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OPINION

Laboratory Biomarkers Predicting COVID-19 Severity in the Emergency Room

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Infection of novel Coronavirus has been declared pandemic by the WHO and now is a world public health crisis. Laboratory activity becomes essential for the timely diagnosis. Few parameters, such Lymphocytes count, SaO₂ and CRP serum level can be used to assess the severity of COVID-19 in emergency room. © 2020 IMSS. Published by Elsevier Inc.

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Infection by the novel Coronavirus (SARS-CoV-2) has been declared pandemic by the WHO on March 11, 2020 and is now a world public health crisis. The World perception changing dramatically.

It is now known that SARS-CoV-2 triggers a heterogeneous clinical manifestation, encompassing a wide range of clinical spectrum, going from an asymptomatic course to an acute respiratory distress syndrome with a high risk of death (1–3).

Lombardy is now considered the Italian Region that major hit by COVID-19, with 78105 cases out of 211938 throughout Italy at May 4, 2020. The first Italian autochthonous patient was recorded in Codogno, Lombardy, on February 18, 2020, 25 km far from Crema.

In the following days, the Maggiore Hospital Emergency Unit was invaded by suspected COVID-19 patients. In the first time at the emergency room, a positive Real-Time PCR (RT-PCR) test for SARS-CoV-2 after nasopharyngeal swab was officially considered the hallmark for COVID-19 diagnosis. However, this technique has affected by several drawbacks. Pre-analytical troubles, suboptimal sensitivity,

long production time results and other intrinsic methodological features affect RT-PCR. Using CT-scan as gold standard for the diagnosis of interstitial pneumonia, we recently calculated the diagnostic accuracy of the nasopharyngeal swab in entire study population of 539 patients, with good sensitivity (80%) but low specificity (45%) (4).

It's a logic deduction that the method cannot be yet considered a rapid and specific tool that can be used for a triage in Emergency room.

It is now recognized that even after an apparently benign initial stage, during which the virus replicates and first symptoms appear, a second more aggressive course due to hyperinflammation can intervene in some patients, with a need of urgent hospitalization or intensive care.

We preliminarily observed that several laboratory tests have been shown as characteristically altered in COVID-19 and we have been proposed as rapid and sensitive alternatives in identifying likely COVID-19 cases. In our paper simple baseline laboratory biomarkers have been clearly linked to clinical feature (4).

Our laboratory exams at admission showed white blood cell count below $10 \times 10^9/L$ in 82% of patients, neutrophil count below $10 \times 10^9/L$ in 83.4%, and lymphocyte count below $1 \times 10^9/L$ in 55.6%. Also, C-reactive protein (CRP), aspartate aminotransferase and lactate dehydrogenase values were elevated in most patients, particularly among those with worst clinical picture and outcome (4).

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The neutrophil/lymphocyte ratio (N/L ratio) was also higher in patients with a more severe disease, as previously reported (5).

As one of the most distinctive acute phase reactants, the short-pentraxin CRP increases rapidly after the onset of inflammation. COVID-19 Pulmonary disease with inflammatory features usually raise serum CRP level in response to inflammatory cytokines, such as IL-6, IL-1 or TNF- α (6). We found by ROC curve analysis that a CRP > 7 mg/dL can identify subjects with a severe disease (4).

Similarly, Oxygen saturation (SaO₂) was found as another candidate marker of progressive severity. The fact that it was so tightly associated to hospitalization or even death in our model is unsurprising, because a low SaO₂ is one of the main criteria for the definition of a severe case. Despite SaO₂ is an indirect way to monitor arterial oxygen pressure (PaO₂) and it may lead to blood oxygen content overestimation in the case of anemia, our data enforce the notion that in most cases the commonly used cutoff (93%) is an important tool to evaluate the severity of COVID-19 (1).

Because all the alterations we described can be linked to the inflammation pathway, our findings also support the need of expanding research on the dysregulation of the first

steps of innate immunity, possibly involving more precocious markers of the pentraxins family, different from CRP.

In conclusion we propose that a few parameters, such Lymphocytes count, L/N ratio, SaO₂ and CRP serum level can be used to assess the severity of COVID-19 in emergency room.

In a second step it's possible to use the RT-PCR on swab to confirm COVID-19 diagnosis.

References

1. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020;395:497–506.
2. Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients with 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *JAMA* 2020;323:1061–1069.
3. Guan W, Ni Z, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med* 2020;382:1708–1720.
4. Benelli G, Buscarini E, Canetta C, et al. SARS-COV-2 comorbidity network and outcome in hospitalized patients in Crema, Italy. *MedRxiv*; 2020. <https://doi.org/10.1101/2020041420053090> 2020.
5. Liu Y, Du X, Chen J, et al. Neutrophil-to-lymphocyte ratio as an independent risk factor for mortality in hospitalized patients with COVID-19. *J Infect*, 2020;. <https://doi.org/10.1016/j.jinf.2020.04.002>.
6. Sarzi-Puttini P, Giorgi V, Sirotti S, et al. COVID-19, cytokines and immunosuppression: what can we learn from severe acute respiratory syndrome? *Clin Exp Rheumatol* 2020;38:337–342.