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Facilitating safe discharge through predicting disease progression in moderate COVID-19: development and validation of a prediction model in resource-limited settings

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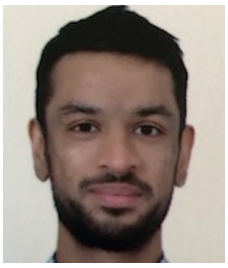
Introduction

In locations where few people have received Covid-19 vaccines, health systems remain vulnerable to spikes in SARS-CoV-2 infections. Triage tools, which could include biomarkers, to identify patients with moderate Covid-19 infection suitable for community-based management would be useful in the event of surges. In consultation with FIND (Geneva, Switzerland) we shortlisted seven biomarkers for evaluation, all measurable using point-of-care tests, and either currently available or in late-stage development.



Arjun is an infectious diseases registrar interested in supporting the development of clinical infection services in under-resourced settings. He has been based in Southeast Asia since 2018 and works on a number of research projects in partnership with MSF. He is currently completing his PhD with Oxford University at the Angkor Hospital for Children in Cambodia, which is focused on developing practical tools to improve the syndromic management of febrile illness and sepsis at the community level.

Methods

We prospectively recruited unvaccinated adults with laboratory-confirmed Covid-19 presenting to two hospitals in India with moderate symptoms, in order to develop and validate a clinical prediction model to rule-out progression to supplemental oxygen requirement. Moderate disease was defined as oxygen saturation (SpO_2) ≥ 94% and respiratory rate < 30 breaths per minute (bpm), in the context of systemic symptoms (breathlessness or fever and chest pain, abdominal pain, diarrhoea, or severe myalgia). All patients had clinical observations and blood collected at presentation, and were followed up for 14 days for the primary outcome, defined as any of the following: SpO_2 < 94%; respiratory rate > 30 bpm; SpO_2/fraction of inspired oxygen (FiO_2) < 400; or death. We specified *a priori* that each model would contain three easily ascertained clinical parameters (age, sex, and SpO_2) and one of the seven biomarkers (C-reactive protein (CRP), D-dimer, interleukin-6 (IL-6), neutrophil-to-lymphocyte ratio (NLR), procalcitonin (PCT), soluble triggering receptor expressed on myeloid cells-1 (sTREM-1), or soluble urokinase plasminogen activator receptor (suPAR)), to ensure the models would be implementable in high patient-throughput, low-resource settings. We evaluated the models' discrimination, calibration, and clinical utility in a held-out external temporal validation cohort.

Ethics

Ethical approval was given by the ethics committees of AIIMS and CMC, India, the Oxford Tropical Research Ethics Committee, UK; and by the MSF Ethics Review Board. ClinicalTrials.gov number, NCT04441372.

Results

426 participants were recruited, of which 89 (21.0%) met the primary outcome. 257 participants comprised the development, and 166 the validation, cohorts. The three models containing NLR, suPAR, or IL-6 demonstrated promising discrimination (c-statistics: 0.72 to 0.74) and calibration (calibration slopes: 1.01 to 1.05) in the held-out validation cohort. Furthermore, they provided greater utility than a model containing the clinical parameters alone (c-statistic = 0.66; calibration slope = 0.68). The inclusion of either NLR or suPAR improved predictive performance such that the ratio of correctly to incorrectly discharged patients increased from 10:1 to 23:1 or 25:1 respectively. Including IL-6 resulted in a similar proportion (~21%) of correctly discharged patients as the clinical model, but without missing any patients requiring supplemental oxygen.

Conclusion

We present three clinical prediction models that could help clinicians identify patients with moderate Covid-19 suitable for community-based management. These models are readily implementable and, if validated, could be of particular relevance for resource-limited settings.

Conflicts of interest

None declared.