Plasma Levels of Glycohydrolase Activities in Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Patients

To the Editor.—Glycohydrolases are distributed everywhere, especially in lysosomes, but also in plasma membranes, in cytosol and plasma. Over the years, plasma glycohydrolases have become increasingly important as potential serologic markers in several diseases characterized by lysosomal apparatus deregulation and altered plasmatic glycohydrolase levels.

It is known that during the inflammatory process, an activation of lysosomal apparatus occurs, with consequent alterations in the plasma levels of several glycohydrolases, including β-D-glucuronidase (GCR). In early 2020, a new coronavirus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), responsible for coronavirus disease 2019 (COVID-19), appeared in Wuhan, China, and rapidly spread worldwide. The hallmark of COVID-19 is tissue damage resulting from overproduction of reactive oxygen species due to the hyperinflammatory process known as cytokine storm. In recent years, a new method for the evaluation of total plasma antioxidant defenses, known as lag time, has proved to be a valid marker of oxidative stress (OS) in different diseases.

In this study we collected plasma samples from 13 COVID-19 patients and 52 non–COVID-19 patients presenting with COVID-19–like symptoms at the emergency room of Istituto di Ricovery e Cura a Carattere Scientifico (IRCCS) Policlinico San Donato, San Donato Milanese, Milano, Italy. All patients were admitted to the intensive care units of the hospital. Thirty age-matched volunteers were used as the control group. The study was approved by the local ethics committee (75/INT/2020).

C-reactive protein (CRP) was measured by a Cobas 600 analyzer (Roche Diagnostic, Milan, Italy). The plasma activities of hexosaminidase, GCR, and α-D-glucosidase, as well as kinetics of plasma oxidation, were fluorometrically determined by Victor (PerkinElmer).

Enzymatic activities and lag-time values showed no significant difference from normal distribution, and the means were compared by Student t test. C-reactive protein showed a nonnormal distribution, and the means were compared by Mann-Whitney U test. The Pearson correlation coefficient (r²) was calculated to determine the correlations between values measured by different assays. Statistical analyses were performed by SPSS STATISTIC 26 package (SPSS Inc, Chicago, Illinois).

In all patients, CRP was significantly altered compared with the reference clinical ranges, and in COVID-19 patients it was significantly higher than in non–COVID-19 patients (Table). All glycohydrolase activities were significantly increased in all patients with respect to the controls and were significantly higher in COVID-19 patients than in non–COVID-19 patients (Table). Lag-time values were significantly lower in all patients compared with controls (Table). In the COVID-19–positive group, lag-time values showed a significant negative linear correlation with GCR level, suggesting that this parameter could be a good indicator of OS in COVID-19 patients (Figure).

Until now there has been little information on the involvement of plasma glycohydrolases in infectious diseases, such as HIV infection. In this regard, to our knowledge, our data highlight for the first time an

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**Inflammation and Oxidative Stress Parameters**

|                      | Reference Interval | Non–COVID-19 | COVID-19 |
|----------------------|--------------------|--------------|----------|
|                      | Control            | Non–COVID-19  | COVID-19  |
| CRP, mg/dL           | 0.0–0.5            | 4.76 ± 7.23  | 11.40 ± 8.78b |
| HEX, U/L             | 27.52 ± 6.35       | 31.15 ± 6.35c | 36.73 ± 9.34c,d |
| GCR, mU/L            | 2060.16 ± 972.06   | 2101.88 ± 1070.72 | 3060.80 ± 1674.98c,e |
| aGLU, mU/L           | 114.47 ± 29.00     | 142.33 ± 57.50d | 185.56 ± 51.84d |
| Lag time, sec        | 137.00 ± 28.00     | 108.78 ± 13.47d | 106.00 ± 13.00d |

Abbreviations: aGLU, α-D-glucosidase; COVID-19, coronavirus disease 2019; CRP, C-reactive protein; GCR, β-D-glucuronidase; HEX, hexosaminidase.

- Results are expressed as mean ± SD. In COVID-19 patients all parameters were significantly higher than in non–COVID-19 patients (CRP, P < .005; HEX, P < .006; GCR, P = .02; aGLU, P = .005). In addition, the same trend was observed in COVID-19 patients versus the control group (HEX, P = .001; GCR, P = .04; aGLU, P < .001). Moreover, in non–COVID-19 patients HEX and aGLU were significantly higher than in the control group (P = .01 and P = .001, respectively). Finally, in both COVID-19 and non–COVID-19 patients lag-time values were significantly higher than in the control group (P < .001).
- P < .01, COVID-19 patients versus non–COVID-19 patients.
- P < .05, patients versus controls.
- P < .01, patients versus controls.
A Holistic Approach to Pathology Education During the Coronavirus Disease 2019 (COVID-19) Pandemic

To the Editor.—We read with great interest the article by Mukhopadhyay et al1 that comprehensively outlined available technologies to promote remote learning in a time of social distancing measures. Indeed, these technologies were rapidly deployed in our department. However, we quickly realized the need to address key technology barriers as well as communication and wellness-related issues before this “new norm” of pathology education could be widely adopted.

The University of Toronto (U of T) Anatomical Pathology (AP) residency program, one of the largest of its kind in Canada, is a 5-year training program. Training occurs at multiple sites including 4 academic hospitals, a children’s hospital, affiliated community hospitals, and the provincial forensic pathology service.

Provincially mandated social distancing restrictions were instituted in March 2019 in response to the coronavirus disease 2019 (COVID-19) pandemic. However, differing Infection Prevention and Control (IPAC) measures amongst the multiple training sites resulted in confusion and mixed messages for our residents. In addition, a decline in surgical procedures led to a decrease in surgical pathology cases.

Stress and anxiety related to the unknown only worsened as our residents were temporarily redeployed to non-AP services to meet the clinical demand of COVID-19 infections. During the months of April and May 2020, as COVID-19 test volumes rapidly increased, 17 residents at 2 training sites were scheduled for in-person shifts to fill an expanded medical microbiology service rotation. Selection was initially site-dependent, which then evolved into a partially voluntary basis, made in collaboration with the Post-Graduate Medical Education Office (PGME), AP Residency Program Committee, and the AP resident body. Anatomical Pathology residents performed tasks such as triaging (where applicable) and accessing microbiology specimens as well as releasing/reporting test results. Several measures were taken to minimize the impacts of redeployment on resident education and wellness. Most residents were redeployed for only a few shifts to perform tasks that posed little health risks. The residents were exempted from pathology work during the days they were scheduled for microbiology shifts and were entitled to lieu days for overnight and weekend shifts. The redeployed residents were encouraged to use provided alternative education resources for self-study. New evaluation assessment forms were used for these rotations, based on new U of T PGME guidelines.

An anonymous survey of our residents’ learning experience during the early phase of COVID-19 was conducted from May 13 to 19, 2020. At the time of the survey, AP residents (redeployed and non-redeployed) had had 1.5 months of lockdown measures, reduced pathology workloads, and self-study (using traditional textbook and available alternative learning resources at the time). Of the 30 current AP residents, 20 (67%) responded. Unsurprisingly, 15 residents (75%) rated the educational yield (defined as perceived learning opportunities from gross rounds, individual or consensus case review and sign-outs, and tumor boards) of rotations during the COVID-19 pandemic as less or significantly less than prepanademic rotations. Most trainees readily identified the need for virtual learning resources. Work modifications such as changing rotations to busier services and sharing cases amongst residents also improved the learning experience. Almost all residents felt that maintaining some form of sign-out was needed for optimum learning, and 13 of 20 residents (65%) reported having modified sign-outs using telephone/email briefing and/or online or conference room meetings. In general, learning using online meeting platforms was well received. While adequate internet connectivity and hardware were important, staff familiarity with these technologies was crucial for effective learning. Two-thirds (13 of 20) of residents were satisfied with workplace safety pre-

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