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Association Between Hemoglobin Levels and Depression Status in Geriatric Patients at Prof. DR. I. G. N. G. Ngoerah General Hospital

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***Abstract*---*Background: There is evidence of decreased hemoglobin levels as long as an ageing process in the elderly. Low hemoglobin level conditions not only influence physical status but also mental function in the elderly. Objective: to know the association between hemoglobin level and depression status in the elderly. Methods: This is an analytic cross-sectional study. Data were derived from medical records of elderly/Geriatric patients (age>60 years old) admitted to the Internal Medicine Department of Prof. Dr. I.G.N.G. Ngoerah General Hospital between January to July 2018. Anemia status was defined using WHO criteria and depression was defined using Geriatric Depression Scale (GDS) questionnaires. We use an independent t-test to know the association between a categorical and numeric variable with normal distribution. Statistically significant if $p < 0.05$. Results: A total of 102 patient was enrolled in this study consisting of 47,05% male and 52,94% female. The prevalence of depression in the elderly was 27,45% and there is no statistically different based on age and sex. There is an association between hemoglobin level and depression in the elderly (p=0,037; CI 0,76-3,14). Logistic regression analysis shows that age and hemoglobin level impact depression status in the elderly. Conclusion: There is an association between hemoglobin level and depression status in the elderly.*
Keywords*---*anemia, depression, elderly, hemoglobin.

Introduction

Depression is one of the most common psychiatric disorders in the world. About 300 million people are estimated to be depressed globally (Shafi et al., 2018). In the elderly population, depression is still a serious health problem issue because of its high prevalence and severe complications (Onder et al., 2005). Approximately 12-20% of the elderly population in the community experience depressive symptoms (Kessler et al., 2003; Blazer, 2003). Several cross-sectional studies have shown that elderly people with depressive symptoms have poorer health status, higher rates of

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disability and various comorbidities (Ruo et al., 2003; Onder et al., 2003). In addition, longitudinal studies show depression is a risk factor for increased morbidity, mortality and delayed recovery and disability (Kuo & Pu, 2011; Penninx et al., 1999).

In the elderly population, the patient is often found with low-level hemoglobin (Chen et al., 2012). Several studies have shown that anemia is associated with changes in quality of life, increased risk of falls, infection, morbidity and death in the elderly population (Onder et al., 2005). In studies with elderly populations undergoing hemodialysis, low levels hemoglobin directly affect brain function and are responsible for cognitive impairment and other mental symptoms (Cesariet al., 2004).

In addition, other studies show the effect of anemia on mental function. The relationship between anemia and depression as well as cognitive function in the geriatric population is still controversial. A study in Japan showed that a significant decrease in hemoglobin levels resulted in the appearance of depressive symptoms in the elderly female population (Umegaki et al., 2011). A cohort-based Italian study showed that depressive symptoms were associated with anemia in the elderly population in the community (Onder et al., 2005). Based on the description above, it can be seen that there is still controversy regarding the relationship between hemoglobin levels and the incidence of depression in the elderly population, which is the reason for conducting this research (Fishbane & Berns, 2005; Foley et al., 2000).

Methods

This study was an observational study with an analytic cross-sectional design to determine the association between hemoglobin levels and depression. The data was taken from the medical records of geriatric patients who were hospitalized by the Geriatric Division of Prof. Dr. I.G.N.G. Ngoerah Hospital.

The research sample was selected utilizing consecutive random sampling. The inclusion criteria were used for patients aged over 60 years who were treated in the Geriatric Room at Prof. Dr. I.G.N.G. Ngoerah Hospital from 1 January to 31 December 2018. The exclusion criteria used were patients with stroke, dementia, patients with acute bleeding, history of alcohol consumption in the last 3 months, patients with impaired consciousness (GCS<15), patients with cognitive impairment, use of drugs that affect hemoglobin status (anticoagulants, aspirin, NSAIDs, SSRIs, hormonal replacement therapy, chemotherapy and corticosteroids), history of previous psychiatric disorder and Parkinson's. Acute bleeding is defined as a sudden decrease in hemoglobin due to various sources of bleeding resulting in anemia (Richard, 2016). In addition, patients with a history of bleeding in the last 3 months were also excluded from this study (Richard, 2016).

Data from medical records were collected containing information regarding age, gender, education level, occupation, diagnosis, comorbid factors and hemoglobin levels. Hemoglobin levels were examined using the Automatic Analyzer (photometer) method. According to WHO, anemia is defined as hemoglobin <13 gr/dl for men and Hb<12 for women. Symptoms of depression are calculated using the Geriatric Depression Scale (GDS) which contains 30 items where the results are categorized into 2, namely normal (score 0-9) and depression (>9). Comorbid factors were calculated using the Charlson Comorbidity Index Scoring System (CACI). In this study, comorbid factors were considered confounding factors. Comorbid factors include systemic diseases that are likely to cause depressive symptoms in patients (Quan et al., 2011).

Statistical analysis using IBM SPSS Statistics version 21. Continuous and normally distributed data is presented in the form of mean + SD whereas if it is not normally distributed it is presented in the form of median and interquartile intervals. The normality test uses the Kolmogorov-Smirnov test, then categorical data is presented in percentage form (MS, 2015).

Hypothesis testing used unpaired t-test to determine the relationship between hemoglobin levels and depression. Multivariate analysis used logistic regression to analyze confounding factors in this study. Data analysis was performed using the Statistics Program for Social Sciences v. 21. (SPSS Inc., USA). The significance level (α) of this study was set at a probability value (p) of less than 0.05 with a 95% confidence interval (MS, 2015).

Results

A total of 102 patients participated in this study, characteristics of the patient can be seen in Table 1. The total sample consists of 48 men and 54 women with an age range of 60-89 years. The prevalence of anemia in geriatric patients who were hospitalized at Prof. Dr. I.G.N.G. Ngoerah General Hospital was 65.68% consisting of 35.29% men and 30.29% women. However, there was no significant difference between the two populations, in terms of age (p=0.45) and sex (p=0.97). The prevalence of depression in geriatric patients who were hospitalized at Prof. Dr.

I.G.N.G. Ngoerah General Hospital was 27.45%, which consisted of men and women who had the same rate of 13.72%. No differences were found in the two populations either in terms of age (0.175) or sex (0.886).

Table 1
Characteristics of the research sample

Variable	N = 102
age (year), *mean*	72,61 +7.06
sex, n (%)	
Male	48 (47,05)
Female	54 (52,94)
Occupation, n (%)	
Unemployment	4 (3,92)
Government employees	42 (41,17)
Private employees	16 (15,68)
National Army	13 (12,74)
Household servant	10 (9,8)
Teachers	11 (10,78)
Others	6 (5,88)
Education, n (%)	
Illiterate	87 (85,29)
Elementary school	5 (4,9)
Junior High School	1 (0.98)
Senior High School	4 (3,92)
Others	5 (4,9)
Hemoglobin level (gr/dl), *mean*	11,22 + 2,72
Anemia status, n (%)	
Yes	67 (65,68)
Male	36 (35,29)
Female	31 (30,39)
No	35 (34,31)
Male	12 (11,76)
Female	23 (22,5)
Depression status, n (%)	
Yes	28 (27,45)
Male	14 (13,72)
Female	14 (13,72)
No	75 (73,52)
Male	34 (33,33)
Female	40 (39,21)
CACI, mean	5 (3-13)

Abbreviation : CACI: *Charlson comorbidity Index scoring system*

The relationship between hemoglobin levels and depression uses an unpaired t-test because the data is normally distributed. The results can be seen in Table 2. From the hypothesis test, it was found that there was a significant relationship between hemoglobin levels and depression (p=0.02; CI 0.76-3.14).

Table 2
Association between hemoglobin level and depression

Depression	Mean (SD)	p-value	CI 95%
Yes	9,80 + 2,71	0,002	1,95 (0,76 – 3,14)
No	11,76 + 2,54		

Unpaired T test

A logistic regression test was used to analyze the confounding factors of the study, in this case, age, sex and comorbid factors. The results of the analysis test can be seen in Table 3. From the results of the statistical tests, it was found that age (OR 1.091 [CI 95% 1.007-1.183] p=0.033) and hemoglobin levels (OR 0.707 [CI 95% 0.58-0.861] p=0.001) significantly affect depression in geriatric patients.

Table 3
Risk Factors Affecting Depression in Geriatric Patients

Risk Factors	OR (95% CI)	P
Age	1.091 (1,007-1,183)	0,033
Sex	1,467 (0,559-3,849)	0,436
Hemoglobin level	0,707 (0,58-0,861)	0,001
CACI	0,858 (0,621-1,186)	0,858

Logistic regression test

Discussion

In this study, the prevalence of anemia in geriatric patients was 65.68%. This result was higher than data from Gaskell et al. (2008), globally, namely 12% in community patients and 40% in hospitalized patients. [15] In this study, anemia classification used WHO criteria because there were no specific criteria regarding anemia in the geriatric population. This is not appropriate because theoretically there is a decrease in hemoglobin levels with age, although this was not proven in this study (p = 0.45).[16] Consistent results were obtained from the Corona et al. study (2014) which found an increase in the prevalence of anemia by age, 60-69 (4.1%), 70-79 (9.4%) and >80 (16.9%) significantly (p<0.001) (Corona et al., 2014).

The mechanism of the decrease in hemoglobin levels related to age may be due to an increase of erythropoietin needed. Increasing age results in cause increase in the need for erythropoietin while the hormonal capacity of the kidneys is not able to meet this need (Ernawati et al., 2022). Another explanation is that during the ageing process, there is an increase in inflammatory cytokines which results in a decrease in the body's sensitivity to erythropoietin. In addition, inflammatory cytokines can induce hepcidin expression (anemia associated with inflammation) and inhibit the formation of erythrocytes in the bone marrow (Corona et al., 2014).

Gaskell et al. (2008), stated that there was a slight difference in the prevalence of anemia in men (28%) and women (25%). This is consistent with our study where there were no significant differences by sex in the elderly population (p=0.97). The same results were also found by Corona et al. (2014), namely the prevalence of anemia in the geriatric population of men (7.3%) and women (7.9%).

Based on the study of Steensma & Tefferi (2007), most anemia in geriatrics covering 30% of the population is caused by nutritional deficiencies such as iron deficiency, folic acid and vitamin B12. Other causes include chronic disease, myelodysplastic syndrome, iatrogenesis, alcohol and idiopathy (Steensma & Tefferi, 2007). Myelodysplastic syndrome is a hematopoietic disorder that often appears in populations over 65 years of age (Steensma & Tefferi, 2007).

The high prevalence of anemia in the geriatric population is a serious health problem. This is because in anemia there is an increased risk of cardiovascular disease, cognitive impairment, decreased physical performance, decreased quality of life and increased risk of falls and fractures. In addition, the condition of anemia in the geriatric population significantly increases the length of stay, morbidity and mortality rates. The first step that can be taken is to determine a clear definition of anemia in the geriatric population (Corona et al., 2014).

Depression is a psychiatric disorder in the elderly population and has serious health complications. Depression is the second global problem in 2010 and is expected to rank first in 2020 (Mirkena et al., 2018). Based on WHO data in 2017, the global prevalence of depression in the geriatric population is around 10-20% depending on the cultural customs of the group, or around 300 million people in 2015 (Mirkena et al., 2018). This study found a higher result approximately 27.45%. This result is still higher than Barua et al. (2011), who said the prevalence of depression in geriatrics was around 10.3% with a QR of around 4.7% and 16%.

In this study, there was no difference in the prevalence of depression either in age (0.175) or gender (0.886). Different results were obtained by Mirkena et al. (2018), where it was found that women have a 1.7 times higher risk than men [AOR = 1.72, 95% CI (1.12, 2.66)]. Different results were also obtained based on age groups, namely 60-64 (46.8%), 65-69 (26.8), 70-74 (14.4%) and > 75 (12%) (Mirkena et al., 2018).

From the results of this study, it was found that there was a relationship between hemoglobin levels and depression in the elderly (p=0.02; CI 0.76-3.14). The results are following the research of Chen et al. (2014), where a negative correlation was found between hemoglobin levels and the GDS depression score of 15 (r=-0.245, p=0.001). After controlling for confounding variables, namely age, education level and smoking status, the results were still significant (r=-0.261, p<0.001) (Chen et al., 2012). When logistic regression analysis was performed, this study also showed consistent results where there was a relationship between hemoglobin levels and depression in the geriatric population (OR 0.707 [95% CI 0.58-0.861] p=0.001).

Different results were obtained from a study in England in 2009 (3816 samples with ages 65.4 + 9 years) but found no significant relationship between hemoglobin levels and depression in geriatric patients undergoing medical treatment. This may be due to differences in sample characteristics including ethnic differences or perceptions of depression (Hamer & Molloy, 2009).

Various theories have been put forward regarding the relationship between low hemoglobin levels and depression. However, the mechanism of this occurrence requires further research (Alexopoulos, 2005; Carman et al., 2000). It is possible that the relationship between low hemoglobin levels and depression is reciprocal and has multiple risk factors that influence one another.[9]

First, depression is likely to result in a decrease in hemoglobin levels due to changes in behavior including impaired nutritional intake and excessive drinking habits. Vulser et al. (2016), stated that populations with nutritional disorders are closely related to low economic status. Impaired nutritional intake includes deficiencies of vitamins (vitamin B12, folic acid) and minerals (zinc). In addition to disrupting nutritional intake, it also results in the activation of the inflammatory response, triggering normochromic normocytic anemia through increased inflammatory markers in the form of C-reactive protein and interleukin-6. In addition, in patients with depression, there is an increase in a sympathetic tone which affects the process of erythropoiesis from the spinal cord through the catecholamine pathway (Vulser et al., 2016).

Depression can also occur due to low hemoglobin levels. In anemia, symptoms of severe fatigue occur, resulting in decreased quality of life and emotional disturbances. Another hypothesis is said to be due to the disruption of cerebral oxygen flow. In anemia conditions, there is an increase in cerebral blood flow in the frontal, middle temporal and hippocampal regions where these pathways play a role in causing depressive symptoms (Vulser et al., 2016).

There is another theory state that anemia and depression may be related because they have risk factors that influence one another (Beghé et al., 2004). First, an increase in glucocorticoid hormones due to acute or chronic stress is associated with depression and anemia. High levels of glucocorticoids result in decreased neurogenesis and disrupt neuroplasticity resulting in depressive symptoms due to disruption of cognitive and emotional functions in the brain. Increased glucocorticoids interfere with mucus secretion and regeneration of gastric cells resulting in gastrointestinal bleeding due to mucosal damage (Vulser et al., 2016).

Stress, both acute and chronic, also causes an increase in oxidative stress biomarkers which results in depression and decreased hemoglobin. Decreased levels and activity of antioxidants were found in patients with depression (McKay et al., 2006; Levinson, 2006). Anti-oxidants such as glutathione peroxidase and glutathione reductase play a role in protecting the hemoglobin cell wall from free radicals. Deficiencies of glutathione peroxidase and glutathione reductase are significantly associated with reduced hemoglobin levels (Vulser et al., 2016).

Other pathological events include activation of the inflammatory response in states of depression and anemia. Increased inflammatory markers such as C-reactive protein, fibrinogen, tissue plasminogen activator and cytokines are found in depressed patients (Tefferi, 2003; Gangat & Wolanskyj, 2013). Anemia due to inflammation is usually normochromic, normocytic, and usually mild. Anemia arises due to the shorter life span of erythrocytes.[22] 22 Women with bleeding due to menstruation also have a risk of anemia and depression (Vulser et al., 2016).

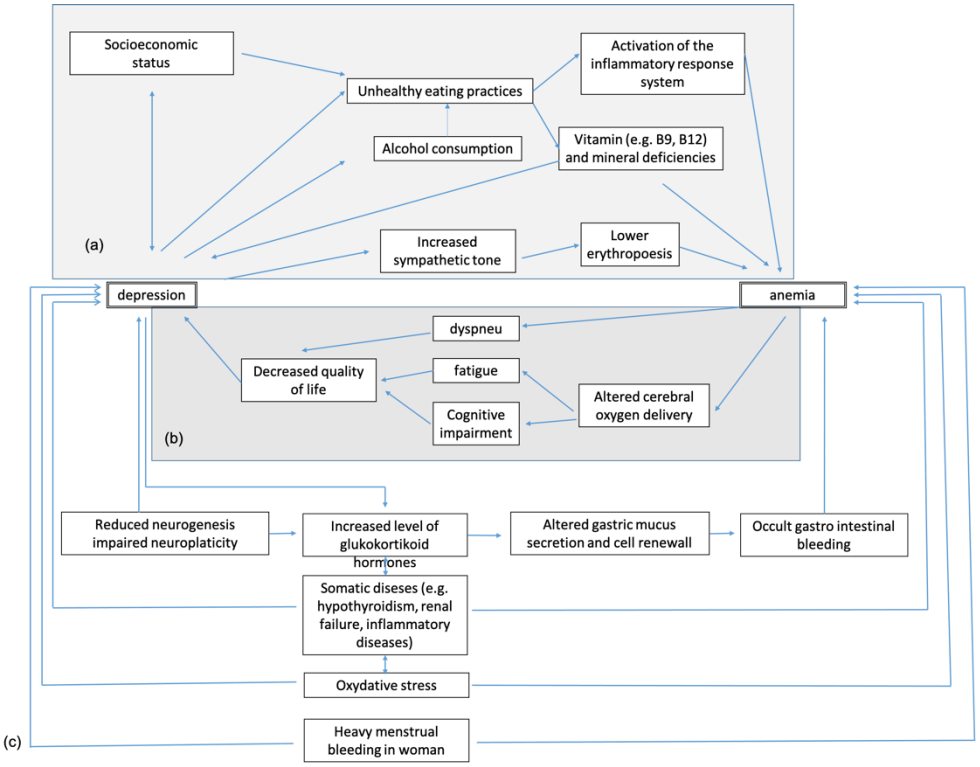

Figure 1. The hypothesis of the relationship between anemia and depression. (a) the hypothesis of depression causing anemia (b) the hypothesis of anemia causing depression. (c) the hypothesis of depression and anemia influence each other (Vulser et al., 2016)

The limitation of this study is that this study uses a cross-sectional method so it does not determine the risk factors that influence depression. In addition, a longitudinal study needed that contains more variables so that it can explain the relationship between hemoglobin levels and depression along with other confounding factors.

Conclusion

The conclusions of this study are:

1) The prevalence of anemia in geriatric patients who are hospitalized at Prof. Dr. I.G.N.G. Ngoerah General Hospital is 65.68%.
2) The prevalence of depression in geriatric patients who are hospitalized at Prof. Dr. I.G.N.G. Ngoerah General Hospital is 27.45%.
3) There is a relationship between hemoglobin levels and depression in geriatric patients.
4) Increasing age and decreasing hemoglobin levels are proven to increase the risk of depression in geriatric patients who are hospitalized at Prof. Dr. I.G.N.G. Ngoerah General Hospital

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