

# The Relationship between Tumor Necrosis Factor-Alpha (Tnf- A) Serum Level and Negative Scale of PANSS in Smoking Schizophrenic Batak Men

\*Elmeida Effendy<sup>1</sup>, Mustafa Mahmud Amin<sup>1</sup>

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

Keywords Schizophrenia, Tumor Necrosis, PANSS

**Abstract:** Chronic schizophrenic patients characterized by non-remitting symptoms and functional decline over time suggest neuroprogression. Schizophrenia has the aberration in the proportion of immuno-competent cells and varied cytokine levels, particularly proinflammatory IL-6, IL-1 and TNF- $\alpha$ , in peripheral blood or cerebrospinal fluid. The negative symptoms of schizophrenia are characterized by deficits in normal emotions and social functions that can be primary or secondary to the treatment of the disease or other manifestations. TNF-  $\alpha$  plays an important role in developing smoking-related illnesses, chronic obstructive pulmonary disease (COPD). Inhaling cigarette smoke can cause TNF- $\alpha$  production by alveolar macrophages, which in turn may increase the production of metalloproteinases (MMPs) involved in the mediation of salmon inflammation and lung damage. MMPs is involved in the mediation of respiratory inflammation and lung damage. This study aimed to determine the relationship between serum levels of TNF- $\alpha$  and PANSS negative scale in men with schizophrenia of Batak tribe smoking. This study was conducted at outpatient instalation RSJ. Prof. Dr. M. Ildrem Medan in the period of February 2018 - June 2018. This is an analytic numerical correlation with a cross-sectional approach. Subjects were 50 schizophrenic Batak men. The data analysis used Spearman correlation. The mean negative scale of PANSS is  $30.42 \pm 1.691$ . This shows that there is a negative symptom in schizophrenic patients. The mean TNF- $\alpha$  serum level was  $22.31938 \pm 23.242901$ . Spearman correlation coefficient between two variables is 0, 403 ( $p = 0.004$ ). There was a significant correlation between serum levels of TNF- $\alpha$  and PANSS negative scale with a correlation value of 0.403 showing a positive correlation with moderate correlation strength ( $r = 0.4 - <0.6$ ).

## 1 INTRODUCTION

Schizophrenia is a variable clinical syndrome, but profoundly damaging to psychopathology involving cognition, emotion, perception, and other aspects of behavior (Sadock, 2015). The negative symptoms of schizophrenia are characterized by deficits in normal emotions and social functions that can be primary or secondary to the treatment of the disease or other manifestations (Farokhnia, 2013).

The prevalence of schizophrenia between men and women is similar, but differs in the onset of the disorder, is earlier in men than in women. Peak onset in men between the ages of 10-25 years and 25-35 years in women. Of the 90% of patients receiving

schizophrenic treatment aged between 15-55 years (Sadock, 2015). The prevalence of schizophrenia in Batak tribe in BLUD RSJ of North Sumatera Province is 60%.

The Batak tribe is a group of people known as Indonesians, with their physical appearance easily distinguished from Caucasians and blacks (Negroid), including the Mongoloid group and still actively practicing customs, especially those domiciled in North Sumatera Territory (Na, 2007). Batak tribe is selected because in addition to the prevalence of visits to polyclinic BLUD RSJ Pemprovu highest, the tribe's most awake purity, due to strong customs to maintain the tribal purity by also marrying with the Batak tribe.

(Petrescu, 2010) showed that serum TNF- $\alpha$  levels were significantly higher in the smoker group compared with the non-smoker group (Petrescu, 2010).

Studies performed by (LV, 2015) showed significantly lower TNF- $\alpha$  levels in chronic schizophrenic patients ( $10.1 \pm 2.0$  pg / ml) compared with healthy controls ( $37.8 \pm 3.4$  pg / ml) with  $p < 0.01$ . Correlation analysis showed a significant negative correlation between TNF- $\alpha$  levels and total PANSS score ( $p < 0.01$ ). TNF- $\alpha$  levels were significantly negative correlated with values in general psychopathology ( $p < 0.01$ ), positive ( $p < 0.01$ ), and on the cognitive sub-scale ( $p < 0.05$ ) (Farokhnia, 2013).

This study wanted to confirm whether there is a correlation between of TNF- $\alpha$  serum level and Negative Scale of PANSS in smoking schizophrenic Batak men.

## 2 MATERIAL AND METHOD

This is numerical correlative analytic study, with cross-sectional, which assessed the correlation between serum levels of TNF- $\alpha$  and Negative Scale of PANSS in smoking schizophrenic Batak Men.

This study was conducted at the inpatient installation of Mental Hospital Prof. Dr. M. Ildrem Medan the period February 2018 - August 2018. The population was schizophrenic patients, while the affordable population were schizophrenic patients at the Inpatient Installation of Mental Hospital Prof. Dr. M. Ildrem Medan. Sampling method by Nonprobability sampling type consecutive sampling that is all subjects that come and meet the eligibility criteria as much as 50 subjects.

We conduct a mini ICD-10 assessment of the subject. There was an assessment using PANSS to assess the negative scale which in this study limited total score of negative scale PANSS  $\geq 21$ . A total of 5ml of blood samples was taken to all subjects in this study, of TNF- $\alpha$  serum levels were analyzed using Quantikine HS Human TNF- $\alpha$  Assay.

Data analysis, before data analysis will be done data normality test by using the Shapiro-Wilk test because the number of samples is less than 50. Furthermore data is analyzed to get correlation value ( $r$ ). When the data is normally distributed, it will be done data analysis using Pearson Correlation test. If the data is not normally distributed data analysis using the Spearman correlation test.

## 3 RESULT

Table 1: Distribution of Subjects Based on Demographic Characteristics

Variables	n	%
Age (years)		
20-30	8	16
31-40	42	84
Education		
Junior high school	28	56
High school	15	30
D3	7	14
Marital Status		
Single	14	28
Married	36	72
Duration of illness		
2-5	44	88
> 5	6	12

Table 1 shows that the proportion of patients with schizophrenia is 20-30 years (16%), 31-40 years (84%). The proportion of schizophrenic patient education is junior high (56%), high school (30%), D3 (14%). The proportion of marital status of schizophrenic patients was unmarried (28%) and married (72%). Based on the length of illness schizophrenia patients are 2-5 years (88%) and > 5 years (12%).

Research conducted by (Na, 2007) to see monocytes, T-helper 1 and T-helper 2 in schizophrenic patients, they measured TNF- $\alpha$  levels in schizophrenic and healthy control patients with

mean age and standard deviation is  $32.86 \pm 12.76$  and  $31.48 \pm 11.83$  (Na, 2007).

Particular “confounding” factors such as age, smoking, body mass index (BMI), sex, and infection also have a bearing on levels of IL-6 and TNF- $\alpha$  (Himmerich, 2009).

Table 2: Mean Negative Scale of PANSS in Schizophrenic Patients

Variable	Mean	SD	p
PANSS Negative	30,42	1.691	0,002

\*Shapiro-Wilk test

Table 2. shows that Negative scale of PANSS with mean of 30,42 and standard deviation 1,691. From the results of normality test data using Shapiro-Wilk found p value = 0.002 ( $p < 0.05$ ), so it can be concluded the data is not normally distributed.

Fan at.el, show serum TNF- $\alpha$  levels showed a significant negative association with PANSS total score ( $r = -0.210$ ,  $p < 0.01$ ) and negative subscore ( $r = -0.300$ ,  $p < 0.01$ ) (Fan, 2015).

Table 3 : Mean TNF- $\alpha$  serum level in Schizophrenic Patients

Variable	Mean	SD	p
TNF- $\alpha$	22.31938	23.24290	0.000

\*Shapiro-Wilk test

Table 3. shows that TNF- $\alpha$  is 22.31938 and deviation standard 23.24290. From the results of normality test data using Shapiro-Wilk found p value = 0.000 ( $p < 0.05$ ), so it can be concluded the data is not normally distributed.

In a study conducted by Theodoropoulou in Athens showed significantly higher levels of TNF- $\alpha$  in treatment-treated chronic schizophrenic patients ( $26 \pm 8$  pg / ml) compared with healthy controls ( $16 \pm 6$  pg / ml) with  $p < 0.001$  (Jiang, 2013).

Prior to the correlative test on the baseline data, firstly tested the normality of data where the variable of Negative Scale PANSS tested normalization using Shapiro Wilk Test because the sample amount is less than or equal to 50 and it is found that the variable of PANSS Negative Scale Distribution is abnormal

therefore correlative test of baseline data using Spearman Correlation test.

Table 4 : Correlation Levels of Serum Tumor Necrosis Factor-Alpha (TNF- $\alpha$ ) And Negative Scale PANSS

Levels of Serum Tumor Necrosis Factor – Alpha (TNF- $\alpha$ )	
Negative Scale PANSS	$r = 0,403$ $p = 0.004$ $n = 50$

\*Spearman test

Spearman correlation test serum level Tumor Necrosis Factor-Alpha (TNF- $\alpha$ ) and PANSS Negative Scale obtained p value  $< 0.05$  and concluded that there is correlation between serum serum Tumor Necrosis Factor-Alpha (TNF- $\alpha$ ) and Negative Scale PANSS Strength relationship between serum levels Tumor Necrosis Factor-Alpha (TNF- $\alpha$ ) and Negative Scale PANSS large 0.403 shows a positive correlation with moderate correlation strength ( $r = 0.4 - 0.6$ ).

#### 4 DISCUSSION

(Al-Asmari, 2014) showed that TNF- $\alpha$  levels in schizophrenic patients ( $27.04 \pm 4.11$ ) were significantly higher than normal controls ( $17.25 \pm 3.20$ ) an imbalance between proinflammatory and antiinflammatory cytokines may be involved in the pathophysiology of schizophrenia through various mechanisms (Asmari, 2014).

The (Petrescu, 2010) study showed a further increase in serum TNF- $\alpha$  levels in patients with daily tobacco exposure of more than 1 pack / day. There was no significant difference between serum TNF- $\alpha$  levels of nonsmokers and those who smoked less than 1 pack / day. This suggests that active smokers who cause inflammation usually require a significant amount of exposure. So based on this study it can be concluded that heavy smoking can lead to a significant increase in serum levels of TNF- $\alpha$  and C-Reactive Protein (CRP), which supports an imbalance between proinflammatory and antiinflammatory factors. TNF- $\alpha$  concentrations are elevated in healthy

serum smokers depending on cigarette doses (Petrescu, 2010).

Studies performed by Lv kk showed significantly lower TNF- $\alpha$  levels in chronic schizophrenic patients (10.1 $\pm$ 2.0 pg/ml) compared with healthy controls (37.8 $\pm$ 3.4 pg/ml) with  $p < 0.01$ . Correlation analysis showed significant negative correlation between TNF- $\alpha$  levels and total PANSS score ( $p < 0.01$ ). TNF- $\alpha$  levels were significantly negative correlated with values in general psychopathology ( $p < 0.01$ ), positive ( $p < 0.01$ ). And on the cognitive sub-scale ( $p < 0.05$ ). Multiple regression analysis gradually identified TNF- $\alpha$  levels as a significant predictor of general psychopathology subscale in PANSS (Tan, 2015).

## 5 CONCLUSIONS

A total of 50 subjects of schizophrenic patients who participated in the study were in the inpatient installation of in Mental Hospital Prof. Dr. M. Ildrem Medan February 2018 – June 2018.

Based on demographic characteristic, it was found that the subjects of the study were age group 31-40 years (84%), based on the highest level of education were 28 subjects (56%) junior high school, based on the highest marital status with marital status of 36 subjects (72%) and based on 2-5 years old sickness of 44 subjects (88%) and > 5 years by 6 subjects (12%). The average score of PANSS negative scale score in schizophrenic patients was 30,42 $\pm$ 1.691 . The average serum level of TNF- $\alpha$  in schizophrenic patients was 22.31938 $\pm$ 23.242901. Strength relationship between serum levels Tumor Necrosis Factor-Alpha (TNF- $\alpha$ ) and PANSS Negative Scale large 0.403 shows a positive correlation with moderate correlation strength ( $r = 0.4-0.6$ ).

## ACKNOWLEDGEMENTS

This study was funded by Lembaga Penelitian Universitas Sumatera Utara Number: 2590/UN5.1.R/PPM/2018 in talent research program.

## REFERENCES

Sadock BJ, Sadock VA. In: Kaplan & Sadock's synopsis of psychiatry behavioral sciences/ clinical psychiatry. 11<sup>th</sup> ed. Philadelphia: Lippincott Williams & Wilkins; 2015.p.467-97

Farokhnia M, Azarkolah A, Adinehfar F, Ardakani MRK, Hosseini SMR, Yekehtaz H, et al. *Clinical neuropharmacology*. 2013;36:185-192

Petrescu F, Voican SC, Silosi I. International journal of chronic obstructive pulmonary disease. 2010; 5: p.217-22

LV MH, Tan YL, Yan SX, Tian L, Chen DC, Tan SP, et.al. *Psychopharmacology*. 2015; 232: p.165-72

Simanjuntak, BA 2006, Struktur sosial dan sistem politik Batak Toba hingga 1945, Yayasan Obor Indonesia, Jakarta

Na KS, Kim YK. *Monocytic*. 2007; 56: p.55-63.

Himmerich H, berthold-Losleben M, Pollmacher T : 2009 *June* :77(6):334-45.doi:10.10555

Fan N, Luo Y, Xu K, Zhang M, Ke X, Huang X, et.al. *HHS Public Access*. 2015

*November*: doi: .10.1016/j.schres.2015.11.006

Jiang J, See YM, Subramaniam M, Lee J. *Plos ONE*. 2013;8(8):1-7

Al-Asmari A, Khan MW. 2014; 33(2): p.115-22