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An urgent call to clinicians and researchers: 2020 acuity required when assessing and reporting laboratory abnormalities in COVID-19

The current outbreak of coronavirus 2019 (COVID-19) calls for actionable information to be published as soon as possible in the interest of public health. There is a surge in literature reviews and meta-analyses summarising the roles of routine laboratory markers in assessing disease severity and guiding treatment in COVID-19. A closer look at the literature reveals some shortcomings in the reporting and interpretation of laboratory results.

When discussing the management of liver injury in COVID-19, Zhang *et al*. provided a summary of patients with abnormal liver aminotransferases from several recent studies and discussed several possible mechanisms for liver injury.[1] Bangash *et al*. later reminded readers of the significance of the liver abnormalities reported in these studies, that, although the prevalence of elevated aminotransferases and bilirubin in patients faring worst was at least double that of others, clinically significant liver injury is uncommon (even when most severely ill patients are selected).[2] In addition, Bangash *et al*. noted that several studies have reported elevated levels of creatine kinase and lactate dehydrogenase or myoglobin. Aminotransferase elevations do not necessarily arise from liver alone; COVID-19 infection might induce a myositis similar to that observed in severe influenza infections.[2]

As study authors compare the significance of laboratory marker results between intensive care unit (ICU) and non-ICU groups, severe and less severe disease groups, or survivors and non-survivors, in addition to assessment of statistical significance of a marker between the two groups, the biological (and analytical) variation of the marker should be considered as well as the biological significance of the value difference.

A meta-analysis of four studies on the role of procalcitonin in patients with severe COVID-19 shows that increased procalcitonin values (above the normal reference limit) are associated with nearly fivefold higher risk of severe SARS-CoV-2 infection (odds ratio (OR), 4.76; 95% confidence interval (CI), 2.74-8.29).[3] A closer look at these four papers found that while Huang *et al*. used a reference limit of <0.1 ng/mL as normal, Guan *et al*. and Wang *et al*. used a different decision limit of ≥0.5 ng/mL as abnormal and Zhang *et al*. used a reference interval of 0–0.1 ng/mL.[4–7] It would be more informative to know the analytical methods used and, provided there is no significant between-method biases, to consider a common reference interval; alternatively, the degree of

procalcitonin elevation may correlate with disease severity in COVID-19.

The analytical method details are scarce in much recent literature on COVID-19. This makes it challenging to adopt, apply or compare published results to the local settings. The European Federation of Clinical Chemistry and Laboratory Medicine and the European Union of Medical Specialists Joint Working Group on Guidelines have suggested a checklist to ensure that all relevant laboratory issues should be addressed for clinical decision making.[8] It includes sample type and handling, methodology, limits of detection and quantification, analytical and biological variations (reference change values).[8]

I call on clinicians and researchers to consider the pre-analytical, analytical and post-analytical aspects of laboratory testing when reviewing or publishing laboratory results in this COVID-19 pandemic.

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