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Investigation of the Association Between COVID-19 and Hepatitis B Vaccination Among Healthcare Workers: A Cross-Sectional Study in Turkey

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Abstract

Backgrounds: *Vaccination is a cornerstone of public health. While COVID-19 vaccination became globally prioritized during the pandemic, Hepatitis B immunization has remained a mandatory occupational requirement in Turkey, particularly among healthcare workers (HCWs). This study evaluated Hepatitis B immunization and factors associated with COVID-19 vaccination among Turkish HCWs.* **Methods:** *A retrospective cross-sectional study was conducted between February 1 and August 15, 2024, at Mersin City Training and Research Hospital. Employees and trainee students who underwent periodic health examinations were included. Participants were grouped as physicians, non-physician HCWs, and non-healthcare professionals. Data included demographics, vaccination history, hematological and biochemical parameters, and clinical characteristics. Logistic regression identified factors associated with COVID-19 vaccination status.* **Results:** *Of 4,048 participants, 92.1% received at least one COVID-19 vaccine dose and 90.0% were vaccinated against Hepatitis B. Physicians demonstrated the highest coverage for both vaccines. Male gender (OR=1.37, 95% CI: 1.04–1.80), non-physician HCW status (OR=2.51, 95% CI: 1.33–4.75), non-healthcare professional status (OR=2.99, 95% CI: 1.55–5.77), and behaviorally linked elevated platelet count (OR=1.54, 95% CI: 1.04–2.28) were independently associated with COVID-19 non-vaccination. A prior history of Hepatitis B vaccination showed a strong protective effect against COVID-19 non-vaccination (OR=0.30, 95% CI: 0.23–0.40).* **Conclusions:** *Vaccine uptake varied across occupational groups, with physicians achieving the highest rates. Prior compliance with mandatory Hepatitis B vaccination was positively associated with COVID-19 vaccine acceptance, emphasizing the role of previous immunization behavior in new vaccine adoption. Occupational health policies integrating vaccination counseling and follow-up are essential to improve coverage among non-physician HCWs.*

1. Introduction

Vaccination remains one of the most effective public health strategies, preventing morbidity and mortality from infectious diseases worldwide. Among healthcare workers (HCWs), immunization is both a personal health measure and a professional obligation to protect patients and the community. The Hepatitis B vaccine has long been recommended for HCWs because of increased exposure to blood- borne pathogens [1, 2]. In Turkey, a nationwide Hepatitis B

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vaccination program was introduced in 1998 as part of the National Immunization Plan, and HCWs are required to demonstrate serologic protection or receive booster doses during periodic occupational health surveillance [3-5]. The COVID- 19 pandemic underscored the urgent need for widespread vaccination in both the general population and frontline professionals [6-8].

Although both vaccines are integral to occupational and public health, comparative studies of Hepatitis B and COVID-19 uptake among HCWs are limited. Most available research examines Hepatitis B vaccination [9-11] or COVID-19 vaccine acceptance [12-15] separately, without cross- vaccine evaluation. Disparities in coverage often stem from hesitancy, accessibility, awareness, and risk perception [16, 17]. Furthermore, differences in vaccine uptake may reflect behavioral, institutional, and perceptual factors that influence compliance with immunization programs [10, 18, 19]. The COVID-19 pandemic also reshaped attitudes toward immunization, providing an opportunity to investigate whether historical vaccination patterns influence acceptance of novel vaccines [20-22].

In this context, the present study was designed to test the hypothesis that healthcare workers with a prior history of Hepatitis B vaccination would be more likely to accept COVID-19 vaccination. By exploring this relationship, we aimed to determine whether prior compliance with a long- established occupational immunization program (HBV) could predict COVID-19 vaccine acceptance. Although HBV vaccination is included in the Turkish National Immunization Plan, real-world coverage and antibody protection among HCWs may vary by occupational experience, training level, and perceived risk. Understanding these variations has both clinical and policy relevance for improving compliance with mandatory immunization programs [23-26].

In Turkey, data comparing vaccination uptake between physician and non-physician HCWs, as well as non-healthcare staff, remain scarce. This study aimed to evaluate both Hepatitis B and COVID-19 vaccination status simultaneously in Turkish HCWs, assess vaccination rates for both Hepatitis B and COVID-19, identify occupational and demographic disparities, and determine clinical and laboratory correlates of COVID-19 vaccine non-uptake.

2. Methods

Between February 1 and August 15, 2024, all hospital employees (physicians, nurses, paramedics, radiation workers, office staff, administrative and accounting personnel) and trainee students (nursing, physiotherapy, medical secretaryship, radiology technology) who presented for periodic health examinations at the Occupational Health and Safety Unit of Mersin City Training and Research Hospital were eligible. Inclusion required completion of screening tests and examination forms. Exclusion applied to those who did not complete the required assessments. Of the 4,230 employees working at the institution during the study period, 4,048 met the inclusion criteria and were enrolled, yielding a participation rate of 95.7%.

Occupational categories were defined in detail to ensure reproducibility: physicians included medical doctors and dentists; non-physician healthcare workers comprised nurses, paramedics, laboratory and radiology technicians, physiotherapists, and trainee healthcare students; non-healthcare professionals included administrative, accounting, technical, and support personnel.

This retrospective cross-sectional study used data from examination forms and electronic medical records. Variables included age, gender, occupation, COVID-19 vaccination status (dose number, type: CoronaVac® [31], Comirnaty® [32]), prior COVID-19 infection, Hepatitis B vaccination status, hematological parameters (Hb, WBC, lymphocytes, neutrophils, platelets), and biochemical parameters (creatinine, urea, AST, ALT). Blood samples were collected after ≥8 hours of fasting. Laboratory parameters were classified according to institutional reference ranges (Mersin City Training and Research Hospital Central Laboratory, 2024): hemoglobin 12.0–16.0 g/dL, leukocytes 4.0–10.0 × 10^9/L, neutrophils 2.0–7.5 × 10^9/L,

lymphocytes 1.0–4.0 × 10^9/L, platelets 150–450 × 10^9/L, ALT 0–41 U/L, AST 0–40 U/L, urea 15–45 mg/dL, creatinine 0.5–1.2 mg/dL, and eGFR ≥ 60 mL/min/1.73 m^2 considered normal. Values outside these ranges were defined as abnormal. Abnormal laboratory values were determined using reference standards. eGFR was calculated using the 2021 CKD-EPI equation [33], with <60 mL/min/1.73 m^2 considered reduced. Occupations were categorized as physicians, non-physician HCWs, and non-healthcare professionals.

According to institutional occupational health policy, HCWs who were non-responders to the Hepatitis B vaccine were offered a full revaccination course and antibody re-testing. For COVID-19, vaccination was strongly recommended but not mandatory; unvaccinated employees were required to sign an informed refusal form and could continue working in compliance with infection control measures.

Normality of numerical variables was assessed with the Kolmogorov-Smirnov test. Data were expressed as medians (IQR) or counts (%). Comparisons by COVID-19 vaccination status used the Mann-Whitney U test (numerical) and Chi-square/Fisher's exact tests (categorical). Logistic regression identified independent predictors of COVID-19 vaccination status, with ORs and 95% CIs reported. Significance was set at $p<0.05$. Analyses were performed using IBM SPSS v21.0 (IBM Corp., Armonk, NY, USA).

Ethics approval was granted by the Mersin University Non-Interventional Clinical Research Ethics Committee (23.10.2024, no. 2024/979). The study complied with the Declaration of Helsinki. Informed consent was waived due to its retrospective nature.

3. Results

3.1. Participant Characteristics

Of 4,048 individuals, 70.3% were female, with a median age of 30 years (IQR 22–42). Chronic diseases were reported by 7.8%. Elevated leukocyte and platelet counts were found in 17.9% and 7.3% of participants, respectively. These values were defined according to institutional reference ranges (leukocytes >10×10^9/L; platelets >450×10^9/L). Among the total institutional workforce of 4,230 employees, the participation rate was 95.7%, indicating strong representativeness of the hospital population. Detailed demographic, occupational, and laboratory characteristics are provided in Table 1, which has been reorganized to improve readability and grouped by variable type (demographic, clinical, laboratory).

3.2. Vaccination Status

Overall, 92.1% received ≥1 COVID-19 vaccine dose, and 90.0% were Hepatitis B vaccinated. Physicians exhibited the highest coverage for both vaccines (COVID-19: 97.7%), followed by non-physician HCWs (91.3%) and non-healthcare professionals (91.8%) . Across all groups, COVID-19 vaccination rates exceeded Hepatitis B rates (Figure 1).

3.3. Comparison by COVID-19 Vaccination

Unvaccinated participants were significantly younger (median 21 vs. 30 years, $p<0.001$), more likely male, less often physicians ($p<0.001$), and had lower Hepatitis B vaccination rates (71.4% vs. 91.6%, $p<0.001$). High platelet counts (11.0% vs. 7.0%, $p=0.019$) and low hemoglobin (21.4% vs. 5.8%, $p=0.017$) were more frequent among unvaccinated individuals (Table 2).

In addition, a subgroup analysis was performed for healthcare workers who were unvaccinated for both COVID-19 and Hepatitis B (n=91, 2.2%). Compared with all other participants, this group was significantly younger (median 21 years, IQR 16–24 vs. 30 years, IQR 15–68; $p<0.001$, Mann–Whitney U test), and predominantly male (34.1%) and non-physician healthcare workers, including trainee students (75.8%). Laboratory findings, including hemoglobin and platelet counts, showed no statistically significant differences compared with the rest of the cohort. These findings suggest that early-career status and limited risk perception may contribute to dual non-vaccination behavior among younger staff (Table 2).

Table 1. Demographic, occupational, clinical and laboratory data in HCWs (N=4048)

Variable	Statistic
Age, median (IQR)	30.0 (22.0-42.0)
Gender, n (%)	
Male	1204 (29.7)
Female	2844 (70.3)
Occupation, n (%)	
Physician	472 (11.7)
Nurse	1244 (30.7)
Paramedic	149 (3.7)
Radiation worker	97 (2.4)
Trainee students of health sciences	1285 (31.7)
Non-healthcare professional	801 (19.8)
Chronic disease, n (%)	
Having at least one chronic disease, n (%)	315 (7.8)
Having multiple chronic diseases, n (%)	33 (0.8)
Hypothyroidism, n (%)	44 (1.1)
Hypertension, n (%)	37 (0.9)
Coronary artery disease, n (%)	30 (0.7)
Diabetes mellitus, n (%)	28 (0.7)
Hepatitis, n (%)	23 (0.6)
Cancer, n (%)	16 (0.4)
Asthma, n (%)	15 (0.4)
Musculoskeletal system disease, n (%)	10 (0.2)
Anemia, n (%)	9 (0.2)
Psychiatric disorders, n (%)	4 (0.1)
COPD, n (%)	2 (0.1)
Others*, n (%)	34 (0.8)
COVID-19 vaccine	
HCWs receiving vaccine, n (%)	3730 (92.1)
Total dose, median (IQR)	3.0 (2.0-4.0)
Sinovac dose, median (IQR)	1.0 (0-2.0)
Biontech dose, median (IQR)	2.0 (1.0-2.0)
History of COVID-19, n (%)	195 (4.8)
History of second episode of COVID-19, n (%)	13 (0.3)
History of hospitalization due to COVID-19, n (%)	17 (0.4)
HCWs receiving Hepatitis B vaccine, n (%)	3643 (90.0)
Hemoglobin level, n (%)	
Low	659 (16.3)
Normal	3308 (81.7)
High	81 (2.0)

Variable	Statistic
Leukocyte count, n (%)	
Low	8 (0.2)
Normal	3315 (81.9)
High	725 (17.9)
Neutrophil count, n (%)	
Low	86 (2.1)
Normal	3750 (92.6)
High	212 (5.2)
Lymphocyte count, n (%)	
Low	86 (2.1)
Normal	3750 (92.6)
High	212 (5.2)
Platelet count, n (%)	
Low	23 (0.6)
Normal	3729 (92.1)
High	296 (7.3)
eGFR<60 mL/min/1.73 m^2, n (%)	11 (0.3)
Elevated urea, n (%)	18 (0.4)
Elevated ALT, n (%)	190 (4.7)
Elevated AST, n (%)	88 (2.2)

**Other uncategorized diseases; ALT, alanine transaminase; AST, aspartate transaminase; COPD, chronic obstructive pulmonarydisease; COVID-19, Coronavirus Disease 2019; eGFR, estimated glomerular filtration rate; IQR, interquartile range; HCW, healthcare worker.*

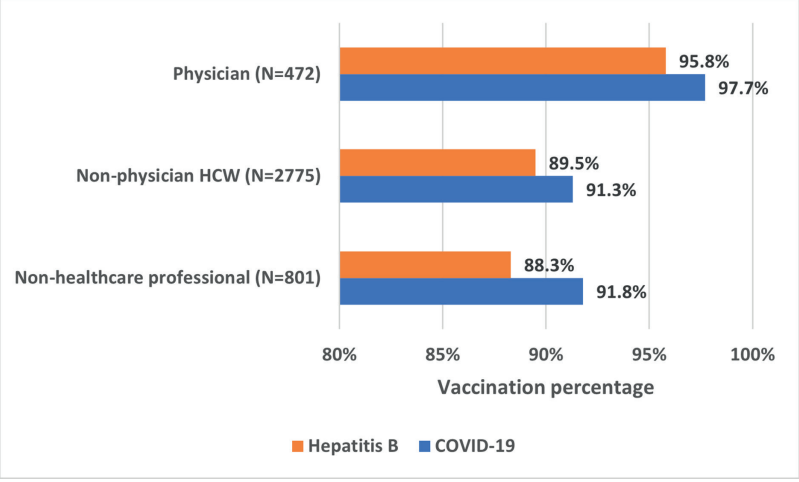

Figure 1. The vaccination rates for both COVID-19 and Hepatitis B.

Table 2. Comparison of characteristics according to COVID-19 vaccination status and subgroup analysis of dual-unvaccinated healthcare workers (N = 4,048).

Variable	Vaccinated (N=3730)	Unvaccinated (N=318)	*p*-value	Unvaccinated, both (N=91)	Others (N=3975)	*p*-value
Age, median (IQR)	30.0 (22.0-42.0)	21.0 (19.0-34.0)	<**0.001***	21(16-24)	30(15-68)	<**0.001***
Gender, n (%)			0.572†			0.362†
Male	1105 (29.6)	99 (31.1)		31(34.1)	1173(29.6)	
Female	2625 (70.4)	219 (68.9)		60(65.9)	2784(70.4)	
Occupation, n (%)			<**0.001†**			**0.017†**
Doctor	461 (12.4)	11 (3.5)		2(2.2)	470(11.9)	
Non-physician HCW	2534 (67.9)	241 (75.8)		69(75.8)	2706(68.4)	
Non-healthcare professional	735 (19.7)	66 (20.8)		20(22)	781(19.7)	
Chronic disease, n (%)	296 (7.9)	19 (6.0)	0.210†	5(7.1)	310(7.8)	031†
History of COVID-19, n (%)	187 (5.0)	8 (2.5)	**0.046†**	4.4(1.1)	194(4.9)	0.131‡
COVID-19 re-infection, n (%)	13 (0.3)	-	0.421‡	0(0)	13(0.3)	1.000‡
COVID-19, hospitalization n (%)	17 (0.5)	-	0.392‡	0(0)	17(0.4)	1.000‡
Vaccinated for Hepatitis B, n (%)	3416 (91.6)	227 (71.4)	<**0.001†**	-	-	-
Laboratory tests						
Hemoglobin level, n (%)			**0.017†**			0.072†
Low	591 (5.8)	68 (21.4)		20(22.0)	639(16.1)	
Normal	3067 (82.2)	241 (75.8)		67(73.6)	3241(81.9)	
High	72 (1.9)	9 (2.8)		4(4.4)	77(1.9)	
Leukocyte count, n (%)			0.793†			0.694†
Low	7 (0.2)	1 (0.3)		0(0)	8(7.8)	
Normal	3058 (82.0)	257 (80.8)		72(79.1)	3243(82)	
High	665 (17.8)	60 (18.9)		19(20.9)	706(17.8)	
Neutrophil count, n (%)			0.359†			0.837†
Low	22 (0.6)	4 (1.3)		1(1.1)	25(0.6)	
Normal	283 (88.0)	278 (87.4)		79(86.3)	3482(88.0)	
High	425 (11.4)	36 (11.3)		11(12.1)	450(11.4)	
Lymphocyte count, n (%)			0.430†			0.245†
Low	77 (2.1)	9 (2.8)		0(0)	86(2.2)	

Variable	Vaccinated (N=3730)	Unvaccinated (N=318)	*p*-value	Unvaccinated, both (N=91)	Others (N=3975)	*p*-value
Normal	3454 (92.6)	296 (93.1)		88(96.7)	3663(92.5)	
High	199 (5.3)	13 (4.1)		3(3.3)	209(5.3)	
Platelet count, n (%)			**0.019†**			0.161†
Low	20 (0.5)	3 (0.9)		1(1.1)	22(0.6)	
Normal	3449 (92.5)	280 (88.1)		79(86.3)	3650(92.2)	
High	261 (7.0)	35 (11.0)		11(12.1)	285(7.2)	
eGFR<60 mL /min/1.73 m^2, n (%)	11 (0.3)	-	1.000‡	0(0)	11(0.3)	1.000‡
Elevated urea, n (%)	18 (0.5)	-	0.392‡	0(0)	1.000‡	1.000‡
Elevated ALT, n (%)	182 (4.9)	8 (2.5)	0.056†	3(3.3)	85(2.1)	0.449‡
Elevated AST, n (%)	79 (2.1)	9 (2.8)	0.403†	2(2.2)	188(4.8)	0.445‡

Column percentages are presented. Bold p-values indicate statistical significance.
**Mann-Whitney-U test.*
†Chi-square test.
‡Fisher's exact test.
ALT, alanine transaminase; AST, aspartate transaminase; COVID-19, Coronavirus Disease 2019; eGFR, estimated glomerular filtration rate; IQR, interquartile range; HCW, healthcare worker.

3.4. Multivariable Analysis

Independent predictors of COVID-19 non-vaccination included younger age (OR=0.96, 95% CI: 0.94–0.97), male gender (OR=1.37, 95% CI: 1.04–1.80), non-physician HCW status (OR=2.51, 95% CI: 1.33–4.75), non-healthcare professional status (OR=2.99, 95% CI: 1.55–5.77), and elevated platelet count (OR=1.54, 95% CI: 1.04–2.28). Hepatitis B vaccination history showed a protective effect (OR=0.30, 95% CI: 0.23–0.40) (Table 3). Here, "protective effect" indicates that prior HBV vaccination was associated with a 70% lower likelihood of COVID-19 non-vaccination after multivariable adjustment (OR<1). The findings remained consistent even after excluding participants with chronic diseases or abnormal laboratory values, indicating that the model results were robust and not driven by these subgroups.

4. Discussion

This study provides the first direct comparison of Hepatitis B and COVID-19 vaccination status among Turkish HCWs. Overall vaccination coverage was high, particularly among physicians, reflecting their higher medical knowledge, perceived risk, and adherence to occupational protocols [9, 12, 17]. Non-physician HCWs and non-healthcare professionals demonstrated lower coverage, highlighting gaps in institutional reinforcement and educational strategies [10, 16, 34].

The higher COVID-19 vaccination uptake relative to Hepatitis B suggests the strong influence of pandemic urgency, institutional campaigns, and perceived threat severity [10, 13, 35]. These findings align with international data showing greater vaccine acceptance among HCWs than the general population [36]. However, the persistent lower uptake in non-physician HCWs underscores the need for targeted strategies, including mandatory onboarding immunization, booster monitoring, and continuous workplace education [2, 9, 11]. In Turkey, HBV vaccination has been included in the National Immunization Plan since 1998, and healthcare workers are required to demonstrate anti-HBs seroprotection or receive booster doses during occupational health surveillance [3-5]. COVID-19 vaccination, although voluntary since 2023, has been strongly

Table 3. Unadjusted and multiple logistic regression analyses for being unvaccinated for COVID-19 (N=4048).

Variable	Unadjusted		Multiple	
	OR (95% CI)	***p*-value**	**OR (95% CI)**	***p*-value**
Age (1-year increase)	0.95 (0.93-0.96)	**<0.001**	0.96 (0.94-0.97)	**<0.001**
Male gender	1.07 (0.84-1.38)	0.572	1.37 (1.04-1.80)	**0.024**
*Occupation**				
Non-physician HCW	3.99 (2.16-7.35)	**<0.001**	2.51 (1.33-4.75)	**0.005**
Non-healthcare professional	3.76 (1.97-7.20)	**<0.001**	2.99 (1.55-5.77)	**0.001**
History of COVID-19	0.49 (0.24-1.00)	0.051	0.91 (0.43-1.91)	0.793
*Hemoglobin**				
Low	1.45 (1.10-1.94)	**0.008**	1.34 (0.99-1.80)	0.057
High	1.59 (0.79-3.22)	0.197	1.12 (0.53-2.37)	0774
*Platelet count**				
Low	1.85 (0.55-6.26)	0.324	1.77 (0.51-6.18)	0.370
High	1.65 (1.14-2.40)	**0.008**	1.54 (1.04-2.28)	**0.033**
Vaccinated for Hepatitis B	0.23 (0.18-0.30)	**<0.001**	0.30 (0.23-0.40)	**<0.001**

Bold p-values indicate statistical significance.
**Physicians, normal hemoglobin level, and normal platelet count were accepted as reference for occupation, hemoglobin, and platelet count variables, respectively.*
CI, confidence interval; HCW, healthcare worker; COVID-19, Coronavirus Disease 2019.

encouraged by the Ministry of Health and hospital administrations to sustain pandemic preparedness. These national regulations likely explain the overall high vaccination rates observed in this cohort.

A novel contribution of this study was the identification of a small subgroup of healthcare workers (2.2%) who were unvaccinated for both COVID-19 and Hepatitis B. This group was significantly younger, predominantly male, and mostly composed of trainee students and non-physician HCWs. Their dual non-vaccination behavior highlights the role of early-career status, limited occupational experience, and possibly lower risk perception. Such behavior underlines the importance of incorporating vaccination counseling into medical and allied-health curricula and reinforcing immunization before clinical placement. From a clinical and occupational health standpoint, recognizing and monitoring this subgroup is crucial for preventing workplace outbreaks and ensuring patient safety. Institutional policies should therefore mandate vaccination verification at the time of recruitment and training. These findings emphasize the need for targeted education and vaccination programs aimed at students and newly employed personnel before clinical exposure begins.

An important novel finding was the association between elevated platelet count and COVID-19 non-vaccination. Thrombocytosis is linked with systemic inflammation and may reflect psychobiological stress responses, which in turn correlate with vaccine hesitancy [37-39]. Although causality cannot be established, this observation suggests potential immune-psychological mechanisms influencing vaccination decisions. It is noteworthy that both vaccines administered in this cohort—Comirnaty® (mRNA) and CoronaVac® (inactivated)—are not associated with vaccine-induced thrombocytosis; therefore, the observed association is likely behavioral or stress-related rather than biological. Clinically, this raises the possibility that subtle hematological variations may indirectly reflect psychosocial determinants of health behavior. Integrating hematologic screening with occupational counseling may thus help identify workers at risk of non-compliance

with vaccination programs. Further longitudinal studies are required to clarify these relationships.

The strong protective effect of prior Hepatitis B vaccination on COVID-19 uptake supports the hypothesis that positive vaccination history fosters acceptance of new vaccines. This behavioral consistency, confirmed in other studies linking past vaccination behavior with COVID-19 acceptance [25, 26], suggests that individuals with strong preventive health orientation are more likely to comply with new immunization campaigns. This finding has direct implications for clinical practice: assessing prior vaccination records during occupational health examinations can help predict vaccine acceptance and guide personalized counseling. Routine verification of immunization status during periodic health assessments could serve as an early intervention to address potential hesitancy. This reinforces the value of comprehensive, routine immunization programs in preparing populations for future public health emergencies [20-22, 27-29]. From a clinical and occupational health perspective, these results highlight the need for systematic follow-up of vaccination records, integration of vaccine counseling into periodic health examinations, and workplace-based campaigns to sustain vaccine confidence. The decision to evaluate Hepatitis B rather than influenza vaccination as a comparator was intentional, as HBV immunization is mandatory, routinely documented, and reflects long-term occupational health compliance, making it a more stable behavioral indicator than seasonal influenza vaccination [30].

Strengths of this study include its large sample size, inclusion of trainee students, and integration of clinical and laboratory data. However, some limitations should be acknowledged. The retrospective and single-center design may restrict causal inference and generalizability. Additionally, behavioral, psychological, and socioeconomic factors influencing vaccine decisions were not assessed because no questionnaire-based data were collected—this represents an important methodological limitation that may have restricted the interpretation of underlying attitudes and motivations. Behavioral, psychological, and socioeconomic factors influencing vaccine decisions were not assessed because no questionnaire-based data were collected, as noted by the reviewer. Furthermore, information on antibody response or long-term seroprotection was unavailable. Future research should combine quantitative clinical data with behavioral and psychometric measures to better understand the determinants of vaccine hesitancy among HCWs.

5. Conclusion

Vaccination uptake among Turkish HCWs varies by occupation, with physicians achieving the highest coverage. Prior immunization history predicts COVID-19 vaccine acceptance, underscoring the importance of institutional strategies and continuous education. Tailored interventions for non-physician HCWs are needed to sustain high coverage in both routine and emergency contexts.

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Institutional Review Board Statement: Ethics approval was granted by the Mersin University Non-Interventional Clinical Research Ethics Committee (23.10.2024, no. 2024/979). The study complied with the Declaration of Helsinki. Informed consent was waived due to its retrospective nature. Clinical trial registration was not applicable.

Informed Consent Statement: Informed consent was waived due to its retrospective nature.

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Author Contribution Statement: SME: Conceptualization, Methodology, Supervision, Writing – original draft, Writing – review & editing, Data curation, Investigation, Resources, Funding acquisition, Project administration, Software, Validation, Visualization. AS: Supervision, Writing – review & editing, Formal analysis, Validation, Visualization.

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