

World Journal of *Transplantation*

World J Transplant 2023 June 18; 13(4): 107-207



REVIEW

- 107 Islet transplantation-immunological challenges and current perspectives

Kabakchieva P, Assyov Y, Gerasoudis S, Vasilev G, Peshevska-Sekulovska M, Sekulovski M, Lazova S, Miteva DG, Gulinac M, Tomov L, Velikova T

MINIREVIEWS

- 122 Intracranial pressure monitoring in the perioperative period of patients with acute liver failure undergoing orthotopic liver transplantation

Mendoza Vasquez LE, Payne S, Zamper R

- 129 Women's health issues in solid organ transplantation: Breast and gynecologic cancers in the post-transplant population

Jones-Pauley M, Kodali S, Basra T, Victor DW

ORIGINAL ARTICLE**Retrospective Cohort Study**

- 138 Pre-Lung transplant reflux testing demonstrates high prevalence of gastroesophageal reflux in cystic fibrosis and reduces chronic rejection risk

Lo WK, Flanagan R, Sharma N, Goldberg HJ, Chan WW

Retrospective Study

- 147 Mortality assessment for pancreas transplants in the United States over the decade 2008-2018

Jarmi T, Brennan E, Clendenon J, Spaulding AC

- 157 Is peri-transplant blood transfusion associated with worse transplant outcomes? A retrospective study

Bukhari MA, Alhomayani FK, Al Eid HS, Al-Malki NK, Alotaibi ME, Hussein MA, Habibullah ZN

- 169 Delayed referral for liver transplant evaluation worsens outcomes in chronic liver disease patients requiring inpatient transplant evaluation

Cooper KM, Colletta A, Hathaway NJ, Liu D, Gonzalez D, Talat A, Barry C, Krishnarao A, Mehta S, Movahedi B, Martins PN, Devuni D

Observational Study

- 183 Haemodynamic management in brain death donors: Influence of aetiology of brain death

Lazzeri C, Bonizzoli M, Batacchi S, Guetti C, Vessella W, Valletta A, Ottaviano A, Peris A

- 190 Randomized intervention to assess the effectiveness of an educational video on organ donation intent among Hispanics in the New York metropolitan area

Pekmezaris R, Cigaran E, Patel V, Clement D, Sardo Molmenti CL, Molmenti E

CASE REPORT

- 201** Efficacy and safety of local candida immunotherapy in recalcitrant warts in pediatric kidney transplantation: A case report

Acharya R, Bush R, Johns F, Upadhyay K

ABOUT COVER

Peer Reviewer of *World Journal of Transplantation*, Mendy Hatibie Oley, MD, PhD, Plastic Reconstructive and Aesthetic Surgery Division, General Surgery Department, Faculty of Medicine, Sam Ratulangi University, Kandou General Hospital, North Sulawesi 95115, Indonesia. mendy.hatibie@unsrat.ac.id

AIMS AND SCOPE

The primary aim of *World Journal of Transplantation* (WJT, *World J Transplant*) is to provide scholars and readers from various fields of transplantation with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJT mainly publishes articles reporting research results obtained in the field of transplantation and covering a wide range of topics including bone transplantation, brain tissue transplantation, corneal transplantation, descemet stripping endothelial keratoplasty, fetal tissue transplantation, heart transplantation, kidney transplantation, liver transplantation, lung transplantation, pancreas transplantation, skin transplantation, etc.

INDEXING/ABSTRACTING

The WJT is now abstracted and indexed in PubMed, PubMed Central, Scopus, Reference Citation Analysis, China National Knowledge Infrastructure, China Science and Technology Journal Database, and Superstar Journals Database.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: Yan-Liang Zhang; **Production Department Director:** Xu Guo; **Editorial Office Director:** Jia-Ping Yan.

NAME OF JOURNAL

World Journal of Transplantation

ISSN

ISSN 2220-3230 (online)

LAUNCH DATE

December 24, 2011

FREQUENCY

Quarterly

EDITORS-IN-CHIEF

Maurizio Salvadori, Sami Akbulut, Vassilios Papalois, Atul C Mehta

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/2220-3230/editorialboard.htm>

PUBLICATION DATE

June 18, 2023

COPYRIGHT

© 2023 Baishideng Publishing Group Inc

INSTRUCTIONS TO AUTHORS

<https://www.wjgnet.com/bpg/gerinfo/204>

GUIDELINES FOR ETHICS DOCUMENTS

<https://www.wjgnet.com/bpg/gerinfo/287>

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH

<https://www.wjgnet.com/bpg/gerinfo/240>

PUBLICATION ETHICS

<https://www.wjgnet.com/bpg/gerinfo/288>

PUBLICATION MISCONDUCT

<https://www.wjgnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/gerinfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>



Retrospective Study

Is peri-transplant blood transfusion associated with worse transplant outcomes? A retrospective study

Muhammad A Bukhari, Faisal K Alhomayani, Hala S Al Eid, Najla K Al-Malki, Mutlaq Eidah Alotaibi, Mohamed A Hussein, Zainab N Habibullah

Specialty type: Transplantation

Provenance and peer review:

Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0

Grade B (Very good): B

Grade C (Good): C

Grade D (Fair): 0

Grade E (Poor): 0

P-Reviewer: Sunder T, India;
Zhang ZX, Canada

Received: March 17, 2023

Peer-review started: March 17, 2023

First decision: April 13, 2023

Revised: April 18, 2023

Accepted: May 4, 2023

Article in press: May 4, 2023

Published online: June 18, 2023



Muhammad A Bukhari, Zainab N Habibullah, Multi-organ Transplantation Center, King Abdullah Medical City, Makkah 29123, Saudi Arabia

Faisal K Alhomayani, Department of Internal Medicine, College of Medicine, Taif University, Taif 23611, Saudi Arabia

Hala S Al Eid, Department of Pharmacy, Alhada Armed Forces Hospital, Taif 29123, Saudi Arabia

Najla K Al-Malki, Mutlaq Eidah Alotaibi, Mohamed A Hussein, Department of Nephrology and Transplantation, Alhada Armed Forces Hospital, Taif 29123, Saudi Arabia

Corresponding author: Muhammad A Bukhari, MD, Attending Doctor, Multi-organ Transplantation Center, King Abdullah Medical City, Third Ring Road, Makkah 29123, Saudi Arabia. bukhary5354@hotmail.com

Abstract

BACKGROUND

Blood transfusion is common during the peri-transplantation period. The incidence of immunological reactions to blood transfusion after kidney transplantation and their consequences on graft outcomes have not been extensively studied.

AIM

To examine the risk of graft rejection and loss in patients who received blood transfusion in the immediate peri-transplantation period.

METHODS

We conducted a single-center retrospective cohort study of 105 kidney recipients, among them 54 patients received leukodepleted blood transfusion at our center between January 2017 and March 2020.

RESULTS

This study included 105 kidney recipients, of which 80% kidneys were from living-related donors, 14% from living-unrelated donors, and 6% from deceased donors. Living-related donors were mostly first-degree relatives (74.5%), while the rest were second-degree relatives. The patients were divided into transfusion (

$n = 54$) and non-transfusion ($n = 51$) groups. The average hemoglobin level at which blood transfusion was commenced was 7.4 ± 0.9 mg/dL. There were no differences between the groups in terms of rejection rates, graft loss, or death. During the study period, there was no significant difference in creatinine level progression between the two groups. Delayed graft function was higher in the transfusion group; however, this finding was not statistically significant. A high number of transfused packed red blood cells was significantly associated with increased creatinine levels at the end of the study.

CONCLUSION

Leukodepleted blood transfusion was not associated with a higher risk of rejection, graft loss, or death in kidney transplant recipients.

Key Words: Transplantation; Transfusion; Rejection; Graft survival

©The Author(s) 2023. Published by Baishideng Publishing Group Inc. All rights reserved.

Core Tip: Blood transfusion in patient undergoing kidney transplantation has long been avoided for the fear for the potential risk of recipient's immunization and potential rejection. This study addresses the risks of peri-transplantation outcomes of blood transfusion.

Citation: Bukhari MA, Alhomayani FK, Al Eid HS, Al-Malki NK, Alotaibi ME, Hussein MA, Habibullah ZN. Is peri-transplant blood transfusion associated with worse transplant outcomes? A retrospective study. *World J Transplant* 2023; 13(4): 157-168

URL: <https://www.wjgnet.com/2220-3230/full/v13/i4/157.htm>

DOI: <https://dx.doi.org/10.5500/wjt.v13.i4.157>

INTRODUCTION

Anemia is common in the early post-kidney transplant period[1-3]. The causes of this anemia are multiple and may include blood loss during the surgical operation, erythropoietin deficiency, iron deficiency as a result of previous end-stage renal disease along with delayed graft function (DGF), and adverse reactions to immunosuppressive agents. In some cases, blood transfusion is an essential life-saving practice. Blood transfusion is widely used in the early post-transplantation period following surgery[2].

However, blood transfusion is not without risks. Exposure to non-self human leukocyte antigens (HLAs) can lead to the formation of anti-HLA antibodies or allosensitization[2-4]. Donor-specific antibodies (DSAs) can develop in kidney recipients after receiving a blood transfusion[2]. HLA sensitization may have negative clinical impacts, including, an increased risk of rejection, and graft loss. Despite these risks, clinical guidelines do not provide specific recommendations for blood transfusion during the perioperative period[4]. This uncertainty could be due to the assumption that post-kidney transplant patients receive immunosuppressive agents, which could reduce the possibility of allosensitization[4,5].

The incidence of immunological reactions to blood transfusion after kidney transplantation and their consequences on graft outcomes have not been extensively studied. Our study aimed to examine the risk of graft rejection and graft loss in patients who receive a blood transfusion in the immediate post-transplantation period and those who were on immunosuppressive therapy.

MATERIALS AND METHODS

Study design

This was a single-center retrospective cohort study of kidney transplantation recipients who received either deceased or living-donor kidneys at Al-Hada Armed Forces Hospital, Taif, Saudi Arabia between January 2017 and March 2020. No other solid-organ transplantation or spontaneous kidney-pancreas transplantation was performed at our center during the study period.

We surveyed kidney transplant recipients who received a blood transfusion in the peri-transplant period (one week prior to transplantation and one month after the surgery). The control group included patients who underwent kidney transplantation during the same period but did not require blood transfusion. At our institution, only leukodepleted blood products are administered to kidney

transplant candidates and kidney transplant recipients; this applied to the kidney recipients enrolled in this study. Data were obtained from the patients' electronic files in the hospital. However, blood product type (leuko-depleted *vs* non-leuko-depleted) was confirmed from the blood bank records. We excluded recipients who were < 18 years of age, those with previous organ transplantation, those who required desensitization prior to transplantation, those on a calcineurin inhibitors (CNIs) avoidance protocol, and those who required permanent withdrawal of one or more of their immunosuppressive therapies.

During the study period, Immunosuppression protocol in our hospital consisted of induction therapy with either antithymocyte globulin (cumulative dose of 4-6 mg/kg) or basiliximab (two intravenous doses of 20 mg on post-op days 0 and 4) and maintenance immunosuppression with tacrolimus (targeting a tacrolimus level of 8-10 ng/mL in the first three months then 4-6 ng/mL), an antimetabolite (mycophenolate mofetil 1 gm twice daily) and prednisone (tapered to a maintenance dose of 5 mg daily).

Outcomes

Primary outcomes were biopsy-proven rejection, DGF, graft loss within the first 18 mo post-transplantation and death of any cause during the same time period. Post-transplant kidney biopsy and DSA identification were not performed routinely in this cohort but rather on a for-cause basis. Secondary outcomes were changes in creatinine levels during the study period, infections, and urological complications. Both cellular and antibody-mediated rejections were accounted for. Graft loss was defined as the need for another renal replacement therapy. Identification of DSAs was performed using a Luminex single-bead antigen solid-phase assay with a cutoff of 1000 mean fluorescence intensity.

Statistical analysis

All analyses were performed using SPSS version 26 (IBM, Armonk, NY, United States). Continuous variables are denoted as mean $\pm$ SD for normally distributed variables or median (interquartile range) for non-normally distributed variables. The Shapiro-Wilk test was used to assess the normality of continuous variables to guide the selection of a parametric or nonparametric test for the comparison of variables. The variables were compared using the Welch's *t*-test, Student's *t*-test, and Mann-Whitney-U test. Categorical variables were presented as frequencies and percentages and were compared using the χ^2 or Fisher's exact tests as appropriate. All independent variables from the univariate linear regression analysis with $P < 0.05$ were entered into a multivariate linear regression model to examine their association with creatinine changes. All reported *P* values were two-sided and *P* values < 0.05 were considered to indicate a statistical significance.

RESULTS

A total of 124 kidney transplant surgeries were performed at Al-Hada Armed Forces Hospital during the study period (between January 2017 and March 2020). Nineteen patients were excluded they were < 18 years (three recipients), had a previous kidney transplant (five recipients), required desensitization prior to surgery (nine recipients), had ABO incompatibility (1 recipient), and lacked sufficient information (one recipient). The final analysis included data from 105 recipients. The patients were divided into two groups: Blood transfusion (54 recipients) and non-transfusion (51 recipients) groups (Table 1). The transplant recipients in our cohort had a higher prevalence of male sex (77 recipients: 73%), and most kidney transplantations were from living-related (84 recipients, 80%) than living-unrelated (15 recipients, 14%) donors or from deceased-donor kidney transplantation (six recipients; 6%). The median number of HLA mismatches was three in both groups. Basiliximab was the most commonly used agent for induction (62 recipients; 59%). All the recipients in our cohort received a tacrolimus-based regimen with an average tacrolimus level during the study time of 7 ng/mL (6-8 ng/mL).

Approximately 85 (69%) recipients in our cohort had anemia [hemoglobin (Hb) of < 12 g/dL]; however, only 57 (54%) recipients received blood transfusions. Among the 57 recipients who received blood transfusion 31 recipients (54%) received only 1 unit, 15 (26%) received two units, 7 (12%) received three units, 3 (5%) received four units, and only 1 (2%) received nine units of blood. The average Hb at the time of transplantation was significantly higher in the non-transfusion group (11.2 mg/dL *vs* 9.8 mg/dL, $P < 0.001$) (Table 2). In the transfusion group, the average Hb level at which blood transfusion was initiated was 7.4 ± 0.9 mg/dL. There were no significant differences in infectious and non-infectious complications between the two groups (Table 3). Additionally, there was no significant difference in graft loss or all-cause death between the two groups (Table 4, Figures 1 and 2). There was no significant difference in creatinine level progression between the two groups during the study period (Figure 3).

Rejection occurred in five recipients in our cohort; three had cellular rejection and two had antibody-mediated rejections (Table 5). All rejection episodes were biopsy-proven, and three occurred in the transfusion group; nevertheless, there was no significant difference in the rate of rejection between the

Table 1 Baseline characteristics of both the transfusion and non-transfusion groups, *n* (%)

	Total cohort, 105	Non-transfusion, 51 (48.6%)	Transfusion, 54 (51.4%)	<i>P</i> value
Age (mean $\pm$ SD)	39.7 $\pm$ 14.5	40.5 $\pm$ 13.9	38.9 $\pm$ 15.1	0.583
Gender				
Female	28 (26.7)	10 (19.6)	18 (33.3)	0.127
Male	77 (73.3)	41 (80.4)	36 (66.7)	
Type of transplantation				
LRKTx	84 (80)	43 (84.3)	41 (75.9)	0.566
LURKTx	15 (14.3)	6 (11.8)	9 (16.7)	
DDKTx	6 (5.7)	2 (3.9)	4 (7.4)	
HLA mismatch	3 (1-4)	3 (0-4)	3 (2-4)	0.152
Cause of ESRD				
Diabetes	18 (17.1)	7 (13.7)	11 (20.4)	0.331
GN	26 (24.8)	11 (21.6)	15 (27.8)	
Hypertension	18 (17.1)	12 (23.5)	6 (11.1)	
PCKD	1 (1)	1 (2)	0 (0)	
Urological	7 (6.7)	2 (3.9)	5 (9.3)	
Other	35 (33.3)	18 (35.3)	17 (31.5)	
Donor's age	33 $\pm$ 8.6	32.4 $\pm$ 8.4	33.5 $\pm$ 8.8	0.562
Induction therapy				
ATG	42 (40)	21 (41.2)	21 (38.9)	1
Basiliximab	62 (59)	30 (58.8)	32 (59.3)	
No induction	1 (1)	0 (0)	1 (1.9)	
Maintenance immunosuppression				
CNI used tacrolimus	105 (100)	51 (100)	54 (100)	
Average CNI level	7 (6-8)	7 (6-8)	7 (6-8)	0.743
Antimetabolite used (MMF)	105 (100)	51 (100)	54 (100)	

LRKTx: Living-related kidney transplantation; LURKTx: Living non-related kidney transplantation; DDKTx: Deceased-donor kidney transplantation; HLA: Human leucocyte antigen; ESRD: End-stage renal disease; GN: Glomerulonephritis; PCKD: Polycystic kidney disease; ATG: Antithymocyte globulin; CNI: Calcineurin inhibitor; MMF: Mycophenolate mofetil.

Table 2 Blood transfusion information

	Total, 105	Non-transfused, 51 (48.6%)	Transfused, 54 (51.4%)	<i>P</i> value
Hemoglobin at transplantation	10.5 $\pm$ 1.7	11.2 $\pm$ 1.6	9.8 $\pm$ 1.6	< 0.001
Hemoglobin at blood transfusion			7.4 $\pm$ 0.9	
Hemoglobin after transfusion			9.2 $\pm$ 1.1	
Number of blood transfusion units given	1 (0-1.5)		1 (0-1.5)	

two groups. Additionally, during the study period, there was an improvement in serum creatinine levels in all the patients with rejection in both groups. None of the recipients with allograft rejection lost their grafts during the study period. However, one of the recipients died due to coronavirus disease 2019 pneumonia with a functioning graft. There were no statistically significant differences in age, sex, type of transplantation, HLA mismatch, induction therapy, or CNI levels between patients who developed rejection and those who did not.

Table 3 Infectious and non-infectious complications among the two groups, *n* (%)

	Total, 105	Non-transfusion, 51 (48.6%)	Transfusion, 54 (51.4%)	<i>P</i> value
No. of infections	0 (0-1)	1 (0-1)	0 (0-1.25)	0.554
Types of infections				
none	55 (52.4)	25 (49)	30 (55.6)	0.745
UTI	30 (28.6)	14 (27.5)	16 (29.6)	0.832
Pneumonia	1 (1)	1 (2)	0 (0)	0.486
TB	1 (1)	0 (0)	1 (1.9)	1
BK	7 (6.7)	5 (9.8)	2 (3.7)	0.261
Bactremia	4 (3.8)	1 (2)	3 (5.6)	0.618
Epididymo-orchitis	2 (1.9)	1 (2)	1 (1.9)	1
Gastroenteritis	2 (1.9)	2 (3.9)	0 (0)	0.234
Herpes zoster	1 (1)	0 (0)	1 (1.9)	1
Infected AVF	1 (1)	1 (2)	0 (0)	0.486
Perianal abscess	1 (1)	1 (2)	0 (0)	0.486
COVID-19	9 (8.6)	6 (11.8)	3 (5.6)	0.311
URTI	2 (1.9)	1 (2)	1 (1.9)	1
CMV	12 (11.4)	6 (11.8)	6 (11.1)	1
Urological complications				
None	95 (90.5)	49 (96.1)	46 (85.2)	0.484
Allograft artery stenosis	1 (1)	0 (0)	1 (1.9)	
Collection	3 (2.9)	1 (2)	2 (3.7)	
Lymphocele	1 (1)	0 (0)	1 (1.9)	
Obstructive uropathy	1 (1)	0 (0)	1 (1.9)	
Perinephric collection and ureteric stricture	2 (1.9)	0 (0)	2 (3.7)	
Unrogenic bladder	1 (1)	0 (0)	1 (1.9)	
Urinary leak	1 (1)	1 (2)	0 (0)	
Urological complications				
No	95 (90.5)	49 (96.1)	46 (85.2)	0.094
Yes	10 (9.5)	2 (3.9)	8 (14.8)	
CNI withdrawal	1 (1)	0 (0)	1 (1.9)	1
Duration from Tx	3 d			
MMF withdrawal	1 (1)	0 (0)	1 (1.9)	1
Duration from Tx	3 d			
Steroids withdrawal	0 (0)	0 (0)	0 (0)	

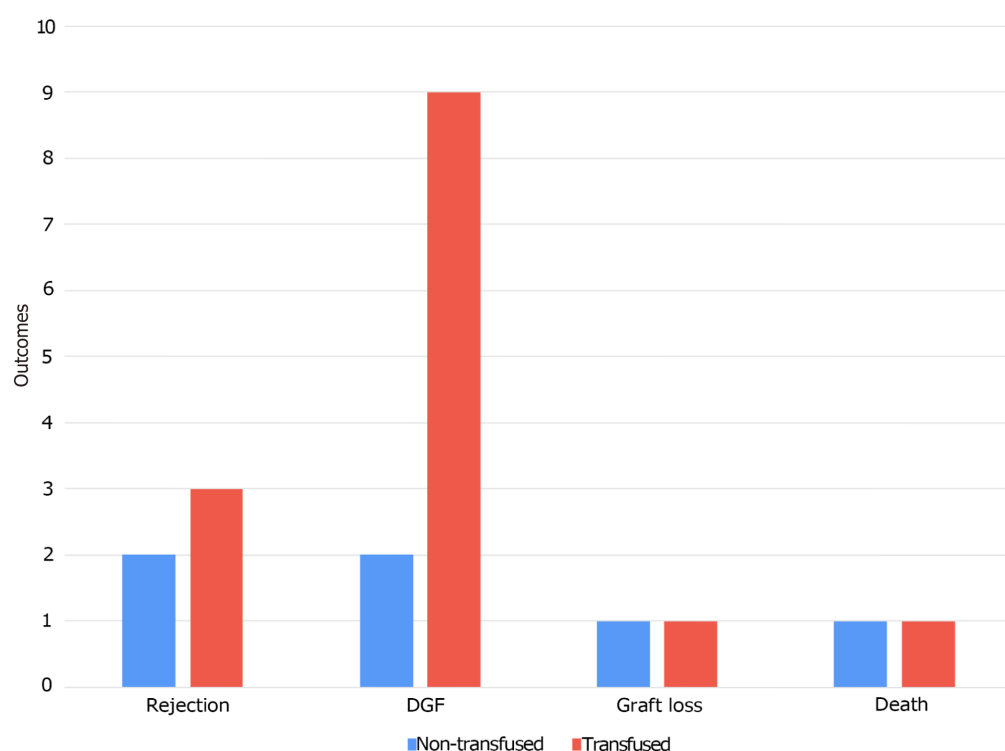
UTI: Urinary tract infection; TB: Tuberculosis; AVF: Arterio-venous fistula; COVID-19: Coronavirus disease 2019; URTI: Upper respiratory tract infection; CMV: Cytomegalovirus; CNI: Calcineurin inhibitor; MMF: Mycophenolate mofetil.

The incidence of DGF was higher in the transfusion group; however, this difference was not statistically significant. In contrast, analysis of the predictors of DGF using multivariate logistic regression showed that age [adjusted odds ratio, 1.06, 95% confidence interval (CI): 1.012-1.111; $P = 0.014$] and blood transfusion (adjusted odds ratio 5.649, 95% CI: 1.106-28.848; $P = 0.037$) were significant independent risk factors for DGF. There were no significant differences in graft loss or all-cause death mortality between the two groups.

Table 4 Comparison in Outcomes of transplantation between the two groups, *n* (%)

	Total, 105	Non-transfusion, 51 (48.6%)	Transfusion, 54 (51.4%)	<i>P</i> value
Rejection	5 (4.8)	2 (3.9)	3 (5.6)	1
Rejection type				
ABMR	2 (40)	1 (50)	1 (33.3)	1
Cellular	3 (60)	1 (50)	2 (66.7)	
Graft loss	4 (3.8)	1 (2)	3 (5.6)	0.618
Death	2 (1.9)	1 (2)	1 (1.9)	1
DGF	11 (10.5)	2 (3.9)	9 (16.7)	0.053
Serum creatinine				
At discharge	141 ± 124.1	123 ± 56.7	158 ± 163	0.770
6 mo	108 ± 40.7	107.1 ± 28	108.9 ± 50.4	0.825
12 mo	109.1 ± 51.3	101.9 ± 22.9	117 ± 69.8	0.182
18 mo	126 ± 168.7	106.2 ± 26.5	147.4 ± 241.5	0.735
Creatinine difference: At 18 mo-at discharge		-19.4 ± 61.5	12.3 ± 253.8	0.439

ABMR: Antibody-mediated rejection; DGF: Delayed-graft function.



DOI: 10.5500/wjt.v13.i4.157 Copyright ©The Author(s) 2023.

Figure 1 Comparison in the outcomes between the blood transfusion vs non-blood transfusion groups. DGF: Delayed graft function.

We conducted a multiple linear regression analysis to examine the association between creatinine change (the difference between creatinine at the end of the study and baseline creatinine) as a dependent variable and eligible study variables as independent variables. We found that a higher number of transfused packed red blood cells was significantly associated with increased creatinine levels at the end of the study ($B = 20.14$; $SE = 6.99$; $P = 0.004$), whereas a higher creatinine level at discharge was associated with milder creatinine increase over the study period ($B = -0.79$; $SE = 0.12$; $P < 0.001$) (Table 6).

Table 5 Characteristics of rejection developers vs non-rejection developers among the study cohort, n (%)

	Non-rejection, 100	Rejection, 5	P value
Age (mean $\pm$ SD)	36.5 (28.25-51.75)	36 (21-46.5)	0.383
Gender			
Female	28 (28)	0 (0)	0.321
Male	72 (72)	5 (100)	
Type of transplantation			
LRKTx	81 (81)	3 (60)	0.172
LURKTx	13 (13)	2 (40)	
DDKTx	6 (6)	0 (0)	
HLA mismatch	3 (1-4)	3 (1-4)	0.729
Cause of ESRD			
Diabetes	18 (18)	0 (0)	0.199
GN	23 (23)	3 (60)	
Hypertension	18 (18)	0 (0)	
PCKD	1 (1)	0 (0)	
Urological	6 (6)	1 (20)	
Other	34 (34)	1 (20)	
Donor's age	32 (26-39)	28 (25.5-43.5)	0.981
Induction therapy			
ATG	41 (41)	1 (20)	0.438
Basiliximab	58 (58)	4 (80)	
No induction	1 (1)	0 (0)	
Average CNI level	7 (6-8)	8 (6.5-9)	0.311
Hb at transplantation	10.65 (9.025-11.3)	10.7 (9.05-12.45)	0.792
Hb at blood transfusion	7.4 (6.8-8)	7.8 ¹	0.138
Hb after transfusion	8.9 (8.4-10)	10 ¹	0.382
No of blood transfusion unites given	1 (0-1)	1 (0-3)	0.491
Serum creatinine			
At discharge	111 (83.25-142.75)	151 (113.5-222.5)	0.096
6 mo	102.5 (80.5-123)	120 (80-156)	0.420
12 mo	99.5 (81.75-119.25)	124.5 (92.5-140.75)	0.201
18 mo	105 (84.25-119)	107 (72-)	0.894
Death	1 (1)	1 (20)	0.093
DGF	9 (9)	2 (40)	0.084
No. of infections	0 (0-1)	1 (0-2)	0.651
Types of infections			
None	53 (53)	2 (40)	0.188
UTI	30 (28.6)	29 (29)	1
Pneumonia	1 (1)	1 (1)	1
TB	1 (1)	1 (1)	1
BK	7 (6.7)	7 (7)	1
Bactremia	4 (3.8)	4 (4)	1

Epideridymo-orchitis	2 (1.9)	2 (2)	1
Gastroenteritis	2 (1.9)	1 (1)	0.093
Herpes zoster	1 (1)	1 (1)	1
Infected AVF	1 (1)	1 (1)	1
Perianal abscess	1 (1)	1 (1)	1
COVID-19	9 (8.6)	8 (8)	0.367
URTI	2 (1.9)	1 (1)	0.093
CMV	11 (11)	1 (20)	0.462
Urological complications			
None	90 (90)	5 (100)	1
Allograft artery stenosis	1 (1)	0 (0)	
Collection	3 (3)	0 (0)	
Lymphocele	1 (1)	0 (0)	
Obstructive uropathy	1 (1)	0 (0)	
Perinephric collection and ureteric stricture	2 (2)	0 (0)	
Unrogenic bladder	1 (1)	0 (0)	
Urinary leak	1 (1)	0 (0)	
Urological complications			
No	90 (90)	5 (100)	1
Yes	10 (10)	0 (0)	

¹Interquartile range could not be calculated due to small number of patients for this outcome.

COVID-19: Coronavirus disease 2019; LKTX: Living-related kidney transplantation; LURKTx: Living non-related kidney transplantation; DDKTX: Deceased-donor kidney transplantation; HLA: Human leucocyte antigen; ESRD: End-stage renal disease; GN: Glomerulonephritis; PCKD: polycystic kidney disease; ATG: Antithymocyte globulin; CNL: Calcineurin inhibitor; MMF: Mycophenolate mofetil; Hb: Hemoglobin; DGF: Delayed-graft function; UTI: Urinary tract infection; TB: Tuberculosis; AVF: Arterio-venous fistula; URTI: Upper respiratory tract infection; CMV: Cytomegalovirus.

Table 6 Multiple linear regression analysis of the association between creatinine change and eligible study variables

	B	SE	95%CI	P value
(Intercept)	70.23	18.72	33.54 to 106.92	< 0.001
Male <i>vs</i> female	-1.74	18.59	-38.17 to 34.69	0.925
No. of PRBCs	20.14	6.99	6.45 to 33.84	0.004
Creatinine at discharge	-0.79	0.12	-1.03 to -0.54	< 0.001

CI: Confidence interval; PRBC: Packed red blood cell.

DISCUSSION

Anemia is a common condition during the peri-transplantation period. The rate of anemia during this period varies significantly. In a retrospective cohort study, Vanrenterghem *et al*[1] reported an anemia rate of 38% in a transplant population[1]. However, in a recent prospective study, 64% of the study cohort had anemia that requiring blood transfusion in the first month after transplantation[2]. The transfusion rate post-transplantation has been repeatedly reported to be between 37%-75%[4,6-8]. This high prevalence of transfusion has also been observed in pediatric populations. For instance, Richards *et al*[7] reported that the prevalence of transfusion was approximately 50% with a higher prevalence in younger children[7]. In our study, the anemia rate was toward the higher end of the above mentioned range at 69% however, only 54% of our cohort required blood transfusion.

Anemia carries significant risk in kidney transplant recipients. A drop of Hb level > 30% of its pre-transplant level was reported to be associated with higher all-cause graft failure and longer length of hospital stay, with a greater risk in those who required blood transfusion of > 3 units and those with

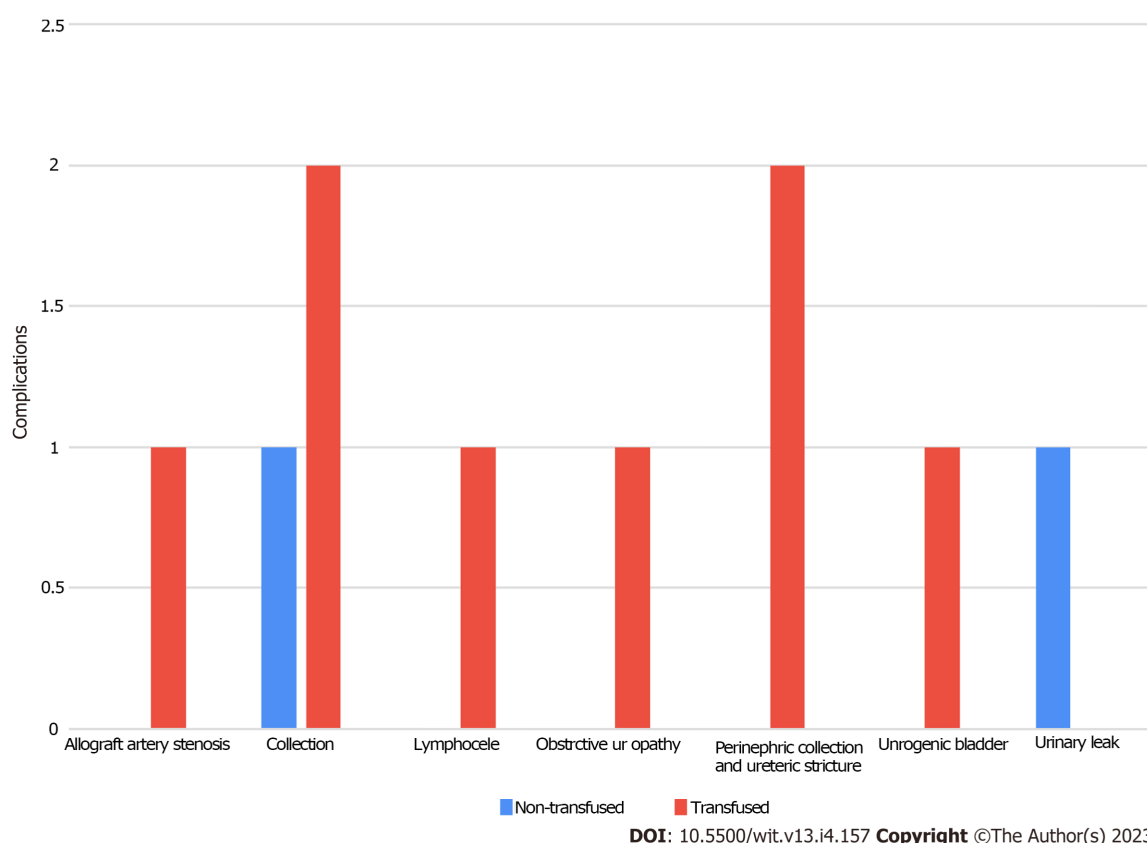


Figure 2 Progression of the mean creatinine between the blood transfusion vs non-blood transfusion groups.

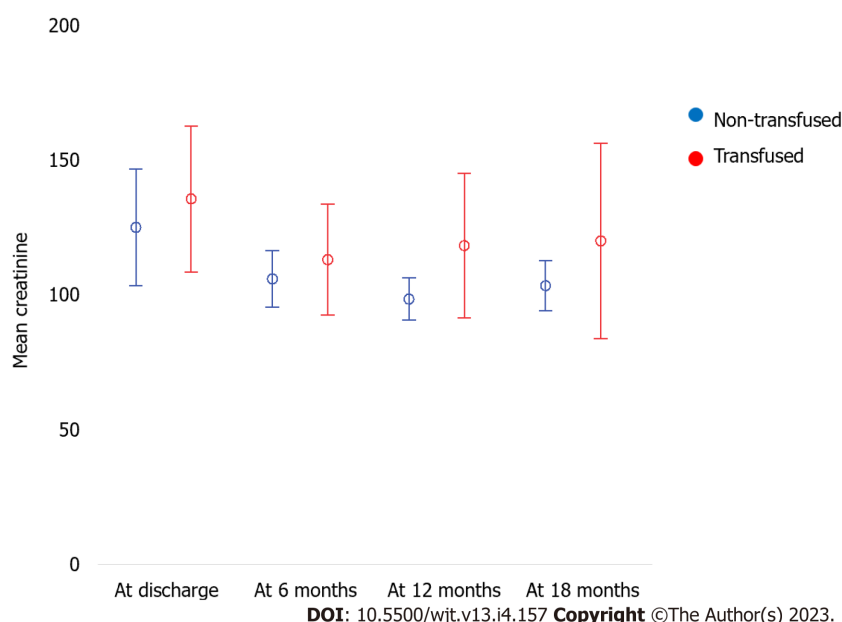


Figure 3 Progression of the mean creatinine between the blood transfusion vs non-blood transfusion groups. Total patients in non-transplantation group are 51. Total patients in transplantation group are 54 patients.

longer cold ischemia time[9]. However, the effect of peri-transplantation blood transfusion on graft outcome have not been well established. For instance, in a study by Daloul *et al*[4], blood transfusion was not associated with a greater risk of worse graft outcomes[4]; however, Massicotte-Azarniouch *et al* [6] revealed that blood transfusion is associated with a greater risk of graft loss[6]. This is also supported by the findings from a recent study that included more than 1000 recipients, which showed that early blood transfusion post-transplantation didn't lead to de novo DSAs formation[10]. Our study did not find any association between blood transfusion and graft loss or mortality. The link between blood

transfusion and graft or patient loss might be a confounding factor because patients with advanced allograft dysfunction are commonly anemic. Similarly, sick patients with multiple comorbidities are usually anemic and may require blood transfusions.

HLA molecules in the blood products are known to cause HLA allosensitization for blood transfusion recipients[11-13]. Various strategies have been attempted to avoid HLA allosensitization after blood transfusion, including leuko-reduced (leuko-depleted) blood products[11,14], HLA-selected blood products[15], and autologous blood transfusion[16]. However, the protective effects of these strategies are not well established[11,14-19]. In our study, we decided to account only for leuko-depleted blood products because this is a widely used technique in our blood bank.

The effect of blood transfusion on DSA formation and antibody-mediated rejection are not well understood. Few studies have examined the development of de-novo HLA antibodies after blood transfusions in transplant populations. While some studies found that *de-novo* HLA antibodies and DSAs have a negative impact on the transplant[2,20], other studies have doubted the significance of HLA antibody development in the setting of immunosuppression therapy[3,8,11]. For instance, In Ferrandiz *et al*[2] reported that antibody-mediated rejection occurred in 6% of kidney transplant recipients who required blood transfusion post-surgery compared with 1.4% in a non-transfusion group ($P = 0.04$)[2]. In contrast, in a study by Jalalonmuhali *et al*[3] involving 699 patients, there was no differences in the development of HLA antibodies or de-novo HLA-DSA and rejection between the transfusion and none transfusion groups[3]. Similarly in our study, the rejection rate in the transfusion group was approximately 5%, with no difference between the two groups.

Multiple factors are associated with an increased risk of poor transplant outcomes after blood transfusion. In a previous prospective observational study, worse transplantation outcomes were linked to the number of transfusion episodes (pre and post-transplantation), regardless of the total number of transfusion units[20]. In another study, poor transplantation outcomes were linked to the number of transfusion units (> 3 units)[9]. In our study, creatinine levels tended to increase toward the end of the follow-up period in the transfusion group, but this finding was not statistically significant.

It is noteworthy that maintenance immunosuppression therapy in studies that found a significant increase in rejection risk after transfusion was cyclosporine-based[2,20] while studies in which the maintenance immunosuppression regimen was tacrolimus-based showed no significant increase in rejection rate between transfusion and non-transfusion groups[3,8]. Our study is consistent with this observation as rejection rate was not significantly different between the two groups in our tacrolimus-based study cohort.

Although blood transfusion after kidney transplantation did not have an impact on patient survival, a cross-sectional study of 1198 liver transplant recipients showed a significant increase in mortality rate in patients who received a large number of blood transfusion units. Average blood transfusion units in expired patients was 5.92 ± 5.91 compared to 3.74 ± 4.23 in alive patients (95% CI: 1.47–2.88)[21].

In this study, there was a tendency toward higher DGF rates in the transfusion group. Although this finding was not statistically significant, it was in line with that of MacIsaac *et al*[9], in which the rate of DGF in transplant patients was up to 26%[9]. Similarly, in a retrospective cohort study on 1258 kidney transplant recipients who were followed for a median of 1405 d, DGF was as high as 41% in a transfusion group *vs* 15% in a non-transfusion group ($P < 0.0001$)[6]. In a study by Fidler *et al*[20], DGF was associated with a higher risk of combined patient and graft loss at a hazard ratio of 2.5 (1.5–4.5) on univariate analysis; However, this difference disappeared on multivariate analysis. It's difficult to determine whether DGF is a cause, or a result of blood transfusion based on the available literature.

This study has limitations. This was a single-center retrospective cohort study. The lack of routine DSA and allograft biopsy restricted the inclusion of clinically insignificant DSAs and non-apparent rejections. Moreover, our cohort was predominantly males, which limits the generalizability of our findings.

CONCLUSION

Leukodepleted blood transfusion in the peri-transplantation period was not associated with a higher risk of rejection, graft loss, or patient loss. Further investigations are needed to address the link between peri-transplantation blood transfusions, DGF and DSA formation.

ARTICLE HIGHLIGHTS

Research background

Blood transfusion is common during the peri-transplantation period. The incidence of immunological reactions to blood transfusion after kidney transplantation and their consequences on graft outcomes have not been extensively studied.

Research motivation

Blood transfusion during the peri-transplantation period is very common and its safety need to be studied.

Research objectives

To examine the risk of graft rejection and loss in patients who received blood transfusion in the immediate peri-transplantation period.

Research methods

A retrospective cohort study of 105 kidney recipients who received leukodepleted blood transfusions at our center between January 2017 and March 2020.

Research results

Of 105 kidney recipients were divided into transfusion ($n = 54$) and non-transfusion ($n = 51$) groups. There were no differences between the two groups in terms of rejection rates, graft loss, or death. There was no significant difference in creatinine level progression between the two groups. A high number of transfused packed red blood cells was significantly associated with increased creatinine levels at the end of the study.

Research conclusions

Leukodepleted blood transfusion was not associated with a higher risk of rejection, graft loss, or death in kidney transplant recipients.

Research perspectives

Leukodepleted blood transfusion in the peri-transplantation period is likely safe.

FOOTNOTES

Author contributions: All the co-authors contributed in data collection, writing, editing, literature review and designing the study.

Institutional review board statement: Approved by the hospital's IRB at AL-Hada Armed Forces Hospital, No. REC 2023-719.

Informed consent statement: Signed informed consent wasn't required for this manuscript.

Conflict-of-interest statement: All the authors report no relevant conflicts of interest for this article.

Data sharing statement: Consent was not obtained but the presented data are anonymized and risk of identification is low.

Open-Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <https://creativecommons.org/licenses/by-nc/4.0/>

Country/Territory of origin: Saudi Arabia

ORCID number: Muhammad A Bukhari 0000-0002-1706-6757; Faisal K Alhomayani 0000-0001-9169-7007.

S-Editor: Fan JR

L-Editor: A

P-Editor: Ji MX

REFERENCES

- 1 **Vanrenterghem Y**, Ponticelli C, Morales JM, Abramowicz D, Baboolal K, Eklund B, Kliem V, Legendre C, Morais Sarmiento AL, Vincenti F. Prevalence and management of anemia in renal transplant recipients: a European survey. *Am J Transplant* 2003; **3**: 835-845 [PMID: 12814475 DOI: 10.1034/j.1600-6143.2003.00133.x]
- 2 **Ferrandiz I**, Congy-Jolivet N, Del Bello A, Debiol B, Trébern-Launay K, Esposito L, Milongo D, Dörr G, Rostaing L, Kamar N. Impact of Early Blood Transfusion After Kidney Transplantation on the Incidence of Donor-Specific Anti-HLA

- Antibodies. *Am J Transplant* 2016; **16**: 2661-2669 [PMID: [26998676](#) DOI: [10.1111/ajt.13795](#)]
- 3 **Jalalonmuhali M**, Carroll RP, Tsiopelas E, Clayton P, Coates PT. Development of de novo HLA donor specific antibodies (HLA-DSA), HLA antibodies (HLA-Ab) and allograft rejection post blood transfusion in kidney transplant recipients. *Hum Immunol* 2020; **81**: 323-329 [PMID: [32327243](#) DOI: [10.1016/j.humimm.2020.04.002](#)]
- 4 **Daloul R**, Braga JR, Diez A, Logan A, Pesavento T. Early Posttransplant Blood Transfusion and Risk for Worse Graft Outcomes. *Kidney Int Rep* 2021; **6**: 986-994 [PMID: [33912748](#) DOI: [10.1016/j.ekir.2020.12.038](#)]
- 5 **Scornik JC**, Meier-Kriesche HU. Blood transfusions in organ transplant patients: mechanisms of sensitization and implications for prevention. *Am J Transplant* 2011; **11**: 1785-1791 [PMID: [21883910](#) DOI: [10.1111/j.1600-6143.2011.03705.x](#)]
- 6 **Massicotte-Azarniouch D**, Sood MM, Fergusson DA, Chassé M, Tinmouth A, Knoll GA. Blood Transfusion and Adverse Graft-related Events in Kidney Transplant Patients. *Kidney Int Rep* 2021; **6**: 1041-1049 [PMID: [33912754](#) DOI: [10.1016/j.ekir.2021.01.015](#)]
- 7 **Richards KM**, Spicer RA, Craig E, Kennedy SE. Prevalence and predictors of blood transfusion after pediatric kidney transplantation. *Pediatr Nephrol* 2018; **33**: 2177-2184 [PMID: [30006835](#) DOI: [10.1007/s00467-018-4017-0](#)]
- 8 **Bynum JP**, Zachary A, Ness PM, Luo X, Bagnasco S, King KE, Segev DL, Orandi BJ, Warren DS, Fuller A, Ciappi A, Montgomery R, Tobian AAR. Transfusion of leukoreduced blood products and risk of antibody-mediated rejection of renal allografts. *Transfusion* 2018; **58**: 1951-1957 [PMID: [30171817](#) DOI: [10.1111/trf.14800](#)]
- 9 **MacIsaac S**, Ramanakumar AV, Saw C, Naessens V, Saberi N, Cantarovitch M, Baran D, Paraskevas S, Tchervenkov J, Chaudhury P, Sandal S. Relative decrease in hemoglobin and outcomes in patients undergoing kidney transplantation surgery: A retrospective cohort study. *Am J Surg* 2021; **222**: 825-831 [PMID: [33707078](#) DOI: [10.1016/j.amjsurg.2021.03.002](#)]
- 10 **Jouve T**, Noble J, Naciri-Bennani H, Dard C, Masson D, Fiard G, Malvezzi P, Rostaing L. Early Blood Transfusion After Kidney Transplantation Does Not Lead to dnDSA Development: The BloodIm Study. *Front Immunol* 2022; **13**: 852079 [PMID: [35432350](#) DOI: [10.3389/fimmu.2022.852079](#)]
- 11 **Scornik JC**, Ireland JE, Howard RJ, Fennell RS 3rd, Pfaff WW. Role of regular and leukocyte-free blood transfusions in the generation of broad sensitization. *Transplantation* 1984; **38**: 594-598 [PMID: [6390819](#) DOI: [10.1097/00007890-198412000-00009](#)]
- 12 **Terasaki PI**, Cai J. Humoral theory of transplantation: further evidence. *Curr Opin Immunol* 2005; **17**: 541-545 [PMID: [16098722](#) DOI: [10.1016/j.coi.2005.07.018](#)]
- 13 **Vaidya S**. Synthesis of new and memory HLA antibodies from acute and chronic rejections versus pregnancies and blood transfusions. *Transplant Proc* 2005; **37**: 648-649 [PMID: [15848488](#) DOI: [10.1016/j.transproceed.2005.01.067](#)]
- 14 **Karpinski M**, Pochinco D, Dembinski I, Laidlaw W, Zacharias J, Nickerson P. Leukocyte reduction of red blood cell transfusions does not decrease allosensitization rates in potential kidney transplant candidates. *J Am Soc Nephrol* 2004; **15**: 818-824 [PMID: [14978185](#) DOI: [10.1097/01.asn.0000115399.80913.b1](#)]
- 15 **Magge BA**, Martin J, Cole MP, Morris KG, Courtney AE. Effects of HLA-matched blood transfusion for patients awaiting renal transplantation. *Transplantation* 2012; **94**: 1111-1116 [PMID: [23111496](#) DOI: [10.1097/TP.0b013e318271d776](#)]
- 16 **Sasaki H**, Chikaraishi T, Furuhashi S, Tsutsumi H, Miyano S, Nakazawa R, Nakano T, Kudo H, Kitajima K, Takahashi T, Satoh Y, Kimura K. Autologous blood transfusion for kidney transplant recipients. *Transplant Proc* 2008; **40**: 1371-1372 [PMID: [18589108](#) DOI: [10.1016/j.transproceed.2008.03.136](#)]
- 17 **van de Watering L**, Hermans J, Witvliet M, Versteegh M, Brand A. HLA and RBC immunization after filtered and buffy coat-depleted blood transfusion in cardiac surgery: a randomized controlled trial. *Transfusion* 2003; **43**: 765-771 [PMID: [12757528](#) DOI: [10.1046/j.1537-2995.2003.00390.x](#)]
- 18 **Ohto H**, Nomizu T, Kuroda F, Hoshi T, Rokkaku Y. HLA alloimmunization of surgical patients by transfusion with bedside leukoreduced blood components. *Fukushima J Med Sci* 2003; **49**: 45-54 [PMID: [14603951](#) DOI: [10.5387/fms.49.45](#)]
- 19 **Sanfilippo FP**, Bollinger RR, MacQueen JM, Brooks BJ, Koepke JA. A randomized study comparing leukocyte-depleted versus packed red cell transfusions in prospective cadaver renal allograft recipients. *Transfusion* 1985; **25**: 116-119 [PMID: [3885483](#) DOI: [10.1046/j.1537-2995.1985.25285169200.x](#)]
- 20 **Fidler S**, Swaminathan R, Lim W, Ferrari P, Witt C, Christiansen FT, D'Orsogna LJ, Irish AB. Peri-operative third party red blood cell transfusion in renal transplantation and the risk of antibody-mediated rejection and graft loss. *Transpl Immunol* 2013; **29**: 22-27 [PMID: [24090807](#) DOI: [10.1016/j.trim.2013.09.008](#)]
- 21 **Kasraian L**, Nikeghbalian S, Karimi MH. Blood Product Transfusion in Liver Transplantation and its Impact on Short-term Survival. *Int J Organ Transplant Med* 2018; **9**: 105-111 [PMID: [30487957](#)]



Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

Telephone: +1-925-3991568

E-mail: bpgoffice@wjgnet.com

Help Desk: <https://www.f6publishing.com/helpdesk>

<https://www.wjgnet.com>

