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# PROFILE OF INCOMPATIBLE REACTIONS TO PACKED RED CELL TRANSFUSION IN PATIENTS WITH CHRONIC KIDNEY DISEASE AT SANGLAH HOSPITAL

PROFIL REAKSI INKOMPATIBEL PASCA TRANSFUSI PACKED RED CELL PADA PENDERITA GAGAL GINJAL KRONIK DI RSUP SANGLAH

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# ABSTRACT

Background: Since the prevalence of chronic renal failure disease has increased. Packed Red Cell (PRC) transfusions were a common way to replace the kidneys' function in filtration. However, the reaction caused was not widely reported. Purpose: To assess the profile of incompatible reactions in PRC transfusions of chronic kidney disease patients at Sanglah Hospital, Denpasar. Method: A descriptive observational study with a cross-sectional design was employed to identify incompatibility reactions in 210 patients using medical records from July-December 2021 at Sanglah Hospital in Denpasar. Sample determination using saturated sampling techniques and data analysis were carried out descriptively. Result: Incompatible reactions in patients with chronic renal failure at Sanglah Hospital Denpasar still affected 57 people (27.14%) out of 210 people with chronic renal failure. This condition could increase fatalities in various health services if not appropriately handled. Incompatible reactions could occur, and the higher risk was in patients of the male sex who were elderly (45-65 years), had blood type O, had hemoglobin (Hb) levels ranging from 6.1–9.0 g/dL, and had conducted PRC transfusions above three pouches with a frequency of more than three times. **Conclusion:** People with chronic kidney failure still had a high chance of having an incompatible reaction after a PRC transfusion. Many different things caused these reactions. Incompatibility reactions in people with chronic kidney failure should happen less often in the future if they were evaluated and found early.

# ABSTRAK

Latar belakang: Setiap tahun, prevalensi penyakit gagal ginjal mengalami peningkatan. Tindakan yang umum dilakukan yakni memberikan transfusi Packed Red Cell (PRC) guna menggantikan fungsi ginjal dalam melakukan filtrasi. Namun, reaksi yang ditimbulkan belum banyak dilaporkan. Tujuan: Untuk menilai profil reaksi inkompatibel pada transfusi PRC pasien gagal ginjal kronik di RSUP Sanglah Denpasar. Metode: Studi deskriptif observasional dengan desain cross-sectional digunakan untuk mengidentifikasi reaksi inkompatibel pada 210 pasien menggunakan rekam medis dari Juli-Desember 2021 di Rumah Sakit Sanglah, Denpasar. Penentuan sampel menggunakan teknik sampling jenuh dan analisis data dilakukan secara deskriptif. Hasil: Reaksi inkompatibel pada penderita gagal ginjal kronik di RSUP Sanglah Denpasar masih ditemukan mencapai 57 orang (27,14%) dari 210 orang penderita gagal ginjal kronik. Kondisi ini apabila tidak ditangani dengan baik maka dapat meningkatkan fatalitas di berbagai layanan kesehatan. Reaksi inkompatibel dapat terjadi dan semakin tinggi risikonya pada penderita dengan jenis kelamin laki- laki, berada pada usia yang tergolong lansia (45-65 tahun), memiliki golongan darah O, kadar hemoglobin (Hb) berkisar 6,1-9,0 g/dL, pernah melakukan transfusi PRC >3 kantong dengan frekuensi >3 kali. Kesimpulan: Reaksi inkompatibel pasca transfusi PRC pada penderita gagal ginjal kronik tergolong tinggi dan diperantarai oleh berbagai faktor. Orang dengan gagal ginjal kronis berisiko tinggi memiliki reaksi inkompatibel setelah melakukan transfusi PRC. Berbagai faktor yang menyebabkan reaksi ini. Reaksi inkompatibel pada orang dengan gagal ginjal kronis harus di evaluasi dan dideteksi sejak dini guna menekan temuan di masa depan.

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# INTRODUCTION

Chronic Kidney Disease (CKD) is one of the noncommunicable diseases that affect people all over the world, including in Indonesia. People worry about CKD, especially those with other health problems that can raise the risk of death (Centers for Disease Control and Prevention, 2021). According to the 2010 Global Burden of Disease study, CKD rose from the 27th leading cause of death in 1990 to the 18th in 2010. The Ministry of Health of the Republic of Indonesia reported that in 2013, as many as 2 out of every 1000 Indonesians suffered from CKD (Ministry of Health Regulation, 2018). Studies reinforce these results that state that the prevalence of CKD in males (0.3%) is higher than that of females (0.2%) and, based on age characteristics, occurs in individuals >75 years (0.6%) and begins to increase at the age of 35 years and over (Centers for Disease Control and Prevention, 2021; Garcia et al., 2022; Larse et al., 2013). More than three times per month, soft and energy drink consumption increases the risk of CKD by 25.8 times. Cases of CKD in Indonesia grew by 3.8% and Bali reported a similar increase of 38.7% in 2018 (Ministry of Health Regulation, 2018).

CKD is when the patient's kidneys do not work as well for more than three months and the glomerular filtration rate is less than 60 ml/min/1.73 m<sup>2</sup> (Pongsibidang, 2016). Kidney damage can be observed through albuminuria, the presence of abnormalities in urine sediment, electrolyte abnormalities, the detection of renal abnormalities histologically and morphologically, as well as the presence of a history of renal transplantation (Egawa et al., 2023; Goesch et al., 2021). This results in alarming impacts, including using hemodialysis to replace kidney function wholly and partially (Buerger and Jain, 2022; Rahman, 2019). Patients with CKD who have anemia complications must receive Packed Red Cells (PRC) blood transfusions. Red blood cell transfusions lower risk, restore kidney function and increase oxygen transport above normal (Hart et al., 2015; Lomas-Francis and Westhoff, 2022; Yan, 2022).

Blood transfusion activities are a common medical procedure carried out to meet the standard of human living needs. However, transfusion activities are a significant risk of causing a fatality, and this is due to a pre-transfusion stage error in the form of giving PRC with incompatible matching test results, resulting in a fatal transfusion reaction (Koury, 2016; Yazer *et al.*, 2022). The incompatibility reaction is significant to avoid blood transfusion errors during hemodialysis. Previous studies reported that incompatible reactions in recurrent transfusions  $\geq 10$  times in *thalassemia* patients obtained 52% incompatible *cross-matching* results. Furthermore, 47 patients (94%) showed inconsistent *cross-matching* results (Geni *et al.*, 2019). The high reports

of incompatible *cross-matching* results in PRC transfusion patients result in people with CKD being particularly at risk of experiencing similar events (Rahman, 2019). However, studies have reported incompatible reactions due to PRC transfusions in people with CKD, but these are still little reported.

This study aimed to assess the profile of incompatible reactions in PRC transfusions of CKD patients at Sanglah Hospital, Denpasar. It is hoped that this research can provide the latest information related to the impact of giving PRC to patients with CKD and encourage all healthcare facilities to pay attention and consider these actions by applying the precautionary principle as an effort to improve the degree of public health.

#### MATERIAL AND METHOD

Descriptive observational research with a crosssectional design (Darwin et al., 2021). The study used secondary data from medical records of CKD patients who received PRC transfusions from Sanglah Central Hospital Denpasar. This research has been declared ethically feasible with protocol number 2022.01.2.0758 and ethical exemption number 1520/UN14.2.2.VII.14/ LT/2022, approved by the Research Ethics Commission (KEP) of the Faculty of Medicine, Udayana University. The study lasted for four months (January-April 2022). The population in this study was all the data on CKD patients with PRC transfusions at Sanglah Denpasar Hospital in July-December 2021, with sample determination using a saturated sampling technique for 210 samples. The determination of the month is based on the availability of research data and the updating of data to minimize the bias of the results obtained.

The data collected in this study are in the form of demographic data including gender (male and female), age when PRC transfusion with CKD ((category of children (6-11 years), adolescents (12-25 years), adults (26-45 years), elderly (46-65 years) and seniors (>65 years)), blood type (A, B, O, and AB), hemoglobin data (Hb) (in g/dL). The intensity of the transfusion performed (times), the frequency of blood pouches received (times), and the results of *cross-matches* in compatible and incompatible reactions. All data obtained are then tabulated and analyzed descriptively in percentages of each variable (Darwin *et al.*, 2021).

## RESULT

Based on the results of the study, the study subjects were dominated by male patients with a total of 117 people (55.7%), age included in the elderly category (46-65 years), and blood type O dominated with 93

people (44.3%). In the *cross-match* results of CKD patients who received PRC at Sanglah Denpasar Hospital in the period from July to December 2021, obtained from 210 patients, there were 57 people (27.1%) with incompatible reaction results, while 153 people (72.9%) had to *cross-match* compatible results.

Identification of incompatible reaction *cross-match*'s results in CKD patients receiving PRC transfusions based on sex characteristics dominated by 34 males (16.19%). In age characteristics, the predominance of incompatible reaction *cross-match*'s results in CKD patients aged 46-65, with the elderly category totaling 37 people (17.63%). Furthermore, in blood type characteristics, CKD patients with blood type O totaled 27 people (12.85%),

dominating the presence of incompatible reactions. In addition, hemoglobin (Hb) levels in patients with CKD who are incompatible are in the range of 6.1-9.0, with a total of 44 people (20.95%). Most patients with CKD who performed PRC transfusions >3 pouches showed an incompatible reaction with 47 people (22.38%). Finally, the frequency of PRC transfusions >3 times in patients with CKD who experienced incompatible reactions was 28 people (13.35%). Thus, the *cross-match* results found that CKD patients who experienced incompatible reactions were still relatively high. Characteristics of patients with CKD at Sanglah Denpasar Hospital based on the *cross-match* results are presented in Table 1.

Table 1. Characteristics of patients with CKD based on cross-match results at Sanglah Hospital

Characteristic     Prequency (vs)     Compatible (vs)     Incompatible (vs)       Gender     Male     117 (55.71)     83 (39.52)     34 (16.19)       Female     93 (44.29)     70 (33.33)     23 (10.96)       Age     Children (6-11 years)     1 (0.47)     1 (0.47)     0 (0.00)       Teenagers (12-25 years old)     17 (8.10)     15 (7.14)     2 (0.96)       Adults (26-45 years)     37 (17.61)     30 (14.30)     7 (3.33)       Elderly (46-65 years old)     115 (54.77)     78 (37.14)     37 (17.63)       Seniors (>65 years old)     40 (19.05)     29 (13.80)     11 (5.23)       Blood type      34 (16.20)     23 (10.95)     11 (5.23)       B     68 (32.38)     54 (25.71)     14 (667)       O     93 (44.28)     66 (31.42)     27 (12.85)       AB     15 (7.14)     10 (4.77)     5 (2.38)       Helevels (g/L)     10 (4.77)     5 (2.38)     13 (6.20)       .1-6.0     33 (15.71)     20 (9.53)     13 (6.20)       .9.1-12.0     4 (1.90)     4 (1.90)     4 (0.00) <th rowspan="2">Characteristic</th> <th rowspan="2">Frequency (%)</th> <th colspan="2">Cross-match result (n = 210)</th>	Characteristic	Frequency (%)	Cross-match result (n = 210)	
Gender       Male     117 (55.71)     83 (39.52)     34 (16.19)       Female     93 (44.29)     70 (33.33)     23 (10.96)       Age          Children (6-11 years)     1 (0.47)     1 (0.47)     0 (0.00)       Teenagers (12-25 years old)     17 (8.10)     15 (7.14)     2 (0.96)       Adults (26-45 years)     37 (17.61)     30 (14.30)     7 (3.33)       Elderly (46-65 years old)     115 (54.77)     78 (37.14)     37 (17.63)       Seniors (>65 years old)     40 (19.05)     29 (13.80)     11 (5.23)       Blood type       34 (16.20)     23 (10.95)     11 (5.23)       B     68 (32.38)     54 (25.71)     14 (6.67)     0     93 (44.28)     66 (31.42)     27 (12.85)       AB     15 (7.14)     10 (4.77)     5 (2.38)     54 (25.71)     14 (6.67)       O     93 (44.28)     66 (31.42)     27 (12.85)     AB     15 (7.14)     10 (4.77)     5 (2.38)       Holevels (g/dL)     10.4.77)     5 (2.38)     19 (9.61.42)     44 (20.95)			Compatible (%)	Incompatible (%)
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	>3 times	51 (24.29)	53 (25.24	28 (13.35)

Source: Data analysis (2022)

#### DISCUSSION

Patients with chronic renal failure who received PRC transfusions at Sanglah Hospital experienced an incompatible reaction. CKD has infected various groups of people, children, and elderly patients (Tuttle et al., 2019). Thus, CKD is characterized by partial or complete damage to the part of the kidney that occurs for more than three months (Malmberg et al., 2020). In addition, pathological abnormalities patients feel with CKD are generally proteinuria, namely the excessive compulsive presence of protein in the urine >150 mg/24 hours (Koshy and Geary, 2008; Melianna and Wiarsih, 2019). The clinical diagnosis of CKD is established by disturbances in the glomerular filtration rate value of <60 ml/min/1.73 m<sup>2</sup> (Jamiatun et al., 2015). The classification of CKD degrees is determined based on the glomerular filtration rate value. The higher stage indicates a lower glomerular filtration rate value (Collein et al., 2021; Sitorus et al., 2015).

In a study conducted at Sanglah Hospital Denpasar from July to December 2021, 210 people with CKD were obtained. The medical records' identification results show that all patients received PRC transfusions with different amounts and frequencies depending on the initial condition of hospital admission. The components contained in PRC are erythrocytes that have been concentrated by separating other components (Goesch et al., 2021). The use of PRC is claimed to reduce disease transmission, minimize the possibility of immunological reactions, and provide less blood volume to reduce the possibility of overload (Camp and Army, 1960; Hart et al., 2015). However, PRC transfusions have several disadvantages, including the availability of plasma, leukocytes, and platelets in the blood, triggering the formation of antibodies in the recipient's blood (Hart et al., 2015).

The characteristics of patients with CKD at Sanglah Hospital Denpasar are dominated by 117 males (55.71%). The results are similar to previous studies that stated that patients with CKD at Sanglah Hospital Denpasar were dominated by males, up to 72% and the rest were female (Saraswati et al., 2021). Similar results were reported in studies in Singapore and China obtained by male-dominated suffering from CKD mediated by smoking, high workload, and less clean-living behaviors, including poorly controlled food (Sabanayagam et al., 2020). Furthermore, Pranandari and Supadmi (2015) research in the hemodialysis unit of RSUD Wates, Kulon Progo showed that there are more people with CKD in males caused by the subordinate role and tendency of men in less hygiene, irregular drug consumption, and consumption of energy drinks that trigger a 2.03fold possible risk. Recent research by Garcia et al. (2022) and Tomlinson and Clase (2019) revealing end-stage CKD is widely found in males, including the reception of kidney transplants. Physiological risk factors in males independently modulate kidney disease or its

development mediated by hypertensive comorbidities and obsessions (Apriastini and Ariawati, 2017; Malmberg *et al.*, 2020; Rahajeng *et al.*, 2020).

The high morbidity of CKD patients with male sex at Sanglah Denpasar Hospital is likely due to other factors that can increase or aggravate CKD (Apriastini and Ariawati, 2017; Tuttle et al., 2019; Zhang et al., 2018). Patients with CKD who received PRC transfusions with incompatible cross-match results were classified as high, reaching 34 people (16.19%). This needs attention by health workers in carrying out PRC transfusion actions, especially identifying comorbidities first and conducting a thorough examination of the patient's condition before the transfusion is carried out. Similar to the research at the Blood Bank of Wahidin Sudirohosodo Makasar Hospital, it was obtained that the frequency of incompatibility was more in males, reaching 51.1%. Different results were revealed by those who found cross-match results by Fatmasari and Lailin (2021) with more incompatible reactions in females, reaching 62% in the PMI Blood Donation Unit in Surakarta City. This is because the female is more likely to experience anemia, heart abnormalities, CKD, rheumatoid arthritis, bone marrow disease, and bleeding during childbirth (Koshy and Geary, 2008; Fatmasari and Laili, 2021; Hidayat et al., 2016; Hinonaung et al., 2020).

Regarding age characteristics, patients with CKD at Sanglah Hospital in Denpasar are dominated by the elderly age group ranging from 46-65 years. Research at Sanglah Hospital in 2019 obtained a dominating age of 46-55 (34.6%) (Saraswati *et al.*, 2021). Research Pranandari and Supadmi (2015) in the hemodialysis unit of RSUD Wates, Kulon Progo obtained patients with CKD dominated by the age of <60. The high number of CKD patients at Sanglah Denpasar Hospital who experienced incompatible *cross-match* results reached 37 people (17.63%) in the elderly category. This must be considered when transfusion to *cross-match* before transfusion to minimize incompatible events that risk fatality (Aljannah and Supadmi, 2021; Raturi *et al.*, 2021).

These results were similar to Kartika et al. (2020) studies that revealed the incidence of incompatibility occurred the most at the age of  $\geq$ 17 years, reaching 92.85%. This age becomes the age of being susceptible to being infected with diseases and a decrease in the body's physiological functions, including the kidneys (Arslan et al., 2022). Geni et al. (2019) explain that the elderly need more blood transfusions. In addition, as you get older, the ability of the kidneys to work usually decreases. As a result, abnormalities or malfunctions in the kidney organs rapidly and progressively have implications for the incidence of CKD from mild to severe stages (McClellan and Flanders, 2003). The decrease in the ability of the kidneys (glomerulus) to filtration in patients with CKD ranges from 41-61 mL/min/1.73 m<sup>2</sup> in adults with a median of 53. While in children, it reaches 50-95 mL/min/1.73 m<sup>2</sup> with a median of 70 (Tuttle et al., 2019).

Blood becomes an essential part of the darkness of human life (Adnyana et al., 2021). Patients with CKD who received PRC with incompatible results dominated by blood type O reached 27 people (12.85%). These results are similar to studies by Kartika et al. (2020) that found incompatible reactions in CKD sufferers with blood type O 40% at Dr. Wahidin Sudirohusodo Hospital. Different antigens in the blood cause differences in blood types. Blood types with A, B, and O systems are based on a series of double alleles, namely IA, IB, and IO, of which all populations in the world own these three alleles (Arslan et al., 2022; Janatpour et al., 2008; Kim et al., 2022; Carvalho-Poyraz et al., 2021). The purpose of cross-matching is to review the presence of complete antibodies of type IgM (immunoglobulin M) and complot antibodies of type IgG (immunoglobulin G) in the patient's serum (mayor) and donor serum against the patient (minor). The results are to minimize anemia and transfusion hemolytic reactions in patients receiving blood donations (Collein et al., 2021; Sitorus et al., 2015). These findings indicate that patients with CKD who receive PRC experience a relatively high incompatible (unsuitable) reaction. If these results are not evaluated, they can harm the patient and result in high fatalities. An effort can be made by cross-matching with repetition to ensure good results before transfusion to the patient (Aljannah and Supadmi, 2021).

The mechanism of incompatible reactions in patients with CKD who receive PRC transfusions at Sanglah Denpasar Hospital, especially in antigen reactions contained in donor red blood cells, reacts with antibodies in the patient's plasma so that a complex antigen reaction with antibodies occurs. The occurrence of agglutination or homolysis indicates a positive *cross-matching* result (incompatible reaction). A refined suspension of erythrocyte cells indicates negative *cross-matching* results after resuspension of erythrocytes precipitating on the bottom of the test gel or no agglutination or hemolysis occurs. A negative *cross-matching* result is a compatible reaction (Kim *et al.*, 2022).

Incompatible reactions are possible due to alloantibodies in the patient's serum that react with donor red blood cell antigens. The patient's serum autoantibodies act with the donor's red blood cells (Geni et al., 2019). Two things cause red blood cell incompatibility. The first is due to incompatibility of blood types A, B, and O when transfusion so that an acute intravascular homolysis reaction occurs and can also be caused by an immune reaction between antigens and antibodies that often occurs in the mother and fetus to be born (Fatmasari and Laili, 2021; Janatpour et al., 2008; Kim et al., 2022). Since the discovery of the ABO blood type by Karl Landsteiner in 1901 and the Rhesus factor (Rh) by Levine in 1939, all blood transfusions taken from known donors of the ABO group and its Rh factor, thus the results of cross-matching are generally appropriate (compatible), transfused to the patient well. Nevertheless, there is an exception process in

exceptional cases, for example, Lewis a or Lewis b antibodies in patients whose classes Lewis a and b are antagonistic (Aljannah and Supadmi, 2021).

Furthermore, patients with CKD who received PRC transfusions were dominated by patients with hemoglobin levels ranging from 6.1-9.0 g / dL to 44 people (20.95%). This is because people with CKD have disorders in eating conditions, including decreased appetite or no interest in consuming anything. This condition occurs due to feelings of nausea, vomiting, and gastrointestinal disorders. If not followed up, hemoglobin levels will continue to decrease in line with the time of the disease. The more kidney function decreases, characterized by an increased stage and a decreased glomerular filtration rate condition, the more aggravating anemia will be (Runtung et al., 2013). If there is moderate to severe anemia, it is necessary to take a blood transfusion to meet normal conditions. However, the high frequency of transfusions has implications for an increase in the possibility of incompatible reactions in patients with CKD at Sanglah Hospital in Denpasar.

The number of blood pouches received by people with CKD indicates the higher severity of the stage suffered. This study found that patients with CKD who received PRC transfusions >3 pouches with incompatible reactions totaled 47 people (22.38%). A large number of blood pouches from patients with CKD allows for an increase in incompatibility that ends in the occurrence of *alloantibodies* due to high exposure to antibodies in the patient's body from the donor's blood (Harbi *et al.*, 2022; Rofinda *et al.*, 2022). *Alloantibody* is a condition of antibodies produced after exposure to genetically different antigens from the same species. At the same time, *autoantibodies* (Herawati and Santhi, 2018).

The frequency of PRC donors in patients with CKD with incompatible reactions was 28 people (13.35%). This result is relatively high compared to patients who received PRC only 1-3 times. The high frequency of PRC donors in patients with CKD is due to the incidence of alloantibodies in patients with CKD who often receive PRC transfusions (Goesch et al., 2021). Incompatible reactions are also possible due to antibodies in the patient's serum that react with donor red blood cell antigens and donor serum antibodies in action with the patient's red blood cell antigens (Herawati and Santhi, 2018; Koury, 2016; Lomas-Francis and Westhoff, 2022). Patients with end-stage CKD to overcome a poor prognosis will more often receive PRC transfusions, as a result of which various factors can favor the occurrence of incompatible reactions in patients, including deterioration of health conditions.

# CONCLUSION

Incompatible reactions in patients with CKD at Sanglah Denpasar Hospital were still found to reach 27.14%. This condition can increase fatalities in various health services if not appropriately handled. Incompatible reactions can occur, and the higher risk in patients of the male sex, being at a relatively elderly age (45-65 years), having blood type O, hemoglobin (Hb) levels ranging from 6.1-9.0 g/dL, having had PRC transfusion more than three pouches with a frequency of more than three times. In the future, further research is needed related to procedures for identifying incompatible reactions early and risk factors that can increase the occurrence of incompatible reactions in patients with CKD. Detection accuracy is needed to ensure the patient's condition is in good condition and minimize fatalities.

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