

This is an Accepted Manuscript for *Infection Control & Hospital Epidemiology* as part of the Cambridge Coronavirus Collection.

DOI: 10.1017/ice.2020.401

**ARTICLE TYPE: RESEARCH BRIEF**

Low seroprevalence of SARS-CoV-2 infection among healthcare workers of the largest children hospital in Milan during the pandemic wave

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Lombardy, Northern Italy, was the first region within a Western country to be severely hit by the spread of SARS-CoV-2. The COVID-19 epidemic started officially in Italy on February 21, 2020 [1], although today it is recognized that the virus had been circulating unnoticed for at least a month prior to that date [2,3]. Several nosocomial outbreaks occurred in the first phase of the epidemic and healthcare workers (HCWs) were the most vulnerable cohort for SARS-CoV-2 infection due to frequent and close contacts with COVID-19 patients without, at least in an initial phase, adhering to strict hygienic measures.

We carried out a cross-sectional seroprevalence study among the HCWs of the largest paediatric hospital in Milan during the period of maximum epidemic activity, when Lombardy accounted for 37% of cases and 53% of deaths of the country [4].

## **Methods**

We analyzed serum samples collected on April 15, 2020 from 663 workers (108 males and 555 females, median age 44 years) at the Buzzi Hospital in Milan, where the first paediatric confirmed COVID-19 case was hospitalized on February 28 and, until the time of this study, 40 COVID-19 cases were managed. All HCWs and non-HCWs who decided to take part to the survey were interviewed to review potential occupational exposures with COVID-19 patients, symptoms and use of personal protective equipment (PPE) as recommended by the WHO [5].

Out of 742 employees, 547 HCWs e 116 non-HCWs (biologists, pharmacists, laboratory technicians, administrative employers) were included. All of them have no symptoms of COVID-19 at the time of blood collection. Approximately 41% of subjects reported symptoms during the weeks preceding the time of sampling, but none had been hospitalized or underwent nasopharyngeal swab for the detection of SARS-CoV-2-RNA. For 304 of the 547 HCWs (55.6%), at least one contact with confirmed COVID-19 patients was known.

Anti-SARS-CoV-2 IgG antibodies were detected using a semi-quantitative enzyme-linked immunosorbent assay (ELISA) (Euroimmun Medizinische Labordiagnostika, Lubeck, Germany) according to manufacturer's instructions.

Comparisons between subject characteristics, work settings and SARS-CoV-2 IgG positivity were made using the  $\chi^2$  test. A P value  $<0.05$  was considered statistically significant (two-tailed test). All statistical analyses were performed using OpenEpi software, v. 3.03a.

## Results

Overall, 34 subjects tested positive for SARS-CoV-2 IgG, with a prevalence of 5.13%; the majority of these (76.5%, 26/34) reported symptoms related to COVID-19, mostly during the month of March. Seroprevalence was almost identical among HCWs and non-HCWs (5.12% vs 5.17%, respectively;  $p=0.95$ ), but significantly higher among males compared to females (9.26% vs 4.32%;  $p=0.049$ ).

Two wards, Surgery and Paediatric Intensive Care, showed a significantly higher frequency of infection than the others (22.2% vs 4.4%,  $p<0.001$  and 14.3% vs 4.5%,  $p<0.01$  respectively). Table 1 shows the percentage of anti-SARS-CoV-2 IgG positivity broken down by HCWs characteristics and hospital wards.

Among HCWs, the percentage of seroconversion was 6.58% (20/304) and 3.29% (8/243) in those with or without contact with confirmed COVID-19 patients, respectively ( $p=0.08$ ). The seroconversion rate was significantly higher among HCWs with PPE-free contact than those who had PPE (21.6%, 8/37 vs 4.5%, 12/267;  $p<0.01$ ). All IgG positive HCWs with symptoms had contact with COVID-19 patients, without PPE, in the first two weeks of March. Of the 7 asymptomatic HCWs that were positive for IgG, 5 had no known contact with confirmed COVID-19 patients and 2 reported PPE-protected contact.

## Discussion

To date there is a lack of serological data and the actual spread of the infection remains undetermined, in particular among the HCWs who managed the COVID-19 emergency in a territorial or hospital setting.

We examined HCWs of the largest paediatric hospital in Milan to determine SARS-CoV-2 seroprevalence in an area with high epidemic density.

Overall, we found a IgG prevalence of approximately 5% on April 15 [4], when Lombardy counted 62,153 confirmed cases and 11,377 deaths. Interestingly, healthcare professionals and other hospital employees

showed the same percentage of IgG positivity (5.13% vs 5.17%). Noteworthy, this percentage is completely comparable (5%) to that found in the first week of April in a recent study conducted on blood donors from the same geographical area (Milan) [6]. Among HCWs who became infected, the highest risk factor was having contacts with COVID-19 patients during the very early stages of the epidemic, when the availability of PPE was still inadequate. Among HCWs who did not have contacts with confirmed cases, the percentage of infection was low (3.29%), even lower (although not significantly) than among non-HCWs (5.17%). Serological analysis allowed to recognize that 25% of infected HCWs were asymptomatic with no contact with confirmed COVID-19 patients (71.4%) or had PPE-protected contacts (28.6%). A limitation to this study could be the lack of information about staff-to-staff transmission and the potential community associated risks.

In conclusion, our data indicates that the prevalence among paediatric HCWs is low and similar to community prevalence, suggesting there is no increased risk within hospitals providing appropriate PPE.

These results are of particular relevance considering that this area was among those with the highest epidemic density worldwide and that the virus had already spread unnoticed since mid-January 2020. The hypothesis of a minor role of children in the spread and transmission of SARS-CoV-2 [7] will need to be explored. Further retrospective serological investigations among children with respiratory symptoms that were hospitalized or had access to the emergency room before the official start of the Italian outbreak will allow to date the introduction of the virus in the paediatric population.

Word count: 889

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Table 1: Subjects characteristics, work settings and SARS-CoV-2 IgG positivity.

		SARS-CoV-2 IgG+
		N (%)
<b>Female (N=555)</b>		24 (4.32)*
<b>Male (N=108)</b>		10 (9.26)*
<b>TOTAL (N=663)</b>		34 (5.13)
<b>PROFESSION</b>		
<b>Healthcare worker (N=547)</b>		28 (5.12)
	Physician (N=214)	10 (4.67)
	Nurse (N=216)	13 (6.02)
	Other health technicians (N=117)	5 (4.27)
<b>Non-health care worker (N=116)<sup>§</sup></b>		6 (5.17)
<b>SETTING</b>		
<b>Specialist Outpatient Services (N=63)</b>		4 (6.34)
<b>Surgery (N=27)</b>		6 (22.22) <sup>°</sup>
<b>Paediatric (N=80)</b>		1 (1.25)
<b>Paediatric Emergency Room (N=55)</b>		1 (1.82)
<b>Neonatal Intensive Care (N=47)</b>		1 (2.13)
<b>Paediatric Intensive Care (N=42)</b>		6 (14.29) <sup>^</sup>
<b>Pre- and Post-Natal (N=181)</b>		6 (3.31)
<b>Administration/Pharmacy/Laboratory (N=70)</b>		6 (8.57)
<b>Others (N=98)</b>		3 (3.06)

\*Female vs male: 4.32% vs 9.26%, p<0.05

<sup>°</sup> Surgery vs all the others: 22.2% vs 4.4%, p<0.001;

<sup>^</sup> Paediatric Intensive Care vs all the others: 14.3% vs 4.5%, p<0.01

<sup>§</sup> Biologists, pharmacists, laboratory technicians and administrative employers