

CLINICAL STUDIES

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Every one counts: A retrospective cohort study examining the safety of extending pre-transfusion compatibility testing from 72 hours to 7 days in hematology patients receiving red blood cell transfusions

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ABSTRACT

Aims: To investigate the safety of extending the pre-transfusion compatibility testing (PTCT) interval from 72 hours to 7 days in hematology patients receiving packed red blood cells (PRBC).

Methods: We undertook a retrospective cohort study over two years when the local protocol for PTCT in recently transfused hematology patients was changed from 72 hours to 7 days. All transfusions from 12 months prior and post this date were exported from eBlood and analyzed. The primary outcome was the incidence of transfusion reactions. Subgroup analysis was conducted for the chronically transfused patient group and patients with PTCT > 72 hours.

Results: A total of 2079 packs were analyzed from 227 patients. Only 37 transfusions that fulfilled the extended crossmatch. There were five (0.69%) transfusion reactions within the post-protocol change cohort and no transfusion reactions in the pre-protocol change cohort. All transfusion reactions occurred in the <72-hour subgroup of the post-protocol change cohort. At the time of reaction, there were no alloantibodies identified. No patients demonstrated new alloantibodies post-reaction.

Conclusion: This study found no evidence for an increased risk of transfusion reactions associated with increasing the PTCT interval from 72 hours to 7 days in a subset of chronically transfused hematology patients. Extending the PTCT interval could decrease costs, decrease patient infection risk, improve comfort, and conserve public health resources. Further evaluation in a larger cohort is necessary.

Keywords: Extended compatibility, Packed red blood cells, Pre-transfusion testing, Transfusion, Transfusion reactions

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Received: 01 June 2023
Accepted: 24 July 2023
Published: 11 October 2023

How to cite this article

Ambrose H, Hedrick A, de Leur M, Elton G, Evans (Bruce) A, Mullen R, Rowlings P, Ross B, Prasad R, Enjeti AK. Every one counts: A retrospective cohort study examining the safety of extending pre-transfusion compatibility testing from 72 hours to 7 days in hematology patients receiving red blood cell transfusions. Int J Blood Transfus Immunohematol 2023;13(2):8–16.

Article ID: 100079Z02HA2023

INTRODUCTION

Blood transfusion is a valuable and life-saving intervention and plays a vital role in managing many conditions, ranging from acute bleeding to chronic blood disorders. However, individuals exposed to red blood cell (RBC) allo-antigens through transfusion, pregnancy, or transplantation may produce antibodies against the allo-antigens expressed by RBC, leading to acute and delayed hemolytic transfusion reactions which can cause significant morbidity and be life-threatening. Pre-transfusion compatibility testing (PTCT), which includes ABO and Rh-typing and antibody screening, is practiced to ensure patient safety and minimize the risk of transfusion reactions. Guidelines in Australia and internationally have similar recommendations for PTCT testing in recently transfused patients. The Australian and New Zealand Society of Blood Transfusion (ANZSBT) states that a patient who has been transfused in the previous three months should have PTCT completed no more than 72 hours before the transfusion [1]. The British Committee for Standards in Haematology (BCSH) [2] and the American Association of Blood Banks (AABB) [3] also recommend a 72-hour limit for PTCT in this group. No guidelines define the reasoning or evidence base behind this recommendation and the BCSH recognizes “there is a dearth of published data regarding when red cell alloantibodies form and are first detectable following a stimulating event” [2]. Overall, there are no widely accepted time interval for repeat antibody identification [4] and these PTCT intervals are based upon expert opinion only.

The Hunter New England Local Health District (HNELHD) follows the Australian and New Zealand Society of Blood Transfusion (ANZSBT) PTCT guidelines [1] and patients who have been transfused or pregnant within the three months prior to their transfusion are required to undergo PTCT within 72 hours prior to PRBC administration. Patients who do not meet these criteria are required to undergo PTCT testing every seven days. The current standard of practice for PTCT presents several challenges. There is a significant burden on the healthcare professionals involved and the blood-banking laboratories in both time and equipment required. The time-sensitive nature of this testing can lead to delays in dispensing transfusion products, which potentially compromises patient outcomes. The need for repeated testing in chronically transfused individuals consumes valuable laboratory resources and contributes to increased healthcare costs. Hematology patients who account for majority of chronically transfused individuals are immunosuppressed, and this increases the risk of complications during the blood collection

process; especially, infection and iatrogenic blood loss [5].

These patients are further subject to many investigations and limiting venepuncture events may improve patient satisfaction and allow greater patient flexibility in timing venepuncture events.

In clinical practice, only ABO and RhD antigens are routinely matched [6], so exposure to foreign RBC antigens occurs frequently. The ANZSBT recommends phenotype matched blood for chronically transfused patients [1]. This is not the local policy at our institution for adults due to practicality and workload concerns, with the exception of sickle cell patients and those receiving anti-CD38 antibody therapy. Despite the inevitable exposure to foreign antigens with blood transfusion, historic studies indicate that the overall prevalence of allo-immunization is relatively small [7], at around 2–3%, with few patients developing alloantibodies despite the receipt of multiple RBC units [8–10]. While there is a small increase in allo-immunization related to the number of blood transfusions received [7, 8], the overall rate remains low. In hematology patients with malignant disorders, rates of allo-immunization are similar to other diseases requiring multiple blood transfusions [11, 12]. However, patients undergoing intensive chemotherapy have been found to form antibodies at a much lower rate than other patients [13, 14], likely secondary to immunosuppression. In contrast, patients with myelodysplastic syndrome [15, 16] and sickle cell disease [17, 18] have been shown to have higher rates of antibody formation.

Extending the protocol for recurrently transfused patients from 72 hours to 7 days offers several advantages. It provides an opportunity to streamline laboratory operations by reducing frequency of testing and optimizing resource allocation and improving cost effectiveness. Additionally, productivity in other areas may be improved with improved turn-around time for issuing blood products and performing other critical testing. It reduces the risk of complications associated with venepuncture and is likely to improve patient satisfaction. In hematology patients, the effect of dilutional anemia from recurrent blood tests is compounded by bone marrow failure, with increased benefit in this group by minimizing blood tests. Nevertheless, implementing an extended timeframe for pre-transfusion compatibility testing in hematology patients must consider the risk to patients of avoidable transfusion reactions. The ANZSBT suggests that specimen validity can be extended in certain situations to seven days such as in transfusion-dependent patients with no clinical antibodies [1], but this is not widespread practice. To evaluate the risk of increasing the time between PTCT, we conducted a retrospective review at our center of patients before and after the protocol was changed from a 72-hour to a 7-day time frame between PTCT in hematology patients.

MATERIALS AND METHODS

Aim

This project aims to investigate the safety of extending the PTCT interval from 72 hours to 7 days in hematology patients receiving PRBC. We hypothesize that the rates of acute and delayed transfusion reactions will be similar before and after the change in protocol.

Design

This study is a two-year retrospective cohort study that compares the incidence of transfusion reactions before and after the PTCT interval protocol change from 72 hours to 7 days. This project obtained low/negligible risk ethics approval for the retrospective review from the Hunter New England Research Ethics and Governance Office.

Prior to July 1, 2018, all patients in the Newcastle Calvary Mater (CMN) hospital receiving transfusion of blood products were required to have had PTCT within 72 hours of the products being released from the blood bank, unless specific permission pre-authorization from hematologist was obtained. The interval was extended in consultation with the Hematology Unit from 72 hours to 7 days after this date for all patients admitted under the Hematology team.

All transfusions from Wards C, D, and E within the CMN hospital between July 1, 2017 and June 30, 2019 were exported from our blood banking database “eBlood.”

This provided identification of patients, blood products, and the release time from eBlood for each pack number. Further data were sourced initially from digital sources such as AusLab, Clinical Applications Portal (CAP), and Digital Medical Records (DMR), where sufficient information was unable to be accessed via digital sources, paper notes for specific admissions were obtained.

Data were collated into a spreadsheet using Microsoft Excel and grouped by medical record number, date and time. Patient demographics, time from PTCT to transfusion, known antibodies, and transfusion reactions were collated. Hemoglobin level and patient diagnosis was also collated. All blood products other than PRBC were excluded. Further exclusion criteria were PTCT intervals outside testing protocol (such pre-authorized extension in the pre-change period), insufficient information to determine the presence or absence of a transfusion reaction, duplicate pack numbers, and patients without a hematological diagnosis, or non-hematological reason for admission (Figure 1).

The main safety outcomes were the number and proportion of acute and delayed transfusion reactions. Secondary outcomes included the presence or development of antibodies across the study and the time frame of antibody development.

Demographics and clinical features of transfused patients were summarized pre- and post-protocol change. Variables included age, gender, diagnosis, and admitting specialty as well as the number of transfusions per patient.

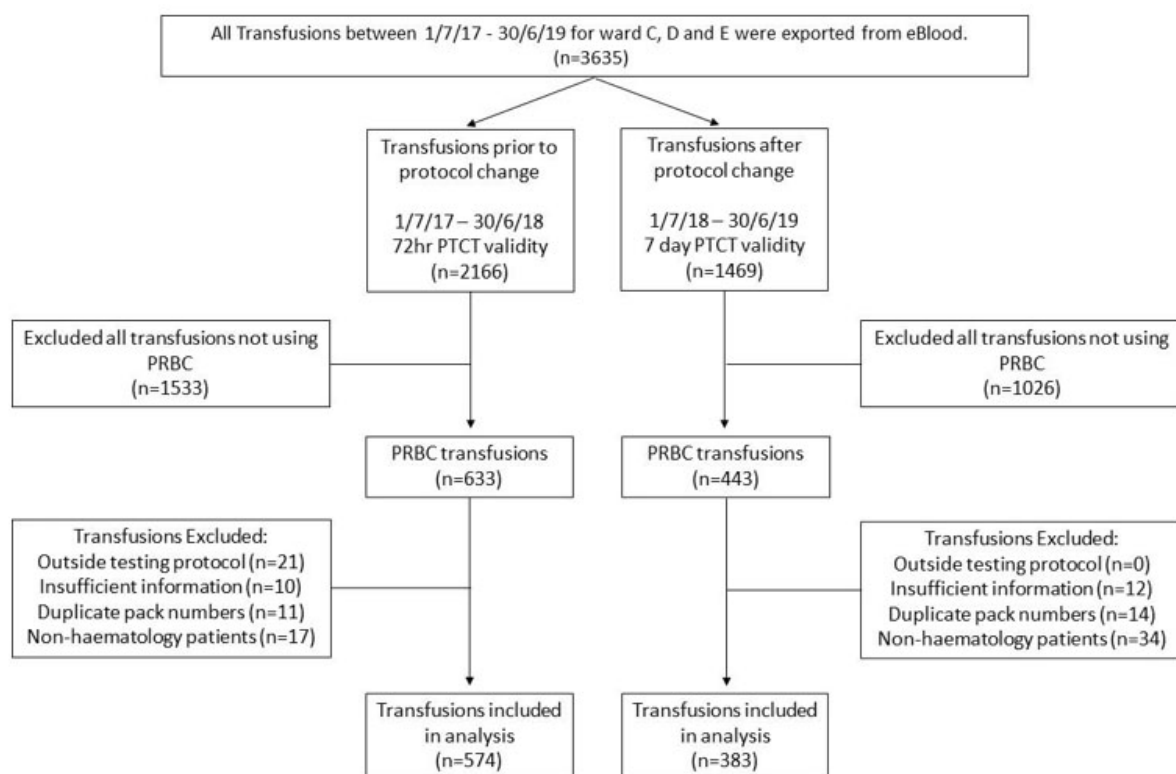


Figure 1: Study design.

Abbreviations: PTCT: Pre-transfusion compatibility testing; PRBC: Packed red blood cells.

The main analysis compared the rates of acute and delayed transfusion reactions between the pre- and post-protocol change cohorts. A descriptive analysis was performed by reporting the number and percentage of reactions as a proportion of the total number of transfusions. To assess the effectiveness of this protocol change on clinical practice, we calculated the PTCT interval in hours for each transfusion in order to calculate the proportion of PRBC's that were released from the blood bank beyond a 72-hour window.

A subgroup analysis examining chronically transfused patients was also conducted. For the purposes of this study, we have defined chronically transfused as more than six transfusions in a 12-month period.

RESULTS

There were 164 patients analyzed in the study (105 in the pre-protocol change period and 59 in the post-protocol change period). A total of 957 transfusions were analyzed with 574 in the pre-change period and 383 in the post-change period.

Demographic and clinical characteristics were similar in both groups. There was no significant difference in gender or age-range between the groups. The most frequent diagnosis was leukemia, representing 57.32% of all patients, followed by multiple myeloma (17.68%) and lymphoma (15.24%). Further detail regarding patient characteristics including diagnoses is presented in Appendices 1 and 2.

PTCT interval comparison within study

The mean PTCT interval in the pre-change period was 21.10 hours (± 17.5) compared to 23.51 hours (± 25.25) in the post-change period. In the post-change period, there were only 16 transfusions events (4.18%) where the PTCT interval was greater than 72 hours. These ranged from 74.0 to 150.2 hours.

Analysis of PTCT interval >72 hours

A subgroup analysis was conducted on the transfusion events which had a PTCT interval greater than 72 hours. There were 37 transfusion events in 19 patients that met this criteria. This included 21 transfusions that occurred within the pre-change period that were initially excluded

for having a PTCT interval greater than 72 hours. In this subgroup, the PTCT interval ranged from 72.59 to 212.18 hours with mean 109.52 hours (± 31.47). No acute or delayed transfusion reactions were associated with these transfusion events. One patient in this group developed an alloantibody which was not associated with a transfusion reaction.

Transfusion reactions

There were five (0.52%) transfusions across the study associated with an acute transfusion reaction. All five occurred in the post-change period and all had a PTCT interval within 72 hours. These reactions occurred in three patients, two of whom received two units in the same episode (Table 1). No patients had an acute hemolytic transfusion reaction. No delayed transfusion reactions were identified in either the pre- or post-change period.

Chronically transfused patients

A subgroup analysis was conducted with chronically transfused (n=44) and non-chronically transfused patients (n=120). Chronically transfused patients accounted for 26.83% (n=44) of the entire cohort and were associated with 67.50% (n=646) of all transfusion events. The most frequent diagnosis in these patients was AML (34%), MDS (22%), and MM (20%) with a similar age range to the study population. The average number of transfusions throughout the study in the chronically transfused subgroup was 14.68 (± 12.53) compared to 2.59 (± 1.26) in the non-chronically transfused. Chronically transfused patients were in the study for an average of 151.34 days compared to non-chronically transfused who were in the study for 23.10 days.

Of the 44 chronically transfused patients there were no delayed transfusion reactions identified. 4.55% (n=2) had acute transfusion reactions. Of the 646 transfusions in this subgroup, 0.46% (n=3) were associated with acute transfusion reactions.

A total of 22.73% (n=10) of the chronically transfused patients developed antibodies, compared to 5.00% (n=6) of the patients who were not chronically transfused. All patients who developed antibodies within the subgroup had leukemia, multiple myeloma, or sickle cell. The antibodies identified were Anti-E, Anti-C(w) and several antibodies that could not be identified at time of analysis.

Table 1: Transfusion reactions experienced during study period

Patient demographics	PTCT Interval (hours)	Units given	Known antibodies	Development of new antibodies	Transfusion reaction description
57 M	20.87	2	No	No	Rigors without fever
68 M	23.82	1	No	No	Paresthesia and vomiting
69 M	24.28	2	No	No	Fever

Abbreviation: PTCT: Pre-transfusion compatibility testing.

DISCUSSION

Recurrently transfused patients are unavoidably exposed to new RBC antigens from regular blood transfusions and are at risk of development of new antibodies. Pre-transfusion compatibility testing is required to detect the development of new, clinically significant antibodies. Hematology patients, particularly in patients undergoing intensive chemotherapy, often require multiple transfusions a week. These patients further have a high burden of blood test monitoring and laboratory resource allocation.

The ability to safely increase the interval between PTCT could lead to significant cost savings and reduced resource utilization. Our study investigated if changing the protocol to an interval of seven days from 72 hours between PTCT would lead to any clinically significant increase in transfusion reactions. While there were more transfusion reactions in the post-change group, none of these were for patients tested outside 72 hours and none were related to a hemolytic transfusion reaction, which would be the main risk of this change. We do not consider these transfusion reactions to be related to the protocol change. We postulate that documentation and reporting may have been more comprehensive in reaction to the changed protocol.

Despite the protocol change to seven days, the PTCT interval for almost all patients remained within 72 hours. The difference between PTCT interval means in the two periods was small (2.41 hours). We hypothesize that doctors may have been habitual in their practice and thus did not deviate from what is familiar to them, i.e., ordering PTCT every 72 hours despite the change in policy. There also may not have been adequate education to the prescribing doctors, who are usually junior doctors who frequently rotate. As the protocol was only established in selected wards and patient groups, doctors who were rotating between teams may have reverted to standard practice to avoid confusion and delays. Patients may also have had the PTCT done in response to a hemoglobin level assessed to require transfusion or prior to a planned transfusion, thus the transfusion would be given shortly after testing. The lack of difference in PTCT interval between our two study groups makes it difficult to draw definite conclusions about variances between groups being related to the protocol change.

We had a subset of 37 patients who had PTCT performed at an interval of greater than 72 hours. We performed a subgroup analysis to assess for evidence of harm in these patients. There was no evidence of acute or delayed transfusion reactions in this group. One patient developed an alloantibody which was not associated with transfusion reaction. This provides proof of concept for extending compatibility testing to seven days in the hematology patients on chronic transfusions, although numbers are too small to form robust recommendations. It should be noted that 21 of these patients were in the pre-change group. This may be as the transfusion was

requested prior to 72 hours but blood was not released until after 72 hours. Further, at our site, a hematologist can verbally extend a crossmatch if they feel it is clinically appropriate.

The retrospective nature of our study has limitations. As the data were collected retrospectively from medical software data, transfusion events that would be relevant to the study may have been missed. There was a significantly smaller number of patients in the post-change group, which is unexplained and may represent missed events. The medical software provided the date and time on which the blood was released from the laboratory. On occasion, blood is released the day before transfusion occurs, such as in patients undergoing planned transfusion. This would alter the timeframe between PTCT and transfusion and hence may have a small effect on the mean time between these two events. It may also contribute to the group of patients in the pre-change group who had testing performed greater than 72 hours pre-transfusion as previously discussed.

Another potential source of missed data is reporting of transfusion reactions, which may have been not included if they were not reported to the blood bank or recorded in the notes. For example, fevers are very common in the hematology patient population and some fevers during transfusion may not have been considered a transfusion reaction by the medical team, while some may be reported as such. This patient group is also commonly 'anaemic' with abnormal biochemistry, so delayed transfusion reactions may not have been recognized. For example, if the patient was recovering post-chemotherapy but did not require transfusion, they would not have had PTCT to identify antibodies.

The generalizability of this study is limited as the patient demographic is exclusively those with a hematological condition. In our cohort, the majority of these patients had malignant conditions, so the applicability of these findings to chronically transfused hematology patients such as hemoglobinopathy patients is uncertain. This study was performed in a single institution with small patient numbers. Further, the patient cohort who had a PTCT interval greater than 72 hours was smaller than expected. As hemolytic transfusion reactions and alloantibody formation are rare events, it is unlikely we would observe small but significant differences between the two groups in our study.

There is minimal literature investigating extending PTCT in different patient groups. Goss et al. [4] explored antibody development following an extension to 14 days in a general inpatient cohort with known antibodies. They concluded that, while the risk of new clinically significant antibody formation was small (0.47%), the clinical risk of potential hemolytic transfusion reaction outweighed the advantages, and they did not change their local policy. They did not report if there was any clinical consequences to the change. Dinh et al. [19] reviewed the incidence and time frame of new antibody formation in patients with existing RBC antibodies over a 9-year period. They found

that emergence of new antibodies was common, with a median time interval to detection of new antibody of 13 days. By day 3, 18% of new antibodies were detected. They did not make recommendations regarding optimal PTCT interval. These studies suggest that patients with known antibodies are at risk of new antibody development and a 72-hour policy for PTCT in this group is appropriate.

As the current literature focuses on patients with known antibodies, the findings are likely to be less relevant to a hematology patient group. The risk of developing subsequent antibodies once a patient has formed an antibody is greatly increased [13, 18, 20]. In hematology patients with malignant disorders, a retrospective analysis of over 1000 patients found that once a patient had formed an antibody, the probability of forming additional antibodies increased threefold [13]. In our study, we looked at all hematology patients regardless of known antibody status, so we would expect a lower rate of new antibody detection than reported in the above literature. Further, many of our patients are undergoing intensive chemotherapy and these patients are known to have a lower rate of antibody formation

[13, 14]. One of the incentives to undertake this study was minimizing blood tests in hematology inpatients to reduce costs and dilutional anemia, particularly in those undergoing intensive chemotherapy such as induction and consolidation chemotherapy for acute leukemia and autologous stem cell transplant patients. This specific patient group may warrant further study as they represent a significant proportion of recurrent PTCT in our institution and are likely to be lower risk of antibody formation and thus associated harms.

CONCLUSION

In conclusion, this study did not show increased hemolytic transfusion reactions associated with increasing the PTCT interval from 72 hours to 7 days. However, small patient numbers and only minor differences in interval of PTCT in both groups limit the strength of our results and does not provide definitive evidence for safety. Further studies are still needed before a widespread policy change can be recommended.

Appendix 1: Patient characteristics and transfusions in the PRE /POST phase of the study

	PRE (n=105)		POST (n=59)		Totals (n=164)	
	n	%	n	%	n	%
Gender						
M	59	56.19	29	49.15	88	53.66
F	46	43.81	30	50.85	76	46.34
Age						
10–19	0	0.00	1	1.69	1	0.61
20–29	0	0.00	1	1.69	1	0.61
30–39	1	0.95	0	0.00	1	0.61
40–49	2	1.90	3	5.08	5	3.05
50–59	18	17.14	7	11.86	25	15.24
60–69	31	29.52	17	28.81	48	29.27
70–79	26	24.76	17	28.81	43	26.22
80–89	20	19.05	12	20.34	32	19.51
90–99	7	6.67	1	1.69	8	4.88
Diagnosis*						
Leukemia	62	59.05	32	54.24	94	57.32
Lymphoma	20	19.05	5	8.47	25	15.24
Multiple myeloma	16	15.24	13	22.03	29	17.68
Hemolytic Anemia	2	1.90	7	11.86	9	5.49
Other	5	4.76	5	8.47	10	6.10
Unknown	1	0.95	0	0.00	1	0.61
Admitting specialty**						
Hematology	92	87.62	59	100.00	151	92.07
Palliative care	11	10.48	0	0.00	11	6.71

Appendix 1: (Continued)

	PRE (n=105)		POST (n=59)		Totals (n=164)	
	n	%	n	%	n	%
Oncology	8	7.62	0	0.00	8	4.88
Medicine	1	0.95	0	0.00	1	0.61
Surgery	1	0.95	0	0.00	1	0.61
PRBC Transfusions during study (Mean, SD)						
	5.47	SD 8.69	6.49	SD 8.04	5.84	SD 8.45

*Note: patients may have more than one active diagnosis.

**Note: within the pre-transfusion 7 patients had joint hematology/oncology admissions, 1 patient had joint hematology/palliative care admission.

Appendix 2: Disease categories used for purpose of analysis (alphabetical by category)

Abbreviation	Full name	Category
ALL	Acute lymphocytic leukemia	Leukemia
AML	Acute myeloid leukemia	Leukemia
	Anaemia	Other
AILT	Angioimmunoblastic T-cell lymphoma	Lymphoma
AA	Aplastic anemia	Other
AIHA	Autoimmune hemolytic anemia	Hemolytic anemia
CAAH	Cerebral amyloid angiopathy-related hemorrhage	Other
CLL	Chronic lymphocytic leukemia	Leukemia
CML	Chronic myelogenous leukemia	Leukemia
CMML	Chronic myelomonocytic leukemia	Leukemia
	Chronic myeloproliferative disorder	Leukemia
CHAD	Cold haemagglutinin disease	Other
CRC	Colorectal cancer	Cancer–other
CTCL	Cutaneous T-cell lymphoma	Lymphoma
DLBCL	diffuse large B-cell lymphoma	Lymphoma
FL	Follicular lymphoma	Lymphoma
	G6PD deficiency	Other
HLH	Hemophagocytic lymphohistiocytosis	Other
	Leukemia unspecified	Leukemia
	Metastatic esophageal cancer	Cancer–other
MM	Multiple myeloma	Multiple myeloma
MDS	Myelodysplastic syndrome	Leukemia
	Myelofibrosis	Leukemia
NHL	Non-Hodgkin's lymphoma	Lymphoma
	Sickle cell disease	Other
SBCL	Small B-cell lymphoma	Lymphoma
	Unknown	Unknown
VWD	von Willebrand disease	Other

Note: not all diseases had an abbreviation and where the full nomenclature was used it is listed as such.

REFERENCES

1. Australian and New Zealand Society of Blood Transfusion. Guidelines for transfusion and immunohaematology laboratory practice. Revised 1ed. 2020. Accessed from ANZSBT Guidelines - ANZSBT.
2. British Committee for Standards in Haematology; Milkins C, Berryman J, et al. Guidelines for pre-transfusion compatibility procedures in blood transfusion laboratories. British Committee for Standards in Haematology. Transfus Med 2013;23(1):3–35.
3. Fung MK, Grossman BJ, Hillyer CD, Westhoff CM. Technical Manual. 20ed. Maryland: AABB; 2020.

4. Goss C, Aveilla ST, Garbaini J, et al. Can the interval between antibody identifications be increased for alloimmunized patients? *Transfusion* 2016;56(2):334–8.
5. Buowari OY. Complications of venepuncture. *Advances in Bioscience and Biotechnology* 2013;4(1A):126–8.
6. National Blood Authority. Patient Blood Management Guidelines: Module 3 Medical. 2012. [Available at: <https://www.blood.gov.au/pbm-module-3>]
7. Hoeltge GA, Domen RE, Rybicki LA, Schaffer PA. Multiple red cell transfusions and alloimmunization. Experience with 6996 antibodies detected in a total of 159,262 patients from 1985 to 1993. *Arch Pathol Lab Med* 1995;119(1):42–5.
8. Zalpuri S, Zwaginga JJ, le Cessie S, Elshuis J, Schonewille H, van der Bom JG. Red-blood-cell alloimmunization and number of red-blood-cell transfusions. *Vox Sang* 2012;102(2):144–9.
9. Schonewille H, van de Watering LM, Loomans DS, Brand A. Red blood cell alloantibodies after transfusion: Factors influencing incidence and specificity. *Transfusion* 2006;46(2):250–6.
10. Higgins JM, Sloan SR. Stochastic modeling of human RBC alloimmunization: Evidence for a distinct population of immunologic responders. *Blood* 2008;112(6):2546–53.
11. Karafin MS, Westlake M, Hauser RG, et al. Risk factors for red blood cell alloimmunization in the Recipient Epidemiology and Donor Evaluation Study (REDS-III) database. *Br J Haematol* 2018;181(5):672–81.
12. Asare M, Hendrickson JE, Tormey CA. Determination of red blood cell alloimmunization rates in transfused patients with hematologic and oncologic malignancies. *Blood* 2016;128(22):1463.
13. Schonewille H, Haak HL, van Zijl AM. Alloimmunization after blood transfusion in patients with hematologic and oncologic diseases. *Transfusion* 1999;39(7):763–71.
14. Evers D, Zwaginga JJ, Tijmens J, et al. Treatments for hematologic malignancies in contrast to those for solid cancers are associated with reduced red cell alloimmunization. *Haematologica* 2017;102(1):52–9.
15. SanzC, NomdedeuM, BelkaidM, MartinezI, Nomdedeu B, Pereira A. Red blood cell alloimmunization in transfused patients with myelodysplastic syndrome or chronic myelomonocytic leukemia. *Transfusion* 2013;53(4):710–5.
16. Zalpuri S, Zwaginga JJ, van der Bom JG. Risk Factors for Alloimmunisation after red blood Cell Transfusions (R-FACT): A case cohort study. *BMJ Open* 2012;2(3):e001150.
17. Aygun B, Padmanabhan S, Paley C, Chandrasekaran V. Clinical significance of RBC alloantibodies and autoantibodies in sickle cell patients who received transfusions. *Transfusion* 2002;42(1):37–43.
18. Rosse WF, Gallagher D, Kinney TR, et al. Transfusion and alloimmunization in sickle cell disease. The Cooperative Study of Sickle Cell Disease. *Blood* 1990;76(7):1431–7.
19. Dinh A, Eliason K, Dzik WS. Time interval between antibody investigations among patients who demonstrate serial red cell antibody formation. *Transfusion* 2019;59(2):738–43.
20. Sood R, Makroo RN, Riana V, Rosamma NL. Detection of alloimmunization to ensure safer transfusion practice. *Asian J Transfus Sci* 2013;7(2):135–9.

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Guarantor of Submission

The corresponding author is the guarantor of submission.

Source of Support

None.

Consent Statement

Written informed consent was obtained from the patient

for publication of this article.

Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.

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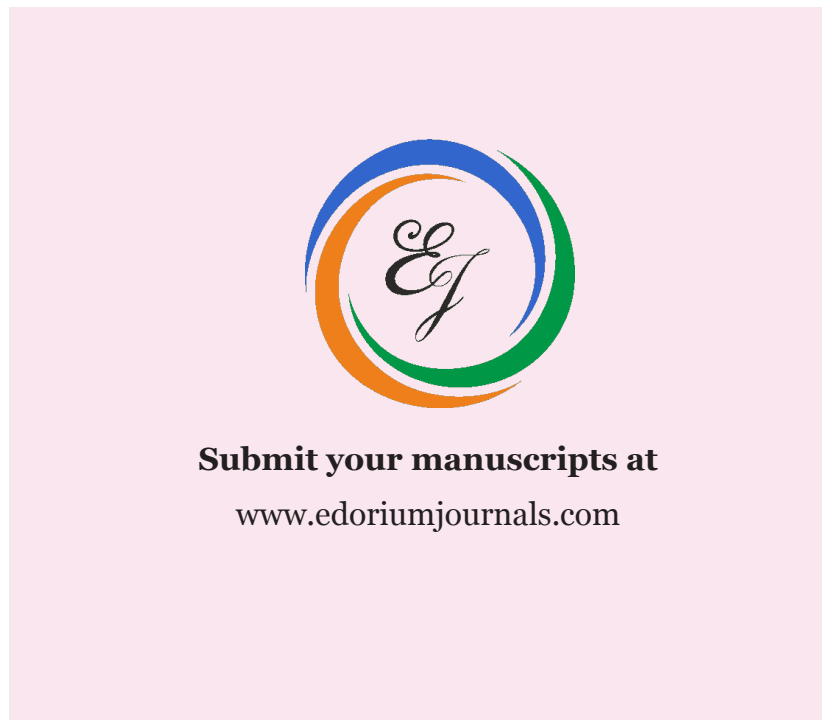
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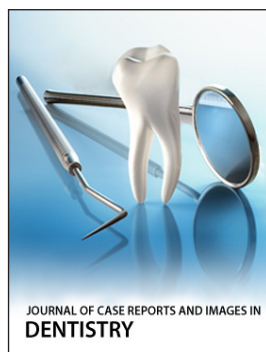
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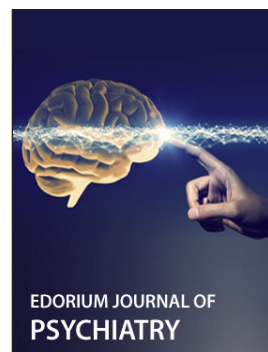
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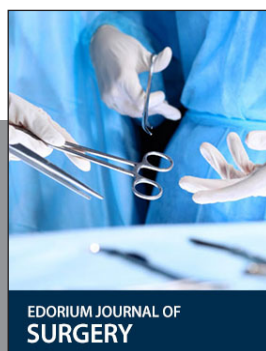
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