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Report

Neutrophil-to-lymphocyte ratio as a promising biomarker for the diagnosis of psoriasis in Pakistan

Benish Nawaz[1], Muhammad Babar Khawar[1,*], Ali Afzal[2], Suneela Aman[3], Syeda Eisha Hamid[2], Muddasir Hassan Abbasi[4,*], Nadeem Sheikh[5,*], Syed Shakeel Shah[1], Mussarat Rafiq[5], Fareeha Azam[5], Rabia Mehmood[5]

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ABSTRACT

Background: Psoriasis is a skin inflammation characterized by papules and plaques on the skin surface. Almost 125 million people are affected by psoriasis worldwide. This study aimed to evaluate whether the neutrophil-to-lymphocyte ratio (NLR) can be used as a biomarker for the diagnosis of psoriasis. **Methods:** Blood samples of patients with psoriasis and healthy controls were collected for complete blood count testing. A t-test was applied to estimate the difference in the hematological parameters between the two groups. **Results:** The hemoglobin level ($p < 0.0001$), hematocrit level ($p < 0.0001$), red blood cell count ($p < 0.0001$), mean corpuscular volume ($p = 0.0002$), platelet count ($p = 0.0039$), white blood cell count ($p = 0.0002$), neutrophil count ($p = 0.0001$), monocyte count ($p < 0.0001$), and eosinophil count ($p = 0.0467$) significantly differed between the groups. Meanwhile, the mean corpuscular hemoglobin concentration ($p = 0.3989$) and lymphocyte count ($p = 0.3842$) did not. The patients with psoriasis had a higher neutrophil count and a lower lymphocyte count than the healthy controls. The NLR was significantly elevated in the patients with psoriasis. **Conclusion:** The NLR is a potential biomarker for the diagnosis of psoriasis.

Key words: Biomarker, Hematology, neutrophils to lymphocyte ratio, Pakistan, Psoriasis

[1]*Applied Molecular Biology and Biomedicine Lab, Department of Zoology, University of Narowal, Narowal, Pakistan*

[2]*Molecular Medicine and Cancer Therapeutics Lab, Department of Zoology, Faculty of Sciences & Technology, University of Central Punjab, Lahore, Pakistan*

[3]*University of Veterinary and Animal Sciences (UVAS), Lahore, Pakistan*

[4]*Department of Zoology, University of Okara, Punjab, Pakistan*

[5]*Cell & Molecular Biology Lab, Institute of Zoology, University of the Punjab, Lahore, Pakistan*

Correspondence

Muhammad Babar Khawar, Applied Molecular Biology and Biomedicine Lab, Department of Zoology, University of Narowal, Narowal, Pakistan

Email: babar.khawar@uon.edu.pk

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INTRODUCTION

Psoriasis (originating from the Greek word "psora" meaning itch) is a highly stigmatizing and common disease that causes skin inflammation [1]. It is a prevalent chronic skin inflammatory disease that poses a substantial illness burden equivalent to that of cancer or diabetes [2]. Hyperproliferation of the epidermis, elongated and conspicuous blood vessels, and thick perivascular lymphocytic infiltration are all symptoms of psoriasis [3]. Furthermore, it is characterized by papules and plaques on the skin surface that vary in form, location, and severity. They are usually symmetrically distributed in the body folds, scalps, elbows, knees, and lumbosacral area [4]. The triggering factor of psoriasis is not completely known but is generally believed to have a genetic origin. This disease is aggravated by beta blockers, lithium salt, and other certain medicines [5]. Its severity is associated with an increased risk of death from a range of causes, the most prevalent of which is cardiovascular death [6].

Psoriasis is a public health issue, affecting almost 125 million people worldwide [7]. Its prevalence varies depending on sex, age, geography, ethnicity, genetics, and environmental variables [8]. Its incidence ranges between 0.27% and 11.4% in adults. Approximately 2% of the European population is affected with psoriasis [9]. The prevalence is approximately 3.2% in men and 2.5% in women [10]. In Spain, psoriasis is common in both men and women, with a prevalence of 1.17–1.43% [11]. In Norway, the total prevalence is 1.4%, with no sex differences, and individuals aged 30–49 years had the highest prevalence [12]. In India, psoriasis affects 0.44–2.8% of people in their third or fourth decades of life, with men having a twofold higher risk for this condition than women [13].

Variations in several hematological parameters, including the hemoglobin level and platelet count, and different kinds of immune cells have been studied in association with psoriasis. There is either an upregulation or a downregulation in all these parameters regardless of dependency. Blood cell counts, such as the neutrophil-to-lymphocyte ratio (NLR), serve as an additional promising parameter.

An extensive literature survey indicates that no population-based study has yet evaluated the prevalence of psoriasis and its association with hematological parameters in Pakistan. We found a severe shortage of local information in the literature. Almost all information on psoriasis was derived from insubstantial hospital-based studies, and a number of articles were published but not in Pakistan [14].

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Correspondence

Muddasir Hassan Abbasi, Department of Zoology, University of Okara, Punjab, Pakistan

Email: dr.muddasir@uo.edu.pk

Correspondence

Nadeem Sheikh, Cell & Molecular Biology Lab, Institute of Zoology, University of the Punjab, Lahore, Pakistan

Email: nadeem.zool@pu.edu.pk

This study aimed to compare the NLR as an inflammatory marker between patients with psoriasis and healthy individuals, evaluate its association with the severity of psoriasis, and determine a cost-effective and easily obtained biomarker for diagnosing this disease.

METHODS

Participant selection

Participants were selected from individuals who visited routine medical clinics in Punjab and Islamabad between January and May 2020. Patient recruitment was approved by the ethical committee (UON/ZOO/101) and interdepartmental review board of Pir Mehr Ali Shah Arid Agriculture University, Rawalpindi, Pakistan. Patients were diagnosed by dermatologists as a part of standard clinical care, and no attempt was made to group the participants into different subtypes of the disease.

Blood sampling

Probable sampling was conducted by collecting venous blood samples from 166 participants (83 patients with psoriasis under treatment and 83 healthy controls) after obtaining oral consent. The blood samples were sent to the laboratory for complete blood count (CBC) testing. Different CBC parameters were compiled into a data sheet for further statistical analysis.

Hematological parameter selection

The hematological parameters selected included the hemoglobin level, total red blood cell (RBC) count, hematocrit level, mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), platelet count, white blood cell (WBC) count, neutrophil count, lymphocyte count, monocyte count, and eosinophil count.

Statistical analysis

The statistical analysis was performed using IBM SPSS (version 21.0; license no. Z125-3301-14). Student's t-test was used for comparing the two groups (case and control). The null hypothesis was that there would be no significant difference in any specific parameter between the groups. Otherwise, an alternative hypothesis was accepted.

RESULTS

Incidence of psoriasis according to age

Figure 1 shows the characteristics of the patients with psoriasis and healthy controls in different age groups. Psoriasis was more common among the individuals aged 21 – 30 years. The percentage analysis showed the lowest incidence of psoriasis in the extreme age groups.

Incidence of psoriasis according to sex

Among the 83 patients with psoriasis, the proportion of women (54%) was higher than that of men (46%) (**Figure 2**).

Hematological parameters

The comparison results of the hematological parameters between the patients with psoriasis and healthy controls are shown in **Figure 3**. The continuous data described as means ± standard deviations are shown in **Table 1**. The t-test showed significant differences in the hemoglobin level ($p < 0.0001$), hematocrit level ($p < 0.0001$), RBC count ($p < 0.0001$), MCV ($p = 0.0002$), platelet count ($p = 0.0039$), WBC count ($p = 0.0002$), neutrophil count ($p = 0.0001$), monocyte count ($p < 0.0001$), and eosinophil count ($p = 0.0467$). Meanwhile, the MCHC ($p = 0.3989$) and lymphocyte count ($p = 0.3842$) did not significantly differ between the groups (**Figure 3 f** and **j**).

NLR

The patients with psoriasis had a significantly higher neutrophil count but a lower lymphocyte count than the healthy controls. The NLR was significantly elevated in the patients with psoriasis compared with that in the healthy controls (**Figure 4**).

DISCUSSION

Our study demonstrated elevated neutrophil and WBC counts in the patients with psoriasis. Therefore, the neutrophil count can be used as an inflammatory biomarker of psoriasis. Neutrophils are most active during the early phases of inflammation and allow macrophages to heal tissue damage. The expression of numerous cytokines and their receptors coordinates these effects, and these molecules may be used to block certain inflammatory processes [15].

Herein, the NLR was elevated in the patients with psoriasis; thus, it can be used as a potential biomarker of this disease. Similar results were obtained in China, in which an elevated NLR was associated with systemic inflammation of psoriasis [16]. A small-scale cohort study found no significant difference in the NLR between patients and healthy controls but suggested an increased mean platelet volume (MPV) accompanied by a decreased Psoriasis Area Severity Index as a contributing prognostic parameter for the clinical prediction of psoriasis [17]. An elevated NLR can be

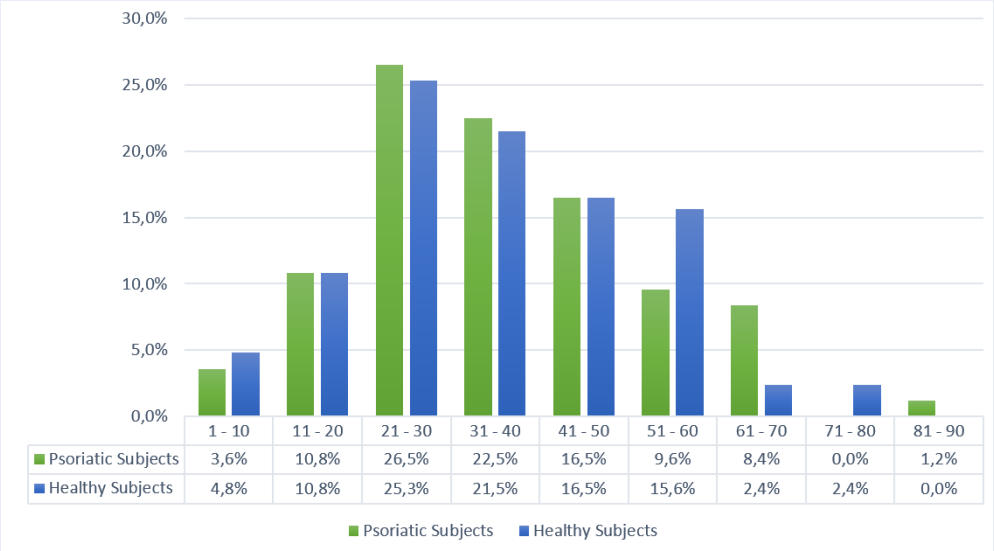

Figure 1: **Prevalence of psoriasis in patients and controls in different age groups**. In our cohort, age group of 21 – 30 shows maximum number of individuals with no significant difference between patients and controls. In group 51 – 60, there is a significant difference between the groups showing that this age group is more susceptible to psoriasis.

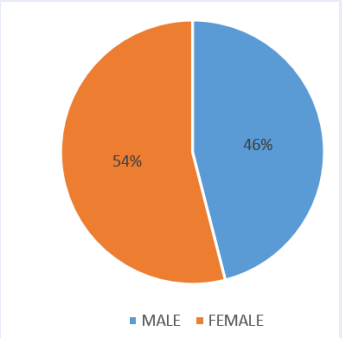

Figure 2: **Incidence of Psoriasis in males and females.** The percentage analysis of probable sampling shows 54% incidence of psoriasis in females and 46% incidence in male.

caused by various conditions and may be an indicator of a severe inflammatory disorder [18]. In our study, the NLR was identified as an indicator of systemic inflammation. Similarly, a strong association was previously found between the NLR, platelet count, and MPV and the incidence of psoriasis [19]. Nevertheless, the platelet count and MPV were less effective predictors of psoriasis than the NLR.

The RBC count was significantly higher in the patients with psoriasis than in the healthy controls in this study. In contrast, patients with psoriasis have been reported to have elevated inflammatory cytokine levels, which increase leukocyte activation products and cause oxidative damage to the components of plasma and erythrocytes [20]. The erythrocyte count may serve as a long-term indicator of oxidative stress in patients with psoriasis. In the present study, the RBC count was substantially lower in the patients with psoriasis than in the healthy controls. Generally, the RBCs of patients with psoriasis have an increased osmotic fragility, and erythrocytes can reflect the deterioration of psoriasis due to oxidative stress in RBCs [21].

In our study, the neutrophil count was significantly higher, and the lymphocyte count was lower in the patients with psoriasis than in the healthy controls. This trend has been recently found in a variety of inflammatory illnesses [22]. In patients with psoriasis, the lymphocyte count is usually low, and the neutrophil

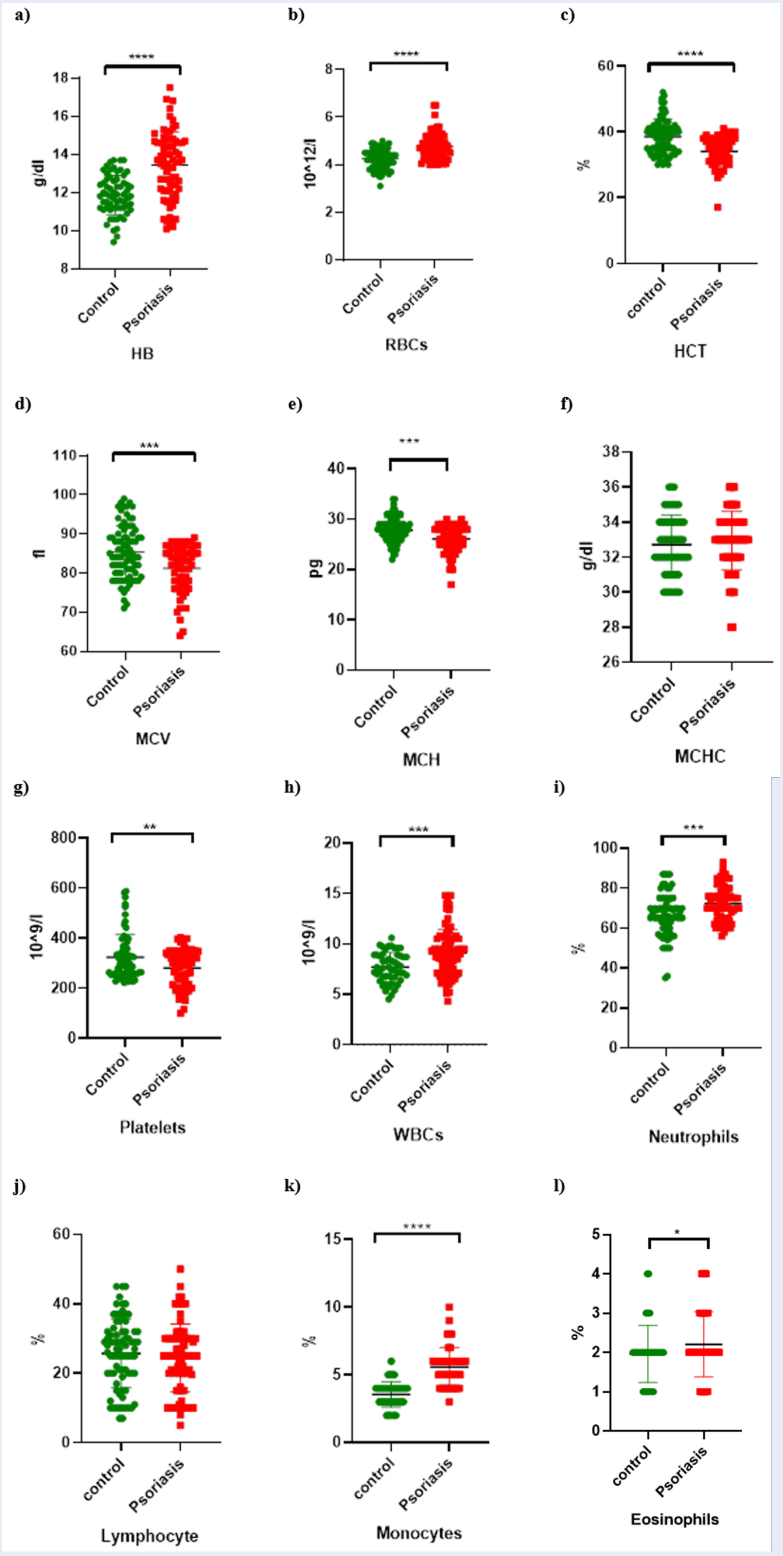

Figure 3: **Different hematological parameter compared with subjects and psoriatic patients**. (**a**) Hb, (**b**) RBCs, (**c**) HCT, (**d**), MCV, (**e**) MCH, (**g**) Platelets, (**h**) WBCs, (**i**) Neutrophils, and (**l**) Eosinophils have shown a significant difference. While there is no significant difference in (**f**) MCHC and (**j**) Lymphocytes.

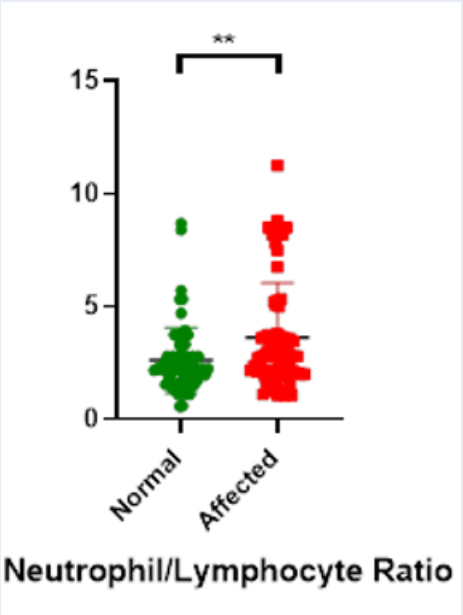

Figure 4: **Estimation of NLR among patients and healthy individuals**. NLR was shown to be elevated in psoriasis patients as compared to control subjects. There is a statistically significant difference in NLR of both groups.

Table 1: Different hematological parameters among the psoriasis and healthy subjects

	Psoriasis patients	Healthy controls (n = 83)	p Value
Hb (g/dl)	12.91 ± 2.25	12.57 ± 1.76	< 0.0001
RBCs (10^{12}/l)	4.64 ± 0.69	4.45 ± 0.58	< 0.0001
HCT (%)	38.09 ± 6.26	38.06 ± 5.53	< 0.0001
MCV (fl)	84.01 ± 7.67	85.34 ± 6.69	0.0002
MCH (pg)	27.69 ± 3.51	27.83 ± 2.54	0.0001
MCHC (g/dl)	32.56 ± 2.43	32.60 ± 1.82	0.3989
PCT (%)	332.97 ± 126.17	297.02 ± 102	0.0039
WBCs (10^{9}/l)	11.36 ± 14.23	9.79 ± 3.57	0.0002
Neutrophils (%)	69.43 ± 11.44	67.87 ± 11.58	0.0001
Lymphocytes (%)	24.40 ± 9.76	26.55 ± 11.02	0.3842
Monocytes (%)	4.66 ± 2.38	3.55 ± 0.92	< 0.0001
Eosinophil (%)	2.19 ± 1.02	2.01 ± 0.84	0.0467

count is high. The presence of reactive platelets in the circulation is indicated by an increase in the platelet volume. Herein, the neutrophil count of the patients with psoriasis was higher when it was tested independently.

Some studies have observed an association of the NLR with other inflammatory disorders. For instance, the NLR has been shown to be a promising diagnostic and prognostic biomarker in the early and late phases of sepsis[23,24]. It was also reported to have an acceptable sensitivity in the diagnosis of another systemic inflammation—preeclampsia[23,25]. In patients with COVID-19 aged $\geq$50 years, the NLR is a predictive factor of critical illness[26]. Recently, a study revealed the diagnostic value of the NLR for psoriasis vulgaris and psoriatic arthritis[27].

Neutrophils form extracellular traps that capture and destroy microbes, thus preventing infections. Dysregulation causes systemic inflammation, including psoriasis, rheumatoid arthritis, gout, and autoimmune hepatitis[28]. Dormant cancer cells can be activated by neutrophil extracellular traps during inflammation[29]. Taken together, we recommend the NLR as a potential diagnostic and prognostic biomarker for these types of inflammation and cancer.

CONCLUSIONS

The neutrophil count is higher, and the lymphocyte count is lower in patients with psoriasis than in healthy individuals. Numerous hematological and biochemical indicators can be used to assess systemic inflammation. The NLR is an emerging marker of inflammation and is elevated in patients with psoriasis. It is considered the most straightforward, accessible, and economical marker for determining inflammation. Therefore, we propose the NLR as a potential biomarker for the diagnosis of psoriasis.

ABBREVIATIONS

CBC: Complete Blood Count, **HB**: Hemoglobin, **HCT**: Hematocrit test, **MCH**: mean corpuscular hemoglobin, **MCHC**: mean corpuscular hemoglobin concentration, **MCV**: mean corpuscular volume, **NLR**: Neutrophil to lymphocyte ratio, **PTC**: Platelet Count, **RBCS**: Red Blood Cells, **WBC**: White Blood Cells

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AUTHOR'S CONTRIBUTIONS

Conceptualization, Supervision and Intellectual Input, MBK, MHA, NS; Methodology and Writing-original draft, BN, MBK, AA, SA, SEH, SSS, MR, FA, RM; Editing and Reviewing, SSS, MBK, FA, RM. All authors read and approved the final manuscript.

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AVAILABILITY OF DATA AND MATERIALS

Data is available on request.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Each participant was asked to sign a written ethical consent form during the interview, before the specimen was taken. The informed ethical consent form was designed and approved by the ethical committee of the University of Narowal, Narowal, Pakistan.

CONSENT FOR PUBLICATION

Not applicable.

COMPETING INTERESTS

The authors declare that they have no competing interests.

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