INTRODUCTION

The ongoing COVID-19 pandemic has caused more than 124 million cases and more than 2.5 million deaths worldwide as of March 2021. To date, there is only one drug whose efficacy has been unequivocally demonstrated in randomized controlled trials (RCT), namely dexamethasone. Many promising therapeutics have failed under RCTs, with COVID-19 convalescent plasma (CCP) having shown clinical benefit if used within 72 hours and with high neutralizing antibodies (nAb) titers;\(^1\)\(^-\)\(^6\) on the contrary, trials lacking one of these requirements have failed to show clinical benefit.\(^1\)\(^,\)\(^7\)\(^-\)\(^9\) Many more trials are still ongoing. CCP donations can be used in different ways,\(^10\) and nAb titers, despite detectable at more than 8 months,\(^11\) show a decline with time after recovery.\(^12\) Hence CCP donor recruitment is being pursued to create bulk storages.

The cost for processing a CCP donation is considerably high due to personnel (donation nurses and laboratory technicians) and, in many regions, accessory testing (additional NAT, viral neutralization tests (VNT)), and pathogen reduction technologies. Additional concerns come from the risk of medical litigations in case of accidents during poorly selected CCP donations or prolonged storage of low-antibody units finally destined to discard.

While the pandemic accelerates, a growing number of eligible convalescents have to be screened as candidate CCP donor. Laboratory screening with high-throughput serology has good correlations with the VNT titer, but upstream screening using clinical surrogates would be advisable. We review here the existing literature on clinical predictors of high-titer nAb. Older age, male sex, and hospitalization are the main proxies of high VNT and should drive CCP donor recruitment.

Clinical predictors of SARS-CoV-2 neutralizing antibody titers in COVID-19 convalescents: Implications for convalescent plasma donor recruitment

Daniele Focosi\(^1\)\(^,\)\(^*\) | Massimo Franchini\(^2\)

\(^{1}\)North-Western Tuscany Blood Bank, Pisa University Hospital, Pisa, Italy
\(^{2}\)Department of Hematology and Transfusion Medicine, Carlo Poma Hospital, Mantua, Italy

Correspondence
Daniele Focosi, via Paradisa 2, 56124 Pisa, Italy.
Email: daniele.focosi@gmail.com

Abstract

While COVID-19 convalescent plasma (CCP) efficacy is still under investigation in randomized controlled trials (RCT), CCP collections continue worldwide with largely variable criteria. Since it is well known that only a minority of patients develop high-titer neutralizing antibodies (nAb), as assessed by the viral neutralization tests (VNT), strategies to maximize cost-effectiveness of CCP collection are urgently needed. A growing amount of the population is having exposure to the virus and is hence becoming a candidate CCP donor. Laboratory screening with high-throughput serology has good correlations with the VNT titer, but upstream screening using clinical surrogates would be advisable. We review here the existing literature on clinical predictors of high-titer nAb. Older age, male sex, and hospitalization are the main proxies of high VNT and should drive CCP donor recruitment.

Keywords
clinical predictors, convalescent plasma, COVID-19, neutralizing antibodies, SARS-CoV-2, viral neutralization tests
### TABLE 1  
Studies reporting correlation of nAb titer with clinical variables in COVID-19

| Country (n) | Median nAb titer | Age (AOR) | Male sex (AOR) | Fever during acute illness (AOR) | Clinical severity by WHO ordinal scale (AOR) | Lymphocyte count | ABO blood group | Days since diagnosis | BMI | Ref |
|-------------|------------------|-----------|----------------|----------------------------------|-----------------------------------------------|------------------|-----------------|---------------------|-----|-----|
| USA (250)   | 60% ±1:80        | 1.03/age  | 2.08           | 2.73                             | 6.59                                          |                  |                 |                     |     | 34  |
| USA (126)   | 0.1 every 10 y   | 0.27a     | 0.86a          |                                  |                                               |                  |                 | −0.192 every 10 d  |     | 41  |
| USA (97)    | No correlation   | Trend     | No correlation |                                  |                                               |                  |                 | No correlation     |     | 17  |
| USA (221)   | No correlation   | No correlation | Mean titer higher in ICU than in hospitalized higher than in HCW | |                                               |                  |                 |                     |     | 26  |
| USA (47)    | Mean titer higher in age 48 to 75 y | No correlation |                                  | Mean titer higher in age 48 to 75 y | Mean titer higher in age 48 to 75 y |                  |                 |                     |     | 18  |
| Austria (100) | 1:230           | r² = .09  | Mean titer 1:60 in females vs. 120 in males | Mean titer 1:208 in WHO scores 1 and 2 vs. 1:696 in WHO scores 3 and 4 (rank) |                                               |                  |                 |                     |     | 42  |
| Brazil (149) |                   |          |                |                                  |                                               |                  |                 |                     |     |      |
| China (175) | ID₅₀ RLU         | >40 y     | r = −.44       | Mean titer 1:208 in WHO scores 1 and 2 vs. 1:696 in WHO scores 3 and 4 (rank) |                                               |                  |                 |                     |     | 15  |
| France (140) |                   | x (ICU)   |                |                                  |                                               |                  |                 |                     |     | 25  |
| Germany (49) | No               | No        |                |                                  |                                               |                  |                 |                     |     | 24  |
| Germany (62) | No               | No        |                |                                  |                                               |                  |                 |                     |     | 44  |
| Italy (494) | 93% >1:80        | 0.26 (linear variable) | −0.14 (linear variable) | 0.28 (linear variable) | No correlation |                  |                 |                     |     | 20  |
| UK (330)    | 1:69             | 1.02 (linear variable) | 2.41            | 2.25                            | AB/B higher than A/O (rank)                   |                  |                 |                     |     | 16  |
| Greece (60) | Age >50          | Hospitalization | No correlation |                                  |                                               |                  |                 |                     |     | 45  |
| China (23)  |                  | Mechanical ventilation higher than isolation wards | No difference ICU vs non-ICU |                                  |                                               |                  |                 |                     |     | 46  |
| Spain (54)  | Age >30          | Yes       | No correlation |                                  |                                               |                  |                 |                     |     | 47  |
| USA (120)   |                  | Yes       | BMI >30        |                                  |                                               |                  |                 |                     |     |      |

Note: Abbreviations: AOR, adjusted odds ratio; nAb, neutralizing antibodies; BMI, body mass index; HCW, healthcare workers. x = AOR or correlation coefficient not reported. Empty cells mean the parameter was not investigated in that given study.

*Linear regression model coefficients.
2 | METHODS

A review of the literature about clinical predictors of PRNT in COVID-19 was done following the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines. PubMed (www.pubmed.gov), medRxiv (https://www.medrxiv.org), and biorXiv (https://www.biorxiv.org/) online databases were systematically searched. The search included articles from January 1, 2020 up to February 5, 2021. No restriction was placed on sample size. Only articles written in English were considered. The search query: “COVID19” AND “neutralizing” AND (“predictors” OR “proxies”) was used for the first screening. The 293 search results were manually screened for consistency. The clinical parameters identified include age at diagnosis, days after initial diagnosis (positive nasopharyngeal swab), gender, hospitalization, and body mass index (BMI). Additionally, being largely available laboratory parameters, ABO blood group, and complete blood count were included as pseudo-clinical parameters.

3 | RESULTS

Table 1 summarizes the findings of 13 studies reporting the association of PRNT titer with clinical variables. Most studies agreed that higher age, male sex, higher BMI, and disease severity (especially hospitalization) are the main predictors for high PRNT titers. Other clinical factors such as fever during acute illness or days since diagnosis (or recovery) instead show correlations only in a minority of studies. Single studies reported a low lymphocyte count or AB/B blood groups as additional proxies. These parameters, albeit not strictly clinical, are widely available for patients discharged from hospitals. One study found that GI symptoms did not predict nAb titer, while another showed that abdominal pain, diarrhea, and low appetite correlated consistently with higher nAb levels. A single study found no relation between nAb and symptom duration (1:7 vs 8-14 vs 15-28 days). Similarly, a single study found no correlation between nAb and higher Charlson Comorbidity Index score.

In the most relevant work to date, Mehew et al reported that, in a logistic regression model, younger age, female gender, blood group O, and not being a previous blood donor were associated with non-detectable neutralizing antibody response. The same authors used a multivariable gamma generalized linear model (GLM) to identify the factors associated with nAb titers: The analysis demonstrated a significant association between increasing mean nAb titers and increasing age, hospitalization (1:383 vs 1:63), male gender (1:97 vs 1:47), and B groups (1:148 for group AB vs 1:104 for group B, 1:70 for group A and 1:47 for group O). Although it has been proposed that higher antibody levels in male and older patients simply relate to COVID-19 severity, their model proposes that they remain associated with higher nAb titer levels after adjusting for hospitalization. In the largest study published so far by Del Fante and colleagues on 494 Italian CCP donors, the nAb titer was found to correlate positively with age and disease severity and negatively with female sex.

4 | DISCUSSION

The VNT, while being a gold standard for nAb titering, is a BSL3-requiring and time-consuming method whose high-throughput variants (eg, pseudotype VNT) are still to be implemented in the vast majority of laboratories. Scaling up of VNT for screening purposes is sustainable only when the recruitment is limited to interventional clinical trials. If the efficacy of CCP will be confirmed in RCT, at that point the number of convalescents to screen before CCP donation would be unsustainable for VNT, and likely an issue even for high-throughput serology (given the potential massive demand during a pandemic), if not filtered upstream with clinical proxies. We then started a review of clinical predictors of high nAb titers, as measured by the VNT.

This review has several limitations. Most studies we identified reported correlations but no cutoffs for clinical predictors. Additionally, the variability between VNT assays (titers, methods, live SARS-CoV-2 virus vs. pseudovirus, etc) is an additional hurdle for the derivation of cutoffs. Many studies were excluded from the analysis because they relied over high-throughput serology as a surrogate of nAb titer (eg).

Nevertheless, the 13 studies we analyzed support the feasibility of first-line screening with cost-free clinical surrogates such as age, sex, and hospitalization to identify the convalescents who are most likely to have high nAb titers as later measured by VNT. In resource-constrained settings, it is hence possible to orient the wave of CCP donations so that time and resource wasting is minimized. This study was limited to clinical proxies, but several studies identified additional, serological (eg, anti-Spike IgG avidity, or microfluidic affinity) or non-serological biomarkers (eg, high C-reactive protein, or non-serological laboratory biomarkers is reduced by their limited availability at the time of CCP donation screening, and, if unavailable, by their incremental cost, which largely overlap the one of high-throughput serology.

In most studies several parameters (ranging from 2% in ICU to 25% in non-hospitalized patients to 40% in healthcare workers) show no nAb at all as assessed by the VNT. Lee et al reported that S-specific antibodies are capable of engaging dimeric FcγRIIa and FcγRIIIa decay linearly over time. S-specific antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent phagocytosis (ADP) activity within plasma decline linearly as well, in line with the decay of S-specific IgG. Although there was significant decay in S-specific plasma ADCC and ADP activity, they remained readily detectable by all assays in 94% at 149 days, in contrast to nAbs, which were only detectable in 70%. While this does not mean at all that the convalescents are not protected from further exposures (having immunity from specific T-lymphocytes), this circumstance further increases the need for cost-effective screening strategies.

On average, the nAb titer peaks 30 days after symptom onset and declines by 25% every 15 days (largely due to the decline in neutralizing IgM and IgA). It is therefore sounding that the days since positive nasopharyngeal swab correlates with the nAb titer. Nevertheless there is large variability in decline kinetics. Grzelak
et al showed that the decline in nAbs was faster in males than in females, independently of age and BMI.\textsuperscript{31} Titters ≥1:160 (which are considered the only useful donations for achieving clinical benefit) begin to decline significantly since day 60 (ie, 30 days after the peak).\textsuperscript{32} Wendel et al reported that Ab titers ≥160 had a median persistence of 77 days after the onset of symptoms, but only 25% remained at this level after 100 days.\textsuperscript{33} While decline around day 100 occurs in 90% of convalescents,\textsuperscript{34} there was a high probability of sustaining nAb titers ≥160 when the initial nAb titer was ≥1280, weight ≥90kg, or BMI classified as overweight or obese. There was no correlation between ABO group, ABO isoagglutinin titers and persistent high nAb titers.\textsuperscript{35} Of course, the initial nAb titer is only useful to evaluate the opportunity for repeated CCP donations.

Several SARS-CoV-2 variants are emerging,\textsuperscript{35-37} and the efficacy of anti-Spike monoclonal antibodies against them seems lower than CCP.\textsuperscript{38} Since even the currently marketed anti-Spike vaccines are likely to offer reduced protection against some of these variants,\textsuperscript{39} the interest in CCP is likely to remain high for months. We anticipate that, with a growing population of convalescents, screening for CCP donation eligibility on the basis of clinical predictors will anticipate laboratory screening with both high-throughput serology and VNT, especially in resource-poor settings.

Additionally, collecting CCP from vaccinees is an intriguing opportunity, although to date the FDA is only allowing collection from vaccinees who have also been convalescents in the last 6 months.\textsuperscript{40} Gaining knowledge about the breadth and duration of the immune response in COVID-19 vaccinees will likely contribute changing such regulations.

CONFLICT OF INTEREST

We declare we have no conflict of interests to disclose.

AUTHOR CONTRIBUTIONS

DF designed the paper, analyzed the data, and wrote the first draft.
MF revised the final version.

ORCID

Daniele Focosi https://orcid.org/0000-0001-8811-195X

REFERENCES

1. Simonovich VA, Burgos Pratx LD, Scibona P, et al. A randomized trial of convalescent plasma in covid-19 severe pneumonia. N Engl J Med. 2021;384(7):619–629.
2. RECOVERY trial closes recruitment to convalescent plasma treatment for patients hospitalised with COVID-19. 15 January, 2021: https://www.recoverytrial.net/news/statement-from-the-recovery-trial-chief-investigators-15-january-2021-recovery-trial-closes-recruitment-to-convalescent-plasma-treatment-for-patients-hospitalised-with-covid-19. Accessed Feb 5, 2021.
3. Libster R, Pérez Marc G, Wappner D, et al. Early high-titer plasma therapy to prevent severe COVID-19 in older adults. N Engl J Med. 2021;384(7):610–618.
4. Joyner MJ, Carter RE, Senefeld JW, et al. Convalescent plasma antibody levels and the risk of death from COVID-19. N Engl J Med. 2021;384(11):1015–1027.
5. Gonzalez SE, Regaizar L, Salazar M, et al. Timing of convalescent plasma administration and 28-day mortality for COVID-19 pneumonia. medRxiv. 2020;2021.2002.2002.21250758.
6. Joyner MJ, Bruno KA, Klassen SA, et al. Safety update: COVID-19 convalescent plasma in 20,000 hospitalized patients. Mayo Clin Proc. 2020;95:1888-1895.
7. Horby PW, Estcourt L, Peto L, et al. Convalescent plasma in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. medRxiv. 2021:2021.2003.20125236.
8. Agarwal A, Mukherjee A, Kumar G, et al. Convalescent plasma in the management of moderate COVID-19 in India: open-label parallel-arm phase II multicentre randomized controlled trial (PLACID Trial). BMJ. 2020;371:m3939.
9. Gharbharan A, Jordans CCE, GeurtsvanKessel C, et al. Convalescent Plasma for COVID-19. A randomized clinical trial. medRxiv. 2020.2020.07.01.20139857.
10. Focosi D, Tuccori M, Antonelli G, Maggi F. What is the optimal usage of COVID-19 convalescent plasma donations?. Clin Microbiol Infect. 2020;S1198–743X(20):30589.
11. Dan JM, Mateus J, Kato Y, et al. Immunological memory to SARS-CoV-2 assessed for up to 8 months after infection. Science. 2021;371(6529):eabf4063.
12. Focosi D, Maggi F, Mazzetti P, Pistello M. Viral infection neutralization tests: A focus on severe acute respiratory syndrome-coronavirus-2 with implications for convalescent plasma therapy. Reviews in Medical Virology. 2021;31(2). http://dx.doi.org/10.1002/rmv.2170
13. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Int J Surg. 2010;8(5):336–341.
14. Amjadi MF, O’Connell SE, Armburst T, et al. Fever, diarrhea, and severe disease correlate with high persistent antibody levels against SARS-CoV-2. medRxiv. 2021;2021.2001.2021.21249240. Available at: https://www.medrxiv.org/content/medrxiv/early/2021/01/06/2021.01.05.21249240.full.pdf. Accessed Feb 5, 2021.
15. Wu F, Wang A, Liu M, et al. Neutralizing antibody responses to SARS-CoV-2 in a COVID-19 recovered patient cohort and their implications. medRxiv. 2020:2020.2003.2030.20047365. Available at: https://www.medrxiv.org/content/medrxiv/early/2020/04/20/2020.03.30.20047365.full.pdf. Accessed Feb 5, 2021.
16. Mehew J, Johnson R, Roberts D, Harvala H. Convalescent plasma for COVID-19: male gender, older age and hospitalisation associated with high neutralising antibody levels, England, 22 April to 12 May 2020. Euro Surveill. 2020;25(45):2001754.
17. Muecksch F, Wise H, Batchelor B, et al. Longitudinal analysis of clinical serology assay performance and neutralising antibody levels in COVID19 convalescents. medRxiv. 2020:2020.2008.2005.20169128. Available at: https://www.medrxiv.org/content/medrxiv/early/2020/08/06/2020.08.05.20169128.full.pdf. Accessed Feb 5, 2021.
18. Gniadek TJ, Thiede JM, Matchett WE, et al. SARS-CoV-2 neutralization and serology testing of COVID-19 convalescent plasma from donors with nonsevere disease. Transfusion. 2021;61(1):7–23. http://dx.doi.org/10.1111/trf.16101
19. Scully EP, Haverfield J, Ursin RL, Tannenbaum C, Klein SL. Considering how biological sex impacts immune responses and COVID-19 outcomes. Nat Rev Immunol. 2020;20(7):442–447.
20. Del Fante C, Franchini M, Baldanti F, et al. A retrospective study assessing the characteristics of COVID-19 convalescent plasma donors and donations. Transfusion. 2021;61(3):830–838.
21. Madariaga MLL, Guthmiller JJ, Schrantz S, et al. Clinical predictors and donations. Transfusion. 2021;61(3):830–838.
22. Benner SE, Patel EU, Laeyendecker O, et al. SARS-CoV-2 antibody avidity responses in COVID-19 patients and convalescent plasma donors. J Infect Dis. 2020;222(12):1974-1984.
23. Schneider MM, Emmenegger M, Xu CK, et al. Microfluidic affinity profiling reveals a broad range of target affinities for anti-SARS-CoV-2 antibodies in plasma of COVID survivors. medRxiv. 2020:2020.2009.2020.20196907. Available at: https://www.medrxiv.org/content/medrxiv/early/2020/09/23/2020.09.20.20196907.full.pdf. Accessed Feb 5, 2021.

24. Ruetalo N, Businger R, Althaus K, et al. Neutralizing antibody response in non-hospitalized SARS-CoV-2 patients. medRxiv. 2020:2020.2008.2017.20169961. Available at: https://www.medrxiv.org/content/medrxiv/early/2020/09/22/2020.09.27.20169961.full.pdf. Accessed Feb 5, 2021.

25. Legros V, Denolly S, Vogrig M, et al. A longitudinal study of SARS-CoV-2-infected patients reveals a high correlation between neutralizing antibodies and COVID-19 severity. Cellular & Molecular Immunology. 2021;18(2):318–327. http://dx.doi.org/10.1038/s41423-020-00588-2.

26. Zeng C, Evans JP, Pearson R, et al. Neutralizing antibody against SARS-CoV-2 spike in COVID-19 patients, health care workers and convalescent plasma donors. JCI Insight. 2020;5(22):e143213.

27. Lee WS, Selva KJ, Davis SK, et al. Decay of Fc-dependent antibody functions after mild to moderate COVID-19. medRxiv. 2020:2020.2012.2013.20248143. Available at: https://www.medrxiv.org/content/medrxiv/early/2020/12/14/2020.12.13.20248143.full.pdf. Accessed Feb 5, 2021.

28. Schwarzkopf S, Krawczyk A, Knop D, et al. Cellular Immunity in COVID-19 Convalescents with PCR-Confirmed Infection but with Undetectable SARS-CoV-2-Specific IgG. Emerging Infectious Diseases. 2021;27(1):122–129. http://dx.doi.org/10.3201/2701.202071.

29. Yao X-Y, Liu W, Li Z-Y, et al. Neutralizing and binding antibody kinetics of COVID-19 patients during hospital and convalescent phases. medRxiv. 2020:2020.2007.20156810.

30. Klinger J, Weiss S, Itri V, et al. Role of Immunoglobulin M and A Antibodies in the Neutralization of Severe Acute Respiratory Syndrome Coronavirus 2. The Journal of Infectious Diseases. 2021;223(6):957–970. http://dx.doi.org/10.1093/infd/jaia784.

31. Grzelak L, Velay A, Madec Y, et al. Sex differences in the evolution of neutralizing antibodies to SARS-CoV-2. The Journal of Infectious Diseases. 2021.http://dx.doi.org/10.1093/infdis/jia127.

32. Gontu A, Srinivasan S, Salazar E, et al. Limited window for donation of convalescent plasma with high live-virus neutralizing antibody titers for COVID-19 immunotherapy. Communications Biology. 2021;4(1). http://dx.doi.org/10.1038/s42003-021-01813-y.

33. Wendel S, Fontâo-Wendel R, Fachiini R, et al. A longitudinal study of convalescent plasma (CCP) donors and correlation of ABO group, initial neutralizing antibodies (nAb), and body mass index (BMI) with nAb and anti-nucleocapsid (NP) SARS-CoV-2 antibody kinetics: Proposals for better quality of CCP collections. Transfusion. 2021; http://dx.doi.org/10.1111/trf.16323.

34. Boonnyaratnakornkit J, Morishima C, Selke S, et al. Clinical, laboratory, and temporal predictors of neutralizing antibodies against SARS-CoV-2 among COVID-19 convalescent plasma donor candidates. Journal of Clinical Investigation. 2021;131 (3):http://dx.doi.org/10.1172/jci144930.

35. Naveca F, da Costa C, Nascimento V, et al. SARS-CoV-2 reinfection by the new Variant of Concern (VOC) P.1 in Amazonas, Brazil. 2021; https://virological.org/t/sars-cov-2-reinfection-by-the-new-variant-of-concern-voc-p-1-in-amazonas-brazil/596. Accessed Jan 27, 2021.

36. Rambaut A, Loman N, Pybus O, et al. Preliminary genomic characterisation of an emergent SARS-CoV-2 lineage in the UK defined by a novel set of spike mutations. 2020; https://virological.org/t/preliminary-genomic-characterisation-of-an-emergent-sars-cov-2-lineage-in-the-uk-defined-by-a-novel-set-of-spike-mutations/563.

37. Kosakovsky Pond S, Wilkison E, Weaver S, et al. A preliminary selection analysis of the South African 501.V2 SARS-CoV-2 clade. 2020; https://virological.org/t/a-preliminary-selection-analysis-of-the-south-african-v501-v2-sars-cov-2-clade/573. Accessed December 31, 2020.

38. Rees-Spear C, Muir L, Griffith SA, et al. The impact of Spike mutations on SARS-COV-2 neutralization. bioRxiv. 2021;2021:2021.2020.15.426849.

39. Wang Z, Schmidt F, Weisblum Y, et al. mRNA vaccine-elicited antibodies to SARS-CoV-2 and circulating variants. Nature. 2021.http://dx.doi.org/10.1038/s41586-021-03324-6.

40. FDA. Recommendations for Investigational COVID-19 Convalescent Plasma. https://www.fda.gov/media/136798/download. Accessed Feb 20, 2021.

41. Klein SL, Pekosz A, Park HS, et al. Sex, age, and hospitalization drive antibody responses in a COVID-19 convalescent plasma donor population. Journal of Clinical Investigation. 2020;130(11):6141–6150. http://dx.doi.org/10.1172/jci142004.

42. Jungbauer C, Weseslindtner L, Weidner L, et al. Characterization of 100 sequential SARS-CoV-2 convalescent plasma donations. Transfusion. 2021;61(1):12–16. http://dx.doi.org/10.1111/trf.16119.

43. Wendel S, Kutner JM, Machado R, et al. Screening for SARS-CoV-2 antibodies in convalescent plasma in Brazil: Preliminary lessons from a voluntary convalescent donor program. Transfusion. 2020;60(12):2938–2951. http://dx.doi.org/10.1111/trf.16065.

44. Bošnjak B, Stein SC, Willenzon S, et al. Low serum neutralizing anti-SARS-CoV-2 S antibody levels in mildly affected COVID-19 convalescent patients revealed by two different detection methods. Cellular & Molecular Immunology. 2021;18(4):936–944. http://dx.doi.org/10.1038/s41423-020-00573-9.

45. Terpos E, Politou M, Sargentanis TN, et al. Anti-SARS-CoV-2 antibody responses in convalescent plasma donors are increased in hospitalized patients; subanalyses of a phase 2 clinical study. Microorganisms. 2020;8(12):1885.

46. Wang Y, Zhang L, Sang L, et al. Kinetics of viral load and antibody response in relation to COVID-19 severity. J Clin Investig. 2020;130(10):5235-5244.

47. Gozalbo-Rovira R, Gimenez E, Latorre V, et al. SARS-CoV-2 antibodies, serum inflammatory biomarkers and clinical severity of hospitalized COVID-19 patients. J Clin Virol. 2020;131:104611.

How to cite this article: Focosi D, Franchini M. Clinical predictors of SARS-CoV-2 neutralizing antibody titers in COVID-19 convalescents: Implications for convalescent plasma donor recruitment. Eur J Haematol. 2021;107:24–28. https://doi.org/10.1111/ejh.13630