

Association Between Severity of Anemia in Patient with Chronic Kidney Failure to Retinal Hemorrhage

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Abstract- Eye disorders can occur in 90% of cases of patients with hematological disease. Anemia is the most common blood disease that causes the most manifestations in the eye. Anemia causes retinal hypoxia, which causes infarction of the nerve lining and blood vessel disorders. Retinal hypoxia also causes dilation of blood vessels; increased transmural pressure which causes hypoproteinemia and microtrauma in the vessel wall, which causes retinal edema and retinal bleeding.

Method : This study is an observational analytic method with cross sectional study. Research subjects were anemia sufferers with chronic renal failure who performed hemodialysis at the Sumatera Utara University Hospital.

Results: From 35 study subjects (65 eyes) there were 4 eyes with Dot blot and 4 eyes with Flame shape retinal hemorrhage. The most research subjects were male 62,9% and the most research subjects were in the degree of moderate anemia which was 15 subjects.

Conclusion: There was no association between the severity of anemia on retinal hemorrhage ($p = 0.376$). By testing somers'd it is found that $r = -0.116$, the opposite correlation is the more severe anemia, the more there is no retinal hemorrhage. And there is no association between age and retinal hemorrhage. ($p = 1,000$). By testing somers'd, it was found that $r = -0.020$, the correlation characteristic was the opposite, where the older the subject, the more there was no retinal hemorrhage.

Index Terms- Retinal Hemorrhage, Anemia, Chronic Renal Failure, Hemodialysis

I. INTRODUCTION

Retinal haemorrhages occur when there is extravasation of blood, either into the retina itself (intraretinal), between the retina and the retinal pigment epithelium (subretinal), or between the retina and the hyaloid face of the vitreous body (subhyaloid or preretinal). The shape and colour of the haemorrhages are determined by the level or levels of the retina affected, and they are often mixed. Often the hyaloid face ruptures and the haemorrhage spreads into the vitreous (intravitreal).¹

Retinal abnormalities have been described for many years in patients with anemia. Extravascular retinal abnormalities

described include flame-shaped hemorrhages, hard exudates, and cotton-wool spots.²

Anemia is a condition of reduced amount of Erythrocytes or Hemoglobin (Oxygen carrier protein) from normal values in the blood so that it cannot fulfill its function to carry oxygen in sufficient quantities to the peripheral tissues so that oxygen delivery to the tissues decreases.^{3,4,5}

Anemia causes retinal hypoxia, which leads to infarction of the nerve fiber layer and clinically manifests as cotton wool spots. Retinal hypoxia also leads to vascular dilatation; increased transmural pressure owing to hypoproteinemia; and microtraumas to the vessel walls, which cause retinal edema and hemorrhages. In many clinical situations, thrombocytopenia is associated with anemia, and that leads to defective coagulation and hemorrhages.⁶

II. METHOD

This study is an analytic observational with cross sectional design study with control was approved by the ethics committee of Medical Faculty of Sumatera Utara University. The study subjects were all patients who admitted to the Vitreo Retina Division and Hematology and Oncology Division of Sumatera Utara University Hospital Medan who was diagnosed with Anaemia from May to July 2018. Total sample was 35 people with age over 18 years. From 70 eyes, there were 5 eyes excluded criteria because of opacity lens. subject with anaemia caused of chronic renal failure with regular hemodialysis and included in the inclusion criteria, then we examined the anterior segment of the eye, recording laboratory results, examining the posterior segment using the canon CX 1 fundus camera, we assessed retinal hemorrhage. All the data were entered with SPSS (IBM SPSS Statistic for Windows, Version 19.0). Two-Sample Kolmogorov-Smirnov test (association between severity of anemia in patient with chronic kidney failure to retinal hemorrhage). Somers'd test (the tendency of correlation between severity of anemia in patient with chronic kidney failure to retinal hemorrhage and tendency correlation between age and retinal hemorrhage). fisher'e exact test (association between age and retinal hemorrhage) were used for analysis. p value of less than 0,05 was considered significant.

III. RESULT

There were 35 subjects with anemia, From 70 eyes, there were 5 eyes excluded criteria because the opacity lens. The most gender in this case were male with total subjects 22 (62,9%). The mean age of subjects was 45 years, and the youngest participant was 22, and the older was 73. The mean time of anemia (hemodialysis) of subjects was 30 month.

Table 1. Distribution Characteristics of Subjects

Characteristic	Total	%
Gender		
Male	22	62,9
Female	13	37,1
Age		
≥18 - 45 years	11	31,4
≥ 45 years	24	68,6
Severity of Anemia		
Mild	11	31,4
Moderate	15	42,9
Severe	7	20,0
life threatening	2	5,7
Time of Anemia (hemodialysis)		
≤ 30 month	29	82,9
> 30 month	6	17,1
Classification of Retinal Hemorrhage		
Subhyaloid and pre retinal hemorrhage	0	0
Flame shape hemorrhage	4	50,0
Dot blot hemorrhage	4	50,0
Subretinal and subretinal pigmen epitelium hemorrhage	0	0

The most retinal hemorrhage occurred in mild anemia was 5 eyes (23.8%), moderate anemia 2 eyes (7.1%), and severe anemia in 1 eye (8.3%) (table 2). of Two-Sample Kolmogorov-Smirnov test obtained $p = 0.376$ which shows there is no relationship between severity of anemia on retinal hemorrhage and it is found that r somers'd - 0.116 where the correlation characteristics are opposite, the worse severity of anemia, the more there is no retinal hemmorrhage.

Table 2. Association Between Severity of Anemia in Patient with Chronic Kidney Failure to Retinal Remorrhage

Severity of Anemia	Retinal Hemorrhage				Total	<i>p</i>	<i>r</i> Somers'd
	Without		With				
	n	%	n	%			
Mild	16	76,2	5	23,8	21	100,0	0,376 - 0,116
Moderate	26	92,9	2	7,1	28	100,0	
Severe	11	91,7	1	8,3	12	100,0	
life threatening	4	100,0	0	0	4	100,0	

The type of flame shape retinal hemorrhage is only found in mild anemia which is 4 eyes. In the type dot blot retinal hemorrhage there is a mild anemia in 1 eye, moderate anemia 2 eyes, and severe anemia 1 eye. (table 3).

Table 3. Characteristic Dot blot and Flame shape retinal hemorrhage

Age	Retinal Hemorrhage				Total	p	r somers'd	
	without		With					
	n	%	n	%				
≥18 - 45 years	19	86,4	3	13,6	22	100,0	1,000	- 0,020
≥ 45 years	38	88,4	5	11,6	43	100,0		

The results of fisher's exact test obtained $p = 1,000$ which showed there was no relationship between age with retinal hemorrhage and by using the somers'd test found $r = - 0,020$ (the opposite correlation), the older age of the research subjects, the less retinal hemorrhage was found.(table 4).

Table 4. Association between Age and Retinal Hemorrhage

Severity of anemia	Retinal Hemorrhage				Total	
	Dot Blot		Flame shape		n	%
	n	%	n	%		
Mild	1	20,0	4	80,0	5	100,0
Moderate	2	100,0	0	0	2	100,0
Severe	1	100,0	0	0	1	100,0
Life threatening	0	0	0	0	0	0

IV. DISCUSSION

Anemia is functionally defined as a decrease in the number of erythrocyte mass (red cell mass) so that it cannot fulfill its function to carry enough oxygen to the peripheral tissue (decrease in Oxygen carrying capacity). Practically anemia is indicated by a decrease in hemoglobin levels, hematocrit or red cell count. But the most commonly used are hemoglobin levels, then hematocrit. Anemia is not a single entity (disease entity), but is a symptom of various underlying diseases.³

In table 1 shows that of the 35 most research subjects were male as many as 22 people (62.9%), while in female as many as 13 people (37.1%). The average (mean) age of the study subjects was 45 years. Where the youngest age is 22 years and the oldest age in this research subject is 73 years. The degree of anemia in this study subject was divided into mild, moderate, severe and life threatening. Where the most research subjects were in moderate anemia levels as many as 15 people. Whereas with a mild anemia as many as 11 people (31.4%), subjects with severe anemia were 7 people (20.0%) and with a degree of life-threatening anemia as many as 2 people (5.7%). The average duration of anemia is 30 months. With the fastest time of 1 month and the longest time is 192 months (16 years). According to data from the 2013 Basic Health Research stated Indonesia that anemia in chronic kidney failure in Indonesia increases with age, besides that, the prevalence in male (0.3%) is higher than that of women (0.2%). This is in line with the research conducted by Arief Tajali which stated in his study of chronic kidney failure, the distribution of respondents by gender was the highest by males (62.1%) than females (37.9%).

In Table 1 shows that there are 4 types of flame shape bleeding (50.0%) and 4 eyes with Dot blot hemorrhage (50.0%). Whereas there was no bleeding of Subhyaloid & pre-retinal types and Subretinal & subretinal pigment epithelium (RPE) bleeding in this study.

This study used 95% confidence intervals ($p < 0.05$) and in Table 2, Two-Sample Kolmogorov-Smirnov Test was conducted which showed no relationship between the degree of anemia in patients with chronic failure of retinal hemorrhage. This is in line with Reznikof's research was of the opinion that since severe anemias alone often do not result in retinal hemorrhage, such hemorrhages might be found to be due to associated thrombocytopenia or leukopenia. which is also in line with research conducted by Robert A which states that anemia does not often cause retinal bleeding but will be more frequent shows bleeding when followed by anoxia due to other causes. However this is contrary to research conducted by Ballantyne and Michaelson which states that retinal changes such as bleeding and exudates occur in severe anemia and Saul merin said patients with severe anemia showed changes in the retina such as bleeding and exudate.^{7,8}

In table 3 it can be seen the distribution of the degree of anemia on the type of retinal dot blot and flame shape bleeding, where the hemorrhage of Dot blot in moderate anemia is 2 eyes, the degree of anemia is mild and severe, each is 1 eye and Dot blot hemorrhage is not found in anemia with life-threatening degree. Whereas Flame shape hemorrhage was found in mild anemia as many as 4 eyes, whereas flame shape retinal bleeding was not found in moderate, severe and life-threatening anemia. In this study no Subhyaloid-pre-retinal hemorrhage and Subretinal-subretinal pigment epithelium (RPE) bleeding were found in this study. This is in line with research conducted by Robert A that in general retinal hemorrhage found in anemia is in the form of a Flame shape.⁷

In Table 4 the distribution of age relationships with retinal hemorrhage was performed by fisher exact test and $p = 1,000$ showed that there was no correlation between age and retinal hemorrhage. This is in line with research conducted by Aisen et al who stated that age does not affect ocular abnormalities. But this is contrary to research by Merin and Freud which states that age is one of the risk factors for fundal lesions in patients with anemia.

V. CONCLUSION

From 35 subjects (65 eyes) there were 4 eyes with Dot blot and 4 eyes with Flame shape retinal hemorrhage. But statistically, There was no association between the degree of anemia on retinal hemorrhage ($p = 0.376$). By testing somers'd it is found that $r = -0.116$, the opposite correlation is the more severe the degree of anemia, the more there is no retinal hemorrhage. And there is no association between age and retinal hemorrhage. ($p = 1,000$). By testing somers'd, it was found that $r = -0.020$, the correlation characteristic was the opposite, where the older the subject, the more there was no retinal hemorrhage.

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