Received: 14 May 2020 | Revised: 28 May 2020 | Accepted: 3 June 2020

DOI: 10.1002/ijc.33148

LETTER TO THE EDITOR

IJC International Journal of Cancer

Low prevalence of IgG antibodies to SARS-CoV-2 in cancer patients with COVID-19

Dear editor,

Currently, coronavirus disease in 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has become a global pandemic. In patients infected with SARS-CoV-2, IgM antibodies are detectable around 7 days postinfection and IgG antibodies usually take 2 weeks to develop.[1-3] COVID-19 IgM/IgG tests have been developed around the world for the diagnosis and management of COVID-19 patients, identifying convalescent cases and seroepidemiological surveillance.[4] It is reported that cancer patients with COVID-19 often get more severe symptoms and have higher mortality risk.[5,6] It is unknown whether there is a difference in the prevalence of IgG antibodies to SARS-CoV-2 between cancer patients and other COVID-19 patients. In our study, we assessed prevalence of IgG antibodies against SARS-CoV-2 in cancer patients with COVID-19 and other hospitalized COVID-19 patients from Zhongnan Hospital of Wuhan University, Wuhan No. 7 Hospital, and Leishenshan Hospital in Wuhan, China.

The study was approved by the institutional ethics board at Zhongnan Hospital of Wuhan University. Requirement for written informed consent was waived by the institutional ethics board. There were 1603 hospitalized patients with COVID-19 who received both COVID-19 IgM/IgG tests and Reverse transcription-polymerase chain reaction (RT-PCR) tests for SARS-CoV-2 from February 29 to April 5, 2020. Eighty-four patients were transferred from Zhongnan Hospital of Wuhan University to Leishenshan Hospital and were only counted once each. We excluded 133 patients with COVID-19 whose IgM/IgG tests were less than 21 days after symptom onset to allow enough time for IgG antibodies against SARS-CoV-2 to develop. In total, we included 40 cancer patients with COVID-19 and 1430 other hospitalized COVID-19 patients.

Diagnosis of COVID-19 was based on epidemiological history, clinical manifestations and the presence of SARS-CoV-2 in clinical samples confirmed by using real-time RT-PCR method.[7] There were changes in diagnosis of COVID-19 in China during time, and the case definition was gradually broadened to all for detection of milder cases.[8] The confirmed cases were estimated to be four times less than that if the later broader case definition had been adopted earlier. All the 1470 patients in our study were hospitalized COVID-19 patients confirmed by RT-PCR tests for SARS-CoV-2. Severity of status of patients with COVID-19 at admission was defined as moderate, severe or critical. Patients with mild diseases were not admitted to the above three hospitals and were generally admitted to Fangcang Hospitals (makeshift hospitals).

Serum samples from these people were collected. Methods for testing serum IgM and IgG antibodies to SARS-CoV-2 were previously described.[9] COVID-19 IgM/IgG test kits contained recombinant SARS-CoV-2 antigens (spike protein and nucleocapsid protein) labeled with magnetic beads (tested on a fully-automated chemiluminescence immunoassay analyzer) or colloidal gold (test card), antihuman IgM monoclonal antibody and antihuman IgG monoclonal antibody. These test kits were reported to have high sensitivity and specificity.[9,10] According to the manufacturers, the sensitivity and specificity are ~90% and >99% for IgM, and ~98% and ~98% for IgG, respectively.

Several physicians extracted the following data using data collection form from electronic medical records: demographic information such as age and sex, RT-PCR test date and results, COVID-19 IgM/IgG test date and results, date of symptom onset for COVID-19 patients and clinical characteristics. Another physician in the research team reviewed the collected data.

Continuous variables were reported using mean and 95% confidence interval (CI) if normally distributed or median and interquartile range if nonnormally distributed. Means for normally distributed continuous variables were compared using Student's *t* test. Mann-Whitney test was used for assessing differences of nonnormal-distributed variables. Categorical variables were described as frequency rates and percentages. The χ^2 test was used for the comparison of categorical variables and Fisher's exact test was used when frequency was too low. Prevalence of positive IgM/IgG test results and 95% CI was also reported. For the assessment of RT-PCR test results of SARS-CoV-2 and IgM/IgG test results, the last test result for each person was used in the analyses. Differences in prevalence of IgM/IgG antibodies to SARS-CoV-2 between cancer patients and other patients were assessed by Wald χ^2 test using logistic regression models. Statistical analyses were conducted using SAS software version 9.4 (SAS Institute; Carey, North Carolina). A two-sided *P* value of <.05 was considered statistically significant.

There were no differences in age and sex in cancer patients with COVID-19 and other COVID-19 patients (Table S1). IgG prevalence was 72.5% (95% CI 58.0%-87.0%) in cancer patients with COVID-19 compared to 90.3% (95% CI 88.7%-91.8%) in other patients ($P < .001$, Table 1). IgM prevalence was 20.0% (95% CI 7.0%-33.0%) in cancer patients with COVID-19 and 31.7% (95% CI 29.3%-34.1%) in other patients.

Among cancer patients, none was positive for SARS-CoV-2 by RT-PCR test. The presence of IgG antibodies to SARS-CoV-2 was not

Abbreviations: COVID-19, coronavirus disease in 2019; IgG, immunoglobulin G; IgM, immunoglobulin M; RT-PCR, reverse transcription-polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

TABLE 1 Prevalence of IgM and IgG antibodies to SARS-CoV-2 AMong cancer patients with COVID-19 and other hospitalized COVID-19 patients

	Prevalence % (95% confidence interval)		
	Cancer patients (n = 40)	COVID-19 Patients (n = 1430)	*P* value
Prevalence IgG			
All	72.5 (58.0-87.0)	90.3 (88.7-91.8)	<.001
Age group (years)			
≤70	67.7 (50.3-85.2)	91.2 (89.6-92.9)	<.001
>70	88.9 (63.3-100.0)	86.4 (82.4-90.5)	.83
Sex			
Female	72.7 (52.5-92.9)	90.9 (88.8-93.0)	.008
Male	72.2 (49.3-95.1)	89.7 (87.4-91.9)	.026
Prevalence IgM			
All	20.0 (7.0–33.0)	31.7 (29.3-34.1)	.12
Age group (years)			
≤70	12.9 (0.4-25.4)	30.6 (27.9-33.3)	.043
>70	44.4 (3.9-85.0)	36.1 (30.4-41.7)	.61
Sex			
Female	9.1 (0.0-22.1)	28.1 (24.8-31.4)	.068
Male	33.3 (9.2-57.5)	35.4 (31.8-38.9)	.86

associated with severity of COVID-19 at first presentation or other clinical characteristics (Table S2).

We assessed prevalence of IgG antibodies to SARS-CoV-2 in cancer patients with COVID-19 and found that only 72.5% had IgG antibodies to SARS-CoV-2 after 21 days post symptom onset, much lower than patients without cancer. It is reported that after 17 to 19 days post symptom onset, IgG was positive in all patients with COVID-19.[3] Lack of blood samples >17 days post symptom onset may be responsible for negative IgG tests in some patients reported in previous literatures. However, this may not apply to cancer patients. Whether they did not get seroconversion or lose the IgG antibodies to SARS-CoV-2 is to be investigated. Currently, the role of IgG antibodies to SARS-CoV-2 in the immune response against the virus infection is unclear. It is hard to interpret the finding of the low prevalence of IgG antibodies to SARS-CoV-2 in cancer patients.

ACKNOWLEDGEMENTS

Part of the study was supported by the National Key Research and Development Program of China (2020YFC0845500, principal investigator: Dr X. W.). Dr F. G. is supported by the National Cancer Institute of National Institute of Health under Award Number K07CA222343. The content is solely the responsibility of the authors and does not necessarily represent the official views of the sponsors. The sponsors had no role in the design and conduct of the study; collection, management, analysis and interpretation of the data; and preparation, review or approval of the manuscript and decision to submit the manuscript for publication.

CONFLICT OF INTEREST

The authors have no conflict of interest to disclose.

DATA AVAILABILITY STATEMENT

The data that support the findings of our study are available from the corresponding authors upon reasonable request.

ETHICS STATEMENT

The study was approved by the institutional ethics board at Zhongnan Hospital of Wuhan University. Requirement for written informed consent was waived by the institutional ethics board.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.