Editorial

Real-world data in COVID-19 pandemic: An essential unmet health-care need

Real-world studies (RWSs) are studies conducted using real-world data (RWD) on patient health status, or health-care delivery, routinely collected from diverse sources such as clinics and hospitals and insurance database.[1] During a pandemic, RWSs have the potential to provide valuable rapid, actionable information to better understand natural history and course of disease and answer urgent questions on effectiveness and safety of treatments and health economics and outcomes research.[2]

Several published studies have provided insights into clinical spectrum of COVID-19.[3,4] Clinical picture of COVID-19 pneumonia showed a predominance of elderly and male patients, coexistence of hypertension, diabetes, and cardiovascular disease and high mortality in severe cases.

With the growth and global expansion of epidemic, the focus of clinical research has expanded to explore the association of COVID-19 with comorbidity and surgery and to predict the prognosis of COVID-19 patients.

A French multicenter observational study in 1317 diabetes patients hospitalized for COVID-19 reported that body mass index was positively associated with tracheal intubation and/or death within 7 days.[5] However, long-term glucose control did not influence the outcomes. In contrast, a Chinese study in 7337 diabetes patients with COVID-10 found that inhospital mortality was significantly lower (1.1%) in well-controlled patients with median blood glucose level 6.4 mmol/L (5.2–7.5 mmol/L) compared to 11% in poorly controlled patients with median blood glucose level 10.9 mmol/L (7.6–14.3 mmol/L).[6] A retrospective study described high all-cause mortality at 30 days in a cohort of 928 cancer patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. The mortality was associated with general risk factors and cancer-specific factors – Eastern Cooperative Oncology Group performance status of 2 or higher and active cancer.[7] In a cohort of 1128 patients undergoing surgery with perioperative SARS-CoV-2 infection, postoperative pulmonary complications occurred in 51.2% of patients and were associated with high 30-day mortality.[8]

Williamson *et al.* analyzed 5683 COVID-19 deaths among British population and reported a strong association between mortality and male gender, older age and deprivation, ethnicity, uncontrolled diabetes, severe asthma, obesity, chronic heart disease, liver disease, stroke/dementia, other neurological diseases, reduced kidney function, autoimmune diseases, malignancy, and hypertension.[4] Liang *et al.* developed a validated predictor risk score from analysis of retrospective cohort of 1590 hospitalized COVID-19 patients.[3] Predictive factors identified were: (1) chest X-ray abnormality, (2) age, (3) hemoptysis, (4) dyspnea, (5) unconsciousness, (6) number of comorbidities, (7) cancer history, (8) neutrophil-to-lymphocyte ratio, (9) lactate dehydrogenase, and (10) direct bilirubin. According to Tan *et al.*, percentage of circulating lymphocytes, C-reactive protein, procalcitonin, interleukin-6, and viral load could predict prognosis and guide classification of COVID-19 patients.[9] These studies on cancer, surgical patients, and prognosis have implications for the management of COVID-19 and concomitant medical conditions.

In pandemic situation, when conducting a randomized clinical trial is scientifically and ethically challenging,[10] costly, and time-consuming, RWS is a useful alternative to assess the effectiveness and safety of repurposed investigational treatments, other commonly used therapies for comorbid conditions, and nonpharmacological measures. COVID-19 Global Rheumatology Alliance conducted an innovative analysis of physician-reported 600 cases suffering from rheumatic diseases and found that glucocorticoid exposure of ≥10 mg/day was associated with a higher risk of hospitalization, and tumor necrosis factor inhibitor use was associated with a reduced risk of hospitalization for COVID-19.[11] The consumption of hydroxychloroquine (HCQ), disease-modifying antirheumatic drugs, or nonsteroidal anti-inflammatory drugs was not associated with a higher risk of hospitalization for COVID-19. In a retrospective cohort study of 1438 hospitalized American patients with COVID-19, treatment with HCQ, azithromycin, or both was not associated with reduced inhospital mortality.[12]

A case-population study did not find an increase in risk of COVID-19 among users of renin–angiotensin–aldosterone

system inhibitors.[13] A systematic review of 172 RWS observation studies of nonpharmaceutical interventions showed that physical distancing of 1 m or more, use of face masks, and eye protection were associated with a much lower risk of infection with SARS-COV-2.[14]

Population health information and COVID-19 patient database have been explored to obtain medically useful information. Hamiel *et al.* compared SARS-CoV-2 rates in 3064 bacillus Calmette–Guérin (BCG)-vaccinated and 2869 BCG-unvaccinated Israeli adults.[15] The proportion of SARS-CoV-2 positive in the BCG-vaccinated group (11.7%]) versus the unvaccinated group (10.4%) did not differ significantly. This study challenges the idea of protective effect of childhood BCG vaccination against COVID-19 in adulthood.

Hanlon *et al.* used the standard World Health Organization (WHO) life tables and published age/sex data from COVID-19 deaths in Italy to estimate the burden of mortality.[16] They found that years of life lost (YLL) per COVID death was 14 for men and 12 for women. In old patients >80 years with no comorbid long-term conditions (LTCs), YLL was >10 years. However, YLL reduced to <3 years in patients with >6 LTCs. Such modeling studies of morbidity and mortality data would help in assessing health economics and outcomes research.

RWSs have generated valuable evidence which has helped in shaping health-care policy for COVID-19 pandemic. Success in planning, conducting, and publishing RWS during COVID-19 pandemic is due to (1) passion of academic researchers during trying times; (2) availability of detailed information on patients – clinical spectrum, demographic variables, comorbidities, laboratory findings, imaging investigations, therapy, intensive care management, etc.; (3) availability of high-quality electronic health records (EHRs); (4) rapid access to large medical data sets through multi-institution multicountry collaboration; (5) technical support for advanced data analytics for extraction of relevant data; (6) open access to data for research; (7) management of ethical, data privacy, and security considerations; (8) application of appropriate statistical methods to handle issues of confounding factors and validity; and (9) rapid publication with and without peer review.

In India, at present, the medical treatment and health-care policy for COVID-19 are largely shaped by data published from other countries. There are a few published research studies on COVID-19 in Indian patients. In a descriptive case series of 21 patients, typical clinical presentation reported was mild upper respiratory tract infection predominantly in young males.[17] All patients recovered with no residual symptoms. The Indian Council of Medical Research case–control study among health-care workers (HCWs) reported that the consumption of four or more maintenance doses of HCQ was associated with a significant decline in the odds of getting infected.[18] Odds of infection with SARS-CoV-2 were higher among HCWs performing endotracheal intubation procedure and reduced among HCWs using personal protective equipment.

For India, generating factual and reliable real-world evidence on COVID-19 pandemic is an urgent and essential unmet health-care need. Private and public hospitals with established EHR systems should conduct collaborative RWS and publish the findings. Medical institutions involved in care of COVID-19 patients, which do not have established EHR systems, can participate in international or India COVID-19 data collection efforts.

The International Severe Acute Respiratory and Emerging Infection Consortium and the WHO have developed case report forms to collect data on suspected or confirmed COVID-19 patients (https://isaric.tghn.org/COVID-19-CRF/). Medical institutions can enter data online or using a mobile app.

Indian COVID-19 database – Cov.Base (https://cdata.icmr.org.in/) – is a joint effort between the Centre for Advanced Research in Imaging, Neurosciences and Genomics and the Institute of Genomics and Integrative Biology. Hospitals can anonymize upload and store their own COVID-19 patient data on Cov.Base.

Hope availability of free and open access online RWD bases will facilitate and accelerate real-world research-based health-care measures to respond to the challenge of controlling COVID-19 pandemic!

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