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Letter to the Editors-in-Chief

The delights and perils of publishing, knowledge-sharing and critique during a pandemic: Observations from COVID-19 coagulopathies



1. Introduction, objectives and systematic observations

The CoronaVirus Disease 2019 (COVID-19) pandemic is a major global concern with 4,369,410 confirmed infections and 297,569 total deaths since the first reported outbreak of the infection (<https://coronavirus.jhu.edu/map.html>, accessed 14th May 2020) [1,2]. It is caused by Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2), previously known as 2019-nCoV [3]. SARS-CoV-2 belongs to the β -coronavirus family, and shares 80% similarity to known SARS-CoV according to genome sequencing [4]. While COVID-19 is primarily a viral respiratory illness, it is proven to have systemic manifestations, most notably coagulation complications, in those with severe disease.

During this unprecedented, global COVID-19 instigated health-crisis, characterized by closed borders, travel restrictions, and at times complete lockdown, we have seen an inspiring response from the scientific community. To understand the current state of discourse, we searched the literature addressing COVID-19-associated coagulopathy, PubMed and the Excerpta Medica dataBASE (EMBASE) databases were searched, from the earliest available report 19th February 2020 to 7th May 2020. We aimed to evaluate the scope and quantity of publications during this period with key terms relating to Coronavirus, coagulopathy, thromboembolic disease, anticoagulant and thrombocytopenia. The other inclusion criteria were Haemostasis and Thrombosis topics in English language, journals with an Impact factor of more than 3 and Haemostasis Specialist journals. The search yielded 586 papers of which 103 were finally included after removing duplicates, inspecting the abstracts and full-text reviews. These are listed in Table 1 according to the journal of publication. Of note, whilst 23 reports documented original findings, the remaining 78 consisted of comments, editorials, letters, expert reviews, and guidelines.

Evidence continues to accumulate as COVID-19 infections escalate, and as more countries present their findings. It is important to note that much of the global data consists of cross-sectional or retrospective reports, with unmeasured, and sometimes underappreciated confounding. While initial reports remain important, our understanding is constantly evolving, with event rates influenced by multiple factors including over-representation of critically ill patients, use of investigational drugs, and a multitude of studies lacking a control group, to name a few.

Earlier studies have noted an association between an abnormal coagulation profile (consistent with the definition of disseminated intravascular coagulation (DIC) previously endorsed by the International Society on Thrombosis and Haemostasis (ISTH)), and subsequent poor outcome in patients with COVID-19 infection [5]. Despite the coagulopathic profile of the laboratory indices, COVID-19 has been shown to create an inherently pro-thrombotic state [6,7]. Hypoxia,

hypercoagulability and stasis due to critical illness in the setting of severe sepsis are indeed known to increase the risk of VTE [8]. This association of venous and arterial thrombosis has now been determined to hold true for individuals affected by COVID-19, and to be linked with higher risk of all-cause mortality [9].

This volatile context has triggered fierce discussions amongst the Haemostasis community, beginning with the type and mechanism of COVID-19-associated coagulopathy and thrombo-embolic risk, spanning the indications for thromboprophylaxis, and extending to the merits and hazards of therapeutic anticoagulation [10,11]; with some even considering therapies such as Tissue-type plasminogen activator (tPA) [12].

As an example, d-dimer was posited as a critical parameter/indicator of thrombotic complication associated with COVID-19. Debates on cut-off values and links to disease-severity and mortality were reported according to diverse patients' presentations, spanning countries, and incorporating varying hospital practices, and accounting for ethnic variability [13]. Deliberation surrounding the merits of using d-dimer as a prognostic indicator in the setting of COVID-19 generated meta-analyses that were published earlier than would typically be expected in non-pandemic conditions [14]. Some investigators have reported the presence of VTE events at the time of admission [15]. Further, concerns of breakthrough risk of venous thromboembolism (VTE) despite prophylactic anticoagulation in critically ill COVID-19 patients have also been raised [16,17]. Decisions about anticoagulation became more complicated, with studies exhibiting improvement in abnormal coagulation parameters or suggesting a survival benefit [18,19]. During these times of myriad uncertainties, debate predominates and social media platforms such as Twitter continue to be filled with puzzled physicians asking crucial questions about anticoagulation dosing as it relates to the severity of infection or d-dimer levels. Discourse on the value of prophylactic low molecular weight anticoagulation also draws on recommendations from international guidelines [20] or interim guidance suggesting systemic anticoagulation with unfractionated heparin [21]. Despite the limited data, the high-stakes milieu and risk of litigation have led several institutions to adopt a more aggressive approach of using intermediate or full-dose anticoagulation for most of their critically ill COVID-19 patients admitted to the Intensive Care Unit [22]. This approach has been tempered by others who have utilised the state of clinical equipoise as a catalyst for collaboration to initiate multicenter Randomised Control Trials (NCT04362085, NCT04345848, NCT04360824, NCT04377997) to more conclusively answer these questions.

The dissemination of knowledge during times of international crisis is guided by the principles first set out in the World Health Organization's 2016 statement on data-sharing during public health emergencies, which incorporated lessons from the Ebola and Zika

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Table 1

List of COVID-19 and coagulopathy related publications during the period 19th February 2020 to 7th May 2020. The table shows the names of journals and number and types of publications.

Name of journal	Publications on COVID-19 and Coagulopathy						
	Total	Case Report	Brief Report/ Study	Expert review/commentary/ guideline	Comment to authors/author response	Editorial	Letter to Editor
New England Journal of Medicine	3	1	0	0	0	0	2
Circulation	1	0	1	0	0	0	0
Annals of Internal Medicine	1	0	1	0	0	0	0
Intensive care Medicine	1	0	1	0	0	0	0
Journal of the American College of Cardiology	2	0	1	1	0	0	0
Blood	1	0	0	1	0	0	0
The Lancet Haematology	1	0	0	0	0	0	1
Canadian Medical Association Journal	1	0	0	1	0	0	0
British Journal of Haematology	8	1	1	3	0	0	3
Research and Practice in Thrombosis and Haemostasis	8	0	0	6	0	1	1
American Journal of Hematology	1	0	0	1	0	0	0
Critical Care (London, England)	1	0	1	0	0	0	0
Translational Research	1	0	1	0	0	0	0
Thrombosis and Haemostasis	6	0	1	2	0	0	3
Thrombosis Journal	1	0	0	1	0	0	0
Journal of Thrombosis and Haemostasis	40	1	11	4	15	1	8
Journal of Vascular Surgery	2	0	0	1	0	0	1
Seminars in Thrombosis and Haemostasis	2	0	0	2	0	0	0
Critical Care and Resuscitation	1	0	1	0	0	0	0
Blood Transfusion	1	0	0	1	0	0	0
Platelets	2	1	1	0	0	0	0
Journal of Thrombosis and Thrombolysis	3	0	1	0	0	1	1
Thrombosis Research	15	1	3	0	1	1	9
Total	103	5	25	24	16	4	29

outbreaks, and was undersigned by many notable foundations and journals [23]. These principles have been adopted for use in the current pandemic through a call to share “research data and findings relevant to the novel coronavirus (COVID-19) outbreak” in the same fashion [24]. The statements implore researchers, journals and funders to expeditiously publish findings relevant to the outbreak, and to ensure these are available free-of-charge, through preprint servers prior to journal publication or as open-access prior to peer-review.

2. Journals' and authors' responsibilities

Academic engagement and advancement of knowledge through increased research output and through extension of open-access policies by medical journals that waive fees to enable and broaden data access has been remarkable, contributing a great deal to the goal of improving outcomes for those affected by the disease [25]. The rapid availability of knowledge ensures that global communities adapt and researchers can mobilise limited resources into effective response strategies [26]. Furthermore, these editorial allowances have extended beyond COVID-19-related matters, to investigations advancing general medical knowledge, with editors and reviewers embracing flexibility in revision timelines and a certain benevolence in the review process itself [27].

Peer-review is an essential quality-assurance process, invaluable to the integrity of scientific work. However; it does have the potential to result in delays during crucial moments of an outbreak, where mere hours may make a difference with respect to dissemination of newly acquired insights. In order to maintain this important quality-assurance measure, we are hoping journal editors have adapted their policies to expedite responses, while consistently upholding their high-standards.

Authors likewise must continue to hold in high-regard their responsibility to maintain the trust of various stakeholders and the public [28]. Data shared publicly should meet appropriate quality, and ethical and legal standards, safeguarding confidentiality of the participants [28]. Authors must remain cognizant of the absolute need to maintain credibility before the scientific community and to exercise caution with

what they submit for publication.

Globally, it is our obligation to treat open-access science with great care. To achieve this, responsible debate and disagreement, and honest yet courteous critique provide a platform for a range of opinions to be expressed [29,30]. Medical journals afford readers the opportunity to submit comments, questions, or criticisms pertaining to published work. The discourse can be passionate and enlightening, exposing new perspectives for further deliberation. Yet in the midst of a deadly crisis, acknowledgement of the circumstances is paramount, and consideration of the underlying pressures more important than ever. Providing the necessary feedback in a respectful and considerate manner, tempered by humanity and kindness for our colleagues, their efforts, and the integrity of their work cannot be underestimated.

SARS-CoV-2 is novel and the recognition of the effects and outcomes of COVID-19 is evolving rapidly, bringing with it urgency for enhanced understanding, to improve current management strategies and save lives. There are both benefits and risks fast-tracked publications on COVID-19, particularly as insights emerge at a record pace. It is imperative to keep in mind that opinions provided based on initial data may need to evolve as new details are reported. For most journals, the risks of missing out, becoming quickly outdated, or potentially being recognized as flawed need to be balanced by the benefits of rapid response to serve the scientific community, to stimulate new ideas and further work, and to maintain leadership in the field.

3. The balance

Accounting for both perspectives, a pragmatic approach is to enable publications, courteous critique and debate, but to also tighten the peer-review process to ensure publication of quality science. Additionally, in the interests of relevance and fairness, and to keep correspondence manageable, journals may wish to consider setting time limits and rules of conduct to guide responses to published material and to govern debate on a given topic. A critical tenet of any scientific debate, which must be upheld in these scary and fast-moving times, is

the need to maintain respect for others' scientific output, to trust in their *bona fide* intentions, and to exercise a humane and dignified manner with which to provide constructive critique. It is likewise important to harness this opportunity to develop innovative collaborations between dedicated professionals, rather than propagating competition. The vulnerability of the world and of humanity is a clear lesson imparted by COVID-19. It would behoove all of us to espouse the metaphorical "we are all in the same boat" scenario and to build supportive teams in the true spirit of collaboration. We should strive to ensure that the positive outcome of this pandemic is a sound foundation for long-term relationships that aim to improve International standards and consensus.

Declaration of competing interest

The authors have nothing to disclose.

References

- [1] World Health Organization, WHO Director-General's Opening Remarks at the Mission Briefing on COVID-19, <https://www.WHO.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19—11-March-2020>, (2020) (<https://doi.org/10.1111/jth.14870>).
- [2] W.J. Guan, Z.Y. Ni, Y. Hu, W.H. Liang, C.Q. Ou, J.X. He, L. Liu, H. Shan, C.L. Lei, D.S.C. Hui, B. Du, L.J. Li, G. Zeng, K.Y. Yuen, R.C. Chen, C.L. Tang, T. Wang, P.Y. Chen, J. Xiang, S.Y. Li, J.L. Wang, Z.J. Liang, Y.X. Peng, L. Wei, Y. Liu, Y.H. Hu, P. Peng, J.M. Wang, J.Y. Liu, Z. Chen, G. Li, Z.J. Zheng, S.Q. Qiu, J. Luo, C.J. Ye, S.Y. Zhu, N.S. Zhong, Clinical characteristics of coronavirus disease 2019 in China, *N. Engl. J. Med.* 382 (19) (2020) 1859–1862 <https://doi.org/10.1056/NEJMoa2002032>.
- [3] WHO, Naming the coronavirus disease (COVID-19) and the virus that causes it, World Heal. Organ. (2020), <https://www.who.int/dg/speeches/detail/who-director-general-s-remarks-at-the-media-briefing-on-2019-ncov-on-11-february-2020> Epublished.
- [4] A.E. Gorbalenya, S.C. Baker, R.S. Baric, R.J. de Groot, C. Drosten, A.A. Gulyaeva, B.L. Haagmans, C. Lauber, A.M. Leontovich, B.W. Neuman, D. Pendar, S. Perlman, L.L.M. Poon, D.V. Samborskiy, I.A. Sidorov, I. Sola, J. Ziebuhr, The species severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2, *Nat. Microbiol.* 5 (2020) 536–544 <https://doi.org/10.1038/s41564-020-0695-z>.
- [5] N. Tang, D. Li, X. Wang, Z. Sun, Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia, *J. Thromb. Haemost.* (2020), <https://doi.org/10.1111/jth.14768>.
- [6] M. Panigada, N. Bottino, P. Tagliabue, G. Grasselli, C. Novembrino, V. Chantarangkul, A. Pesenti, F. Peyvandi, A. Tripodi, Hypercoagulability of COVID-19 patients in intensive care unit. A report of thromboelastography findings and other parameters of hemostasis, *J. Thromb. Haemost.* (2020), <https://doi.org/10.1111/jth.14850>.
- [7] B. Bikdeli, M.V. Madhavan, D. Jimenez, T. Chuich, I. Dreyfus, E. Driggin, C. Der Nigoghossian, W. Ageno, M. Madjid, Y. Guo, L.V. Tang, Y. Hu, J. Giri, M. Cushman, I. Quere, E.P. Dimakakos, C.M. Gibson, G. Lippi, E.J. Favaloro, J. Fareed, J.A. Caprini, A.J. Tafur, J.R. Burton, D.P. Francese, E.Y. Wang, A. Falanga, C. McLintock, B.J. Hunt, A.C. Spyropoulos, G.D. Barnes, J.W. Eikelboom, I. Weinberg, S. Schulman, M. Carrier, G. Piazza, J.A. Beckman, P.G. Steg, G.W. Stone, S. Rosenkranz, S.Z. Goldhaber, S.A. Parikh, M. Monreal, H.M. Krumholz, S.V. Konstantinides, J.I. Weitz, G.Y.H. Lip, COVID-19 and thrombotic or thromboembolic disease: implications for prevention, antithrombotic therapy, and follow-up, *J. Am. Coll. Cardiol.* (2020), <https://doi.org/10.1016/j.jacc.2020.04.031> Epublished.
- [8] D. Kaplan, T. Charles Casper, C. Gregory Elliott, S. Men, R.C. Pendleton, L.W. Kraiss, A.S. Weyrich, C.K. Grissom, G.A. Zimmerman, M.T. Rondina, VTE Incidence and Risk Factors in Patients with Severe Sepsis and Septic Shock, *Chest*, (2015), <https://doi.org/10.1378/chest.15-0287>.
- [9] F.A. Klok, M.J.H.A. Kruip, N.J.M. van der Meer, M.S. Arbous, D.A.M.P.J. Gommers, K.M. Kant, F.H.J. Kaptein, J. van Paassen, M.A.M. Stals, M.V. Huisman, H. Endeman, Incidence of thrombotic complications in critically ill ICU patients with COVID-19, *Thromb. Res.* (2020) (doi:10.1016/j.thromres.2020.04.013) S0049-3848(20)30120-1.
- [10] J. Thachil, N. Tang, S. Gando, A. Falanga, M. Levi, C. Clark, T. Iba, M. Cattaneo, Type and dose of heparin in COVID-19, *J. Thromb. Haemost.* (2020), <https://doi.org/10.1111/jth.14870> n/a.
- [11] Y.Y. Greenstein, Inaccurate conclusions by Tang and colleagues, *J. Thromb. Haemost.* (2020), <https://doi.org/10.1111/jth.14857> n/a.
- [12] C.D. Barrett, H.B. Moore, E.E. Moore, R.C. McIntyre, P.K. Moore, J. Burke, F. Hua, J. Appgar, D.S. Talmor, A. Sauaia, D.R. Liptzin, L.A. Veress, M.B. Yaffe, Fibrinolytic therapy for refractory COVID-19 acute respiratory distress syndrome: scientific rationale and review, *Res. Pract. Thromb. Haemost.* (2020), <https://doi.org/10.1002/rth2.12357> n/a.
- [13] H. Fogarty, L. Townsend, C. Ni Cheallaigh, C. Bergin, I. Martin-Loeches, P. Browne, C.L. Bacon, R. Gaule, A. Gillett, M. Byrne, K. Ryan, N. O'Connell, J.M. O'Sullivan, N. Conlan, J.S. O'Donnell, COVID-19 coagulopathy in Caucasian patients, *Br. J. Haematol.* (2020), <https://doi.org/10.1111/bjh.16749> n/a.
- [14] G. Lippi, E.J. Favaloro, D-dimer is associated with severity of coronavirus disease 2019: a pooled analysis, *Thromb. Haemost.* (2020), <https://doi.org/10.1055/s-0040-1709650>.
- [15] J.-F. Llitjos, M. Leclerc, C. Chochois, J.-M. Monsallier, M. Ramakers, M. Auvray, K. Merouani, High incidence of venous thromboembolic events in anticoagulated severe COVID-19 patients, *J. Thromb. Haemost.* (2020), <https://doi.org/10.1111/jth.14869>.
- [16] F.A. K., M.J.H.A. K., N.J.M. van der M., M.S. A., D.A.M.P.J. G., K.M. K., F.H.J. K., J. van P., M.A.M. S., M.V. H., H. E., Incidence of thrombotic complications in critically ill ICU patients with COVID-19, *Thromb. Res.* (2020), <https://doi.org/10.1016/j.thromres.2020.04.013> [https://tufts-primo.hosted.exlibrisgroup.com/openurl/01TUN/01TUN_SP?sid=EMBASE&sid=EMBASE&issn=18792472&id=doi:10.1016%2Fj.thromres.2020.04.013&title=Incidence+of+thrombotic+complications+in+critically+ill+ICU+patients+with+COVID-19&title=Thromb.+Res.&title=Thrombosis+Research&volume=&issue=&epage=&aualst=Klok&aufirst=F.A.&aunit=F.A.&aufull=Klok+F.A.&coden=THBRA&isbn=&pages=-&date=2020&aunit1=F&aunitm=A+S0049-3848\(20\)30120-1](https://tufts-primo.hosted.exlibrisgroup.com/openurl/01TUN/01TUN_SP?sid=EMBASE&sid=EMBASE&issn=18792472&id=doi:10.1016%2Fj.thromres.2020.04.013&title=Incidence+of+thrombotic+complications+in+critically+ill+ICU+patients+with+COVID-19&title=Thromb.+Res.&title=Thrombosis+Research&volume=&issue=&epage=&aualst=Klok&aufirst=F.A.&aunit=F.A.&aufull=Klok+F.A.&coden=THBRA&isbn=&pages=-&date=2020&aunit1=F&aunitm=A+S0049-3848(20)30120-1).
- [17] J. Helms, C. Tacquard, F. Severac, I. Leonard-Lorant, M. Ohana, X. Delabranche, H. Merdji, R. Clere-Jehl, M. Schenck, F. Fagot Gandet, S. Fafi-Kremer, V. Castelain, F. Schneider, L. Grunebaum, E. Angles-Cano, L. Sattler, P.-M. Mertes, F. Meziani, C.T.G. (Clinical R. in I.C. and S.T.G. for G.E. and R. in Sepsis), High risk of thrombosis in patients with severe SARS-CoV-2 infection: a multicenter prospective cohort study, *Intensive Care Med.* (2020), <https://doi.org/10.1007/s00134-020-06062-x> Epublished.
- [18] M. Ranucci, A. Ballotta, U. Di Dedda, E. Bayshnikova, M. Dei Poli, M. Resta, M. Falco, G. Albano, L. Menicanti, The procoagulant pattern of patients with COVID-19 acute respiratory distress syndrome, *J. Thromb. Haemost.* n/a (2020). doi:10.1111/jth.14854.
- [19] N. T., H. B., X. C., J. G., D. L., Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy, *J. Thromb. Haemost.* 18 (5) (2020) 1094–1099 <https://doi.org/10.1111/jth.14817>.
- [20] E. Vlachodimitropoulou Koumoutsea, A.J. Vivanti, N. Shehata, A. Benachi, A. Le Gouez, C. Desconclois, W. Whittle, J. Snelgrove, K.A. Malinowski, COVID19 and acute coagulopathy in pregnancy, *J. Thromb. Haemost.* (2020), <https://doi.org/10.1111/jth.14856> Epublished.
- [21] C.D. B., H.B. M., M.B. Y., ISTH interim guidance on recognition and management of coagulopathy in COVID-19: a comment, *J. Thromb. Haemost.* (2020), <https://doi.org/10.1111/jth.14860> Epublished.
- [22] J.M. Connors, J.H. Levy, COVID-19 and its implications for thrombosis and anticoagulation, *Blood* (2020), <https://doi.org/10.1182/blood.2020060600>.
- [23] K. Modjarad, V.S. Moorthy, P. Millett, P.S. Gsell, C. Roth, M.P. Kienny, Developing global norms for sharing data and results during public health emergencies, *PLoS Med.* (2016), <https://doi.org/10.1371/journal.pmed.1001935>.
- [24] Sharing research data and findings relevant to the novel coronavirus (COVID-19) outbreak (n.d.). <https://wellcome.ac.uk/coronavirus-covid-19/open-data>.
- [25] D. Lillicrap, Open letter to the thrombosis and hemostasis community from the editors of JTH, *J. Thromb. Haemost.* (2020), <https://onlinelibrary.wiley.com/journal/15387836> Epublished.
- [26] J. Berens, U. Mans, S. Verhulst, Mapping and comparing responsible data approaches, *SSRN Electron. J.* (2018), <https://doi.org/10.2139/ssrn.3141453>.
- [27] M. Cushman, Publishing in the COVID era, *Res. Pract. Thromb. Haemost.* (2020), <https://doi.org/10.1002/rth2.12341> n/a.
- [28] ICMJE, Recommendations for the conduct, reporting, editing, and publication of scholarly work in medical journals, current version, *Int. Comm. Med. J. Ed.* (2018).
- [29] C. Graf, E. Wager, A. Bowman, S. Fiack, D. Scott-Lichter, A. Robinson, Best practice guidelines on publication ethics: a publisher's perspective, *Int. J. Clin. Pract.* (2007), <https://doi.org/10.1111/j.1742-1241.2006.01230.x>.
- [30] COPE Council, Ethical Guidelines for Peer Reviewers, https://Publicationethics.Org/Files/Ethical_Guidelines_For_Peer_Reviewers_2.Pdf, (2017).

Sajida Kazi^a, A. Kinga Malinowski^b, Maha Othman^{c,d,*}

^a MSc Clinical Education Student, University of Edinburgh, Edinburgh, UK

^b Department of Obstetrics & Gynecology, Division of Maternal Fetal Medicine, Mount Sinai Hospital, Toronto, Canada

^c Department of Biomedical and Molecular Sciences, School of Medicine, Queen's University, Kingston, Canada

^d School of Baccalaureate Nursing, St. Lawrence College, Kingston, Canada

E-mail address: othman@queensu.ca (M. Othman).

* Corresponding author at: Department of Biomedical and Molecular Sciences, School of Medicine, Queen's University, Kingston, Ontario, Canada.