# **INDONESIAN JOURNAL OF**

# CLINICAL PATHOLOGY AND MEDICAL LABORATORY

Majalah Patologi Klinik Indonesia dan Laboratorium Medik

## **EDITORIAL TEAM**

Editor-in-chief: Puspa Wardhani

## **Editor-in-chief Emeritus:**

Prihatini Krisnowati

### **Editorial Boards:**

Maimun Zulhaidah Arthamin, AAG Sudewa, Rahayuningsih Dharma, Mansyur Arif, July Kumalawati, Nurhayana Sennang Andi Nanggung, Aryati, Purwanto AP, Jusak Nugraha, Sidarti Soehita, Endang Retnowati Kusumowidagdo, Edi Widjajanto, Budi Mulyono, Adi Koesoema Aman, Uleng Bahrun, Ninik Sukartini, Kusworini Handono, Rismawati Yaswir, Osman Sianipar

**Editorial Assistant:** 

Dian Wahyu Utami

Language Editors: Yolanda Probohoesodo, Nurul Fitri Hapsari

> Layout Editor: Akbar Fahmi

**Editorial Adress:** 

d/a Laboratorium Patologi Klinik RSUD Dr. Soetomo Jl. Mayjend. Prof. Dr Moestopo 6–8 Surabaya, Indonesia Telp/Fax. (031) 5042113, 085-733220600 E-mail: majalah.ijcp@yahoo.com, jurnal.ijcp@gmail.com Website: http://www.indonesianjournalofclinicalpathology.or.id

Accredited No. 36a/E/KPT/2016, Tanggal 23 Mei 2016

# **INDONESIAN JOURNAL OF**

# CLINICAL PATHOLOGY AND MEDICAL LABORATORY

Majalah Patologi Klinik Indonesia dan Laboratorium Medik

## CONTENTS

### RESEARCH

05–207
08–211
12–218
19–226
27–231
32–236
37–240
41–245
46–253
54–257

Printed by Airlangga University Press. (OC 202/08.16/AUP-B1E). Kampus C Unair, Mulyorejo Surabaya 60115, Indonesia. Telp. (031) 5992246, 5992247, Fax. (031) 5992248. E-mail: aup.unair@gmail.com Kesalahan penulisan (isi) di luar tanggung jawab AUP

Glycated Albumin and HbA1c in Diabetic Nephropathy	
(Albumin Glikat dengan HbA1c dan Penyakit Nefropati Diabetik) <b>Elvan Dwi Widyadi, Jusak Nugraha, Ferdy Royland Marpaung</b>	258–262
Small Dense Low Density Lipoprotein with Angiographically Atherosclerosis in Coronary Heart Disease (Small Dense Low Density Lipoprotein dengan Aterosklerosis Secara Angiografi di Penyakit Jantung Koroner)	
Yuliani Zalukhu, Siti Muchayat Purnamaningsih, Nahar Taufik, Suwarso	263–267
Total IgG and IgG Anti PGL-I with Duration of Therapy and Reactions of Multibaciller Leprosy (Jumlah Keseluruhan IgG dan IgG Anti PGL-I Mycobacterium leprae dengan Lama Pengobatan dan Reaksi Kusta Multibasiler)	
Endang Retnowati, Halik Wijaya, Indropo Agusni	268–273
Factors in Acute Transfusion Reaction (Faktor Reaksi Transfusi Darah Akut) <b>Wiwi Payung, Rachmawati AM, Mansyur Arif</b>	274–278
Neopterin and CD4+ T-Lymphocytes in Stage I HIV Infection (Neopterin dan Limfosit T-CD4+ di Infeksi HIV Stadium I) <b>Harianah, Endang Retnowati, Erwin Astha Triyono</b>	279–283
LITERATURE REVIEW	
The Role of Platelets SCD40L to Atherogenesis (Peran sCD40L Trombosit terhadap Aterogenesis) Liong Boy Kurniawan	284–288
CASE REPORT	
Multiple Myeloma in a Young Adult (Mieloma Multipel di Dewasa Muda) <b>Hendra Rasubala, Agus Alim Abdullah, Mansyur Arif</b>	289–292

## Thanks to editors in duty of IJCP & ML Vol 22 No. 3 July 2016

Aryati, Ida Parwati, Purwanto AP, July Kumalawati, Puspa Wardhani, Rismawati Yaswir, Kusworini Handono, Ninik Sukartini, Adi Koesoema Aman, Rahayuningsih Dharma, AAG. Sudewa, Sidarti Soehita, Endang Retnowati INDONESIAN JOURNAL OF

# CLINICAL PATHOLOGY AND MEDICAL LABORATORY

Majalah Patologi Klinik Indonesia dan Laboratorium Medik

2016 July; 22(3): 274–278 p-ISSN 0854-4263 | e-ISSN 4277-4685 Available at www.indonesianjournalofclinicalpathology.or.id

## RESEARCH

## FACTORS IN ACUTE TRANSFUSION REACTION

(Faktor Reaksi Transfusi Darah Akut)

Wiwi Payung, Rachmawati A.M., Mansyur Arif

#### ABSTRAK

Data kejadian reaksi transfusi darah akut di Indonesia khususnya di Sulawesi Selatan belum pernah dilaporkan. Pencatatan dan pelaporan tentang kejadian reaksi transfusi darah akut di RSUP Dr. Wahidin Sudirohusodo Makassar baru terlaksana mulai bulan Januari 2014. Begitu pun dengan faktor yang mungkin berpengaruh terhadap kejadian reaksi transfusi darah akut belum pernah diteliti sebelumnya. Penelitian ini bertujuan untuk mengetahui faktor yang berpengaruh terhadap kejadian reaksi transfusi darah akut. Rancangan penelitian adalah kajian potong lintang. Sampel sebanyak 93 subjek, masa waktu antara bulan Januari–Juni 2014 di RSUP Dr. Wahidin Sudirohusodo Makassar. Variabel yang diteliti antara lain diagnosis, riwayat transfusi darah sebelumnya, komponen darah yang ditransfusikan dan golongan darah. Metode menghitung yang digunakan adalah diskriptif dan analitik. Metode mendiskriptifkan dilakukan dengan perhitungan sebaran kekerapan. Metode menganalitik dilakukan dengan menggunakan uji Chi Kuadrat dan Multiple Logistic Regression. Pasien yang mengalami reaksi transfusi darah akut ada 43 orang. Faktor yang berpengaruh adalah diagnosis p=0,765, riwayat transfusi darah sebelumnya p=0,563, komponen darah yang ditransfusikan p=0,046, golongan darah p=0,018. Berdasarkan kajian ini dapat disimpulkan, bahwa golongan darah merupakan faktor kebahayaan utama reaksi transfusi darah akut. Yaitu golongan darah O berkebahayaan 2,7 kali lebih besar untuk mengalami reaksi transfusi darah akut dibandingkan dengan golongan darah yang bukan.

Kata kunci: Reaksi transfusi darah akut, faktor, golongan darah

#### ABSTRACT

The data on the incidence of acute transfusion reaction in Indonesia, particularly in South Sulawesi, have not been reported. It was not until January 2014 that the acute transfusion reactions incidence at Dr. Wahidin Sudirohusodo General Hospital Makassar was recorded and reported. Likewise, the factors potentially contributing to the prevalence of acute transfusion reactions have not been studied previously. This study aimed to know the factors that contribute to the incidence of acute transfusion reaction by determine. This study was a cross-sectional study involving 93 subjects conducted during January to June 2014 at Dr. Wahidin Sudirohusodo General Hospital Makassar. The variables examined it included diagnosis, the history of previous transfusion, transfused blood components, as well as the blood type. The obtained data were then analyzed descriptively and analytically. The descriptive analysis was performed by calculating the frequency distribution, whereas the analytical method was performed by using Chi Square and Multiple Logistic Regression. In this study, the number of subjects with acute transfusion (p=0.563), transfused blood component (p=0.046), and blood type (0.018). The study was found that the blood type was the primary risk factor to the incidence of acute transfusion reaction, in which the blood type O had 2.7 greater riskfor having acute transfusion reaction compared with the non-O blood type.

Key words: Acute transfusion reaction, factors, blood type

## **INTRODUCTION**

The blood transfusion is the way transfusion related to blood or its components from one individual (donor) transfused to certain other individual (recipient). The decision to take blood transfusion should consider the risks and benefits received. One of the risks of blood transfusion is the reactions that follow. Blood transfusion reaction is a unwanted response of patients due to the administration of blood or its components. Blood transfusion reactions may occur acutely in the first 24 hours after the transfusion takes place or

Department of Clinical Pathology, Faculty of Medicine, Hasanuddin University, Jl. Perintis Kemerdekaan Tamalanrea, Makassar, Indonesia. Email: wiwipayung.patklin13@gmail.com

delayed reactions that may occur between 4–7 days, or even weeks, after the transfusion.  $^{1\!-\!3}$ 

Acute reaction is the incidence that occurs during blood transfusion or within 24 hours after acute reaction can be divided into three categories, namely: mild, moderate-severe and reaction that is harmful to the life of the patients. Mild reaction is characterized by the emergence of pruritus, urticaria and rash. This reaction is caused by excessive sensitivity. The moderate - severe reaction is characterized by restlessness, weakness, pruritus, palpitation, mild dyspnea, and headache and on examination finds redness on the skin, urticaria, fever, tachycardia, muscle rigidity. The moderate - severe reaction is commonly caused by excessive sensitivity, fever due to nonhemolytic blood transfusion reactions (antibodies against leukocytes, protein, platelets), pyrogens pollution and/or bacteria.4

The research conducted by Savage *et al*<sup>5</sup> stated that allergic reaction was the most common blood transfusion reaction using platelets and plasma between 0.1–0.5%. This reaction is associated with the excessive sensitivity type I where particular antigen allergens bind to IgE molecules that have previously been attached to the surface of mast cells or basophils, leading to a variety of mediators by mast cells and basophils released collectively resulting in increased capillary permeability, vasodilation, contraction of bronchial smooth muscle and gastrointestinal tract as well as local inflammation.<sup>3,5</sup> The research conducted by Meza et al<sup>6</sup> in Windhoek Namibia (2011) in six hospitals found 785 cases of blood transfusion and 28 incidences of acute transfusion reaction, making the estimated incidence of acute transfusion reaction in the country was 11,5/1000 transfusion units. The research conducted by Payandeh *et al*<sup>7</sup> at the Teaching Hospital of Kermanshah University of Medical Sciences in Iran during 2010 to 2012 found the that 6238 units of blood components were transfused. A total of 59 (0.94%) cases of blood transfusion reaction were reported during the period. The common reactions were allergic reaction with various skin manifestations such as urticaria, rash and pruritus (49.2%), nonhemolytic febrile blood transfusion reaction (37.2%), pain in the area of blood transfusion (6.8%) and hypotension (6,8%).<sup>6,7</sup> The research conducted by Kumar et al (2013)<sup>8</sup> on the incidence of acute blood transfusion reaction in patients in ICU found that the common reactions were nonhemolytic febrile transfusion reaction (60.4%), hemolytic febrile transfusion reaction (0.4%) allergic reaction (31.2%) and nonspecific reaction (8%). These reactions occurred to 1.09% of adult patients and 0.36% of children patients. The most blood components to cause acute blood transfusion

reactions were PRC (73.8%), FFP (19.1%) and platelets (7.1%).<sup>8.9</sup>

The death rate due to blood transfusion reactions in the United States was 1 to 1.2 cases/100,000 recipients. It was also reported that urticaria reaction occurred to 10,000–20,000 recipients/1 million blood transfusions and fever reaction occured to 50,00–10,000 recipients/1 million blood transfusion, whereas deadly acute hemolytic reaction occured approximately 1–2 cases/1 million blood transfusions.<sup>1</sup>

The data on the incidence of acute blood transfusion reaction in Indonesia, especially in South Sulawesi have not been reported, as well as the factors that may affect the prevalence of the incidence. Recording and reporting on the incidence of acute blood transfusion reaction at Dr. Wahidin Sudirohusodo General Hospital Makassar were started in January 2014. Thus, the author was interested in studying the factors that contributed to the incidence. This study is expected to be a source of new explanations for the health workers about factors that could affect acute blood transfusion reactions in the recipients.

## **METHODS**

This study was cross-sectional observational. The study was conducted by collecting the data of patients receiving blood transfusion who experienced acute reactions from SIRS and medical records at Dr. Wahidin Sudirohusodo General Hospital Makassar from January to June 2014. Data analysis was performed using SPSS version 22. The statistical counting method was descriptive and analytical (statistical tests). Descriptive method was performed by calculating the frequency distribution. The analytical method was conducted using Chi Square test and Multiple Logistic Regression. Statistical test results were considered significant if p <0.05.

Based on the age, the subjects were divided into two groups, under 17 years and over 17 years. The independent variables in this study include patient diagnosis, history of blood transfusion, the types of components transfused and blood type. Diagnosis of patients was grouped based on the major and divided into groups of malignancy, metabolic endocrine, infection, trauma and others. The history of blood transfusion was divided into first time transfusion and more than one time. Types of blood components transfused were divided into three groups: Whole blood, Packed Red Cell (PRC) and platelets. Blood type of the patients were grouped into O and other than O.

#### **RESULTS AND DISCUSSION**

The research was conducted by collecting the data from SIRS and medical records at Dr. Wahidin Sudirohusodo general Hospital Makassar on patients who received blood transfusions and experienced acute transfusion reactions from January to July 2014. The data showed 43 samples experienced acute

Table 1. Characteristics of subjects

Variabel	n (%)
Number of subjects $(n = 93)$	
Age:	
$\leq$ 17 years old	20 (21.5)
>17 years old	73 (78.5)
Sex:	
Male	52 (55.9)
Female	41 (44.1)
Diagnosis:	
Malignancy	36 (38.7)
Metabolic endocrine	13 (14.0)
Infection	18 (19.4)
Trauma	8 (8.6)
Others	18 (19.4)
History of blood transfusion:	
First time	36 (38.7)
Multiple	57 (61.3)
Blood groups:	
0	44 (47.3)
Others	49 (52.7)
Blood components	
WB	2 (2.2)
PRC	88 (94.6)
Platelet	3 (3.2)
Acute transfusion reaction	
Yes	43 (46.2)
No	50 (53.8)

Table 2. Characteristics of transfusion

Variables	n (%)
Types of acute tansfusion reaction:	
Mild	23 (24.7)
Moderate - severe	20 (21.5)

Table 3. Distribution of transfusion reaction based on diagnosis

Transfusion reaction					
Diagnosis	yes		no		n
Diagitosis	n	%	n	%	- P
Malignancy	18	50.0	18	50.0	
Metabolic endocrine	6	46.2	7	3.8	
Infection	7	38.9	11	61.1	0.765
Trauma	5	62.5	3	37.5	
Others*	7	38.9	11	61.1	
Total	43	46.2	50	53.8	

Chi Square Test

\* Others (benign tumor, postpartum bleeding, thalassemia)

blood transfusion reactions and 50 samples did not. Characteristics of research subjects can be seen in Table 1.

The characteristics of blood transfusion can be seen in Table 2. The 93 research subjects, 46.2% experienced acute reaction, 24.7% experienced mild reaction and 21.5% experienced moderate-severe reaction.

The results of the analysis of factors that contribute to acute transfusion reaction can be seen in table 3-6.

To assess the risk of blood type resulted from acute blood transfusion reactions, the Odds Ratio (OR) was calculated as shown in Table 8.

In this study, out of 93 subjects, 55.9% were males and 44.1% were females, 21.5% was at the age of less than 17 years and 78.5% was at the age of over 17 years (see Table 1). 46.2% experienced acute blood transfusion reactions, 24.7% experienced mild blood transfusion reactions and 21.5% experienced moderatesevere blood transfusion reactions (see Table 2).

Table 4. Distribution of transfusion reaction based on the history of blood transfusion

Transfusion reaction					
History of	У	es	ť	10	n
transfusion	n	%	n	%	- P
First	18	50.0	18	50.0	
Multiple	25	43.9	32	56.1	0.563
Total	43	46.2	50	53.8	

Chi Square Test

**Table 5.** Distribution of transfusion reaction based on blood
 components

Transfusion reaction					
Blood components	J	/es	r	10	n
biood components	n	%	n	%	- P
WB*	2	100.0	0	0.0	
PRC*	38	43.2	50	56.8	0.046
Platelet	3	100.0	0	0.0	
Total	43	46.2	50	53.8	

Chi Square Test

\* WB<sup>1</sup>: Whole Blood \* PRC: Packed Red Cell

Table 6. Distribution of transfusion reaction based on blood type

Transfusion reaction					
Plood type	У	yes		10	n
blood type	n	%	n	%	- P
0	26	59.1	18	40.9	
Others*	17	34.7	32	65.3	0.018
Total	43	46.2	50	53.8	

Chi Square Test

• Others (A, B and AB)

Steps	Variables	Wald	р
1	Diagnosis	0.079	0.779
	Transfusion history	0.169	0.681
	Blood components	0.492	0.483
	Blood group	5.465	0.019
2	Transfusion history	0.134	0.715
	Blood components	0.564	0.452
	Blood group	5.724	0.017
3	Transfusion history	0.669	0.413
	Blood group	5.840	0.016
4	Blood group	5.435	0.020

**Table 7.** Significant multivariate analysis to the acute reaction transfusion

Multiple Logistic Regression-Backward Wald Method (R<sup>2</sup>=0.078)

**Table 8.** Correlation between blood group and acute transfusion reaction

Transfusion reaction					
Blood group	yes	no	Total		
0	26	18	44		
Others	17	32	49		
Total	43	50	93		

OR=2.7 (95% confidence interval =1.17-6.30)

24 cases of mild acute blood transfusion reactions were in the form of itching, hives and swelling around the eyes, whereas the moderate-severe blood transfusion reactions included fever, chills, spasms and vomiting. The research conducted by Savage *et al*<sup>5</sup> and Mehrdad Payandeh *et al*<sup>7</sup> found that the most common acute blood transfusion reaction was allergy with various skin manifestations such as urticaria, rash and itching (49.2%), followed by febrile nonhemolytic (37.2%). Other reactions include pain in the area of blood transfusion (6.8%) and hypotension (6.8%).

The percentage of acute blood transfusion reactions in the diagnosis of malignancy group was 50.0%. This group consisted of cases of ALL, malignant lymphoma, carcinoma of the cervix, carcinoma of the colon, breast, bladder, gastric and thyroid. The percentage of acute blood transfusion reactions in metabolic endocrine group was 46.2%. This group consisted of cases of diabetes mellitus and chronic renal failure. The percentage of acute blood transfusion reactions in the infection group was 38.9%. This group consisted of cases of pulmonary tuberculosis, lymphadenitis, dengue, Community Acquired pneumoniae (CAP) and peptic ulcer et causaH. pylori. The percentage of acute blood transfusion reactions in trauma group was 62.5%. This group consisted of cases of stab wounds, head injury and fractures of the femur. The percentage of acute blood transfusion reactions in other group was 38.9%. This group consisted of cases of mesenteric cysts, ovarian cysts, postpartum hemorrhage, bleeding due to malfunctioning womb/PUD and thalassemia. Some diseases are capable of stimulating blood transfusion reactions, among others: *Paroxysmal nocturnal hemoglobinuria*, autoimmune hemolytic anemia, *glucose-6-phosphate dehydrogenase deficiency*, *malignant hyperthermia*, hemoglobinopathies and erythrocyte membrane defects. The statistical test did not find a significant difference in the distribution of blood transfusion reactions based on diagnosis (p>0.05), although it may appear that the percentage of transfusion reactions is the highest in subjects with trauma (see Table 3).

The blood transfusion reactions with nonhemolytic febrile occurred within 8–24 hours after the transfusion, can be followed by chills, nausea, vomiting, headache and backache. This condition often occurred in patients who often give birth or who have repeatedly received a blood transfusion as the *human leukocyte antigens* (HLA) antibody is the recipient of the HLA antigen: lymphocytes, monocytes and granulocytes of donor or no cytokines release from leukocytes during storage. Statistical test results found no significant differences in the distribution of acute blood transfusion reactions based on the history of previous transfusion (p>0.05) (see Table 4).

The stored blood components, particularly platelets, may contain cytokines IL-1 $\beta$ , IL-6, IL-8 and TNF  $\alpha$  that can cause fever. Another theory of the mechanism of blood transfusion reactions followed by non-hemolytic febrile as a result of the stored blood is the release of CD 40 ligands that can provide the stimulation of endothelial cells to produce cytokines such as pyrogen prostaglandin E2. The allergic reactions such as itching, erythema occur within 15-20 minutes after blood transfusion due to antibodies recipient of protein or foreign substances (drugs, food consumed by donor). The incidence of this reaction is 1-3% of blood products containing plasma. Table 5 shows significant difference of the distribution of acute blood transfusion reactions based on the type of components of transfusion (p < 0.05). The percentage of incidence of acute blood transfusion reactions was significantly the highest in the subjects who were given WB or platelets (respectively 100%) compared to PRC (43.2%). On the other hand, the research conducted by Rajesh Kumar et al<sup>8</sup> found that blood components that was most likely to cause acute blood transfusion reactions were PRC (73.8%), FFP (19.1%) and platelets (7.1%). Table 6 shows significant difference of the distribution of acute blood transfusion reactions based on blood type (p < 0.05). The percentage of incidence of acute blood transfusion reactions was significantly higher in O-blood group (59.1%) compared with non O-blood group (34.7%). Non-O blood groups who experienced acute blood transfusion reactions were as follow: 9 subjects of A blood group, 6 subjects of B blood group and 2 subjects of AB blood group. Multivariate analysis was performed in four (4) stages. At each stage, insignificant variables were excluded (the highest p) (see Table 7). This showed that of the four variables whose correlation with acute blood transfusion reactions was analyzed, only blood type had a major risk factor of acute blood transfusion reactions, although the role was quite small (7.8%). The results of the OR calculation performed to assess the risk of blood type due to acute blood transfusion reactions found that O blood subjects had 2,7 times greater risk of such reactions compared with non-O blood subjects.

## CONCLUSION

This study showed that blood type was a major risk factor of acute blood transfusion reactions. O blood people had a 2,7 times greater risk of acute blood transfusion reactions compared to the non O-blood people.

### REFERENCES

1. Najwa Dalimoenthe Zamalek, *et al.* Basic-Basic Blood Transfusion. First Ed., Division of hematology Clinic Department of Clinical Pathology, Bandung, Faculty of Medicine, University of Padjadjaran. 2011; 111.

- Djoerban Zubairi. Basics of Blood Transfusion in Textbook of Medicine. Fourth Ed., Vol. II, Jakarta, Central issuance of Medicine Faculty of Medicine, University of Indonesia. 2007; 672–79.
- SM Lewis, BJ Brain, I Bates. Laboratory Aspects of Blood Transfusionin Dacie and Lewis Practical Haematology. Tenth Ed., Philadelphia, Churchill Livingstone Elsevier. 2006; 549–51.
- WHO. The clinical use of blood: handbook. Geneva, 2002. Available from URL: http://www.who.int/bct/Main\_areas\_of\_ work/Resource\_Centre/CUB/English/Handbook.pdf
- Savage William J, AA Tobian, JH Savage, RA Wood, JT Schroeder, et al. Scratching the surface of Allergic Reaction Transfusion, Published In Transfusion, 2013; 53 (6): 1361–1371. (Cited 2014 Sept 16). Available from: www.ncbi.com
- Benjamin Meza PL, Britta Lohrke, R Wilkinson, JP Pitman, RW Shiraishi, *et al.* Estimation of the Prevalence and Rate of Acute Transfusion Reactions occuring in Windhoek, Namibia, On Transfus Blood 2014; 12: 352–61. (Cited 2014 Sept 16) Available from: www.ncbi.com.
- Payan deh Mehrdad, Zare ME, Kansestani AN, Pakdel SF, Jahanpour F, et al. Description of Acute Transfusion Reactions in the Teaching Hospitals of Kermanshah University of Medical Sciences, Iran, On the International Journal of Hematology-Oncology and Stem Cell Research. (Cited 2014 Sept 16) Available from: www.ncbi.com, 2013; 7 (2): 11–16.
- Rajesh Kumar, Gupta M, Gupta V, Amarjit K, Gupta S. Acute Transfusion Reaction (ATRs) in the Intensive Care Unit (ICU): a Retrospective Study In Journal of Clinical and Diagnostic Research, February 2014; 8 (2): 127–129. (Cited 2014 Sept 16) Available from: www.ncbi.com
- Tanhehco Yvette C and Berns Jeffrey S. Red Blood Cell Transfusion Risks in a Patient with End-Stage Renal Disease, Published in Semin Dial 2012; 25 (5): 539–544. (Cited 2014 Sept 16). Available from: www.ncbi.com