Clinical trials and Consolidated Standards of Reporting Trials: Continuing concerns of compliance in COVID-19 era

COVID-19 global pandemic's serious health consequences created an urgent unmet medical need to discover effective therapies for managing disease and preventing complications. This has led to an exponential increase in clinical research publications related to COVID-19. PubMed lists 202,277 articles. The urgency of planning and the speed of publication have raised major concerns regarding the scientific rigor and quality of clinical research in COVID-19.[1,2] Jung *et al.* performed a systematic review to evaluate the methodological quality of 686 COVID-19 articles. Quality scores of methodology in COVID-19 articles were lower as compared to historical controls.[1] However, this study included only three randomized controlled trials (RCTs). PubMed includes 1424 clinical trials, and Clinitrials.gov has registered 1461 RCTs. As RCTs are gold standard for supporting evidence of efficacy of different interventions, it is imperative to assess quality of published RCTs on COVID-19.

The quality of clinical trials could be assessed by reviewing the publications and preprints against Consolidated Standards of Reporting Trials (CONSORT).[3] The CONSORT statement consists of a flow diagram and a checklist of 37 items (25 items + 12 subitems) that guide the reporting of essential items of an RCT. The checklist consists of six sections: (1) title and abstract (one item), (2) introduction (one item), (3) methods (ten items), (4) results (seven items), (5) discussion (three items), and (6) other information (three items). Endorsement of CONSORT by over 600 biomedical journals and prominent editorial organizations such as International Committee of Medical Journal Editors and the World Association of Medical Editors[2,3] has contributed to improvement in overall reporting quality of RCTs. However, recent studies of quality of published RCTs of COVID-19 interventions appear to reverse this trend.

Yin *et al.*, in a study of evaluation of reporting quality of 53 RCTs in COVID-19 patients, found that the average reporting rate for 37 items in the CONSORT checklist was 53.85%. For the methodological section, the reporting rate was 31.35%.[2] For some critical items – trial design, sample size, allocation concealment, randomization implementation, blinding, ancillary analyses, and protocol – the reporting rate was very low <20%. Only a small number –7 studies (13.21%) reported method of masking concealment, while 9 studies (16.98%) reported the details of blinding.[2] The authors also assessed adherence to CONSORT scoring for each item and subitem and reported a mean overall adherence score of 13.02 ± 3.546 (range 7–22). Gaps in reporting quality of clinical trials are not unique to COVID-19 trials.

In this issue of Journal, Gupta *et al.* have reported an appraisal of RCTs published *in Indian Journal of Pharmacology* (IJP).[4] The authors screened 1102 articles published in IJP between 2011 and 2016 and selected 28 RCTs with full-text articles for analysis. They evaluated the quality of these articles against a checklist based on the CONSORT 2010 guidelines for reporting parallel group randomized trials. Deficiencies in the reporting of methods were (1) no description of sample size determination in 7 (25%); (2) mechanism to implement the random allocation sequence not reported in 8 (64.29%) articles; and (3) details of blinding process not available in 12 (42.86%). In the "Results" section, the deficiencies were (1) not reporting precision of effect size in 22 (78.57 %); (2) no participant flow diagram and "intention-to-treat" analysis in 18 (64.29%) articles; and (3) no data on baseline demographics in 8 (28.57%). Trial limitations were not discussed in 9 (32.14%) articles. Another significant omission was no registration of RCT in 19 (67.86%) articles.

Suboptimal adherence to reporting guidelines remains a concern among the clinical research community. In a 2018 systematic review, Jin *et al.* analyzed whether reporting of medical research adheres to well-known reporting guidelines.[5] They included reviews published over 20 years – between January 1996 and September 2016 – which assessed compliance to reporting standards for clinical trials, systematic reviews, observational studies, meta-analysis, diagnostic accuracy, economic evaluations, and preclinical animal studies.[5] Of the 124 studies assessed, overall adherence to any reporting standards was suboptimal in 87.9%. Compliance to the CONSORT

statement was suboptimal in 71 (88%) of 81 RCTS examined.[5]

Several factors related to (1) ethical aspects, (2) authorship, (3) study, and (4) journal were associated with improved adherence to reporting guidelines.[5]

Ethical factors were: Articles describing details of ethics committee approval, informed consent of participant, and source of funding.[5]

Authorship factors were: The level of expertise of author team in research methods and having multiple authors.[5] Low reporting rates for critical items of methodology, results, and discussion may reflect the lack of relevant knowledge of the authors in clinical research methodology and reporting guidelines such as CONSORT. For original research articles, "Methods" section is the most frequently responsible for rejection of the manuscript.[6] Young clinical researchers should be aware of relevant reporting guidelines – CONSORT while preparing the manuscript.

Study design factors were: Well-designed, adequately powered trials providing detailed study methods.[5] Poor reporting of methodological items, e.g., randomization sequence generation, sample size, allocation concealment, and blinding, could result from a perception that the clinical aspects of RCTs are of greater importance and interest compared to study design issues.[7] Some studies have demonstrated a strong association between poorly reported trials and poorly designed or conducted trials.[7]

Journal factors were: Journals with high impact or endorsing reporting guidelines.[5] Such journals usually request authors to submit a completed CONSORT checklist, which would be instrumental in enhancing the quality of reporting.

Suboptimal quality of reporting of RCT in publications can result in inaccurate conclusions regarding treatment effect. Reporting guidelines such as CONSORT are an essential tool in the endeavor to ensure consistency in reporting of RCTs. The authors, peer reviewers, and editors should make concerted efforts to meet CONSORT standards.

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