



First considerations on the SARS-CoV-2 epidemic in the Dialysis Units of Piedmont and Aosta Valley, Northern Italy

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Piedmont (4,356,406 inhabitants) and Aosta Valley (125,666 inhabitants [1]) are two Regions of North-Western Italy, covering an area of almost 29,000 km² where 5793 patients are presently receiving renal replacement therapy (RRT): 2893 are on haemodialysis, 387 on peritoneal dialysis and 2513 have a functioning kidney graft [2].

In just over a month since the first case of SARS-CoV-2 positivity was recorded in Piedmont on February 22nd, 7782 (0.17%) inhabitants in these two Regions have been infected, and 637 of them have died (lethality of 8.19%) [3].

Since the outbreak of the epidemic nephrologists identified dialysis and kidney transplanted patients as a category at greater risk of contracting the infection and suffering its lethal consequences [4]. They also realized that the general health rules issued by the authorities were not sufficient to protect the nephrology-dialysis community. Nephrologists' warnings went initially unheeded. The main difficulties they had to deal with while trying to set up the most appropriate solutions included:

- regulating transport from home and access to the hospital, in particular for febrile patients, organizing telephone

pre-triage in order to arrange individual transport of suspected SARS-CoV-2 cases and to avoid group transportation,

- triaging patients before allowing them to enter the dialysis rooms,
- identifying designated areas where suspected and confirmed SARS-CoV-2 patients could undergo dialysis,
- guaranteeing adequate levels of protection (including personal protective equipment) for health care professionals, especially in designated areas, as well as a suitable number of surgical masks for the patients,
- broadening the indications for, and quickly getting the results of, nasopharyngeal and oropharyngeal swabs in individuals in contact with suspected or confirmed SARS-CoV-2 cases.

This was of paramount importance when dealing with such a tightly knit community of operators and patients continuously interacting with each other.

In a context in which data on dialysis and kidney transplant patients are few and scattered, we report our first experience concerning patients and professionals in the 22 Nephrology and Dialysis Units in Piedmont and Aosta Valley. The two Regions employ about 1200 health care workers including 226 nephrologists and 959 non-medical staff. The present report is updated 35 days after the beginning of the epidemic (March 27, 2020).

Data were updated in real time by all the Units via a IT platform developed by the local Nephrology Network and the Network of Rare Diseases of Piedmont and Aosta Valley, and were analyzed using SPSS Statistics version 26 (IBM, Armonk, USA), and Wizard version 1.9.40 (Evan Miller, Chicago, IL, USA).

No SARS-COV-2 cases were observed in the only Paediatric Nephrology Unit in the Region (having in charge 4 hemodialysis, 4 peritoneal dialysis, and 35 transplanted

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patients), which was not surprising due to the lower susceptibility of children to clinically evident infection.

In Piedmont and Aosta Valley, mainly symptomatic patients or patients at high risk of exposure (e.g. health care workers exposed to positive patients without adequate protection) have been tested until now. This approach may have caused a substantial underestimation of positive patients, preventing exact calculation of mortality rates. However, in the last days, the health authorities have extended indications, at least among healthcare professionals. Moreover, clinicians of the emergency and intensive care units are commonly using radiographic signs suggestive of interstitial pneumonia as surrogate criteria of SARS-CoV-2 disease.

In adults, 156 SARS-COV-2 cases were recorded: 130 RRT patients including 98 in hemodialysis, 4 in peritoneal dialysis, 26 transplanted, and 2 waiting for transplantation, and 26 health care workers (6 physicians, 18 nurses and 2 members of auxiliary staff). SARS-COV-2 cases were unevenly distributed within the Regions ranging from 0 to maximum of 25 cases per Nephrology Unit. The difference in number of cases among the Units may reflect a true variability in the incidence of positive cases in Piedmont and Aosta Valley. However, the high number of cases in single Centers might also be due to intra-hospital spreading of the infection. In this context, it is worth emphasising the need to comply with the correct hygienic rules, including hand disinfection and use of surgical masks by personnel and patients.

The incidence of confirmed cases showed an increasing trend between March 16th to 26th, slowing down in the last week, possibly due to the very restrictive measures adopted by the Italian government (Fig. 1).

The prevalence of SARS-CoV-2 positivity was the same in RRT patients and nephrology staff: 2.2%. This is much higher than the rates for the general population in Piedmont and Aosta Valley (7782 subjects affected by SARS-CoV-2, i.e., 0.17% of the population), with an odds ratio of 13.43, 95% CI 11.27 to 16.00; z score $p < 0.0001$ for RRT patients,

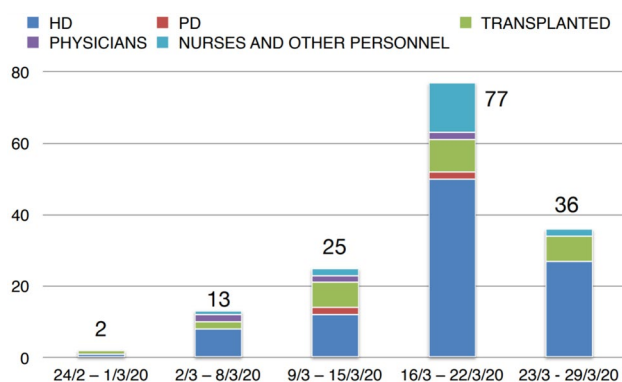


Fig. 1 Number of new confirmed (positive swab) cases per week

and of 12.80 (95% CI 8.67 to 18.89; z score $p < 0.0001$) for staff.

Presently, all personnel affected by SARS-CoV-2 have been quarantined at home (waiting for two negative swabs at 24 h-intervals to be allowed to come back to work), but one nurse who has been hospitalized.

The average age of affected patients was 69.7 (range 26–92 years). It was higher in dialysis (70 years, range 41–92) than in transplanted patients (61, range 26–80), with a higher number of males (59.3 vs 40.7%), which is consistent, at least in part, with the prevalence of males in the RRT population.

Of these patients, 74.6% have been hospitalised. Being under RRT did not preclude per se admission to the intensive care unit (ICU). However, the incidence of ICU admission was higher in transplanted than dialysis patients, presumably due to lower comorbidity burden that favoured accessibility to intensive care. Anyway, the difference was not statistically significant (20.8% vs 8.2%; z-score $p = 0.086$). The death rate was 24.6%, much higher than that observed in the whole SARS-CoV-2-positive population of the same area in the same period (8.19%; 637 deaths in 7,782 confirmed subjects affected by SARS-CoV-2). The Odds Ratio for death in RRT patients vs the general population was 3.80 (95% CI: 2.53 to 5.72; z score, $p < 0.0001$).

Lethality was higher in males than in females (31.1% vs 4%, respectively; z score, $p = 0.008$).

Lethality was not related to dialysis vintage, while the presence of cardiovascular diseases was associated with higher lethality (29.9% vs 10.7%; $p = 0.040$). Diabetes was a risk factor in transplanted patients (66.7% vs 13.6%; $p = 0.031$). History of neoplasia was also associated with an increase in risk, albeit not statistically significant (40% vs 19%). Treatment almost invariably included anti-retroviral agents and hydroxychloroquine. The database was not designed to provide data on rescue therapies, such as anti-cytokine treatments. Deaths were due to multi-organ failure and cardiovascular collapse.

In summary, these preliminary data must be interpreted with caution and require further in-depth re-evaluation after the individual follow-up of each patient is completed. However, we felt that they could add to the current scant knowledge since they come from the first regional inquiry in RRT patients and may help better understanding of the epidemic. Furthermore, these data confirm that RRT patients and hospital staff have a higher incidence of infection and show that RRT patients have higher lethality than the general population. This observation may support maximizing preventive measures and early diagnosis in this fragile population.

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Compliance with ethical standards

Conflict of interest All the authors declare that they have no conflicts of interest.

Ethical approval All data used in this study were collected in accordance with the ethical standards of the institutional and regional research committees, with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. According to the European GDPR, all data were anonymized before the collection.

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