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RESEARCH ARTICLE

Comparison of Monocyte/High-Density Lipoprotein Cholesterol Ratio Between Patients with First-Episode and Chronic Schizophrenia

İlk Epizod ve Kronik Şizofreni Hastalarında Monosit/Yüksek Yoğunluklu Lipoprotein Kolesterol Oranı Karşılaştırması

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ABSTRACT
Objective: To investigate the monocyte/high-density lipoprotein ratio (MHR), which has been shown in the literature to be a novel inflammatory marker in patients with first-episode (FES) and chronic (CS) schizophrenia.
Materials and Methods: The study involved 38 patients with FES, 65 patients with CS and 40 healthy controls (HC). Retrospective investigations of blood parameters were carried out using the database and associated records. The monocyte count was divided by the HDL-C level to determine the MHR.
Results: Monocyte levels were significantly higher and platelet and HDL-C levels were significantly lower in both the FES and CS groups compared with the HC group. MHR levels were significantly higher in both the FES and CS groups compared with healthy controls, although no statistically significant difference was detected between the two groups. Correlation analyses revealed several modest associations between MHR and certain clinical variables, though no consistent relationship with illness duration or hospitalisation-related variables was observed.
Conclusion: The findings of this study demonstrate that MHR is significantly increased in patients with schizophrenia, supporting the notion that schizophrenia is associated with inflammatory activation. These results suggest that MHR may be associated with the inflammatory alterations observed in schizophrenia.

Keywords: Schizophrenia, inflammation, monocyte-to-high-density-lipoprotein ratio

ÖZET
Amaç: Literatürde ilk atak (İEŞ) ve kronik (KŞ) şizofreni hastalarında yeni bir inflamasyon belirteci olduğu gösterilen monosit/yüksek yoğunluklu lipoprotein oranını (MHO) araştırmaktır.
Gereç ve Yöntemler: Çalışmaya 38 IEŞ hastası, 65 KŞ hastası ve 40 sağlıklı kontrol (SK) dahil edildi. Kan parametrelerinin retrospektif incelemeleri, veri tabanı ve ilgili kayıtlar kullanılarak gerçekleştirilmiştir. MHO'yu belirlemek için monosit sayısı HDL-K düzeyine bölünmüştür.
Bulgular: Monosit düzeyleri önemli ölçüde daha yüksekken, trombosit ve HDL-K düzeyleri hem İEŞ hem de KŞ gruplarında sağlıklı kontrollere kıyasla önemli ölçüde daha düşüktü. MHO düzeyleri hem İEŞ hem de KŞ hastalarında sağlıklı kontrollere kıyasla önemli ölçüde daha yüksekti, ancak iki gurup arasında istatistiksel olarak anlamlı bir fark tespit edilmedi. Korelasyon analizleri, MHO ile belirli klinik değişkenler arasında birkaç mütevazı ilişki olduğunu gösterdi, ancak hastalık süresi veya hastaneye yatışla ilgili değişkenlerle tutarlı bir ilişki gözlemlenmedi.
Sonuç: Bu çalışmanın bulguları, şizofreni hastalarında MHO'nun önemli ölçüde arttığını göstermekte ve şizofreninin inflamatuar aktivasyonla ilişkili olduğu görüşünü desteklemektedir. Bu sonuçlar, MHO'nun şizofrenide gözlenen inflamatuar değişikliklerle ilişkili olabileceğini düşündürmektedir.

Anahtar Kelimeler: Şizofreni, inflamasyon, monosit/yüksek yoğunluklu lipoprotein oranı

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INTRODUCTION

Schizophrenia is a severe and chronic psychiatric disorder characterized by disturbances in perception, thought processes, emotional regulation, and behavior, and it affects approximately 1% of the global population (1, 2). In addition to its profound impact on functional outcomes and quality of life, schizophrenia is associated with complex and multifactorial pathophysiological mechanisms involving genetic, neurodevelopmental, and environmental factors. In recent years, increasing evidence has indicated that immune dysregulation and inflammatory processes may be important in the pathophysiology of schizophrenia (3, 4). Several lines of evidence support the involvement of inflammatory mechanisms in schizophrenia. Studies have demonstrated alterations in peripheral immune markers, including increased levels of pro-inflammatory cytokines and changes in immune cell profiles in patients with schizophrenia (5–8). Neuroinflammatory processes, particularly microglial activation and dysregulated immune signalling within the central nervous system, have also been suggested as potential causes of neuronal dysfunction and symptom development in schizophrenia (9). These findings have led to growing interest in identifying accessible peripheral biomarkers that may reflect the inflammatory alterations associated with the disorder.

In recent years, routine blood-based inflammatory indices derived from standard hematological and biochemical parameters have gained attention as potential biomarkers in psychiatric research. Among these markers, the neutrophil-to-lymphocyte ratio (NLR), the platelet-to-lymphocyte ratio (PLR) and the monocyte-to-lymphocyte ratio (MLR) have been investigated as potential indicators of systemic inflammation in patients with schizophrenia. Several studies have reported elevated NLR and PLR levels in patients with schizophrenia compared to healthy controls, suggesting the presence of low-grade systemic inflammation in the condition (10–12). Additionally, composite biomarkers derived from routine laboratory parameters, such as C-reactive protein-based indices and other haematology-derived inflammatory markers, have been increasingly explored to better characterise immune dysregulation in psychiatric disorders. The monocyte-to-high-density lipoprotein cholesterol ratio (MHR) is one of the emerging inflammatory biomarkers that has recently attracted considerable attention as a composite marker reflecting the balance between pro-inflammatory and anti-inflammatory processes. Monocytes are key components of the innate immune system and play a crucial role in inflammatory responses through the secretion of pro-inflammatory cytokines and oxidative mediators (13). In contrast, high-density lipoprotein cholesterol (HDL-C) exerts anti-inflammatory, antioxidant, and endothelial-protective effects, partly by inhibiting monocyte activation and reducing oxidative stress (14, 15). Consequently, the MHR, which is calculated by dividing the monocyte count by the HDL-C level, has been suggested as an effective indicator of systemic inflammatory burden.

Previous studies have shown that MHR is associated with inflammatory activity and disease severity in several cardiovascular, metabolic, and inflammatory disorders (16,17-20). These findings suggest that MHR may serve as a practical and accessible biomarker reflecting immune and inflammatory processes in various clinical conditions. Given the growing evidence linking schizophrenia with immune dysfunction and chronic low-grade inflammation, investigating MHR in patients with schizophrenia may provide additional insight into the inflammatory mechanisms underlying the disorder. Only a limited number of studies have examined MHR levels in patients with schizophrenia. Previous studies have reported higher MHR levels in patients with schizophrenia compared with healthy controls and have suggested that this marker may be associated with disease severity or clinical characteristics (21-24). However, the existing literature remains limited, with most studies have evaluated schizophrenia patients as a single group without considering potential differences across illness stages.

From an inflammatory perspective, comparing patients with first-episode schizophrenia (FES) and chronic schizophrenia (CS) may provide valuable insights into whether inflammatory alterations represent an early feature of the disorder or develop progressively during the course of the illness. Previous studies examining inflammatory biomarkers such as cytokines and hematological ratios have reported increased inflammatory markers both in first-episode and chronic stages of schizophrenia, although findings regarding differences across disease stages remain inconsistent (25-27). Therefore, further research is needed to clarify whether inflammatory markers differ between early and chronic phases of schizophrenia. Based on this background, the present study aimed to investigate serum monocyte-to-HDL cholesterol ratio (MHR) levels as a potential inflammatory biomarker in patients with first-episode and chronic schizophrenia and to compare these findings with healthy controls. It was hypothesised that MHR levels would be higher in patients with schizophrenia than in healthy individuals, and that any differences between patients experiencing their first episode of the disorder and those with chronic schizophrenia might reflect stage-related inflammatory alterations in the disorder.

MATERIALS AND METHODS

Design and Participants

This retrospective study reviewed the medical records of patients hospitalized with a diagnosis of schizophrenia according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), at the Psychiatry Clinic of the University of Health Sciences Beyhekim Training and Research Hospital between January 2018 and July 2020. Patient inclusion was performed consecutively among eligible individuals who met the study criteria during the study period in order to minimize potential selection bias. A total of 103 male patients aged between 18 and 65 years were included in the study. The patients were divided into two groups: those with first-episode schizophrenia (FES) and those with chronic schizophrenia (CS). The CS group consisted of patients previously diagnosed with

schizophrenia who had not used any antipsychotic medication within the last six months and were followed through the hospital automation system. This criterion was applied to minimize the potential effects of antipsychotic medications on inflammatory markers and lipid metabolism.

To reduce biological variability related to hormonal fluctuations that may influence lipid metabolism and inflammatory parameters, only male participants were included in the study. In particular, variations in estrogen levels and menstrual cycle phases may affect HDL-C levels and inflammatory markers; therefore, restricting the sample to male participants was intended to improve the homogeneity of the study population. Clinical information regarding the patients, including duration of illness, number of episodes, and number of hospitalizations, was obtained from the hospital automation system.

Control Group

The control group consisted of healthy male individuals who attended routine health examinations during the same time. The control group was matched to the patient group in terms of age and smoking status. Individuals in the control group were required to have no history of psychiatric disorders, chronic inflammatory diseases, metabolic disorders, cardiovascular diseases, or other systemic illnesses that could affect inflammatory or lipid parameters.

Exclusion Criteria

Participants with an acute infection, autoimmune disease, chronic inflammatory disorder, metabolic syndrome, liver or kidney disease, malignancy, or a substance use disorder were excluded from the study. Additionally, individuals who had recently used medications known to influence inflammatory markers or lipid metabolism were excluded. These medications included systemic corticosteroids, anti-inflammatory drugs, lipid-lowering agents, and immunomodulatory medications. Smoking status was obtained from medical records and recorded as a potential confounding variable.

Laboratory Measurements

A retrospective analysis of demographic characteristics, clinical data, and laboratory findings was performed using the hospital's computerized medical database. Venous blood samples were obtained from all participants after overnight fasting. Hematological parameters, including monocyte counts, and biochemical parameters, including high-density lipoprotein cholesterol (HDL-C), were measured using standard automated laboratory methods. The monocyte-to-high-density lipoprotein cholesterol ratio (MHR) was calculated by dividing the absolute monocyte count (10^3/μL) by the HDL-C level (mg/dL). As a ratio, MHR was expressed as a unitless index.

Ethical Approval: The research had the approval of the Faculty of Medicine's clinical research ethics committee, KTO Karatay University (approval number E.2345-41901325-050.99, date: 17 July 2020). Research was conducted according to the standards of the Declaration of Helsinki. No invasive procedures were performed.

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS), version 18.0, was used for data analysis. Categorical variables were presented as numbers and percentages, whereas continuous variables were expressed as the mean ± standard deviation (SD). The chi-square test was used to assess the associations between the categorical variables. The Kolmogorov–Smirnov test was applied to evaluate normality. One-way analysis of variance (ANOVA) was used to compare normally distributed continuous variables among the three groups, while the Kruskal–Wallis test was used for non-normally distributed variables. Post-hoc pairwise comparisons were performed using the Tukey test when the assumption of homogeneity of variances was met, and the Games–Howell test when this assumption was violated. A p-value of less than < 0.05 was considered statistically significant. Although most continuous variables were normally distributed and analyzed using parametric tests, correlation analyses were conducted using Spearman's rank correlation coefficient. This decision was made because several clinical variables (e.g., disease duration, number of hospitalizations) demonstrated skewed distributions and/or potential non-linear relationships. Therefore, a non-parametric correlation method was preferred to provide a more robust assessment of associations across variables with heterogeneous distributional properties.

Sample size estimation was performed using G*Power software (version 3.1.9.7). An a priori power analysis was conducted based on the comparison of MHR values among the three independent groups using the F-tests family and one-way ANOVA fix fixed effects, omnibus, one-way statistical test. Assuming an effect size of $f = 0.30$, an alpha error probability of 0.05, a power of 0.80 and three groups, the minimum total sample size required was calculated to be 111 participants. The present study included a total of 143 participants, indicating that the sample size was sufficient for the planned analyses.

RESULTS

The study sample consisted of 143 male participants, including 38 patients with first-episode schizophrenia (FES), 65 patients with chronic schizophrenia (CS), and 40 healthy controls (HC). For categorical variables, chi-square statistics (χ^2) are reported alongside p-values. For continuous variables analyzed using ANOVA, F-statistics are presented to provide a complete description of the statistical analyses. A statistically significant difference in age was observed between the groups ($F = 18.76$, $p < 0.001$) (see Table 1). The younger age observed in the FES group was consistent with the earlier onset of first-episode schizophrenia. Smoking status did not differ significantly between the FES and CS groups ($p = 0.081$). In the CS group, the mean duration of illness was 115.6±68.1 months. The mean number of hospitalizations was 3.4±2.0, and the mean number of relapses was 3.9±2.1. Demographic and clinical characteristics of groups are presented in Table 1.

Comparisons of hematological and biochemical parameters among the three groups are shown in Table 2. There were significant differences among the groups in platelet levels ($F = 25.04$, $p < 0.001$), monocyte levels ($F = 17.82$, $p < 0.001$), HDL-C levels ($F = 31.19$, $p < 0.001$), and MHR ($F = 34.02$, p

Table 1. Clinical and demographic characteristics of patients with schizophrenia

	FES (n=38)	CS (n=65)	HC (n=40)	χ^2/F (overal	p (overall)	χ^2/t (FES vs CS)	p (FES vs CS)
Age (years)	25±6.3	34.8±8.4	30.6±8.1	18.76	<0.001	6.21	<0.001
Smoking							
Yes	29 (76.3%)	58 (89.2%)	22 (55%)	12.23	0.002	3.05	0.081
No	9 (23.7%)	7 (10.8%)	18 (45%)				
Marital Status							
Single	35 (92.1%)	39 (60%)	-			13.67	<0.001
Married	2 (5.3%)	25(38.5%)	-				
Other	1(2.6%)	1(1.5%)	-				
Education Status							
≤8 years	16 (42.1%)	52 (80%)	-			15.65	<0.001
>8 years	22 (57.9%)	13 (20%)	-				
Disease duration	-	115.6±68.1	-				
Number of Hospitalizations	-	3.4±2.0	-				
Number of Episodes	-	3.9±2.1	-				

FES: First-episode schizophrenia; CS: Chronic schizophrenia; HC: Healthy control.
Continuous variables were expressed as mean±SD and compared using one-way ANOVA for overall group comparisons and independent samples t-test for pairwise comparisons (FES vs CS).
Categorical variables were expressed as n (%) and analyzed using the chi-square test (χ^2) for both overall and pairwise comparisons. p<0.05 was considered statistically significant.

Table 2. Comparison of blood count parameters between patients with schizophrenia and healthy controls.

	FES (n=38)	CS (n=65)	HC (n=40)	F	p	post hoc
WBC (10^3/μL)	7.1±1.2	7.4±1.3	6.8±1.6	2.33	0.100	
Hemoglobin (g/dL)	15±1.3	15.1±1.1	14.3±1.1	5.25	0.006	
Platelets (10^3/μL)	226.6±50.8	221.3±49.6	284.2±34.9	25.04	<0.001	HC > FES, HC >CS
Neutrophils (10^3/μL)	3.7±1.1	4.2±1.1	4.1±1.2	1.88	0.156	
Monocytes (10^3/μL)	0.7±0.1	0.7±0.1	0.5±0.1	17.82	<0.001	FES>HC, CS> HC
Lymphocytes (10^3/μL)	2.5±0.8	2.4±0.6	2.3±0.5	0.83	0.434	
Triglyceride (mg/dL)	102.8±38.6	112.2±41.3	101.2±32.9	1.28	0.279	
LDL-C (mg/dL)	100.7±32.9	99.4±30.7	104.8±25.5	0.40	0.666	
HDL-C (mg/dL)	41.7±9.4	38.3±7.7	50.8±6.5	31.19	<0.001	HC > FES, HC>CS
MHR	17.5±4.6	19.4±6.6	10.9±2.2	34.02	<0.001	FES>HC, CS > HC

FES: First-episode schizophrenia; CS: Chronic schizophrenia; HC: Healthy control; WBC: White blood cell; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; MHR: Monocyte-to-high-density lipoprotein ratio. Statistics: One-way ANOVA was used for group comparisons. Results are presented with F-statistics and corresponding p-values. Post-hoc comparisons were performed using the Tukey test. Data are expressed as mean ± SD. p < 0.05 was considered statistically significant.
MHR was calculated as monocyte count (10^3/μL) divided by HDL-C (mg/dL) and expressed as a unitless ratio.

< 0.001). Compared with the HC group, both FES and CS patients exhibited significantly higher monocyte counts and significantly lower platelet and HDL-C levels. Mean MHR values were 17.5 ± 4.6 in the FES group, 19.4 ± 6.6 in the CS group, and 10.9 ± 2.2 in the HC group. MHR levels were significantly higher in both the FES and CS patients compared with healthy controls (p < 0.001). Given the significant age difference between the groups, an analysis of covariance (ANCOVA) was conducted with age as a covariate to control for its potential confounding effect. After adjustment for age, the difference in MHR levels between the groups remained statistically significant (p < 0.001). Post hoc pairwise comparisons using the Tukey test showed that MHR levels were significantly higher in both the FES and CS groups than in the HC group. However, no statistically significant difference was detected between the FES and CS groups. Although the mean MHR value was numerically higher in the CS group than in the FES group, no statistically significant difference was detected between these two groups. The mean difference between the CS and FES groups was 1.9, indicating a higher MHR value in the CS group; however, no evidence of a statistically significant between-group difference was detected. Comparisons of MHR and other hematological parameters among the three groups are presented in Table 2.

Correlation analyses were performed to examine the relationship between MHR levels and clinical variables in patients with chronic schizophrenia. A statistically significant positive correlation was observed between disease duration and age in the FES, CS and FES+CS groups (p<0.01). A weak positive correlation was also observed between age and MHR in the healthy control (HC) group (p: 0.03). The results of the correlation analysis showed no statistically significant

Table 3. Spearman's correlation coefficients for the groups

	Correlations	Correlation coefficient (r)	Level	p value
Patients (FES+CS)				
(n: 103)	Age-Disease duration	0.79	Strong	p<0.01
	WBC-MHR	0.31	Weak	p<0.01
FES (n: 38)	Age-Disease duration	0.43	Moderate	p<0.01
CS (n: 65)	Age-Disease duration	0.71	Strong	p<0.01
	WBC-Disease duration	0.25	Weak	0.04*
HC (n: 40)	WBC-MHR	0.53	Moderate	p<0.01
	Age-MHR	0.35	Weak	0.03*

FES: First Episode schizophrenia, CS: Chronic schizophrenia, HC: Healthy control, Statistics: Spearman's correlation test, *p<0.05, **p<0.01, For correlation analyses, the Spearman correlation coefficient (r) was considered as an effect size indicator.

link between MHR levels and either the number of hospital admissions or the number of relapses. The detailed results of the correlation analyses are presented in Table 3.

DISCUSSION

The present study demonstrated that MHR levels were significantly higher in both first-episode schizophrenia (FES) and chronic schizophrenia (CS) patients compared with healthy controls. These findings indicate that alterations in the balance between pro-inflammatory monocytes and anti-inflammatory HDL-C may be associated with schizophrenia. However, no statistically significant difference was detected between the FES and CS groups, suggesting that within the limits of the present sample size, we did not observe evidence of stage-related differences in MHR levels. Recent research suggests that inflammatory responses may contribute to the development of, and worsen the prognosis for several mental illnesses (28). Pro-inflammatory cytokines contribute to the activation of microglia. However, as cytokines and other direct inflammatory mediators were not measured in the present study; therefore, these mechanisms should be considered biologically plausible hypotheses rather than mechanisms demonstrated by the current data. This activation is strongly correlated with initiating and progressing the inflammatory process. The possibility that an aberrant immunological response contributes to the development of schizophrenia is often raised (29,30). In many clinical studies of schizophrenia patients, the detection of elevated peripheral cytokine levels in plasma is accepted as an indicator of an increased peripheral immune response (31-33). Numerous studies have consistently shown a significant increase in monocyte levels (they secrete proinflammatory and prooxidant cytokines) and total white blood cell counts (13,23). These findings have prompted the search for simple and reliable inflammatory markers that may reflect immune dysregulation in schizophrenia (10,21).

In this context, hematological inflammatory indices such as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and monocyte-to-lymphocyte ratio (MLR) have been investigated as potential biomarkers in schizophrenia (10-12). Several inflammatory ratios such as NLR, PLR, and MLR have been reported to be elevated in schizophrenia and are considered indirect indicators of systemic inflammation. These findings provide a broader context for investigating composite inflammatory markers such as the MHR. Monocytes and macrophages are the cells responsible for pro-inflammatory and pro-oxidative responses. These cells are central to the initiation and regulation of inflammatory responses. Their activation triggers the production and release of inflammatory cytokines (34). On the other hand, HDL-C modulates monocyte activation and adhesion, controls the proliferation of progenitor cells that differentiate into monocytes, and increases nitric oxide synthase expression in endothelial tissue. These properties give it antioxidant and anti-inflammatory activity (35). Taken together, MHR has been proposed as a potentially useful composite inflammatory index reflecting the balance between pro-inflammatory monocytes and anti-inflammatory HDL-C (36).

Consistent with this conceptual framework, MHR has been investigated as a systemic inflammatory marker in various chronic inflammatory and vascular conditions, where elevated levels were generally interpreted as reflecting an increased inflammatory burden (16,17,37). These findings from different clinical contexts support the rationale for examining MHR in psychiatric disorders characterized by potential immune dysregulation, such as schizophrenia. However, studies evaluating MHR in schizophrenia remain limited, particularly in patients at different stages of the illness. Only a small number of studies have examined MHR in patients with schizophrenia. Sahpolat et al. reported significantly higher MHR levels in patients with schizophrenia compared to healthy controls and demonstrated a positive correlation between MHR and total PANSS scores, suggesting a relationship between inflammation and disease severity (23). In another study, Wei et al. found higher MHR levels in patients with schizophrenia compared to HC. In addition, they emphasized that MHR may be a predictor for differentiating schizophrenia patients from HC (24). Similar to our study, a 2023 study comparing the MHR levels of 85 patients with schizophrenia and 50 healthy controls and reported that the patient group had significantly higher MHR and platelet levels, and significantly lower HDL-C levels, compared to the control group (21). In another study conducted in the same year, 214 schizophrenia patients were divided into 2 groups as aggressive and non-aggressive, and it was reported that platelet, monocyte, and MHR levels of the aggressive patients were significantly higher than the non-aggressive schizophrenia group, and MHR levels may be used

to predict aggressive behavior in schizophrenia patients. They also did not compare these results with the HC (22). However, in these two studies, which were similar to our study, they did not evaluate the patient group by dividing them into two different groups as FES and CS as in our study.

According to the results of our research, MHR levels were significantly higher in people diagnosed with schizophrenia compared to HC. These findings are consistent with previous studies and are compatible with the presence of systemic inflammatory alterations reported in schizophrenia, although the present design does not allow for causal inferences regarding the role of inflammation in the pathophysiology of the disorder. However, there was no scale in the medical records to indicate the severity of the attacks. Therefore, we could not investigate the possible effect of episode severity on inflammation. In addition, age differences between the groups may have affected the results. Contrary to the findings of Sahpolat et al., no correlation was found between other clinical characteristics that might indicate disease severity and MHR levels in CS patients (23). Further studies may be needed to clarify this relationship. Unlike most previous studies, this study compared MHR levels between first-episode schizophrenia (FES) and chronic schizophrenia (CS) patients. Although the mean MHR value was numerically higher in the CS group than in the FES group, no statistically significant between-group difference was detected. Therefore, within the limits of the present sample, we did not observe any of stage-related differences in MHR levels. However, the study was not specifically powered to detect differences between patient subgroups, so the possibility of a type II error cannot be excluded. Further adequately powered prospective studies are required to determine whether inflammatory alterations differ across illness stages.

Correlation analyses revealed several associations between MHR levels and certain clinical variables. However, these relationships were modest and should be interpreted cautiously given the retrospective design and potential residual confounding. Previous studies have also reported elevated inflammatory markers in both first-episode and chronic schizophrenia, although findings regarding changes across disease progression remain inconsistent (25-27). The differences between the present findings and those reported by Sahpolat et al. (23) may be due to methodological factors such as variations in sample composition or study design, or the absence of standardized psychopathology severity scales in the present study.

Study Limitations

This study has several limitations that should be considered when interpreting the findings. Firstly, the retrospective design may introduce potential selection bias. As the sample of patients consisted of individuals who were hospitalised, the study population may represent patients with more severe clinical presentations, which may limit the generalisability of the findings to all individuals with schizophrenia. Secondly, the healthy control group was recruited from individuals attending routine health examinations, which may introduce a potential health-seeking bias. Thirdly, although smoking status was available and considered in the analyses, other potential confounding factors that may influence inflammatory markers and lipid metabolism, such as physical activity, dietary habits, and socioeconomic status, were not systematically recorded in the medical records and therefore could not be included in the analysis.

Finally, the study included only male participants in order to minimize hormonal variability that could influence lipid and inflammatory parameters. While this approach improved sample homogeneity, it may limit the generalizability of the findings to female patients with schizophrenia. Future research should employ prospective longitudinal designs that include repeated MHR measurements across relapse and remission phases, standardized psychopathology scales (e.g., PANSS or BPRS), and multivariable models adjusting for metabolic and lifestyle-related covariates. Despite these limitations, this study contributes to the limited literature examining MHR in schizophrenia and provides additional evidence to support the potential role of this accessible biomarker in inflammatory alterations associated with the disorder.

CONCLUSION

Previous studies have suggested that a high MHR may be a new biomarker for inflammatory disorders. Our study showed that MHR is significantly elevated in patients with schizophrenia. The findings of the present study demonstrate that MHR levels are significantly higher in patients with schizophrenia compared to healthy controls, supporting the growing body of evidence that schizophrenia is associated with inflammatory activation. Moreover, this study is among the first to evaluate MHR levels in patients with first-episode schizophrenia, indicating that inflammatory alterations may be present even in the early stages of the disease. Although no significant difference was observed between the first-episode and chronic schizophrenia groups, the overall elevation of MHR in patients with schizophrenia suggests that this marker may be compatible with the presence of persistent low-grade inflammatory alterations reported in schizophrenia. Future longitudinal and multicenter studies with larger and more diverse populations, incorporating standardized clinical assessments and comprehensive inflammatory panels, including cytokine profiling, are needed to clarify whether MHR reflects a stable trait marker or varies according to clinical state and treatment response, and to further evaluate its potential clinical utility as an accessible inflammatory marker.

DECLARATIONS

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