Original Article

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Anemia and Aggression Among Patients with Schizophrenia in Amino Gondohutomo A Hospital

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Abstract

Background: Anemia has been identified as a potential modifiable factor influencing aggression levels in individuals with schizophrenia.

Objective: To investigate the association between anemia and incidence of aggression in patients with schizophrenia in Amino Gondohutomo Psychiatric Hospital, Semarang, Indonesia.

Methods: A cross-sectional study was conducted between January 2022 and December 2023 on patients with schizophrenia in Amino Gondohutomo Psychiatric Hospital, Semarang, Indonesia. Subjects were selected using consecutive sampling technique, and individuals with affective mood disorder and lost to follow-up were excluded from the study. Data were obtained through patients' medical records, PANSS-EC scores, and hemoglobin measuring devices. Chi-square test and logistic regression were applied for statistical analyses.

Results: Of 100 participants, patients with schizophrenia presented with aggression were predominantly above 40 years old (26 patients, 81.3%), women (17 patients, 51.1%), and non-anemic (17 patients, 57.1%). Gender and anemia were significantly associated with aggression in patients with schizophrenia ($p<0.05$). Schizophrenic patients with anemia had a 7.68-fold greater risk (95% CI: 2.70–21.8) of aggression. Men with schizophrenia was associated with a 2.37-fold greater risk (95% CI: 1.00–5.60) of aggression.

Conclusion: Anemia and men seems to be risk factors of aggression in patients with schizophrenia. Further multicenter studies with larger sample size is needed to support this finding.

Keywords: Aggression, anemia, schizophrenia

Introduction

Schizophrenia is a severe psychiatric disorder characterized by symptoms such as delusions and hallucinations, affecting approximately 1% of the global population.[1] According to the 2018 Indonesian Basic Health Research, the prevalence of schizophrenia in Indonesia increased by 1.7 per million compared to the 2013 data.[2] During the acute phase, schizophrenia patients had either positive symptoms or negative symptoms. Positive symptoms such as delusions and auditory or visual hallucinations. As the symptoms begin to worsen, the patient's coping also becomes progressively worse. Anger and aggression made their delusions and hallucinations start to overtake their thinking and functioning. Patients become aggressive and threaten themselves and others. At this stage, inpatient care is often necessary to ensure stabilization and safety for both the patient and others.[3,4]

The patient with schizophrenia at the acute phase had increased dopaminergic activity but decreased serum iron. The BBB (Blood-brain barrier) is impermeable to iron. There is slow bidirectional transport of iron across the BBB. In schizophrenic patients, there is increased BBB permeability and decreased serum iron.[5] Iron deficiency anemia can affect dopamine receptor levels and disrupt sensitivity functions of brain regions leading to psychosis.[6] Poor perfusion caused by anemia also may lead to fatigue, decrease in stamina, dizziness, dyspnea, or syncope.[7] Megaloblastic anemia due to vitamin B12 deficiency can manifest with psychosis through mechanisms related to one-carbon metabolism and neurotransmitter synthesis.[8]

Jiang *et al*. found no significant association between anemia and cognitive function in schizophrenia patients.[9] A previous study conducted by Lee *et al*.[10] showed that iron deficiency anemia subjects had a significantly increased risk of psychiatric disorders, including panic disorder, sleep disorder, and psychosis. However, data on the association between anemia and aggression in patients with schizophrenia are scarce. The purpose of this study was to investigate the association between anemia and the incidence of aggression in patients with schizophrenia.

Methods

This observational analytic study with a cross-sectional design was conducted at Dr. Amino Gondohutomo Psychiatric Hospital in Semarang between January 2022 and December 2023. A total of 100 inpatients diagnosed with schizophrenia were included using a consecutive sampling method. The inclusion criteria were patients admitted with a diagnosis of schizophrenia during the study period who had experienced psychiatric symptoms for at least two years. Patients with affective mood disorders or those lost to follow-up were excluded from the study.

The target population for this study was all individuals diagnosed with schizophrenia, while the accessible population comprised schizophrenic inpatients at Dr. Amino Gondohutomo Psychiatric Hospital within the defined period. The sample size of 100 was obtained through consecutive sampling based on the specified inclusion and exclusion criteria.

Data were obtained through interviews, patients' medical records, hemoglobin measuring devices, and PANSS-EC. Each subject's hemoglobin level was examined using a hemoglobin measuring device. Patients were categorized into two groups: those with anemia (hemoglobin <11 g/dL) and those without anemia (hemoglobin ≥11 g/dL). PANSS-EC scores were used by evaluating each sign on a scale from 1 to 7. Participants were categorized into schizophrenia patients with aggression (PANSS-EC score ≥20) and without aggression (PANSS-EC score <20).

Data were analyzed using descriptive analysis and presented in frequency and percentages. Hypothesis test was performed to determine the *p* value using chi-square test and logistic regression. Ethical clearance was obtained from the This study received ethical approval from the Health Research Ethics Committee of Dr. Amino Gondohutomo Psychiatric Hospital, Semarang (Reference number: 420/1116).

Results

Table 1 summarizes the demographic and clinical characteristics of the study participants. Among patients with schizophrenia who exhibited aggression, the majority were over 40 years old (26 patients, 81.3%), female (17 patients, 51.1%), and non-anemic (17 patients, 57.1%). Comparable results were found regardless of the marital and occupational status (16 patients, 50.0%).

Table 2 presents the association between participant characteristics and no aggression, as measured by the PANSS-EC score. A chi-square test with continuity correction was used to calculate the prevalence ratio (PR), confidence intervals (CI), and identify variables with statistically significant associations to be included in the logistic regression model. Gender (PR 2.37, 95% CI [1.00–5.60]; p= 0.047), marital status (PR 2.57, 95% CI [1.07–6.16]; p=0.031), and anemia (PR 7.68, 95% CI [2.70–21.80]; p=0.001) were significantly associated with aggression levels based on PANSS-EC. Age and occupational status were not significantly associated (p>0.05).

Logistic regression was carried out to determine the association between gender, marital status, and anemia, with PANSS-EC, as described in Table 3. Gender (95% CI [1.301–9.873]; p=0.014) and anemia (95% CI [3.298–32.634]; p<0.001) were risk factors of incidence of aggression based on PANSS-EC in patients with schizophrenia in Amino Gondohutomo Psychiatric Hospital.

Marital status, however, did not show a statistically significant association (95% CI

Table 1 Characteristics of Participants

Characteristics	Aggression*		No Aggression	
	(n=32)	%	(n=68)	%
Age				
<40 years old	26	81.3	48	70.6
>40 years old	6	18.8	20	29.4
Gender				
Men	15	46.9	46	67.6
Women	17	53.1	22	32.4
Marital Status				
Married	16	50.0	49	72.1
Unmarried	16	50.0	19	27.9
Occupational Status				
Employed	16	50.0	36	52.9
Unemployed	16	50.0	32	47.1
Anemia				
Anemic	15	46.9	7	10.3
Non-Anemic	17	53.1	61	89.7

Note: Aggression is defined as a PANSS-EC score≥20

[0.787–5.714]; p=0.137).

Discussion

Symptoms of aggression in patients with schizophrenia including poor control of impulses, tension, hostility, uncooperativeness, and aggressive behavior, can be measured using the validated subscale of PANSS score, namely PANSS-EC. Each item is scored from 1 to 7, and a total score of more than 20 is considered indicative of acute aggression.[12] Prevalence of aggression and factors associated with aggression were essential to effectively

Table 2 Association Between Characteristics of Participants and No Aggression Based on PANSS-EC

Variable	PANSS-EC		Total	p-value	PR (95% CI)
	(n=68)	%			
Age				0.257	1.80 (0.64–5.05)
<40 years old	48	70.6	74		
>40 years old	20	29.4	26		
Gender				0.047*	2.37 (1.00–5.60)
Men	46	67.6	39		
Women	22	32.4	61		
Marital Status				0.031*	2.57 (1.07–6.16)
Married	49	72.1	35		
Unmarried	19	27.9	56		
Occupational Status				0.748*	1.12 (0.48–2.60)
Employed	36	52.9	48		
Unemployed	32	47.1	52		
Anemia				0.001*	7.68 (2.70–21.8)
Anemic	7	10.3	22		
Non-Anemic	61	89.7	78		

Note: p-values are from Chi-square tests between groups; *statistically significant (p <0.05)

Table 3 Logistic Regression Analysis of Variables Associated with Aggression Based on PANSS-EC

Variables	p-value	PR	95% CI
Gender	0.014*	3.583	1.301–9.873
Marital Status	0.137	2.121	0.787–5.714
Anemia	<0.001*	10.375	3.298–32.634

Note: Statistically significant results (p<0.05)

control the risk of aggression in patients with schizophrenia. Previous study stated that aggression in patients with schizophrenia was associated with severe psychotic symptoms, substance abuse, previous history of violence, men, young age, unmarried status, and poverty.[13]

Out of 100 patients with schizophrenia involved in this study, 46 (67.6%) of 68 patients without aggression were men. Furthermore, 15 (46.9%) of 32 patients with aggression were men, compared to 17 women (53.1%). In this study, gender was associated with aggression in patients with schizophrenia (p <0.05), and men with schizophrenia was associated with a 2.37-fold greater risk (95% CI: 1.00–5.60) of aggression. Similar results were found in a previous study in England which stated that there was significant association between men with physical aggression (49.2%), assault attack (21.2%), and violence behavior against others (11.8%).[14] On the contrary, a study conducted by Krakowski stated that there were no significant gender differences in incidence of aggression. This result might be due to similar percentage of men and women in the study. Another previous study also reported that women experienced higher verbal violence and early disclosure of physical violence. Positive psychotic symptoms in women and men were associated with violence incidence. Physical violence was found to be more common in men, related to addiction of substance, criminal acts, and history of school truancy.[15]

Anemia can manifest in neuropsychiatry symptoms, including mood disorder, anxiety disorder, sleep disorder, and psychosis. Iron deficiency anemia, typical nutrient deficiency anemia, can present with fatigue, dizziness, or immune disorder. Iron is essential for every living organism to deliver oxygen, cellular respiration, immune system, neurotransmitter metabolism, and DNA synthesis.[13] A previous study reported that iron deficiency anemia was significantly associated with negative symptoms in patients with schizophrenia.[16]

Out of 100 patients with schizophrenia in this study, 61 (89.7%) of 68 patients without aggression had no anemia. Furthermore, 17 (53.1%) of 32 patients with aggression had no anemia, compared to 15 anemic patients (46.9%). Anemia was significantly associated with aggression in patients with schizophrenia (p<0.05). In addition, anemia in patients with schizophrenia had a 7.68-fold greater risk (95% CI: 2.70–21.8) of aggression. This study concludes that anemia influences the incidence of aggression in schizophrenia. So tailor-made management for schizophrenia patients is needed, especially for screening anemia.

Iron deficiency anemia is associated with schizophrenia related to dopamine receptor level and disrupt sensitivity function of brain region resulting in psychosis. Iron deficiency anemia also aggravates myelination in brain and monoamine metabolism disruption.[6] A previous study showed that iron deficiency anemia affects glutamate and GABA neurotransmitter homeostasis resulting in cognitive, memory, and behavioral disorder, as well as emotional and psychological disorder.[17] On the other hand, anemia is also a side effect of drugs that control psychosis and affect the production and longevity of red blood cells leading to anemia. Furthermore, lifestyles such as malnutrition and unhealthy eating habits can make inadequate intake of iron, vitamin B 12 and folate contribute to the development of anemia. This correlation between drug and lifestyle with aggression in schizophrenia patients can be conducted in future studies.

This study has several limitations. It was conducted at a single center and involved a relatively small sample size, which may limit the generalizability of the findings. Future multicenter studies with larger cohorts are necessary to further explore the relationship between anemia and aggression, and to evaluate other contributing factors, such as medication effects, nutritional deficiencies, and comorbid medical conditions. In conclusion, this study identified anemia and

male gender as significant risk factors for aggression in patients with schizophrenia at Amino Gondohutomo Psychiatric Hospital.

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