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Short Communication

A cross sectional evaluation of the corona-score for swift identification of SARS-CoV-2 infection at a tertiary care hospital in Pakistan

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ABSTRACT

Background: The Corona-Score is one of the first and most widely used predictive model for coronavirus 2 (SARS-CoV-2) infection. The purpose of this study was to validate the performance of Corona-Score in a cohort of Pakistani patients pursuing care for suspected infection.

Methods: After seeking institution's ethical committee exemption, results of serum lactate dehydrogenase (LDH), C-reactive protein (CRP), ferritin, absolute lymphocyte and neutrophil counts, chest x-ray findings and demographics of suspected COVID-19 cases with respiratory symptoms were recouped from electronic medical record. The pre-validated score as proposed by Kurstjens S et al., was calculated. The subjects were divided into SARS-CoV-2 positive and negative on the basis of reverse transcription-polymerase chain reaction (RT-PCR) findings. Median and interquartile range (IQR) was calculated for the score in the two groups and the difference was assessed using the independent sample median test. Receiver operating characteristics (ROC) curve analysis was plotted. Statistical analyses were carried out using SPSS 26, with statistical significance set at p *value* < 0.05.

Results: A total of sixty cases, 30 (50%) RT-PCR positive and 30 (50%) negative with a median Corona-Score of 3.5 (IQR: 0–6) and 1.5 (IQR: 0–4) respectively, were evaluated. A p-value of 0.61 showing no statistically significant between group differences was observed. The area under the curve of Corona-Score in our population of patients was 0.59 (95% CI: 0.45–0.74). Using the cut-off values of four originally identified by Kurstjens et al. the model displayed 43.3% sensitivity and 70% specificity with an overall accuracy of 56.67%.

Conclusion: Corona-Score displayed a lower diagnostic accuracy which may be attributable to the different genetic framework, viral strain and severity of the disease in Pakistanis compared to the population where this score was originally validated. However, large multi-center studies across the country are dire need of time to evaluate the score in overly exhausted health care setup and limited availability of PCR testing.

1. Introduction

The novel Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), after its origin in China in 2019, became a global pandemic in 2020 [1]. The disease can present as mild, flu-like illness, to critical condition requiring intensive care admission and mechanical ventilation [2,3]. The diagnosis of COVID-19 is still clearly based on detection of SARS-CoV-2 RNA in upper or lower respiratory tract specimens via nucleic acid amplification tests (NAATs) [4]. However, these techniques have a few crucial disadvantages, such as the relatively low diagnostic sensitivity in nasopharyngeal swabs, shortage of testing materials and personnel, as well as time consuming, which constitute issues for purposes of huge populace screening [5].

Clinical laboratories have provided a significant contribution towards diagnosis of COVID-19. To accelerate the diagnostic process, a point-based algorithm, the Corona-Score, was developed [6]. It is one of the first and most widely used predictive model that includes age, gender, chest X-ray and five laboratory investigations: lactate dehydrogenase (LDH), C-reactive protein (CRP), ferritin, and neutrophil and lymphocyte counts. This algorithm has the ability to predict whether a patient presenting with respiratory symptoms is probable to have COVID-19. A current study utilizing the Corona-Score in The Netherlands showed 91% accuracy, 96% sensitivity, and 95% specificity

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for differentiating patients testing positive or negative for SARS-CoV-2 by NAAT [6]. In fear of a shortage of testing capacity, embracing this algorithm could diminish the number of patients for whom RT-PCR testing is required. Moreover, in already resource constrained health care set ups with limited testing capacities in majority of the Indo-Pak sub-continent can facilitate rapid decision making in triage.

Although these data are inspiring, the model needs to be validated in other clinical and healthcare settings. Therefore, the purpose of this study was to evaluate the performance of Corona-Score in a cohort of Pakistani patients pursuing care for suspected COVID-19 infection.

2. Material and methods

The study was conducted at the Section of Chemical Pathology in collaboration with the Section of Molecular Pathology, Department of Pathology and Laboratory Medicine, Aga Khan University (AKU), Karachi, Pakistan, from August 2020 to January 2021. Permission form AKU's Ethical Review committee was sought. The subjects were divided into SARS-CoV-2 positive and negative on the basis of reverse transcription-polymerase chain reaction (RT-PCR) results on a standard-of-care nasopharyngeal swab.

Retrospective biochemical, hematological and imaging data was retrieved from the Integrated Laboratory Management System (ILMS). Biochemical parameters retrieved included serum LDH, CRP and ferritin. Hematological parameters recovered included absolute neutrophil and lymphocyte count. Presence of infiltrates on chest X-ray was the only radiological parameter included. The laboratory services at AKU operates according to the highest degree of quality and are accredited by Joint Commission International (JCIA) and College of American Pathologists (CAP).

The pre-validated score as proposed by Kurstjens S et al. was calculated using Microsoft Excel for windows [6]. According to the Corona-Score instructions, concentrations of ferritin were multiplied by a harmonization factor of 1.2 for Siemens equipment. Based on age, gender, biochemical and radiological data scores were assigned to each parameter according to a pre-defined criteria as outlined by Kurstjens et al. [6]. The Corona-Score is obtained by the summation of the score for each parameter. The final score is calculated from a minimum of 0 to a maximum of 14 points.

Median and interquartile range (IQR) was calculated for the score in the two groups and the difference was assessed using the independent sample median test. Receiver operating characteristics (ROC) curve analysis was plotted. Statistical analyses were carried out using Statistical Package for the Social Sciences (SPSS) version 26, with statistical significance set at $p < 0.05$. The study was exempted by the institutional ethical review committee of the AKU, Karachi (ERC#2020-5168-14099) with waiver of informed consent. The study was also registered with Chinese Clinical Trial Registry (Registration No: ChiCTR2100042375). Furthermore, this work has been reported in line with the STROCSS criteria [7].

3. Results

A total of 60 cases i.e. 30 (50%) positive and 30 (50%) negative by a nasopharyngeal swab RT-PCR testing were evaluated. The distribution of gender amongst RT-PCR positive and negative groups are shown in Table 1.The median Corona-Score of 3.5 (IQR: 0–6) was found in the RT-PCR positive group and 1.5 (IQR: 0–4) in the group that tested negative.

Table 1
Details of study subjects and median Corona-Score.

	RT-PCR Positive	RT-PCR Negative
Male (n)	12	13
Female (n)	18	17
Corona-Score (Median IQR)	3.5 (0–6)	1.5 (0–4)
Age (years)	**33.1±6.5**	**60.5±16.5**

The Corona-Score value was found to be elevated in participants with SARS-CoV-2 infection compared to those without. However, no statistically significant between group differences was observed on independent-samples median test with a p-value of 0.605 as shown in Fig. 1.

The area under the curve of Corona-Score in our population of patients was 0.59 (95% CI: 0.45–0.74). Using the cut-off values of 4 originally identified by Kurstjens et al. for their study population, the model displayed 43.3% sensitivity and 70% specificity with an overall accuracy of 56.67%. The results of ROC curve analysis is shown in Fig. 2.

4. Discussion

Thinking about the susceptible public health and healthcare system of Pakistan, and abrupt rise in number of infected cases, the country certainly has high possibility of morbidity and mortality associated with COVID-19. A number of interlaced reasons that put the Pakistani population at increased risk can be categorized into public reluctance (poverty, illiteracy, carelessness, rural lifestyle), healthcare personnel associated demurrals (reduced caregiver to patient ratio, inadequate knowledge and training of healthcare professionals, meager collaboration) and ineffective organizations and authorities (unstable healthcare infrastructure, lack of infection control strategies, poor scrutiny system and resource constraints) [8]. Another issue is the restricted capacity of laboratories and it seems difficult to expand the laboratory facilities for large scale testing [9,10].

Population-scale testing for COVID-19 is probably the most ideal approach to restrict mortality rates. Large scale testing identifies and isolates infections quickly, restricting the virus' spread and shielding susceptible populations [11]. The diagnosis of COVID-19 relies on detection of SARS-CoV-2 RNA in upper or lower respiratory tract specimens via RT-PCR [12]. However, RT-PCR is time consuming and scarcity of testing materials and facility enforce a grave hazard [13]. The Corona-Score, a point-based algorithm, incorporates routinely conducted blood tests that are widely available and performed on automated platforms with very swift turn-around time [6]. The Corona-Score helps predict the likelihood of SARS-CoV-2 infection, and utilizing this score accelerates determination of isolation needs and also reduces

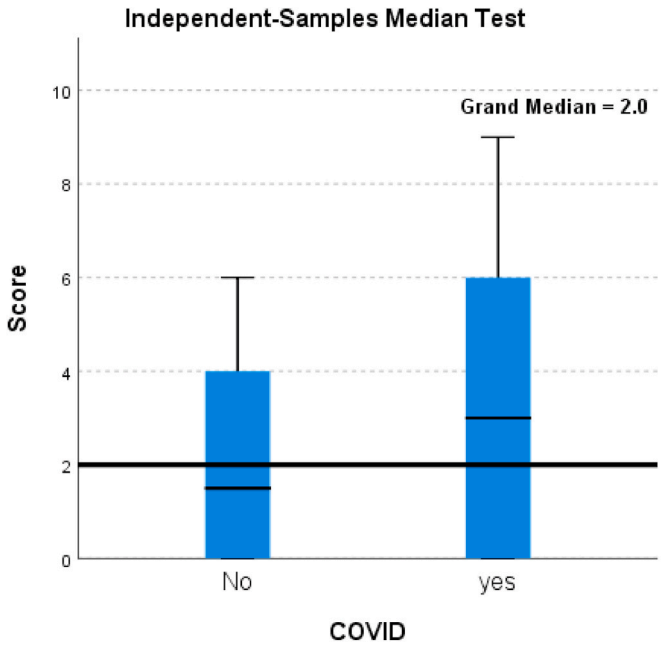

Fig. 1. Independent sample median test for corona-score between groups p-value 0.605.

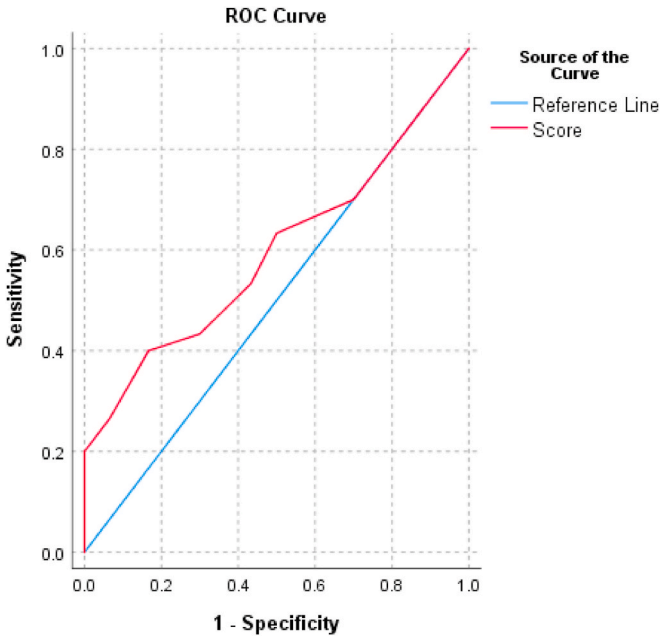

Fig. 2. Receiver operating characteristics (ROC) curve analysis of the Corona-Score against COVID-19 PCR

RT-PCR testing. It also eliminates the expertise and training of a person required to obtain a right, representative sample. Moreover, the PCR test can itself suffer from low diagnostic yield particularly false negatives in presence of classic sign and symptoms due to discrepancy in sample collection practices and timeline of infectivity, this is where corona score can produce vital information and necessitates protective measures for a likely true positive case.

In this study the Corona Score exhibited an AUC of 0.59, which was considerably lower compared to the scores evaluation in Dutch and United States health care set ups [5,6]. **The score was developed by Kurstjens S et al in a set of 967 Dutch patients seeking emergency care at multiple centers in Netherlands, using artificial intelligence based computational sampling, followed by validation of the model in 592 patients. The external validation by Lippi G et al in the United States of America, had also reported a lower AUC (0.74) and sensitivity (82%), but slightly higher specificity (96%) compared to the original Dutch cohort [5,6]. The authors have linked the variation to the populations' specific differences, location specific viral strains and the variance of health care structure and care provision between the three different health settings from Europe, United States and Asia.**

Findings of our study were reported from a single institute with a relatively small sample size which could be the limitations of our study and there exists a likelihood that significant improvement in diagnostic accuracy and predictive performance may arise with larger sample size. Secondly, as it was a retrospective analysis, differences in underlying patient co-morbidities could not be evaluated which may also contribute to these observation. Keeping in view the resource constraints and additional biochemical parameters, the score is unlikely to replace molecular analysis, but it can provide a practical supplement for assessing pre- and post-test probabilities and can serve as a screening tool for the control groups in COVID-19 clinical studies as suggested by Lippi G et al [5]. Moreover, we also propose to investigate the prognostic utility of corona score in a representative cohort to assist optimal intensive resource allocation and attain patient centered outcomes.

5. Conclusion

Corona-Score displayed a lower diagnostic accuracy which may be attributable to the different genetic framework, viral strain and severity of the disease in Pakistanis compared to the population where this score was originally validated. Corona Score is an easy-to-use algorithm for identification of Covid-19 patients with respiratory symptoms and needs to be further validated on a bigger sample size. Large multi-center studies across the country are dire need of time to evaluate the score in overly exhausted health care setup and limited availability of PCR testing.

Ethical approval

The study was granted exemption by the institutional ethical review committee of the AKU, Karachi (ERC#2020-5168-14099).

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None.

Author contribution

SA performed the literature search, data analysis and write-up of the work in the first draft. MUNE performed data collection and assisted in write-up of the first draft. ZAA and IS were involved in the laboratory workup, patient selection and critical revision of the article for the intellectual content. LJ conceived the idea, coordinated the writing of the paper and reviewed the final draft. All the authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.

Registration of research studies

1. Name of the registry: Chinese Clinical Trial Registry.
2. Unique Identifying number or registration ID: ChiCTR2100042375;
3. Hyperlink to your specific registration (must be publicly accessible and will be checked):
http://www.chictr.org.cn/showprojen.aspx?proj=120493.

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Consent

N/A.

Declaration of competing interest

None.

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