Caspian Journal of Internal Medicine 2026 (Winter); 17(1): 90-96
DOI: 10.22088/cjim.17.1.90

Original Article

Interleukin-38 serum levels in breast cancer: A comparative analysis of women under 40 and over 50

Seyedeh Niloufar Mousavi (MD) [1]
Aida Khademolhosseini (MSc) [1]
Mohammad Javad Fattahi (PhD) [1]
Soolmaz Khansalar (MSc) [1]
Sedigheh Tahmasebi (MD) [2]
Abbas Ghaderi (PhD) [1]
Mohammad Reza Haghshenas (PhD) [1*]

1. Shiraz Institute for Cancer Research, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran
2. Breast Diseases Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

*** Correspondence:**
Mohammad Reza Haghshenas,
Shiraz Institute for Cancer Research, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran

E-mail : haghshenasmr@sums.ac.ir
Tel: +98 7132303687

Received: 24 Dec 2024
Revised: 5 March 2025
Accepted: 6 April 2025
Published: 21 Jan 2026

Abstract

Background: Interleukin-38 (IL-38) is an anti-inflammatory cytokine with immunomodulatory properties, but its role in breast cancer (BC) is unclear. This study aimed to evaluate IL-38 serum levels in BC patients aged ≤40 and ≥50 years and to correlate the findings with clinicopathological features.

Methods: IL-38 levels were measured using an enzyme-linked immunosorbent assay (ELISA) in the serum of 30 BC patients aged ≤40, 30 aged ≥50, and 30 healthy controls. Non-parametric tests were used for statistical comparisons, and Spearman's correlation was used to examine the correlation between IL-38 and age and tumor size.

Results: There was no significant difference in serum IL-38 levels between patients aged ≥50 and those aged ≤40 or their age-matched controls. However, patients aged ≤40 years had significantly lower IL-38 levels than healthy individuals of the same age (P=0.003). In addition, serum IL-38 levels were significantly different between healthy individuals aged ≤40 and ≥50 years. Patients with stage I and II BC had significantly lower serum IL-38 levels than healthy controls (P=0.04 and P=0.003, respectively). However, there were no significant associations between IL-38 serum levels and histological grade (P=0.09), nuclear grade (P=0.11), lymphovascular invasion (P=0.72), perineural invasion (P=0.21), lymph node involvement (P=0.71) and tumor size (P=0.70).

Conclusion: Our results suggest that any change in IL-38 serum levels is likely to affect the anti-inflammatory response in BC patients, especially those under 40 years of age. However, this is a preliminary study, and further studies with larger cohorts are needed to validate these findings.

Keywords: Breast cancer, IL-38 protein, Age groups, Cytokine, Serum concentration.

Citation:
Mousavi SN, Khademolhosseini A, Fattahi MJ, et al. Interleukin-38 Serum Levels in Breast Cancer: A comparative analysis of women under 40 and over 50. Caspian J Intern Med 2026; 17(1): 90-96.

Breast cancer (BC) is the most frequent cancer among women globally and is responsible for the majority of cancer-related deaths in women throughout the world (1). BC is generally considered an age-related disease, with age over 40 recognized as a significant risk factor for its development (2, 3). In developed countries, the incidence of BC among women under 40 is infrequent (6-10%), however, in less developed countries a higher proportion of patients are under 40 (approximately 20%), with the average age of onset being about 10 years lower than in developed countries. In Iran, the average age of BC incidence is also lower compared to developed countries (4, 5). BC in women under 40 is often more aggressive with unfavorable prognosis compared to older women (6). The immune system's role in biology of BC in young women has yet to be fully understood. Importantly, inflammation predisposes to tumor growth and participates in all stages of tumorigenesis, making the association between inflammatory components of the immune system and breast cancer a crucial area of cancer research (7).

 Publisher: Babol University of Medical Sciences

Pro-inflammatory and anti-inflammatory cytokines, key components of the immune system, have been extensively studied in BC. However, the role of newly identified cytokines, such as IL-38, in cancer progression and/or protection is still under investigation (8-12). IL-38 has been known for over a decade and is a member of the IL-1 family. IL-38 is believed to act as a natural inhibitor of inflammation, attenuating the created inflammation at the early phases of diseases such as multiple sclerosis and systemic sclerosis (13). The anti-inflammatory properties of IL-38 are mediated by binding to several receptors, including interleukin-36 receptor (IL-36R), interleukin-1 receptor accessory protein-like 1 (IL-1RAPL1), and interleukin-1 receptor 1 (IL-1R1), to block binding to other pro-inflammatory cytokines and inhibit downstream signaling pathways such as nuclear factor-κB (NF-κB) (14, 15).In addition, IL-38 enhances the immunosuppressive activity of regulatory T cells and stimulates the generation of Th2-related cytokines and anti-inflammatory components (e.g. IL-10 and TGF-β) (16). IL-38 is expressed in various tissues, including tonsils, spleen, thymus, fetal liver, lungs, heart, placenta, and skin, and shows significant homology with IL-36Ra and IL-1R, exerting anti-inflammatory effects through interaction with IL-36R and IL-1R1(15, 17). Due to the novelty of IL-38, investigations into its role in cancer pathogenesis are limited. In colorectal cancer (CRC), IL-38 expression was shown to be 95% lower in tumor tissues than in unaffected adjacent tissues correlating with longer survival and smaller tumor size (18). Conversely, in lung adenoma carcinoma, higher expression of IL-38 was detected in tumor cells which were associated with worse prognosis (19). Furthermore, IL-38-transfected Lewis lung carcinoma cells exhibited lower tumor growth compared to empty vector-transfected cells (20). Hence, the involvement of IL-38 in cancer pathology remains underexplored and findings to date are controversial. To the best of our knowledge, no published studies have assessed the role of IL-38 in BC. Therefore, the purpose of this study was to investigate the serum levels of IL-38 in BC. Given that the immune system is expected to be more robust in younger individuals, yet young BC patients exhibit a more malignant phenotype, it is crucial to evaluate the immune system components in this population. Considering the significant impact of age-related inflammation on the biology of BC and the increasing incidence of BC among young women, IL-38 serum levels were analyzed in two age groups: ≤40 and ≥50. Moreover, the associations between IL-38 serum levels and the clinicopathological characteristics of the patients were examined.

Methods

Study population: In total, 60 new cases of BC (mean age 45.72±11.47) and 30 age- and sex-matched healthy controls (mean age 45.80±12.04) were enrolled in this case-control study. All patients were diagnosed with invasive ductal carcinoma and the diagnosis was performed clinically and pathologically at Faghihi Hospital, Shiraz, Iran. BC patients were equally divided into 2 age groups ≤40 and ≥50 years, each containing 30 patients. The control group consisted of two equal groups of healthy people under 40 years of age and over 50 years of age, with 15 subjects in each group. As research has shown that both hematological and biological parameters are drastically altered by chemotherapy in people with BC, the blood samples were collected before any medical intervention (21, 22). Those with other malignancies, immune-related diseases, and infectious diseases within the month before blood sampling were excluded from the study. The control group included healthy women who had no family history of malignancies, immune-related diseases, infectious diseases, and anti-inflammatory drug administration within the month before the sample collection. The clinicopathological characteristics of patients (including stage, histological grade, nuclear grade, tumor size, skin involvement, muscle involvement, lymphovascular invasion, perineural invasion, and lymph node involvement) were obtained by reviewing their medical records and are indicated in table 1. All the participants signed the written informed consent form.

IL-38 measurements in serum: Venous blood samples were collected and immediately centrifuged for 10 minutes at 2500 × g at 4°C. The serum samples were collected and stored at -80°C until further analysis. IL-38 serum levels were measured using enzyme-linked immunosorbent assay (ELISA) kits from SHANGHAI CRYSTAL DAY BIOTECH CO., LTD. The assay range of the kit was 0.5 to 200 pg/mL and the sensitivity was 0.23 pg/mL.

Statistical analysis: Data analysis was conducted using the SPSS22 software package. IL-38 serum levels did not show normal distribution as assessed by the Kolmogorov–Smirnov test. Accordingly, non-parametric tests, including Mann–Whitney U and Kruskal–Wallis H, were used to compare IL-38 serum levels between the patients and control group and to investigate their association with the clinicopathological characteristics of patients. The correlation between IL-38 serum levels and age and tumor size was examined using Spearman's correlation. The results were presented as the mean±SEM and median. A p-value of less than 0.05 was used to determine statistical significance.

Table 1. Clinicopathological characteristics of patients

Parameters	Categories		Frequency	Percent
Age Group	≤40		30	50
	≥50		30	50
Stage	Early	I	20	33.3
		II	23	38.4
	Advanced	III	17	28.3
Histologic Grade	Well-differentiated		17	28.3
	Moderately-differentiated		23	38.4
	Poorly-differentiated		18	30.0
	Unknown		2	3.3
Nuclear Grade	I		8	13.3
	II		21	35.0
	III		21	35.0
	Unknown		10	16.7
T	1		31	51.7
	2		23	38.3
	3		2	3.3
	4		1	1.7
	Unknown		3	5.0
N	Unknown		3	5.0
	0		23	38.4
	1		20	33.3
	2		8	13.3
	3		6	10.0
M	0		57	5.0
	Unknown		3	95.0
Skin Involvement	Involved		1	1.7
	Free		59	98.3
Muscle Involvement	Involved		1	1.7
	Free		59	98.3
Lymphovascular Invasion	Involved		20	33.3
	Free		40	66.7
Perineural Invasion	Involved		12	20.0
	Free		48	80.0
Lymph Node Involvement	Involved		34	.56.6
	Free		23	38.4
	Unknown		3	5.0

Results

Serum levels of IL-38 in different groups: The IL-38 serum levels were observed to be significantly lower among BC patients (16.40±3.16) in comparison to the control group (27.31±5.60) (P=0.007) (figure 1 and table 2). No statistically significant differences were found in IL-38 serum levels between patients aged≤40 (16.65±3.82) and patients aged ≥50 (16.15±5.11) (P=0.89). Moreover, IL-38 serum levels were found to be significantly lower in patients aged ≤40 (16.65±3.82) than in healthy individuals aged ≤40 (39.03±9.74) (P=0.003). IL-38 serum levels were not significantly different between patients aged ≥50 (16.15±5.11) and healthy individuals aged ≥50 (15.59±3.93) (P= 0.48). Moreover, serum IL-38 levels were significantly higher in healthy individuals aged ≤40 than in those ≥50 (figure 1 and table 2).

Association of IL-38 serum levels with pathological characteristics of patients: Breast cancer is generally classified into four stages, with stages I and II considered early stages and stages III and IV as advanced stages. In this study, patients were in stages I to III of BC: 20 patients in stage I, 23 in stage II, and 17 in stage III. There was no statistically significant difference in IL-38 serum levels among the three stages (P=0.27).

Accordingly, IL-38 serum levels were not statistically significant between stage I and II (P=0.495), between stage II and III (P=0.090), or between stage I and III (P=0.478). The next step was to compare the data from each stage separately in different age subgroups. Our results showed among patients with stage I disease, IL-38 serum levels were significantly lower in patients aged≥50 years (10.38±3.53) than in those aged≤40 years (27.61±8.13, P=0.042). Furthermore, IL-38 serum levels in stage II did not show any significant difference between patients aged≤40 (11.08±3.65) and those aged ≥50 (9.46±1.46, P=0.785). The same results were observed in stage III between patients aged≤40 (25.14±13.20) and those aged ≥50 (26.45±12.87, P=0.660).

However, compared to the control group (27.31±5.60), IL-38 serum levels were significantly lower in stages I and II (14.69±3.65, P=0.04 and10.80±3.01, P=0.003). IL-38 serum levels in stage III (25.99±9.29) were not significantly different from the control group (27.31±5.60, P=0.36). Although IL-38 levels were higher in the advanced stage (25.99 ±9.29) compared to the early stage (12.60±2.33), the difference was not statistically significant (P=0.16). There were no associations between IL-38 serum levels and other pathologic characteristics of patients, including histological grade (P=0.09), nuclear grade (P=0.11), lymphovascular invasion (P=0.72), perineural invasion (P=0.21), lymph

node involvement (N) (P=0.71) and tumor size (T) (P=0.70) (data are provided in Table 2). It should be noted that groups containing ≤2 patients were not included in the comparisons.

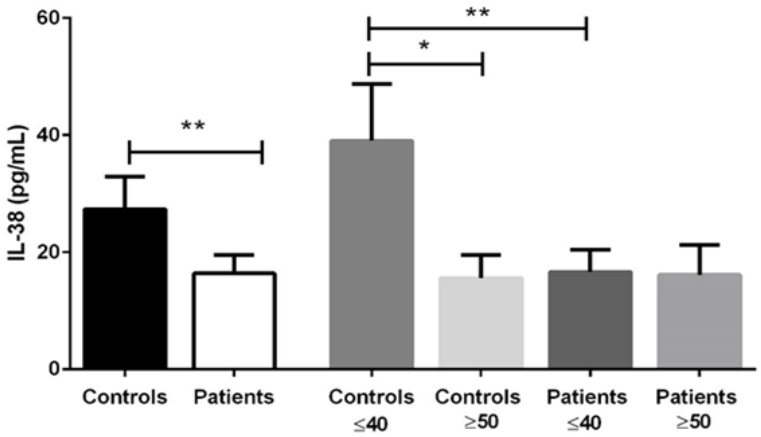
Correlation between IL-38, age and, tumor Size: There were no significant correlations between IL-38 serum levels and age (N=60, R=-0.06, P=0.65) as well as IL-38 serum levels and tumor size (N=57-, R=0.06, P=0.66), as investigated by Spearman's correlation test.

Table 2. Association of IL-38 serum levels with clinicopathological characteristics of patients

		Number	IL-38 Serum Level (pg/mL)				P-value	
			Mean±S.E.M	Median	Minimum	Maximum		
Characteristics	Total patients	60	16.40±3.16	9.31	0.53	152.88	0.007	
	Total Controls	30	27.31 ±5.60	19.79	0.54	159.20		
Age	Patients ≤40	30	16.65±3.82	8.85	0.53	78.66	0.890	
	Patients≥50	30	16.15±5.11	10.54	0.53	152.88		
	Controls ≤40	15	39.03±9.74	35.24	1.88	159.20	0.010	
	Controls ≥50	15	15.59±3.93	15.10	0.54	55.49		
	Patients≥50	30	16.15±5.11	10.54	0.53	152.88	0.480	
	Controls ≥50	15	15.59±3.93	15.11	0.54	55.49		
	Patients ≤40	30	16.65±3.82	8.85	0.53	78.67	0.003	
	Controls ≤40	15	39.03± 9.74	35.24	1.88	159.20		
Stage	Stage I	20	14.69±3.65	11.30	0.53	55.96	I vs. II	0.495
	Stage II	23	10.80±3.01	8.32	0.53	72.58	I vs. III	0.478
	Stage III	17	25.99±9.29	12.30	0.86	152.88	II vs. III	0.09
	Stage I	20	14.69±3.65	11.30	0.53	55.96	0.040	
	Controls	30	27.31 ±5.60	19.79	0.54	159.20		
	Stage II	23	10.80±3.01	8.32	0.53	72.58	0.003	
	Controls	30	27.31 ±5.60	19.79	0.54	159.20		
	Stage III	17	25.99±9.29	12.30	0.86	152.88	0.360	
	Controls	30	27.31 ±5.60	19.79	0.54	159.20		
	Early Stage (I, II)	43	12.60±2.33	8.32	0.53	72.58	0.160	
	Advanced Stage (III)	17	25.99±9.29	12.30	0.86	152.88		
Histologic Grade	Well-differentiated	17	27.74±9.37	12.77	0.59	152.88	0.090	
	Moderately-differentiated	23	11.97±2,67	8.08	0.53	51.63		
	Poorly-differentiated	18	11.67±3.86	8.14	0.53	72.58		
Nuclear Grade	I	8	24.87±9.31	14.35	0.59	78.67	0.110	
	II	21	10.97±3.27	6.68	0.53	55.96		
	-III	21	12.26±3.36	9.14	0.53	72.58		

Caspian Journal of Internal Medicine 2026 (Winter); 17(1): 90-96
Mousavi SN, et al.

		Number	IL-38 Serum Level (pg/mL)				P-value
			Mean±S.E.M	Median	Minimum	Maximum	
Lymphovascular Invasion	Involved	20	13.72±3.46	8.44	0.53	55.96	0.720
	Free	40	17.74±4.43	10.43	0.53	152.88	
Perineural Invasion	Involved	12	8.13±1.75	7.67	0.53	20.96	0.210
	Free	48	18.47±3.88	9.84	0.53	152.88	
Lymph Nodes involvement	0	23	13.38±3.24	8.08	0.53	55.96	0.710
	I	20	19.98±7.74	9.31	0.74	152.88	
	II	8	22.94±9.97	13.18	0.86	78.67	
	III	6	14.42±3.37	11.71	4.69	27.39	
Tumor size (T)	T1	31	15.08±3.28	9.49	0.53	78.67	0.700
	T2	23	14.30±3.41	9.60	0.75	72.58	



1. Comparison of IL-38 serum levels between patients with breast cancer and control group

Discussion

IL-38 has been investigated for its potential involvement in the development of various diseases, but its exact role in cancer remains unclear and controversial (14, 23, 24). Although a few limited studies have explored the expression of IL-38 in tumor tissues, none have measured it in sera until now (15). To the best of our knowledge, this research is the first to investigate IL-38 levels in the sera of BC patients and their association with the clinicopathological characteristics. Our data revealed that IL-38 serum levels - were significantly lower in BC patients than in controls. Consistent with our findings, an immunohistochemical study of IL-38 in CRC showed significantly lower expression of IL-38 in tumor tissue compared to neighboring normal tissue, however, the expression of IL-38 was correlated with smaller tumor size and longer survival in CRC (18). In contrast to our results, higher IL-38 expression was detected in tumor cells in lung adenocarcinoma, which was associated with poor prognosis in this cancer (19). The higher expression of IL-38 in lung cancer was shown to promote tumor progression by reducing CD8+ tumor-infiltrating lymphocytes (TILs) (20). These discrepancies may be due to differences in sample types, measurement methods, and tumor pathogenesis. BC incidence has increased among Iranian young women (5). The average age of BC appearance in Iran is approximately 10 years lower than in developed countries (5). Moreover, BC in young women tends to be more aggressive (25). Due to the rising trend of BC in Iranian women, particularly those under 40, we assessed IL-38 serum levels in two different age groups of women with BC. One group consisted of patients aged ≤40, representing young women. Given the onset of immunosenescence after 50 and aging-associated inflammation as a contributing factor to BC development, the second group included patients aged ≥50 (3, 26). A 10-year gap was applied to clearly examine the

effect of age on IL-38 serum levels in BC. IL-38 serum levels were significantly lower in patients aged ≤40 compared to their counterparts in the control group, while no significant differences were found in patients aged ≥50 compared to controls. Although more studies with larger sample sizes are required, this may suggest a potential protective effect of IL-38 against BC in young women. IL-38 serum levels were significantly lower in patients in stages I and II of BC compared to the control group. Moreover, among BC patients with stage I disease, serum IL-38 levels were significantly lower in patients aged ≥50 years than in those aged ≤40 years. In addition, we observed a non-significant decrease in serum IL-38 concentrations in the early stages of BC compared to the advanced stages. The close and complex interplay between inflammation and cancer may explain these observations, at least in part. On the one hand, acute inflammatory reactions can mediate anti-tumor effects by stimulating dendritic cell maturation, antigen presentation, and cytokines and chemokine production (27, 28).

On the other hand, inflammation is considered a hallmark of cancer that plays a pivotal role in every step of carcinogenesis (29). Non-specific, chronic inflammation is a contributing factor to the development and progression of different types of cancer including BC (27, 30). In other words, the in-time resolution of acute inflammation is necessary to prevent chronic inflammation and its consequent pro-tumoral effects (31).

Thus, the decrease in anti-inflammatory mediators, including IL-38, in the early phase of tumorigenesis may be involved in tumor development and progression. However, the elevation of IL-38 in BC patients may inhibit specific inflammatory responses, leading to tumor progression. Overexpression of IL-38 might contribute to tumor development and progression of tumors by inhibiting the function of IL-36, another member of the IL-1 cytokine family, which participates in anti-tumor responses through CD8+ T cell activation and Th1 polarization (32). However, inflammation and cytokines like IL-38 are considered a double-edged sword in cancer and IL-38 might exert different effects at different stages of BC. Our results suggest that any change in IL-38 serum levels is likely to affect the anti-inflammatory response in BC patients, especially those under 40 years of age. However, this is a preliminary study and the findings should be validated by further studies in larger patient cohorts.

Acknowledgments

This project was conducted as the MD thesis of Seyedeh Niloufar Mousavi, and was ethically and financially supported by grants from Shiraz University of Medical Sciences, Shiraz, Iran (Grant No:19891), as well as Shiraz Institute for Cancer Research, Shiraz University of Medical Sciences, Shiraz, Iran (ICR-100-503).

Funding: This project was financially supported by grants from Shiraz University of Medical Sciences, Shiraz, Iran (IR.SUMS.MED.REC.1399.086, Grant No:19891), as well as Shiraz Institute for Cancer Research, Shiraz University of Medical Sciences, Shiraz, Iran (ICR-100-503).

Ethics approval: All the participants signed the written informed consent form. The study was approved by the local Ethics Committee at Shiraz University of Medical Sciences, Shiraz, Iran (IR.SUMS.MED.REC.1399.086).

Conflict of interests: There are no competing interests to declare.

Consent for publication: All authors confirm that they have provided their consent for the publication of this work.

Authors' contribution: S.N.M., A.Kh., and S.Kh.; Contributed to lab experiments, data and statistical analysis. M.R.H. and A. Gh.; Contributed to the conception and study design. M.R.H. and M.J.F.; Contributed to the data interpretation. S.T.; Contributed to patient's diagnosis and sample collection. M.R.H. and A. Gh.; Supervised the project. M.R.H.; Contributed to funding acquisition. S.N.M., and A.Kh.; Drafted the manuscript, and then it was revised by M.J.F., S.Kh , A. Gh., and M.R.H. All authors read and approved the final manuscript.

Availability of data and material: The data generated in this study are available upon reasonable request.

References

1. Sung H, Ferlay J, Siegel RL. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2021; 71: 209-49.
2. Youn HJ, Han W. A review of the epidemiology of breast cancer in Asia: Focus on risk factors. Asian Pac J Cancer Prev 2020; 21: 867-80.
3. Leonardi GC, Accardi G, Monastero R, Nicoletti F, Libra M. Ageing: from inflammation to cancer. Immun Ageing 2018; 15: 1.
4. Siddig A, Tengku Din T, Mohd Nafi SN, et al. The unique biology behind the early onset of breast cancer. Genes (Basel) 2021; 12: 372.
5. Fazel A, Hasanpour-Heidari S, Salamat F, et al. Marked increase in breast cancer incidence in young women: A 10-year study from Northern Iran, 2004-2013. Cancer Epidemiol 2019; 62: 101573.

6. Tesch ME, Partridge AH. Treatment of breast cancer in young adults. Am Soc Clin Oncol Educ Book 2022; 42: 1-12.
7. Liubomirski Y, Lerrer S, Meshel T, et al. Tumor-stroma-inflammation networks promote pro-metastatic chemokines and aggressiveness characteristics in triple-negative breast cancer. Front Immunol 2019; 10: 757.
8. Cruceriu D, Baldasici O, Balacescu O. The dual role of tumor necrosis factor-alpha (TNF-α) in breast cancer: molecular insights and therapeutic approaches. Cell Oncol (Dordr) 2020; 43: 1-18.
9. Méndez-García LA, Nava-Castro KE, Ochoa-Mercado TL, et al. Breast cancer metastasis: Are cytokines important players during its development and progression? J Interferon Cytokine Res 2019; 39: 39-55.
10. Zhang Y, Liu C, Gao J, et al. IL-22 promotes tumor growth of breast cancer cells in mice. Aging (Albany NY) 2020; 12: 13354-64.
11. Kan T, Feldman E, Timaner M, et al. IL-31 induces antitumor immunity in breast carcinoma. J Immunother Cancer 2020; 8: e001010.
12. Autenshlyus A, Davletova K, Varaksin N, Marinkin I, Lyakhovich V. Cytokines in various molecular subtypes of breast cancer. Int J Immunopathol Pharmacol 2021; 35: 20587384211034089.
13. Zarrabi M, Nazarinia M, Rahimi Jaberi A, Gholijani N, Amirghofran Z. Elevated IL-38 serum levels in newly diagnosed multiple sclerosis and systemic sclerosis patients. Med Princ Pract 2021; 30: 146-53.
14. Xie L, Huang Z, Li H, Liu X, Zheng S. IL-38: A new player in inflammatory autoimmune disorders. Biomolecules 2019; 9: 345.
15. Haghshenas MR, Zamir MR, Sadeghi M, et al. Clinical relevance and therapeutic potential of IL-38 in immune and non-immune-related disorders. Eur Cytokine Netw 2022; 33: 54-69.
16. Ge Y, Huang M, Wu Y, Dong N, Yao YM. Interleukin-38 protects against sepsis by augmenting immunosuppressive activity of CD4(+) CD25(+) regulatory T cells. J Cell Mol Med 2020; 24: 2027-39.
17. Diaz-Barreiro A, Huard A, Palmer G. Multifaceted roles of IL-38 in inflammation and cancer. Cytokine 2022; 151: 155808.
18. Chen F, Zhang F, Tan Z, et al. Interleukin-38 in colorectal cancer: a potential role in precision medicine. Cancer Immunol Immunother 2019; 69: 69-79.
19. Takada K, Okamoto T. Clinical implications of the novel cytokine IL-38 expressed in lung adenocarcinoma: Possible association with PD-L1 expression. PLoS One 2017; 12: e0181598.
20. Kinoshita F, Tagawa T. Interleukin-38 promotes tumor growth through regulation of CD8(+) tumor-infiltrating lymphocytes in lung cancer tumor microenvironment. Cancer Immunol Immunother 2021; 70: 123-35.
21. Pullakanam T, Mannangatti M, Ramesh A, Nekkala R, Vijayalakshmi P. Chemotherapy on hematological and biochemical parameters in breast cancer patients. Caspian J Intern Med 2025; 16: 132-40.
22. Pakmanesh F, Moslemi D, Mahjoub S. Pre and post chemotherapy evaluation of breast cancer patients: Biochemical approach of serum selenium and antioxidant enzymes. Caspian J Intern Med 2020; 11: 403-9.
23. van de Veerdonk FL, de Graaf DM, Joosten LA, Dinarello CA. Biology of IL-38 and its role in disease. Immunol Rev 2018; 281: 191-6.
24. de Graaf DM, Teufel LU, Joosten LAB, Dinarello CA. Interleukin-38 in health and disease. Cytokine 2022; 152: 155824.
25. Fabiano V, Mandó P, Rizzo M, et al. Breast cancer in young women presents with more aggressive pathologic characteristics: Retrospective analysis from an argentine national database. JCO Glob Oncol 2020; 6: 639-46.
26. Goronzy JJ, Weyand CM. Understanding immunosenescence to improve responses to vaccines. Nat Immunol 2013; 14: 428-36.
27. Zhao H, Wu L, Yan G, et al. Inflammation and tumor progression: signaling pathways and targeted intervention. Signal Transduct Target Ther 2021; 6: 263.
28. Shrihari T. Dual role of inflammatory mediators in cancer. Ecancermedicalscience 2017; 11: 721.
29. Singh R, Mishra MK, Aggarwal H. Inflammation, immunity, and cancer. Cell 2017; 2017: 6027305.
30. Suman S, Sharma PK, Rai G, et al. Current perspectives of molecular pathways involved in chronic inflammation-mediated breast cancer. Biochem Biophys Res Commun 2016; 472: 401-9.
31. Liotti F, Marotta M, Melillo RM. The impact of resolution of inflammation on tumor microenvironment: Exploring new ways to control cancer progression. Cancers (Basel) 2022; 14: 3333.
32. Zhao X, Chen X, Shen X, et al. IL-36β promotes CD8(+) T cell activation and antitumor immune responses by activating mTORC1. Front Immunol 2019; 10: 1803.