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EDITORIAL

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Papa Giovanni XXIII Bergamo Hospital at the time of the COVID-19 outbreak: Letter from the warfront…

1 | INTRODUCTION

In early December 2019, the 2019 novel coronavirus (COVID-19) was identified as the agent responsible for the first pneumonia cases of unknown origin in Wuhan, the capital of the Hubei region in China. The virus has been identified as a novel enveloped RNA betacoronavirus 2, that has been promptly named SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2). The World Health Organization (WHO), on January 12, 2020, declared the COVID-19 a public health emergency of international concern. On March 11, the WHO made the assessment that COVID-19 can be characterized as a pandemic.

The COVID-19 infection, documented both in hospitals and in home settings, has spread diffusely worldwide with local minor differences, totaling over 234 073 laboratory-confirmed cases as of March 19, 2020.[1]

The first documented case in Italy was identified in a 38-year-old manager in the province of Lodi, Lombardy, in the north of Italy. The first documented case in our hospital (Bergamo Province, of over 1.1 million inhabitants) was identified on Friday, February 21, 2020.

In this report, we describe the call for action activated to tackle the epidemic. The rapid increase of positive cases has caused, on the one hand, widespread panic among the people and on the other hand, the need for profound structural and logistical reorganizations of the Papa Giovanni XXIII Hospital. In this context, we describe the role of the laboratory.

Starting from Saturday February 22, half of the infectious disease ward was dedicated to COVID-19 patients, moving 24 non-COVID-19 patients to other medical units of the same hospital or discharging them. On February 23, it became clear that this conversion was not enough and by Friday February 28, all of the 48 beds of the infectious disease unit were occupied. From that day on, every 48 hours, a new 48-bed unit was prepared, transferring out of the hospital the non-COVID-19 patients. In a rapid and tremendously organized fashion, several medical and surgical units were dismantled to create dedicated COVID-19 units, rapidly occupied by patients undergoing respiratory support (mainly continuous positive airway pressure, CPAP), up to 140 devices working simultaneously and some bi-level noninvasive ventilation, (NIV). As of March 10, 2020, five COVID-19-dedicated units (48 beds each) were progressively activated moving non-COVID-19-related patients to either other departments, external hospitals, or discharged. More than 35% of the medical personnel (approximately 400 physicians of any discipline), together with over 900 nurses, have been recruited and specifically formed to be fully dedicated to the newly born COVID-19 units. As of today, we are activating the sixth 48-bed unit. An additional 45 beds were prepared in San Giovanni Bianco Hospital (a section of our hospital, a few miles away from the main location).

Simultaneously, the hospital increased the number of insensitive care unit (ICU) beds from the initially dedicated 8-bed unit to the current number of 88 ICU beds plus 12 respiratory semi-intensive unit beds.

On an average day, as of February between 80 and 90 patients are attended in the emergency room (ER), distributed as follows:

- 5%-10% in the shock room (for intubated or in CPAP patients)
- 25% in the emergency medicine unit (up to 24 patients on CPAP/NIV)
- Over 60% in the atrium (up to 50 patients, 50% on oxygen supplementation)

The rapid spread of the infection has led to a progressive increase in the number patients of accessing to the ER.

In this context, the hematology laboratory has seen a progressive reduction of tests required for outpatients versus inpatients due to COVID-19.

The laboratory plays an essential role in the diagnosis, even early, in the management, follow-up, and in the prognosis of many diseases.[2]

The diagnosis and the management of patients with COVID-19 are no exception to this paradigm; indeed, the molecular diagnostics testing allows for the direct identification of RNA virus, while the detection of specific antibodies for COVID-19 is the cornerstone for serological surveillance.

The increase of critically ill patients has put the ICUs to the test. Therefore, there is an urgent need to identify the clinical and laboratory predictors which allow for risk assessment, the most appropriate clinical pathways, and the optimization of resource allocation.

Currently, the clinical characteristics of patients with COVID-19 are well described,[3-5] while few and contradictory information are available on the laboratory tests[6] such as the complete blood count (CBC) parameters.[7-10] Data on the most innovative parameters of the CBC profile (CBC extended) (ie, immature granulocytes, reactive lymphocytes and the nucleated red cells automatic counts, the platelet fraction or reticulated platelets, the erythrocyte and reticulocyte indices), are not currently available in literature.

The only published and studied data on CBC parameters are focused on small case series which often do not exceed more than 100 subjects and are able to show that absolute lymphopenia is predictive of an increased risk of complications in ICU patients.[8,9]

As a matter of fact, the evidence on all other CBC parameters shows contradictory results, perhaps due to timing in which the test is performed with respect to the development of the disease and factors such as ethnicity, gender, age, comorbidity, and possible therapeutic treatments. A puzzling factor lies adequate, but different multivariate statistical analyses that have been used in published articles. Nevertheless, we have no choice but to use whatever information is available.

On a cohort of 300 COVID-19 patients randomly selected from those evaluated in the ER in the first week of the Bergamo outbreak, the lymphopenia was observed, but not anemia or thrombocytopenia. The leukocyte counts were normal, and only about 1% of subjects was observed to have the presence of circulating erythroblasts (ie, 0.02×10^9/L). Manual microscopy review showed the presence of reactive lymphocytes of which a subset appeared lymphoplasmacytoid according to Fan et al[9]

These are, of course, preliminary data of a timely observation from which no conclusions or indications can be drawn. These data must be supplemented with clinical information for the correct multivariate statistical analyses to be done.

With regard to the safety of laboratory staff manipulating peripheral blood samples, a recent study by Wang et al[11] showed that a small percentage of blood samples had positive reverse transcriptase-polymerase chain reaction (RT-PCR) test results (ie, 1%), suggesting that infection sometimes may be systemic, this study does not address the viability of the virus. The presence of viral RNA in the peripheral blood does not imply that infection may be transmitted by the parenteral route. Aerial transmission is considered the major exposure risk for coronaviruses such as SARS-CoV-2.

The WHO released documents to provide interim guideline for the management of samples that might contain SARS-CoV-2.[12]

Iwen et al[13] in a recent article points out that MERS-CoV and SARS-CoV cases as a laboratory-acquired infections are very rare and caused by incorrect safety behaviors of laboratory staff.

The level of biosafety for virology labs depends on the type of activity performed. Biosafety level 2 or level 3 hoods are used for nonpropagative and propagative work of diagnostic laboratory, respectively.[12] While a precise indication for all other laboratories at the moment is not available, the hematology laboratory staff must follow the rules of the biosafety and regulatory standards provided, according to the local risk assessment.[13]

Despite the emergency and limited time availability, more information is needed about the actual CBC pattern of COVID-19-positive subjects at different stages of disease development, for proper risk stratification, appropriateness of hospitalization and monitoring. Only this way, will it be possible to identify which, among the many parameters of the CBC extended profile, may have a real predictive value for the clinical progression and risk of complications of acute lung damage/acute respiratory distress syndrome.

Only the proper production of strong scientific evidence can avoid the risk of interpretative errors, leading to potential delays in identifying the best therapeutic strategies.

It should also be considered that the preparation of Papa Giovanni XXIII Hospital as the COVID-19 Hospital in Bergamo, with the total closure of health care, except for emergencies and oncological patients, will eventually lead to a delayed diagnosis of a great number of pathologic conditions, especially in hematology and oncology patients. There will be a progressive complexity of the cases which will gradually be diagnosed and require more attention and care from clinicians and many other resources to prevent worse outcomes.

In the claim of great technological development and rapid sharing of information, it is necessary to enhance national and international cooperation and networks for sharing data and big data technologies from a multidisciplinary perspective.

In these days, humanity is facing a long fraught road with obstacles, with an unknown destination. In this situation, time factor is the key factor in order to save as many lives as possible. Time is critical.

The lessons learned that should be shared with both health personnel and the general population:

- We were forced to mobilize a whole hospital (a 1000-bed hospital) for COVID-19 patient.
- There is no need to panic, or to rush to somewhere. Just stay home, and reinforce hand hygiene (*if no alcoholic solution is available, 40-60 seconds of washing with soap and water is enough*).
- Dutifully comply with the institutional indications for avoiding close contact and large gatherings of people (*movies, theaters, sports events, schools, universities, meeting, and similar should be avoided*).
- Strictly adhere to the antispread protection rules when in close contact with an infected or possibly infected individual.
- If you are infected (or a close contact is infected) and asymptomatic, please DO RESPECT the quarantine for at least 14 days. Do not go to the ER or take public transportation. If you are symptomatic call, the emergency number provided by your local government.
- The main message should be: "I am part of the solution" …. if one believes that the problem is upon someone else it shall never work ("*If we ALL feel involved, together we can beat it*").
- But most of all, if you PREPARE yourself at all levels (population, institutions, health workers), you will defend all.

In times of globalization, when the critical phase of this emergency is overcome, a deep reflection on global risk assessment strategies, economic, social development priorities, and development policies will be needed. It is also necessary to define and ensure a global health care and hygiene is essential at all levels, to warrant a health system which is necessarily barrier-free between states. If humanity is able to analyze this global crisis in the right perspective, maybe we can discover new horizons and new opportunities for a better future.

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REFERENCES

1. Situation report -60. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200320-sitrep-60-covid-19.pdf?sfvrsn=8894045a_2. Accessed March 21, 2020.
2. Plebani M, Laposata M, Lippi G. A manifesto for the future of laboratory medicine professionals. *Clin Chim Acta*. 2019;489:49-52.
3. Li LQ, Huang T, Wang YQ, et al. 2019 novel coronavirus patients' clinical characteristics, discharge rate and fatality rate of meta-analysis. *J Med Virol*. 2020;1-7. https://doi.org/10.1002/jmv.25757. [Epub ahead of print].
4. Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *Lancet Respir Med*. 2020;20:30079–30085.
5. Chang LM, Wei L, Xie L, et al. Epidemiologic and clinical characteristics of novel coronavirus Infections infections involving 13 patients outside Wuhan, China. *JAMA*. 2020;323:1092-1093. [Epub aheadof print].
6. Wu F, Zhao SU, Yu B, et al. A new coronavirus associated with human respiratory disease in China. *Nature*. 2020;579:265-269.
7. Lippi G, Plebani M. Laboratory abnormalities in patients with COVID 2019 infection. *Clin Chem Lab Med*. 2020. https://doi.org/10.1515/cclm-2020-0198
8. Lippi G, Plebani M, Herny MB. Thrombocytopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: a meta-analysis. *Clin Chim Acta*. 2020. https://doi.org/10.1016/j.cca.2020.03.022
9. Fan BE, Chong VCL, Chan SSW, et al. Hematologic parametersin patients with COVID-19 infection. *Am J Hematol*. 2020 Mar 4. [Epub ahead of print].
10. Park GE, Kang C-I, Ko J-H, et al. Differential cell count and CRP level in blood as predictors for middle east respiratory syndrome coronavirus infection in acute febrile patients during nosocomial outbreak. *J Korean Med Sci*. 2017;32:151-154.
11. Wang W, Xu Y, Gao R, et al. Detection of SARS-CoV-2 in different types of clinical specimens. *JAMA*. 2020. https://doi.org/10.1001/jama.2020.3786
12. World Health Organization. Laboratory biosafety guidance related to the novel coronavirus (2019-nCoV): interim guidance. https://www.who.int/docs/default-source/coronaviruse/laboratory-biosafety-novel-coronavirus-version-1-1.pdf?sfvrsn=912a9847_2. Accessed March 21, 2020.
13. Iwen PC, Stiles KL, Pentella MA. Safety considerations in the laboratory testing of specimens suspected or known to contain the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). *Am J Clin Pathol*. 2020; 1-4. https://doi.org/10.1093/AJCP/AQAA047