		Value	df	Asymp. Sig. (2-sided)
	Pearson Chi-Square	462.333a	4	,000
	Likelihood Ratio	454,597	4	,000
	N of Valid Cases	22367		

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 994.89.

Based on the analysis of the coverage of the target group with MMR revaccin, in the cohort group, and observed by years, we conclude that in the cohort group the number of revaccinated patients was statistically significantly different by years ($\chi2$ = 462,333, df = 4, p <0.001, table value $\chi2$ = 18,467). The number of revaccinated patients in the cohort group has been declining since 2015, and in 2017 only 67% of the realized revaccinations can be observed.

BANOVICI	Number	337	996	1333
	% municipality	25,3%	74,7%	100,0%
	% MMR coverage	7,7%	5,8%	6,2%
ČELIĆ	Number	40	346	386
	% municipality	10,4%	89,6%	100,0%
	% MMR coverage	,9%	2,0%	1,8%
DOBOJ ISTOK	Number	17	517	534
	% municipality	3,2%	96,8%	100,0%
	% MMR coverage	,4%	3,0%	2,5%
GRAČANICA	Number	396	2156	2552
	% municipality	15,5%	84,5%	100,0%
	% MMR coverage	9,1%	12,6%	11,9%

Table 5: MMR vaccine coverage by cohort group by municipality

			MMR coverage		TOTAL
			Difference in number of planned	Vaccinated	
MUNICIPALITY	GRADAČAC	Number	135	1791	1926
		% municipality	7,0%	93,0%	100,0%
		% MMR coverage	3,1%	10,4%	9,0%
	KALESIJA	Number	356	1315	1671
		% municipality	21,3%	78,7%	100,0%
		% MMR coverage	8,1%	7,7%	7,8%
	KLADANJ	Number	173	325	498
		% municipality	34,7%	65,3%	100,0%
		% MMR coverage	4,0%	1,9%	2,3%
	LUKAVAC	Number	823	921	1744
		% municipality	47,2%	52,8%	100,0%
		% MMR coverage	18,8%	5,4%	8,1%
	SAPNA	Number	68	332	400
		% municipality	17,0%	83,0%	100,0%
		% MMR coverage	1,6%	1,9%	1,9%
	SREBRENIK	Number	102	1858	1960
		% municipality	5,2%	94,8%	100,0%
		% MMR coverage	2,3%	10,8%	9,1%
	TEOČAK	Number	77	220	297
		% municipality	25,9%	74,1%	100,0%
		% MMR coverage	1,8%	1,3%	1,4%
	TUZLA	Number	1265	3872	5137
		% municipality	24,6%	75,4%	100,0%
		% MMR coverage	28,9%	22,6%	23,9%
	ŽIVINICE	Number	584	2495	3079
		% municipality	19,0%	81,0%	100,0%
		% MMR coverage	13,4%	14,6%	14,3%
TOTAL		Number	4373	17144	21517
		% municipality	20,3%	79,7%	100,0%
		% MMR coverage	100,0%	100,0%	100,0%

Table 6: Hi-square test of association between MMR vaccination in cohort group by municipality

Chi-Square Tests			
	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	1577.708a	12	,000
Likelihood Ratio	1611,438	12	,000
N of Valid Cases	21517		

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 60.36.

Based on the analysis of coverage of the target group with MMR vaccine, in the cohort group, observed by municipalities, we conclude that in the cohort group the number of vaccinations was statistically significantly different by municipalities ($\chi 2$ = 1,577,708, df = 12, p <0,001, table value $\chi 2$ = 32.909). In terms of municipalities, the lowest percentage of cohort vaccinations in the cohorts is in the municipalities of Lukavac (53%) and Kladanj (65%).

Table 7: MMR revaccine coverage by cohort by municipality

MUNICIPALITY	BANOVIĆI	Number	588	551	1139
		% municipality	51,6%	48,4%	100,0%
		% MMR coverage	11,1%	3,2%	5,1%
	ČELIĆ	Number	142	424	566
		% municipality	25,1%	74,9%	100,0%
		% MMR coverage	2,7%	2,5%	2,5%
	DOBOJ ISTOK	Number	50	646	696
		% municipality	7,2%	92,8%	100,0%
		% MMR coverage	,9%	3,7%	3,1%
	GRAČANICA	Number	297	2073	2370
		% municipality	12,5%	87,5%	100,0%
		% MMR coverage	5,6%	12,0%	10,5%
	GRADAČAC	Number	78	1983	2061
		% municipality	3,8%	96,2%	100,0%
		% MMR coverage	1,5%	11,5%	9,1%
	KALESIJA	Number	548	1383	1931
		% municipality	28,4%	71,6%	100,0%
		% MMR coverage	10,3%	8,0%	8,6%
	KLADANJ	Number	158	341	499
		% municipality	31,7%	68,3%	100,0%
		% MMR coverage	3,0%	2,0%	2,2%
	LUKAVAC	Number	960	925	1885
		% municipality	50,9%	49,1%	100,0%
		% MMR coverage	18,0%	5,4%	8,4%
	SAPNA	Number	70	392	462
		% municipality	15,2%	84,8%	100,0%
		% MMR coverage	1,3%	2,3%	2,0%
	SREBRENIK	Number	88	1987	2075
		% municipality	4,2%	95,8%	100,0%
		% MMR coverage	1,7%	11,5%	9,2%
	TEOČAK	Number	61	239	300
		% municipality	20,3%	79,7%	100,0%
		% MMR coverage	1,1%	1,4%	1,3%
	TUZLA	Number	1679	3792	5471
		% municipality	30,7%	69,3%	100,0%
		% MMR coverage	31,6%	22,0%	24,3%
	ŽIVINICE	Number	600	2493	3093
		% municipality	19,4%	80,6%	100,0%
		% MMR coverage	11,3%	14,5%	13,7%
TOTAL		Number	5319	17229	22548
		% municipality	23,6%	76,4%	100,0%
		% MMR coverage	100,0%	100,0%	100,0%

Tabela 8: Hi-kvadrat test povezanosti MMR revakcinacije u grupi kohorta po opštinama

Chi-Square Tests			
	Value	df	Asymp. Sig (2-sided)
Pearson Chi-Square	2668.884a	12	,000
Likelihood Ratio	2854,791	12	,000
N of Valid Cases	22548		

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 70.77.

DISCUSION

Epidemiological monitoring of measles, rubella and mumps, and especially laboratoryconfirmed diseases, should be encouraged worldwide to monitor the burden of disease and the impact of immunization. Epidemic research can also provide valuable information, and therefore needs to be validated. There is an urgent need to improve monitoring, especially in developing countries, with a particular focus on child mortality. Identification of the necessary conditions for re-emergence: measles, rubella and parotitis, and effective strategies for preventing re-emergence of disease are important to model research. The percentage coverage of the target group with two doses of MMR vaccine per year in the TC area is not very satisfactory. The highest percentage of two-dose vaccination with MMR vaccine, in the cohort group, in the TC area, was recorded in 2014, and a slightly lower percentage in 2013. The situation showing that the percentage of coverage of the target group with two doses of MMR vaccine, in the TC area has been decreasing from year to year since 2015 is of considerable concern. Compared to 2014, this percentage in 2015 decreased by 4.9%, and in 2016 and 2017 by 5.8% compared to the previous year. Collective immunity is achieved by vaccination in a percentage of 95% of the whole population, while in the observed period in the area of TC, this percentage is far from realized. From the highest score in 2014 in the cohort group (83.7%) in 2017, this percentage is significantly lower, ie in the cohort group 67.2%. Namely, from the coverage of 82.0% achieved in 2013, this rate is constantly falling and reaching the value of 67.2% in 2017, which is 14.8% lower. Such a percentage requires the urgent establishment of appropriate strategies and steps in order to improve it, that is, to raise awareness of the MMR vaccine and its benefits. The highest percentage of coverage of the target group with two doses of MMR vaccine was observed in the municipality of Gradačac (96.2%), followed by Srebrenik (95.8%) and Doboj Istok (92.8%). A high percentage (over 80%) was also observed in the municipalities of Gracanica, Sapna and Živinice. The lowest percentage of coverage of the target group with two doses of MMR vaccine in the cohort group was observed in the municipalities of Banovići (48.4%) and Lukavac (49.1%). In other municipalities, the percentage ranges between 68% and 75%. WHO reports show that there has been a decline in vaccine coverage for many diseases over the past 10 years. The best example of this is the fall in the coverage of the MMR vaccine. In 2016, the coverage of the MMR vaccine in BiH was 68%, in Serbia 82%, in Croatia 90%, and in Italy 85%. The decline in the coverage of children by immunization resulted in measles outbreaks. In the countries mentioned above, except for Italy, immunization is mandatory. For the sake of comparison, for example, in Germany and Belgium, there has been a constant high prevalence of MMR vaccines (96-97%) over the last 10 years, despite the fact that there is no mandatory immunization. Despite adequate coverage, limited epidemics are still occurring. In 2015, there were 2460 cases of measles in Germany reported [10]. Among those suffering from the epidemic of measles and rubella in our country and in the world, the highest number of patients is registered in the group of unvaccinated or incompletely vaccinated. In Europe, 24.592 people suffered from measles in 2017, of whom 35 died, a fourfold increase over 2016. The largest epidemics were reported in 15 European countries. Most cases were in Romania (5562), Italy (5006) and Ukraine (4767), countries that have seen a decline in routine immunization coverage in recent years, consistently low coverage in marginalized groups, interruptions in vaccine supply, and inadequate disease monitoring systems [11]. This trend continued in 2018, where 54.354 people suffered from measles in Europe, which represents a new increase over 2017 of over 120%. Globally, in 2017, 184 countries reported a total of 152.766, and in 2018, 189.392 measles patients [12]. Thus, in 2018, the world had a total of 36.626 more people suffering from measles compared to 2017, of which 29.762 were more affected in Europe, from which it can be concluded that the global increase in the number of patients with measles was most influenced by the increase in the number of patients in Europe, at about 81%. According to the European Center for Disease Prevention and Control (ECDC), 8.326 cases of measles have been registered in Europe in 2012, 10.271 in 2013, 3.616 in 2015, 3.969 in 2015 and 3.767 in 2016 [13]. Between January and July 2017, more than 11.000 cases of measles were reported. The highest number in Romania – 6.378, followed by Italy - 3346, Germany - 766, France - 295, Belgium - 293, Hungary - 54, etc. the list also includes Serbia, which had 6 cases in 2016, and in 2017 had 702 cases of diseased patients. In the first five months of 2017, the number of patients increased by 50% compared to the same period in 2016. Over 80% of patients have certain data that they have not been vaccinated [13, 14]. A comprehensive report from the European Center for Disease Prevention and Control, covered all measles cases in Europe according to which the incidence of the MMR vaccine in Romania in 2013 was 92%, in 2014 89%, while in 2015 this percentage dropped to only 83%, and the same trend continued in 2016. The number of vaccinated persons in some Romanian districts has fallen below 70%, and it is in these districts that the epidemic was the strongest [13]. Experiences from other countries' health systems suggest that it is possible to achieve a high level of protection without the legal obligation of immunization, but the fact is that these experiences are not universally applicable because of existing cultural, social and economic differences. The vaccine protects every individual who is immunized, and if it is achieved in one community that all individuals are immunized, then we have created good collective immunity that will prevent the pathogens from circulating and thus protect those who could not be immunized.

CONCLUSION

The key strategic directions for prevention are as follows:

- ▢ maintaining a high rate of coverage (≥ 95%) with two doses of MMR vaccine through high quality routine immunization services; providing opportunities, ie creating conditions for vaccination through additional
- ▢ immunization activities in population groups that have not been vaccinated or undervaccinated; strengthening a monitoring system that includes mandatory case research and laboratory confirmation of clinical cases and
- ▢ Increasing the availability of high quality and valuable information to healthcare professionals and the public about the benefits and risks of MMR vaccination.

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