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Commentary

Differentiating diagnosis of COVID-19 or influenza in patients based on laboratory data during flu season

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Both coronaviruses and influenza A viruses (IAVs) are general pathogens which are responsible for the seasonal cold. However, a new coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is pulling the world into the torment of the COVID-19 pandemic [1]. As the SARS-CoV-2 is still circulating in almost every continent with its ability for airborne and asymptomatic transmission [2], it would be very likely that the COVID-19 pandemic will overlap with the influenza epidemic in the coming winter [3]. COVID-19 shares many clinical symptoms with pneumonia caused by IAVs, but its fatality rate is much higher than that of seasonal flu [4]. Therefore, to precisely treat patients with respiratory diseases during the epidemic season, it would be very important that doctors are able to differentiate COVID-19 from seasonal influenza based on laboratory data as early as possible.

Currently published clinical and laboratory data on COVID-19 are limited to studies with small sample sizes mostly originating from China. In the study, Ji et al. in Northwestern University reveals significant differences in laboratory parameters between hospitalized COVID-19 and influenza patients in the US, with a sample size of more than 1000 cases [5]. Instead of comparing clinical endpoints to evaluate risks, they compiled and temporally tracked all available laboratory results of the hospitalized patients from the day of presentation to day 14.

Compared to influenza patients, the most significant differences over the course of 14 days of hospitalization in COVID-19 patients were faster worsening anemia and leukocytosis, and a more rapid increase in D-dimer, BUN, and ALT. The level of lactate dehydrogenase (LDH) was significantly higher in patients with influenza. However, the most commonly reported laboratory abnormalities in COVID-19 include lymphopenia, prolonged prothrombin time (PT), and elevated LDH.

To further evaluate the risk, COVID-19 patients were sub-classified into 5 clusters through a unique hierarchical clustering by analysis of the 14-day laboratory data that are different between COVID-19 and influenza, such as complete blood count, D-dimer, BUN, and ALT. The clinical manifestation of patients in these clusters is different from each other. Cluster 1 showed the highest mortality rate (27.8%), which was followed by group 2 and 5 (12.5%). There were also significantly increased rates of ICU admission, intubation, and other respiratory infections in cluster 1 compared to cluster 4. In addition, while cluster 4 showed the best outcome, patients in cluster 1 presented features which are consistent with previously published reports, including high WBC, BUN, creatinine, alkaline phosphatase, bilirubin, and troponin.

The authors also found that the hospitalized COVID-19 patients with the worst prognosis often show worsening anemia, increasing RDW, worsening neutrophilia and monocytosis, and significantly higher levels of BUN, creatinine, D-dimer, alkaline phosphatase, bilirubin, and troponin. The data were also analyzed based on sex and age (< 60 or ≥ 60), and laboratory features associated with a worse prognosis were more prominent in old males.

It would be interesting to further investigate whether the different risk clusters of COVID-19 correlate with the pathophysiology in these patients. Future studies on specific organ systems in correlation with other clinical manifestations, including the level of inflammatory cytokines, may be useful to confirm the underlying pathology in patients in these clusters.

There are also some limitations. The sample size is still small, and only 154 COVID-19 and 23 influenza inpatients with at least 7 days of data points were used to analyze, thus no distinct clusters were identified in influenza patients due to lack of sufficient patients. It is also not a multi-center study, and it is not known that similar laboratory patterns as in COVID-19 cluster 1 are also present in severe hospitalized influenza patients. Furthermore, no patients coinfected with SARS-CoV-2 and influenza virus were analyzed. In conclusion, a multi-center, large sample size with different human races, risk stratification of hospitalized COVID-19 patients, influenza patients, and co-infection patients with SARS-CoV-2 and IAV, are needed in future studies.

Declaration of Interests

None.

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