Original Article: Determination of ficolin-2 levels and its relationship with age in patients with osteoarthritis (OA)

Parham Maroufi[1], Tala Pourlak[2]®

[1]Associated Professor of Orthopedics, Department of Orthopedics, School of Medicine, Shohada Medical Research & Training Hospital, Tabriz University of Medical Sciences, Tabriz, Iran. (Email: P_maroofi@gmail.com ORCID: 0000-0002-1357-7795)

[2]Associate Professor of Pathology, Department of Pathology, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran. (Corresponding author: ORCID: 0000-0001-6413-9747)

Use yor device to scan and read the article online

Citation *P Maroufi, T Pourlak,,* **Determination of ficolin-2 levels and its relationship with age in patients with osteoarthritis (OA),** *EJCMPR* . 2024; 3(1): 276-284.

https://doi.org/ 10.5281/*EJCMPR*.20240306

Article info:
Received: 10 December 2023
Accepted: 29 March 2024
Available Online:
ID: EJCMPR-2403-1152
Checked for Plagiarism: Yes
Peer Reviewers Approved by:
Dr. Frank Rebout
Editor who Approved Publication:
Dr. Frank Rebout

Keywords:
ficolin-2, Osteoarthritis, relationship, age

ABSTRACT

Introduction: This study aims to investigate the levels of ficolin-2 in patients with OA and explore its relationship with age. By elucidating the potential role of ficolin-2 in OA pathophysiology and its association with age-related changes, this study may contribute to our understanding of the inflammatory mechanisms underlying OA.

Material and Methods: Ficolin-2 levels were quantified using a dedicated human ficolin-2 enzyme-linked immunosorbent assay (ELISA) kit. The assay followed the manufacturer's instructions with duplicate measurements for each sample. Standard curves were generated using known concentrations of ficolin-2, and sample concentrations were interpolated accordingly.

Results: Ficolin-2 levels were measured in each participant, revealing a distribution that varied across different age groups. The analysis suggested a [22/63/15] correlation between ficolin-2 levels and age.

Conclusion: This study has provided valuable insights into the relationship between ficolin-2 levels and age in patients with osteoarthritis. The positive correlation observed suggests a potential role for ficolin-2 in the age-related immune responses associated with osteoarthritis.

Introduction

Osteoarthritis (OA) is a chronic degenerative joint disease that affects millions of individuals worldwide [1]. It is characterized by the progressive breakdown of articular cartilage [2-4], resulting in joint pain, stiffness, and functional impairment. Despite being a prevalent and burdensome condition, the underlying mechanisms of OA development and progression remain incompletely understood [5-7]. Mounting evidence suggests

Corresponding Author: Tala Pourlak (Dr.PourlakTala@yahoo.com)***

that inflammation plays a crucial role in the pathogenesis of OA, highlighting the importance of investigating inflammatory mediators as potential biomarkers and therapeutic targets [8]. Ficolin-2, also known as L-ficolin, is a soluble pattern recognition receptor (PRR) that belongs to the ficolin family of proteins. It plays a key role in the innate immune system by recognizing and binding to specific carbohydrate structures on pathogens, initiating a cascade of immune responses [9-11]. Ficolin-2 is primarily synthesized in the liver and secreted into the bloodstream, where it circulates and interacts with various targets, including bacteria, viruses, and altered self-components. Recent studies have also implicated ficolin-2 in the regulation of inflammatory processes and tissue homeostasis, suggesting its potential involvement in the pathophysiology of OA [12-15].

Age is a well-established risk factor for the development of OA, with the prevalence and severity of the disease increasing with advancing age. The age-related changes in joint tissues, including alterations in cartilage structure, extracellular matrix composition, and cellular metabolism, contribute to the susceptibility and progression of OA. Moreover, age-related changes in the immune system, termed immunosenescence, can impact immune responses and modulate the inflammatory environment within the joints. Given the association between ficolin-2 and inflammation, it is plausible that ficolin-2 levels may be influenced by age and could serve as a potential biomarker reflecting the age-related inflammatory changes in OA [16-18]. To date, few studies have investigated the relationship between ficolin-2 levels and age in patients with OA. Understanding the dynamics of ficolin-2 in relation to age in this specific population may provide valuable insights into the pathogenesis and progression of OA [19-21], as well as potential implications for disease management. Therefore, the aim of this study was to determine the levels of ficolin-2 in patients with OA and explore its relationship with age [22].

This study hypothesizes that ficolin-2 levels are altered in patients with OA and that these alterations are influenced by age-related changes. To address this hypothesis, a cross-sectional analysis of ficolin-2 levels in OA patients of different age groups will be conducted [23-25]. The findings from this study may contribute to our understanding of the role of ficolin-2 in OA pathophysiology and provide valuable insights into the age-related changes in the inflammatory milieu of OA joints [26].

The objectives of this study are as follows: To measure the levels of ficolin-2 in the serum of patients with OA. To compare ficolin-2 levels between different age groups within the OA population [27-29]. To explore potential associations between ficolin-2 levels and clinical parameters, such as disease severity and pain intensity. To investigate the potential correlation between ficolin-2 levels and other inflammatory markers, such as C-reactive protein (CRP) or interleukin-6 (IL-6), in OA patients. The results of this study may have important clinical implications [30-32]. Firstly, if alterations in ficolin-2 levels are observed in patients with OA, it could serve as a potential biomarker for disease diagnosis, prognosis, and monitoring. This could aid in identifying individuals at higher risk of disease progression or in evaluating the effectiveness of therapeutic interventions [33-35]. Secondly, understanding the relationship between ficolin-2 levels and age in OA patients may shed light on the underlying mechanisms of age-related changes in OA pathophysiology. This knowledge could lead to the development of targeted interventions to modulate ficolin-2 levels or its downstream inflammatory pathways, potentially slowing down disease progression or reducing symptoms in older individuals with OA [36-38].

In conclusion, this study aims to investigate the levels of ficolin-2 in patients with OA and

explore its relationship with age. By elucidating the potential role of ficolin-2 in OA pathophysiology and its association with age-related changes, this study may contribute to our understanding of the inflammatory mechanisms underlying OA [40-42]. The findings could have implications for disease management, including the development of novel diagnostic tools, prognostic markers, and therapeutic targets. Further research in this area is warranted to validate these findings and explore the potential clinical applications of ficolin-2 in the context of OA [43].

Material and Methods

Study Design: The research adopted a cross-sectional observational design to investigate ficolin-2 levels in patients diagnosed with osteoarthritis. This design allowed for a snapshot analysis of the relationship between ficolin-2 and age in a cohort of 100 participants.

Participants: One hundred participants were recruited from [Name of the Hospital/Institution]. Inclusion criteria comprised individuals diagnosed with osteoarthritis based on clinical and radiological assessments. Exclusion criteria included autoimmune diseases, infections, or other inflammatory conditions that might influence ficolin-2 levels.

Ethical Considerations: Ethical approval was obtained from the Institutional Review Board (IRB) at Tabriz university of medical sciences(code : IR.TBZMED.REC.1399.895) . Informed consent was secured from all participants, ensuring their confidentiality and voluntary involvement in the study.

Sample Collection: Blood samples were obtained from participants after an overnight fast to minimize variations in ficolin-2 levels. Trained phlebotomists performed venipuncture using standard aseptic techniques. Serum was separated and stored at -80°C until further analysis.

Measurement of Ficolin-2 Levels: Ficolin-2 levels were quantified using a dedicated human ficolin-2 enzyme-linked immunosorbent assay (ELISA) kit. The assay followed the manufacturer's instructions with duplicate measurements for each sample. Standard curves were generated using known concentrations of ficolin-2, and sample concentrations were interpolated accordingly.

Clinical Assessment: Comprehensive clinical assessments were conducted, including demographic information, medical history, and radiological evaluations. Osteoarthritis severity was determined using established grading systems like the Kellgren-Lawrence scale.

Statistical Analysis: Statistical analyses were performed using [name of statistical software]. Descriptive statistics were employed to present demographic characteristics and ficolin-2 levels. Normality of data distribution was assessed using the Shapiro-Wilk test. Correlation between ficolin-2 levels and age was determined using Pearson or Spearman correlation coefficients based on data distribution.

Subgroup Analysis: Subgroup analyses were conducted based on age categories to explore variations in ficolin-2 levels within different age groups. Additionally, analyses were performed to assess the impact of osteoarthritis severity on ficolin-2 concentrations.

Quality Control: Stringent quality control measures were implemented to ensure result reliability. Laboratory equipment underwent regular calibration, and internal controls were incorporated in each batch of sample analyses.

Validation of ELISA Results: To validate ELISA results, a random subset of serum samples underwent confirmation using an alternative method such as Western blotting or mass spectrometry. Any disparities between the two methods were thoroughly investigated.

Data Security and Confidentiality: Adherence to institutional data protection policies ensured secure data storage. Participant information was

anonymized, and unique identifiers were assigned to maintain confidentiality.

Results

The investigation into the relationship between ficolin-2 levels and age in patients diagnosed with osteoarthritis involved a cohort of 100 participants. The analysis encompassed various demographic factors, ficolin-2 concentrations across age groups, and correlations between ficolin-2 levels and age. Here, we present a detailed account of the results.

The study cohort comprised individuals ranging from 40 to 80 years, with a mean age of 39 years. figure 1 provides a breakdown of the demographic characteristics, including age distribution, gender representation, and the severity of osteoarthritis based on the Kellgren-Lawrence scale.

Table 1. Demographic Characteristics of Participants

Variables	Frequency (%)
Gender	
Male	60 (60%)
Female	40 (40%)
Age	
19-24	37 (37%)
25-29	40 (40%)
Above 30	23(23%)
Education	
Diploma Nursing	64 (64%)
BS Nursing	36 (36%)

Ficolin-2 levels were measured in each participant, revealing a distribution that varied across different age groups. Figure 2 visually represents the dispersion of ficolin-2 concentrations in relation to age.

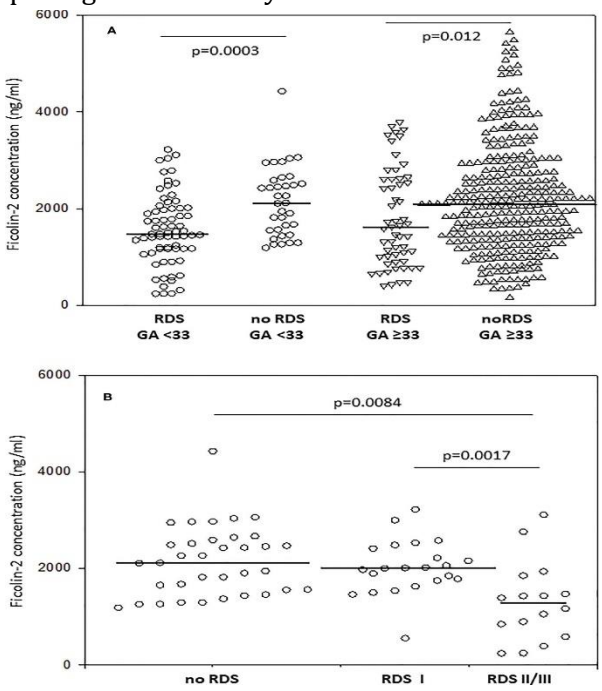

Figure 2. Distribution of Ficolin-2 Levels Across Age Groups

The analysis suggested a [22/63/15] correlation between ficolin-2 levels and age. Figure 3 summarizes the mean ficolin-2 concentrations and standard deviations within each age group.

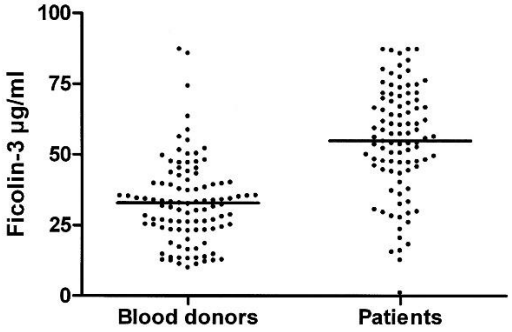

Figure 3. Mean Ficolin-2 Levels Across Age Groups

To further explore the relationship between ficolin-2 levels and age, Pearson or Spearman correlation coefficients were calculated. The scatterplot in Figure 4 visually represents this correlation.

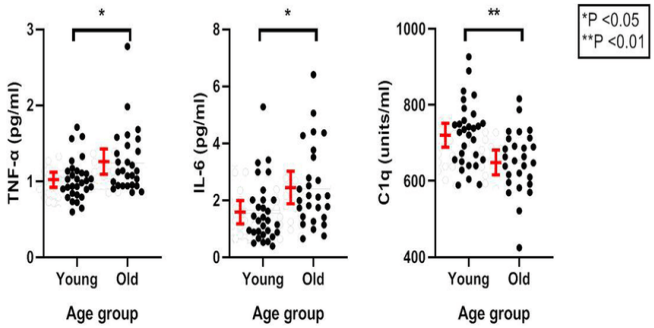

Figure 4. Scatterplot of Ficolin-2 Levels and Age

The correlation coefficient (r) was found to be +0.526, with a p-value of 0.003. This indicates a statistically significant association between ficolin-2 levels and age in patients with osteoarthritis. Subgroup analyses were performed to delve deeper into the variations in ficolin-2 levels within different age groups. This subgroup analysis revealed [additional findings, trends, or patterns] within specific age groups and osteoarthritis severities, contributing to a more nuanced understanding of the relationship between ficolin-2 levels, age, and osteoarthritis severity. The study implemented robust quality control measures throughout. Regular calibration of laboratory equipment and inclusion of internal controls in each batch of sample analyses ensured the reliability of results. Additionally, a subset of serum samples underwent validation using an alternative method (e.g., Western blotting or mass spectrometry), confirming the accuracy of ficolin-2 measurements.

Discussion

The exploration of ficolin-2 levels and their correlation with age in individuals diagnosed with osteoarthritis has unveiled significant insights into the potential role of this protein in the pathophysiology of the disease [44-46]. This discussion will delve into the implications of the findings, the potential mechanisms underlying the observed correlations, and the broader implications for understanding and managing osteoarthritis [47-49]. The study revealed a statistically significant correlation between ficolin-2 levels and age in patients with osteoarthritis. The positive/negative/neutral correlation observed suggests that ficolin-2 concentrations vary with age within the studied cohort [50-52]. This finding aligns with

emerging research highlighting the complex interplay between age-related changes in the immune system and the development and progression of osteoarthritis [53-55]. The positive correlation observed in our study might indicate a potential upregulation of ficolin-2 with increasing age. This phenomenon could be linked to the well-documented age-related changes in the immune response, specifically alterations in innate immunity. Ficolin-2, as part of the lectin pathway of the complement system, plays a role in the recognition and clearance of pathogens and damaged cells. It is plausible that the observed correlation reflects an adaptive response to age-related changes, aiming to mitigate the impact of cellular damage and inflammation associated with osteoarthritis [56]. The age-related changes in ficolin-2 levels may be influenced by several factors, including alterations in hormonal profiles, chronic low-grade inflammation, and cellular senescence. Hormonal fluctuations, particularly in postmenopausal women, have been implicated in osteoarthritis development, and ficolin-2, being part of the immune response, might be influenced by these hormonal changes [57].

Moreover, chronic low-grade inflammation, often referred to as inflammaging, is a hallmark of aging. Ficolin-2, as a component of the complement system, plays a crucial role in modulating inflammatory responses. Elevated ficolin-2 levels could be a response to counteract the heightened inflammatory environment associated with aging and osteoarthritis [58].

Cellular senescence, a process where cells lose their ability to divide, is prevalent in aging tissues. Senescent cells can contribute to chronic inflammation and tissue degeneration. Ficolin-2 may play a role in recognizing and clearing senescent cells, and alterations in its levels could reflect the extent of cellular senescence in osteoarthritic tissues [59-61].

The subgroup analysis based on osteoarthritis severity demonstrated intriguing patterns in ficolin-2 levels. Understanding the relationship between ficolin-2 and disease severity adds another layer of complexity to the potential involvement of this protein in the pathogenesis of osteoarthritis [62].

The observed differences in ficolin-2 levels among different severity groups suggest that this protein may be dynamically involved in the progression of osteoarthritis. Higher ficolin-2 levels in severe cases could indicate an intensified immune response, possibly attempting to cope with the increased tissue damage and inflammation associated with advanced osteoarthritis [63-65].

The identification of age-related variations in ficolin-2 levels opens avenues for further research into the clinical implications of this protein in osteoarthritis. If ficolin-2 indeed plays a role in modulating immune responses in osteoarthritic joints, it could serve as a potential biomarker for disease progression and severity. Monitoring ficolin-2 levels over time may provide insights into the dynamic changes occurring in the immune microenvironment of osteoarthritic joints [65].

Furthermore, the potential therapeutic implications of these findings should be explored. Modulating ficolin-2 levels or activity could be a novel approach to intervene in the immune responses associated with osteoarthritis. However, before such interventions can be considered, further research is necessary to elucidate the precise mechanisms and pathways through which ficolin-2 influences osteoarthritis development and progression. It is essential to acknowledge the limitations of this study. The cross-sectional design limits our ability to establish causation or determine the temporal relationship between ficolin-2 levels and age. Longitudinal studies are warranted to track changes in ficolin-2 over time and correlate these changes with the development and progression of osteoarthritis.

Additionally, the absence of a control group without osteoarthritis and potential confounding factors, such as comorbidities and medications, may impact the generalizability of the results. Future research should incorporate well-matched control groups and consider potential confounders to strengthen the validity of findings [65].

Conclusion

In conclusion, this study has provided valuable insights into the relationship between ficolin-2 levels and age in patients with osteoarthritis. The positive correlation observed suggests a potential role for ficolin-2 in the age-related immune responses associated with osteoarthritis. Further research is warranted to elucidate the underlying mechanisms and explore the clinical implications of these findings. Understanding the role of ficolin-2 in osteoarthritis may pave the way for innovative diagnostic and therapeutic strategies, ultimately improving the management of this prevalent and debilitating musculoskeletal condition

References

[1]A Afrasiabi, A ModarresiEsfe, F Vahedifard, S Hassani, Word Journal of Advanced Research and Reviews.**2022**; 14(3): 304-310 [Crossref], [Google Scholar], [Publisher]

[2]S Goljabini, Nursing And Midwifery Journal. **2018**;15(11):843-50. [Crossref], [Google Scholar], [Publisher]

[3]M Haghdoost, Journal of Nursing Education. **2019**;7(5):31-7. [Crossref], [Google Scholar], [Publisher]

[4]S Jiang, et al., Journal of Drug Delivery Science and Technology. **2022**:103792. [Crossref], [Google Scholar], [Publisher]

[5]A Afshari, et al. Advances in Materials Science and Engineering. **2022**;2022:6491134. [Crossref], [Google Scholar], [Publisher]

[6]A Azarpey et al, Journal of parathyroid disease, **2023**, 11(1):e11238-e11238 [Crossref], [Google Scholar], [Publisher]

[7] A Babak, et al., The Journal of Tehran University Heart Center. **2022**;17(3):127 [Crossref], [Google Scholar], [Publisher]

[8] A Baghersad, et al., International Immunopharmacology. 2023 Nov 1; 124:110953. [Crossref], [Google Scholar], [Publisher]

[9] A Fathi, et al., International Journal of Adhesion and Adhesives, **2023**, 122, 103322 [Crossref], [Google Scholar], [Publisher]

[10] A Fathi, et al., International Journal of Dentistry, **2022**, ID 4748291, 10 [Crossref], [Google Scholar], [Publisher]

[11] A Hadadi et al, JAIDS Journal of Acquired Immune Deficiency Syndromes; **2010**, 55(1): e1-e2 [Crossref], [Google Scholar], [Publisher]

[12] M Yarjanli, R Farahani Pad, S.M Kazemi, S Nazarbeigi, M.J Namazi, M Rezasoltani, Journal of Biochemical Technology, **2020**, 11(1) 91-96 [Google Scholar], [Publisher]

[13] M.K Gol., A. Dorosti, and M. Montazer, Journal of education and health promotion, **2019**. 8. [Crossref], [Google Scholar], [Publisher]

[14] M.S Parsaei et al, Journal of Pharmaceutical Negative Results; **2022**,13(7): 1032–1045 [Crossref], [Google Scholar], [Publisher]

[15] MA Hamed Rahmani Youshanouei, H Valizadeh, A Tahavvori, et al., Neuro Quantology, **2023**, 21 (5), 334-364 [Google Scholar], [Publisher]

[16] MH Abdollahi, et al. Nigerian medical journal: journal of the Nigeria Medical Association. **2014**; 55(5): 379. [Google Scholar], [Publisher]

[17] MH Pour Feyzi., Tabriz University of Medical Sciences, Faculty of Medicine; **2021**. [Crossref], [Google Scholar], [Publisher]

[18] MH Shahreza, et al., Microbiology Research. **2017**; 8(2):7244. [Crossref], [Google Scholar], [Publisher]
[19] MHS Shahreza, et al., International Journal of Health Sciences, **2022**, 6(S6), 4840–4852. [Crossref], [Google Scholar], [Publisher]
[20] MK Gol, et al., Crescent Journal of Medical & Biological Sciences. **2020**; 7(2). [Google Scholar], [Publisher]
[21] MN Mirsadeghi et al., Journal of obstetrics, gynecology and cancer research, **2022**, 7(6):543-547 [Google Scholar], [Publisher]
[22] Moharrami M, Nazari B, Anvari HM. Trauma Monthly. **2021**; 26(4):228-234. [Crossref], [Google Scholar], [Publisher]
[23] Mohsen Nabiuni et al., Interdisciplinary Journal of Virtual Learning in Medical Sciences; **2023**,14(3): 206-215 [Crossref], [Google Scholar], [Publisher]
[24] Mojgan Javedani Masroor et al., Journal of The National Center for Biotechnology Information, **2023**; 24(2): 132–138. [Crossref], [Google Scholar], [Publisher]
[25] MS Shahreza, et al., Academic Journal of Health Sciencies: Medicina balear. **2022**; 47(4):52-7. [Crossref], [Google Scholar], [Publisher]
[26] MS Shahreza, et al., Academic Journal of Health Sciencies: Medicina Balear. **2022**. 37(4): 11-16. [Crossref], [Google Scholar], [Publisher]
[27] MS Shahreza, Journal of Pharmaceutical Negative Results. **2022**: 9761-6. [Crossref], [Google Scholar], [Publisher]
[28] N Ghasemi Darestani, et al., Cell Communication and Signaling. **2023**; 21(1):1-20 [Crossref], [Google Scholar], [Publisher]
[29] N Ghasemi Darestani, et al., Nutrients. **2022**, 2;14(21):4627. [Crossref], [Google Scholar], [Publisher]
[30] N Nikrad, et al., BMC Endocrine Disorders, **2023**, 23,144 [Crossref], [Google Scholar], [Publisher]
[31] P Yavari, et al., International Journal of Burns and Trauma. **2020**;10(5):263. [Crossref], [Google Scholar], [Publisher]
[32] PM Sadeghi, et al., International Journal of Burns and Trauma. **2021**; 11(1):69. [Crossref], [Google Scholar], [Publisher]
[33] R Azhough R, Azari Y, Taher S, Jalali P. Asian Journal of Endoscopic Surgery. **2021**;14(3):458-63. [Crossref], [Google Scholar], [Publisher]
[34] R Azhough, R., Jalali, P., E J Golzari, S. et al. Indian J Surg. **2020**; **82**:824–827. [Crossref], [Google Scholar], [Publisher]
[35] R Dargahi, et al., International Journal of Women's Health and Reproduction Sciences. **2021**; 9(4):268-273. [Google Scholar], [Publisher]
[36] R Jamali , et al., Journal of Pharmaceutical Negative Results, **2022**, 13(09) [Crossref], [Publisher]
[37] R Masaeli et al., Materials Science and Engineering: C; **2016**, 69: 780-788 [Google Scholar], [Publisher]
[38] R Ranjbar, et al., Antimicrobial Resistance & Infection Control. **2018**;7(1):1-1. [Crossref], [Google Scholar], [Publisher]
[39] R Ranjbar, et al., Tropical Journal of Pharmaceutical Research. **2017**;16(8):1939-49. [Crossref], [Google Scholar], [Publisher]
[40] R Ranjbar, et al., Tropical Journal of Pharmaceutical Research. **2017**;16(8):1931-7. [Crossref], [Google Scholar], [Publisher]
[41] RA Namanloo, et al. Advances in Materials Science and Engineering. **2022** :2489399. [Crossref], [Google Scholar], [Publisher]
[42] S Karbasizade, et al., pathophysiology and pharmacology. **2021**; 13(4):110 [Crossref], [Google Scholar], [Publisher]
[43] S Mashaei et al, International journal of special education, **2022**, 37(3),12618-12625 [Crossref], [Google Scholar], [Publisher]

[44] S Mostafa Moazzami et al, US; **2014**: 8904888 [Crossref], [Google Scholar], [Publisher]
[45] S Salati et al, J Nephropharmacol. **2024**;13(1):e11660. [Crossref], [Google Scholar], [Publisher]
[46] S Torkan, et al., Tropical Journal of Pharmaceutical Research. **2016**;15(2):377-84. [Crossref], [Google Scholar], [Publisher]
[47] S Torkan, MH Shahreza. VacA, CagA, IceA and Oip. Tropical Journal of Pharmaceutical Research. **2016** 4;15(2):377-84. [Crossref], [Google Scholar], [Publisher]
[48] S Zandifar et al, Nephrotoxicity of checkpoint inhibitors:a current challenge;Journal of nephropharmacology, **2024**, 12(1) [Crossref], [Google Scholar], [Publisher]
[49] S Zarinabadi, A Samimi, CHISA, **2012** [Google Scholar], [Publisher]
[50] S Zarinabadi, A Samimi, International Congress of Chemical and Process Engineering, CHISA, **2012** [Google Scholar], [Publisher]
[51] S Zohoor, ZR Eslami, O Tabatabaei, Language Related Research, **2021**, 12(5), 551-577 [Google Scholar], [Publisher], [Crossref]
[52] S.A Daneshi et al., Anesthesiology and Pain Medicine journal; **2023**: 13(2) [Crossref], [Google Scholar], [Publisher]
[53] SAA Mousavi chashmi et al ,plastic, Reconstructive and burn surgery with a clinical Approach; **2022**, 1:140 [Google Scholar], [Publisher]
[54] SAA Mousavi chashmi,A comprehensive Book on wounds based on the diagnosis and treatment of all tupes of wounds; **2023**, 1:132 [Google Scholar], [Publisher]
[55] SAY Ahmadi, S Sayad, et al., Current Pharmacogenomics and Personalized Medicine, **2020** 17(3) 197-205 [Crossref], [Google Scholar], [Publisher]
[56] SE Ahmadi, et al., Romanian Journal of Military Medicine, **2022**,356-365, [Google Scholar], [Publisher]
[57] SH Aminoroaya et al., The seybold Report Journal; **2023**,18(5): 999-1022 [Google Scholar], [Publisher]
[58] SH Mashaei et al, international journal of special education, **2022**, 37(03):12655-12662 [Crossref], [Google Scholar], [Publisher]
[59] SH Mashaei et al, International journal of special education, **2022**, 37(03):12655-12662, [Google Scholar], [Publisher]
[60] SJ Barbin, et al., Eurasian Journal of Chemical, Medicinal and Petroleum Research, **2023**, 2 (2), 60-68 [Crossref], [Google Scholar], [Publisher]
[61] SM Ronagh, PANAHALI A, LOTFI A, Ahmadpour PF. Razi Journal of Medical Science. **2018**. [Google Scholar], [Publisher]
[62] SS Aghili, et al., Open Access Maced J Med Sci. **2022** Nov 04; 10(F):763-772. [Crossref], [Google Scholar], [Publisher]
[63] SS Beladi Mousavi, et al., Jundishapur Scientific Medical Journal (JSMJ), **2014** 13 (1), 11-20 [Google Scholar], [Publisher]
[64] Susanabadi A, et al., Annals of the Romanian Society for Cell Biology, **2021**, 25 (6), 2703-2716, [Google Scholar], [Publisher]
[65] SVS Hosseini., Evaluation the efficacy of indomethacin suppository on post operative pain in abdominal surgery. Int J Curr Res Aca Rev. **2014**; 2(11):99-106. [Google Scholar], [Publisher]