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# Vaccination coverage and its association with COVID-19 morbidity and mortality in Primorje-Gorski Kotar County: a retrospective study

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## Abstract

**Introduction**. The COVID-19 pandemic remains a global challenge despite extensive vaccination efforts. Although vaccination coverage has increased, coverage varies by population group, affecting hospitalization and mortality rates. Understanding the distribution of immunization coverage and its association with severe disease outcomes is essential for public health planning.

**Aim.** To analyze the association between COVID-19 vaccination status, hospitalizations and mortality among adult residents of Primorje-Gorski Kotar County admitted to the Rijeka Clinical Hospital Center. Specific objectives included assessing the distribution of vaccinations by gender and age, the proportion of vaccinated persons among hospitalized patients and the proportion of vaccinated persons among those who died from COVID-19 between December 27, 2020 and March 27, 2022.

**Methods.** This retrospective study included 6,025 adult patients admitted with a confirmed COVID-19 diagnosis (ICD-10 code U07.1: COVID-19, virus identified). The data were obtained from the Integrated Hospital System of the Clinical Hospital Center Rijeka and the Croatian Institute of Public Health.

**Results.** Among hospitalized patients, men accounted for 57.8% of cases. Vaccination coverage was higher in persons aged ≥65 years than in younger patients. Unvaccinated patients were hospitalized more frequently (50.19%) than vaccinated patients (44.9%). Mortality was significantly higher in unvac-

cinated patients (1.36%) than in vaccinated patients (0.2%). The statistical analysis confirmed a significant correlation between vaccination status, hospitalization and mortality.

**Conclusion.** The results suggest that vaccination coverage was higher in individuals aged ≥65 years, while hospitalization and mortality rates were higher in unvaccinated patients. A statistically significant association was found between vaccination status and severe COVID-19 outcomes; however, causality cannot be established. Public health efforts should focus on maintaining high vaccination coverage, counteracting vaccination fatigue and ensuring access to booster vaccinations, especially for high-risk groups.

## Introduction

On January 30, 2020, the World Health Organization (WHO) declared the outbreak of COVID-19 an international health emergency. Just weeks later, on March 11, 2020, it was officially classified as a global pandemic. COVID-19, which stands for coronavirus disease 2019, is caused by the novel virus SARS-CoV-2 (1). Due to its high transmissibility and the lack of prior immunity in the population, the virus spread rapidly worldwide.

Those at highest risk of severe COVID-19 disease requiring hospitalization or intensive care include older adults, men and people with pre-existing conditions such as obesity, hypertension or diabetes (2). Croatia took early public health measures to bring the outbreak under control; the first confirmed case was reported on February 25, 2020. The nationwide vaccination campaign started at the end of December 2020, and by March 2022, over 60% of the Croatian population was fully vaccinated, with similar vaccination trends in Primorje-Gorski Kotar County (3, 4).

The first COVID-19 vaccine administered outside of a clinical trial was given on December 8, 2020. To ensure global vaccine equity, initiatives such as COVID-19 Vaccine Global Access (COVAX) and the WHO have set targets for distributing vaccines to low- and middle-income countries (5, 6). Despite these efforts, vaccine distribution remains uneven and vaccine hesitancy continues to pose a significant global challenge (7).

While COVID-19 vaccination has been associated with a decrease in severe disease and mortality, vaccination coverage varies by demographic and socioeconomic group, influencing morbidity and mortality trends (8-11). Regional differences in immunization coverage and their impact on severe disease remain critical for public health planning and resource allocation.

## Aim

The aim of this study was to analyze vaccination coverage in Primorje-Gorski Kotar County and its association with COVID-19 morbidity and mortality. In particular, the study examined the distribution of vaccinations by gender and age, the proportion of vaccinated persons among admitted patients and the proportion of vaccinated persons among patients who died of COVID-19 at the Clinical Hospital Center Rijeka. Understanding these patterns provides valuable insights into how vaccination status relates to hospitalization and mortality, thus contributing to public health strategies aimed at improving vaccination coverage and reducing the burden of COVID-19, especially in high-risk groups.

## Methods

### Participants and characteristics of the sample

This retrospective study included all adult residents of Primorje-Gorski Kotar County who were admitted to the Clinical Hospital Center Rijeka between December 27, 2020 and March 27, 2022 with the diagnosis 'U07.1 COVID-19, virus identified' The total

sample included 6,025 participants, representing the entire population of COVID-19 patients admitted to the hospital during the study period.

## Data collection

Data were collected from the integrated hospital information system of the Clinical Hospital Center Rijeka via the centralized emergency department. Information retrieved included patient demographics, COVID-19 test results, place of residence, hospitalization details and disease outcome (cure or death). Additional vaccination data were obtained from publicly available records from the Croatian Institute of Public Health, covering the same period as the hospital data.

Patients were categorized as unvaccinated or vaccinated based on their vaccination status, regardless of the number of vaccine doses received.

## Ethics

This study complied with the ethical principles of biomedical research as laid down in the Declaration of Helsinki. The Ethics Committee of the Clinical Hospital Center Rijeka granted ethical approval on June 27, 2022 (Class: 003-05/22-1/58; No.: 2170-29-02/1-22-2). The Ethics Committee ensures compliance with medical ethics and deontology and approves the scientific research conducted at the Clinical Hospital Center Rijeka. All data were anonymized to protect the confidentiality of the participants and did not contain any personal identifiers (e.g. names, dates of birth or addresses).

## Statistics

Descriptive and inferential statistical methods were used to analyze the data. The descriptive statistics included absolute and relative frequencies for categorical variables as well as mean and standard deviation for continuous variables.

For inferential analysis, chi-square tests ($\chi^2$ test) were used to assess associations between categorical variables, including gender, age, vaccination status, hospitalization, and mortality. Independent-samples t-tests were performed to compare age differences between groups (e.g., vaccinated vs. not vaccinated, recovered vs. deceased).

All statistical analyzes were performed using SPSS software (version 20.0; SPSS Inc., Chicago, IL, USA). Statistical significance was set at $p<0.05$.

# Results

A total of 6,025 participants from Primorje-Gorski Kotar County who were admitted to hospital between December 27, 2020 and March 27, 2022 with the diagnosis 'U07.1 COVID-19, virus identified' were included in the study. The majority of patients were men, and a chi-square test confirmed that their proportion was statistically significantly higher than that of women ($\chi^2$= 146.34, df=1, $p<0.0001$). Additionally, the average age of female patients was significantly higher than that of male patients (t=-12.74, $p<0.001$) (Table 1). The largest proportion of participants belonged to the 65-74 age group (28.6%), followed by the 75-84 age group (25.8%). Overall, more than two thirds (68.3%) of the patients admitted were aged 65 or older.

Table 1. **Descriptive statistics on gender**

| Gender | Frequency | Percentage (%) | Mean age | Standard Deviation (Age) |
|---|---|---|---|---|
| Male | 3,482 | 57.8 | 68.00 | 14.07 |
| Female | 2,543 | 42.2 | 71.85 | 14.89 |
| **Total** | **6,025** | **100.0** | **69.62** | **14.55** |

## Hospitalization status

Of the total number of participants, the majority required hospitalization, while a smaller group was discharged for home treatment as their condition did not require hospitalization. A t-test confirmed a statistically significant age difference between these groups, with the hospitalized patients having a higher mean age (t=2.14, $p$=0.032) (Table 2).

Table 2. **Hospitalization statistics**

| Hospitalization Status | Frequency | Percentage (%) | Mean age | Standard Deviation (Age) |
|---|---|---|---|---|
| Hospitalized | 5,729 | 95.1 | 69.69 | 14.55 |
| Not Hospitalized | 296 | 4.9 | 68.23 | 14.31 |
| **Total** | **6,025** | **100.0** | **69.62** | **14.55** |

## Results of the treatment

The mean age of the deceased patients (82.03 years, SD=7.75) was significantly higher than that of the recovered patients (69.42 years, SD=14.54), a difference that was confirmed by a t-test (t=7.89, $p<0.001$) (Table 3).

Table 3. **Treatment outcomes**

| Treatment Outcome | Frequency | Percentage (%) | Mean Age | Standard Deviation (Age) |
|---|---|---|---|---|
| Fatal | 94 | 1.6 | 82.03 | 7.75 |
| Recovered | 5,931 | 98.4 | 69.42 | 14.54 |
| **Total** | **6,025** | **100.0** | **69.62** | **14.55** |

## Vaccination status

A larger proportion of admitted patients were unvaccinated (53.5%) compared to vaccinated persons (46.5%). A chi-square test confirmed that unvaccinated individuals were significantly more likely to be hospitalized ($\chi^2$=3441.83, df=1, $p<0.0001$) (Table 4). A t-test confirmed that vaccinated individuals were significantly older than unvaccinated individuals (t=4.55, $p<0.001$), further supporting the trend that vaccination rates increase with age, although the age difference between the two groups was very small.

Table 4. **Vaccination status**

| Vaccination Status | Frequency | Percentage (%) | Mean Age | Standard Deviation (Age) |
|---|---|---|---|---|
| Vaccinated | 2,799 | 46.5 | 69.99 | 13.28 |
| Unvaccinated | 3,226 | 53.5 | 69.30 | 15.55 |
| **Total** | **6,025** | **100.0** | **69.62** | **14.55** |

## Vaccination by gender

A statistically significant difference in vaccination rates between men and women was found ($\chi^2$=13.940, df=1, $p<0.05$). More men than women were vaccinated, both in absolute numbers and as a proportion of their gender group (48.4% of men vs. 43.7% of women) (Table 5).

Table 5. **Vaccination by gender**

| Gender | Vaccinated (n, %) | Unvaccinated (n, %) | Total (n, %) |
|---|---|---|---|
| Male | 1,687 (60.3%) | 1,795 (55.6%) | 3,482 (57.8%) |
| Female | 1,112 (39.7%) | 1,431 (44.4%) | 2,543 (42.2%) |
| **Total** | **2,799 (100%)** | **3,226 (100%)** | **6,025 (100%)** |

## Vaccination and fatal outcomes

A statistically significant association was found between vaccination status and fatal outcomes ($\chi^2$=43.573, df=1, $p<0.05$). Among hospitalizations, unvaccinated patients had a significantly higher mortality rate (1.36%) than vaccinated patients (0.24%), indicating a lower risk of fatal outcomes in vaccinated individuals (Table 6).

Table 6. **Fatal outcomes and vaccination**

| Vaccination Status | Fatal Outcome (n, %) | Survived (n, %) | Total (n, %) |
|---|---|---|---|
| Vaccinated | 3 (0.24%) | 1,254 (99.76%) | 1,257 (100%) |
| Unvaccinated | 22 (1.36%) | 1,597 (98.64%) | 1,619 (100%) |
| **Total** | **25 (100%)** | **2,851 (100%)** | **5,729 (100%)** |

## Discussion

Our study included 6,025 hospitalized COVID-19 patients from Primorje-Gorski Kotar County, 57.8% of whom were men. This is in line with previous research indicating that men are disproportionately affected by severe COVID-19 cases worldwide (12, 13). Biological and immunological factors may contribute to this difference, including a weaker initial immune response and higher levels of angiotensin-converting enzyme 2 (ACE2) receptors in men, which facilitate viral entry into cells (14, 15). Studies from China and Europe have come to similar conclusions, emphasizing the role of gender-specific immunological differences in disease severity (16, 17).

The mean age of hospitalized patients was 69.62 years, and 68.25% were ≥65 years old, confirming the known association between older age and severe COVID-19 disease. Similar trends have been observed worldwide, where older populations consistently have higher hospitalization and mortality rates compared to younger populations (16-19). This pattern is largely attributed to the age-related decline of the immune system (immunosenescence), multimorbidity and reduced physiological resilience (17, 18).

In our study, hospitalization rates were higher in unvaccinated individuals (55.1%) than in vaccinated individuals (44.9%), supporting the growing body of evidence that vaccination significantly reduces the risk of severe disease. This finding is consistent with studies from Germany and the UK, which consistently report lower hospitalization rates in vaccinated individuals (20-22). The effect of vaccination on reducing the hospital burden has been widely documented, with studies highlighting that in countries with high vaccination rates, the number of hospital admissions during COVID-19 waves was lower (21, 22).

In addition, the mortality rate was significantly lower in vaccinated patients (0.2%) than in unvaccinated patients (1.36%), underlining the protective role of COVID-19 vaccines against severe outcomes. Studies from North America and Europe consistently show that COVID-19-related deaths occur predominantly in unvaccinated individuals (20-22). In Pennsylvania, for example, 97% of COVID-19-related deaths were reported in unvaccinated or partially vaccinated individuals, underscoring the critical importance of vaccination in reducing mortality (23). In Croatia, the introduction of vaccines led to a drastic decrease in the national COVID-19 mortality rate from 1.79% before vaccination to 0.01% during the study period (24), reflecting similar trends observed worldwide.

In terms of gender-specific vaccination patterns, the absolute number of vaccinated men was higher than that of vaccinated women. This result is consistent with several international studies that have found lower vaccination rates among women (25-27). Various factors may contribute to this difference, including cultural and occupational influences, access to healthcare and differences in risk perception. However, other studies suggest the opposite trend, with women in certain contexts showing higher health awareness and willingness to be vaccinated (25–27), suggesting that gender differences in vaccination rates are context-dependent and may vary by region and population.

In addition, vaccination rates were significantly higher in people aged ≥65 years than in younger age groups, which is consistent with global trends (28-31). This pattern is likely influenced by early strategies to prioritize vaccines for older adults as well as higher perceived risk in older populations (29-31). Studies from Canada and Australia have shown that older adults are more likely to adhere to public health measures and immunization campaigns, contributing to higher vaccination rates in this group (28-31).

Our results confirm that unvaccinated individuals were disproportionately represented among COVID-19-related deaths during hospitalization. Similar results have been observed in several studies showing that mortality rates remain significantly higher in unvaccinated populations (20-22). European and North American data support the critical role of COVID-19 vaccination in preventing deaths, particularly in high-risk groups (20-22).

## Study limitations

This study provides important insights into the association between vaccination status and severe COVID-19 disease in a specific population. By analyzing admitted patients in a specific region, we were able to assess real trends in hospitalizations and mortality in vaccinated and unvaccinated individuals.

However, several limitations should be noted. First, since this is a retrospective observational study, no causal relationships cannot be established. The observed differences in hospitalizations and mortality may have been influenced by unmeasured confounders, such as pre-existing conditions, socioeconomic status, unequal access to healthcare, and behavioral factors.

Second, this study did not account for differences in vaccine types, dosing regimens, or booster doses that may have influenced the immunity levels of vaccinated individuals. In addition, data on previous SARS-CoV-2 infections were missing, meaning that some unvaccinated individuals may have had natural immunity, potentially affecting hospitalization and mortality rates.

Finally, our results refer only to the patients admitted to the hospital and cannot be generalized to the entire population of Primorje-Gorski Kotar County or Croatia. Future research should include longitudinal studies and multivariable models to better understand the long-term effects of vaccination and the impact of booster vaccinations. Further research on comorbidities, socioeconomic variables and access to healthcare would provide a more comprehensive understanding of factors contributing to hospitalization and mortality risk.

## Conclusion

This study examined the association between COVID-19 vaccination status and hospitalization and mortality rates in patients admitted to the Rijeka Clinical Hospital Center. The results indicate that unvaccinated individuals were significantly more likely to experience hospitalization and death due to COVID-19 compared to vaccinated individuals. Furthermore, vaccination rates were significantly higher in people aged ≥65 years, in contrast to younger age groups. Additionally, a statistically significant gender difference in vaccination coverage was found.

While these results confirm that vaccination is associated with lower hospitalization and mortality rates, further research is needed to investigate additional factors that influence the incidence of severe disease, such as comorbidities, vaccine type and the effect of booster doses.

Public health strategies should continue to monitor vaccination trends, combat vaccine hesitancy and ensure equitable distribution of vaccines, particularly for high-risk groups. Future studies should focus on longitudinal analyzes to assess the durability and efficacy of vaccines, especially against emerging SARS-CoV-2 variants.

## Author contributions

Conceptualization (KI, KV); Data Curation (KV, SV); Formal Analysis (KV, SV); Writing – Original Draft (KI, KV, SV); Writing – Review & Editing (KI, KV, SV). All authors have approved the final manuscript.

## Conflict of interest

The authors declare no conflicts of interest.

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