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ELEVATED NEUTROPHIL/LYMPHOCYTE RATIO IN PATIENTS WITH SCHIZOPHRENIA

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SUMMARY

Background: *Inflammatory mechanisms are reported to play important roles in the pathophysiology of schizophrenia. The neutrophil–lymphocyte ratio (NLR) is a simple and easily accessible indicator of the systemic inflammatory response. Our goal was to investigate whether NLR was higher in patients with schizophrenia than in healthy comparison subjects similar in age, sex, and body mass index.*

Subjects and methods: *In this multicenter cross-sectional study, we analyzed 156 non-obese patients with schizophrenia and 89 healthy control subjects for complete blood count. The Brief Psychiatric Rating Scale was used to determine the severity of clinical pathology.*

Results: *The mean±SD NLR of patients with schizophrenia was significantly higher than that of healthy controls (2.6±1.1 vs. 1.9±0.6, respectively, p<0.001). NLR did not significantly correlate with severity and duration of schizophrenia (r=0.065. p>0.05).*

Conclusions: *Our findings suggest that NLR levels are increased in physically healthy, non-obese, patients with schizophrenia when compared with physically and mentally healthy individuals. To our knowledge, this is the first study that demonstrated the association between NLR and schizophrenia.*

Key words: *lymphocyte – neutrophil - neutrophil/lymphocyte ratio – schizophrenia – inflammation - immunology*

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INTRODUCTION

Schizophrenia is a complex and multifactorial mental disorder with well-defined symptoms and a lifelong course, but without a satisfactory biological explanation. A growing body of evidence suggests that immunological and inflammatory mechanisms may play important roles in the pathophysiology of schizophrenia (Rothermundt et al. 2001). Various immune alterations, such as increased frequency of activated lymphocytes (Nikkilä et al. 2001), abnormal levels of inflammatory cytokines (Potvin et al. 2008, Müller 2013), and pathogenic autoantibodies (Zandi et al. 2011), have been observed in patients with schizophrenia. However, further research is necessary to clarify the role of the immunological and inflammatory mechanisms in schizophrenia (Müller & Schwarz 2010).

The neutrophil–lymphocyte ratio (NLR) is a new, simple and inexpensive marker of the systemic inflammatory response (Zahorec 2001). Elevated levels of NLR were suggested to be associated with poor prognosis in patients with pancreatitis (Azab et al. 2011), coronary heart disease (Ayhan et al. 2013, Fowler and Agha 2013), and malignancy (Szkandera et al. 2013, Seretis et al. 2013). NLR has also been shown to be associated with chronic stress in animal studies (Puppe et al. 1997, Erminio & Bertoni 2009). However, no studies have examined the relationship between neuropsychiatric disorders and NLR, except a study in which patients with Alzheimer's disease were compared with individuals with normal cognitive functioning (Kuyumcu et al. 2012).

In this study, we aimed to investigate whether NLR was higher in non-obese patients with schizophrenia than in a healthy control group matched for age, sex, and body mass index. We also sought to determine if there was an interaction between NLR and severity of the disorder in patients with schizophrenia.

SUBJECTS AND METHODS

Patients

The current study employed a descriptive cross-sectional design. From March 2013 to May 2013 consecutive 156 patients with schizophrenia admitted to three hospitals in different cities, one a university hospital (Abant Izzet Baysal University, Bolu), the others city hospitals (Sivas State Hospital, Sivas and Diyarbakir State Hospital, Diyarbakir), were evaluated for eligibility. All patients were assessed by trained psychiatrists. The Structured Clinical Interview for DSM-IV-TR (SCID) was used to diagnose schizophrenia (First et al. 1997).

The eligible participants were physically healthy and aged 18 years or older. Patients were excluded from the study if they met one or more of the following criteria: alcohol or substance abuse, hypertension, diabetes mellitus, manifest heart disease, hepatic or renal failure, clinical evidence of active infection, active or chronic inflammatory or autoimmune diseases, obesity (BMI >30 kg/m2), heavy smoking (more than 15 cigarettes per day), and treatment with anti-inflammatory or immunosuppressive medication. Clinically significant abnormalities on the baseline physical examination (e.g., tachycardia, tachypnea, fever) or laboratory test results (e.g., anemia, leukocytosis, leukopenia, thrombocytosis) were also criteria for exclusion from study participation. We considered as "antipsychotic-free" those patients who had not taken antipsychotic medication for a minimum of 2 weeks prior to the admission. The duration of the disorder was determined by calculating the difference between the age of onset of the disorder and the age at which evaluation was done. The Brief Psychiatric Rating Scale (BPRS) (Overall and Gorham 1962) was used to rate clinical pathology. The BPRS is an 18 item orally administered instrument; each item is rated in Likert format on seven categories from 'not present (0)' to 'extremely severe (6)'.

Healthy controls

Eighty-nine (89) age and sex matched control subjects were recruited from within the hospitals, and the general community. None of them was taking any form of prescribed or over-the-counter medication. In the sampling of the control group, there was an attempt to find individuals who were living in the same neighborhood. They were screened for physical condition through clinical examinations and laboratory tests. In addition, they had a mental health screening through a psychiatric interview (SCID-I) for exclusion of any present, past and family (first degree) history of axis-I diagnoses. As with the schizophrenic patients, none of the healthy volunteers met the exclusion criteria listed above.

The study complied with the Declaration of Helsinki, and was approved by institutional ethics committee of Abant Izzet Baysal University. All patients –or their legal representatives- and controls gave informed consent prior to entry into this study.

Blood tests

Twelve-hour fasting blood samples were drawn at about 9:00 AM from a large vein of each patient by applying minimal tourniquet force. For measurement of complete blood count, blood was drawn into a vacutainer tube, containing EDTA as an anticoagulant, and analyzed in an automated blood cell counter (Abbott CELL-DYN 3700, Abbott Diagnostics Division, Abbott Laboratories, Illinois, USA).

Statistical analysis

The statistical analyses were performed using software (SPSS 16.0, SPSS Inc., Chicago, IL). Data are presented as mean ± SD for continuous variables. Categorical variables are shown as number and percentage. Variables were checked for normal distribution, and normally distributed variables were compared using the Student t test. Abnormally distributed variables were compared using Mann-Whitney U test. Pearson's chi-square test was used to compare categorical variables. Pearson correlation analysis was used to determine correlations between neutrophil/lymphocyte ratio and severity and duration of the schizophrenia. Multivariate analysis was used to test if gender, age, red blood cell-related hematologic parameters, and BPRS score could affect NLR. Statistical significance was set at 0.05.

RESULTS

There were no differences between patients and controls with regard to age, sex, body mass index, marital status, and education level (Table 1). As presented in Table 2, compared with the healthy subjects, patients with schizophrenia had significantly higher mean NLR and percentage of neutrophils, but lower percentage of lymphocytes.

The NLR was higher in female patients than in female comparison subjects (2.5±1.2 versus 2.0±0.6) ($p<0.001$). Also, compared with the healthy male subjects, the schizophrenic male patients had significantly higher neutrophil/lymphocyte ratio (1.9±0.7 versus 2.6±1.0) ($p<0.001$).

Number of the red blood cells, hemoglobin and the percentage of hematocrit were significantly higher in female than in male patients with schizophrenia. There were no significant differences between men and women with schizophrenia with regard to other blood count parameters (Table 3). Overall, multivariate analysis did not detect any meaningful effect of age, BMI, red blood cell-related parameters, and BPRS score ($p>0.05$).

As expected, mean BPRS score was higher in drug-free patients than in those who were on antipsychotic medication ($p<0.001$). However, there was no significant difference between patients who had been receiving and those who had not been receiving antipsychotics with regard to the neutrophil/lymphocyte ratio (Table 4). Compared with healthy controls, drug-free patients with schizophrenia also had a significantly higher NLR ($p<0.01$).

In the patients with schizophrenia, NLR did not significantly correlate with severity (as measured with the BPRS) ($n=156$; $r=0.065$, $p=0.151$) and duration of the disorder ($r=-0.085$, $p=0.156$). Schizophrenia-related items of BPRS (emotional withdrawal, conceptual disorganization, mannerisms and posturing, grandiosity, hostility, suspiciousness, hallucinatory behaviors, motor retardation, uncooperativeness, unusual thought content, blunted affect) were evaluated separately. None of these items were found to be correlated with NLR ($p>0.05$).

Table 1. Characteristics of Patients With Schizophrenia and Healthy Comparison Subjects

Characteristic	Patients (n=156)	Controls (n=89)	p
Age†	34.7±7.9	33.4±9.7	0.281
Female‡	68 (43.6%)	41 (46.1%)	0.707
Body mass index (kg/m2)†	25.4±2.8	24.9±2.1	0.220
Marital status‡			
Single	50 (32.1%)	18 (20.2%)	
Married	96 (61.5%)	66 (74.2%)	0.118
Divorced or widowed	10 (6.4%)	5 (5.6%)	
Education‡			
5 years	84 (53.8%)	36 (40.4%)	
8 years	34 (21.8%)	22 (24.7%)	0.156
11 years	28 (17.9%)	20 (22.5%)	
>11 years	10 (6.4%)	11 (12.4%)	

†Mean ± Standard deviation, student's t-test; ‡number (percentile), chi-square test

Table 2. Comparison of Blood Count Parameters Between Patients With Schizophrenia and Healthy Controls†

Parameters	Patients (n=156) Mean±SD	Controls (n=89) Mean±SD	p
Red blood cell count, 10^6/mL	4.9±0.4	5.0±0.4	0.202
Hemoglobin (g/dl)	14.7±1.4	14.6±1.4	0.639
Hematocrit, %	42.9±4.1	43.3±4.1	0.390
White blood cell count (x10^3)	7.1±1.4	6.9±1.3	0.319
Neutrophils (%)	62.7±8.8	58.4±6.9	<0.001
Lymphocytes (%)	27.5±7.8	32.4±6.8	<0.001
N/L ratio	2.6±1.1	1.9±0.6	<0.001
Platelet count, 10^9/L	240.7±55.6	252.1±43.6	0.101

SD, standard deviation; †student's t-test

Table 3. Comparison of Men and Women with Schizophrenia†

	Men (n=88) Mean±SD	Women (n=68) Mean±SD	p
Age (years)	35.2±7.5	34.0±8.3	0.335
BPRS score	41.4±6.6	41.1±6.9	0.776
Duration of the disorder, years	9.2±7.2	8.8±7.2	0.773
Body mass index (kg/m2)	25.1±2.6	25.6±3.0	0.425
Red blood cell count, 10^6/mL	5.0±0.4	4.8±0.4	0.007
Hemoglobin (g/dl)	14.9±1.5	14.2±1.2	0.001
Hematocrit, %	43.9±4.2	41.5±3.4	<0.001
White blood cell count (x10^3)	7.2±1.4	6.9±1.3	0.308
Neutrophils (%)	63.6±8.3	61.6±9.4	0.171
Lymphocytes (%)	26.6±6.7	28.7±8.9	0.093
N/L ratio	2.6±1.0	2.5±1.2	0.411
Platelet count, 10^9/L	237.8±53.9	244.4±57.9	0.461

BPRS: Brief Psychiatric Rating Scale; SD, standard deviation; †student's t-test

Table 4. Comparison of Patients on Antipsychotics and Antipsychotic-Free patients

	Patients on Antipsychotics (n=91) Mean±SD	Antipsychotic-Free patients (n=65) Mean±SD	p
Age (years) †	34.4±5.3	34.9±10.5	0.718
Female/Male‡	37/54	31/34	0.382
BPRS score†	37.9±5.8	45.7±5.1	<0.001
Duration of the disorder, years†	8.2±4.8	10.1±9.6	0.147
Body mass index (kg/m2) †	25.4±2.8	25.3±2.9	0.847
White blood cell count (x10^3) †	7.1±1.3	7.1±1.5	0.724
Neutrophils (%)†	63.7±6.4	61.5±11.3	0.182
Lymphocytes (%)†	26.5±5.9	28.9±9.8	0.074
N/L ratio†	2.6±1.0	2.5±1.2	0.910
Platelet count, 10^9/L†	242.8±54.8	237.7±56.9	0.572

BPRS: Brief Psychiatric Rating Scale; SD, standard deviation; †Mean ± Standard deviation, student's t-test; ‡number (percentile), chi-square test.

DISCUSSION

The present study aimed to provide preliminary data on the NLR in patients with schizophrenia. We found that patients with schizophrenia had significantly higher NLR than healthy comparison subjects. There was not a correlation between NLR and severity of psychopathology.

Abnormal ultrastructure of blood cell formation in patients with schizophrenia was reported almost 40 years ago (Naneishvili & Zurabashvili 1976). It has been postulated that the cellular immune alterations are associated with the course of the psychopathology and are a possible marker of the therapeutic outcome in schizophrenia (Muller et al. 1993). Disturbances in T-lymphocyte related immunological response has been broadly described (Smith & Maes 1995). Muller and Riedel (1999) have defined the concept of a T-Helper-1 (TH-1)/T-Helper-2 (TH-2) imbalance with a shift to the TH-2 system in schizophrenic patients. Most of the studies have focused on the T cell subgroup lymphocytes in schizophrenia with inconsistent results. Some reported a decrease (Mazzarello et al. 2004, Maino et al. 2007, Steiner et al. 2010), while others observed an increased in T cell numbers in patients with schizophrenia (Henneberg et al. 1990, Sperner-Unterweger et al. 1999). Unchanged T cell counts were also described (Schattner et al. 1996, Rudolf et al. 2004, Maxeiner et al. 2009). Associations of total white blood cell numbers and schizophrenia were shown as well. In a multi-center study (Fan et al. 2010), white blood cell counts were shown to be positively correlated with the risk for metabolic syndrome and psychopathology severity in patients with schizophrenia. In the present study, when compared with healthy comparison subjects we found decreased lymphocyte, but increased neutrophil percentages in patients with schizophrenia although white blood cell counts were similar in both groups. These findings indicate an imbalance of white cell distribution in schizophrenic patients. Given that lymphopenia is observed in inflammatory states due to increased lymphocytes apoptosis (Hotchkiss & Karl 2003), our findings may be interpreted as a contribution to the understanding of the inflammatory mechanisms in schizophrenia. There was not a significant correlation between elevated NLR levels and psychopathology severity, and NLR levels were not different between patients who had been taking antipsychotics and those had not. Thus, NLR seems to be a state rather than trait measure for schizophrenia.

Kuyumcu et al. (2012) have evaluated NLR in 241 patients with Alzheimer's disease (AD) in comparison with 175 patients with normal cognitive function and found that NLR was significantly higher in patients with AD than in controls. By means of multivariate regression analysis, they also found that NLR was an independent predictor of AD. Because neurodegeneration may play a role in the pathophysiology of schizophrenia (Lieberman 1999, Weinberger & McClure 2002), as of AD, elevated NLR levels found in our study may indicate a neurodegenerative process.

Female patients were reported to exhibit more circulating neutrophils, less lymphocytes, and higher NLR following major surgery (Gwak et al. 2007). However, in our study, no significant difference was found between men and women with schizophrenia with respect to NLR. Moreover, both women and men with schizophrenia exhibited increased NLR levels when compared with female and male controls, respectively. To explore the effect of sex on NLR, further studies need to be conducted among different populations.

It has been shown that stress-induced changes in blood leukocyte distribution are apparent very shortly (within an hour) after an acute stressor (Dhabhar 2009). As the patients with schizophrenia are prone to acute stress reactions (Jubin & Bonnie 1977), our results might be confounded with certain stress factors which were not considered in the study.

Although we examined a relatively large number of non-obese schizophrenic patients, the results of the present study need to be considered in the context of following limitations. Foremost, this was a cross-sectional study; hence we could not interpret the causal relationships between increased NLR and schizophrenia in the cross-sectional design. Second, subtypes of lymphocytes were not investigated. Third, other indicators of immune system such as cytokines were not evaluated; thus it is not possible to determine whether increased NLR is an independent marker of alterations in the immune system in patients with schizophrenia. Fourth, neutrophil counts are very variable in the individual and they have a short life-span (about 5 days). However, the measures were not repeated to see how stable the results are. Also, the patients were not assessed for a history of recent surgical procedure, lifestyle and general health (e.g., dental status) which may affect NLR levels.

CONCLUSIONS

We believe this study is the first to investigate NLR in patients with schizophrenia. The findings of our study show that NLR is increased in physically healthy, non-obese patients with schizophrenia when compared with physically and mentally healthy controls. According to this finding, elevated levels of NLR may be involved in inflammatory pathophysiology of schizophrenia. Further studies are needed to investigate the effect of antipsychotic treatment on NLR in drug-naive schizophrenic patients. It will also be of interest in future studies to determine whether NLR is different among schizophrenia subgroups.

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Conflict of interest: None to declare.

References

1. *Ayhan SS, Oztürk S, Erdem A, Ozlü MF, Ozyaşar M, Erdem K, et al: Relation of neutrophil/lymphocyte ratio with the presence and severity of coronary artery ectasia. Turk Kardiyol Dern Ars 2013; 41:185-190.*
2. *Azab B, Jaglall N, Atallah JP, Lamet A, Raja-Surya V, Farah B, et al: Neutrophil-lymphocyte ratio as a predictor of adverse outcomes of acute pancreatitis. Pancreatology 2011; 11:445-452.*
3. *Dhabhar FS: Enhancing versus Suppressive Effects of Stress on Immune Function: Implications for Immunoprotection and Immunopathology. Neuroimmunomodulation 2009; 16:300-317.*
4. *Erminio T, Bertoni G: Some physiological and biochemical methods for acute and chronic stress evaluation in dairy cows. Ital J Anim Sci 2009; 8:265-286.*
5. *Fan X, Liu EY, Freudenreich O, Park JH, Liu D, Wang J, et al: Higher white blood cell counts are associated with an increased risk for metabolic syndrome and more severe psychopathology in non-diabetic patients with schizophrenia. Schizophr Res 2010; 118:211-217.*
6. *First MB, Spitzer RL, Gibbon M, Williams JBW: Structured Clinical Interview for DSM-IV Clinical Version. American Psychiatric Press, Washington, DC, 1997.*
7. *Fowler AJ, Agha RA: Neutrophil/lymphocyte ratio is related to the severity of coronary artery disease and clinical outcome in patients undergoing angiography - the growing versatility of NLR. Atherosclerosis 2013; 228: 44-45.*
8. *Gwak MS, Choi SJ, Kim JA, Ko JS, Kim TH, Lee SM, et al: Effects of gender on white blood cell populations and neutrophil-lymphocyte ratio following gastrectomy in patients with stomach cancer. J Korean Med Sci 2007; 22:104-108.*
9. *Henneberg A, Riedl B, Dumke HO, Kornhuber HH: T-lymphocyte subpopulations in schizophrenic patients. Eur Arch Psychiatry Neurol Sci 2007; 239:283-284.*
10. *Hotchkiss RS, Karl IE: The pathophysiology and treatment of sepsis. N Engl J Med 2003; 348:138-150.*
11. *Kuyumcu ME, Yesil Y, Oztürk ZA, Kizilarslanoğlu C, Etgül S, Halil M, et al: The evaluation of neutrophil-lymphocyte ratio in Alzheimer's disease. Dement Geriatr Cogn Disord 2012; 34:69-74.*
12. *Jubin Z, Bonnie S: Vulnerability: A new view of schizophrenia. J Abnorm Psychol 2012; 86:103-126.*
13. *Lieberman JA: Is schizophrenia a neurodegenerative disorder? A clinical and neurobiological perspective. Biol Psychiatry 1999; 46:729-739.*
14. *Maino K, Gruber R, Riedel M, Seitz N, Schwarz M, Müller N: T- and B-lymphocytes in patients with schizophrenia in acute psychotic episode and the course of the treatment. Psychiatry Res 2007; 152:173-180.*
15. *Mazzarello V, Cecchini A, Fenu G, Rassu M, Dessy LA, Lorettu L, et al: Lymphocytes in schizophrenic patients under therapy: serological, morphological and cell subset findings. Ital J Anat Embryol 2004; 109:177-188.*
16. *Maxeiner HG, Rojewski MT, Schmitt A, Tumani H, Bechter K, Schmitt M: Flow cytometric analysis of T cell subsets in paired samples of cerebrospinal fluid and peripheral blood from patients with neurological and psychiatric disorders. Brain Behav Immun 2009; 23:134–142.*
17. *Müller N, Hofschuster E, Ackenheil M, Eckstein R: T-cells and psychopathology in schizophrenia: relationship to the outcome of neuroleptic therapy. Acta Psychiatr Scand 1993; 87:66-71.*
18. *Müller N, Riedel M, Ackenheil M, Schwarz MJ: The role of immune function in schizophrenia: an overview. Eur. Arch. Psychiatry. Clin Neurosci 1999; 249:62-68.*
19. *Müller N, Schwarz MJ: Immune System and Schizophrenia. Curr Immunol Rev 2010; 6:213-220.*
20. *Müller N: The role of anti-inflammatory treatment in psychiatric disorders. Psychiatr Danub 2013; 25:292-298.*
21. *Naneishvili BR, Zurabashvili ZA: The ultrastructure of formed white blood elements (neutrophils) in schizophrenia. Folia Haematol Int Mag Klin Morphol Blutforsch 1976; 103:160-165.*
22. *Nikkilä HV, Müller K, Ahokas A, Rimón R, Andersson LC: Increased frequency of activated lymphocytes in the cerebrospinal fluid of patients with acute schizophrenia. Schizophr Res 2001: 49:99-105.*
23. *Overall JE, Gorham DR: The brief psychiatric rating scale. Pyschol Rep 1962; 10:799-812.*
24. *Potvin S, Stip E, Sepehry AA, Gendron A, Bah R, Kouassi E: Inflammatory cytokine alterations in schizophrenia: a systematic quantitative review. Biol Psychiatry 2008; 63:801-808.*
25. *Puppe B, Tuchscherer M, Tuchscherer A: The effect of housing conditions and social environment immediately after weaning on the agonistic behaviour, neutrophil/lymphocyte ratio, and plasma glucose level in pigs. Livestock Prod Sci 1997; 48:157-164.*
26. *Rothermundt M, Arolt V, Bayer TA: Review of immunological and immunopathological findings in schizophrenia. Brain Behav Immun 2001; 15:319-339.*
27. *Rudolf S, Schlenke P, Broocks A, Peters M, Rothermundt M, Arolt V, et al: Search for atypical lymphocytes in schizophrenia. World J Biol Psychiatry 2004; 5:33-37.*
28. *Schattner A, Cori Y, Hahn T, Sirota P: No evidence for autoimmunity in schizophrenia. J Autoimmun 1996; 9:661-666.*
29. *Seretis C, Gourgiotis S, Gemenetzis G, Seretis F, Lagoudianakis E, Dimitrakopoulos G: The significance of neutrophil/lymphocyte ratio as a possible marker of underlying papillary microcarcinomas in thyroidal goiters: a pilot study. Am J Surg 2013; 205:691-696.*
30. *Smith RS, Maes M: The macrophage-T-lymphocyte theory of schizophrenia: additional evidence. Med Hypotheses 1995; 45:135-141.*
31. *Sperner-Unterweger B, Whitworth A, Kemmler G, Hilbe W, Thaler J, Weiss G, et al: T-cell subsets in schizophrenia: a comparison between drug-naive first episode patients and chronic schizophrenic patients. Schizophr Res 1999; 38:61-70.*
32. *Steiner J, Jacobs R, Panteli B, Brauner M, Schiltz K, Bahn S, et al: Acute schizophrenia is accompanied by reduced T*

cell and increased B cell immunity. Eur Arch Psychiatry Clin Neurosci 2010; 260: 509-518.

33. *Szkandera J, Absenger G, Liegl-Atzwanger B, Pichler M, Stotz M, Samonigg H, Glehr M, et al: Elevated preoperative neutrophil/lymphocyte ratio is associated with poor prognosis in soft-tissue sarcoma patients. Br J Cancer 2013; 108:1677-1683.*
34. *Weinberger DR, McClure RK: Neurotoxicity, neuroplasticity, and magnetic resonance imaging morphometry: what is happening in the schizophrenic brain? Arch Gen Psychiatry 2002; 59:553-558.*
35. *Zahorec R.: Ratio of neutrophil to lymphocyte counts--rapid and simple parameter of systemic inflammation and stress in critically ill. Bratisl Lek Listy 2001; 102:5-14.*
36. *Zandi MS, Irani SR, Lang B, Waters P, Jones PB, McKenna P, et al: Disease-relevant autoantibodies in first episode schizophrenia. J Neurol 2011; 258:686-688.*

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