View Point

Dubious Medical Literature Publications during COVID-19 — Another 'Epidemic' !

Surajit Bhattacharya[1], Kaushik Bhattacharya[2], Neela Bhattacharya[3]

More than 5,82,645 articles were published about the Coronavirus pandemic till 2022 and were demarcated as global literature on COVID-19 by the World Health Organisation. The majority of the journals rushed to get COVID-19 related manuscripts through fast-track peer review, and this resulted in many dubious publications in medical journals about the Coronavirus thereby spreading misinformation and manipulation of evidence-based medicine.

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The World Health Organisation (WHO) has demarcated about 5,82,645 articles published in various medical journals on Corona virus as Global literature on COVID-19 and they feature on the website of WHO[1]. There was a hurry to get any article on COVID-19 through peer review during the pandemic. MedRxiv took just a median review time of 72 days for pre-prints of articles on COVID-19 to appear in peer-reviewed journals which was twice as fast as pre-prints on any other topic from the server. In a study of 11 medical journals in the first six months of 2020, it was found that they published papers on COVID-19 much faster than normal, at the expense of publishing other research more slowly[2]. It was disconcerting to note that 30,000 papers on COVID-19 published in 2020 were pre-prints which accounted for 17% to 30% of total COVID-19 research papers. This fast-track publication of data and half-cooked evidence resulted in many dubious publications about COVID-19 in the medical literature.

Research-based or Pharma-based Publications ?

There were innumerable research-publishing scandals[3]. The dubious intention was evident when many high-profile articles on COVID-19 were retracted, including studies that relied extensively on electronic health records from a website Surgisphere in Chicago, Illinois. By December 2020, the Retraction Watch site reported that about 15 pre-prints and 24 so-called peer-reviewed papers on COVID-19 were withdrawn or retracted[4]. It was due to a concern about authenticity that 5 papers were 'temporarily" retracted while 5 more papers had authors expressing concern.All these retracted literature had a conflict of interest and had relied heavily on health-record analyses of a company that would not reveal its original data for a scientific audit. Exactly 2 weeks after a high-profile multinational registry analysis manuscript in *The Lancet*[5] reported that hydroxychloroquine, the antimalarial drug that was extensively used then for COVID-19, might actually be dangerous to patients, three of its four authors retracted the work because they were unable to independently verify their data which was a large proprietary collection of electronic health records analyzed by Surgisphere.Similarly, on 4th June 2020, researchers and other co-authors retracted a paper in the *New England Journal of Medicine* (*NEJM*) for the same reason[6]. That study, finally published a month ago, had researched the impact of certain heart medications on people with COVID-19 and had found no safety concerns.

In a significant move, on 22nd May 2020, a hydroxychloroquine study was published which had purportedly analyzed electronic health records of 96,000 patients in 671 hospitals across the globe. Finding many inconsistencies in the data, critics raised questions and asked for more details on its origins which led to 120 researchers signing a letter to *The Lancet* highlighting their concerns 6 days after the publication. Several queries were also raised on the *NEJM* study which relied on Surgisphere data that

Editor's Comment :

- A pandemic of the stature of COVID-19 affecting every nook and corner of the planet also saw a pandemic of half-cooked and half-baked unscientific research publications in medical journals without any peer review and these publications were suddenly retracted after the initial hype.
- There is no shortcut to scientific research and every peer review protocol should be strictly followed before any COVID-19 publication makes its entry in a reputed medical journal.

[1]MS, MCh (Plastic Surgery), Senior Consultant Plastic, Reconstructive & Aesthetic Surgery, Sahara Hospital, Lucknow 226010

[2]MS, DNB, MNAMS, FAIS, FACS, FRCS, (Glasg) FRCS(Edin), Associate Professor (Surgery), Mata Gujri Memorial Medical College and LSK Hospital, Kishanganj 855107 and Corresponding Author

[3]MS, DNB, MCh (Plastic Surgery), Consultant Plastic and Reconstructive Surgeon, Anandaloke Multispeciality Hospital, Siliguri 734001

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apparently covered 9,000 patients across 169 hospitals. Even when the scientific validity of the data was challenged, Surgisphere did not present its raw data available to third-party auditors for verification. The retraction notice in the *Lancet* cited Surgisphere as feeling that transferring the data would violate "client agreements and confidentiality requirements".

Mysterious disappearance of the Ivermectin study:

A significant reduction in COVID-19 mortality rates was found by the study of Desai, *et al* using Surgisphere data when patients were given the anti-parasitic drug Ivermectin, but that study suddenly vanishedfrom the social-sciences preprint server SSRN, where it was first posted on 6th April 2020 and a second version was posted on 19th April 2020[6]. Mehra told *Nature* that he removed the study because he "did not feel it was ready for peer review". The scenario was completely ironic to claiminitially that Ivermectin reduced COVID-19 deaths by 90% on April 6th, 2020 and then to watch the paper being withdrawn from the pre-print server on July 14, 2020! The immediate concern at that juncture was whether this was a genuine error of judgment or wanton scientific dishonesty.

Even though the paper was not published in a peer-reviewed indexed journal,nonetheless it contributed to a huge surge in the popularity of ivermectin for COVID-19 treatment! Such hurried publications, inadequate peer reviews and subsequent withdrawal can at best cause confusion in the reader's mind and at worst can be a pharmaceutical company-driven propaganda to skyrocket the popularity of a drug for a short period of time, reap the financial benefits and then withdraw the publication citing confidentiality issues. This is neither good for the journals involved nor for the integrity of science! Both *The Lancet* and the *NEJM* had their credibility severely damaged but maintained that their peer-review processes were strictly confidential and they could not divulge details on how the papers were so quickly reviewed and accepted for publication.

Before the so-called reputed journals published such studies, researchers and reviewers should have asked more questions about how such comprehensive data could be obtained from hospitals across the World in the middle of a pandemic. The retraction won't get anywhere near as much news as the original study, and we may never get an answer about the treatment of COVID with Hydroxychloroquine or reduction in mortality following treatment with Ivermectin!

Dubious publications on Mask :

The Annals of Internal Medicine back-tracked on a highly cited paper it had published in 2020 which inferred that face masks were ineffective in preventing the spread of COVID[7]. This paper, which must have passed the peer-review system of the esteemed journal, had included just 4 study subjects but the misinformation it sent out led to careless exposure and infection of millions of people! How can such acts of omission be justified which demean the very basis of science?

Failure of Ethics in Publication :

Retraction Watch shows that 137 papers related to COVID-19 have been retracted since July 2020. Twelve more were retracted due to journal error and in 7 publications 'expressions of concern' were raised. Five papers were retracted and reinstated during the same time[4]. Since Retraction Watch does not distinguish between withdrawal and retraction, journals have typically done so without assigning a reason for retracting a paper, and sometimes make a paper disappear without a trace or controversy. Journals may retract a paper at the authors' request and/or if the editors identify fundamental flaws that would have precluded acceptance if spotted during the review. A pre-print is usually withdrawn only at an author's request. Since no claim is made to have peer-reviewed and certified the scientific content in the first place,a pre-print server will not typically withdraw a flawed preprint against the wishes of the author but may do so in instances of fraud, ethics violations, dangerous material, or legal issues. Typically, it takes three years for editors to retract a paper, but during the pandemic, it took just months — in part because these papers were facing so much scrutiny[8]. But retractions are a proxy for attention perhaps more than anything else and the damage they do in a short span of time is incalculable!

Retraction Watch has wondered, 'One does not know how many more COVID-19 papers are likely to be retracted'. One also cannot say with any certainty that COVID-19 papers are any more likely to be retracted than others. In the world of medical documentation, it seems that scientific integrity has declined,and quality was replaced by quantity during COVID times. Ethics in scientific research is more essential than ever now. The pandemic was the first of its kind in our lifetime and we did not have a similar experience to fall back upon. Today we need more information about a new disease. We need it quickly and we need it from genuine sources. Journals are our only source, and we take printed words as gospels and blindly trust them. So, whatever goes through a journal peer review system should be honest, unbiased, and totally reliable. This is not like a social media post – posted today and retracted tomorrow, with or even without an apology. Journals have a responsibility towards their readers and posterity will hold them accountable for scientific insincerity and misadventure.

Failure of newer drugs and misinformation :

There was huge enthusiasm for the magic treatment of Coronavirus with monoclonal antibodies,

Remdesivir/ Tocilizumab, and Convalescent plasma therapy. But all of them failed in detailed trials.No clinical benefit was observed from the use of Remdesivir in patients who were hospitalized for COVID-19 when symptomatic for more than 7 days and required oxygen support[9]. Evidence from the RECOVERY trial showed that, among patients hospitalized with COVID-19, high-titer convalescent plasma did not improve survival or other prespecified clinical outcomes[10]. In a randomized trial involving hospitalized patients with severe COVID-19 pneumonia, the use of Tocilizumab did not result in significantly better clinical status or lower mortality than placebo at 28 days[11].

All these medicines which have now been proved'useless' in COVID-19 were in huge demand once in India during the Second wave and were the root cause behind pandemic profiteering.

Ethics cannot be compromised for speed of publication.

Complete vaccination of the World sounds more like a myth than an achievable goal today, because of both vaccine hesitancy as well as the vaccine-deprived status of the third World despite the World Health Organization's fervent pleas to the developed countries to share the vaccine. Even if this Utopian objective is achieved Coronavirus is going to be with us in its various mutant avatars. So, science must regain its ethical center and shrug off the pressures of urgency and haste. Clinical trials should be seriously re-looked – is there incomplete enrolment of patients in clinical trials? Are we strictly adhering to the inclusion and exclusion criteria? Do we have adequate consumables and kits for carrying out the desired scientific steps? Have research workers returned to their workstations from lockdowns? Do funding agencies still have the funds to support the trials? These are practical roadblocks that researchers have encountered of late, but these should not compromise science. Another elephant in the room is the role of politics in scientific research – science cannot dish out politically convenient conclusions every time. If irresponsible election rallies have resulted in an increased number of infections, scientists should be able to fearlessly conclude the same. The scientific community of the US recently requested the U.S. President not to politicize research[12].

Conclusion

Scientists published well over 5,82,645 articles about the Coronavirus pandemic in 2020-22 and newer publications keep rolling out now on the sequels. Fast-track peer review to beat the deadline and be the first to publish was the objective of both the researchers and the journal editors. This haste resulted in many articles slipping through the peer-review and getting published but because of heightened interest and intense scrutiny they had to be hastily retracted, but not before they managed to do incalculable harm to patient care. Retraction Watch shows that 137 papers related to COVID-19 have been retracted since July 2020. Twelve more were retracted due to journal error and 'expression of concern' was raised against 7. While a few of them could be because of unintentional errors on the part of the authors, when we see a pattern of papers on the use of Hydroxychloroquine, Ivermectin, monoclonal antibodies, Remdesivir/ Tocilizumab and Convalescent plasma therapy appearing in print with a lot of promise and then getting retracted or being followed by publications refuting their utility, a concern should be expressed unambiguously – were these windows of glory designed by the sponsors of these researches to facilitate windfall profits for the pharmaceutical industry?

"*Positive findings are around twice as likely to be published as negative findings. This is a Cancer at the core of evidence-based medicine*".

— Ben Goldacre

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