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# Распространенные гематологические нарушения у пациентов с шизофренией: стационарное исследование «случай-контроль»

Ramdas Ransing[1]✉, Ashwini Kamble[2], Rajashree Kulkarni[1], Praveen Khairkar[2], Suvarna Patil[1], Krishna Pevekar[1], Kishord K. Misha[3], Nitin Gangane[3]

[1] Загородный медицинский колледж Валавалкар, Махараштра, Индия;
[2] Институт медицинских наук Каминени, Телангана, Индия;
[3] Институт медицинских наук имени Махатмы Ганди, Махараштра, Индия

***АННОТАЦИЯ***

***Введение.*** Несмотря на то, что распространенные гематологические нарушения (РГН) такие, как анемия, макроцитоз и дисфункция тромбоцитов, нередко встречаются у людей с шизофренией, эмпирические данные о них ограничены. До сих пор о подобных отклонениях сообщалось лишь в отчетах или серии клинических случаев.

***Цель.*** Изучить частоту РГН у пациентов с шизофренией.

***Материалы и методы.*** В это исследование был включен 491 пациент с шизофренией [в том числе не получавших лекарственных препаратов (n = 115) и пациенты с хронической шизофренией (n = 376)], а также 504 здоровых добровольца. Образцы крови были взяты у каждого участника и проанализированы на РГН с помощью автоматического счетчика Coulter. Для сравнения переменных в трех группах были использованы тесты $\chi^2$ и дисперсионный анализ (ANOVA).

***Результаты.*** Доля макроцитоза была почти одинаковой у пациентов с шизофренией (не получающих лекарственных препаратов — 10,5%, пациентов с хронической шизофренией — 10,6%), и при этом была значительно выше, чем у здоровых добровольцев контрольной группы (4,2%). Количество тромбоцитов было существенно выше в группе хронической шизофрении ([282,5 ± 87,9] × $10^3$/мкл), чем в группе, не получавших лекарственных препаратов ([277,0 ± 92,8] × $10^3$/мкл) и здоровых ([249,6 ± 85,2] × $10^3$/мкл), тогда как различия в концентрации гемоглобина и количества лейкоцитов в крови были незначительные.

***Заключение.*** У пациентов с шизофренией более высокая доля макроцитоза в сочетании с повышенным количеством тромбоцитов, что свидетельствует о том, что основные заболевания следует диагностировать и начинать лечить как можно ранее. Кроме того, необходимы проспективные исследования большего размера выборки для изучения основной этиологии этих состояний у пациентов с шизофренией.

**Ключевые слова:** *шизофрения; общий анализ крови; количество тромбоцитов; анемия; макроцитоз*

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# Common Hematological Disorders in Patients with Schizophrenia: In-Patient Case — Control Study

Ramdas Ransing[1]✉, Ashwini Kamble[2], Rajashree Kulkarni[1], Praveen Khairkar[2], Suvarna Patil[1], Krishna Pevekar[1], Kishord K. Misha[3], Nitin Gangane[3]

[1] BKL Walawalkar Rural Medical College, Maharashtra, India;
[2] Kamininenі Institute of Medical Sciences, Telangana, India;
[3] Mahatma Gandhi Institute of Medical Sciences, Maharashtra, India

***ABSTRACT***

***INTRODUCTION:*** Although common hematological abnormalities (CHA) such as anemia, macrocytosis, and platelet dysfunction are often present in patients with schizophrenia, empirical data are limited. Thus far, such deviations have been mentioned either in reports or in a series of clinical cases.

***AIM:*** To study the incidence of CHA in patients with schizophrenia.

***MATERIALS AND METHODS:*** This study involved 791 patients with schizophrenia [including those who did not receive medical drugs (n = 115) and patients with chronic schizophrenia (n = 376)] and 504 healthy volunteers. From each participant, blood samples were taken and analyzed for CHA using an automatic Coulter counter. In the three groups, $\chi^2$ tests and analysis of variance (ANOVA) were conducted to compare the variables.

***RESULTS:*** The incidence of macrocytosis was nearly the same in the schizophrenia group (patients not receiving medications, 10.5%; patients with chronic schizophrenia, 10.6%) and was significantly higher than that in the control group (4.2%). The platelet count was considerably higher in the chronic schizophrenia group ([282.5 ± 87.9] × $10^3$/μL) than in the group not receiving medical drugs ([277.0 ± 92.8] × $10^3$/μL) and control group ([249.6 ± 85.2] × $10^3$/μL), whereas the differences in the concentration of hemoglobin and leukocytes in the blood were insignificant.

***CONCLUSION:*** Patients with schizophrenia have a higher proportion of macrocytosis in combination with increased platelet count, which shows that the underlying diseases should be diagnosed and treated as early as possible. Moreover, prospective studies with a larger sample size are necessary to determine the etiology of these conditions in patients with schizophrenia.

**Keywords:** *schizophrenia; complete blood count; platelet count; anemia; macrocytosis*

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## LIST OF ABBREVIATIONS

CBC — complete blood count
CHA — common hematological abnormalities
EDTA — ethylenediaminetetraacetic acid
Hb — hemoglobin
ICD-10 — International Statistical Classification of Diseases and Related Health Problems 10th Revision
MCV — mean corpuscular volume
RBC — red blood cell
WBC — white blood cell

## INTRODUCTION

Schizophrenia is one of the most common chronic and disabling illnesses, characterized by a constellation of positive, negative, and cognitive symptoms that cause significant disability [1]. Patients with schizophrenia have an increased risk of mortality and the development of medical comorbidities than the general population [2, 3]. Self-neglect, physical illness, poor diet, lack of exercise, obesity, smoking, and access to medical services are all factors that contribute to this high mortality and morbidities [3]. Most risk factors are a direct or indirect result of antipsychotic use, genetic predisposition, sedentary lifestyle, and comorbid mood disorders [4]. Specific nutrient/food components such as antioxidants, omega-3 fatty acids, and vitamins are commonly used to improve symptoms and lower mortality in these patients [5].

Furthermore, cardiovascular disease-related mortality is common among patients with schizophrenia [6]. Increased platelet activity is one of the primary mechanisms of a cardiovascular accident in patients with schizophrenia [7]. These risk factors must be identified early because they have a significant impact on the outcome of schizophrenia patients.

These risk factors and medical comorbidities of schizophrenia can be detected using a variety of tests. However, most previous studies did not use routine and widely available tests to identify these risk factors and the underlying etiology.

The complete blood count (CBC) is simple, most commonly advised, and well-studied by various medical specialties [8]. It is most commonly used to assess the composition and concentration of blood cellular components such as red blood cell (RBC), total and differentiated white blood cell (WBC), and platelet counts, as well as red cell indices. It reflects the signs of infections, anemia, dehydration, and malnutrition. In addition, Antipsychotics have been reported to produce several hematological and other side effects. The CBC can detect these common hematological abnormalities (CHA) among patients with schizophrenia [9]. Although several researchers have attempted to study individual components (e. g., Hemoglobin (Hb) concentration, mean corpuscular volume (MCV)), the overall proportion of CHA on CBC is still unclear. In light of this, we compared the proportion of CHA among patients with schizophrenia to healthy participants.

This study **aimed** to examine the proportion of common hematological abnormalities in patients with schizophrenia.

## MATERIALS AND METHODS

After approval from the Institutional Ethical Committee, the case-control study was carried out in a tertiary care teaching hospital. The study included patients with schizophrenia diagnosed using International Statistical Classification of Diseases and Related Health Problems 10$^{th}$ Revision (ICD-10) criteria, either gender, aged 18–45 years, and attending outpatients or inpatients services of psychiatry department. In the study, the healthy controls were age- and gender-matched relatives of the patients who had other medical (e. g., diabetes mellitus, arterial hypertension) or mental illness (e. g., depression, anxiety, bipolar) and were accompanying these patients. The patients and controls with a history of alcohol use, delirium, or comorbid psychiatric disorders, those who were receiving antidepressants, mood stabilizers, anti-coagulants, oral iron supplements, and vitamin $B_{12}$ and folic acid supplements, and those with a history of hepatic or renal failure, acute infection, leukemia, and aplastic anemia were excluded from the study. Furthermore, patients with schizophrenia living in long-term rehabilitation centers (i. e. centers providing stay for more than a month) and not accompanied by relatives, were excluded from the study.

The patients attending Out-Patient Department or In-Patient Department services were recruited using convenience sampling (non-probability) method. After obtaining informed consent, the blood sample (5 mL) was drawn into a bulb containing 0.04 mL of 7.5% Ethylenediaminetetraacetic acid (EDTA) and analyzed using an automated Coulter counter within 2 hours of collection. The outcome parameters were the Hb concentration, WBC count, platelet count, and MCV.

Initially, 540 people from each category (patients with schizophrenia and healthy controls) were identified and asked to take part in the study. Of the 540, 65 patients with schizophrenia and 9 healthy controls refused to participate. The amount of blood required was less than that required to run a Coulter for blood count analysis in 34 patients and 20 healthy controls. Blood from 18 patients with schizophrenia

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and 11 healthy controls was clotted before reaching the pathology lab. Therefore, 491 patients with schizophrenia and 504 ***age- and sex-matched controls*** were included in the present study. The patients with schizophrenia were sub-grouped into drug-naive (n = 115) and ***chronic schizophrenia*** (n = 376) groups based on their previous history of antipsychotic use.

Table 1 summarizes the socio-demographic and clinical characteristics of study groups. There was no significant difference in age between the three groups (p = 0.41) and the study included a nearly equal number of men and women ($\chi^2$ = 0.33, df = 2, p = 0.84). The duration of illness was longer in the chronic schizophrenia group (29.54 ± 10.88 months) than in the drug naïve group (3.68 ± 4.74 months).

**Table 1.** Sociodemographic and clinical characteristics

| Parameter | Drug naive | Chronic schizophrenia | Healthy control | Significance |
|---|---|---|---|---|
| n | 115 | 376 | 504 | – |
| Age, years | 33.8 ± 14.5 | 34.3 ± 11.4 | 33.2 ± 10.2 | p = 0.41 |
| Male, n (%) | 53 (46.1) | 176 (46.8) | 246 (48.42) | $\chi^2$ = 0.33, df = 2, p = 0.84 |
| Female, n (%) | 62 (53.9) | 200 (53.2) | 262 (51.93) | |
| Duration of illness, months | 3.68 ± 4.74 | 29.54 ± 10.88 | – | p < 0.001 (S) |
| ***Dietary Pattern*** | | | | |
| Vegetarian, n (%) | 36 (45.55) | 120 (31.91) | 189 (37.50) | $\chi^2$ = 3.61, df = 2, p = 0.16 |
| Mixed, n (%) | 79 (68.69) | 256 (68.08) | 315 (62.50) | |

SPSS Software Version 20.0 (SPSS Inc., USA) was used for statistical analyses. The chi-square test was used for comparing categorical variables [e. g., proportion of CHA: Hb concentration (anemia), WBC count (leukopenia or leucocytosis), MCV (macrocytosis or microcytosis), and platelet count (thrombocytopenia and thrombocytosis)] among the groups. The Shapiro–Wilk normality test (p > 0.05) and a visual inspection of Q-Q plots, histograms, and box plots revealed that the Hb concentration, WBC count, MCV, and platelet count were normally distributed. Independent Student's t-test was conducted for normally distributed continuous variables. Continuous variables were expressed as Mean ± SD or Median (Minimum–Maximum) and categorical variables as percentages. The three groups were compared using the analysis of variance test. Tukey's multiple comparisons test was used to draw comparisons among the subgroups. A p-value of < 0.05 was considered significant for all statistical analyses.

## RESULTS

There was no difference in Hb concentration or WBC count between the three groups. The platelet count was significantly higher (p < 0.0001) in the chronic schizophrenia group ([282.5 ± 87.9] × $10^3$/μL) than in the drug-naive ([277.0 ± 92.8] × $10^3$/μL) and healthy control ([249.6 ± 85.2] × $10^3$/μL) groups. The MCV was significantly higher (p < 0.001) in the chronic schizophrenia group (88.60 ± 10.68 fL) than in the drug-naive (87.41 ± 11.24 fL) and healthy control (84.18 ± 9.09 fL) groups (Tables 2, 3).

**Table 2.** Complete blood count findings

| Parameter | Drug naive | Chronic schizophrenia | Healthy control | Significance |
|---|---|---|---|---|
| Hemoglobin concentration, g/dL | 12.08 ± 1.93 | 11.92 ± 2.03 | 12.20 ± 1.95 | F = 2.15, p = 0.11 |
| Red blood cell count, × $10^{12}$ $L^{-1}$ | 4.2 ± 0.7 | 4.2 ± 0.7 | 4.1 ± 1.0 | F = 2.39, p = 0.09 |
| White blood cell count, × $10^9$ $L^{-1}$ | 8.1 ± 2.4 | 8.6 ± 2.9 | 8.3 ± 3.2 | F = 2.30, p = 0.10 |
| Platelet count, × $10^{12}$ $L^{-1}$ | 277.0 ± 92.8 | 282.5 ± 87.9 | 249.6 ± 85.2 | F = 16.55, p < 0.001 |
| Mean corpuscular hemoglobin, pg | 29.2 ± 4.2 | 28.6 ± 4.3 | 27.5 ± 3.4 | F = 15.19, p < 0.001 |
| Mean corpuscular hemoglobin concentration, g/L | 32.88 ± 1.44 | 32.66 ± 1.74 | 32.00 ± 1.87 | F = 20.62, P < 0.001 |
| Red cell distribution width, fL | 16.99 ± 2.98 | 16.95 ± 2.97 | 14.66 ± 3.23 | F = 68.17, p < 0.001 |
| Mean Platelet Volume, fL | 7.11 ± 0.96 | 7.28 ± 1.09 | 6.45 ± 1.23 | F = 59.69, p < 0.001 |
| Platelet distribution width, fL | 17.01±0.86 | 17.02±0.84 | 16.57±0.45 | F = 54.85, p < 0.001 |
| Mean Corpuscular Volume, fL | 87.41 ± 11.24 | 88.60 ± 10.68 | 84.18 ± 9.09 | F = 21.83, p < 0.001 |
| Vitamin $B_{12}$ level, pg/ml | 260.5 ± 176.1 | 280.6 ± 168.0 | 328.0 ± 259.1 | F = 7.36, p < 0.001 |
| Neutrophil / lymphocyte ratio | 2.79 ± 1.50 | 2.53 ± 1.34 | 2.40 ± 1.32 | F = 3.934, p = 0.019 |

**Table 3.** Multiple comparisons among the healthy control, drug naïve, and chronic schizophrenia group

| Parameter | Groups | Mean difference | q value | 95% confidence interval of difference |
|---|---|---|---|---|
| Hemoglobin concentration, g/dL | A vs. B | –0.45 | 3.16 | –0.94 to 0.03 |
| | A vs. C | –0.30 | 3.16 | –0.62 to 0.017 |
| | B Vs C | 0.15 | 1.04 | –0.34 to 0.65 |
| Red blood cell count, × $10^{12}$ $L^{-1}$ | A vs. B | 0.16 | 2.54 | -0.05 to 0.37 |
| | A vs. C | 0.10 | 2.41 | -0.04 to 0.24 |
| | B Vs C | 0.06 | 0.92 | -0.15 to 0.27 |
| White blood cell count, × $10^{9}$ $L^{-1}$ | A vs. B | –0.35 | 1.68 | –1.07 to 0.35 |
| | A vs. C | 0.22 | 1.56 | –0.25 to 0.69 |
| | B Vs C | –0.58 | 2.63 | –1.31 to 0.16 |
| Mean Corpuscular Volume, fL | A vs. B | –4.41 | 5.96*** | –6.89 to –1.94 |
| | A vs. C | –3.22 | 6.61*** | –4.86 to –1.59 |
| | B Vs C | –1.19 | 1.56 | –3.74 to 1.36 |
| Mean corpuscular hemoglobin, pg | A vs. B | 1.75 | 6.25** | 0.82 to 2.68 |
| | A vs. C | 1.15 | 6.23** | 0.54 to 1.76 |
| | B Vs C | 0.60 | 2.07 | -0.36 to 1.56 |
| Mean corpuscular hemoglobin concentration, g/L | A vs. B | 0.88 | 6.78*** | 0.45 to 1.31 |
| | A vs. C | 0.66 | 7.71*** | 0.37 to 0.94 |
| | B Vs C | 0.22 | 1.64 | -0.22 to 0.66 |
| Red cell distribution width, fL | A vs. B | 2.33 | 10.27*** | 1.57 to 3.08 |
| | A vs. C | 2.29 | 15.30*** | 1.79 to 2.78 |
| | B Vs C | 0.04 | 0.17 | -0.73 to 0.81 |
| Mean Platelet Volume, fL | A vs. B | 0.66 | 7.85*** | 0.38 to 0.94 |
| | A vs. C | 0.83 | 14.98*** | 0.64 to 1.01 |
| | B Vs C | -0.17 | 1.96 | -0.46 to 0.12 |
| Platelet distribution width, fL | A vs. B | 0.44 | 8.93*** | 0.27 to 0.60 |
| | A vs. C | 0.45 | 13.85*** | 0.34 to 0.55 |
| | B Vs C | -0.01 | 0.19 | -0.17 to 0.15 |
| Platelet count, × $10^{12}$ $L^{-1}$ | A vs. B | –32.88 | 5.09** | –54.46 to –11.29 |
| | A vs. C | –27.41 | 6.43*** | –41.66 to –13.16 |
| | B Vs C | –5.470 | 0.82 | –27.77 to 16.82 |
| Vitamin $B_{12}$ level, pg/ml | A vs. B | -67.50 | 4.20** | -120.80 to -14.20 |
| | A vs. C | -47.40 | 4.47** | -82.54 to -12.26 |
| | B Vs C | -20.10 | 1.21 | -75.05 to 34.85 |
| Neutrophil / lymphocyte ratio | A vs. B | 0.38 | 3.88* | 0.06 to 0.72 |
| | A vs. C | 0.12 | 1.88 | -0.10 to 0.34 |
| | B vs. C | 0.26 | 2.57 | -0.08 to 0.60 |
| Significance level: * = significant ($p < 0.05$); ** = highly significant ($p < 0.01$); *** = very highly significant ($p < 0.001$), A = Healthy controls, B = Drug Naïve, C = Chronic Schizophrenia | | | | |

*Note:* group A — Healthy controls; group B — Drug Naïve; group C — Chronic Schizophrenia; * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

Subgroup analyses revealed that there are no significant differences in the Hb concentration and WBC count between the drug-naive and chronic schizophrenia groups (Table 3). Also, there was no significant difference in WBC count between the healthy control, drug-naive, and chronic schizophrenia groups. However, the difference in MCV and platelet count between the two groups was highly significant ($p < 0.001$).

There were no significant differences in Hb concentrations between men and women with schizophrenia and healthy controls. Mild anemia was relatively higher in the male patients with chronic schizophrenia (40.3%) than in the drug-naive male patients (34,0%). Similar findings were noted for a moderate degree of anemia (drug naive [7.5%] and chronic schizophrenia [13.1%]). Also, moderate anemia was higher in the female patients with chronic schizophrenia (35.5%) than in the drug-naive female patients (27.4%). The proportion of mild anemia was higher in the drug-naive group (30.6%) than in the chronic schizophrenia group (22.5%, Table 4).

The macrocytosis was significantly higher in the drug-naive (10.5%) and chronic schizophrenia (10.6%) groups than in the healthy control group (4.1%, $\chi^2 = 17.96$, $p < 0.001$). Furthermore, the microcytosis was higher in the healthy control group (27.8%) than in the drug-naive (20.0%) and chronic schizophrenia (22.1%) groups (Table 5).

**Table 4.** Gender wise analysis of Anaemia among the healthy control, drug naïve, and chronic schizophrenia group

| Degree of anemia (Hb concentration) | Drug naive | Chronic schizophrenia | Healthy control | Significance |
|---|---|---|---|---|
| *Men* | | | | |
| Normal (> 13 g/dL), n (%) | 30 (56.6) | 79 (44.9) | 99 (42.0) | $\chi^2 = 5.74$, df = 6, p = 0.45 |
| Mild anemia (11–12.9 g/dL), n (%) | 18 (34.0) | 71 (40.3) | 98 (41.2) | |
| Moderate anemia (8.0–10.0 g/dL), n (%) | 4 (7.5) | 23 (13.1) | 32 (13.4) | |
| Severe anemia (< 8 g/dL), n (%) | 1 (1.9) | 3 (1.7) | 9 (3.8) | |
| Total, n | 53 | 176 | 238 | |
| *Women* | | | | |
| Normal (> 12 g/dL ), n (%) | 23 (37.09) | 77 (38.5) | 74 (27.81) | $\chi^2 = 8.93$, df = 6, p = 0.17 |
| Mild anemia (11–11.9 g/dL), n (%) | 19 (30.64) | 45 (22.5) | 71 (26.69) | |
| Moderate anemia (8.0–10.0 g/dL), n (%) | 17 (27.41) | 71 (35.5) | 108 (40.6) | |
| Severe anemia (< 8 g/dL), n (%) | 3 (4.83%) | 7 (3.5) | 13 (4.88) | |
| Total, n | 62 | 200 | 266 | |

**Table 5.** Distribution common heamatogical abnormalities among of the study groups

| Degree of anemia (Hb concentration) | Drug naive | Chronic schizophrenia | Healthy control | Significance |
|---|---|---|---|---|
| n | 115 | 376 | 504 | – |
| *Mean corpuscular volume (MCV)* | | | | |
| Microcytosis (MCV < 80 fL), n (%) | 23 (20.0) | 83 (22.1) | 140 (27.8) | $\chi^2 = 17.96$, df = 4, p = 0.001 |
| Normal (MCV 80–100 fL), n (%) | 80 (69.6) | 263 (69.9) | 343 (68.1) | |
| Macrocytosis (MCV > 100 fL), n (%) | 12 (10.5) | 40(10.6) | 21 (4.2) | |
| *White blood cell (WBC) count* | | | | |
| Leukopenia (WBC < $4.5 \times 10^9$ $L^{-1}$), n (%) | 2 (1.7) | 6 (1.6) | 20 (4.0) | $\chi^2 = 18.14$, df = 4, p = 0.001 |
| Normal (WBC 4.5–$11.5 \times 10^9$ $L^{-1}$), n (%) | 97 (84.3) | 343 (91.2) | 410 (81.3) | |
| Leucocytosis (WBC > $11.5 \times 10^9$ $L^{-1}$), n (%) | 16 (13.9) | 27 (7.2) | 74 (14.7) | |
| *Platelet count* | | | | |
| Thrombocytopenia (platelet count < 1 50 000 $10^3$/μL), n (%) | 6 (5.2) | 17 (4.5) | 35 (6.9) | $\chi^2 = 2.53$, df = 4, p = 0.64 |
| Normal platelet count (1 50 000–4 50 000 $10^3$/μL), n (%) | 106 (92.2) | 347 (92.3) | 453 (89.9) | |
| Thrombocytosis (platelet count > 4 50 000 $10^3$/μL), n (%) | 03 (2.7) | 12 (3.2) | 16 (3.2) | |

# DISCUSSION

In our study, the proportion of mild to moderate anemia was slightly higher in the men with schizophrenia than in the healthy controls, but there was no difference in Hb concentration between the three groups. These findings are consistent with the findings of a previous study conducted with 60 patients and 60 controls in which no significant difference in the Hb concentration was observed between healthy controls (13.4 ± 1.96 g/dL) and patients with

schizophrenia (13.53 ± 1.36 g/dL) [9]. The National Family Health Survey (NFHS-32005/2006) found 13% mild, 10% moderate, and 1% severe anemia in men and 39% mild, 15% moderate, and 2% severe anemia in women, which is lower than our findings [10]. Iron deficiency, chronic illness, and micronutrient (e. g., pyridoxine) deficiency are the common causes of anemia in the Indian population. In addition, hemoglobinopathies (e.g., thalassemia) are common in our region. Although these findings are not statistically significant in our study when compared to healthy participants. The future controlled prospective studies may show that patients with schizophrenia have poor nutritional status (iron, vitamin $B_{12}$, and folic acid deficiency), medical morbidities, and dietary preferences. Anemia in women has been linked to a genetic predisposition to schizophrenia in their offspring. A maternal Hb concentration of ≤ 10.0 g/dL is associated with an approximately 4-fold increased risk of development of schizophrenia spectrum disorders in their offspring [11]. In addition, anemia is strongly linked to cognitive decline in patients with schizophrenia [12].

The second important finding in our study was that patients with schizophrenia had higher MCV than healthy controls, with no significant difference in patients who were drug-naive or used antipsychotics. The significance of macrocytosis is frequently underestimated by clinicians because it is a relatively common finding, with 1.7–3.6% prevalence in the general population [13]. However, in our study, patients with schizophrenia (10.63%) and healthy controls (4.16%) had macrocytosis, which is consistent with previous study findings [9]. Comorbid illnesses such as alcohol use, reticulocytosis, nonalcoholic liver diseases, hypothyroidism, vitamin $B_{12}$ and folate deficiency, multiple myeloma, myelodysplastic syndrome, aplastic anemia, and acute leukemia, as well as drugs (anticonvulsants), maybe the causes of macrocytosis in patients with schizophrenia [14, 15]. Also, these disorders are more common in patients with schizophrenia than in the general population [16].

It is important to note that vitamin $B_{12}$ and folic acid deficiency is linked with the pathogenesis of schizophrenia and neuropsychiatric disorders, such as memory changes, cognitive decline, mood disorder, violent behavior because of structural damage to the brain characterized by brain atrophy, and silent brain infarct via multiple pathways [9, 17, 18].

Although MCV is neither a specific nor a sensitive indicator of vitamin $B_{12}$ and folic acid deficiency, it provides a fair idea of the vitamin $B_{12}$ deficiency, folate levels(blood), and homocysteine levels along with other medical disorders [19]. The published literature suggests that in patients with chronic psychiatric illnesses, the odds ratio for macrocytosis with low serum vitamin $B_{12}$ levels was 6.90 times higher than in individuals with normal serum vitamin $B_{12}$ levels [20]. Therefore, in routine clinical practice, macrocytosis could be a useful marker in patients with schizophrenia.

Our findings did not show a significant difference in MCV between the drug-naive and chronic schizophrenia groups. It implies that the underlying causes of high MCV are frequently undiagnosed, untreated, and frequently overlooked by clinicians. Higher MCV levels in patients with schizophrenia have been linked to genetic vulnerability, the outcome of schizophrenia, and a poor lifestyle [21–23].

Iron, vitamin $B_{12}$, and folic acid deficiency are more common in the Indian population. Iron deficiency causes microcytosis while vitamin $B_{12}$ and folic acid deficiency causes macrocytosis. A combined deficiency results in a normocytic picture, which may be the cause of undiagnosed among these patients [24]. Also, it is important to note that MCV is neither a specific nor a sensitive indicator of vitamin $B_{12}$ and folic acid deficiency, but it provides a fair idea of the vitamin $B_{12}$ deficiency, folate levels(blood), and homocysteine levels [19]. Therefore, along with CBC, serum vitamin $B_{12}$, folic acid, ferritin, and iron levels should be measured in patients with schizophrenia for more targeted management.

Previous research has linked subclinical inflammation, prenatal infections, and maternal immunological alterations to an increased risk of schizophrenia [25, 26]. Patients with schizophrenia have a proinflammatory state characterized by elevated levels of interleukin 12, interferon, tumor necrosis factor, and soluble interleukin 2 [27]. These cytokines have been linked to elevated WBC counts in schizophrenia, and they have been linked to a poor prognosis and a risk factor for metabolic syndrome and cardiovascular disease [28]. However, our findings did not show a significant difference in WBC Count between patients with schizophrenia and healthy controls. Furthermore, when interpreting WBC counts, psychotropic drugs such as clozapine that cause a life-threatening decrease in WBC count and transient reversible leucocytosis must be considered [29].

Platelet count was higher in patients with drug-naive schizophrenia than in healthy controls, which is consistent with previous research [30]. The rise in platelet count appears to be unrelated to antipsychotic use in our study. Platelet count is thought to be a key mediator in the pathogenesis of the cardiovascular disease, metabolic syndrome, and a peripheral marker of major psychiatric disorders such as schizophrenia [30, 31]. Furthermore, the platelet count in chronic schizophrenia patients was significantly higher than in drug-naive patients in this study. Atypical antipsychotics are known to increase the risk of cardiovascular morbidity in schizophrenia patients by increasing the risk of obesity, metabolic syndrome, and type 2 diabetes mellitus [32]. Overall, platelet count estimation may be a useful tool in assessing the risk of medical comorbidities and the effects of antipsychotics in patients with schizophrenia.

Strengths, Limitations, and Future Directions. The uniqueness of this study is that we focused on CHAs in a routinely administered test i. e. CBC. Although most previous studies have investigated various nutritional deficiencies (vitamin $B_{12}$ and folic acid), iron deficiency, immunological abnormalities (WBC count), and risks of cardiovascular diseases (platelet count abnormalities) in patients with

schizophrenia, our study attempted to bridge the gap between ongoing research and routine clinical practice using a routinely administered test.

In this study, we have not compared the effects of typical and atypical antipsychotics on the CBC parameters. However, the typical and atypical antipsychotics have different metabolic and cardiovascular effects [33]. In addition, the correlation between the severity of psychotic symptoms and various blood indices was not studied. Our primary focus was on the most common components of the CBC. However, abnormalities in other CBC parameters, such as mean platelet volume, WBC differential count, RBC count, red cell distribution width, and hematocrit, may considerably affect patients with schizophrenia, and therefore must be studied. Also, we did not include a group of patients with chronic schizophrenia living in long-term rehabilitation centers or on long term inpatients treatment, who may have poor nutritional status and more CHAs compared to patients receiving outpatients or short-term inpatient treatment. Therefore, future research should compare the nutritional status and CHAs of patients among these groups.

Our study provides preliminary data on the comparison of CBC abnormalities in patients with drug-naive schizophrenia, patients with chronic schizophrenia on antipsychotics, and healthy controls visiting a tertiary care rural hospital in India. Future well-controlled prospective studies are required to estimate the relationship between CHA and serum vitamin $B_{12}$, folic acid, iron, and ferritin levels to investigate possible etiological and prognostic significance in patients with schizophrenia.

## CONCLUSION

The proportion of common hematological abnormalities is higher in the patients with schizophrenia than in the healthy participants. Patients with schizophrenia had a significantly higher proportion (nearly three times) of macrocytosis, as well as higher platelet counts than healthy participants. Our findings provide indirect evidence that patients with schizophrenia have a higher risk of cardiovascular morbidity, medical comorbidities, and nutrient deficiency than healthy controls. Thus, the complete blood count, which is a simple, readily available, inexpensive measure, may predict certain etiologies, immunological factors, medication effects, and cardiovascular morbidities in patients with schizophrenia, following a careful interpretation in routine clinical practice.

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**Contribution of the authors:** *R. Ransing* — concept and design of research, collection and analysis of material, data analysis and interpretation, writing text, editing; *S. Patil, R. Kulkarni* — concept and design of research, collection and analysis of material; *A. Kamble, P. Khairkar* — data analysis and interpretation. All authors made a substantial contribution to the conception of the work, acquisition, analysis, interpretation of data for the work, drafting and revising the work, final approval of the version to be published and agree to be accountable for all aspects of the work.

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## ОБ АВТОРАХ

***Ransing Ramdas**, доцент;
ORCID: https://orcid.org/0000-0002-5040-5570;
e-mail: ramdas_ransing123@yahoo.co.in

**Kamble Ashwini**, д.х.н., профессор;
ORCID: https://orcid.org/0000-0003-3396-8010;
e-mail: dr.ashwinipravin@gmail.com

**Kulkarni Rajashree**, доцент;
ORCID: https://orcid.org/0000-0001-6361-100X;
e-mail: krajashree23@gmail.com

**Khairkar Praveen**, д.м.н., профессор;
ORCID: https://orcid.org/0000-0003-3166-3547;
e-mail: praveen.khairkar280@gmail.com

**Patil Suvarna**, доцент;
ORCID: https://orcid.org/0000-0002-9564-986X;
e-mail: suvarnapatil@walawalkarhospital.com

**Pevekar Krishna**, доцент;
ORCID: https://orcid.org/0000-0001-8990-7685;
e-mail: krishnapevekar@yahoo.co.in

**Misha Kishord Kumar**, д. псих.н., профессор;
ORCID: https://orcid.org/0000-0002-9994-9640;
e-mail: drkkmishra2003@yahoo.co.uk

**Gangane Nitin**, д.м.н., профессор;
ORCID: https://orcid.org/0000-0003-0190-4215;
e-mail: nitingangane@gmail.com

## AUTHOR'S INFO

***Ramdas Ransing**, MD, Associate Professor;
ORCID: https://orcid.org/0000-0002-5040-5570;
e-mail: ramdas_ransing123@yahoo.co.in

**Ashwini Kamble**, MD, Dr. Sci. (Biochem.), Professor;
ORCID: https://orcid.org/0000-0003-3396-8010;
e-mail: dr.ashwinipravin@gmail.com

**Rajashree Kulkarni**, MD, Associate Professor;
ORCID: https://orcid.org/0000-0001-6361-100X;
e-mail: krajashree23@gmail.com

**Praveen Khairkar**, MD, Dr. Sci. (Med.), Professor;
ORCID: https://orcid.org/0000-0003-3166-3547;
e-mail: praveen.khairkar280@gmail.com

**Suvarna Patil**, MD, Associate Professor;
ORCID: https://orcid.org/0000-0002-9564-986X;
e-mail: suvarnapatil@walawalkarhospital.com

**Krishna Pevekar**, MD, Associate Professor;
ORCID: https://orcid.org/0000-0001-8990-7685;
e-mail: krishnapevekar@yahoo.co.in

**Kishord K. Misha**, MD, MD, Dr. Sci. (Psych.), Professor;
ORCID: https://orcid.org/0000-0002-9994-9640;
e-mail: drkkmishra2003@yahoo.co.uk

**Nitin Gangane**, MD, Dr. Sci. (Med.), Professor;
ORCID: https://orcid.org/0000-0003-0190-4215;
e-mail: nitingangane@gmail.com

* Автор, ответственный за переписку / Corresponding author