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ORIGINAL ARTICLE

Safety and efficacy of COVID-19 vaccines in patients on dialysis: a multicentre cohort study in Italy

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Abstract

Background The aim of this study was to evaluate the efficacy and safety of COVID-19 vaccines in patients undergoing haemodialysis in Italy compared to the general population.

Methods In this cohort study, 118 dialysis centres from 18 Italian Regions participated. Individuals older than 16 years on dialysis treatment for at least 3 months, who provided informed consent were included. We collected demographic and clinical information, as well as data on vaccination status, hospitalisations, access to intensive care units and adverse events. We calculated the incidence, hospitalisation, mortality, and fatality rates in the vaccinated dialysis cohort, adjusted for several covariates. The incidence rates of infection in the dialysis cohort and the general population were compared through Standardised Incidence Rate Ratio.

Results The study included 6555 patients vaccinated against SARS-CoV-2 infection according to the schedule recommended in Italy. Between March 2021 and May 2022, there were 1096 cases of SARS-CoV-2 infection, with an incidence rate after completion of the three-dose vaccination cycle of 37.7 cases per 100 person-years. Compared to the general population, we observed a 14% reduction in the risk of infection for patients who received three vaccine doses (Standardised Incidence Rate Ratio: 0.86; 95% Confidence Interval: 0.81–0.91), whereas no statistically significant differences were found for

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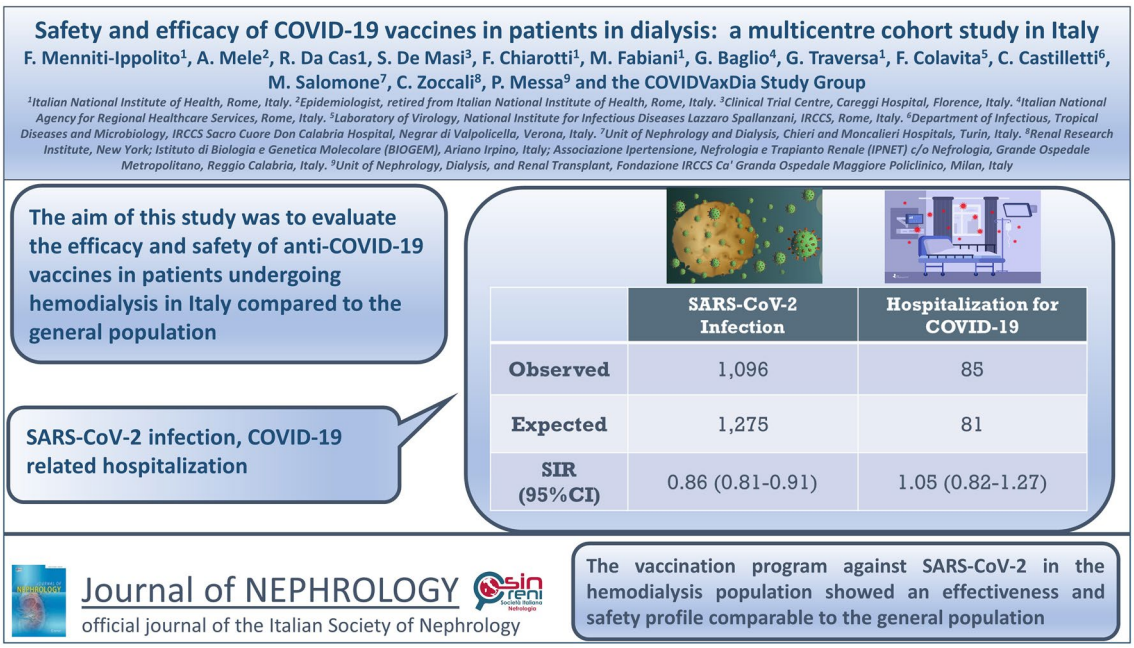
COVID-19-related hospitalisations, intensive care unit admissions or death. No safety signals emerged from the reported adverse events.

Conclusions The vaccination program against SARS-CoV-2 in the haemodialysis population showed an effectiveness and safety profile comparable to that seen in the general population.

Graphical abstract



Keywords Cohort study · Dialysis · COVID vaccines · Effectiveness · Safety

Introduction

Chronic Kidney Disease (CKD) is a public priority [1]. In 2017, there were 846 million people globally with CKD, and 3.9 million were on dialysis [2]. In a survey conducted in Italy from 2008 to 2012 by the Cardiovascular Epidemiology Observatory/Health Examination (OEC/HES), 2.5% of the Italian population (i.e., 1,482,000 people) had stage G3-5 CKD [3], and in 2010, 42,488 patients were on regular dialysis treatment [4].

The COVID-19 pandemic has had severe effects on patients with chronic kidney disease undergoing replacement therapies [5]. The high risk of infection in this population is due to an altered immune system and exposure to the virus during transportation to the dialysis centre and prolonged contact (4–5 h) with other patients in common areas while waiting for, and during dialysis treatment.

Patients on dialysis treatment (stage G5D CKD) have been particularly affected by the COVID-19 pandemic, as early (within 28 days) COVID-19-attributable mortality was 20% in the European Registry of Dialysis and Transplantation [5]. Therefore, as soon as vaccines against SARS-CoV-2 infection became available, the Italian Society of Nephrology (SIN) requested and obtained prioritisation from the Italian Ministry of Health for COVID-19 vaccination of stage G5D patients. A study was conducted to evaluate the efficacy and safety of COVID-19 vaccines in dialysis patients to describe the vaccination program in this high-risk population. Thus, in early 2021, in collaboration with the Italian Institute of Health (Istituto Superiore di Sanità-ISS), SIN proposed a national study on dialysis patients undergoing COVID-19 vaccination.

Herein, we report the results of the efficacy and safety of the COVID-19 vaccination program in dialysis patients in Italy.

Methods

This multicentre cohort study was performed between 1st March, 2021 and 31st May, 2022. All Italian dialysis centres were invited to participate. Most of the participating centres were public hospitals (105/118), representing 36% of all Italian public dialysis centres (about 290) [6]. The remaining

centres ($n = 13$) were private organisations. Participation in the study was voluntary and we did not investigate why centres did not participate. We included persons vaccinated with any vaccine against COVID-19 according to the schedule recommended by the Ministry of Health at the start of the study [5]. To be recruited, patients had to be older than 16 years, on dialysis treatment (haemodialysis or peritoneal dialysis) for at least 3 months, willing to undergo the required clinical and laboratory tests and provide informed consent. The study protocol and informed consent were approved by the ethics committee of the National Institute for Infectious Diseases Lazzaro Spallanzani, Rome and by the Local Ethics Committees.

Subjects with SARS-CoV-2 infection at the time of enrolment and with a life expectancy ≤ 6 months (based on the clinical evaluation of nephrologists at the centre level) were excluded. For patients who reported a previous SARS-CoV-2 infection, the Ministry of Health recommended administering the first dose at least 3 months from recovery [5]. These patients were not excluded from the analysis. The study planned a 48-week follow-up period, starting from administration of the 2nd dose (for vaccines requiring two doses), subsequently amended to 6 months from the third dose (first booster dose). Since a second booster dose was also strongly recommended by the Italian Ministry of Health (IMH), some patients also received this 4th dose during the study period. For the evaluation of the major clinical outcomes, we grouped the study periods into two-time intervals, according to the vaccination schedule, as follows: Time 1, from the first dose up to 14 days after the third dose; Time 2, from 15 days after the third dose up to the end of follow up.

Investigators at each centre took care of the recruitment of dialysis patients and provided detailed information on the nature of the study to all participants. The same investigators also collected informed consent from each participant.

We used an electronic Case Report Form for the collection of demographic and clinical information, vaccination status (including other vaccinations in addition to COVID-19), baseline comorbidities and ongoing therapies (e.g. immunosuppressive and other drugs) at the time of enrolment and after vaccination, hospitalisations, access to intensive care units, laboratory tests, adverse events, and study outcomes. All data concerning comorbidities were retrieved through a review of the clinical records of the individual patients, without further validation. With regard to cancer diagnoses, these were established on documented clinical and laboratory findings. Moreover, the number of drugs was also considered as a proxy for comorbidities. SARS-CoV-2 infection and/or disease were detected through routine surveillance activities in participating dialysis centres. Ascertainment of diagnosis was performed through routine antigenic/molecular tests or retrieved from clinical records for hospitalised patients. Patients were classified as infected/non-infected across the 2-time intervals indicated above, along with the recommendations of the ISS-IMH surveillance system [7]. This system collects data on all Italians who were positive for the SARS-CoV-2 swab tests. In addition to measuring the incidence of the spread of the disease, the system also collects data on deaths. In reporting COVID-19 deaths to the surveillance system, the ISS-IMH follows the indications of the European Centre for Disease Control (ECDC) and the World Health Organization (WHO) in identifying the deaths associated with COVID-19 [7]. The criteria to define a death from COVID-19 are indicated in the ECDC Report and include microbiological confirmation (molecular swab test) of SARS-CoV-2; the presence of a clinical phenotype suggestive of SARS-CoV-2 infection; absence of a clear cause of death other than COVID-19; absence of a period of complete clinical recovery between disease onset and death [7].

The COVID-19-related causes of death include complications or consequences of pre-existing conditions that could have favoured or predisposed a negative course of the infection in a patient with a clinical phenotype compatible with SARS-CoV-2.

Statistical analysis

The distribution of each variable (age, number of doses, comorbidities, duration of dialysis, BMI > or ≤ 30 kg/m^2 and other relevant factors) of infected patients was compared with that of uninfected ones. Adverse events were reported in the electronic Case Report Form and coded according to the System Organ Class Medical Dictionary of Regulatory Activities [SOC MedDRA [8]].

Infection rates were calculated as the number of events divided by person-time for each time interval and exposure category. Person-time was calculated for each patient; the contribution to Time 1 lasted from the first vaccine dose until the earliest of the following dates: occurrence of infection, death, or censoring (loss to follow-up or 14 days after the third dose); Time 2 lasted from 15 days after the third dose until the earliest of the following dates: occurrence of infection, death, or censoring (loss to follow-up or study end, 31st May, 2022).

The number of deaths (related and unrelated to the infection) was reported as an absolute number, proportion, and rate (number of events/person-time). The COVID-19 mortality rate was calculated as the number of deaths for SARS-CoV-2 infection divided by the person-time of the study population (until the date of death or censoring, as defined above).

The lethality rate was calculated as the number of COVID-19-related deaths divided by the number of SARS-CoV-2 infected population.

Crude Rate Ratios (RR) were calculated for each variable as ratio between incidences. Adjusted Hazard Ratios (HR) associated with patients' risk factors were estimated by multivariate analyses using Cox regression models, and the associations were tested through the Chi-Square and T-tests. In the multivariate Cox regression models the HRs were adjusted for geographic area of the clinical centre, age, sex, previous COVID-19 infection, BMI ($>$ or ≤ 30 kg/m^2), immunosuppressive therapy in the 6 months preceding the first dose of COVID-19 vaccine, number of other drugs (as a proxy of comorbidities). The significance level of tested associations was fixed at a p-value < 0.05.

Finally, we compared the incidence rates in the dialysis population with concurrent data of the Italian general population (ISS-IMH surveillance system) on COVID-19 cases, hospitalisations, Intensive Care Unit (ICU) admissions and deaths [8]. We did not take the unvaccinated population as a comparison group since, in Italy, the vaccination coverage was very high in the general population, frail persons and the age groups represented in our cohort. The Standardised Incidence Ratio (SIR) was calculated as the ratio between events observed in dialysis patients and events expected based on the incidence rates of events observed in the vaccinated general population, stratified by age and sex and matched by calendar time. In other words, the incidence rate for specific gender and age strata of the vaccinated general population was used to estimate the corresponding expected numbers in the dialysis population. All statistical analyses were performed using STATA (version 16.1).

Results

One hundred and eighteen dialysis centres in 18 Italian Regions agreed to participate in the study. Overall, 6555 patients were enrolled, 65% were males, over 70% were 60 years of age or older; 7% were on peritoneal dialysis and 93% were on extracorporeal dialysis treatment, and the mean dialysis vintage was 6 years (± 7 years Standard Deviation [SD]). The percentage of patients who received the second, third and fourth dose was 97% ($n = 6.369$), 65% ($n = 4.286$) and 14% ($n = 934$), respectively. Multimorbidity, defined as at least two diseases in addition to stage G5D CKD, was present in 90% of patients. Nine per cent of the whole population was obese (BMI > 30 kg/m^2), and 11% of infected patients had a BMI > 30 kg/m^2 (Table 1). Most of the background nephropathies of dialysis patients were secondary to diabetes mellitus, hypertension, and glomerular diseases; collectively, these diseases represented more than 70% of the total. All nephropathies with known aetiology but not listed in Table S1 were classified as "Other nephropathies". (Supplementary S1). The most frequent types of dialysis

Table 1 Baseline characteristics of the study population

	Uninfected patients	Infected patients	Total	p
All patients (n, %)	5459 (83)	1096 (17)	6555 (100)	
Age, mean (standard deviation [SD])	68.0 ($\pm$13.4)	66.1 ($\pm$14.3)	67.7 ($\pm$13.6)	0.382
Age $>$ 60 years (n, %)	4084 (75)	750 (68)	4834 (74)	$<$0.001
Female (n, %)	1934 (35)	367 (34)	2301 (35)	0.219
BMI $>$ 30 kg/m^2 (n, %)	494 (9)	122 (11)	616 (9)	0.031
Comorbidity (n, %)				
Hypertension	3558 (65)	823 (75)	4381 (67)	$<$0.001
Heart disease	2188 (40)	480 (44)	2668 (41)	0.022
Diabetes mellitus	1481 (27)	340 (31)	1821 (28)	0.009
Neoplasia	942 (17)	192 (18)	1134 (17)	0.834
Peripheral vasculopathy	981 (18)	204 (19)	1185 (18)	0.614
Lung disease	557 (10)	125 (11)	682 (10)	0.234
Cerebral vasculopathy	554 (10)	123 (11)	677 (10)	0.286
Auto-Immune disease	292 (5)	60 (6)	352 (5)	0.866
All comorbidity, median (IQR)	3 (1–4)	3 (2–4)	3 (1–4)	$<$0.001
Comorbidities ≥ 2 (n, %)	4865 (89)	1056 (96)	5921 (90)	$<$0.001
Drugs, median (IQR)	7 (5–9)	7(5–10)	7(5–9)	$<$0.001
Immunosuppressive therapy (n, %)	371 (7)	92 (8)	463 (7)	0.060
Previous COVID-19 infection (n, %)				
Yes	593 (11)	73 (7)	666 (10)	$<$0.001
No	4372 (80)	950 (87)	5322 (81)	
Missing	494 (9)	73 (7)	567 (9)	
Dialysis vintage (years), mean (SD)	6 ($\pm$7)	6 ($\pm$7)	6 ($\pm$7)	0.959

were bicarbonate dialysis and haemodiafiltration (Supplementary S2).

Incidence of SARS-CoV-2 infection, hospitalisation, admission to intensive care units, COVID-19-related deaths and lethality

During the study, 1096 cases of COVID-19 were reported; infected patients were slightly younger than uninfected ones, while the percentage of persons > 60 years old was significantly higher in the uninfected patients with respect to infected ones (75% vs. 68%, $p < 0.001$). Infected patients were characterised by a greater number of comorbidities, the most frequent ones being hypertension (75%), heart disease (44%) and diabetes mellitus (31%). As expected, patients with a previous SARS-CoV-2 infection presented a lower risk of being infected after vaccination (11% vs. 7%, $p < 0.001$) (Table 1). The dialysis type distribution was the same in both infected and uninfected patients (Table S2).

The highest incidence of SARS-CoV-2 infection (37.7 per 100 person-years) was observed during Time 2 (Table 2) when the new omicron BA.1 was the main circulating variant in Italy [8].

From Time 1 to Time 2, we observed an over six-fold increase in the risk of infection (RR: 6.21; 95% CI 5.42–7.13).

The number of hospitalisations due to COVID-19 was 82 (7.5%), and 6 patients (0.6%) were admitted to the ICU, and again, a near seven-fold increase in the risk of hospitalisation was recorded from Time 1 to Time 2 (RR: 6.71; 95% CI 3.98–11.32), while the risk of admission to the ICU was stable (RR: 0.94; 95% CI 0.17–5.16).

Mortality for COVID-19 increased across the two study periods (RR: 3.22; 95% CI 1.62–6.40), while lethality showed an opposite trend (RR: 0.56; 95% CI 0.28–1.09).

As detailed in Table 3, the risk of infection was lower in elderly patients (adjusted HR 0.68; 95% CI 0.58–0.79; $p < 0.0001$) but higher in hypertensive patients (adjusted HR 1.37; 1.15–1.62; $p = 0.001$) and in patients with heart disease (adjusted HR: 1.18; 1.02–1.37; $p = 0.034$). Similarly, higher risks of infection were recorded in individuals with a BMI > 30 kg/m^2 (adjusted HR 1.22; 0.99–1.52), in those on polytherapy (≥ 5 drugs) (adjusted HR 1.23; 0.99–1.53) and patients treated with immune-active medications (adjusted HR 1.39; 1.09–1.77). Mortality by COVID-19 was higher in the older age group (adjusted HR 2.89; 0.66–12.53), but due to the small number of events, the excess risk in the older population failed to achieve statistical significance, as was the case for other covariates considered in this study (Table 4).

Comparison of dialysis patients and the Italian general population (ISS-IMH surveillance system)

As shown in Table 5, the observed risk of infection in dialysis patients was less than that expected in comparison with the general population (SIR = 0.86; 0.81–0.91), even though the vaccination rates of the general population were high and

Table 2 Incidence of infection, mortality, hospitalization and lethality for COVID-19 in Time 1 and Time 2

	n	p-y	Rate (*n*/100 p-y)	Crude RR (95% CI)
Infection				
Time 1	272	4485	6.1	1.0
Time 2	824	2186	37.7	6.21 (5.42–7.13)
Mortality by COVID-19				
Time 1	13	4601	0.3	1.0
Time 2	22	2416	0.9	3.22 (1.62–6.40)
Hospital admission for COVID-19 (*n*, %)				
Time 1	18	4595	0.4	1.0
Time 2	64	2435	2.6	6.71 (3.98–11.32)
ICU admission				
Time 1	4	4601	0.09	1.0
Time 2	2	2435	0.08	0.94 (0.17–5.16)
	n	Infected patients	%	Crude RR (95% CI)
Lethality by COVID-19^ (number of deaths/over number of patients with COVID-19)				
Time 1	13	272	4.8	1.0
Time 2	22	824	2.7	0.56 (0.28–1.09)

p-y Person-years; *RR* rate ratio; *CI* confidence intervals

*Date of death not reported in 2 cases ^ p-y only for infected cases

Table 3 COVID-19 infection from 14 days after the third dose ($n = 824$)

Demographic and clinical characteristics	*N*	p-y	Rate (*n*/100 p-y)	Crude RR (95% CI)	Adjusted* HR (95% CI)
Age (years)					
< 60	258	540	47.8	1.0	0.68 (0.58–0.79)
≥ 60	566	1646	34.4	0.72 (0.62–0.83)	
Sex					
Male	545	1432	38.0	1.0	0.99 (0.86–1.15)
Female	279	754	37.0	0.97 (0.84–1.12)	
BMI (kg/m^2)					
≤ 30	727	1979	36.7	1.0	1.22 (0.99–1.52)
> 30	97	207	46.8	1.27 (1.03–1.57)	
Hypertension					
No	195	676	28.8	1.0	1.37 (1.15–1.62)
Yes	629	1510	41.7	1.44 (1.23–1.70)	
Heart disease					
No	448	676	66.2	1.0	1.18 (1.02–1.37)
Yes	376	904	41.6	0.63 (0.55–0.72)	
Diabetes mellitus					
No	563	1556	36.2	1.0	1.09 (0.93–1.27)
Yes	261	630	41.4	1.15 (0.99–1.33)	
Lung disease					
No	721	1945	37.1	1.0	1.09 (0.88–1.34)
Yes	103	241	42.8	1.15 (0.94–1.42)	
Drugs					
< 5	110	409	26.9	1.0	1.23 (0.99–1.53)
≥ 5	714	1777	40.2	1.50 (1.22–1.83)	
Immunosuppressive therapy					
No	751	2045	36.7	1.0	1.39 (1.09–1.77)
Yes	73	141	51.9	1.41 (1.11–1.80)	

Incidence density (per 100 p-y), crude rate ratio and adjusted hazard ratio

p-y Person-years; *RR* rate ratio; *HR* hazard ratio; *CI* confidence intervals

*Geographic area of clinical centre, age, sex, previous COVID-19 infection, BMI, immunosuppressive therapy, other drugs

similar to those of dialysis patients [8]. The risk of admission to the ICU (SIR = 0.62; 0.12–1.11) showed the same trend but did not achieve statistical significance. Overall, the risk of death among dialysis patients who experienced the infection was numerically higher than the general population, though not statistically significant (SIR = 1.39; 0.93–1.85).

COVID-19 vaccination safety

Altogether, 309 adverse events were reported over eighteen thousand vaccine administrations. Among adverse events, 104 (33.7%) were general disorders and administration site conditions, 33 (10.7%) were vascular disorders, and 29 (9.4%) were nervous system disorders. No data were available on the severity of the events, and causality assessment was impossible due to incomplete information. No difference was observed between the second and third vaccine dose (Supplementary S3). These reactions are comparable to those reported within the Italian pharmacovigilance system [8]

Discussion

The overall incidence of SARS-CoV-2 infection in the Italian dialysis population after three doses of the COVID-19 vaccine was 37.7/100 person-years. Both the infection rate and the risk of ICU admission in this high-risk population were lower than expected in the corresponding general population included in the Italian surveillance system. Thus, the dialysis population's timely and extensive vaccination program and standard recommendations for preventing SARS-CoV-2 infection by the Italian Ministry of Health afforded a

Table 4 Mortality for COVID-19 from 14 days after the third dose

Demographic and clinical characteristics	*N*	p-y	Rate (*n*/100 p-y 100)	Crude RR (95% CI)	Adjusted* HR (95% CI)
Age (years)					
< 60	2	617	0.3	1.0	2.89 (0.66–12.53)
≥ 60	20	1800	1.1	3.43 (0.80–14.66)	
Sex					
Male	15	1586	0.9	1.0	1.04 (0.42–2.58)
Female	7	830	0.8	0.89 (0.36–2.19)	
BMI					
≤ 30 kg/m^2	18	2183	0.8	1.0	1.90 (0.62–5.82)
> 30 kg/m^2	4	233	1.7	2.08 (0.70–6.15)	
Hypertension					
No	4	729	0.5	1.0	1.77 (0.58–5.44)
Yes	18	1687	1.1	1.95 (0.66–5.75)	
Heart disease					
No	8	729	1.1	1.0	1.91 (0.77–4.70)
Yes	14	1009	1.4	1.26 (0.53–3.01)	
Diabetes mellitus					
No	11	1712	0.6	1.0	1.76 (0.73–4.23)
Yes	11	704	1.6	2.43 (1.05–5.61)	
Lung disease					
No	16	2146	0.7	1.0	2.40 (0.92–6.29)
Yes	6	270	2.2	2.98 (1.16–7.61)	
Drugs					
< 5	3	440	0.7	1.0	0.74 (0.20–2.76)
≥ 5	19	1977	1.0	1.41 (0.42–4.76)	
Immunotherapy					
No	20	2255	0.9	1.0	1.93 (0.44–8.42)
Yes	2	162	1.2	1.39 (0.33–5.96)	

Incidence density (per 100 p-y), crude rate ratio and adjusted hazard ratio

p-y Person-years; *RR* rate ratio; *HR* hazard ratio; *CI* confidence intervals

*Geographic area of clinical centre, age, sex, previous COVID-19 infection, BMI, drugs

Table 5 Standardised incidence ratio (SIR) of infection, hospitalisation, ICU admission and death

	N. observed cases	N. expected cases	SIR*	95% CI
SARS-CoV-2 infections	1096	1275	0.86	0.81–0.91
Hospitalisation for COVID-19	85	81	1.05	0.82–1.27
ICU admission for COVID-19	6	10	0.62	0.12–1.11
Death for COVID-19	35	25	1.39	0.93–1.85

CI Confidence intervals

*Standardised incidence ratio

degree of protection from COVID-19 and secondary hospitalisations in these high-risk patients.

The present study covers an extended period in which several viral variants with various pathogenic potentials and infectivity were present. We collected information on symptomatic and asymptomatic patients, but we have no granular information on the various SARS-CoV-2 variants, and we cannot, therefore, compare the relative protection of vaccines for these variants. Since the end of 2021, the omicron variant has rapidly spread, explaining the higher incidence of infection in Time 2 of the study. The increased risk of hospitalisation from Time 1 to Time 2 and the increase in mortality for COVID-19 can be explained by the higher infection rate, while ICU admission was stable between the two times. At the same time, lethality was lower in Time 2.

In this study, the younger population presented higher infection rates, most likely because young people were less adherent to policies recommended by health authorities for spreading the virus, such as social distancing, use of masks, and hand washing. In addition, young people had

higher exposure to the virus in their social and working life compared to the older population. Hypertension, heart disease, and patients treated with immune-active medications presented a slightly increased risk of infection. Age and lung disease presented a doubling in the mortality risk for COVID-19, but, probably due to the small number of events, this excess risk did not reach statistical significance.

The description of country-wide experiences of COVID-19 vaccination programs in the dialysis population, like the one carried out in Italy, is limited. In a Swiss study, the incidence density was calculated by region and by the different epidemic waves [9]. During the third wave (January 1, 2021, to June 30, 2021), corresponding to the beginning of enrolment in our study, the incidence density among dialysis patients in Switzerland was 10.6/100,000 person-days, i.e., 3.9/100 person-years, lower than 6.1/100 person-years estimated in our study. During the omicron variant period (corresponding to Time 2 in our study) (October 10, 2021, to February 2, 2022), in Switzerland, the incidence density was 105.7/100,000 person-days, equal to 38.6/100 person-years, similar to the incidence calculated in our study among patients that completed the vaccination cycle with three doses (37.7/100 person-years).

In a cohort of 1121 haemodialysis patients in the United Kingdom included in a weekly screening for SARS-CoV-2, 13% were infected over a 6-week observation period (from December 1, 2021, to January 16, 2022) [10]. Compared with unvaccinated patients, those who received three vaccine doses had a halved risk of infection (HR 0.50; CI 95% 0.29 to 0.92) [11] and these findings were consistent with general population data from the UK Health Security Agency [12]. This finding is in keeping with the reduced standardised incidence rate recorded in dialysis patients in our study, even though the effect size, 14%, was lower in Italian dialysis patients (HR:0.86; CI 95% 0.81–0.91).

We used the standardised incidence ratios of infection, hospitalisation, ICU admission and death, adjusted for age and sex in the haemodialysis population in Italy. Compared with the general population, the vaccination program in Italy provided adequate protection for this high-risk population. This protection should be seen not solely as the effect of vaccination but as the combined effect of vaccines, the use of personal protection devices, and proactive tracking of patients at high risk of SARS-CoV-2 infection.

The present study has several limitations. First, the cohort of patients included in the study represented only 14% of the general population of Italian patients on dialysis treatment. Though all Italian dialysis centres were invited to participate in the study, only a part of them declared they were in the operational conditions to implement the study protocol. The wide distribution of the participating centres throughout Italy suggests that the representativeness may be satisfactory. Second, the number of patients on peritoneal dialysis included in the study was relatively low, precluding a reliable statistical analysis of the potential differences compared to haemodialysis patients. In this respect, the distribution of type of dialysis was quite the same in infected and uninfected patients. Third, since not all patients were regularly tested for SARS-CoV-2 infection in all clinical centres, we cannot exclude a possible misclassification of undetected infections.

Finally, in our study we included only vaccinated patients, and thus no comparison could be conducted with unvaccinated ones; however, given the very high vaccination coverage in Italy in the general population, and in particular in frail subjects, any comparison between vaccinated and unvaccinated subjects would have been of limited, if any, value.

In conclusion, a country-wide vaccination program in the Italian haemodialysis population integrated with other measures, including personal protective devices and periodic testing for SARS-CoV-2, afforded a global degree of protection from this infection and its related complications comparable to that seen in the Italian general population. Our findings highlight that prevention strategies in high-risk populations, as large-scale COVID-19 vaccination in haemodialysis patients, are as effective as in the general population and underline the relevance of timely prevention.

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