PPN

Personalized Psychiatry and Neurology

Systematic review

Monocyte-to-Lymphocyte Ratio Any Association with Metabolic Syndrome in Schizophrenia

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Abstract: The problem of adverse drug reactions (ADR) development in psychopharmacotherapy is one of the current issues in the treatment of patients with schizophrenia. One of the most common ADRs when taking antipsychotics is the development of metabolic syndrome. This reduces the quality of life of patients and increases the risk of premature death of patients due to cardiovascular diseases. Markers of systemic inflammation are a predictor of the development of metabolic syndrome in patients with schizophrenia. One of these hematological coefficients is the monocyte-to-lymphocyte ratio (MLR). **Objective**: to conduct a systematic review of scientific publications based on the relationship between MLR and metabolic syndrome in patients with schizophrenia. **Methods**: The initial search identified 120 articles from the Pubmed and ScienceDirect databases. The inclusion criterion for the study is the relationship between the MLR and metabolic syndrome in patients with schizophrenia. **Result**: Screening did not yield any publications suitable for systematic review.

Keywords: *monocyte-to-lymphocyte ratio (MLR), schizophrenia, metabolic syndrome, hematologic inflammation coefficients (HICs), systemic inflammation, psychiatric disorders, immune dysregulation, biomarkers, antipsychotic therapy, psychoneuroimmunology.*

1. INTRODUCTION

Schizophrenia is a severe, chronic mental illness that affects approximately 24 million people, or 1 in 300 people (0.32%) worldwide. Among adults, the rate is 1 in 222 people (0.45%) [1].

However, the etiology, pathogenesis and optimal therapy of this disease are still being studied. In recent years, the role of the sensor in the occurrence of schizophrenia and the development of adverse events when it appears has been actively studied. There is growing evidence that disturbances in the immune system, including the inflammatory response, are realized in these processes [2].

Metabolic syndrome is common in patients with schizophrenia, increasing patients' risk of premature death due to cardiovascular disease [3 - 6]. One of the most promising predictors of metabolic syndrome is the hematological coefficients of the sensor, obtained from a clinical blood test. The monocyte-to-lymphocyte ratio (MLR) is an inexpensive, easy-to-observe, and easy-to-calculate marker of systemic attention [7]. Understanding the relationship between MLR and metabolic syndrome can help identify individuals at high risk of developing it and implement preventive measures. This systematic review aims to determine the utility of MLRs as early indicators of the development of metabolic syndrome in patients with schizophrenia.

Purpose of the study is to determine a link between monocyte/leukocyte ratio and metabolic syndrome in patients with schizophrenia..

2. MATERIALS AND METHODS

The work was carried out from June to September 2024 in accordance with the principles of the PRISMA guidelines for systematic reviews [8] (Fig. 1) by a team of five psychiatrists, a clinical pharmacologist and one neurologist.

According to PRISMA criteria, this systematic review was conducted in five stages: search design and strategy, article search and analysis, assessment of inclusion and exclusion criteria, quantitative or qualitative assessment, and statistical data analysis. Each article found independently through a search query in two search publication databases was included in an online Excel table indicating the title of the article, authors, document doi, year of publication.

The search was carried out using the search query ("Monocyte to lymphocyte ratio"[Title/Abstract] OR "MLR"[Title/Abstract]) AND ("metabolic syndrome"[Title/Abstract]) OR ("schizophrenia"[Title/Abstract]]) in the international databases PubMed and ScienceDirect. All available studies had been analyzed.

We were looking for prospective and retrospective studies examining the MLR in patients with a verified diagnosis of schizophrenia according to ICD-10 criteria and metabolic syndrome according to the International Diabetes Federation criteria in comparison with a healthy control group.

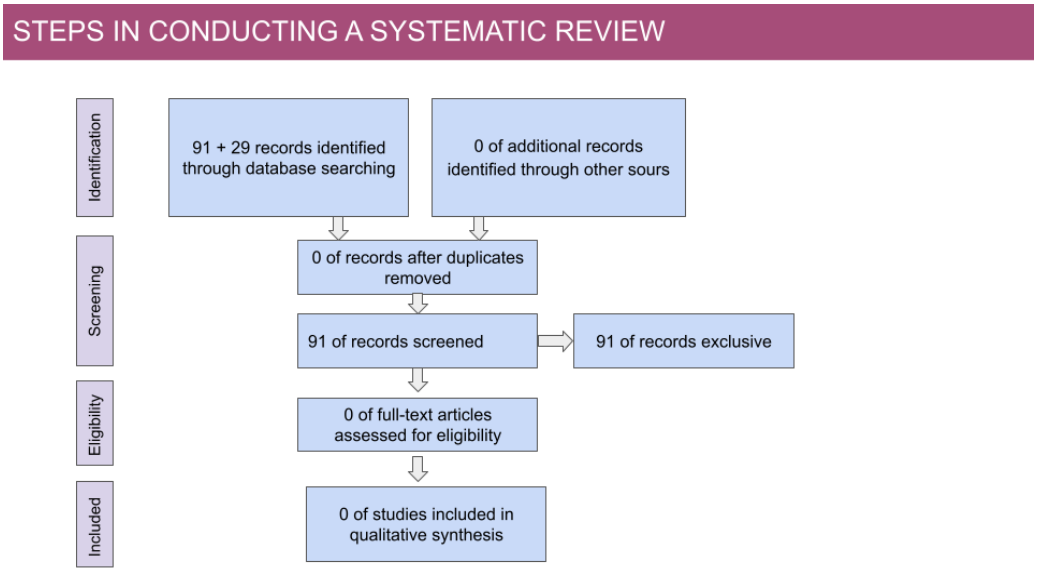

Figure 1. This a Block diagram of PRISMA 2020 [9]

2.1 Eligibility Assessment

The systematic review was intended to include studies that could assess the association (or lack thereof) between the MLR and the development of metabolic syndrome in patients with schizophrenia. The quality of the selected studies was planned to be assessed using the Newcastle-Ottawa Scale (NOS) checklist. The NOS checklist consists of eight sections in which studies are assigned a score of 0, indicating low quality, and a score of 8, indicating high quality. Studies are classified into three categories depending on their quality score: 5 or less indicates low quality, 5-6 indicates moderate quality, and 7-8 indicates high quality. Articles of moderate quality and above

were to be reviewed. Disagreements arising during the assessment process were planned to be discussed until a consensus was reached.

2.2 Schizophrenia criteria:

Criteria for the diagnosis of Schizophrenia (F20) according to ICD-10 [10] :

1. For the majority of a psychotic episode lasting at least one month (or for some time on most days), at least one of the features listed in checklist (1) or at least two of the features listed in checklist (2) must be present. 1) At least one of the following signs: a) "echo" of thoughts, insertion or withdrawal of thoughts, or openness of thoughts; b) delusions of influence or influence, distinctly referring to movement of the body or limbs or to thoughts, actions or sensations; delusional perception; c) hallucinatory "voices", which are a current commentary on the patient's behavior or a discussion of it among themselves, or other types of hallucinatory "voices" emanating from any part of the body; d) persistent delusional ideas of another kind that are culturally inadequate and completely impossible in content, such as identifying oneself with religious or political figures, claims of superhuman abilities (for example, the ability to control the weather or communicate with aliens). (2) or at least two of the following signs: a) chronic hallucinations of any kind, if they occur daily for at least one month and are accompanied by delusions (which may be unstable and half-formed) without clear affective content; b) neologisms, breaks in thinking, leading to discontinuity or inconsistency in speech; c) catatonic behavior such as agitation, rigidity or waxiness, negativism, mutism and stupor; d) "negative" symptoms, such as severe apathy, speech impoverishment and flattened or inappropriate emotional reactions (it should be obvious that these are not caused by depression or antipsychotic therapy.

Exclusion criteria: 1) If the case also meets the criteria for a manic episode (F 30-) or a depressive episode (F 32-), criteria 1.1 and 1.2 above must be identified BEFORE the development of a mood disorder. 2) The disorder cannot be attributed to organic brain disease (as set out in F 00-09) or to alcohol or drug intoxication (F 1x.0), dependence (F 1x.2) or withdrawal state (F 1x.3 and 1x. 4).

2.3 Metabolic syndrome criteria:

Metabolic syndrome in subjects was defined according to the International Diabetes Federation criteria as the presence of central obesity, defined by a waist circumference (WC) ≥ 94 cm for men and ≥ 80 cm for women or a body mass index (BMI) > 30 kg/m2, in combination with any two of four factors: systolic blood pressure ≥ 130 mm Hg. Art. or diastolic ≥ 85 mm Hg. Art., triglyceride (TG) level in the blood ≥ 1.7 mmol/l, high-density lipoprotein (HDL) < 1.03 mmol/l (in men) or < 1.29 mmol/l (in women), glucose level fasting blood ≥ 5.6 mmol/l or diagnosed non-insulin-dependent diabetes mellitus [11].

3. RESULTS

Thus, an initial search of the two databases identified 120 publications. Information about the found publications will be saved in an online Excel table, which takes into account the necessary information for the subsequent selection of articles. The study will include original research on a given topic without time restrictions. The criterion for inclusion in the study is the relationship between the MLR and metabolic syndrome in patients with schizophrenia. The study must indicate the sample size, the specific number of subjects examined in each study group. The sample size, the number of patients in the study and control groups, age indicators, features of the clinical picture, features of psychopharmacotherapy, psychometric tools, criteria for metabolic syndrome and measurement of the MLR will necessarily be taken into account. Each

article will be reviewed by three psychiatrists to eliminate potential errors. Where necessary, additional information and raw data will be requested by contacting the author (first author or responsible person or department of the authors). Further, articles that meet the inclusion criteria will be studied by the entire team of authors. Data processing will be carried out using the statistical and analytical solution XLSTAT and Statistica.

No publications suitable for systematic review were found based on the screening results.

4. DISCUSSION

In the course of our study, we came to a null result for the originally planned query and we could not answer the question affirmatively whether there is a relationship between the MLR and the development of metabolic syndrome in patients with schizophrenia. Probably, the review error is the limitation of the number of databases to two and in the future it is necessary to include other databases to search for publications for the planned query. Also, the chosen topic is little studied, but the proposed research is innovative and has both practical and theoretical significance.

However, our colleagues published another systematic review, which considered other GCI, namely the neutrophil to lymphocyte ratio taking into account the dynamics of schizophrenia in comparison with the indicators of a group of healthy volunteers. According to the results of the review, it was not possible to establish causal relationships between the change in hematological indices and the development of metabolic disorders [12].

5. CONCLUSION

The hypothesis we formulated that the use of HICs in combination with the analysis of clinical and psychosocial factors allows us to identify the risks of the formation of MN in a group of patients with mental disorders cannot be refuted or confirmed to date due to insufficient study of the topic, which is confirmed by isolated publications. In the future, it is necessary to study the relationship between MLS and the development of metabolic disorders in patients with schizophrenia.

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REFERENCES:

1. Nasyrova, R.F.; Kidyaeva, A.V.; Petrova, M.M.; Shnayder, N.A. Antipsychotic-induced QT prolongation and torsade de pointes in patients with mental disorders: A review. *Safety and Risk of Pharmacotherapy*. **2024**, 12(4):380-395. doi:10.30895/2312-7821-2024-410
2. Frota, I.J.; de Oliveira, A.L.B.; De Lima, D.N. Jr.; et al. Decrease in cognitive performance and increase of the neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios with higher doses of antipsychotics in women with schizophrenia: a cross-sectional study. *BMC Psychiatry*. **2023**, 23(1):558. doi:10.1186/s12888-023-05050-x
3. Mazo, G.E.; Kibitov. A.O. Risk management of metabolic disorders in the use of antipsychotics. *V.M. Bekhterev review of psychiatry and medical psychology*. **2016**, (3):85-97. (In Russ.)
4. Khasanova, A.K.; Dobrodeeva, V.S.; Shnayder, N.A.; et al. Blood and urinary biomarkers of antipsychotic-induced metabolic syndrome. *Metabolites*. **2022**, 12(8). doi:10.3390/metabo12080726
5. Petrova, N.N.; Semenova, N.V. Metabolic syndrome and antipsychotic therapy of schizophrenia. *S.S. Korsakov Journal of Neurology and Psychiatry*. **2024**, 124(11):165-170. doi:10.17116/jnevro2024124111165
6. Kidyaeva, A.V.; Nasyrova, R.F. The role of cariprazine in the prevention and correction of antipsychotic-induced cardiometabolic disorders. *Sovrem. ter. psih. rasstrojstv*. **2024**, 3:51-57. doi:10.21265/PSYPH.2024.75.87.005
7. Balcioglu, Y.H.; Kirlioglu, S.S. C-Reactive protein/albumin and neutrophil/albumin ratios as novel inflammatory markers in patients with schizophrenia. *Psychiatry Investig*. **2020**, 17:902–910. doi:10.30773/pi.2020.0185
8. Moher, D.; Liberati, A.; Tetzlaff, J.; Altman, D.G. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ.* **2009,** b2535. doi: 10.1136/bmj.b2535
9. Page, M.J.; McKenzie, J.E.; Bossuyt, P.M. et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. **2021**, n71. doi: 10.1136/bmj.n71
10. Geneva, I. ICD-10. Classification of Mental and Behavioral Disorders-2010, **1993**.
11. Dobrowolski, P.; Prejbisz, A.; Kuryłowicz, A.; et al. Metabolic syndrome - a new definition and management guidelines: A joint position paper by the Polish Society of Hypertension, Polish Society for the Treatment of Obesity, Polish Lipid Association, Polish Association for Study of Liver, Polish Society of Family Medicine, Polish Society of Lifestyle Medicine, Division of Prevention and Epidemiology Polish Cardiac Society, "Club 30" Polish Cardiac Society, and Division of Metabolic and Bariatric Surgery Society of Polish Surgeons. *Arch Med Sci*. **2022**, 18(5):1133-1156. doi: 10.5114/aoms/152921
12. Zakharova, N.V.; Nasyrova, R.F.; Rakhmatullin, A.I. et al. Neutrophil-to-Lymphocyte ratio any association with metabolic syndrome in schizophrenia. *Personalized Psychiatry and Neurology*. **2024,** 4(3):12-23. doi:10.52667/2712-9179-2024-4-3-12-23