





## Differences in Selenium Levels between People with Schizophrenia and Control Groups

Nabilah Aulia Hasanuddin<sup>1</sup>, Elmeida Effendy<sup>1\*</sup>, Vita Camellia<sup>1</sup>

<sup>1</sup>Department of Psychiatry, Faculty of Medicine, Universitas Sumatera Utara

\*Corresponding author: [elmedia.effendi@usu.ac.id](mailto:elmedia.effendi@usu.ac.id)

### Abstract

**Background:** Cognitive, emotional, and behavioural symptoms of schizophrenia affect various areas of mental function. Schizophrenia is a mental condition. The lifetime prevalence of this condition ranges from 0.3% to 0.7%, with rates fluctuating depending on migration, urbanization, and socioeconomic position. The oxidative stress theory, which contends that it contributes to brain damage, is one of many hypotheses addressing the pathophysiology of schizophrenia. Through selenoproteins, Selenium, an essential element for the body, participates in the defence against oxidative stress. According to earlier research, selenium supplementation can help persons with schizophrenia (PWS) have better memory. However, it was discovered that PWS had lower levels of Selenium than the control groups. Cognitive impairment is an essential aspect of the clinical course of schizophrenia. Therefore, this study aims to examine the correlation between selenium levels and schizophrenia in Indonesia.

**Method:** This comparative analytical observational study with a cross-sectional approach assessed differences in selenium levels between PWS and control groups. Selenium levels were evaluated using the Inductively Coupled Plasma Mass Spectrometry (ICP-MS) technique on the sample, comprising 100 people with schizophrenia and 100 controls. The Mann-Whitney U and Chi-Square tests were used for data analysis in the Statistical Package for the Social Sciences (SPSS).

**Results:** The demographic data showed no significant differences in gender ( $p=0.887$ ) and age ( $p=0.509$ ). The PANSS score and selenium levels did not significantly correlate with one another ( $r=0.188$ ,  $p=0.061$ ). However, selenium levels between the PWS and control groups differed significantly ( $z=-2.324$ ,  $p=0.020$ ).

**Conclusion:** The findings offer insightful early data on the possible involvement of Selenium in PWS development. Additional research is required to validate these results and deepen our understanding of the relationship between Selenium and PWS.

**Keywords.** selenium levels, PANSS, people with schizophrenia, control

## Introduction

The mental disorder known as schizophrenia exhibits positive, negative, and cognitive symptoms that affect almost all aspects of mental activity, including perception, attention, memory, and emotions. This disorder is also accompanied by long-lasting psychotic symptoms, cognitive dysfunctions, and profound psychosocial impairment [1,2]. In 2019, the World Health Organization (WHO) reported that schizophrenia affects approximately 20 million people worldwide, although its occurrence is less prevalent compared to other mental disorders [3]. According to representative national survey meta-analyses, the lifetime prevalence of schizophrenia is estimated to be between 0.3% and 0.7%, with rates changing by more than fivefold. Based on factors such as migration and refugee status, urbanization, socioeconomic position, and geographic latitude, several studies revealed an increasing frequency and incidence of schizophrenia in various populations. [4]. Numerous theories are associated with the occurrence of schizophrenia, ranging from genetic, prenatal and perinatal factors, neural development, brain neurochemistry to neuro-progressive theories [5]. Efforts to describe the molecular roots of schizophrenia are continuously being developed. According to some accounts, oxidative stress—which is brought on by an excess of reactive chemicals like reactive oxygen species (ROS) and reactive nitrogen species (RNS)—causes neuronal damage in the pathophysiology of schizophrenia. Lipid peroxidation, protein carbonylation, DNA strand breaks, and altered cell signalling cascades that control neurotransmitter systems are all ways that ROS can harm neurons. This disorder may result in changes in dopaminergic, glutamatergic, and GABAergic neurotransmission. The pathogenesis of schizophrenia is influenced by disruptions in the biosynthesis and function of selenoproteins like glutathione peroxidases (GPXs), thioredoxin reductases (TrxRs), and iodothyronine deiodinases, which are also involved in the mechanism of protection against oxidative stress. [6,7].

A vital mineral for the body is Selenium, a chemical element with atomic number 34 on the periodic chart. The various chemical forms of this element affect its bioavailability, use, and toxicity to people. Organic Selenium, such as selenomethionine and selenocysteine, as well as inorganic Selenium, such as selenate and selenite, are both derived from food sources. [8,9]. The biological functions of selenoproteins engaged in oxidative stress defence, which is a significant factor in the initiation and development of numerous diseases, are the main drivers of Selenium's impacts on human health. [6]. People with schizophrenia (PWS) and healthy individuals have selenium levels that are correlated, according to earlier studies. However, the findings showed that PWS has lower amounts of Selenium than the healthy control groups. [10-12]. Cognitive impairment is an aspect of the clinical course of schizophrenia that progresses independently of the primary symptoms. A study also indicated that targeting symptom therapy for schizophrenia with cognitive impairment progresses independently [1]. The intricate roles that Selenium and

selenoproteins play in disease, including the control of several layers of homeostasis and the central nervous system, are a result of some of these interactions. [13]. Li et al. (2017) demonstrated that selenium supplementation in PWS can improve appetite and enhance memory function [14]. Based on these various backgrounds, this study aims to investigate the correlation between selenium levels and schizophrenia in Indonesia.

## Methods and Statistical Analysis

### Methods

This comparative analytical observational study adopted a cross-sectional approach to assessing the correlation between plasma selenium level and PWS. The sample consisted of 100 individuals with schizophrenia and 100 controls, and plasma selenium levels were examined using the Inductively Coupled Plasma Mass Spectrometry (ICP-MS) method. In preparation, subjects are prohibited from consuming seafood for three days prior to the examination. A venous blood sample of 7 mL is collected and then placed into a specialized trace element tube for immediate centrifugation within a maximum of 30 minutes after sample collection. Subsequently, the samples are sent to the central laboratory on the same day for processing via ICP-MS.

### Statistical Analysis

The Statistical Package for the Social Sciences (SPSS) was used in this study to compare the data. It was determined whether there was a connection between selenium levels and schizophrenia using the Mann-Whitney U and Chi-Square tests.

### Results

In this study, there were more male participants in both PWS and control groups. The age median was 30, with a minimum and maximum of 20 and 40 for PWS groups and 19 and 40 for control groups, respectively. As presented in Table 1, the onset age had a mean and standard deviation of  $24.59 \pm 4.634$ , while the PANSS score had a median of 90.5 with a minimum and maximum of 80 and 110, respectively.

The results in Table 1 showed differences in gender and age ( $p=0.887$  and  $p=0.509$ ) in the demographic data. There were also differences in selenium levels between PWS and control groups ( $z= -2.324$ ,  $p=0.020$ ), as illustrated in Table 2. However, based on the values in Table 3, there was no correlation between the PANSS score and selenium levels ( $r=0.188$ ,  $p=0.061$ ).

**Table 1.** Demographics

Variable	Groups		p
	PWS (n=100)	Control (n=100)	

Gender			
Male	54 (49.1%)	56 (50.9%)	0.887
Female	46 (50.9%)	44 (49.1%)	
Age	30 (20-40)	30 (19-40)	0.509
Onset	24.59±4.634	-	
Total PANSS Score	90.50 (80-110)	-	

**Table 2.** Differences in selenium levels (µg/L) between PWS and control groups

	PWS (n=100)	Control (n=100)	Statistics (Mann Whitney U)	
	Median (minimum- maximum)	Median (minimum- maximum)	Z	p
Selenium Levels	88 µg/L (76-110)	89 µg/L (77-110)	-2.324	0.020

**Table 3.** Correlation between selenium levels with PWS and control groups

Variable	r	P value
Total Moca-INA Score	0.188	0.061

**Discussion**

The two sample groups analyzed had no discernible age or gender disparities. These findings supported Charlson et al. (2018) study "Global Epidemiology and Burden of Schizophrenia," which detailed the prevalence of schizophrenia worldwide. [15]. The study showed that there were no gender differences in the global prevalence of schizophrenia. Furthermore, more than 70.8% of schizophrenia cases occurred in the age groups of 25-54 years, with the highest prevalence in the 40s age group and a decrease in older age groups. Other studies also indicated that the morbidity risk of schizophrenia was 1%, and there were no differences in prevalence between genders, but the incidence rate was higher in males [15,16].

This study showed significant differences in selenium levels between PWS and control groups. These results were consistent with Ma et al. (2020) and Li et al. (2018), demonstrating a significant decrease in serum selenium concentration associated with schizophrenia risk. Several reports showed that selenoproteins played a role in suppressing oxidative stress related to the pathophysiology of schizophrenia. Moreover, oxidative stress is a mechanism that can disrupt neuroprotection processes. Selenium and selenoproteins were also believed to be involved in the dopamine pathway. Previous animal studies showed that decreased Selenium can reduce dopamine metabolism levels and trigger impairments in central nervous system functions such as coordination, memory, and cognition [17,18].

This study's findings, which were in line with a work by Cardoso et al. (2018) in Australia with 154 participants over the age of 60, did not identify a significant association between selenium levels and MOCA INA. Multiple linear regression analysis of the findings revealed no correlation between plasma selenium levels and cognitive function. Furthermore, Gao et al. (2007) reported that a cross-sectional study of 2,000 steady rural Chinese seniors aged 65 found a substantial relationship between selenium status and cognitive function. According to Hall et al., 2012, high selenium exposure in groundwater was associated with better memory function and a reduced risk of cognitive decline in 484 community residents in Texas and New Mexico. Another investigation also found that Selenium played a role in optimizing brain growth and development, thereby impacting cognitive function [19,20].

## Conclusion

The results of this investigation demonstrated that the selenium levels in the PWS and control groups differed. However, the PANSS score in PWS individuals did not correlate with selenium levels. The demographic information revealed no appreciable gender or age variations between the two sample groups. These findings gave valuable early insights into the possible involvement of Selenium in PWS aetiology. Additional research is required to validate these findings and learn more about the relationship between Selenium and PWS.

## Declaration

This research has received approval from the Research Ethics Committee for Health Studies at the Universitas Sumatera Utara.

## References

1. Lieberman J, Stroup T, Perkins D. Essentials of Schizophrenia. London: American Psychiatric Publishing; 2012: p. 337-42
2. Sadock BJ, Sadock VA. Kaplan & Sadock's Comprehensive Textbook of Psychiatry. 10th ed. Lippincott Williams & Wilkins Volume 1;2017: p. 5602-3
3. WHO. Schizophrenia 4. 2021;(October 2019):2019-22.
4. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders 5th ed.* American Psychiatric Publishing; 2013: p.99-105
5. Lieberman J, Stroup T, Perkins D. Textbook of Schizophrenia. London: American Psychiatric Publishing; 2006.p.55-167
6. Barchielli G, Capperucci A, Tanini D. The Role of Selenium in Pathologies: An Updated Review. *Antioxidants*. 2022;11(2). doi:10.3390/antiox11020251
7. Huang D, Liu S. Oxidative Stress and Schizophrenia. *J Psychiatry Brain Sci*. 2017;2(2):2-6. doi:10.20900/jpbs.20170006
8. Arteel GE, Sies H. The biochemistry of Selenium and the glutathione system. *Environ Toxicol Pharmacol*. 2001;10(4):153-158. doi:10.1016/S1382-6689(01)00078-3

9. Perrone D, Monteiro M. Section I Chemistry and Biochemistry. In Food and Nutritional Components in Focus No. 9 Selenium: Chemistry, Analysis, Function and Effects;2015;p.3-13
10. Cai L, Chen T, Yang J, et al. Serum trace element differences between Schizophrenia patients and controls in the Han Chinese population. *Sci Rep*. 2015;5(September):1-8. doi:10.1038/srep15013
11. Arinola G, Idonije B, Akinlade K, Ihenyen O. Essential trace metals and heavy metals in newly diagnosed schizophrenic patients and those on anti-psychotic medication. *J Res Med Sci*. 2010;15(5):1-5.
12. Liu T, Lu Q Bin, Yan L, et al. Comparative study on serum levels of 10 trace elements in schizophrenia. *PLoS One*. 2015;10(7):1-8. doi:10.1371/journal.pone.0133622
13. Solovyev ND. Importance of Selenium and selenoprotein for brain function: From antioxidant protection to neuronal signalling. *J Inorg Biochem*. 2015;153:1-12. doi:10.1016/j.jinorgbio.2015.09.003
14. Li Z, Liu Y, Li X, et al. Association of Elements with Schizophrenia and Intervention of Selenium Supplements. *Biol Trace Elem Res*. 2018;183(1):16-21. doi:10.1007/s12011-017-1105-0
15. Charlson FJ, Ferrari AJ, Santomauro DF, et al. Global Epidemiology and Burden of Schizophrenia: Findings From the Global Burden of Disease Study 2016. 2018;44(6):1195-1203. doi:10.1093/schbul/sby058
16. Owen MJ, Sawa A, Mortensen PB. Schizophrenia. *Lancet*. 2016; 388(10039): 86-97.
17. Subramaniam M, Abdin E, Vaingankar JA, Sambasivam R, Zhang YJ, Shafie S. Lifetime prevalence and correlates of schizophrenia and other psychotic disorders in Singapore. *Front Psychiatry*.2021; 12: 1-10.
18. Ma J, Yan L, Guo T, et al. Association between Serum Essential Metal Elements and the Risk of Schizophrenia in China. *Sci Rep*. 2020;10(1):1-11. doi:10.1038/s41598-020-66496-7
19. Cardoso BR, Szymlek-Gay EA, Roberts BR, et al. Selenium status is not associated with cognitive performance: A cross-sectional study in 154 older Australian adults. *Nutrients*. 2018;10(12). doi:10.3390/nu10121847
20. Gashu D, Stoecker BJ. Selenium and Cognition: Mechanism and Evidence. In Handbook of Famine, Starvation, and Nutrient Deprivation. Handb Famine, Starvation, Nutr Deprivation. Published online 2017. doi:10.1007/978-3-319-40007-5

**Open Access** This chapter is licensed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License (<http://creativecommons.org/licenses/by-nc/4.0/>), which permits any noncommercial use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license and indicate if changes were made.

The images or other third party material in this chapter are included in the chapter's Creative Commons license, unless indicated otherwise in a credit line to the material. If material is not included in the chapter's Creative Commons license and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder.

