

ASSOCIATION OF SEX, AGE, AND ABO BLOOD GROUPS WITH SERUM CXCL8 LEVELS IN PATIENTS WITH MULTIPLE MYELOMA (MM)

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ABSTRACT

Multiple myeloma is a hematological malignancy characterized by the uncontrolled proliferation of plasma cells in the bone marrow. Interleukin-8 (IL-8/CXCL8) is a pro-inflammatory chemokine that plays an important role in immune regulation, angiogenesis, and tumor progression. This study aimed to evaluate serum CXCL8 levels in patients with multiple myeloma and investigate their association with sex, age, and ABO blood groups. A total of 40 blood samples were collected from patients diagnosed with multiple myeloma between October and December 2025. Blood samples were analyzed for ABO and Rh blood group determination using the slide agglutination method. Serum CXCL8 concentrations were measured using enzyme-linked immunosorbent assay (ELISA). Statistical analyses were performed using SPSS software, and significant differences among groups were evaluated using analysis of variance (ANOVA). The results demonstrated significantly higher serum CXCL8 levels in females compared with males. Significant variations were also observed among ABO blood groups, with the highest CXCL8 levels detected in individuals with blood group B+, followed by O+ and A+. In addition, age-related differences were observed, with the highest CXCL8 levels recorded in the youngest age group. These findings suggest that serum CXCL8 levels may be influenced by sex, age, and ABO blood groups in patients with multiple myeloma, highlighting its potential value as a biomarker of disease-associated inflammatory and immunological alterations.

KEYWORDS: Multiple myeloma, CXCL8, age, sex, blood groups.

INTRODUCTION

Multiple myeloma accounts for approximately 1–2% of all cancers and 10–13% of all hematological malignancies, making it the second most common hematological malignancy, with an incidence of about 6 cases per 100,000 people annually in the United States. The incidence is significantly higher among African Americans aged 50 and older than

among white Americans, and this continues to increase with age, particularly after age 80. Males also have a higher incidence than females.^[1] Plasma cells normally produce antibodies to fight infection. However, in multiple myeloma, plasma cells become malignant and accumulate within the bone marrow, the tissue inside bones responsible for producing blood cells. The cancerous cells crowd out healthy blood cells in the bone marrow. Furthermore, malignant plasma cells produce abnormal monoclonal immunoglobulins or light chains that may impair normal immune function, instead of producing beneficial antibodies. This leads to a condition known as anemia. These abnormal cells can also cause damage to the bones and kidneys.^[2]

Interleukin-8 (CXCL8) belongs to the CXC chemokine family, known for its diverse biological functions. It plays a pivotal role in guiding immune cells and promoting angiogenesis. CXCL8 exists in both monomeric and dimeric forms and plays an important role in inflammatory responses and tumor progression.^[3] Unlike most inflammatory cytokines, which have a short half-life in the body, CXCL8 exhibits resistance to temperature changes and proteolytic enzymes, remaining active for several days or even weeks after its initial production during the inflammatory response.^[4]

CXCL8 consists of 72 amino acids (in some cases, 77 depending on the protein processing).^[5] Studies have indicated that CXCL8 may contribute to cancer development primarily by promoting angiogenesis. CXCL8 signaling can stimulate the proliferation and migration of multiple myeloma (MM) cells and contribute to disease progression. A number of cancer cells produce CXCL8, which attracts cells to the tumor site.^[6] Inflammatory signaling via CXCL8 can activate cancer cells in the bone marrow microenvironment, leading to the secretion of factors that support the survival of abnormal or atypical stem cells, thus contributing to disease persistence and promoting the progression of malignant hematological disorders.^[7] Interleukin-8 has been shown to promote tumor growth, angiogenesis, and cancer metastasis in a variety of human cancers.^[8]

MATERIALS AND METHODS

The study involved collecting 40 blood samples from a specialized hospital between October 10 and December 15, 2025. The samples were divided into 20 male and 20 female samples, categorized by age group. Four milliliters of peripheral venous blood were collected from each participant. A portion was directly transferred to EDTA tubes for blood typing and Rh factor determination using agglutination on slides with specific antibodies (Anti-A, Anti-B, and Anti-O).^[9] The remaining blood sample was centrifuged at 3000 x g for serum separation to obtain serum for biochemical and immunological analysis. Serum IL-8 (CXCL8) concentrations were measured using a commercially available ELISA kit from Sunlong Biotech, China, at a wavelength of 450 nm.^[10] The data obtained were then subjected to statistical analysis via SPSS software to extract the arithmetic means and standard errors, and the analysis of variance (ANOVA) was applied to determine the significant differences between the study groups.^[11]

RESULTS

Table 1: Serum CXCL8 levels in the male and female.

	Males (Mean $\pm$ SE)	Females (Mean $\pm$ SE)
CXCL8 (pg/mL)	32.3 $\pm$ 1.45	34.6 $\pm$ 1.47**

** indicates a significant difference at $P \leq 0.01$

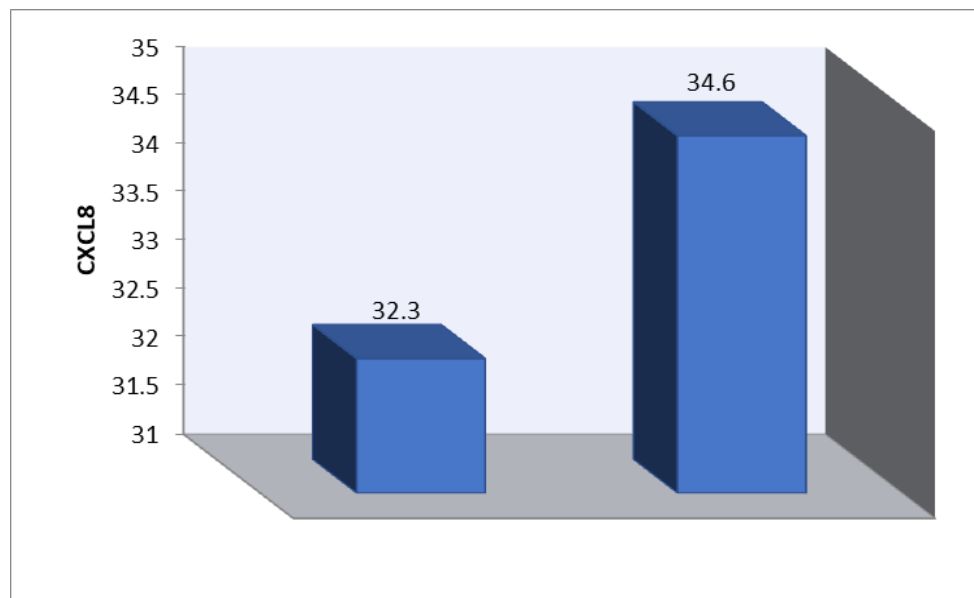


Figure 1: illustrates the mean serum CXCL8 levels according to sex, Female patients showed higher CXCL8 levels (34.6 pg/mL) than male patients (32.3 pg/mL).

Table 2: CXCL8 levels in blood groups ABO in the study groups, expressed as (Mean $\pm$ SE).

	A + (Mean $\pm$ SE).	B + (Mean $\pm$ SE).	O + (Mean $\pm$ SE).
CXCL8 (pg/mL)	30.6 $\pm$ 1.33b	35.8 $\pm$ 4.68 ab	32.7 $\pm$ 0.84 a

different letters indicate significant differences.

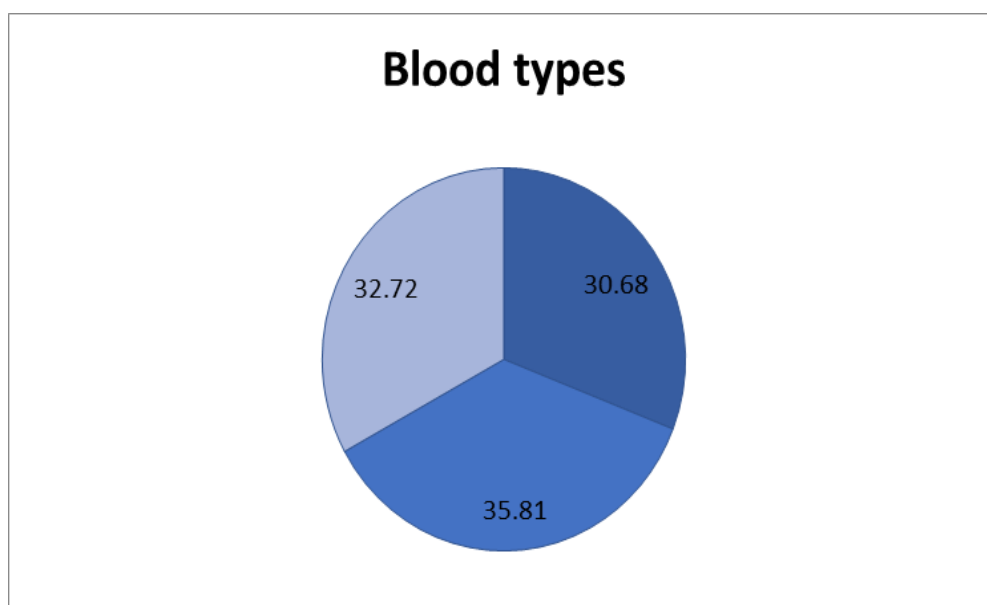


Figure 2: Presents the mean serum CXCL8 levels according to ABO blood groups.

Table 3: CXCL8 levels according to age in the study groups, expressed as (Mean $\pm$ SE).

	Children (1_12 years)	Adolescents (13_17 years)	Adults ($\geq$ 18 years)
CXCL8 (pg/mL)	36.2 $\pm$ 2.66 a	32.9 $\pm$ 1.42 $\pm$ b	32.3 $\pm$ 1.52 b

Similar letters indicate no significant differences, while different letters indicate significant differences.

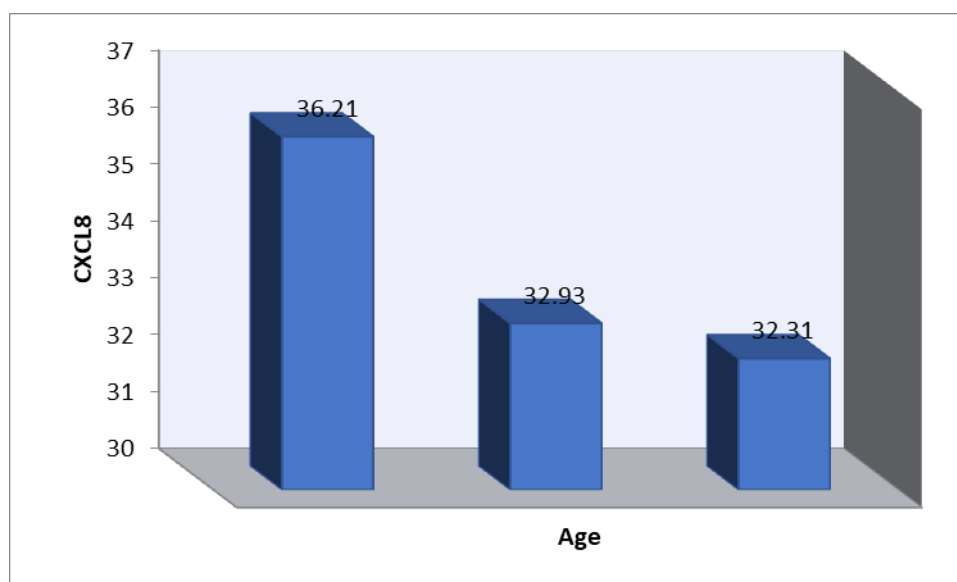


Figure 3: Presents the mean serum CXCL8 levels across the different age groups.

DISCUSSION

As shown in Table (1), a comparative analysis of the effect of sex on CXCL8 levels in patients with multiple myeloma revealed that the findings related to CXCL8 levels are of particular importance in light of the growing body of evidence regarding the role of inflammation in the sex-related differentiation in multiple myeloma. Recent studies have shown that females have stronger immune responses due to the presence of two X chromosomes, as approximately 15% of genes on the inactive X chromosome escape silencing, thus enhancing immune surveillance in females.^[12] This fundamental immune difference is thought to contribute to the increased susceptibility of males to acute myeloid leukemias, while females exhibit better survival rates despite experiencing greater therapeutic toxicity.^[13]

Recent research suggests that higher CXCL8 levels in females may reflect a more robust immune response, consistent with the general clinical observation that women exhibit stronger immune responses against cancer cells. Studies have also shown significant differences in gene mutation patterns between the sexes, with some mutations associated with poor prognosis, such as ZRSR2 mutations on the X chromosome, being more common in males.^[14] These mutations contribute to impaired dendritic cell activation and inflammatory response, which may partially explain the differences in inflammatory levels between the sexes.

As shown in Table (2), a significant difference in CXCL8 levels observed among the ABO blood groups, with the highest level observed in B+ blood groups, followed by O+ and A+. Recent studies have shown that the regulation of gene expression of ABO antigens may be affected by DNA methylation processes in cancer cells. The elevated CXCL8 levels observed in the B+ blood groups may be associated with a stronger response or with a specific gene pattern that affects the production of this cytokine.^[15] It is important to note that impaired ABO antigen expression, observed in some types of leukemia, can affect the results of hematologic cross matching tests and cause difficulties in their interpretation. Furthermore, a study^[16] indicated that changes in the regulation of ABO antigen gene expression may occur during hematopoietic progenitor cell differentiation, affecting the antigen profile in patients with multiple myeloma.

As shown in Table (3), the results revealed a variation in CXCL8 levels among the three age groups: younger than 12 years, 12-17 years, and older than 18 years. The results indicated lower CXCL8 level in adults than in children. CXCL8 is a potent chemokine and vasodilator, and its elevation in children may reflect a more severe inflammatory response or a genetic predisposition.^[17] Elevated CXCL8 levels have been associated with poor prognosis in hematological malignancies, although their role may vary according to age.

CONCLUSION

The present study concludes that variations exist in the distribution of ABO blood groups among patients with multiple myeloma (MM), with blood B being the most prevalent among the study participants. These findings suggest a possible association between specific ABO blood groups and susceptibility to multiple myeloma. The study also indicates the presence of sex-related differences in disease susceptibility and factors that may influence its development.

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