RAP CONFERENCE PROCEEDINGS, VOL. 9, PP. 87–94, 2024
ISSN 2737-9973 (ONLINE) | DOI: 10.37392/RAPPROC.2024.18
RAP-PROCEEDINGS.ORG

THE IMPORTANCE OF COMPULSORY VACCINATION IN CHILDREN IN THE FIGHT AGAINST PERTUSSIS AFTER COVID-19

Jasmina Jovanović Mirković[1*], Jagoda Nikolić[1], Slađana Pirić[1], Christos Aleksopoulos[1], Jelena Milojković[1], Dragana Đorđević Šopalović[1], Nataša Rančić[2]

[1]The Academy of Applied Preschool Teaching and Health Studies, Department of Medical Studies, Ćuprija, Serbia
[2]Faculty of Medicine, University of Niš, Niš, Serbia

Abstract. *Introduction. Whooping cough (pertussis) is a contagious respiratory disease caused by Bordatella pertussis, a gram-negative bacterium. It can occur at any age. The clinical picture is diverse, with a wide range of symptoms and severity, especially in newborns, infants, and the elderly. Due to the potential complications, a high morbidity and mortality rate of this disease has been recorded in developed and developing countries. The diagnosis is made based on the clinical picture and confirmed by a nasal swab or a nasopharyngeal aspirate, PCR detection, or serological tests. Epidemics occur worldwide every 3 to 5 years. Early detection of the disease itself and appropriate and rapid treatment with suitable antibiotics are key to success in controlling the epidemic. Objective. To determine whether, with the emergence of COVID-19, the rate of vaccinations and booster vaccinations against whooping cough according to the prescribed vaccination calendar on Šumadija District. County has decreased compared to previous years before the outbreak of the coronavirus pandemic. Results and Discussion. Prevention of this disease is childhood vaccination according to the vaccination calendar prescribed in our country. Whooping cough is a notifiable disease in the Republic of Serbia and is recorded in the Report on Infectious Diseases of the Institute of Public Health of Serbia "Dr. Milan Jovanović-Batut". The incidence of diseases in Serbia has steadily decreased since the introduction of compulsory vaccination in the middle of the 20th century. The pertussis vaccine has proven to be an effective and powerful weapon in the fight against whooping cough in all age groups. The statistical data obtained shows that the vaccination coverage rate in the first year of life was 89% in 2021, compared to 2018 when it was 98% in the first year of life. Booster vaccination in the second year of life was 90% in 2021 compared to 98% in 2018 in the Šumadija District. According to the latest vaccination guidelines and considering the recurrence and spread rate of this disease, as well as possible complications in certain systems, we should talk about the possibility of supplementary vaccination at some point in life. Conclusion. Based on the processed data, it can be stated that children's response to vaccination and booster vaccination has decreased during the COVID-19 pandemic in the Šumadija District. It is necessary to check the vaccination status and thus improve immunity against this disease to reduce the possibility of the occurrence and spread of the said disease on an epidemic scale, which is extremely serious in newborns, young children, and the elderly.*

Keywords: *whooping cough, immunization, vaccination calendar, Šumadija District, COVID-19*

1. INTRODUCTION

Whooping cough is an acute infectious disease of sporadic or epidemic character, clinically manifested by persistent coughing and wheezing ending with the expulsion of small amounts of sticky mucus or vomiting [1]. The causative agent of whooping cough is *Bordetella pertussis*, an immotile bacterium that does not produce spores and is very insensitive to the external environment [2]. *Bordetella pertussis* produces biologically active substances that play an important role in the pathogenesis of the disease: Filamentous hemagglutinin (FHA) and agglutinogen enable the bacterium to adhere to the ciliated epithelium of the respiratory tract [3]. *Bordetella pertussis* adenylate cyclase plays a role in cell damage, while its dermonecrotic toxin affects vascular smooth muscle contraction, ischemia, and necrosis [4]. Tracheal cytotoxin and hemolysin are also important in the pathogenetic mechanism of the development and manifestation of the disease. *Bordetella parapertussis* is also pathogenic for humans. It is morphologically and biochemically similar to *Bordetella pertussis* but differs antigenically [5].

Bordetella is transmitted by droplet infection [6], i.e. by inhalation of an infectious aerosol. The disease occurs most frequently and most severely in the first two years of life, and the highest mortality rate is in children under one year of age [7]. Hospitalization is recommended for infants, as a severe clinical picture with complications can develop quickly. Accompanying symptoms may include vomiting after coughing and subconjunctival bleeding. The infant mortality rate from whooping cough in developing countries is around 3% [8]. Milder clinical forms of the disease occur in older people and partially vaccinated children and go unrecognized. The risk of infection decreases with increasing esteem. Symptoms in adolescents and adults are usually milder, as these patients are partially protected by previous vaccinations or infections [3]. In adults, pertussis is often a persistent disease with a

* ninajovanovic.vms@gmail.com

cough that can last up to 100 days (a hundred-day cough).

A high vaccination rate and collective immunity are therefore of particular importance. Regardless of the past epidemic wave [8], the situation is incomparably more favorable than in the period before the introduction of vaccination, when the number of deaths was in the hundreds [9]. The almost complete absence of deaths is very significant, as there are undoubtedly many more cases of whooping cough than are reported. A resurgence of pertussis cases in recent years has been observed in many countries with a long history of vaccination and high coverage [2, 10].

When pneumonia occurs in neonatal whooping cough, pulmonary hypertension develops, requiring treatment by artificial ventilation [11]. The highest mortality rate of about 1% of infants is in the age group up to 6 months [12]. Possible complications include pneumonia and ear infections (*Otitis media*), especially in young children, and whooping cough encephalopathy. The changes in the CNS are the most serious and are caused by the direct effect of pertussis toxin (PT) and hypoxia of the brain due to impaired blood flow at the level of brain tissue. Mechanical complications are the result of increased intracranial, intrathoracic, and intra-abdominal pressure.

Isolation of *Bordetella pertussis* and culture on culture media is only used in the first two weeks of illness, as the sensitivity of this method decreases after the second week of the disease. Amplification chain reaction (PCR) can be used to diagnose whooping cough in the early stages of the disease [13]. It is recommended to perform serological tests to determine antibodies (ELISA and microagglutination tests).

Antibiotic therapy for whooping cough is successful if it is used in the early stages of the disease, i.e. in the first two weeks of the illness. The therapy uses macrolide antibiotics (erythromycin, azithromycin, and clarithromycin) [14, 5] which reach high concentrations both in respiratory secretions and intracellularly. Therapy with trimethoprim-sulfamethoxazole [11] can also be used. Coughing fits can be reduced by the use of antitussives and corticosteroids. Two types of vaccines are now commercially available worldwide for the prevention of whooping cough: a) a whole-cell vaccine containing an inactivated whole bacterial cell of *Bordetella pertussis*, and b) an acellular vaccine containing purified components of the bacterial cell of *Bordetella pertussis* [10].

Vaccination is the best measure of protection [15]. Thanks to vaccination, whooping cough is no longer a major medical problem. Its occurrence is proportional to the use of vaccination [16]. Vaccination is started in the 3rd month of life with the combined Di-Te-Per (DTP) vaccine. If the vaccination is carried out regularly, whooping cough does not occur. Despite vaccination, whooping cough remains a major problem in both developing and industrialized countries.

This paper aims to compare the success trends of mandatory vaccination with the Di-Te-Per vaccine (DTP) and Pentaxim vaccine from 2014 to 2018 (before the COVID-19 epidemic) and in the period after the COVID-19 epidemic (years 2021 and 2022) in the Šumadija District. Vaccination against pertussis (whooping cough) is legally administered in Serbia according to the vaccination calendar.

2. Methods

For the methodology of this research work, a descriptive method was applied, in which the annual reports on immunization carried out for the Šumadija District of the Institute for Public Health Kragujevac were used, as well as data from the website of the Institute for Public Health of Serbia "Dr. Milan Jovanović Batut" (National annual report on immunization carried out at territory of the Republic of Serbia). Statistical analysis was performed in the Statistical Package for Social Sciences, version 23.0 for Windows (SPSS Inc. Chicago, Illinois, United States). The probability level (p) of < 0.05 was considered significant. The results are presented graphically.

3. Results and discussion

Active immunization is carried out with the combined Di-Te-Per (diphtheria, tetanus, whooping cough) (DTP) vaccine that begins in the 3rd month of life, in three doses at an interval of 1 to 3 months. Revaccination is in the second year of life, and in the fourth, revaccination with mono vaccine against pertussis. A dead pertussis vaccine is used, which contains a suspension of whole bacterial cells [17]. There is data on the neurotoxicity of a vaccine made from whole bacterial cells. Serious but rare defects of that vaccine are the occurrence of convulsions, hypotonic effect, and acute encephalopathy (0-10.5 cases per million doses given). That is why the acellular pertussis vaccine was created in the 80s of the last century, which today is even more perfected and contains 1-5 components of bacteria. This vaccine has been licensed in many countries since 1991. Efficiency reaches up to 93%. However, immunity is not lifelong even after vaccination.

The whole-cell vaccine contains a suspension of whole *Bordetella pertussis* bacteria that have been killed by temperature or chemicals [18]. The vaccine also contains tetanus and diphtheria toxoids. In the nineties of the 20th century, the use of an acellular vaccine against whooping cough began, which does not contain the entire cell of *Bordetella pertussis*, but only individual antigens or virulence factors of the bacterium [19] such as pertussis toxoid, filamentous hemagglutinin, and pertactin, which are said to be the basis of protection [20].

Di-Te-Per (DTP) vaccine, adsorbed on aluminum phosphate, is produced in Belgrade (Institute for Immunology and Virology, Torlak). The vaccine consists of well-purified diphtheria toxoids (25 Lf or 30 IJ), tetanus (5 Lf or 40 IJ), and merthiolate-killed and preserved (0.01%) 15-20 billion *Bordetella pertussis* bacteria. Less than 2 mg of aluminum phosphate was added as a carrier. All of this is contained in a buffer solution of 0.5 ml per dose. This composition provides an optimal immune response against diphtheria and tetanus already after two doses, and against pertussis after the third dose [21].

By the recommendations of the World Health Organization (WHO) Advisory Committee on Immunization in 2006, a strategy for immunization against whooping cough has been adopted. In most countries, the current recommendations are to initiate pertussis immunization with the first dose of vaccine at six to 12 weeks of life and to continue the primary series

with two additional doses, with a minimum interval of four weeks between doses in the primary series. After the primary series of three vaccine doses, the fourth (booster) dose of the vaccine is administered one year after the third vaccine dose, the booster vaccination against whooping cough [22, 23].

Our classical vaccine, which is produced and used in our country against whooping cough, is produced in such a way that all serological types of *Bordetella pertussis* (4 strains) are represented, which are in circulation in an appropriate ratio. The strains selected for the vaccine are fresh (in the first immune phase), the most recently isolated in recent years. This ensures that the antigenic composition of the vaccine and the circulating strains (and serotypes) are identical, providing maximum protection for this type of inactivated vaccine. Many manufacturers in the world produce this type of classical vaccine from standard strains, disregarding the principle of diversity and currency of strains [24]. That is why our vaccine is the most ideal means of protection against whooping cough in our area. A report on immunization against whooping cough, diphtheria, and tetanus on the territory of Šumadija District in 2014 and 2016 is shown in Figure 1.

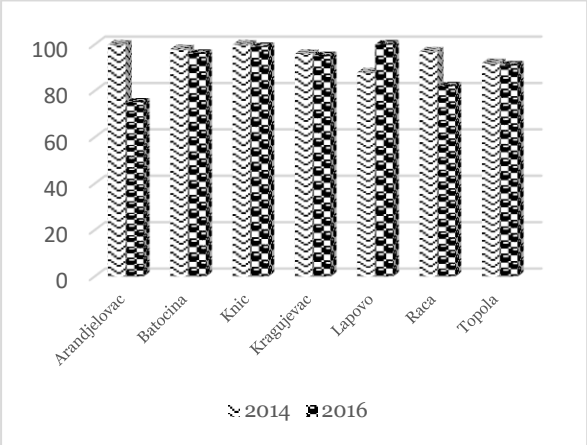

Figure 1. DTP booster vaccination in the 2nd year

The results of immunizations carried out for the Šumadija District in the calendar year 2014 show that the highest response for booster immunization with the DTP vaccine in the 2nd year of life was in the municipalities of Aranđelovac, where 413 out of 413 planned persons were boosted, and in Knić, where 92 out of 92 planned persons were boosted, which corresponds to 100%. In the municipality of Batočina, 81 out of 83 planned people were vaccinated, 98%. In Rača, 63 out of 65 planned subjects were revaccinated, corresponding to 97%. In Kragujevac, 1631 of the planned 1700 people were vaccinated, corresponding to 96%. In the city of Topola with 92%, where the planned number is 167, 154 respondents were revaccinated. The lowest response rate to the 2nd year booster vaccination was in the area of Lapovo municipality, where out of 57 planned 50 people were vaccinated, which is 88%. The coverage of the 2nd year booster vaccination with the DTP vaccine in the Šumadija District in 2014 is satisfactory, the overall percentage is 96%, which indicates that the booster vaccination was successfully carried out.

In 2016, the booster vaccination of children in the 2nd year of life was performed, with the best performance in the municipality of Lapovo, which amounted to 100%. The lowest percentage of those vaccinated in the second year of life was in the city of Aranđelovac, of the planned 400, 301 were vaccinated, corresponding to 75%. In Knić, 80 of the planned 81 were vaccinated, corresponding to 99%. In Batočina, 81 of the 84 planned vaccinations were completed, corresponding to 96%. In Kragujevac, 1660 of the planned 1750 were vaccinated, corresponding to 95%. In Topola, 128 of the planned 152 people were vaccinated, corresponding to 91%. In Rača, 82 of the planned 100 respondents were vaccinated, which is 82%. The overall percentage of vaccinated people in the Šumadija District is 91%, which indicates that the booster vaccination in the second year of life against whooping cough was not successfully carried out.

Vaccination against diphtheria, tetanus, and pertussis DTP and with the combined pentavalent DTaP-IPV-Hib vaccine (Pentaxim) was carried out in the Republic of Serbia in 2016 with a coverage of 94.1% and an estimated coverage of 92.5%. In the central part of Serbia, the vaccination coverage rate with the DTP vaccine and the combined pentavalent DTaP-IPV-Hib vaccine was 93.4%, i.e. out of 47396 planned compulsory vaccinations, 44282 were vaccinated, which, according to the estimate based on 48124 live births in 2015, corresponds to 92%, i.e. 3850 children remained unvaccinated. A vaccination coverage rate of below 95% for DTP as well as for the combined pentavalent vaccine DTaP-IPV-Hib, Pentaxim, at the first booster vaccination, had 54 municipalities in Central Serbia (47%) and 17 in Vojvodina (38%). The lowest vaccination coverage was recorded in the municipalities of Doljevac (38.3%) and Apatin (64.4%) [25].

Vaccination against diphtheria, tetanus, and whooping cough with the DTP vaccine was carried out in the Republic of Serbia in 2014 with a coverage of 95% and an estimated coverage of 92.5%. 33 municipalities (28.7%) in central Serbia and eight municipalities (17.7%) in Vojvodina had DTP vaccination results below 95%. The lowest values were recorded in Golubac (53.7 %), i.e. Irig (69.2 %). 49 municipalities in Central Serbia (42.6%) and 9 in Vojvodina (20%) had a vaccination coverage rate below 95% at the first DTP booster vaccination. The lowest vaccination coverage was recorded in the municipalities of Niš (62.1%) and Bački Petrovac (78.5%). Based on the estimated total number of live births in the Republic of Serbia in 2013, 4900 children were not vaccinated in 2014 [26].

Recommendations for booster vaccination against pertussis in the elderly depend on the epidemiological situation and economic development and vary from country to country [23]. Some developed countries have introduced booster vaccination at preschool and school age, and some have introduced systematic booster vaccination for persons over 30 years of age or certain categories of adults (healthcare workers, childcare workers). The fact that 60% of children under five months of age who are treated in intensive care due to complications of the disease have a reservoir of pertussis infection in the child's family [27, 28]. For children who are not age-appropriately vaccinated against pertussis, the so-called maintenance strategy (eng. *cooing* strategy) [29], according to which close contacts of the newborn (family members, closest relatives, persons involved in the care of children and health personnel who have contact with children of the

youngest age) are vaccinated with a suitable pertussis vaccine (DTap). Due to the particular risk of disease and the possible transmission of the infection to the newborn, in some countries, vaccination against whooping cough is given to pregnant women in the last trimester of pregnancy [30]. A graphical representation of the arithmetic mean and standard deviation of whooping cough vaccination in the first year of life of infants and revaccination against whooping cough in the 2nd year of life of children for the 2014 year is shown in Figure 2.

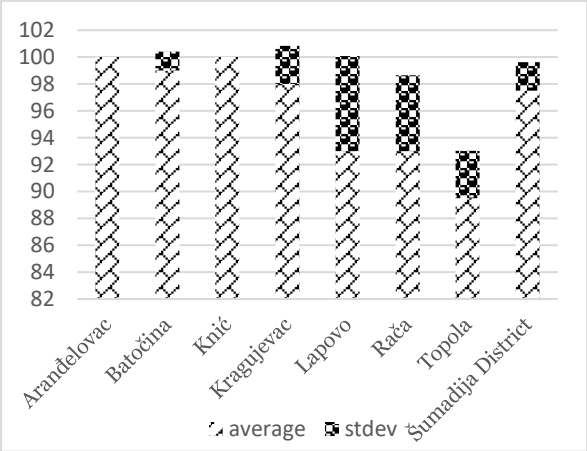

Figure 2. Immunization of children against whooping cough in 2014

Based on the summarized data on booster vaccination of children in the 2nd year of life with the DTP/DTaP-IPV-HiB vaccine, the number of planned vaccinations in the city of Aranđelovac was 350 and the number of booster vaccinations was 337, which corresponds to 96%. In Batočina, 81 of the planned 85 were revaccinated, corresponding to 95%. In Kragujevac, 1604 of the planned 1680 were vaccinated, corresponding to 95%. In the city of Knić, 79 of the planned 79 were vaccinated, corresponding to 100%. In Rača, 70 of the planned 70 were vaccinated, corresponding to 100%. In Lapovo, the planned number is 50, and 49 have been revaccinated, corresponding to 98%. In Topola, 141 of the planned 162 have been revaccinated, which is 87%. The percentage at the level of the entire district in 2015 was 95%, which indicates that the booster vaccination was successfully carried out.

We note that in 2021, 2312 or 90% were vaccinated in the 2nd year of life. In the city of Aranđelovac, about 98% were vaccinated, also in Knić the percentage of vaccinated is 96%, while in the city of Lapovo, this percentage is higher and amounts to 100.00%. In Batočina, out of the planned 80, 76 were revaccinated, which is 95%. In the city of Rača, out of the planned 65, 58 were revaccinated, which is 89%. The same percentage of revaccinated children was observed in Topola, 89%, out of the planned 135, 120 children were revaccinated. In the city of Kragujevac, the lowest percentage of revaccinated people was observed for the territory of Šumadija District, out of the planned 1760, 1548 were revaccinated, which is 88%. A report on vaccination against whooping cough, diphtheria, and tetanus on the territory of Šumadija District in 2015 and 2021 is shown in Figure 3. A graphical representation of the arithmetic mean and standard deviation of the vaccination against whooping cough in the first year of life of infants and the booster vaccination against whooping cough in the second year of life of children for the 2021 year is shown in Figure 4.

The data analysis showed a statistical significance ($p<0.05$) for 2017 and 2021 for DTP vaccination in the first year of life.

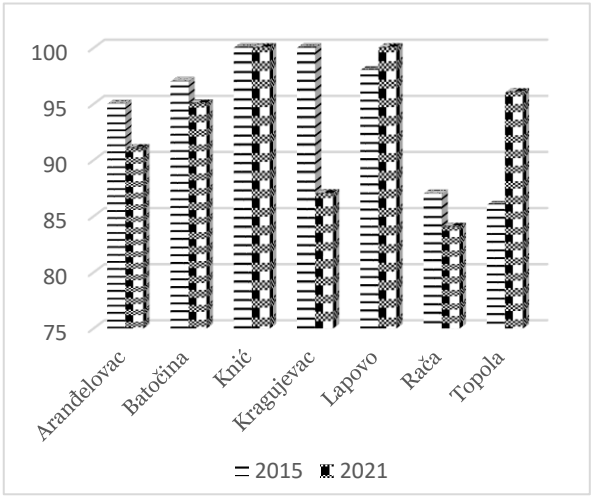

Figure 3. DTP booster vaccination in the 2nd

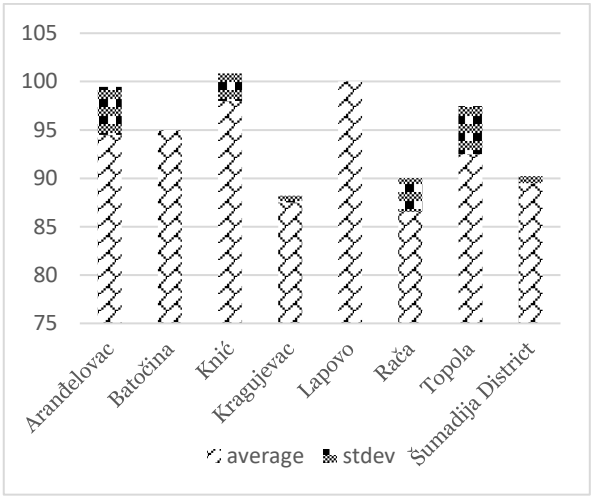

Figure 4. Immunization of children against whooping cough in 2021

Vaccination against diphtheria, tetanus, and pertussis with DTP as well as with the combined pentavalent DTaP-IPV-Hib vaccine, i.e. Pentaxim vaccine, was carried out in the Republic of Serbia in 2015 with a coverage of 95% and an estimated coverage of 95.2%. In the central part of Serbia, the vaccination coverage with the DTP vaccine as well as the combined pentavalent DTaP-IPV-Hib vaccine was 94.6%, i.e. 46721 of the 49407 planned vaccinees were vaccinated, which was 95.5% according to an estimate based on 48926 live births in 2014, i.e. 2700 children remained unvaccinated. The results of vaccination with the DTP vaccine and with the combined pentavalent DTaPIPV-Hib vaccine were below 95% in 33 municipalities (28.7%) in central Serbia and nine municipalities (20%) in Vojvodina.

The lowest values were recorded in Doljevac (28.2%), i.e. Pećinci (82.5%). The analysis of the success of the first revaccination with the DTP vaccine, as well

as the combined pentavalent DTaP-IPV-Hib vaccine, Pentaxim vaccine by district shows that in 2015, the coverage in 68% of the districts was below 95%, and the lowest in Niš District was 79.9%. [31]. The first booster vaccination against diphtheria, tetanus, and pertussis with the combined pentavalent vaccine Pentaxim, DTaP-IPV-HiB vaccine (DTaP-IPV-Hib) in the 2nd year of life was carried out in the Republic of Serbia with a vaccination coverage rate of 82.3%. The analysis of the vaccination coverage rate for the first booster vaccination with the combined pentavalent vaccine by district shows that in 2021, no district achieved a vaccination coverage rate of 95% of the intended population, while only eight districts achieved a vaccination coverage rate of more than 90%. The lowest vaccination coverage rate was registered in Raška District (64.4%) [32].

Historically, the occurrence of the whooping cough epidemic dates back to the 15th century in Persia, and deaths of infants and young children from this disease in Paris were recorded in the 16th century [19, 1]. As with other diseases for which mass immunization has been implemented, the incidence of whooping cough illnesses and deaths has decreased dramatically. It is estimated that, for example, in 2008, 16 million people suffered from pertussis, much less than before, and that almost 200000 of them died, although close to 700000 deaths were avoided by vaccination. Seven years later, in 2015, it is believed that 89000 people have died from this infection and that the average vaccine coverage in the world is 86%.

In developing countries, almost a quarter of affected infants get pneumonia (four times more than in the developed world), and for every 25th child, the outcome of the disease is fatal. Some developed countries, for example, France, Germany, and Australia recommend the strategy of "cocooning" the infant, i.e. isolating it from the environment in which the causative agents of pertussis circulate, by vaccinating relatives, including grandparents, before the new arrival from the maternity ward [29]. The idea is based on the observation from France that 80% of infants get infected with pertussis from their household. There is still no scientific evidence of the effect of this measure.

In Serbia, in 2013, whooping cough was diagnosed in 39 people, and in 2014, 281 patients were reported, which is almost double the number during the previous 10 years. In 2015, the official number of patients was reduced to 89, but with one death. Regardless of the past epidemic wave, the situation is incomparably more favorable than in the period before the introduction of vaccination, when the number of deaths was measured in the hundreds [33, 34].

In the municipalities of Aranđelovac, Knić, and Lapovo, all intended persons were vaccinated, corresponding to 100.00%. In Kragujevac, 1711 of the planned 1750 people were vaccinated, which is 98%. In Topola, 141 of the planned 144 were vaccinated, which is 98%. In the municipality of Batočina, 80 of the planned 84 were vaccinated, corresponding to 95%. It is noticeable that in Rača, the number of vaccinated people is significantly lower than the planned number and amounts to 93%. This shows that this municipality recorded the lowest percentage of vaccinated people in the first year of life for the 2017 calendar year. The percentage at the Šumadija District level in 2017 was 98%, which shows that the vaccination was successfully carried out. A report on vaccinations against whooping cough, diphtheria, and tetanus carried out on the territory of Šumadija District in 2017 and 2022 is shown in Figure 5.

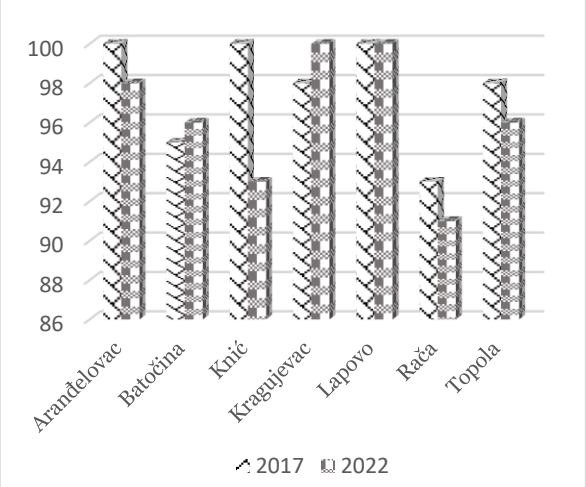

Figure 5. DTP vaccination in 2017 and 2022

In the calendar year of 2022, in the municipalities of Kragujevac and Lapovo, all intended persons were vaccinated, corresponding to 100%. In Aranđelovac, 383 of the planned 384 people were vaccinated, which was 98%. In the city of Batočina, 72 of the planned 75 were vaccinated, and in the city of Topola, 139 of the planned 144 were vaccinated, which corresponds to 96%. In Knić, 68 of the planned 73 were vaccinated, corresponding to 93%. In Rača, 59 of the planned 65 were vaccinated, which is 91%. The percentage at the level of the entire district in 2022 is 99%, which means that immunization in the first year of life was successfully carried out and implemented.

Immunization against diphtheria, tetanus, and whooping cough with the combined pentavalent DTaP-IPV-HiB vaccine, the Pentaxim vaccine, was carried out in the Republic of Serbia in 2017 with a coverage of 95.1% and an estimated coverage of 95.3%. In the central part of Serbia, vaccination coverage with the combined pentavalent DTaP-IPV-HiB vaccine, the Pentaxim vaccine, was achieved at 95%, i.e. 45200 of the 47570 planned obligees were vaccinated, which, according to an estimate based on 47627 live births in 2016, amounted to 94.9%, that is, 2450 children remained unvaccinated. Based on the estimate of the total number of live births in the Republic of Serbia in 2016, 3250 children were not vaccinated in 2017. The lowest coverage in central Serbia was in the municipalities of Ub (63.8%), Bujanovac (66.3%), and Preševo (79.7%), which at the same time conditions the lowest coverage in Kolubara and Pčinja Districts. On the territory of Vojvodina, the smallest coverage of 77.1% was in the municipality of Ada. The first revaccination against diphtheria, tetanus, and pertussis and the second against diphtheria and tetanus in the Republic of Serbia was carried out with almost the same results compared to those achieved in 2016 [35].

Pentaxim vaccine is used for the preventive protection of children against diphtheria, *Haemophilus influenzae* type *b* (conjugated, adsorbed), whooping cough (acellular), poliomyelitis (inactivated), and tetanus [36]. It is used for the primary vaccination of

infants from the age of three months and the booster vaccination one year after the primary vaccination in the second year of the child's life. The vaccine is administered intramuscularly.

The planned vaccination in the Republic of Serbia against diphtheria, tetanus, whooping cough, polio, and diseases caused by *Haemophilus influenzae* type *b* (DTaP-IPV-Hib) was carried out with a vaccination coverage rate of 91.9%. The target vaccination coverage rate of 95% with the DTaP-IPV-Hib vaccine in the first year of life was achieved in 12 districts, in two districts it was below 90%. The revaccination of children in the second year of life with the same vaccine was carried out with a vaccination coverage rate of 80.6% [37].

Coronaviruses (CoV) are a family of pathogens of various diseases, from a mild cold to a severe form of the disease, severe acute respiratory syndrome (SARSCoV) or Middle East Respiratory Syndrome. *Coronaviruses* cause diseases in animals. To date, seven types of viruses are known to cause disease in humans, and only some (SARS-CoV and MERS-CoV) have been shown to transmit from person to person. The new coronavirus SARS-CoV-2 represents a completely new strain of the virus that has not been identified in the human population so far. According to its genetic structure, it is similar to SARS-CoV. In December 2019, cases of pneumonia of unknown etiology appeared in the human population in China, and on January 7, it was confirmed that SARS-CoV-2 is the cause of the infectious disease [38].

The average length of incubation is 5-6 days (maximum 14 days). The disease is transmitted interpersonally, usually after close direct contact with an infected person, droplets, or through indirect contact (freshly contaminated hands or objects). The disease can be asymptomatic, or it can manifest itself as a mild, moderate, or severe disease with cough, shortness of breath, difficulty breathing, elevated body temperature, as well as other symptoms and signs (sudden loss of smell, taste, or change in taste, headache, muscle pain, fatigue, vomiting and/or diarrhea). In more severe cases, the infection can also cause pneumonia, severe acute respiratory syndrome, kidney failure, and even death [39].

4. Conclusion

The results of the implemented immunization for the Šumadija District in the calendar year 2014 show that the coverage of the implemented immunization in the first year of life is 99%, the total number planned about the number of vaccinated, which is considered successful. It was also successfully carried out in 2015 and is 98%, which indicates that the Pentaxim vaccine immunization was successfully carried out. The percentage of immunization carried out in 2016 was 99%, which shows us that the immunization was successfully carried out, also in 2017, the percentage of vaccinated persons was 98%, which shows that the immunization was carried out successfully. A year after the COVID-19 pandemic, a significant difference was observed at the level of the entire Šumadija District regarding the immunization performed in the calendar year 2021, which is 89%. We can conclude that immunization was not successfully implemented in 2021, and therefore we expect a decline in collective immunity, with the risk of an epidemic of vaccine-preventable diseases.

References

1. A. Aslanabadi, K. Ghabili, K. Shad, M. Khalili, M. M. Sajadi, "Emergence of whooping cough: notes from three early epidemics in Persia," *Lancet Infect. Dis.*, vol. 15, no. 12, pp. 1480 – 1484, Dec. 2015. DOI: 10.1016/S1473-3099(15)00292-3 PMid: 26298206 PMCid: PMC7164782
2. D. J. Nieves, U. Heininger, "Bordetella pertussis," *Microbiol. Spectr.*, vol. 4, no. 3, Jun. 2016. DOI: 10.1128/microbiolspec.EI10-0008-2015 PMid: 27337481
3. K. Zycinska et al., "Whooping Cough in Adults: A Series of Severe Cases," in *Pathobiology of Pulmonary Disorders*, vol. 955, M. Pokorski, Eds., 1st ed., Cham, Switzerland: Springer, 2017, ch. 6, pp. 47 – 50. DOI: 10.1007/5584_2016_167 PMid: 28039663
4. N. Carbonetti, "What Causes the Cough in Whooping Cough?," *mBio*, vol. 13, no. 3, e0091722, Jun. 2022. DOI: 10.1128/mbio.00917-22 PMid: 35604095 PMCid: PMC9239215
5. I. Stock, "Pertussis (Whooping cough) - an update," *Med. Monatsschr. Pharm.*, vol. 38, no. 12, pp. 484 – 488, Dec. 2015. PMid: 26837155
6. B. Chivima, "Whooping cough," *Nurs. Stand.*, vol. 29, no. 7, 61, Oct. 2014. DOI: 10.7748/ns.29.7.61.s46 PMid: 25315570
7. P. Nee, E. Weir, M. Vardhan, A. Vaidya, "Could this be whooping cough?," *Emerg. Med. J.*, vol. 35, no. 10, pp. 639 – 642, Oct. 2018. DOI: 10.1136/emermed-2018-207792 PMid: 30097456
8. D. Bhagat et al., "Pertussis epidemiology in Canada, 2005-2019," *Can. Commun. Dis. Rep.*, vol. 49, no. 1, pp. 21 – 28, Jan. 2023. DOI: 10.14745/ccdr.v49i01a05 PMid: 36815868 PMCid: PMC9902035
9. V. Bouchez, N. Guiso, "Bordetella pertussis, B. parapertussis, vaccines and cycles of whooping cough," *Pathog. Dis.*, vol. 73, no. 7, ftv055, Oct. 2015. DOI: 10.1093/femspd/ftv055 PMid: 26242280
10. M. Prygiel et al., "Effectiveness of experimental and commercial pertussis vaccines in the elimination of Bordetella pertussis isolates with different genetic profiles in murine model," *Med. Microbiol. Immunol.*, vol. 210, no. 5 – 6, pp. 251 – 262, Dec. 2021. DOI: 10.1007/s00430-021-00718-1 PMid: 34338880 PMCid: PMC8326312
11. U. Heininger, "Pertussis (whooping cough)," *Pneumologe*, vol. 17, no. 6, pp. 465 – 476, Nov. 2020. DOI: 10.1007/s10405-020-00345-2 PMid: 33041739 PMCid: PMC7537784
12. M. Rochat, S. De Vallière, B. Favrat, "What does a general practitioner need to know about whooping cough?," *Rev. Med. Suisse*, vol. 16, no. 718, pp. 2398 – 2402, Dec. 2020. PMid: 33300701
13. A. S. Pimenova et al., "PCR-based diagnosis of whooping cough in the Russian Federation," *Klin. Lab. Diagn.*, vol. 66, no. 1, pp. 52 – 58, Feb. 2021. DOI: 10.18821/0869-2084-2021-66-1-52-58 PMid: 33567174

14. V. T. N. Nguyen, L. Simon, "Pertussis: The Whooping Cough," *Prim. Care*, vol. 45, no. 3, pp. 423 – 431, Sep. 2018.
DOI: 10.1016/j.pop.2018.05.003
PMid: 30115332
15. A. A. J. Vaillant, M. J. Grella, "Vaccine (Vaccination) (Archived)," in *StatPearls [Internet]*, Treasure Island (FL), USA: StatPearls Publishing, Jan. 2024.
PMid: 30422490
16. J. D. Cherry, S. Doustmohammadi, "Pertussis vaccines," *Curr. Opin. Pediatr.*, vol. 34, no. 2, pp. 126 – 131, Apr. 2022.
DOI: 10.1097/MOP.0000000000001108
PMid: 35081553
17. M. Prygiel, E. Mosiej, P. Górska, A. A. Zasada, "Diphtheria-tetanus-pertussis vaccine: past, current & future," *Future Microbiol.*, vol. 17, pp. 185 – 197, Feb. 2022.
DOI: 10.2217/fmb-2021-0167
PMid: 34856810
18. N. Guiso, "Pertussis vaccination and whooping cough: and now what?," *Expert Rev. Vaccines*, vol. 13, no. 10, pp. 1163 – 1165, Oct. 2014.
DOI: 10.1586/14760584.2014.941816
PMid: 25020131
19. M. D. Decker, K. M. Edwards, "Pertussis (Whooping Cough)," *J. Infect. Dis.*, vol. 224, no. 12, pp. S310 – S320, Sep. 2021.
DOI: 10.1093/infdis/jiaa469
PMid: 34590129
PMCid: PMC8482022
20. K. A. Gregg, T. J. Merkel, "Pertussis Toxin: A Key Component in Pertussis Vaccines?," *Toxins*, vol. 11, no. 10, 557, Sep. 2019.
DOI: 10.3390/toxins11100557
PMid: 31546599
PMCid: PMC6832755
21. S. M. A. Hanifi et al., "Diphtheria-Tetanus-Pertussis (DTP) Vaccine Is Associated with Increased Female-Male Mortality. Studies of DTP Administered Before and After Measles Vaccine," *J. Infect. Dis.*, vol. 223, no. 11, pp. 1984 – 1991, Jun. 2021.
DOI: 10.1093/infdis/jiaa684
PMid: 33125458
22. *10 Facts on Immunization*, WHO, Geneva, Switzerland, 2018.
Retrieved from: https://www.who.int/news-room/facts-in-pictures/detail/immunization
Retrieved on: Jan. 15, 2024
23. *Vaccines to Children: Protective Effect and Adverse Events: A Systematic Review*, SBU Yellow Report no. 191, Swedish Council on Health Technology Assessment, Stockholm, Sweden, 2009.
PMid: 28876765
24. S. Taye, B. Tessema, B. Gelaw, F. Moges, "Assessment of Pertussis Vaccine Protective Effectiveness in Children in the Amhara Regional State, Ethiopia," *Int. J. Microbiol.*, vol. 2020, 8845835, Oct. 2020.
DOI: 10.1155/2020/8845835
PMid: 33110430
PMCid: PMC7579676
25. *Izveštaji o sprovedenoj imunizaciji na teritoriji Republike Srbije u 2016. godini*, Institut za javno zdravlje Srbije "Dr Milan Jovanović Batut", Beograd, Srbija, 2017.
(Reports on immunization carried out on the territory of the Republic of Serbia in 2016, Institute for Public Health of Serbia "Dr Milan Jovanović Batut", Belgrade, Serbia, 2017.)
Retrieved from: https://www.batut.org.rs/index.php?category%20id=140;
Retrieved on: Jan. 20, 2024
26. *Izveštaji o sprovedenoj imunizaciji na teritoriji Republike Srbije u 2014. godini*, Institut za javno zdravlje Srbije "Dr Milan Jovanović Batut", Beograd, Srbija, 2015.
(Reports on immunization carried out on the territory of the Republic of Serbia in 2014, Institute for Public Health of Serbia "Dr Milan Jovanović Batut", Belgrade, Serbia, 2015.)
Retrieved from: https://www.batut.org.rs/index.php?category%20id=140;
Retrieved on: Jan. 05, 2024
27. M. Veljkovic, G. Loncarevic, M. Kanazir, D. Kisic-Tepavcevic, T. Gazibara, "Trend in mandatory immunisation coverage: linear and joinpoint regression approach, Serbia, 2000 to 2017," *Euro Surveill.*, vol. 26, no. 26, 2000417, Jul. 2021.
DOI: 10.2807/1560-7917.ES.2021.26.26.2000417
PMid: 34212841
PMCid: PMC8326657
28. P. E. Kilgore, A. M. Salim, M. J. Zervos, H. J. Schmitt, "Pertussis: Microbiology, Disease, Treatment, and Prevention," *Clin. Microbiol. Rev.*, vol. 29, no. 3, pp. 449 – 486, Jul. 2016.
DOI: 10.1128/CMR.00083-15
PMid: 27029594
PMCid: PMC4861987
29. G. Di Mattia et al., "Pertussis: New preventive strategies for an old disease," *Paediatr. Respir. Rev.*, vol. 29, pp. 68 – 73, Feb. 2019.
DOI: 10.1016/j.prrv.2018.03.011
PMid: 29914744
30. N. Sompagdee et al., "Seroprevalence of Bordetella pertussis antibodies and anti-pertussis antibody response after a single dose of reduced-antigen combined diphtheria, tetanus, and acellular pertussis vaccine (Tdap) in pregnant Thai women," *Vaccine*, vol. 38, no. 12, pp. 2725 – 2733, Mar. 2020.
DOI: 10.1016/j.vaccine.2020.01.074
PMid: 32070680
31. *Izveštaji o sprovedenoj imunizaciji na teritoriji Republike Srbije u 2015. godini*, Institut za javno zdravlje Srbije "Dr Milan Jovanović Batut", Beograd, Srbija, 2016.
(Reports on immunization carried out on the territory of the Republic of Serbia in 2015, Institute for Public Health of Serbia "Dr Milan Jovanović Batut", Belgrade, Serbia, 2016.)
Retrieved from: https://www.batut.org.rs/index.php?category%20id=140;
Retrieved on: Jan. 20, 2024
32. *Izveštaji o sprovedenoj imunizaciji na teritoriji Republike Srbije u 2021. godini*, Institut za javno zdravlje Srbije "Dr Milan Jovanović Batut", Beograd, Srbija, 2022.
(Reports on immunization carried out on the territory of the Republic of Serbia in 2021, Institute for Public Health of Serbia "Dr Milan Jovanović Batut", Belgrade, Serbia, 2022.)
Retrieved from: https://www.batut.org.rs/index.php?category%20id=140;
Retrieved on: Jan. 20, 2024
33. B. Savić i sar., *Medicinska mikrobiologija*, Beograd, Srbija: Univerzitet u Beogradu, Medicinski fakultet, 2022.
(B. Savić et al., *Medical Microbiology*, Belgrade, Serbia: University of Belgrade, Faculty of Medicine, 2022.)
34. D. Delić, *Infektivne bolesti, Laboratorijska dijagnostika i lečenje*, 1 izdanje, Beograd, Srbija: Zavod za udžbenike i nastavna sredstva, 2001.
(D. Delić, *Infectious Diseases, Laboratory Diagnostics and Treatment*, 1st ed., Belgrade, Serbia: Institute for textbooks and teaching aids, 2001.)
35. *Izveštaji o sprovedenoj imunizaciji na teritoriji Republike Srbije u 2017. godini*, Institut za javno

zdravlje Srbije "Dr Milan Jovanović Batut", Beograd, Srbija, 2018.
(Reports on immunization carried out on the territory of the Republic of Serbia in 2017, Institute for Public Health of Serbia "Dr Milan Jovanović Batut", Belgrade, Serbia, 2018.)
Retrieved from: https://www.batut.org.rs/index.php?category%20id=140;
Retrieved on: Jan. 20, 2024

36. S. A. Plotkin, J. Liese, S. A. Madhi, E. Ortiz, "A DTaP-IPV//PRP~T vaccine (Pentaxim): A review of 16 years' clinical experience," *Expert Rev. Vaccines*, vol. 10, no. 7, pp. 981 – 1005, Jul. 2011.
DOI: 10.1586/erv.11.72
PMid: 21749196
37. *Izveštaji o sprovedenoj imunizaciji na teritoriji Republike Srbije u 2022. godini*, Institut za javno zdravlje Srbije "Dr Milan Jovanović Batut", Beograd, Srbija, 2023.
(Reports on immunization carried out on the territory of the Republic of Serbia in 2022, Institute for Public Health of Serbia "Dr Milan Jovanović Batut", Belgrade, Serbia, 2023.)
Retrieved from: https://www.batut.org.rs/index.php?category%20id=140;
Retrieved on: Jan. 20, 2024
38. G. S. Dite, N. M. Murphy, R. Allman, "Development and validation of a clinical and genetic model for predicting risk of severe COVID-19," *Epidemiol. Infect.*, vol. 149, e162, Jul. 2021.
DOI: 10.1017/S095026882100145X
PMid: 34210368
PMCid: PMC8292840
39. R. Puthiyedath et al., "Ayurvedic clinical profile of COVID-19 - A preliminary report," *J. Ayurveda and Integr. Med.*, vol. 13, no. 1, 100326, Jan.-Mar. 2022.
DOI: 10.1016/j.jaim.2020.05.011
PMid: 32624376
PMCid: PMC729022