Regular RNA screening detects asymptomatic SARS-CoV-2 infection in haemodialysis patients

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INTRODUCTION

Those receiving in-centre haemodialysis are uniquely vulnerable to COVID-19 due to co-morbidity and inability to self-isolate, resulting in high rates of infection and mortality (1). Evidence for dialysis unit transmission (2) highlights the importance of effective case detection in order to protect this population. However, around 17% of SARS-CoV-2 infections are asymptomatic (3) and this may be higher in in an elderly dialysis population (4). US and UK antibody screens have found only 9.2% and 56.6% of seropositive haemodialysis cases were previously detected by symptom-led RT-PCR testing (5,6).

Asymptomatic infected individuals can transmit SARS-CoV-2, at an estimated 42% of the risk in symptomatic cases (7,8), therefore screening for asymptomatic SARS-COV-2 has been proposed or adopted in a range of populations, predominantly to protect others by case isolation (9,10).

The efficacy of frequent asymptomatic screening has not been established in the dialysis population, nor whether end stage kidney disease influences antibody responses. To address these questions, we briefly report our experience of regular screening for both acute infection and post-infectious antibody response in a haemodialysis population.

METHODS

From May 2020 asymptomatic SARS-CoV-2 RT-PCR screening was offered fortnightly to every hospital haemodialysis patient in our region, with monthly SARS-CoV-2 IgG from July 2020. Verbal consent was obtained as part of clinical care.

Viral RNA obtained from nasopharyngeal swabs was detected by RT-PCR predominantly using the Abbott Real Time assay. For Altona and Public Health England RdRp results, comparative standard curves were used to interpolate Abbott cycle numbers (CN).

SARS-CoV-2 nucleocapsid IgG was quantified using Abbot Architect Immunoassay. Titre is an index of chemiluminescent light units for sample relative to calibrator. Positive threshold >= 1.4

RESULTS

Of 490 haemodialysis patients across our region, 388 had both regular RT-PCR viral RNA screening and at least one IgG antibody test and were included in the dataset. 388 patients had a mean±SD of 8±5.4 RT-PCR tests between 1st May and 7th October, equating to testing on average every 19.9 days. 27 had a positive RT-PCR; of these, 9(33.3%) had no symptoms at or following the positive test (Table 1).

21/34 (sensitivity 61.8%, NPV 96.4%) patients with a positive IgG result were picked up at the time of infection by RT-PCR. Of 13 patients with prior SARS-CoV-2 infection detected by antibody but 'missed' by RT-PCR, retrospective review indicated only 2 (15%) reported or exhibited clinical features consistent with covid-19 (including fever or chest X-ray changes).

Since the first UK pandemic wave began in March and April we hypothesise that these patients may have been infected prior to our regular screening programme. Consistent with this, all 13 patients were identified from the first monthly IgG screen in early July, with no additional 'missed' patients detected by subsequent IgG screens, despite a continued rate of new PCR positive cases. From May onwards the frequency of swab testing did not differ between PCR+IgG+ and PCR-IgG+ cases (1st May to 7th October mean±SD 13.4±4.9 vs. 14.2+-2.4 tests, p=0.59 by unpaired two-tailed t test), but in March and April, prior to asymptomatic screening, PCR+IgG+ patients were more likely to be swabbed than PCR-IgG+ (mean±SD 1.0±0.6 vs. 0.3±0.7 tests, p=0.004) (Figure 1a).

21/27 PCR confirmed patients subsequently had a detectable IgG response (sensitivity 77.8%, NPV 98.3%). Positive IgG was more likely in symptomatic than asymptomatic cases (Fisher's exact p=0.044) (Figure 1b), and associated with lower first positive RT-PCR cycle number (CN), (mean 14.31 vs 27.02, p=0.039 by two-way ANOVA), but CN did not distinguish symptomatic from asymptomatic cases (22.80 vs 18.58, p=0.66) (Figure 1c). Although in individuals with >1 positive IgG, titre declined with time, likelihood of serological positivity was unrelated to time from the first positive PCR swab (mean 103.4 vs. 109.0 days for positive vs. negative IgG, p=0.34) (Figure 1d) and at a cohort level there was no significant relationship between IgG titre and time (Figure 1e).

DISCUSSION

Our data shows that offering fortnightly SARS-CoV-2 swabbing on haemodialysis picks up the majority of cases. Our sensitivity of 61.8% is likely to be an underestimate, skewed by cases prior to screening, though infections could be missed between tests, and weekly screening may improve detection. One third of cases were asymptomatic, and would not be identified by symptom based testing, but can still transmit virus (11). Whilst we endeavour to minimise risk of infection to other patients or staff by hand hygiene and personal protective clothing, proactive screening permits additional targeted measures including patient isolation (in our case cohorting in a dedicated haemodialysis area).

IgG to nucleocapsid protein was detectable in 77.8% of infected patients tested between 16 and 194 days post infection, similar to non-dialysis cohorts (12). Seroconversion is more likely in symptomatic cases and with higher viral titre. Our data indicates that this antibody test performs similarly in the dialysis population as it does more generally.

It is not yet known whether seropositivity confers adequate immune protection, and neutralising antibodies, for example against spike protein, may be more clinically important. The negative IgG result in 6 patients cannot be interpreted alone as a lack of longer-term immunity and the role of serological screening to predict re-infection risk or vaccine response in this population remains to be established.

Based on our findings, we advocate regular RT-PCR screening of all dialysis patients. This supports local planning and targeted additional infection control measures including cohorting, though further studies will be needed to confirm that screening reduces transmission risk and unit outbreaks. Further the data ensures haemodialysis patients are included in the broader epidemiological understanding of the pandemic.

Table 1. In centre haemodialysis patients with both SARS-CoV-2 RT-PCR and subsequent IgG results between 1st April and 7th October 2020

	All RT-PCR negative	>= 1 RT-PCR positive
All IgG negative	348	6
>= 1 IgG	13	21

Figure 1 Legend

a) Number of SARS-CoV-2 RT-PCR tests performed per dialysis patient in two monthly groups, for IgG positive patients, by RT-PCR result. Mean and SEM shown.

b) Symptomatic versus asymptomatic PCR positive patients by IgG status

c) Cycle number (CN), calculated from Ct value, for first positive SARS-CoV-2 RT-PCR, by symptom and IgG status, data available for 20 patients.

d) Number of days between first positive SARS-CoV-2 RT-PCR and SARS-CoV-2 IgG testing, by IgG result. Lines show mean and SD. In patients with more than one IgG result each result is presented as a separate data point.

e) SARS-CoV-2 IgG titre against time from first positive RT-PCR to IgG result. In patients with more than one IgG result each result is presented as a separate data point. Broken line indicates threshold for positive IgG result.

CONFLICT OF INTEREST STATEMENT

None declared.

DATA AVAILABILITY STATEMENT

Non-identifiable data underlying this article will be shared on reasonable request to the corresponding author.

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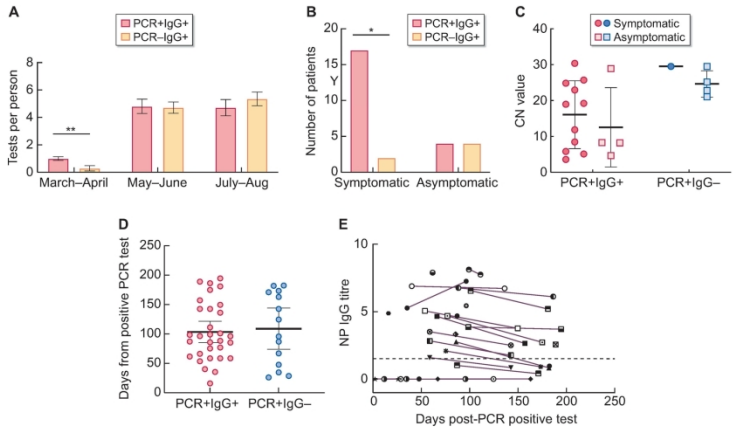

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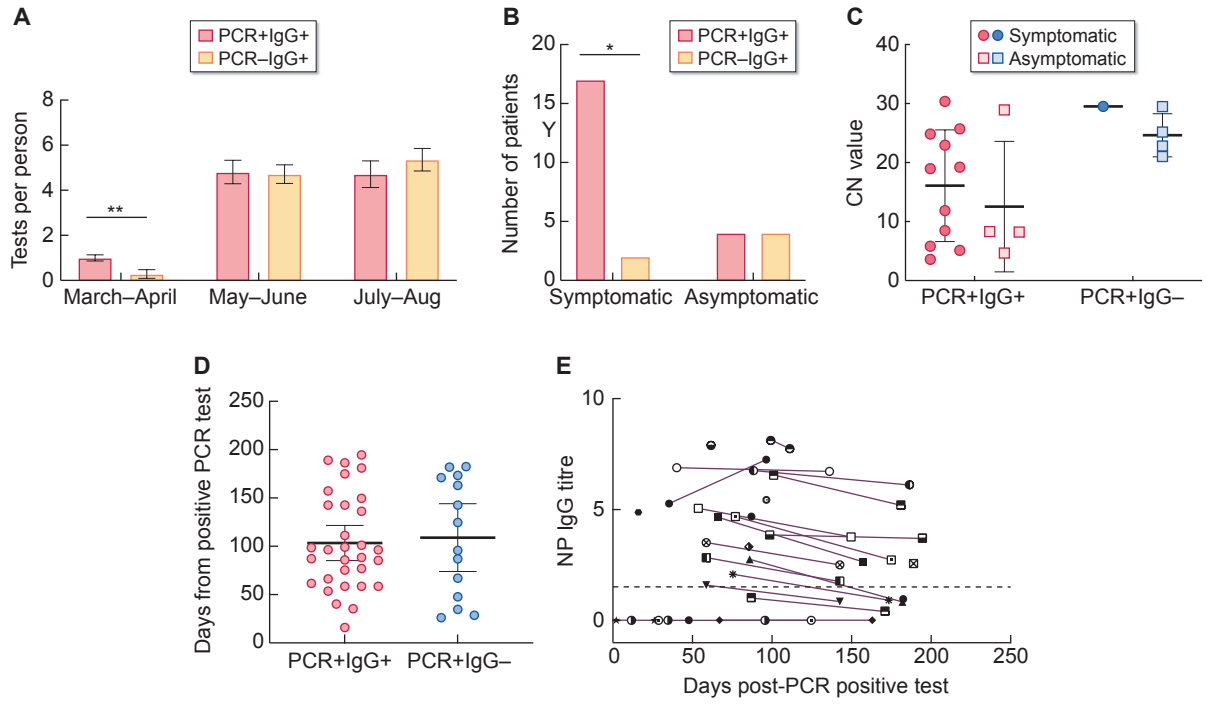

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