Original article

doi:10.5633/amm.2026.0420

SOCIODEMOGRAPHIC CHARACTERISTICS AND INFLAMMATORY MARKERS IN DRUG-NAIVE PATIENTS WITH FIRST-EPISODE PSYCHOSIS FROM THE SCHIZOPHRENIA SPECTRUM

Jovana Petrović[1,2], Iva Binić[1,2], Suzana Tošić-Golubović[1,2], Olivera Žikić[1,3], Filip Petrović[1,4], Bogdan Pinterović[5]

[1]University of Niš, Medical Faculty, Niš, Serbia

[2]University Clinical Center Niš, Clinic of Psychiatry, Niš, Serbia

[3]University Clinical Center Niš, Center for Mental Health Protection, Niš, Serbia

[4]University Clinical Center Niš, Radiology Center, Niš, Serbia

[5]Institute of Forensic Medicine, Niš, Serbia

Contact: Jovana Petrović

81 Zorana Djindjića Blvd., 18000 Niš, Serbia

E-mail: jovanapetrovic0912@gmail.com

First-episode psychosis (FEP) represents a critical period for understanding the early course of psychotic disorders. Sociodemographic factors may influence both clinical presentation and biological processes, including inflammatory responses. To examine sociodemographic characteristics of drug-naive patients with FEP and explore their association with inflammatory markers. The study included 60 participants, comprising 38 drug-naive patients with FEP and 22 healthy controls matched by age and sex. Sociodemographic variables included sex, age, marital status, parenthood, place of residence, education, and employment status. Serum levels of IL-1β, IL-2, IL-6, and IL-10 were measured prior to treatment initiation. Statistical analyses were performed to assess differences and associations between variables. No statistically significant differences in cytokine levels were found across sociodemographic categories ($p > 0.05$). However, higher mean values of IL-1β and IL-2 were observed among unemployed participants and those with higher educational levels. IL-10 showed similar trends, while IL-6 levels were higher among females, individuals with higher education, and those living in urban areas. Although no statistically significant associations were found, observed trends suggest a potential influence of sociodemographic factors on inflammatory processes in early psychosis. Further research with larger samples is warranted.

Key words: first episode psychosis, inflammation, cytokine, sociodemographics

Originalni rad

doi:10.5633/amm.2026.0420

SOCIODEMOGRAFSKE KARAKTERISTIKE I INFLAMATORNI MARKERI KOD PRETHODNO NETRETIRANIH PACIJENATA SA PRVOM PSIHOTIČNOM EPIZODOM IZ SPEKTRA SHIZOFRENIJE

Jovana Petrović[1,2], Iva Binić[1,2], Suzana Tošić Golubović[1,2], Olivera Žikić[1,3], Filip Petrović[1,4], Bogdan Pinterović[5]

[1]Univerzitet u Nišu, Medicinski fakultet, Niš, Srbija

[2]Univerzitetski klinički centar Niš, Klinika za psihijatriju, Niš, Srbija

[3]Univerzitetski klinički centar Niš, Centar za zaštitu mentalnog zdravlja, Niš, Srbija

[4]Univerzitetski klinički centar Niš, Centar za radiologiju, Niš, Srbija

[5]Zavod za sudsku medicinu, Niš, Srbija

Kontakt: Jovana Petrović

Bulevar dr Zorana Đinđića 81, 18000 Niš, Srbija

E-mail: jovanapetrovic0912@gmail.com

Prva psihotična epizoda (FEP) predstavlja kritičan period za razumevanje ranog toka psihotičnih poremećaja. Sociodemografski faktori mogu uticati kako na kliničku prezentaciju, tako i na biološke procese, uključujući inflamatorne odgovore. Ispitati sociodemografske karakteristike pacijenata sa FEP koji prethodno nisu tretirani farmakoterapijom, kao i njihovu povezanost sa inflamatornim markerima. Studija je obuhvatila 60 ispitanika, uključujući 38 pacijenata sa FEP bez prethodne terapije i 22 zdrave kontrole uparene po uzrastu i polu. Sociodemografske varijable obuhvatale su pol, uzrast, bračni status, roditeljstvo, mesto stanovanja, obrazovanje i radni status. Serumski nivoi IL-1β, IL-2, IL-6 i IL-10 mereni su pre započinjanja terapije. Sprovedene su statističke analize. Nisu utvrđene statistički značajne razlike u nivoima citokina između sociodemografskih kategorija ($p>0,05$). Međutim, više srednje vrednosti IL-1β i IL-2 uočene su kod nezaposlenih ispitanika i onih sa višim nivoom obrazovanja. IL-10 je pokazao slične trendove, dok su nivoi IL-6 bili viši kod žena, osoba sa višim obrazovanjem i onih koji žive u urbanim sredinama. Iako nisu pronađene statistički značajne povezanosti, uočeni trendovi ukazuju na potencijalni uticaj sociodemografskih faktora na inflamatorne procese u ranoj psihozi. Potrebna su dalja istraživanja na većim uzorcima.

Ključne reči: prva psihotična epizoda, inflamacija, citokini, sociodemografija

Introduction

Psychotic disorders are characterized by a constellation of positive, negative, and disorganized symptoms that significantly impair functioning and quality of life (1, 2). These disorders most commonly emerge during late adolescence and early adulthood, often disrupting key developmental processes such as education, employment, and social integration (3).

First-episode psychosis (FEP) represents the early phase of psychotic disorders and provides a unique opportunity to examine both clinical and biological aspects of the illness before the influence of long-term treatment and chronicity(4–6) . Early intervention during this phase has been consistently associated with better outcomes, while longer duration of untreated psychosis is linked to poorer prognosis, including greater symptom severity and functional impairment (7–9).

In addition to clinical features, sociodemographic characteristics such as sex, educational level, employment status, and marital status play an important role in shaping both the onset and course of psychotic disorders (3, 10). These factors may reflect premorbid functioning, as well as early disease-related decline.

Recent research has increasingly focused on the role of inflammatory processes in the pathophysiology of psychosis, particularly in drug-naive patients (11–13, 4). However, the interaction between sociodemographic factors and inflammatory markers remains insufficiently explored.

The aim of this study was to examine the sociodemographic characteristics of drug-naive patients with first-episode psychosis and to explore their association with selected inflammatory markers.

Methods

This cross-sectional study included 60 participants: 38 drug-naive patients with first-episode psychosis from the schizophrenia spectrum and 22 healthy controls matched by age and sex. Patients were recruited during hospitalization at the Clinic of Psychiatry, University Clinical Center Niš, and all clinical and laboratory assessments were performed before the initiation of antipsychotic treatment. The control group consisted of healthy volunteers without current psychiatric disorders or relevant somatic conditions.

The diagnosis of first-episode psychosis was established through clinical psychiatric examination, including auto- and heteroanamnestic data, mental status assessment, and structured diagnostic evaluation. Only patients with primary psychotic disorders from the schizophrenia spectrum were included. Secondary psychoses, psychotic symptoms induced by psychoactive substances, acute or chronic inflammatory and somatic diseases, and previous antipsychotic treatment were considered exclusion criteria. In order to reduce the influence of potential confounding factors on inflammatory parameters, participants with conditions known to affect immune response were not included.

For the purpose of this analysis, sociodemographic variables were collected for all participants and included sex, age, marital status, parenthood, number of children, place of residence, educational level, and employment status. In the analysis of cytokine levels according to the number of children, only patients with FEP who had children were included, while patients without children were not included in this specific subanalysis.

Blood samples were obtained in the morning by venipuncture of the antecubital vein, using tubes with EDTA as anticoagulant. After centrifugation at 4500 rpm for 10 minutes, serum samples were separated, aliquoted, properly labelled, and stored at -80°C until analysis. Serum concentrations of interleukin-1β (IL-1β), interleukin-2 (IL-2), interleukin-6 (IL-6), and interleukin-10 (IL-10) were determined using commercially available enzyme-linked immunosorbent assay (ELISA) kits (Wuhan Fine Biotech, Wuhan, China), according to the manufacturer's instructions. Absorbance was measured using an ELISA reader at a wavelength of 450 nm. Cytokine concentrations were expressed in pg/mL.

Statistical analysis was performed using descriptive and inferential statistical methods. Categorical variables were presented as frequencies and percentages, while continuous variables were expressed as mean ± standard deviation. The distribution of continuous variables was assessed before selecting appropriate statistical tests. Differences in cytokine concentrations according to sociodemographic categories were examined using parametric or non-parametric tests, depending on data distribution and the number of compared groups. For comparisons between two groups, the Student's t-test or Mann–Whitney U test was used, while comparisons involving more than two categories were performed using one-way ANOVA or the Kruskal–Wallis test, as appropriate. Categorical variables were compared using the chi-square test or Fisher's exact test when required. Statistical significance was set at $p < 0.05$. Given the exploratory nature of the analysis and the relatively small sample size, the results were interpreted cautiously, particularly in the context of multiple comparisons.

Results

Sociodemographic characteristics of the study sample are summarized in Table 1. The distribution of cytokine levels across sex, marital status, number of children among patients with children, and place of residence is presented in Table 2, while cytokine levels according to educational level and employment status are shown in Table 3.

Table 1. Sociodemographic characteristics of the study sample

Variable	Category	FEP group (n=38)	Control group (n=22)	p
Sex	Male	23 (60.5)	14 (63.6)	0.811
	Female	15 (39.5)	8 (36.4)	
Age	Mean ± SD	27.63 ± 6.84	29.91 ± 6.46	0.210
Marital status	Unmarried	31 (81.6)	9 (40.9)	0.005
	Divorced	2 (5.3)	3 (13.6)	
	Married	5 (13.2)	10 (45.5)	
Parenthood	Yes	7 (18.4)	14 (63.6)	<0.001
	No	31 (81.6)	8 (36.4)	
Place of residence	Rural	8 (21.1)	8 (36.4)	0.196
	Urban	30 (78.9)	14 (63.6)	
Educational level	Primary school	2 (5.3)	0 (0.0)	0.429
	Secondary school	24 (63.2)	11 (50.0)	
	College/higher school	2 (5.3)	2 (9.1)	
	University degree	9 (23.7)	9 (40.9)	
	Postgraduate studies	1 (2.6)	0 (0.0)	
Employment status	Employed	7 (18.4)	16 (72.7)	<0.001
	Unemployed	28 (73.7)	6 (27.3)	
	Temporary work	3 (7.9)	0 (0.0)	

Values are presented as n (%) unless otherwise indicated. FEP - first-episode psychosis; SD - standard deviation.

Table 2. Cytokine levels according to sex, marital status, number of children, and place of residence in patients with FEP

Variable	Category	IL-1β (pg/mL)	IL-2 (pg/mL)	IL-6 (pg/mL)	IL-10 (pg/mL)
Sex	Male	139.6 ± 97.6	421.96 ± 366.85	7.84 ± 8.43	139.83 ± 175.48
	Female	115.7 ± 87.3	461.09 ± 407.82	12.08 ± 20.45	141.90 ± 185.10
	p value	**0.43**	**0.83**	**0.36**	**0.95**
Marital status	Unmarried	137.9 ± 97.7	435.41 ± 403.69	9.52 ± 13.57	160.93 ± 189.78
	Married	78.6 ± 65.2	220.03 ± 168.44	8.97 ± 10.42	50.54 ± 43.02
	Divorced	138.5 ± 52.6	175.30 ± 43.69	1.77	51.45 ± 0.79
	p value	**0.76**	**0.29**	**0.32**	**0.50**
Number of children among patients with children	One	89.9 ± 70.2	205.07 ± 133.70	12.61 ± 9.53	58.01 ± 30.99
	Three	139.2 ± 98.3	435.35 ± 403.74	8.61 ± 13.46	159.31 ± 190.86
	p value	**0.61**	**0.19**	**0.42**	**0.09**
Place of residence	Urban	132.2 ± 97.2	429.14 ± 409.56	10.85 ± 14.49	155.31 ± 192.26
	Rural	122.5 ± 81.7	262.79 ± 197.20	4.27 ± 4.72	85.67 ± 88.29
	p value	**0.33**	**0.24**	**0.04**	**0.10**

Values are presented as mean ± standard deviation where applicable. p values are shown in separate rows and correspond to the cytokine column above. FEP - first-episode psychosis; IL - interleukin.

Table 3. Cytokine levels according to educational level and employment status in patients with FEP

Variable	Category	IL-1β (pg/mL)	IL-2 (pg/mL)	IL-6 (pg/mL)	IL-10 (pg/mL)
Educational level	Primary school	50.6 ± 18.2	130.14 ± 93.22	3.17	24.19 ± 12.90
	Secondary school	128.1 ± 90.5	375.03 ± 357.45	7.79 ± 8.87	130.73 ± 167.86
	College/higher school	166.6 ± 219.4	625.80 ± 513.64	-	245.20 ± 180.45
	University degree	132.8 ± 84.3	454.13 ± 468.08	13.70 ± 21.70	162.20 ± 228.02
	Postgraduate studies	241.3	623.10	-	208.90
	p value	**0.27**	**0.25**	**0.30**	**0.40**
Employment status	Employed	79.6 ± 60.9	160.98 ± 121.35	5.94 ± 9.19	43.64 ± 27.48
	Unemployed	147.1 ± 97.7	465.95 ± 415.32	10.13 ± 13.98	169.98 ± 197.54
	Temporary work	89.7 ± 74.1	258.30 ± 88.29	3.98	93.23 ± 34.07
	p value	**0.21**	**0.16**	**0.18**	**0.11**

Values are presented as mean ± standard deviation where applicable. p values are shown in separate rows and correspond to the cytokine column above. A dash indicates that the value was not available/reported in the source table. FEP - first-episode psychosis; IL - interleukin.

Overall, cytokine concentrations did not differ significantly across most examined sociodemographic variables. The only nominally significant finding was observed for IL-6 according to place of residence, with higher mean values among participants from urban areas compared to those from rural areas ($p = 0.04$). However, given the exploratory nature of the analysis, the relatively small sample size, and the number of comparisons performed, this finding should be interpreted with caution. Although no consistent pattern of statistically significant associations was identified, several differences in mean cytokine values were observed across sociodemographic categories.

Regarding sex, male participants showed higher mean levels of IL-1β, whereas female participants had higher mean levels of IL-2, IL-6, and IL-10. These differences were modest and did not reach statistical significance.

Analysis by marital status showed variability in cytokine concentrations across categories. Higher mean values of IL-1β and IL-2 were observed among unmarried participants compared with married and divorced participants, while IL-10 also varied between groups without a clear linear pattern. None of these differences were statistically significant.

The variable related to number of children did not show a uniform pattern of cytokine distribution. Given the small number of participants in some subcategories, these findings should be interpreted cautiously. Place of residence showed the most noticeable difference in cytokine distribution. Participants living in urban areas had higher mean levels of IL-2, IL-6, and IL-10 compared with participants from rural areas. The difference reached nominal statistical significance only for IL-6 ($p = 0.04$), while differences in other cytokines were not statistically significant.

Educational level demonstrated a heterogeneous pattern. Participants with higher educational attainment, including university and postgraduate education, showed higher mean levels of some cytokines, particularly IL-1β, IL-2, and IL-10. However, variability within categories was substantial, and no statistically significant differences were detected.

Employment status showed a trend toward higher mean levels of IL-1β, IL-2, and IL-10 among unemployed participants compared with employed participants, while participants engaged in temporary work generally showed intermediate values. Although these differences did not reach statistical significance, this pattern may indicate a trend that warrants further investigation in larger samples.

Discussion

The present study did not demonstrate statistically significant associations between cytokine levels and sociodemographic characteristics in patients with first-episode psychosis. However, several consistent patterns in the distribution of inflammatory markers across different sociodemographic groups were observed, suggesting that these factors may still exert a modulatory influence on immune processes in the early phase of psychotic disorders.

One of the more notable findings was the tendency toward higher levels of proinflammatory cytokines, particularly IL-1β and IL-2, among unemployed participants. This observation may reflect the complex interaction between psychosocial stress, functional impairment, and biological vulnerability. Unemployment in patients with FEP is often not only a consequence of illness onset but may also represent a marker of premorbid dysfunction or early decline in cognitive and social functioning (14, 15). Employment status should also be interpreted cautiously in this context. Among patients with FEP, unemployment may partly reflect greater clinical severity, poorer functional capacity, or early illness-related decline, rather than representing an isolated sociodemographic factor. Accordingly, the observed tendency toward higher cytokine levels in unemployed participants should be viewed with this possible confounding effect in mind. Previous research has consistently linked psychosocial stressors, including socioeconomic disadvantage and occupational instability, with activation of inflammatory pathways, which may contribute to both the onset and progression of psychiatric symptoms (16–18).

Similarly, although higher mean cytokine values were observed in some categories of higher educational attainment, this pattern should be interpreted cautiously given the small sample size and the absence of statistical significance. Rather than indicating a clear association, these findings may reflect variability within the sample. Future research should further examine whether educational level, as a proxy for cognitive reserve and psychosocial functioning, is related to inflammatory activity in early psychosis (3, 18, 14).

The analysis of IL-10, an anti-inflammatory cytokine, revealed a pattern similar to that observed for proinflammatory markers, particularly in relation to employment status. This may suggest the presence of a compensatory anti-inflammatory response, which has been described in the context of psychiatric disorders as part of a broader immune

dysregulation process. (19–22). The simultaneous elevation of pro- and anti-inflammatory markers supports the hypothesis of a dynamic and bidirectional immune response in early psychosis.

Higher IL-6 levels observed in female participants are in line with previous findings indicating sex-related differences in immune functioning. Hormonal influences, particularly the role of estrogen, as well as differences in stress reactivity and immune regulation, have been proposed as potential mechanisms underlying these differences (10, 23). In addition, the higher IL-6 levels observed in individuals living in urban environments may reflect increased exposure to environmental and psychosocial stressors, such as social density, noise, and reduced social cohesion, all of which have been implicated in both the risk of psychosis and inflammatory activation (24, 14).

Although none of the observed differences reached statistical significance, the consistency of these patterns suggests that the lack of significance may be related to the relatively small sample size rather than the absence of a true effect. Studies in early psychosis populations are often limited by sample size, particularly when focusing on drug-naive patients, which may reduce statistical power and the ability to detect subtle but clinically relevant associations.

These findings highlight the importance of considering sociodemographic and psychosocial context when interpreting biological data in psychiatric research. Inflammatory processes in psychosis are unlikely to be driven solely by biological factors, but rather emerge from complex interactions between genetic vulnerability, environmental exposures, and individual life circumstances.

From a clinical perspective, understanding these interactions may contribute to more comprehensive assessment and personalized treatment approaches. Sociodemographic factors such as unemployment, educational level, and living environment may serve as indirect indicators of increased vulnerability and could be integrated into early intervention strategies alongside biological markers.

The present study has several limitations that should be acknowledged. The relatively small sample size limits the generalizability of the findings and reduces statistical power. Additionally, the cross-sectional design does not allow for causal inferences regarding the relationship between sociodemographic factors and inflammatory markers. Future longitudinal studies with larger samples are needed to further explore these associations and clarify their clinical significance.

Conclusion

The present study did not identify statistically significant associations between inflammatory markers and sociodemographic characteristics in drug-naive patients with first-episode psychosis. However, several observable trends suggest that factors such as employment status, educational level, sex, and place of residence may influence inflammatory responses in the early stages of the disorder.

These findings support the notion that inflammatory processes in psychosis are shaped not only by biological mechanisms but also by broader psychosocial and environmental factors. Although preliminary, the observed patterns highlight the importance of integrating sociodemographic context into the interpretation of biological data in psychiatric research.

Further studies with larger samples and longitudinal design are needed to better understand these relationships and their potential clinical implications in early psychosis.

REFERENCES

1. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. Diagnostic and Statistical Manual of Mental Disorders. 2013.
2. Tandon, R, HA Nasrallah, MS Keshavan. Schizophrenia, “just the facts” 4. Clinical features and conceptualization. Schizophr Res. 2009;110(1–3):1–23.
3. Moe, AM, NJK Breitborde. Psychosis in Emerging Adulthood: Phenomenological, Diagnostic, and Clinical Considerations. Evid Based Pract Child Adolesc Ment Health. 2019;4(2):141–56.
4. Trovão, N, J Prata, O Vondoellinger, S Santos, M Barbosa, R Coelho. Peripheral Biomarkers for First-Episode Psychosis—Opportunities from the Neuroinflammatory Hypothesis of Schizophrenia. Psychiatry Investig. 2019;16(3):177.
5. Lieberman, JA, GD Tollefson, C Charles, R Zipursky, T Sharma, RS Kahn, et al. Antipsychotic Drug Effects on Brain Morphology in First-Episode Psychosis. Arch Gen Psychiatry. 2005;62(4):361–70.
6. Yang, C, J Tang, N Liu, L Yao, M Xu, H Sun, et al. The Effects of Antipsychotic Treatment on the Brain of Patients With First-Episode Schizophrenia: A Selective Review of Longitudinal MRI Studies. Front Psychiatry. 2021;12:593703.
7. Howes, OD, T Whitehurst, E Shatalina, L Townsend, EC Onwordi, TLA Mak, et al. The clinical significance of duration of untreated psychosis: an umbrella review and random-effects meta-analysis. World Psychiatry. 2021;20(1):75.
8. McGorry, PD, E Killackey, A Yung. Early intervention in psychosis: concepts, evidence and future directions. World Psychiatry. 2008;7(3):148.
9. Fusar-Poli, P, PD McGorry, JM Kane. Improving outcomes of first-episode psychosis: an overview. World Psychiatry. 2017;16(3):251–65.
10. Zhilyaeva, T, G Rukavishnikov, E Manakova, G Mazo. Serum Interleukin-6 in Schizophrenia: Associations with Clinical and Sociodemographic Characteristics. Consortium Psychiatricum. 2023;4(4):5.
11. Foley, ÉM, GM Khandaker. Cytokines in psychosis: from mechanism towards treatment and prediction. Lancet Psychiatry. 2023;10(4):237–9.
12. Misiak, B, F Bartoli, G Carrà, B Stańczykiewicz, A Gładka, D Frydecka, et al. Immune-inflammatory markers and psychosis risk: A systematic review and meta-analysis. Psychoneuroendocrinology. 2021;127.
13. Miller, BJ, DR Goldsmith. Evaluating the Hypothesis That Schizophrenia Is an Inflammatory Disorder. Focus (Am Psychiatr Publ). 2020;18(4):391–401.
14. Muscatell, KA, SN Brosso, KL Humphreys. Socioeconomic status and inflammation: a meta-analysis. Mol Psychiatry. 2018;25(9):2189.

15. Hintikka, J, SM Lehto, L Niskanen, A Huotari, KH Herzig, H Koivumaa-Honkanen, et al. Unemployment and ill health: a connection through inflammation? BMC Public Health. 2009;9:410.
16. Zubin, J, B Spring. Vulnerability: A new view of schizophrenia. J Abnorm Psychol. 1977;86(2):103–26.
17. Walker, EF, D Diforio. Schizophrenia: A Neural Diathesis-Stress Model. Psychol Rev. 1997;104(4):667–85.
18. Pruessner, M, AE Cullen, M Aas, EF Walker. The neural diathesis-stress model of schizophrenia revisited: An update on recent findings considering illness stage and neurobiological and methodological complexities. Neurosci Biobehav Rev. 2017;73:191–218.
19. Reale, M, E Costantini, NH Greig. Cytokine Imbalance in Schizophrenia. From Research to Clinic: Potential Implications for Treatment. Front Psychiatry. 2021;12(March):1–17.
20. Adib-Conquy, M, JM Cavaillon. Compensatory anti-inflammatory response syndrome. Thromb Haemost. 2009;101(1):36–47.
21. Momtazmanesh, S, A Zare-Shahabadi, N Rezaei. Cytokine Alterations in Schizophrenia: An Updated Review. Front Psychiatry. 2019;10.
22. Marcinowicz, P, M Więdłocha, N Zborowska, W Dębowska, P Podwalski, B Misiak, et al. A Meta-Analysis of the Influence of Antipsychotics on Cytokines Levels in First Episode Psychosis. J Clin Med. 2021;10(11):2488.
23. Lockwood, KG, AL Marsland, S Cohen, PJ Gianaros. Sex differences in the association between stressor-evoked interleukin-6 reactivity and C-reactive protein. Brain Behav Immun. 2016;58:173–80.
24. Cooper, JD, S Ozcan, RM Gardner, N Rustogi, S Wicks, GF Van Rees, et al. Schizophrenia-risk and urban birth are associated with proteomic changes in neonatal dried blood spots. Transl Psychiatry. 2017;7(12):1–14.