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Research Article

Effectiveness of Vaccination in Preventing Coronavirus Disease 2019 Six Months or More After the Second Dose and Up to Five Months After the Third Dose in The Municipality of Voždovac (Belgrade, Serbia): A Real-Life Comparison of Four Vaccines

Jelena Milić[1,2], Zoran Kokić[3], Predrag Kon[4], Srdja Janković[5*]

[1]Institute of Public Health of Serbia "Dr Milan Jovanović Batut", Dr Subotića 5, 11 000 Belgrade, Serbia

[2]European University KALLOS, Ratarski put 8a, 11000 Belgrade, Serbia

[3]Community Health Center Voždovac, 11010 Belgrade, Serbia

[4]Belgrade City Institute of Public Health, 11108 Belgrade, Serbia

[5]University Children's Hospital, Tiršova 10, 11000 Belgrade, Serbia

[*]**Corresponding author:** Srdja Janković, University Children's Hospital, Tiršova 10, 11000 Belgrade, Serbia

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Abstract

Background: Availability of vaccines less than a year after the beginning of the coronavirus disease 2019 (COVID-19) pandemic, followed by the widest vaccination campaign in history, significantly altered the global course of the pandemic. Data on Vaccine Effectiveness (VE) are important for immunization policies, as well as vaccine acceptance, especially among populations susceptible to severe infection. **Aims:** To assess the relative risk of COVID-19 in the vaccinated vs. unvaccinated population and compare the effectiveness of four vaccines (BBIBP-CorV, BNT162b2, Gam-COVID-Vac, ChAdOx1) against symptomatic infection. **Study Design:** Retrospective, cross-sectional observational study. **Methods:** We examined the incidence of SARS-CoV-2 infection and clinically overt COVID-19 in a five-month period (November 1st, 2021 – March 31st, 2022) in the Belgrade municipality of Voždovac. The observed period corresponded to the predominance of Delta and Omicron variants. Data on vaccinal status were retrieved from the National Registry for Immunization against COVID-19 at the Institute for Public Health of Serbia, while information on vaccine type was obtained by telephone interview in people with polymerase chain reaction (PCR)-confirmed infection. Only those who received two or three vaccine doses were included in the study. **Results:** Of the total population of Voždovac (169,567), 88,870 people (52.4%) were vaccinated with two or three doses by the end of the study

period. Two doses of BBIBP-CorV were received by 28.8% of the total population, while 14.9% received BNT162b2, 5.8% Gam-COVID-Vac, and 2.7% ChAdOx1. People vaccinated with three doses comprised 13.9%, 14.9%, 3.1%, and 0.4% of the population for BBIBP-CorV, BNT162b2, Gam-COVID-Vac, and ChAdOx1, respectively. Importantly, none of the vaccinated individuals exhibited any side effects other than transient reactogenicity, and no adverse events requiring medical assistance were reported to the relevant national authority (Medicines and Medical Devices Agency of Serbia). The relative risk (RR) of infection for two-dose vaccination against the unvaccinated population was 0.93 (95% CI 0.88–0.99), while the overall VE was 7%. When analyzed by age group, RR was statistically significant only for people older than 75 (0.45; CI 0.34-0.61; VE 55%). For three doses, overall RR was 0.65 (CI 0.61-0.69; VE 35%), decreasing from 0.71 in the 18-49 age group to 0.69 in the 50-64 group and 0.46 in people above 75, corresponding to a VE of 29%, 31%, and 54%, respectively. The overall RR of three-dose vs. two-dose regimen was 0.69 (95% CI 0.64-0.75) with a VE of 31%. A significant difference in the risk of symptomatic disease was found in the 18-49 (RR 0.72; 95% CI 0.65-0.79; VE 28%) and 50-64 age groups (RR 0.76; 95% CI 0.64-0.91; VE 24%). Among vaccines, greatest effectiveness was exhibited by BNT162b2, followed by Gam-COVID-Vac and BBIBP-CorV. Results for ChAdOx1 could not be statistically assessed due to insufficient number of people who received three doses of this vaccine. **Conclusion:** Taken together, our real-world data attest to a modest overall effectiveness of three-dose COVID-19 vaccination against symptomatic infection in the observed population and time period, with considerable effectiveness of both three- and two-dose regimes among the elderly.

Keywords: Coronavirus disease 2019; Vaccines; Pandemic

Introduction

Active immunization is, in many respects, the most successful method of preventing infectious disease and suppressing epidemics and pandemics throughout history. Its success, however, hinges on a number of factors, including the effectiveness of a given vaccine in preventing symptomatic illness, mode and rate of disease transmission, magnitude of risk of hospitalization or death, and of course, the extent and duration of vaccinal protection. The recent pandemic of coronavirus disease 2019 (COVID-19), a systemic disease caused by severe acute respiratory syndrome-associated coronavirus 2 (SARS-CoV-2), offered an instructive illustration of the power of vaccines to mitigate such global threats and a rich source of new insights into the real-world impact of a global mass vaccination campaign in the face of an extremely contagious, rapidly spreading pathogen in an increasingly interconnected world [1].

Owing in part to previous research on SARS-CoV-1 and an unprecedented global scientific, medical and institutional mobilization, by the end of 2022 a total of 13 vaccines for coronavirus disease 2019 (COVID-19) were granted emergency approval and were massively used throughout the world, though the number subsequently dropped to 12 [2,3]. In the period of peak global effort to contain the pandemic, four different vaccines were available in Serbia: BBIBP-CorV (Sinopharm), a traditionally designed inactivated viral vaccine; BNT162b2 (Phizer-BioNTech), an mRNA-based vaccine; Gam-COVID-Vac, also known as Sputnik V, an adenoviral vector vaccine designed by the Gamaleya institute; and AstraZeneca's ChAdOx1, also an adenoviral vector vaccine. The citizens were invited to freely select one of these vaccines. After huge initial public interest and rapid vaccine rollout, COVID-19 vaccination coverage in Serbia soon started to stall, reaching the proverbial "glass half full" at just above fifty percent nationwide (52.4% in the municipality of Voždovac) by the conclusion of the observed period [4,5].

Initially, the overall assessment was that, in order to significantly influence the epidemic process as a sole intervention, a COVID-19 vaccine needed to be at least 60% effective assuming a 100% coverage, or 70% effective for a coverage of 75% [6]. While vaccine effectiveness (VE) did indeed meet this requirement, at least initially, studies also demonstrated vast variations in different clinical settings, age groups, professions, as well as depending on the type of vaccine, number of doses administered and, perhaps crucially, time elapsed since vaccination [7-11]. Considerable differences in VE were also noted between different types of vaccine [12]. VE was also influenced (and ultimately considerably limited) by the ongoing evolution of SARS-CoV-2, giving rise to new variants of concern (VoC), notably Delta and Omicron with their subvariants [13-14].

In view of the reported rapid waning of immune memory with the according reduction of VE, we undertook to assess the risk of infection and overall vaccination effectiveness in the Belgrade city municipality of Voždovac, six months or more after the beginning of vaccination and up to five months after the third dose. In order to do so, we compared the incidence of COVID-19 in vaccinated and unvaccinated persons who received two or three doses in relation to their age. Furthermore, we assessed the comparative effectiveness of the four vaccines available at the time in Serbia in terms of prevention of symptomatic infection.

Methods

Population and Study Design

A retrospective cross-sectional study of the incidence of symptomatic SARS-CoV-2 infection in vaccinated and unvaccinated individuals in the Belgrade city municipality of Voždovac was conducted during a five-month period between November 1st 2021 and March 31st 2022. Data on the Voždovac population were obtained from the Statistical Office of the Republic of Serbia, while vaccination status (total number of vaccinated individuals by type of vaccine and number of doses received) was obtained from the National Registry for Immunization against COVID-19 at the Institute for Public Health of Serbia. Information regarding individuals affected by COVID-19 was collected by reviewing the medical records (database) of the COVID-19 unit at the local community health center (CHC Voždovac); all individuals with polymerase chain reaction-confirmed symptomatic infection were included. Vaccination status and type of vaccine received were ascertained by telephone interview with an epidemiologist (ZK). Only people who received two or three vaccine doses were included in the study. The study coincided with a high prevalence and transmission of SARS-CoV-2 Delta and Omicron variants both globally and locally (in Serbia), although the virus had not been typed for the patients in this study.

Detection of SARS-CoV-2

All individuals presenting at the CHC COVID-19 unit with symptomatic infection were tested for SARS-CoV-2. Nasopharyngeal and buccal swabs were collected and dispatched to the official PCR laboratory at the Institute of Virology, Vaccines and Sera "Torlak", Belgrade. A positive PCR result was considered a confirmation of infection for the purposes of this study.

Statistical Analysis

All analyses were conducted using an electronic database organized in the SPSS statistical software package (version 11.5, SPSS Inc., Chicago, IL, USA). The overall and vaccine-specific risks of infection were calculated by dividing the infection rates among vaccinated persons by the rates among the unvaccinated; the results are presented as odds ratios (OR) with 95% confidence intervals (95% CI). Vaccine effectiveness (VE) against symptomatic disease was calculated according to the formula 1-V/N, where V is the disease incidence in vaccinated persons and N the disease incidence in unvaccinated individuals. For each vaccine, VE was compared between vaccinated and unvaccinated population, as well as among different age groups.

Results

The temporal incidence of COVID-19 and the timeline of vaccination in the Belgrade city municipality of Voždovac are shown in Figure 1. The total population of the Voždovac community at the time of study was estimated at 169,567. Of these, a total of 88,870 individuals have been vaccinated by March 31st 2022 with two or three doses, comprising about a half of the population (52.4%). There was, however, significant variation in vaccination coverage among age groups. The lowest coverage was in children under 17 (2.1%), where only a negligible 0.1% received three doses, and the highest was in the age group of 65-74 (82.0% for two and 65.3% for three doses; Table 1). The percentage of the population vaccinated with two and three doses by age and type of vaccine is presented in Table 2. The majority of those vaccinated with two doses received the BBIBP-CorV vaccine (28.8%), while 14.9% received the BNT162b2 vaccine, 5.8% the Gam-COVID-Vac and 2.7% the ChAdOx1 vaccine. The third dose was received by 13.9% of the total population for BBIBP-CorV vaccine, 14.9% for BNT162b2, 3.1% for the Gam-COVID-Vac, and 0.4% for ChAdOx1 (Table 3). Importantly, none of the individuals vaccinated with any of the vaccines exhibited any side effects other than immediate and transient reactogenicity and no adverse events requiring medical assistance were reported to the relevant national authority (Medicines and Medical Devices Agency of Serbia). Table 4 depicts the incidence of COVID-19 cases by age in the vaccinated and unvaccinated population, respectively. The incidence in the vaccinated population by age and number of doses received is presented in Table 5. The numbers of COVID-19 cases by age among people vaccinated with three doses is given in Table 6.

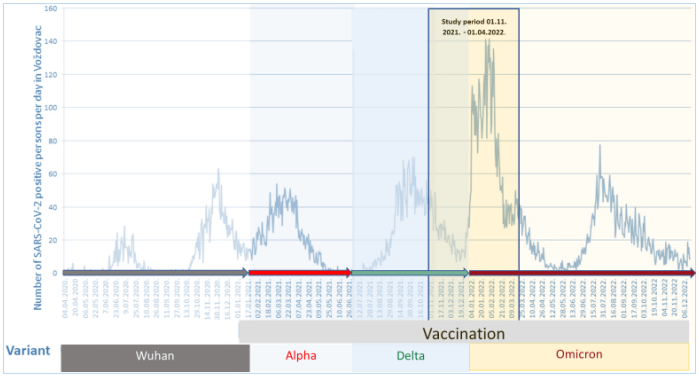

Figure 1: Timeline of the COVID-19 pandemic in the Voždovac municipality. The study period (November 1st, 2021– March 31st, 2022) is highlighted, while the vaccination campaign and the predominant SARS-CoV-2 variant at a given time are indicated below. Daily numbers of SARS-CoV-2-positive persons in Voždovac (from April 2020 through December 2022) are shown as reported by the Institute of Public Health of Serbia (https://covid19.data.gov.rs, accessed on 27 December 2022).

Age	Population	Not vaccinated	Vaccinated		
			2 doses		3 doses
0-17	29380	28761 (97.9%)	619 (2.1%)		21 (0.1%)
18-49	75050	35170 (46.9%)	39880 (53.1%)		19387 (25.8%)
50-64	31677	10312 (32.6%)	21365 (67.4%)		14049 (44.4%)
65-74	20230	3633 (18%)	16597 (82%)		13219 (65.3%)
75+	13230	2821 (21.3%)	10409 (78.7%)		8091 (61.2%)
Total	169597	80697 (47.6%)	88870 (52.4%)		54767 (32.3%)
Total18+	140187	51936 (37.05%)	88251 (63%)		54746 (39.1%)

Table 1: Numbers of vaccinated and unvaccinated persons in different age groups in the population of Voždovac.

Age	Population	BBIBP-CorV	BNT162b2	Gam-COVID-Vac	ChAdOx1 nCoV-19
0-17	29380	0 (0%)	619 (2.1%)	0 (0%)	0 (0%)
18-49	75050	15669 (20.8%)	17043 (22.7%)	4163 (5.9%)	3005 (4%)
50-64	31677	11791 (37.2%)	5165 (16.3%)	3155 (9.9%)	1254 (3.9%)
65-74	20230	12852 (63.5%)	1636 (8.1%)	1844 (9.1%)	265 (1.3%)
75 +	13230	8587 (64.9%)	971 (7.3%)	744 (5.6%)	107 (0.8%)
Total	169597	48899 (28.8%)	25424 (14.9%)	9906 (5.8%)	4631 (2.7%)
Total 18+	140187	48899 (34,8%)	24815 (28.1%)	9906 (11.1%)	4631(5.2%)

Table 2: Absolute and relative numbers of people vaccinated against COVID-19 in different age groups by type of vaccine.

Age	Population	BBIBP-CorV	BNT162b2	Gam-COVID-Vac	ChAdOx1 nCoV-19
0-17	29380	0 (0%)	21 (0.1%)	0 (0%)	0 (0%)
18-49	75050	4904 (6.5%)	12434 (16.6%)	1637 (2.2%)	412 (0.5%)
50-64	31677	5642 (17.8%)	6429 (20.3%)	1749 (5.5%)	229 (0.7%)
65-74	20230	7650 (37.8%)	4210 (20.8%)	1308 (6.5%)	51 (0.3%)
75 +	13230	5295 (40%)	2230 (16.9%)	546 (4.1%)	20 (0.2%)
Total	169597	23491 (13.9%)	25324 (14.9%)	5240 (3.1%)	712 (0.4%)
Total 18+	140187	23491 (16.8%)	25303 (18%)	5240 (3.7%)	712 (0.5%)

Table 3: Number and percentage of people who received the third COVID-19 vaccine dose by age and type of vaccine.

Age	Cases	Per 1000 people
0-17	78	2.7
18-49	655	18.6
50-64	190	18.4
65-74	41	11.3
75+	43	15.2
Total	1007	12.5
Total 18+	929	17.9

Table 4: Numbers of COVID-19 cases in the unvaccinated population by age group.

Age	2 or 3 doses		2 doses		3 doses	
	Cases	Per 1000 people	Cases	Per 1000 people	Cases	Per 1000 people
0-17	0	0	0	0	0	0
18-49	633	15.9	378	18.4	255	13.2
50-64	300	14	122	16.7	178	12.7
65-74	191	11.5	45	13.3	146	11
75 $^{+}$	73	7	16	6.9	57	7
Total	1197	13.5	561	16.5	636	11.6
Total 18^{+}	1197	13.6	561	16.7	636	11.6

Table 5: Numbers of COVID-19 cases in the vaccinated population by age group.

Age	BBIBP-CorV	BNT162b2	Gam-COVID-Vac	ChAdOx1 nCoV-19
0-17	0	0	0	0
18-49	88	138	22	7
50-64	85	67	22	4
65-74	91	45	9	1
75 $^{+}$	41	12	3	1
Total	305	262	56	13
Total 18^{+}	305	262	56	13

Table 6: Numbers of Covid-19 cases in different age groups in people vaccinated with three doses by type of vaccine.

The overall relative risk (RR) of infection in recipients of two doses compared to the unvaccinated population was 0.93 (95% CI: 0.88-0.99), while the overall VE was 7%. By age group, the relative risk was statistically significant for people over 75 (0.45; 95% CI: 0,34-061), corresponding to a VE of 55% (Table 7). There was no statistical significance for other age groups. Those vaccinated with three doses had an RR vs. the unvaccinated of 0.65 (95% CI: 0.61-0.69), with a VE of 35%. Analysed according to age group, the relative risk decreased from 0.71 in the 18-49 group, through 0.69 in the 50-64 group, to 0.46 in people above 75, corresponding to the VE of 29%, 31% and 54%, respectively. Comparing people vaccinated with three doses with those who received two doses, RR was 0.69 (95% CI: 0.64-0.75), with a VE of 31%. A statistically significant difference in the risk of disease was found in the age groups 18-49 (RR 0.72; 95% CI: 065-0.79; VE 28%) and 50-64 (RR 0.76; 95% CI: 0.64-091; VE 24%). Table 8 shows RR and VE by age and vaccine type for the population vaccinated with three doses compared to those who did not receive the third dose. The highest overall effectiveness was achieved by the BNT162b2 vaccine (42%; 95% CI: 38-45%) and the lowest with BBIBP-CorV (27%; 95% CI: 23-32%), while the VE of Gam-COVID-Vac was in the middle (40%; 95% CI: 36-44%). The AstraZeneca ChAdOx1 vaccine could not be statistically evaluated in this context due to the small number of persons who received three doses of this vaccine. Importantly, the VE of all vaccines depended on the age group observed. For instance, although the overall effectiveness of BBIBP-CorV was 27%, it was only 18% effective in the age group 50-64, but as much as 49% in people over 75. The effectiveness of BNT162b2 was not significant in persons aged 65-74, while in the other age groups it varied between 40% and 64%, increasing with the age of the vaccines. The vector vaccine Gam-COVID-Vac yielded a similar a pattern, from its minimal VE of 28% in the youngest population (18-49) to the maximal VE of 64% in people over 75.

	2 doses vs. unvaccinated		3 doses vs. unvaccinated		3 vs. 2 doses	
Age	**RR (95% CI)**	**VE %**	**RR (95% CI)**	**VE %**	**RR (95% CI)**	**VE %**
18-49	0.99 (0.92 – 1.07)	1	0.71 (0.66 – 0.77)*	29*	0.72 (0.65 – 0.79)*	28*
50-64	0.91 (0.79 – 1.04)	9	0.69 (0.60 – 0.79)*	31*	0.76 (0.64 – 0.91)*	24*
65-74	1.18 (0.87 – 1.60)	-18	0.97 (0.72 – 1.32)	3	0.83 (0.62 – 1.11)	17
75 +	0.45 (0.34 – 0.61)*	55*	0.46 (0.34 – 0.62)*	54*	1.01 (0.62 – 1.65)	-1
Total 18+	0.93 (0.88 – 0.99)*	7*	0.65 (0.61 – 0.69)*	35*	0.69 (0.64 – 0.75)*	31*
*Statistically significant at p<0.05						

Table 7: COVID-19 vaccine effectiveness in different age groups by number of doses.

	BBIBP-CorV		BNT162b2		Gam-COVID-Vac		ChAdOx1 nCoV-19	
Age	**RR (95% CI)**	**VE %**	**RR (95% CI)**	**VE %**	**RR (95% CI)**	**VE %**	**RR (95% CI)**	**VE %**
18-49	0.96 (0.89 – 1.04)	4	0.60 (0.55 – 0.64)*	40*	0.72 (0.67 – 0.78)*	28*	0.91 (0.85 – 0.99)*	9*
50-64	0.82 (0.71 – 0.94)*	18*	0.57 (0.49 – 0.65)*	43*	0.68 (0.59 – 0.79)*	32*	0.95 (0.83 – 1.09)	5
65-74	1.05 (0.78 – 1.43)	-5	0.95 (0.70 – 1.28)	5	0.61 (0.45 – 0.83)*	39*	1.73 (1.28 – 2.35)*	-73*
75 +	0.51 (0.38 – 0.68)*	49*	0.36 (0.26 – 0.48)*	64*	0.36 (0.27 – 0.49)*	64*	3.29 (2.45 – 4.43)*	-229*
Total 18+	0.73 (0.68 – 0.77)*	27*	0.58 (0.55 – 0.62)*	42*	0.60 (0.56 – 0.64)*	40*	1.02 (0.96 – 1.09)	-2
* Statistically significant at p<0.05								

Table 8: Vaccine effectiveness (by type of vaccine) in different age groups in people who received three COVID-19 vaccine doses as compared to those who did not receive the third dose.

Discussion

Vaccine development has endowed humankind with an invaluable tool to protect lives and wellbeing in the recent COVID-19 pandemic. Vaccines have successfully reduced the rates of symptomatic infection, hospitalization and mortality in various populations and clinical settings [15,16]. However, measured VE displayed considerable variation, particularly after the onslaught of novel SARS-CoV-2 variants, and investigations of VE in different real-life circumstances could be crucial for appropriate vaccination policy against this still evolving virus, as well as for the timely response to future pandemics, including those potentially brought about by as yet unknown pathogens ("disease X") [17,18]. The Belgrade municipality of Voždovac may be considered a reasonable testbed for investigating VE, given that its demographic structure is roughly representative of urban communities in Serbia and that overall COVID-19 vaccination coverage in this municipality (52.4%) was very close to the national average. For the investigated period, we found a very modest VE against symptomatic infection (in aggregate, 7% for two doses and 35% for three doses), much below the value typically found in real-world studies [19]. However, at least six months had elapsed since the second dose, and the limited VE is likely to be due to the expected waning of the humoral immune response against SARS-CoV-2 with time [20-22], since neutralizing anti-SARS-CoV-2 antibodies prevent virus from entering into host cells [23] and thus alone may block the infection prior to appearance of any symptoms. Unfortunately, we were not able to obtain data on VE against hospitalization and death for the same time period in the same population. The latter would arguably be more appropriate outcome measures, considering a somewhat greater durability of the cellular immune response compared to the humoral [24]. The latter takes more time to mobilize, exerts its protective effects only after the virus has entered host cells, and is therefore thought to affect general disease outcome much more than the likelihood of appearance of symptoms *per se.*

The measured VE in our observed population increased with age. Indeed, after receiving only two vaccine doses, it turned out to be significant only in people over 75 (55%). After three doses, VE was 29% in the group aged 18-49, 31% in the 50-64 group, insignificant in the 65-74 group, and 54% in those over 75, virtually coinciding with VE after two doses for this age group. This evidence of a considerable protective effect in the elderly, even after six months,

arguably represents the most significant finding of our study, given that people of advanced age have been shown early in the pandemic to be particularly vulnerable to harmful consequences of COVID-19 [25] and subsequently confirmed to benefit extensively from vaccination [26]. It is therefore encouraging to find that the protection in this population appears to have held even after it had waned in other age groups. However, differential exposure of the elderly population to SARS-CoV-2 may have also played a role in this result, since it is plausible to assume that elderly citizens who accepted the recommendation to get vaccinated exhibited less pandemic-related paranoid ideation and therefore also largely accepted to wear protective masks, limit interpersonal contacts and avoid mass gatherings [27].

The VE measured after three vaccine doses also exhibited marked differences according to the type of vaccine, ranging from 27% for BBIBP-CorV to 40% for Gam-COVID-Vac and 42% for BNT162b2 (VE for ChAdOx1 could not be evaluated due to insufficient subsample size). While this direct comparison of effectiveness of vaccines built upon three different platforms (conventional inactivated, RNA-, and vector-based) may also be considered an important strength of our study, relating its results to those obtained in other real-world studies remains a challenge due to a number of factors [28]. Foremost among the latter are constant shifting of predominant viral variants, possible variation in spatiotemporal distrubution of risk factors in respective populations, and a dynamic relationship between ongoing viral evolution and the state of collective immunity. Still, our results are consistent with those of a number of studies attesting to a superior VE of RNA- and/or vector- based vaccines over vaccines with a conventional inactivated virus design, including those from Hong Kong [29], Buenos Aires [30] and Colombia [31], as well as an extensive meta-analysis of a plethora of other studies [32]. Our results are also, in a way, complementary to literature data attesting that all vaccines against COVID-19 showed considerable effectiveness against symptomatic infection up to six months after the second dose [33].

In this light, VE we found after three vaccine doses primarily reflects the well-documented boosting effect [34], coupled with the fact that humoral immune response had not yet had the time to massively wane following the third dose [21]. By the same token, relatively poor protection after two doses can be explained by the combination of waning of immunity with time and the predominance of the then novel Delta variant of SARS-CoV-2 at the time of study, partially bypassing the immune memory elicited by earlier infection or vaccination [35], a phenomenon later found to be even more pronounced after the emergence of the Omicron variant [36]. Since both processes appear to affect humoral immunity more than cellular, one could expect a more solid protection against severe or life-threatening consequences of SARS-CoV-2 infection [37-39] – something that we, again, were unfortunately unable to assess in this study. However, in nearby Hungary, Vokó and collaborators, whose results regarding symptomatic infection are very similar to ours, indeed found more solid and durable protection against lethal outcome of COVID-19 [40].

The downward temporal trend in VE against symptomatic infection can be easily traced by comparing our results with those of studies pertaining to earlier time periods in the course of the global vaccination campaign: the study of Petrović et al. [5], covering the initial four months, and that by Kokić, Kon and Djurković-Djaković [4], conducted from six to eleven months after the onset of COVID-19 vaccination. In this light, our data may be considered a natural extension of data gathered in the latter two studies, offering further insight into the dynamics of post-vaccinal immunity to SARS-CoV-2. In summary, we appear to have found both evidence of limited duration of immunity acquired by vaccination against COVID-19 against symptomatic infection and an attestment that, at least in the most vulnerable age group, a significant level of protection may still linger beyond six months after the primary vaccine series.

Conclusion

The results of this study demonstrate a significant overall effectiveness of vaccination against symptomatic COVID-19 infection in people over 75 years of age six months or more after the second dose, as well as a significant protection in most age groups up to five months after the third dose. Vaccination effectiveness also varied considerably by type of vaccine and was the highest for BNT162b2, closely followed by Gam-COVID-Vac. However, further research is needed to better understand the long-term effectiveness of different vaccine types, as well as to assess potential variations in protection across different populations and emerging variants.

Ethics Statement and Conflict of Interest

This study was approved by the Institutional Review Board of the Community Health Center Voždovac. The authors declare no conflict of interest.

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