Sudan Journal of Medical Sciences
Volume 16, Issue no. 2, DOI 10.18502/sjms.v16i2.9284
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Editorial

Diagnosis of COVID-19 in Countries with Limited Health Resources – Blood Markers versus rRT–PCR

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Since the outbreak of coronavirus disease 2019 (COVID-19) in China in December 2019 and its rapid worldwide spread, the real-time reverse transcription–polymerase chain reaction (rRT–PCR) test has become the gold standard for the etiological diagnosis of COVID-19 infection [1]. However, for countries with limited health resources, rRT–PCR test is relatively expensive and requires specialized laboratories and highly trained personnel [2].

Recent studies have shown that some routine blood test markers might help in the diagnosis of COVID-19 infection in suspected patients with a very high predictive value (>95%) [3]. This editorial aims to assess the role of blood markers in diagnosing COVID-19 infection as an alternative for rRT–PCR in countries with limited health resources by performing online search in electronic databases such as Medline, Scopus, and Web of Science, using keywords such as “blood markers’ role in diagnosis of COVID 19.” Additionally, the references of identified documents were cross-checked for detecting additional studies. Overall, 203 articles were found using the aforementioned search criteria, of which 200 were excluded after scrutinization by the authors. Only three studies were finally selected and used in the present editorial based on the comparison of the final diagnosis reached by rRT–PCR and the high predictive value of blood markers. Another reason for excluding most studies was that they focused on the disease outcome rather than the diagnostic value.

Santotoribio *et al.* (2019) evaluated the role of six routine blood tests (blood lymphocyte, eosinophil count, ferritin serum level, lactate dehydrogenase (LDH), C-reactive protein (CRP), and D-dimer) in diagnosing cases of suspected COVID-19 [4. The study showed that 91% of patients infected with COVID-19 met one or more of these biomarker criteria. Thus, it is possible to rule out coronavirus infection with a high degree of probability in patients who meet none of these criteria. They concluded that these

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Received 2 May 2021
Accepted 22 June 2021
Published 30 June 2021

Production and Hosting by Knowledge E

Editor-in-Chief:
Prof. Mohammad A. M. Ibnouf

OPEN ACCESS

markers could very well be used as a tool for diagnosing and screening suspected COVID-19 in adult patients at hospital admission.

Another study by Ferrari *et al*. compared the routine blood analysis of the plasma levels of white blood cells (WBCs), platelets, CRP, aspartate aminotransferase (AST), alanine aminotransferase (ALT), γ-glutamyl transpeptidase (GGT), alkaline phosphatase (ALP), and LDH of 207 patients who had tested positive for COVID-19 using the rRT–PCR test [5].

The results showed statistically significant differences in the plasma levels of WBC, CRP, AST, ALT, and LDH between those who were positive and those who were negative at the genetic testing. Using rRT–PCR as the gold standard, almost 70% of the patients could be classified as COVID-19-positive or -negative on the basis of their hematological parameters.

The last study was conducted in Sudan under the supervision of the authors of this editorial [6]. The study included 56 patients who had all tested positive for COVID-19 using rRT–PCR. For all patients, the complete blood count (CBC), CRP, erythrocyte sedimentation rate (ESR), total protein, albumin, total and direct bilirubin, AST, ALT, ALP, urea, creatinine, and electrolytes were measured upon admission. In this study, intense statistical analyses were done using the SPSS program. With a significance level of $p \leq 0.05$ and confidence limits (CLs) of 95%, group comparison was tested using Mann–Whitney test for quantitative variables while qualitative variables were tested using Chi-square (fisher exact) test. The receiver operating characteristic/area under the curve (ROC/AUC) was used to obtain the true positive, and false positive predictive values were calculated using the best cutoff values.

The ROC/AUC ensured the appellant result of lymphocytes (%) as a predictor with 92% AUC, 90% neutrophils, 95.8% ESR, 89% CRP, and 86.8% WBCs. About 98% of the suspected individuals diagnosed with COVID-19 using ROC showed a cutoff of <=21.8 for lymphocytes (%), >=67.7 for neutrophils, >=37.5 for ESR, >=6.2 for CRP, and >=7.15 for WBCs. The applicable value of these studies based on the fact that hospitals in developing countries, including the ones with limited health resource, have the facilities of automated analyzers that can test for these inexpensive highly sensitive and specific blood markers in <60 min. If physicians combine the blood markers with the medical history and imaging tests, they can very well diagnose and/or screen patients suspected of COVID-19. In addition to that, using blood markers in diagnosis may be crucial in detecting a new genetic variant of Coronavirus, that is, the Indian strain in which molecular testing encounters a high percentage of false-positive/negative cases.

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