



Letter to the Editor

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Laboratory parameters as predictors of mortality in COVID-19 patients on hospital admission

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To the Editor,

In December 2019 a novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SAR-CoV-2), emerged in Wuhan (China), later named as COVID-19 by the World Health Organization (WHO). The number of cases spread rapidly across the world becoming a pandemic disease in March 2020. Since then, many studies have broadly described the clinical and laboratory characteristics of these patients, especially in the region of China. Some attempts have been made in order to identify risk factors associated with severe and adverse outcomes on the basis of these characteristics [1–3].

In this study we present the laboratory characteristics from 382 adult patients admitted with COVID-19 to Isala Hospital, the largest Dutch referral hospital located in the Northern area of the Netherlands, from March 12th (first case admitted) up to April 14th 2020. The laboratory measurements were collected retrospectively from the electronic patient record with the help of CTcue software (www.ctcue.com). The laboratory parameters on admission were compared between survivors (admitted and discharged) and non-survivors. Our aim was to identify predictors of mortality based on the laboratory results on admission.

The first confirmed COVID-19 case in the Netherlands occurred on February 2020 in the South of the country. Since that moment till mid-April 2020, 382 adult patients with COVID-19 were hospitalized in Isala Hospital. The overall mortality rate of the admitted COVID-19 patients

was 26%, consistent with previous studies [1–3]. The median age of the survivor group was statistically lower compared to the non-survivor group with 67.6 and 80.0 years, respectively. In both groups males predominated. The majority of patients presented with laboratory values within the reference interval. This percentage was higher in the survivor group compared to the non-survivor group. Several significant differences in laboratory values were noted between the non-survivor and survivor group on admission, especially encompassing higher values of creatine kinase (CK) (2.7-fold), lactate dehydrogenase (LDH) (1.6-fold), C-reactive protein (CRP) (1.6-fold), aspartate aminotransferase (AST) (1.4-fold), creatinine (1.3-fold), glucose (1.1-fold) and higher absolute neutrophil counts (1.1-fold), as well as lower absolute lymphocyte counts (0.7-fold) and platelet counts (0.8-fold) and values of albumin (0.9-fold), pO₂ (0.9-fold) and O₂ saturation (0.98-fold) (Table 1).

The observed differences are in line with data shown in previous studies [1–5]. These studies also reported that an increase in CK, LDH, CRP, AST and creatinine, together with a decreased number of lymphocytes, platelets and albumin levels are associated with a severe or fatal prognosis [1–5]. In addition, Zhou and others showed older age as a potential risk factor for COVID-19 patients [1, 3]. Our data is consistent with both findings and the reported mortality. Increased white blood cell (WBC) count seems to be a consistent finding in severely ill patients [2, 4, 5]. In contrast, our data shows no significantly increased WBC counts in the non-survivor group on admission, whereas the differences between neutrophils, lymphocytes and platelets in both groups are similar as previously described [1–5]. Similarly, there are no differences in alanine aminotransferase (ALT) or bilirubin values between the two groups, although this has been described by others [1, 2, 5]. A possible explanation is that we report data on admission whereas others reported data during hospitalization. Interestingly, the number of neutrophils increased as disease progressed (data not shown). Together with the increased CRP this tendency is indicative for a

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Table 1: Age, sex and laboratory values of COVID-19 patients on hospital admission.

| | Reference interval | Survivors (n=282) | Non-survivors (n=100) | p-Value ^a |
|-------------------------------------|----------------------------|-------------------|-----------------------|-----------------------|
| Age, years | n.a. | 67.6 | 80.0 | <0.0001 ^b |
| Sex | n.a. | 60% (m), 40% (f) | 65% (m), 35% (f) | n.a. |
| WBC, ($\times 10^9$ per L) | 4.0–10.0 | 6.5 (n=265) | 6.6 (n=72) | 0.46 |
| <4 | – | 14% | 10% | 0.35 |
| 4–10 | – | 72% | 71% | 0.89 |
| >10 | – | 14% | 19% | 0.29 |
| Lymphocytes, ($\times 10^9$ per L) | 1.00–4.00 | 0.90 (n=246) | 0.65 (n=68) | <0.0001 ^b |
| <0.8 | – | 31% | 43% | 0.07 |
| Neutrophils, ($\times 10^9$ per L) | 1.5–9.0 | 4.7 (n=249) | 5.3 (n=68) | 0.032 ^b |
| Platelets, ($\times 10^9$ per L) | 150–400 | 206 (n=261) | 169 (n=70) | 0.0004 ^b |
| <100 | – | 4% | 4% | 0.86 |
| <150 | – | 18% | 33% | 0.008836 ^b |
| Hemoglobin, mmol/L | 8.5–11.0 (m), 7.5–10.0 (f) | 8.5 (n=266) | 8.4 (n=72) | 0.59 |
| CRP, mg/L | <0.5 | 62 (n=263) | 100 (n=72) | 0.0002 ^b |
| Albumin, g/L | 35–55 | 38 (n=244) | 36 (n=71) | 0.0005 ^b |
| ALT, U/L | 0–45 | 30 (n=257) | 28 (n=70) | 0.97 |
| AST, U/L | 0–45 | 40 (n=248) | 54 (n=70) | <0.0001 ^b |
| >45 | – | 39% | 67% | <0.0001 ^b |
| LDH, U/L | 50–250 | 253 (n=253) | 410 (n=71) | <0.0001 ^b |
| >250 | – | 67% | 86% | 0.001709 ^b |
| Bilirubin, μ mol/L | <17 | 8 (n=243) | 9 (n=71) | 0.0514 |
| Creatinine, μ mol/L | 65–105 (m), 50–90 (f) | 85 (n=265) | 112 (n=73) | <0.0001 ^b |
| CK, U/L | <200 (m), <170 (f) | 109 (n=170) | 297 (n=39) | 0.0002 ^b |
| Glucose, mmol/L | 4.0–7.8 | 6.7 (253) | 7.5 (72) | 0.0137 ^b |
| PH | 7.35–7.45 | 7.48 (n=109) | 7.47 (n=32) | 0.19 |
| pCO ₂ , kPa | 4.7–6.4 | 4.4 (n=220) | 4.3 (n=67) | 0.65 |
| pO ₂ , kPa | 9.3–13.3 | 9.1 (n=220) | 8.1 (n=67) | 0.0024 ^b |
| <9.3 | – | 53% | 69% | 0.02517 ^b |
| O ₂ Saturation | 0.95–0.98 | 0.95 (n=218) | 0.93 (n=65) | <0.0001 ^b |
| <0.95 | – | 38% | 60% | 0.00173 ^b |

Data represent median laboratory results (and total number of patients measured) or % of patients. ^ap-Values are calculated by Wilcoxon-Mann-Whitney test, or χ^2 -test, as appropriate. A p-Value less than 0.05 were considered statistically significant. ^bsignificant different (p-Value<0.05). n.a., not applicable; WBC, white blood cell count; CRP, C-reactive protein; ALT, alanine aminotransferase; AST, aspartate aminotransferase; LDH, lactate dehydrogenase; CK, creatine kinase.

superimposed bacterial infection as previously described [4]. Although it is well known that the disease causes pneumonia, little has been described about blood gas parameters of COVID-19 patients on hospital admission. Arterial blood gas analysis showed no differences between the pH and the CO₂ pressure between survivors and non-survivors. However, our data indicate that a low O₂ pressure and O₂ saturation on admission could be considered as potential risk factors for fatal outcome. As expected, both the O₂ pressure and O₂ saturation decreased along the course of the disease for the non-survivor group (data not shown).

Although some limitations in this study must be acknowledged (i.e. the viral load, the date of onset of the disease and comorbidities are unknown and coagulation

parameters shown to be important were not routinely tested), the presented data are a good representation of the laboratory diagnostics of COVID-19 patients on hospital admission in a large referral hospital of a Western European country. To our knowledge this report is one of the largest COVID-19 cohorts presented in laboratory medicine. We believe the presented data can be used for faster, more accurate and early assessment of disease progression of COVID-19 patients.

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