





# Prevalence of SARS-CoV-2-IgG Antibodies in Children with CKD or Immunosuppression

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Coronavirus disease 2019 (COVID-19) rapidly spread from China as a pandemic, with Italy one of the most affected countries worldwide. Unlike adults, children have a milder presentation of COVID-19, even when affected by CKD or on immunosuppressive therapy for glomerulopathies and kidney transplantation (1). In a nationwide study by the Italian Society of Pediatric Nephrology, involving 1572 pediatric patients with kidney diseases requiring immunosuppressive treatment or CKD stages 3–5d, we have previously reported a low prevalence (0.2%) of clinically detectable COVID-19, and no patients with severe disease (2). As asymptomatic infections are common and testing early in the pandemic was restricted to a limited number of children, we implemented a study to evaluate the prevalence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) IgG antibodies in the initial cohort.

The study population included two subgroups of children who were enrolled in our previous study (2). The randomized group consisted of 200 children selected by random sampling, stratified by geographical area, to be representative of the whole cohort. Testing was extended to their siblings and cohabitants. The symptomatic group included all 197 children who had reported symptoms suggestive for a viral infection in the original cohort, including 29 subjects from the randomized group (Figure 1).

The serological testing for SARS-CoV-2-IgG was initiated 3 months after the clinical study and was conducted from July 15 to September 15, 2020, by a COVID-19 Rapid Test (Model: GCCOV-402a). The test has a sensitivity of 93% and a specificity of 99% for IgG, compared with real-time PCR (3). The rate of seroprevalence was compared with the pediatric report from the Italian Ministry of Health together with the Italian National Institute of Statistics (4), and the clinical prevalence of our previous study (2). The study was approved by the local ethics committees of each participating center.

In the randomized group, a total of 178 patients (median age 11 years), 90 siblings (median age 10 years), and 271 cohabitants (median age 42 years)

were tested. In total, 22 families denied consent and 85 cohabitants were not tested due to the restrictions in place for the pandemic. Among the patients who were enrolled, 98 had a glomerular disease treated with immunosuppressive agents (from one to three), 36 were kidney transplant recipients, 32 had CKD, and 12 were on dialysis. In total, 29 out of 178 had reported nonspecific infectious symptoms during the pandemic peak.

A positive test for SARS-CoV-2-IgG was detected in three out of 178 patients (2%), six out of 90 (7%) siblings, and nine out of 271 (3%) cohabitants. Only the difference between patients and siblings was statistically significant ( $P=0.03$ ; chi-squared test). As expected, in the randomized group, patients who had previously reported nonspecific infectious symptoms were more likely to be found positive compared with those who had not (two out of 29 versus one out of 149;  $P=0.02$ ; chi-squared test). The seroprevalence in patients who were asymptomatic was 0.7%.

Among the three patients who tested positive, two were transplant recipients, with a history of fever and upper respiratory tract infection, respectively, and one was an asymptomatic child on immunosuppression for idiopathic nephrotic syndrome. In all patients, SARS-CoV-2 infection was not previously documented by swab real-time PCR testing. No child required hospitalization or experienced multisystem inflammatory syndrome or worsening of kidney function.

Furthermore, the percentage of children with kidney diseases who tested positive for SARS-CoV-2-IgG in our sample was not statistically different from the corresponding Italian healthy population aged 0–17 years (2% versus 2%;  $P=0.54$ ; chi-squared test) (4). Similar to the general Italian population (4), in our series, the prevalence of humoral response was found to be 8.5-fold higher than the clinical prevalence of SARS-CoV-2 infection identified in our previous study (1.7% versus 0.2%).

Overall, during the study, we identified SARS-CoV-2 spreading in nine families, all living in the most affected areas of Italy: Milan (six), Bergamo (two), and

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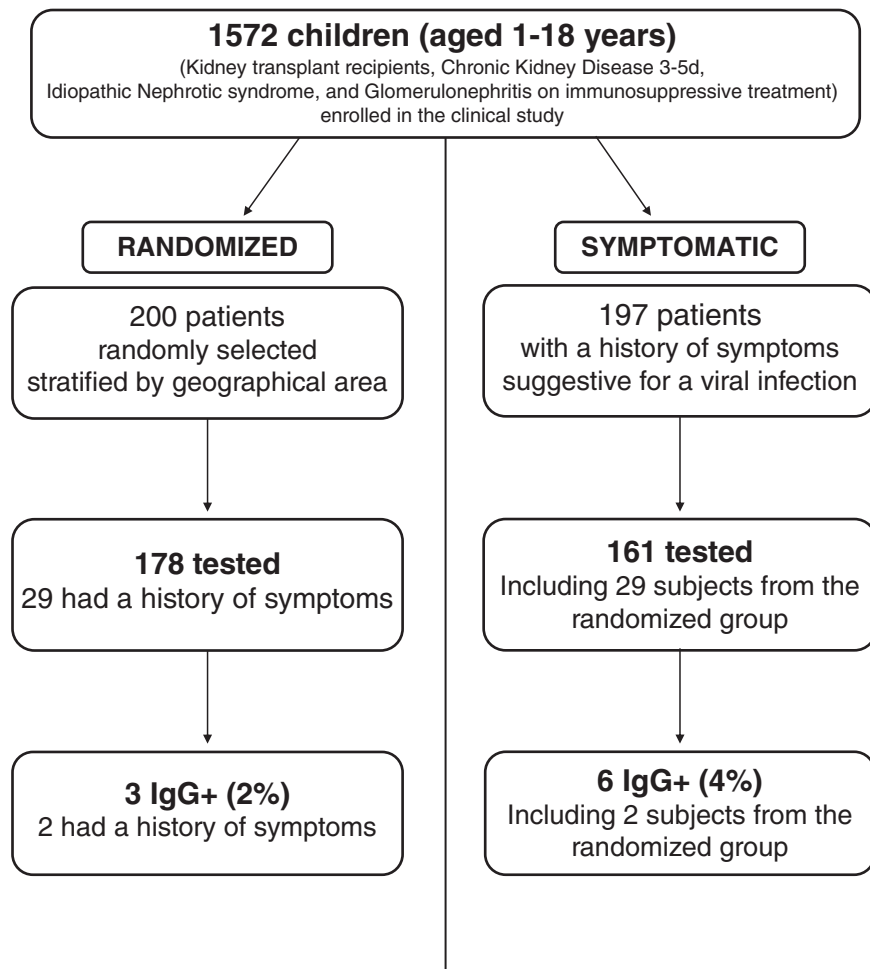
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**Figure 1. | Study population: The randomized group included 200 children, selected by random sampling, stratified by geographical area to be representative of the whole cohort.** The symptomatic group included all children who had reported symptoms suggestive for a viral infection during the previous study, for a total of 197 subjects. In total, 29 enrolled patients belonged to both groups.

Turin (one). In four families, only one subject tested positive, none of which was the nephropathic child. This supports the low risk of infection in our population.

In the symptomatic group, 161 of 197 children who reported symptoms (mainly upper respiratory tract infections and fever) from our previous study were tested, including 29 subjects from the randomized group. Even in this population, potentially considered at higher risk of previous SARS-CoV-2 infection, the seroprevalence was low, with only six children (4%) positive for SARS-CoV-2-IgG.

The study has some limitations, such as the relatively small numbers and the timing of serological testing. However, because the humoral response to SARS-CoV-2 is proven to last at least 4 months after infection (5), our results should not be affected.

In conclusion, the serological assessment may detect previous asymptomatic infections not clinically identified. Nevertheless, the seroprevalence of SARS-CoV-2 antibodies in pediatric patients with kidney diseases is low and similar to that of general pediatric population.

According to our data, we do not suggest reducing immunosuppressive therapy in this population. Moreover, we do not recommend more stringent protective measures compared with healthy peers.

#### Disclosures

A.P. Mastrangelo reports employment with Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico Milano. G. Montini reports consultancy agreements with Alnylam and Bayern. G. Pucio reports receiving honoraria from Associazione per il Bambino Nefropatico (ABN-Onlus) and serving as a scientific advisor or member of *EuroMediterranean Biomedical Journal*. I. Guzzo reports employment with Bambino Gesù Children's Hospital. L.A. Petruzzelli reports employment with Santobono Pausilipon. L. Martelli reports employment with Ospedale Papa Giovanni XXIII, Bergamo. L. Massella reports employment with Bambino Gesù Children's Hospital and Research Institute and serving on the Editorial Board of *Nephron*, section "Case Studies in Genetics." L. Peruzzi reports employment with Regina Margherita Children's Hospital and Citta della Salute e della Scienza di Torino and reports receiving honoraria from Alnylam, Chiesi, and Dicerna. R. Dall'Amico reports employment with Azienda Sanitaria Friuli Occidentale. W. Morello

reports employment with Pediatric Nephrology, Dialysis and Transplant Unit, Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico Milano and reports receiving honoraria from Sanofi-Genzyme. All remaining authors have nothing to disclose.

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Dr. A. Mastrangelo, Prof. G. Montini, Dr. W. Morello, and Dr. L. Peruzzi conceptualized and designed the study; Dr. A. Mastrangelo and Dr. W. Morello designed the data collection instrument; Prof. G. Montini and Dr. L. Peruzzi coordinated data collection; Drs. E. Benetti, C. Benvenuto, L. Cusinato, R. Dall'Amico, I. Guzzo, L. Martelli, L. Massella, C. Pecoraro, L. Petruzzelli, and F. Vianello collected data; Dr. A. Mastrangelo, Prof. G. Montini, Dr. W. Morello, and Dr. L. Peruzzi supervised data collection; Dr. G. Puccio the performed statistical analysis; Dr. A. Mastrangelo and Dr. W. Morello drafted the initial manuscript; Drs. E. Benetti, C. Benvenuto, L. Cusinato, R. Dall'Amico, I. Guzzo, L. Martelli, L. Massella, A. Mastrangelo, W. Morello, C. Pecoraro, L. Annicchiarico Petruzzelli, G. Puccio, and F. Vianello reviewed and revised the manuscript; Prof. G. Montini and Dr. L. Peruzzi critically reviewed the manuscript for important intellectual content; and all authors approved the final manuscript and agree to be accountable for all aspects of the work.

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