



## Research Article

# Monocyte, neutrophil, eosinophil and lymphocyte volume levels in multiple myeloma patients

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### Abstract

**Objectives:** Multiple myeloma (MM) is a malignant proliferation of monoclonal plasma cells in the blood that may also cause renal failure. The most frequent complications of MM are painful pathological fractures, anemia, hyperkalemia, renal failure and recurrent bacterial infections. Seen from this aspect, it is indicated that inflammation is a significant component of the neoplastic process.

**Methods:** The present study aims to evaluate the association of monocyte, neutrophil, eosinophil and leucocyte volume values in patients with MM as a retrospective study. Sixty patients with MM aged 64.5±11.2 and 107 healthy control aged 64.9±10.3 years who were admitted to the Polyclinic of Hematology in the Faculty of Medicine of the Selcuk University were included in this study.

**Results:** The monocyte, lymphocytes, neutrophil volume levels were significantly higher in patients as 175.62±8.06; 95.05±6.08; 152.51±8.18, respectively, compared with the control group 170.41±8.15; 89.78±4.92; 148.19±8.04, respectively. The eosinophil volume levels were 157.5±22.4 in the patients group and 157±17.3 in the control group (p=0.953). The findings obtained in this study suggest that monocyte, lymphocytes, neutrophil volume values except eosinophil volume may be used as a potentially prognostic biomarker in patients with Multiple myeloma.

**Conclusion:** The present study aimed to evaluate a biomarker that is easily analyzed. This study suggests that monocyte, lymphocytes, neutrophil volume values except eosinophil volume may be used as a potentially prognostic biomarker in patients with Multiple myeloma. And also, monocyte, lymphocyte and neutrophil volume levels are significant parameters that can be applied lower in cost.

**Keywords:** Eosinophil, lymphocytes, multiple myeloma, monocyte, neutrophil, retrospective data

Multiple Myeloma (MM) is a malignant plasma cell structure disorder that gives rise to approximately 10% hematological malignancy [1]. MM is malignant proliferation that still occurs as a result of the uncontrolled growth of white blood cell monoclonal plasma cells [2-4]. Bone ion or monoclonal protein in urine and/or serum is diagnosed by clonal plasma cells [5]. MM is mostly seen between the ages of 25-81, but it occurs more frequently in men than in women [6]. In patients with MM, the most common complications are kidney failure, anemia, painful pathological fractures, hyperkalaemia

and recurrent bacterial infections [7, 8]. Patients with MM have a high amount of protein in their blood.

Antibody-producing plasma cells (immunoglobulin) can be expressed as cells that destroy the effects of immune reactions and pressurized), which has a significant role in the immune system, which balances the T cell's responses to the tumor cells [2, 9]. Monocytes are the precursors of dendritic cells (DC). Lymphocytes are significant in the destruction of the M-protein [10]. Neutrophils have a remarkable task in evaluating the susceptibility of cells to infection [11]. Eosinophils

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(Eoz) has a remarkable task in assessing the survival, proliferation, and retention of malignant plasma cells in the bone marrow (BM) [12].

In MM, myeloid cells are often transformed into new tumor cells. Due to its biology, myeloid-derived suppressor cells (MDSC) are crucial in suppressing and epitomizing the effects of cancer immunotherapy. These cells are associated with neutrophils and monocytes [11]. Clinical significance in MM has rarely been investigated. In this study, we aimed to investigate the prognostic effects of neutrophil, lymphocyte, monocyte and eosinophil volumes in patients with MM according to data of retrospective.

## Materials and Methods

Sixty patients with MM providing the criteria of the International Myeloma Working Group (IMWG) were included in the retrospective review of patient records. In the present study, 107 people with years and gender-matched healthy control were included.

This study was divided into two groups. Group 1 included 60 patients with MM aged  $64.5 \pm 11.2$  years. Group 2 included 107 healthy control aged  $64.9 \pm 10.3$  years. All the groups were composed of whom were admitted to the Polyclinic of Hematology in the Faculty of Medicine at the Selcuk University between 2017 February-February 2018. Patients who were taken steroids, anabolic hormones, beta two agonists were not included in this study because of effecting of Neutrophil levels. New markers were added to the CRAB (Hypercalcemia, Kidney Failure, Anemia, Bone Disease) findings of the multiple myeloma patients which described the myeloma requiring treatment included in our study as: 1- SLiM presence of over 60% clonal plasma cells in bone marrow, 2- being above 100 of free light chain ratio (FLC ratio), 3-and the presence of more than 5 mm or greater focal lesions in the whole body MR. VCD (bortezomib, cyclophosphamide, dexamethasone) protocol was applied to suitable patients for autologous stem cell transplantation. No secondary cancer was detected in our patients. Healthy control group who were admitted to the Polyclinic of Hematology for any health problem and check-up. Monocyte Volume, Neutrophil Volume, Eosinophil Volume, and Lymphocyte Volume levels were measured with a Beckman Coulter LH-780 hematology analyzer in the laboratory of Medical Biochemistry of the Selcuk University.

## Statistical analysis

Statistical analysis was performed using SPSS v16. Student's t-test and Mann-Whitney U-test were used parametric variables for Monocyte Volume (MO VOL), Neutrophil Volume (NEU VOL) and Lymphocyte Volume (LY VOL) and non-parametric variables for Eosinophil Volume (EO VOL). Data were expressed as  $x \pm SD$ . Results were considered statistically significant at  $p < 0.05$ .

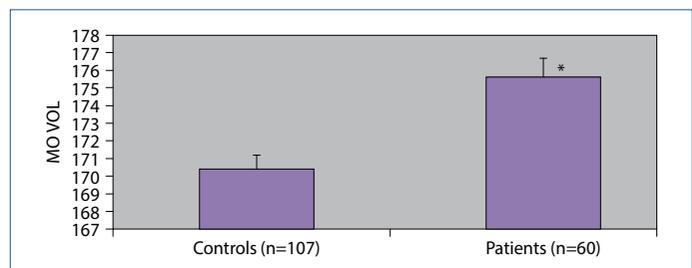
## Results

As shown in Figure 1, the monocyte volume was higher in patients with MM ( $175.62 \pm 8.06$ ) according to healthy subjects ( $170.41 \pm 8.15$ ).

The levels of Lymphocyte Volume were  $95.05 \pm 6.08$  in patients and  $89.78 \pm 4.92$  in the healthy group (Fig. 2).

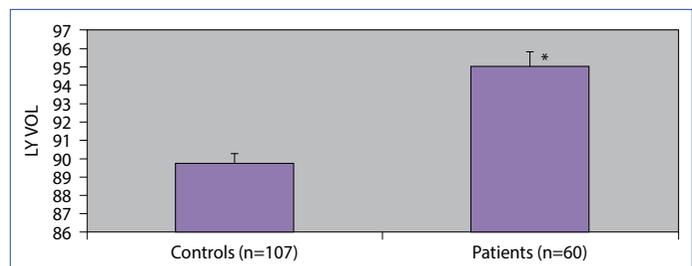
Neutrophil volume levels were significantly higher in patients as  $152.51 \pm 8.18$  compared with the control group as  $148.19 \pm 8.04$  (Fig. 3). The differences between the groups were significantly important according to the level of monocyte, lymphocyte and neutrophil volume levels.

However, eosinophil volume levels were  $157.5 \pm 22.4$  in the patients group and  $157 \pm 17.3$  in the control group ( $p = 0.953$ ) (Fig. 4). The differences between the groups were not important.



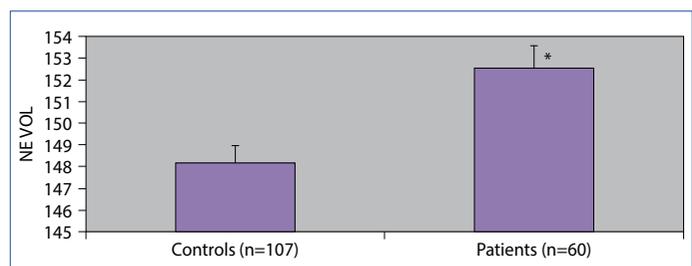
**Figure 1.** MO VOL in patients with multiple myeloma and control groups.

MO VOL: monocyte volume, patients ( $175.62 \pm 8.06$ ) according to healthy subjects ( $170.41 \pm 8.15$ ),  $p = 0.000$ .



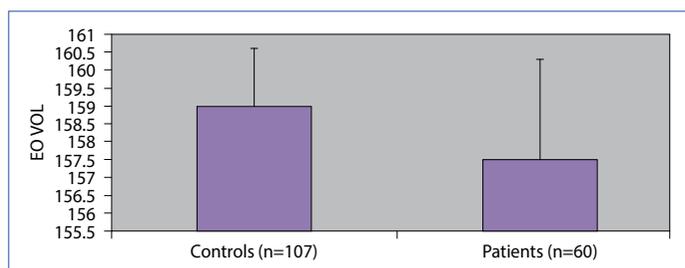
**Figure 2.** LY VOL in patients with multiple myeloma and control groups.

LY VOL: Lymphocyte volume, patients  $95.05 \pm 6.08$  according to healthy subjects  $89.78 \pm 4.92$ ,  $p = 0.000$ .



**Figure 3.** NE VOL in patients with multiple myeloma and control groups.

NE VOL: Neutrophil volume, patients  $152.51 \pm 8.18$  according to healthy subjects  $148.19 \pm 8.04$ ,  $p = 0.001$ .



**Figure 4.** EO VOL in patients with multiple myeloma and control groups.

EO VOL: Eosinophils volume, patients  $157.5 \pm 22.4$  according to healthy subjects  $157 \pm 17.3$ ,  $p=0.953$ .

## Discussion

BM consists of white blood cells, red blood cells, plasma cells, lymphocytes and hemopoietic cells, phibroblasts, histiocytes/macrophages, fat cells and blood vessels, which contain many stages of mast cells [13]. In MM, cell cycle, plasma-cell differentiation, and DNA-damage repair pathways occur, and the immune system-related monocyte, neutrophil, eosinophil and lymphocyte levels are determined by evaluating these differences [14, 15]. MM is primary events, secondary events, and disease caused by clonal heterogeneity [16, 17]. MM is a complex disease that arises from many genomic conditions when evaluated genetically [14]. MM has a molecular subtypes with many prognoses. These primary immunoglobulin heavy chain (IgH) translocations are trisomy (40%) or an IgH combination translocation and trisomy [18-20]. Factors that represent the disease biology of MM and affect the prognosis (age, performance status, molecular subtypes, comorbidities, disease stage) and exposure to mutagens (smoking or ultraviolet) in order to decide the treatment strategy (e.g., drug selection, duration and therapy) in patients light [21, 22]. Monocytes are the largest leukocyte feature in peripheral blood [23]. Myeloid cells contain monocytes, granulocytes, macrophages and DC. Monocytes may differ from the monocyte derivative, DC or inflammatory macrophage [24]. The ability of MM cells to attract monocytes through various secreted factors can contribute to increased dysfunction of DC during illness [3]. With this differentiation feature, monocytes can modify and regulate immune responses according to their own advantage, as MM cells may affect the early stages of DC differentiation [16]. The spectrum of renal lesions in MM is heterogeneous, so myeloma nephropathy cannot be diagnosed at an early stage [7]. Although myeloid cells produced under these conditions are morphologically and phenotypically similar to neutrophils and monocytes, they have different genomic and biochemical structures and functions [11]. Eoz is anti-tumor functions in many malignancies [25]. In the human BM, 1-4% of the cellular compartment consists of eozs [26, 27]. Morphological maturation of eozs precursors and myeloid cells occurs in the same way [13]. Neutrophils make up an average of 50-60% of leukocytes in the blood. Neutrophils

are included in the bloodstream after being produced in the bone marrow. Generally, the neutrophil count does not increase in viral infections, but when there is a systemic infection or systemic inflammatory response, the number of neutrophils in the blood increases [28-31]. As a result, neutrophils play a role in assessing the susceptibility of cells to infection [11]. Lymphoid cells are located in the bone marrow [32]. BM lymphocytes increase when it comes to chronic lymphocytic leukemia [33]. T lymphocytes are involved in intercellular communication in the immune system and have an anti-tumor effect in patients with lymphoid malignancy [34, 35]. B lymphocytes are responsible for humoral immunity. T and B lymphocytes work effectively among themselves and other cell types to stimulate immunity [35]. In addition, many studies show that the neutrophil-lymphocyte ratio (NLR) plays a role in predicting overall survival and prognosis in individuals with hematological cancer [36-40]. MDSC is absent in healthy individuals and occurs only in pathological events associated with cancer, chronic inflammation or stress [11]. There are many biochemical conditions that distinguish MDSC from controls. These include high arginine and iNOS expression and activity, high and persistent ROS (reactive oxygen species), such as myeloperoxidase, superoxide, hydroxyl peroxidase and peroxynitrite [41, 42]. Patients with MM with higher NLR are more likely to have a worse prognosis than patients with lower NLR [43]. Ramachandran et al. revealed that neutrophils affect the effectiveness of chemotherapy in patients with MM and thus the outcome of this disease [43]. Treatment of the disease is a long-term treatment that should be kept under control without considerably impairing the quality of life of the individual throughout his life [44].

## Conclusion

The present study aimed to evaluate a biomarker that is easily analyzed. This study indicated that monocyte, lymphocytes, neutrophil volume values except eosinophil volume might be used as a potentially prognostic biomarker in patients with Multiple myeloma.

Monocyte, lymphocyte and neutrophil volume levels are significant parameters that can be applied lower in cost.

**Conflict of Interest:** There is no conflict of interest.

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