No increase in anti-A isohemagglutinin titer after SARS-CoV-2 infection: A retrospective cohort analysis of group O apheresis platelet donors

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Abstract
The risk of a hemolytic reaction during the transfusion of ABO non-identical PC is determined by the presence of natural anti-A IgM antibodies, the titer of which may increase after infections. The aim of the study was to evaluate the titer of anti-A isohemagglutinins in platelet concentrate (PC) obtained by apheresis from group O donors who experienced SARS-CoV-2 infection, and to compare the titer before and after infection. A retrospective single-center analysis of 21 PC donors with a previous COVID-19 history was performed. The results showed neither a statistically important increase in the anti-A IgM antibody titers nor a significant correlation between the anti-A IgM antibody level and anti-SARS-CoV-2S1 antibody titer in the donors with an asymptomatic or mild COVID-19. Further population-based studies on anti-A titers are necessary for a comprehensive assessment of this phenomenon.

KEYWORDS
COVID-19, isohemagglutinin, platelet, SARS-CoV-2, transfusion

1 | INTRODUCTION

Although transfusion of ABO-identical platelet concentrate (PC) is widely recognized as the most effective and safest therapeutic strategy its widespread use is not always possible.¹ For this reason, a vast majority of blood banks enable the transfusion of non-identical PCs, especially the ones obtained through apheresis from group O donors to non-O recipients. Such PCs pose a risk of post-transfusion hemolytic reaction, which may be especially intense in group A recipients.² In order to minimize the risk of hemolytic complications, it is possible to reduce the plasma content of the transfused component³ and to assess the titer of natural isohemagglutinins.⁴

Interestingly, there is a possibility of a potential increase in anti-A isohemagglutinin levels in response to SARS-CoV-2 infection due to the incorporation of the group A antigen into the S protein structure of SARS-CoV-2 virus.⁵ This is supported by an increased level of the anti-A IgM antibodies observed in SARS-CoV infection.⁶ Since there is significant sequence identity between the S protein of the SARS-CoV and SARS-CoV-2 viruses, possible expression of the histo-blood group antigens should be expected during SARS-CoV-2 replication.⁷
2 | BRIEF REPORT

2.1 | Objective

In the present study, we aimed to assess the anti-A isohemagglutinin titer in PCs obtained through apheresis from group O donors who had experienced the SARS-CoV-2 infection, and to compare the results with the titer determined in earlier PCs donations (from the same donors, prior to the SARS-CoV-2 infection).

2.2 | Study group and methodology

A total of 21 group O donors, including 5 women and 16 men, were identified for analysis. The median age was 34 years (range 24-48). Assessment of the severity of COVID-19 (based on the guidelines of the National Institute of Health) allowed us to distinguish: 14 asymptomatic donors, 6 donors with a mild disease, and 1 donor with a moderate disease, who had a radiographically documented pneumonia.

Median time from SARS-CoV-2 diagnosis (positive nucleic acid testing of nasopharyngeal swab) to PC donation and anti-A titer assessment was 39 days (range 28-64). The median time elapsed between assessing anti-A titer in pre-COVID and post-COVID donations was 125 days (range 47-275).

In the samples obtained from PCs (in accordance with the applicable SOP, plasma volume content in the component at the level of 25%-35%) serial 2-fold dilutions were made using a conventional tube technique to

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**FIGURE 1** Anti-A IgM titer prior and subsequent to SARS-CoV-2 infection in platelet concentrate donations.
(A) Comparison of anti-A IgM titer in platelet donations obtained before and after SARS-CoV-2 infection.
(B) Fluctuations in anti-A IgM levels after SARS-CoV-2 infection. The donor with a moderate COVID-19 severity is marked in black.
(C) Results of anti-A IgM titers in subgroups of donors with different levels of disease severity.
determine the level of anti-A IgM antibodies. A positive reaction was defined as a 1+ macroscopic reaction while the titer was interpreted as the reciprocal of the highest dilution.

2.3 | Results

No significant differences in the anti-A IgM titer were established based on the analysis of PCs donated before and after the infection ($P = .3125$) (Figure 1A). Furthermore, there was no significant difference in the anti-A IgM titer between the donors with an asymptomatic ($P = .625$) and mild course ($P = .999$) of the infection when analyzed separately (Figure 1C). As far as the change in the anti-A IgM titer is concerned, 2 donors had an increased anti-A titer, 1 donor had a decreased anti-A titer, while in 18 of our donors the titers remained unchanged following the SARS-CoV-2 infection (Figure 1B). It ought to be emphasized that the highest, 2-fold increase in the anti-A isohemagglutinin titer was found in a donor with a history of moderate infection, who simultaneously showed the highest level of anti-SARS S1 IgG antibodies (Ratio = 8.53 S/Co, titer = 4000) (Figure 1B). However, as indicated earlier, it was the only donor with a moderate course of the infection, which makes it difficult to interpret the result unambiguously. Additionally, no statistically significant correlation was found between the titer of anti-SARS-CoV-2S1 IgG antibodies analyzed in the donors and the increase in the titer of anti-A IgM antibodies in the obtained PCs ($\rho = 0.173; P = .453$).

2.4 | Study limitations

Undoubtedly, there were limitations to our study. Since it was a retrospective analysis, the anti-A IgM titration was determined by different laboratory diagnosticians employed at our Centre, which could possibly have led to an inconsistent interpretation of the results. As it is not mandatory under current transfusion legislation, total levels of circulating immunoglobulins (IgM, IgG, etc) have not been measured in presented donors before or after COVID-19. Additionally, the limited group size and follow-up time did not allow us to draw firm conclusions on the fluctuation in anti-A IgM titers. Equally important is the fact that none of the analyzed donors experienced a severe SARS-CoV-2 infection, which may possibly be connected with an enhanced anti-A IgM production. Finally, the issue of the elapsed time between pre-COVID and post-COVID anti-A assessments seems to be no less relevant given the potential influence of other factors on anti-A levels during this time period.

3 | CONCLUSION

Our study demonstrated no significant increase in anti-A IgM isohemagglutinin titer in the PC donations obtained from donors with a history of asymptomatic or mild SARS-CoV-2 infection. Our current findings could be hypothetically ascribed to the decreased humoral and cell-mediated immune responses observed during an asymptomatic SARS-CoV-2 infection. Asymptomatic individuals exhibit both lower proportions of the SARS-CoV-2-specific CD4+ T cells and have a decreased humoral immune response. Due to the fact that the titer of natural isohemagglutinins shows a significant correlation with the total concentration of immunoglobulins, a weakened humoral response may in this case translate into the lack of increase in the titer of IgM anti-A antibodies.

Given this, group-O PCs obtained by apheresis from donors with asymptomatic or mild COVID-19 course do not seem to present an extended risk of post transfusion hemolytic reactions compared with the regular apheresis group-O PCs donated by donors with no SARS-CoV-2 history, which is extremely important in the context of the PCs transfusion policy and PCs stock management.

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CONFLICT OF INTEREST

All authors have seen and approved the study submitted. No part of the submitted work has been published or is under consideration for publication elsewhere. The authors have no competing interests.

AUTHORS CONTRIBUTIONS

Tomasz Wasiluk: Designed the study, collected the data, analyzed and interpreted the data, and drafted the manuscript. Kamila Rybinska: Collected and analyzed the data. Magdalena Bujno: Collected and analyzed the data. Anna Rogowska: Collected and analyzed the data. Zebrowska: Interpreted the data. Agnieszka Zcebrowska: Interpreted the data. Barbara Boczkowska-Radziwon: Interpreted the data. Jaroslaw Piszcz: Interpreted the data. Lukasz Bolkun: Interpreted the data and drafted the manuscript. Piotr Radziwon: Designed the study, interpreted the data, and drafted the manuscript. All authors approved the final manuscript.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author.
REFERENCES

1. Seigeot A, Desmarets M, Rumpler A, et al. Factors related to the outcome of prophylactic platelet transfusions in patients with hematologic malignancies: an observational study. *Transfusion*. 2018;58(6):1377-1387.

2. Berséus O, Boman K, Nessen SC, Westerberg LA. Risks of hemolysis due to anti-A and anti-B caused by the transfusion of blood or blood components containing ABO-incompatible plasma. *Transfusion*. 2013;53(S1):114S-123S.

3. Tynuv M, Flegel WA. Quality improvement with platelet additive solution for safer out-of-group platelet transfusions. *Immunohematology*. 2019;35(3):108-115.

4. Josephson CD, Mullis NC, Van Demark C, Hillyer CD. Significant numbers of apheresis-derived group O platelet units have “high-titer” anti-a/a,B: implications for transfusion policy. *Transfusion*. 2004;44(6):805-808.

5. Breiman A, Ruvën-Clouet N, Le Pendu J. Harnessing the natural anti-glycan immune response to limit the transmission of enveloped viruses such as SARS-CoV-2. *PLoS Pathog*. 2020;16(5):e1008556.

6. Guillan P, Clément M, Sébille V, et al. Inhibition of the interaction between the SARS-CoV spike protein and its cellular receptor by anti-histo-blood group antibodies. *Glycobiology*. 2008;18(12):1085-1093.

7. Jaimes JA, André NM, Chappie JS, Millet JK, Whittaker GR. Phylogenetic analysis and structural modeling of SARS-CoV-2 spike protein reveals an evolutionary distinct and proteolytically-sensitive activation loop. *J Mol Biol*. 2020;432:3309-3325.

8. COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. National Institutes of Health. Available at https://www.covid19treatmentguidelines.nih.gov/. Accessed July 23, 2021.

9. Mazzoni A, Maggi L, Capone M, et al. Cell-mediated and humoral adaptive immune responses to SARS-CoV-2 are lower in asymptomatic than symptomatic COVID-19 patients. *Eur J Immunol*. 2020;50(12):2013-2024.

10. Rieben R, Buchs JP, Fluckiger E, Nydegger UE. Antibodies to histo-blood group substances A and B: agglutination titers, Ig class, and IgG subclasses in healthy persons of different age categories. *Transfusion*. 1991;31(7):607-615.

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