Original Article

Association Between Fluid Administration and Hemoglobin Changes During Perioperative Kidney Transplantation

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ABSTRACT

Background: Chronic Kidney Disease (CKD) is a leading cause of mortality worldwide, particularly in Indonesia, so it requires effective treatment options like kidney transplantation. Optimal fluid therapy during the perioperative period is important for stable hemodynamics and graft function. However, guidelines for fluid administration remain lacking.

Objective: This study investigates the association between fluid therapy and changes in hemoglobin levels in patients undergoing renal transplantation.

Methods: A retrospective observational cross-sectional study was conducted at RSUP Prof. DR. I.G.N.G. Ngoerah Denpasar from January 2016 to August 2024. Data were collected from medical records of patients who underwent kidney transplantation, excluding those with incomplete data. Key variables included daily fluid intake and hemoglobin levels. The coefficient of variance was calculated and continued with correlation analyses utilizing Pearson correlation and linear regression to assess relationships between fluid administration and hemoglobin changes.

Results: Of 28 patients, 10 met inclusion criteria, consisting of 4 males and 6 females. Analysis showed a strong correlation between the variance of fluid intake and the variance of hemoglobin levels ($R = 0.86$; $R^2 = 0.74$; $P < 0.001$).

Conclusion: This study demonstrates a significant relationship between post-operative variance of fluid administration and variance of hemoglobin levels following kidney transplantation. It may have an impact on the management of post-operative reduction in hemoglobin levels.

Keywords: Fluid, Hemoglobin Changes, Kidney Transplant, Association, Perioperative.

Introduction

Chronic Kidney Disease (CKD) has become one of the leading causes of death worldwide, especially in Indonesia. Hypertension and Diabetes Mellitus have been identified as the main contributing factors. End-Stage Renal Disease (ESRD), or late stage of CKD, requires renal replacement therapy, such as hemodialysis, peritoneal dialysis, or kidney transplantation. Kidney transplantation is one of the most effective therapies, as it can restore the excretory, secretory, and endocrine functions of the kidney nearly perfectly. The kidney donor may come from a living donor or a cadaveric donor.[1,2]

Administering optimal fluid therapy to achieve stable hemodynamics during kidney transplant surgery is important. Proper fluid

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administration can increase microvascular flow, give a better oxygen distribution, and prevent cellular hypoxia, leading to immediate graft function. It also helps avoid hypovolemia during the perioperative period. However, there is no standardized guideline specifying how much fluid should be given during the perioperative period after a kidney transplant.[3,4]

The old theory suggested that providing fluids to fulfill the kidney's need for 25% of cardiac output would optimize graft function. However, this approach increases the risk of hypervolemia and pulmonary edema. Several studies have compared various parameters, such as Central Venous Pressure (CVP) and Mean Arterial Pressure (MAP), to assess fluid adequacy, but no definitive numbers have been established, making fluid administration more individualized. Retrospective studies on kidney transplant patients indicated that intraoperative CVP values of less than 8 mmHg, even reaching less than 6 mmHg, were significant predictors of delayed graft function or primary non-function. A retrospective study of 1,966 patients showed that CVP above 11 mmHg was a predictor of chronic graft dysfunction, while fluid administration of more than 2,500 mL was an independent risk factor for graft failure. Other prospective and retrospective studies suggested that aggressive fluid administration during graft ischemia, increasing CVP from 5 mmHg to 15 mmHg, was associated with better graft function, reduced use of vasopressors and diuretics, and less post-operative tissue edema.[3–5]

Fluid administration may also trigger a relative, but not absolute, condition known as dilutional anemia, characterized by decreased hemoglobin concentration. Iatrogenic hemodilution is often seen in critically ill patients receiving colloid therapy as part of perioperative treatment goals, where there is no increase in cardiac output after intravenous fluid loading. In septic shock patients receiving fluid therapy to reach a target CVP of 8–12 mmHg, MAP of 65–70, urine output of >0.5 mL/kg/hr, and oxygen saturation >70% within the first 6 hours, a complete blood count often reveals a 30% reduction in hematocrit within 3 hours post-resuscitation. The administration of 500 ml IV fluid can reduce hemoglobin level by 1 gr/dL.[5,6] Iatrogenic hemodilution can increase the risk of unnecessary blood transfusions without significant bleeding. In a randomized controlled trial (RCT) study comparing patients receiving goal-directed therapy (GDT) with a control population, it was found that the GDT group had twice the rate of blood transfusions. It was concluded that many patients in the GDT group experienced a drop in hemoglobin levels below the threshold for transfusion due to hemodilution.[6–8]

Kidney transplant patients also receive large volumes of fluid during the perioperative period to prevent delayed graft function. However, no studies have explored the association between fluid administration and changes in hemoglobin levels during the perioperative period following kidney transplantation. This study investigates the correlation between fluid administration and hemoglobin changes to avoid unnecessary blood transfusions without signs of significant bleeding.

Methods

Design and participants

This retrospective observational cross-sectional study involves all patients who underwent kidney transplantation at RSUP Prof. DR. I.G.N.G. Ngoerah Denpasar from January 16, 2016, to August 31, 2024. Data were collected from medical records, and patients with incomplete data were excluded. Descriptive statistical analysis was performed on social patient data, including age, sex, relationship with the donor, human leukocyte antigen **(**HLA) matching, baseline hemoglobin levels, daily hemoglobin levels, and the amount of fluid administered daily during hospitalization. The variables studied were hemoglobin levels and daily fluid intake.

Ethics approval and consent to participate

Not applicable.

Data collection

Data were gathered from medical records, with patients with incomplete information excluded. A descriptive statistical analysis was conducted on social patient data, encompassing factors such as age, sex, relationship with the donor, human leukocyte antigen (HLA) matching, baseline hemoglobin levels, daily hemoglobin levels, and the amount of fluid administered daily during hospitalization. The study focused on the variables of hemoglobin levels and daily fluid intake.

Statistical analysis

A coefficient variation analysis was conducted for both parameters to assess the variability of hemoglobin levels and fluid intake in each sample. The linearity of the results was analyzed using Pearson correlation and linear regression, as well as nonlinear correlation (power correlation), to determine the correlation coefficient (R), coefficient of determination (R^2), and regression coefficient (B). A p-value of less than 0.05 was considered statistically significant. The data were presented in the form of box plots and scatter plots.

Results

A total of 28 patients with chronic kidney disease underwent kidney transplant surgery at RSUP Prof. DR. I.G.N.G. Ngoerah Denpasar, consisting of 17 male and 11 female patients, with a mean recipient age of 31.14 (±7.26) years. Of these, 18 patients were excluded due to incomplete data, leaving only 10 patients in the study. Table 1 shows the basic characteristics of the patients.

Table 1. Characteristics data of patients

Characteristics	Mean	SD	n
Age	28.9	5.54	
Sex			
Male			4
Female			6
Body mass index (BMI)	23.52	2.01	
Hemoglobin (g/dL)	12.26	1.54	
Creatinine (mg/dL)	13.91	2.58	
HD Duration (mo's)	37.8		
Relation with donor			
Father			4
Mother			5
Sibling			1

Hemoglobin levels and the amount of fluid administered after kidney transplant surgery were recorded and analyzed to determine the average values, standard deviation, and co-efficient of variation. Table 2 below shows the daily hemoglobin levels and the daily fluid intake.

Table 2. Daily hemoglobin levels and daily fluid intake

		N	Mean	SD	Minimum	Maximum
Fluid intake (ml/24h)	1	10	8,246	3,625	4,005	15,167
	2	10	6,703	3,395	3,625	15,670
	3	10	5,555	1,539	3,650	8,960
	4	10	5,720	1,685	3,225	8,766
	5	10	5,948	2,056	3,830	9,950
	6	10	5,552	1,375	3,280	7,100
	7	10	5,825	2,245	3,300	11,100
	8	10	5,989	1,593	3,590	9,180
	Total	80	6,192	2,386	3,225	15,670

Cont.

Hb (g/dl)	1	10	11.2	2.1	8.1	14.5
	2	10	9.5	2.1	6.1	12.3
	3	10	8.7	1.9	5.4	11.2
	4	10	8.8	1.8	5.7	12.4
	5	10	9.2	1.1	7.1	10.5
	6	10	9.4	1.0	7.5	10.5
	7	10	9.2	1.4	7.0	11.3
	8	10	9.5	1.8	7.1	12.8
	Total	80	9.5	1.8	5.4	14.5

The changes in hemoglobin levels per day and the amount of fluid intake can be seen in the following figures 1 and 2.

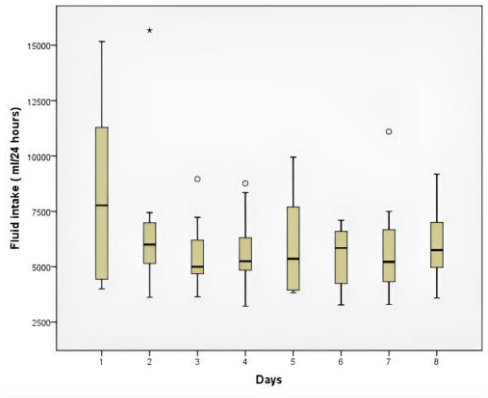

Figure 1. Changes in fluid intake per day

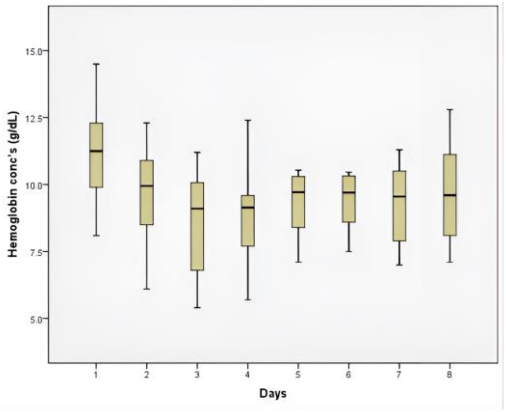

Figure 2. Changes in hemoglobin per day

Figure 1 shows that the fluid intake has the largest variance range on the first day, which then decreases and tends to stabilize on the second, third, and fourth days. It increases again on the fifth day before stabilizing until the eighth day. Meanwhile, in Figure 2, hemoglobin levels show a downward trend, reaching their lowest point on the third day before rising again until the eighth day. An analysis was conducted to determine the coefficient of variation for daily fluid intake and hemoglobin levels, as shown in Table 3.

Table 3. average and standard deviation of fluid intake and hemoglobin levels, as well as coefficient of variation for each patient

No.	Mean*	SD*	Mean**	SD**	CoV*	CoV**
1.	6,389	2,271	10.96	1.11	0.36	0.10
2.	8,467	4,520	10.45	0.95	0.53	0.09
3.	5,000	1,223	9.75	0.76	0.24	0.08
4.	6,778	1,758	7.77	1.39	0.26	0.18
5.	5,913	1,742	11.36	1.43	0.29	0.13
6.	5,652	1,780	11.45	1.37	0.32	0.12
7	5,900	1,106	8.98	0.68	0.19	0.08
8.	8,625	1,900	7.53	0.85	0.22	0.11
9.	4,584	890	8.34	1.71	0.19	0.21
10.	4,614	1,086	8.41	1.35	0.24	0.16

*Fluid intake (ml/day); **Hb level (g/dL)

Using Pearson Correlation and Linear Regression, followed by a power correlation test, the results showed a strong relationship between the coefficient of variation for fluid intake and the coefficient of variation for hemoglobin levels ($R = 0.86$; $R^2 = 0.74$; $B = 0.38$; $P < 0.001$), as illustrated in the line diagram below (Figure 3).

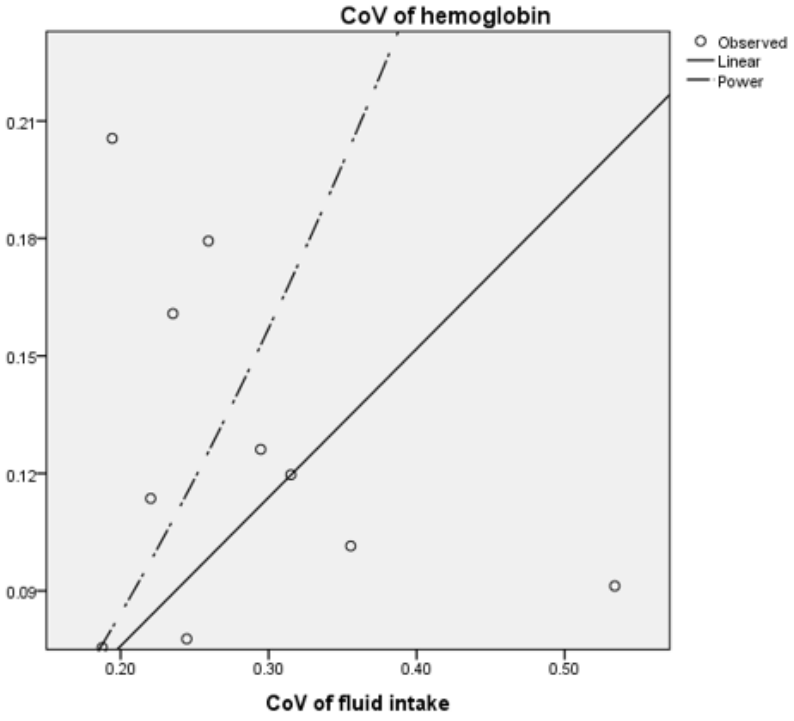

Figure 3. The relationship between the coefficient of variation for fluid intake and variance of hemoglobin levels was analyzed using linear regression ($R = 0.86$; $R^2 = 0.74$; $B = 0.38$; $P < 0.001$) and power correlation ($R = 0.96$; $R^2 = 0.91$; $B = 1.54$; $P < 0.001$).

Discussion

Optimal fluid administration targets achieving immediate graft function, which is the most critical aspect of perioperative management after kidney transplantation. Since there is no standardized consensus or guidelines on the exact volume of fluid that should be administered, the amount of fluid given is individualized for each kidney transplant recipient. It is known that administering 500 ml of fluid can result in a hemoglobin decrease of 1 g/dL, a condition known as relative and temporary hemodilution. However, hemodilution can reduce the oxygen delivery capacity to tissues due to the lowered hemoglobin levels.[4–6,8]

In major surgery, preoperative fluid administration to achieve acute normovolemic hemodilution (ANH) is often to be done. The main concept is that exchange with crystalloids or colloids is given for every blood loss to maintain normovolemia. The target hematocrit with ANH is variable, but it is often around 25% to 30%. More extreme hemodilution is likely to be more efficacious in preventing allogenic blood transfusion, but the risks are greater, particularly in some patients with pre-existing medical conditions. Hemoglobin concentrations are influenced by plasma. An increase in the plasma volume by the intravenous administration of fluids may cause significant hemodilution and decreased hemoglobin levels. Critical hemoglobin level denotes the efficacy of ANH, and for humans, the decrease of hemoglobin levels between 4 to 5 gr/dL was considered safe.[9,10]

To our knowledge, our study is the first to investigate the effect of fluid administration in the perioperative period after kidney transplantation on hemoglobin. This study observed a strong relationship between the decrease in hemoglobin levels and fluid administration to achieve immediate graft function. This hemoglobin decrease is temporary and will recover on its own without the need for blood transfusion. Iatrogenic hemodilution, which is temporary, was confirmed during the perioperative period after kidney transplantation in this study. Careful monitoring is necessary to avoid unnecessary blood transfusions.

Conclusion

There is a relationship between perioperative fluid administration after kidney transplantation and a temporary decrease in hemoglobin levels, suggesting that blood transfusion should only be administered when significant bleeding is evident.

Limitations of the Study

This study is a preliminary observation of hemodilution during the perioperative period after kidney transplantation, and it has limitations, including a small sample size and the lack of analysis regarding intraoperative bleeding and the volume of fluids administered during the procedure.

Declarations

Ethics approval and consent to participate

Not applicable.

Competing interests

There are no conflicts of interest in writing this article.

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Author's Contribution

Idea/concept: AS. Design: AS. Control/supervision: IGRW, GWM, YK, NPA, IGNATE. Data collection/processing: AS. Analysis/interpretation: AS, IGRW. Literature review: AS. Writing the article: AS. Critical review: IGRW, AS. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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