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CORRELATION BETWEEN POSITIVE AND NEGATIVE SYNDROME SCALE (PANSS) SCORES AND HOMOCYSTEINE LEVELS IN MEN WITH SCHIZOPHRENIA BATAKNESE TRIBE AT PSYCHIATRIC HOSPITAL OF PROF. M. ILDREM MEDAN

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Ridha Rizki, Elmeida Effendy, Vita Camellia, Freddy Subastian: Correlation between Positive and Negative Syndrome Scale (PANSS) Scores and Homocysteine Levels in Men with Schizophrenia Bataknese Tribe at Psychiatric Hospital of Prof. M. Ildrem Medan --Palarch's Journal Of Archaeology Of Egypt/Egyptology 17(6), 1-14. ISSN 1567-214x

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ABSTRACT

In people with schizophrenia, high serum homocysteine levels are associated with poor clinical symptoms, especially in the negative symptom domain and general psychopathology with PANSS score assessment. Many studies have been studied about consensus that homocysteine is an important indicator for mental disorders such as autism, schizophrenia, depression, and bipolar disorder. To find out the correlation between PANSS scores and homocysteine levels in men with schizophrenia in the Batak tribe in the mental hospital prof. M. Ildrem Medan. A correlation analytic study with cross sectional design using PANSS score measurement and examination of serum homocysteine levels in men with schizophrenia of the Batak tribe during the July-September 2019 period in the inpatient installation of psychiatric hospital of Prof. Ildrem Medan. A total of 105 subjects who met the inclusion criteria of men with schizophrenia of the Batak tribe who were diagnosed with PPDGJ III, ages 20-45 years, length of illness ≥ 2 years. Participants who suffergeneral medical disorders and or other comorbidities, the use of other psychoactive substances and use of supplements that contain folic acid and vitamin B exclusion from this study. There is a significant correlation between positive PANSS scores and Homocysteine levels in Batak schizophrenic men, a correlation coefficient of r = 0.529 shows a positive correlation with moderate correlation strength (r = 0.4 - (0.6)) with a value of p =

0.001). There is a correlation between negative PANSS scores and Homocysteine levels in the Batak schizophrenic men, the correlation coefficient is r = 0.544 with moderate correlation strength ($r = 0.4 - \langle 0.6 \rangle$) with p = 0.001. There is a significant correlation between PANSS scores of general psychopalogy and Homocysteine levels in schizophrenic men of the Batak tribe, the correlation coefficient of r = 0.633 with the strength of strong correlations ($r = 0.6 - \langle 0.8 \rangle$) with p = 0.001. There is a significant correlation between the PANSS Total Score and Homocysteine Levels in men with schizophrenia of the Batak tribe, the correlation coefficient of r = 0.668 shows a positive correlation with strong strength ($r = 0.6 - \langle 0.8 \rangle$) with a value of p = .001.

Introduction

Schizophrenia is a complex disorder of brain function with wide variations in symptoms and signs, and in the course of the disease, there are apparent deficits in neurological, psychological and social function, appearing to have a number of genetic and environmental causes. This disorder involves the most basic functions that give normal people a feeling of personality (individuality), uniqueness, and self-direction (self-direction). Schizophrenia is the most common and most important disorder in the clinical spectrum that is similar (and may be genetically related), which includes schizoaffective disorder, schizotypal disorder and acute transient psychotics. The term schizophrenia includes a variety of clinical presentations and personal experiences resulting from complex interactions between genes and the environment.¹

Many studies have found a positive correlation between Homocysteine levels with the severity of negative symptoms and general psychopathology as assessed by the PANSS score. Elevated levels of homocysteine are considered a risk factor for Alzheimer's disease and changes in this pathway are also associated with mental disorders such as autism, schizophrenia, depression, and bipolar disorder.² Increased plasma levels of amino acid homocysteine have been linked to schizophrenia, especially in young male patients.³

Homocysteineis an amino acid sulfur that is formed by demethylation of the nutrient methionine. Folate and B12 are cofactors in their metabolism. At high concentrations it is considered a neurotoxic substance, causes activation of the causes excitotoxicity.3 N-methyl-D-aspartate (NMDA) receptor and Homocysteineproduced from S-adenosyl-L-homocysteine (SAH) by Sadenosyl-homocysteine hydrolase. SAH is a transmethylation product from Sadenosylmethionine (SAM) made from*methionine* and adenosine triphosphate(ATP). In the metabolic cycle, Homocysteine toore-methylated to methionine through methionine synthase or degraded to cysteine through cystathionine beta-synthase. Homocysteine is also released into the blood and urine. Vitamin B12, folate, and B6 are needed in the Homocysteine remethylation pathway and *transsulphuration pathway*.⁴

Studies by Levine and colleagues have found that elevated Homocysteine levels of 5 μ M / 1, compared to normal levels (> 15 μ mol / L), can represent 70% of the risk of developing schizophrenia. High blood Hcy levels can

represent biological markers for oxidative stress, or signaling activated proinflammatory pathways characterized by increased expression of nitric oxide synthase and cyclo-oxygenase, as evidenced in patients' peripheral mononuclear blood cells. influenced by the first psychotic episode. According to the latest view, hyperhomocysteinaemia can cause changes in DNA⁶ methylation in peripheral leukocytes.

The Indonesian nation is a plural nation consisting of various ethnic groups, religions and languages. Ethnic groups are ethnic and cultural groups of people formed from generation to generation.⁷ The Batak tribe originated from the island of North Sumatra. Based on the Central Statistics Agency, the Batak tribe as much as 8.5 million (3.6 percent). The Batak tribe includes the Angkola of Batak, Karo of batak, Mandailing of batak, Pakpak Dairi of Batak, Simalungun of Batak, Tapanuli of Batak, Toba of Batak and Dairi. The Batak are known for their openness, spontaneity and aggressiveness both physically and verbally. When angry, Bataks often choose to express their anger. Batak people are more likely to expressively express their emotions. the Batak are known for their perseverance, loud talk, courage and decisive action. Therefore Batak people prefer to be frank about the emotions they are feeling

Method

This study is a numerical correlative analytic study with a cross-sectional study approach, the judge Correlation between Positive and Negative Syndrome Scale (PANSS) scores and homocysteine levels in men with schizophrenia in the Batak tribe. This study was conducted at Prof. M. Ildrem Medan's mental hospital, July 2019 - September 2019. A total of 105 subjects fulfilled the inclusion and exclusion criteria by including Batak tribe men with schizophrenia who had been diagnosed based on PPDGJ III, aged between 20 - 45 years. , Schizophrenic patient with illness ≥ 2 years old, Willing to be a respondent and can be interviewed and exclude patients with general medical disorders and or other comorbidities, History of alcohol use and other substances, History of use of supplements containing folic acid and vitamin B (vitamin B 6 and B 12).

Data retrieval of subjects was preceded by screening using inclusion and exclusion criteria, subjects who met the inclusion criteria and did not have exclusion criteria were explained about the aims and objectives of the study. Selected subjects were asked for approval to participate in the study after obtaining an informed consent explanation. Fill in the subject's demographic data.Conducting PANSS assessment of research subjects.In the PANSS measurement, a suitability test is conducted between the researcher and the interester. All study subjects (men with schizophrenia of the Batak tribe were collected for blood sampling as much as 3 ml. Blood sampling was carried out after the subjects took the drug \pm 6-8 hours. Results.

This study was conducted at the M M. Ildrem Psychiatric Hospital in Medan. In June 2019 until September 2019. The research sample was taken by using nonprobability sampling, consecutive sampling. This study has succeeded in getting 48 male subjects with schizophrenia who are undergoing treatment at the Inpatient Mental Hospital of Prof. M. Ildrem Medan.

Demographic characteristics of the research subject

Test the normality of demographic characteristics

For demographic characteristics in this study are presented in table 1. Before conducting further analysis for demographic characteristics normality tests were conducted with the Kolmogorov-Smirnov test because the subjects in this study were above 50 subjects (\geq 50). The numerical variables in this study are presented in the mean and standard deviation if the data are normally distributed (p> 0.05) which can be seen in the appendix. If the data are not normally distributed, (p <0.05) then they are presented in the median (minimum-maximum). For categorical variables presented in the form of numbers and percent.

Table 1 Distribution of Research Subjects Based on Demographic Characteristics of Men with Batak Schizophrenia.

Demographic Characteristics	Average (s, b) Median (minimun-maximum)	n (%)
Age (years)		
21 - 45	32 (21-45) years old	
Level of education		
Elementary school		30 (28.60%)
Middle School		53 (50.50%)
High school		22 (21.0%)
Marital status		
Married		47 (44.80%)
Not Married		58 (55.20%)
Job status		
Work		40 (38.10%)
Does not work		65 (61.90%)
Length of illness (years)	5.00 (2.00 - 10.00)	

* Shapiro-Wilk Test

Table 1 shows the demographic characteristics for the age of medium 32 with a maximum (21-45) years old. Based on the level of elementary school education is 30 people (28.60%), 53 people SMP (50.50%), 22 people high school (21.0%). In marital status, subjects with married status were 47 people (44.80%) and not married 58 people (55.20%). Likewise with the status of work, as many as 40 people working subjects (38.10%) and subjects who did not work as many as 65 people (61.90%). For the duration of illness, a medium of 5.00 with a minimum (2-10) years is found.

After the data normality test was done with the Kolmogorov-Smirnov test, it was found that the PANSS score variable was positive with normal distribution with p value = 0.06, negative PANSS score variable was normal distribution with p value = 0.08, general psychopathology PANSS score variable was not normally distributed with p = 0.03, PANSS total score of positive variables is normally distributed with p = 0.17 and homocysteine levels are normally distributed, it can be obtained the average value of the total PANSS score and the average of homocysteine levels as follows:

Table 2. Average PANSS scores positive for men with schizophrenia in the Batak tribe.

	Ν	Average (sb)	IK95%
PANSS score is positive	105	29.11 (3,09)	28,52-29,71

Table 2 shows the average PANSS positive scores on the subjects of this study obtained by 29.11 and the standard deviation of 3.09.

 Table 3. Average PANSS scores negative in men with Batak schizophrenia.

	Ν	Average (sb)	IK95%
PANSS score is negative	105	30.58 (2.86)	30.03 - 31.13

Table 3 showing the negative PANSS score on the subjects of this study was 30.58 and the standard deviation was 2.86.

Table 4. Average PANSS psychopatalogi scores common in men with Batak schizophrenia.

		Ν	Median	(Minimum-	IK95%
			Maximum)		
PANSS	general	105	36:00 (30-44)	
psychopatholog	y score				

Table 4 shows the average PANSS score of general psychopathology in the study subjects obtained a median of 36.00 and a minimum of 30 and a maximum of 44.

Table 5 Mean PANSS total scores in men with Batak schizophrenia.

NAverage (sb)IK95%PANSS Total Score10595.33 (7.86)93.81-96.85Table 5 shows the average PANSS negative score on the subjects of this study
was 95.33 and the standard deviation was 7.86.Table 6 Mean Homocysteine levels in men with Batak schizophrenia.

NAverage (sb)IK95%Homocysteine levels10521.24 (7,17)19.86-22.63Table 6 shows the mean homocysteine levels in the study subjects obtained by
21.24 and standard deviation 7.17.

Table 7 Correlation between positive PANSS scores and Homocysteine levels

Homocysteine levels

PANSS score is positive r = 0.529p = 0.001n = 105

Pearson correlation test

In table 7 for the Correlation test between positive PANSS scores and Homocysteine levels the correlation test was performed using the Pearson test because the two variables to be correlated were normally distributed. The test results obtained positive correlation between positive PANSS scores and Homocysteine levels with a value of r = 0.529 with a value of p = 0.001.

Table 8 Correlation between negative PANSS scores and Homocysteine levels

Homocysteine levels

PANSS score is negative r = 0.544p = 0.001n = 105

Pearson correlation test

In Table 8 for the correlation test between PANSS negative scores and homocysteine levels, a correlation test was performed using the Pearson test because the two variables to be correlated were normally distributed. The test results obtained were positively correlated between PANSS negative scores and homocysteine levels with a value of r = 0.544 with a value of p = 0.001.

Table 9 Correlations between PANSS scores of general psychopathology and Homocysteine levels

Homocysteine levels

PANSS score of general psychopathology r = 0.633p = 0.001n = 105

Pearson correlation test

In Table 9 for the Correlation Test Between PANSS Score of General Psychopathology and Homocysteine Levels the correlation test was performed using the Pearson test because the two variables to be correlated were normally distributed. The test results obtained were positively correlated between

PANSS scores of general psychopathology and Homocysteine levels with r = 0.633 with p = 0.001.

Table 10 Correlations Between PANSS Total Scores and Homocysteine Levels

PANSS Total Score $r = 0.668$		
p = 0.001		
n = 105		

Pearson correlation test

Homocysteine levels

In table 10 for the Correlation test between positive PANSS total scores and Homocysteine levels, a correlation test was performed using the Pearson test because the two variables to be correlated were normally distributed. The test results obtained positively correlated between Homocysteine Levels and Total PANSS Score with a value of r = 0.668 with a value of p = 0.001.

Discussion

This study is a correlative analytic study with a cross-sectional approach, which is describing and analyzing a situation in a certain moment. In this study, what was analyzed was the Correlation between the Positive and Negative Syndrome Scale (PANSS) Score and Homocysteine Levels in men with schizophrenia of the Batak tribe who were undergoing treatment in the Hospital. The Soul of Prof. M. Ildrem Medan, involving 105 subjects who met the inclusion and exclusion criteria. This research was carried out after obtaining approval from the research ethics committee of the Faculty of Medicine, University of North Sumatra, from the director of the Hospital. Jiwa Prof. M. Ildrem Medan and from research subjects through filling in informed consent.

For statistical analysis IBM SPSS Statistics version 22 is used with Pearson correlation test data analysis when the data are normally distributed. For normality test data used Sapphiro-Wilk normality test because the number of subjects from this study was \geq 50 subjects.

In table 1, sociodemographic characteristics for medium age 32 years with a maximum-maximum (21-45) years. Based on studies byGouaille and Bottiglieri and Diazyme laboratories explained that levels of homocysteine increase with age. Higher total homocysteine concentrations are seen in the elderly (age more than 60 years) can be a consequence of general slowing of metabolism, increased prevalence of intestinal malabsorption or inadequate supply of folate nutrition, vitamins B12, and B6.4,9

Based on a study by Levine and colleagues in 2006 in Israel studied a large sample of inpatients with schizophrenia and suggested that there are sex and age effects that mediate an increase in plasma homocysteine concentrations. The difference between cases and controls is mainly due to schizophrenic male patients younger than 50 years

Based on table 1 in this study researchers only took male subjects. Based on studiesby Gouaille and Bottiglieri it was explained that sex affected the average homocysteine level in males higher than females this was associated with hormonal factors.9

Based on studies by Applebaum and colleagues in Israel in 2004 found an increase in plasma homocysteine concentrations in adolescent patients with schizophrenia, which is almost entirely caused by a subgroup of male patients. It has been suggested that the increase in homocysteine levels found mainly in males can be explained by the decreased effect of homocysteine from estrogen.10

In table 1 based on the level of education in this study were elementary school 30 people (28.60%), junior high school 53 people (50.50%), high school 22 people (21.0%). In marital status, subjects with married status were 47 people (44.80%) and not married 58 people (55.20%). Likewise with the status of work, as many as 40 people working subjects (38.10%) and subjects who did not work as many as 65 people (61.90%).

In the Song and colleagues study found a positive relationship between the serum level of total Homocysteine score and PANSS (r = 0.312, p = 0.035). This relationship remained significant in controlling gender, age, education, smoking status and duration of illness

In table 1 the medium value for the duration of illness in this study is 5.00 years with a maximum-maximum (2-10) years. In the study of Di Lorenzo and colleagues in 2015 in Italy, this study divided the subjects into two groups, namely people with schizophrenia with a long illness for tahun1 years and people with Schizophrenia with illness for> 1 year, and the results obtained that there was a significant increase in homocysteine levels in the group of people with schizophrenia with> 1 year of illness compared to the other groups ($\chi 2$ test, p = 0.02) .12 While in another study by Ma and colleagues in 2009 in Hong Kong it was found that there is no correlation between the length of illness of people with schizophrenia with homocysteine levels with the average length of illness 12.4 years.

In table 2 the mean value of a positive PANSS score on the subject of this study was 29.11 and the standard deviation was 3.09.

In table 3 the mean PANSS negative scores on the subjects of this study were 30.58 and the standard deviation was 2.86.

In table 4 the average PANSS score for general psychopathology in the subjects of this study obtained a median of 36.00 and a minimum of 30 and a maximum of 44.

In table 5 the mean value of the total PANSS score on the subject of this study was 95.33 and the standard deviation was 7.86. The subjects in this study were in the acute phase of treatment. In a study by Song and colleagues in 2014 of first episode schizophrenia patients who were hospitalized with a mean PANSS score of 78.72 and a standard deviation of 4.74.11

Based on table 6, the average value of homocysteine was obtained, which was $21.24 \mu mol / L$ and the standard deviation of 7.17 $\mu mol / L$. In some of the subjects of this study the results obtained increased levels of homocysteine. In the Kim and Moon study in Korea in 2011 comparing schizophrenia and healthy controls. The results obtained were significant differences in homocysteine levels between the two groups (p < 0.001) with mean values and standard deviations for the schizophrenia group 14.30 ± 13.10 and mean values and standard deviations for the healthy control group 9.12 \pm 6.36 μ mol / L. However, this study did not assess the PANSS score in the schizophrenia group.¹⁴The Levine J study and colleagues in Ireland in 2004 found that there were no statistically significant differences between schizophrenia and control patients in two different patient populations and in different decades. No difference was also found in young male patients with schizophrenia who were hospitalized. In study Athere were no significant differences in the average CSF homocysteine in Study A between schizophrenic patients ($X \pm SD = 0.038$ \pm 0.05 µm / L) and Control (0.012 \pm 0.04 µm / L) or in Study B (schizophrenia patients, $0.022 \pm 0.03 \ \mu\text{m}$ / L vs control, $0.018 \pm 0.03 \ \text{mm}$ / L). There was no average difference in CSF homocysteine between Study A and Study B.15

In a 2014 study by Narayan in India, the mean and standard deviation of homocysteine levels in the paranoid schizophrenia, catatonic schizophrenia and unspecified schizophrenia groups were respectively (16.5 ± 9.5 , 18.4 ± 12 , and 15, $4 \pm 7.7 \mu mol / L$).16

Table 7 shows the results of the Pearson correlation test between positive PANSS scores and Homocysteine levels in schizophrenic men of the Batak tribe were statistically very significant showing a positive correlation of 0.529 with moderate correlation strength ($r = 0.4 - \langle 0.6 \rangle$, p = 0.001) with interpretation that the higher homocysteine levels means the higher PANSS positive scores in men with schizophrenia. In contrast to a 2014 study by Narayan in India where Homocysteine levels were not significantly different in homocysteine levels between schizophrenic subtypes. PANSS positive symptom scores from schizophrenia did not significantly correlate with Homocysteine levels (r = 0.007, p = 0.9).17

Table 8 shows the results of the Pearson correlation test between PANSS negative scores and Homocysteine levels in schizophrenic men of the Batak tribe statistically very significantly showing a positive correlation of 0.544 with

moderate correlation strength ($r = 0.4 - \langle 0.6 \rangle$, p = 0.001) with interpretation that the higher homocysteine level means the higher PANSS score is negative in men with schizophrenia.

A study from Bouaziz N and colleagues, in 2010 in Tunisia of men with schizophrenia, showed that there was a significant positive correlation between homocysteine levels and the 'anhedonia-asociality' subscale of the Scale for the Assessment of Negative Symptoms (SANS), (r = 0.37; p = 0.01) and there is also a positive correlation between homocysteine levels and the 'avolution-apathy' subscale (r = 0.30; p = 0.04) using the PANSS score.17

In the study by Misiak B and friends in 2014 found a positive correlation between Homocysteine levels and the severity of negative symptoms (r = 0.363, p = 0.006) in first-episode schizophrenia patients where the assessment was using the Positive and Negative Syndromes Scale (PANSS) .18

Table 9 shows the results of the Pearson correlation test between PANSS scores of general psychopalogy and Homocysteine levels in schizophrenic men of the Batak tribe statistically very significantly showing a positive correlation of 0.633 with a strong correlation strength ($r = 0.4 - \langle 0.6 \rangle$, p = 0.001) with interpretation that the higher the homocysteine level means the higher PANSS psychopathological score in men with schizophrenia.In the study by Misiak and friends in Poland in 2014 found a positive correlation between Homocysteine levels with the severity of negative symptoms and general psychopathology as assessed by the PANSS score (respectively; r = 0.363, p = 0.006 and r = 0.349, p = 0.008,). It was found that an increase of 5 µmol / 1 plasma homocysteine can increase the risk of schizophrenia by up to 70% .18

Table 10 shows the Pearson correlation test between PANSS Total Score and Homocysteine levels in the Batak schizophrenia statistically very significantly showing a positive correlation of 0.668 with strong correlation strength (r = 0.4 - <0.6), p = 0.001) with interpretation that the higher homocysteine levels means the higher the total PANSS score in men with schizophrenia.

In a study by Song and colleagues in 2014 of first episode schizophrenia patients who were hospitalized with a mean PANSS score of 78.72 and a standard deviation of 4.74. This study controlled for several confounding factors such as gender, age, history of substance use, and duration of pain. Statistically significant results showed a positive correlation with homocysteine and PANSS levels with a mean of 25.31 μ mol / L and standard deviation of 9.30 μ mol / L, (r = 0.312, p = 0.035).11

A study by Song found that Higher serum Homocysteine levels are associated with worse clinical symptoms of schizophrenia, especially in the negative symptom domain. Exposure to folic acid deficiency in the fetus and increased levels of Homocysteine in pregnant women have been identified as risk factors for hereditary schizophrenia. This study reports that there is a negative correlation between serum folate levels and the severity of negative symptoms in individuals with schizophrenia. Homocysteine is formed by methionine demethylation and acts as a neurotoxin through action on NMDA receptors and by increasing oxidative stress, folate and B12 are cofactors in metabolism. Folate deficiency causes high levels of Homocysteine, which is likely to contribute to the development of schizophrenia. 11

In contrast to a 2014 study by Narayan in India where Homocysteine levels were not significantly different in homocysteine levels between schizophrenic subtypes. The mean and standard deviation of homocysteine levels in the paranoid schizophrenia, catatonic schizophrenia and unspecified schizophrenia are respectively (16.5 ± 9.5 , 18.4 ± 12 , and $15.4 \pm 7.7 \mu mol / L$). PANSS positive symptom scores from schizophrenia did not correlate significantly with Homocysteine levels (r = 0.007, p = 0.9). However, the negative PANSS score had a significant correlation with Homocysteine levels (r = 0.7; p < 0.001) .16

The strength of this research is the first study conducted in Indonesia to find out the Correlation Between Homocysteine Levels and the Total Positive and Negative Syndrome Scale (PANSS) Score in men with schizophrenia of the Batak tribe. The limitation of the study is that it is only done in one hospital and is not a multi-center study.

Conclusion

Involved 105 male subjects with schizophrenia who were hospitalized in the hospital. The soul of Prof. Ildrem Medan.Based on demographic characteristics, it is found that the age is 32 medium with a maximum maximum (21-45) years. Based on the highest level of education, there were 53 junior high schools (50.50%), 30 elementary schools (28.60%), and 22 high schools (21.0%). In marital status, the majority of subjects with no marriage were 58 people (55.20%) and married status were 47 people (44.80%). Likewise with employment status, the most subjects were subjects who did not work as many as 65 people (61.90%) and worked as many as 40 people (38.10%). For the duration of illness, a medium of 5.00 with a minimum (2-10)years is found. It was found that the average PANSS score was positive in men with Batak schizophrenia in the subjects of this study was 29.11 and standard deviation was 3.09. It was found that the PANSS score was negative in men with Batak schizophrenia in the subjects of this study obtained by 30.58 and standard deviation of 2.86. It was found that the average PANSS score of general psychopathology in men with Batak slizophrenia in the study subjects was obtained a median of 36.00 and a minimum of 30 and a maximum of 44. The mean total PANSS score in men with Batak schizophrenia in the study subjects was found to be 95.33 and the standard deviation was 7.86. The mean Homocysteine level in men with Batak schizophrenia was $21.24 \,\mu$ mol / L and the standard deviation was 7.17 µmol / L. There is a significant correlation with the Pearson correlation test between positive PANSS scores and Homocysteine levels in Batak schizophrenic men, the correlation coefficient of r = 0.529 shows a positive correlation with moderate correlation strength (r =

 $(0.4 - \langle 0.6 \rangle)$ with p = 0.001). With the interpretation that the higher levels of homocysteine means the higher total PANSS score in men with schizophrenia. There is a significant correlation with the Pearson correlation test between negative PANSS scores and Homocysteine levels in schizophrenic men of the Batak tribe, the correlation coefficient of r = 0.544 with moderate correlation strength ($r = 0.4 - \langle 0.6 \rangle$) with p = 0.001. With the interpretation that the higher levels of homocysteine means the higher PANSS score is negative in men with schizophrenia. There is a significant correlation with the Pearson correlation test between PANSS scores of general psychopalogy and Homocysteine levels in schizophrenic men of the Batak tribe, the correlation coefficient of r = 0.633with the strength of a strong correlation ($r = 0.6 - \langle 0.8 \rangle$) with a p value = 0.001. With the interpretation that the higher levels of homocysteine means the higher PANSS psychopathological scores in men with schizophrenia. There is a significant correlation with the Pearson correlation test between the PANSS Total Score and Homocysteine Levels in men with schizophrenia of the Batak tribe, the correlation coefficient of r = 0.668 shows a positive correlation with strong strength (r = $0.6 - \langle 0.8 \rangle$) with a value of p = 0.001. With the interpretation that the higher levels of homocysteine means the higher total PANSS score in men with schizophrenia.

Hyperhomocysteinaemiacaused by a rare genetic defect that results in deficiency of cystathionine β synthase, methylenetetrahydrofolate reductase, or in other enzymes involved in the synthesis of methyl-B12 and homocysteine methylation. The polymorphic variant of the methylenetetrahydrofolate (C677T) reductase gene is responsible for hyperhomocysteinaemia due to a 70% reduction in enzyme activity. Several studies have hypothesized that this condition could represent a risk factor for schizophrenia. The C677T genetic variant can be responsible for early schizophrenia in certain populations. Related polymorphic variants of catechol-O-methyl-transferase (COMT 324AA) and methylentetrahydrofalote reductase (MTHFR 677TT) gene, both of which are responsible for hyperhomocysteinaemia, can increase susceptibility to schizophrenia and can represent predictors of negative psychotic symptoms. Hyperhomocysteinaemia during the third trimester of pregnancy can be a risk factor for schizophrenia in children, possibly due to damage to blood vessels in the placenta or defects in the development of NMDA receptors. The first few studies have shown an increase in the frequency of schizophrenia in homocystinuria syndrome patients. Another study that ingesting 10-12 g of methionine, a precursor of homocysteine, worsens psychotic symptoms in chronic schizophrenic patients.10 The first few studies have shown an increase in the frequency of schizophrenia in homocystinuria syndrome patients. Another study that ingesting 10-12 g of methionine, a precursor of homocysteine, worsens psychotic symptoms in chronic schizophrenic patients.10 The first few studies have shown an increase in the frequency of schizophrenia in homocystinuria syndrome patients. Another study that ingesting 10-12 g of methionine, a precursor of homocysteine, worsens psychotic symptoms in chronic schizophrenic patients.10

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