JBACHS
Journal of Basic and Clinical Health Sciences

J Basic Clin Health Sci 2024; 8: 759-764
https://doi.org/10.30621/jbachs.1550234
RESEARCH ARTICLE

A STUDY ON THE SYSTEMIC INFLAMMATORY INDEX (SII) AND RELATED FACTORS IN PATIENTS WITH MALIGNANT OTITIS EXTERNA

Asuman Feda Bayrak[1], Muhammed Mirza Dogan[1], Baturalp Cetin[1]

[1] Department of Otorhinolaryngology, Izmir Katip Celebi University Ataturk Training and Research Hospital

ORCID: A.F.B. 0000-0001-8403-3018; M.M.D. 0009-0008-1302-3566; B.C. 0009-0003-0474-3661

Corresponding author: Asuman Feda Bayrak, **E-mail:** fedabolat@yahoo.com
Received: 15.09.2024; **Accepted:** 19.09.2024; **Available Online Date:** 30.09.2024

Cite this article as: Bayrak AF, Dogan MD, Cetin B. A Study on the Systemic Inflammatory Index (SII) and Related Factors in Patients with Malignant Otitis Externa. J Basic Clin Health Sci 2024; 8: 759-764.

ABSTRACT

Purpose: This study aims to investigate the relationship between systemic inflammatory index and various clinical and microbiological factors in patients with malignant otitis externa (MOE).
Materials and Methods: In this retrospective study, patients diagnosed with MOE and treated between January 2017 and March 2023 were examined. The data include clinical evaluations, laboratory tests, and imaging results. All patients underwent computed tomography of the temporal bone, and MOE was staged according to Tengku's radiological classification .SII was calculated using neutrophil, platelet, and lymphocyte counts.
Results: 11 patients were examined retrospectively, including 8 males (72.7%) and 3 females (27.3%). The mean age of the patients was 72.3±7.5 years. Comorbidities such as Diabetes Mellitus (DM) and Chronic Kidney Disease (CKD) were associated with higher SII values. CT phases and cranial nerve involvement were also related to high SII values. Microbiological analyses showed that pathogens such as Pseudomonas aeruginosa and Candida tropicalis were associated with high SII values.
Conclusion: SII is an important biomarker in evaluating the prognosis and treatment response in MOE. Early diagnosis, a multidisciplinary approach, and personalized treatment strategies are critical in managing MOE. Further studies involving larger patient groups will contribute to validating these relationships and improving treatment processes.

Keywords: Malignant otitis externa, systemic inflammatory index, diabetes mellitus, cranial nerve involvement, skull base osteomyelitis, CT phases.

INTRODUCTION

Malignant otitis externa (MOE) is an aggressive osteomyelitis that typically begins in the external auditory canal and subsequently spreads to the base of the skull. This disease is most commonly observed in elderly and diabetic patients and is associated with significant morbidity and mortality. MOE occurs more frequently in high-risk patients, particularly in immunocompromised individuals and can lead to serious complications if left untreated (1,2,3).

The diagnosis and management of MOE require the use of broad-spectrum antibiotics and antifungal agents, surgical debridement, and long-term follow-up. However, early diagnosis and appropriate treatment strategies are of great importance in the management of MOE (4,5). High-resolution computed tomography (HRCT) plays a crucial role in the diagnosis and staging of MOE, allowing for the evaluation of the extent and severity of the disease (6,7).

The Systemic Inflammatory Index (SII) is a biomarker used to assess the inflammatory response and is calculated using neutrophil, platelet, and lymphocyte counts (8). SII is particularly useful in determining the severity of infections and inflammatory diseases and can serve as an important indicator in assessing the prognosis of serious infections such as MOE (8,9,10). Chronic infections and inflammation can increase the systemic inflammatory response, leading to various complications. MOE is particularly common in diabetic patients, where the severity of the inflammatory response may affect the progression of the disease and the response to treatment. Diabetes imposes stress on the immune system, reducing the body's resistance to infections and increasing the inflammatory response (1,2,3). Elevated levels of inflammatory markers may indicate the severity and extent of the disease, which can guide the determination of treatment strategies. Specifically, SII can be used as an objective measure of the inflammatory response, aiding in the assessment of the prognosis and treatment response in MOE patients (8,9,10).

The treatment of MOE involves the use of broad-spectrum antibiotics, antifungal agents, and surgical interventions when necessary. Serious complications such as cranial nerve involvement can occur in patients with MOE, affecting the severity and prognosis of the disease. Patients with cranial nerve involvement require more aggressive treatment and close monitoring (11,12, 13).

The prevalence and severity of MOE are important factors that determine the prognosis and response to treatment. CT phases are used to assess the extent and severity of MOE, and these phases reflect the degree of inflammatory response and the stage of the disease. Higher CT phases may be associated with higher SII values, which can serve as a guide in determining the prognosis of the disease. (5,6,7,8,14,15,16)

Elevated SII values indicate the severity of the inflammatory response and the extent of the disease, which can guide the determination of treatment strategies. In this study, the relationship between comorbidities, CT phases, cranial nerve involvement, HbA1c levels, and microbiological findings with SII in patients diagnosed with MOE was investigated. Evaluating these relationships may contribute to the identification of more effective treatment strategies in the management of MOE.

MATERIALS AND METHODS

In this retrospective study, patients diagnosed with MOE and treated between January 2017 and March 2023 were examined. The data include clinical evaluations, laboratory tests, and imaging results. All patients underwent high-resolution computed tomography (HRCT) of the temporal bone, and MOE was staged according to Tengku's radiological classification (6).

Definition of CT Phases

According to Tengku's radiological classification, MOE is examined in five phases:

- Phase I: Inflammation is limited to the soft tissue in the external ear canal, with no bone involvement.
- Phase II: Inflammation extends beyond the soft tissue and is limited to the mastoid with bone involvement.
- Phase III: Inflammation progresses medially to involve the petrous temporal bone or the temporomandibular joint, sometimes involving the parapharyngeal soft tissue.
- Phase IV: Inflammation progresses medially to involve the nasopharynx, sometimes with abscess formation.
- Phase V: Inflammation extends to the contralateral ear base or the contralateral skull base.

Systemic Inflammatory Index (SII)

The systemic inflammatory index (SII) is a relatively new parameter that has been shown to increase in inflammatory diseases. SII uses three blood cell subtypes (neutrophils, lymphocytes, and platelets) that reflect the balance between inflammation and immune response. SII was calculated using the following formula: SII = (platelet count × neutrophil count) / lymphocyte count (8,9,10).

Statistical analyses

All statistical analyses were conducted using SPSS 15.0 software. The normal distribution of the data was evaluated using the Kolmogorov-Smirnov test. For continuous variables following a normal distribution, data were expressed as mean ± standard deviation (SD) and analyzed using a t-test. For non-parametric data, values were presented as median (minimum-maximum), and the Mann-Whitney U test was applied. A p-value of <0.05 was considered statistically significant.

Ethical approval for the study was received from Izmir Katip Celebi University Non-Invasive Clinical Research Ethics Committee (Date: 21.03.2024, Decision No:0143).

RESULTS

A total of 11 patients diagnosed with malignant otitis externa (MOE) were included in this retrospective study. The cohort consisted of 8 males (72.7%) and 3 females (27.3%), with a mean age of 72.3±7.5 years. Comorbidities were prevalent in the patient population, with Diabetes Mellitus (DM) identified in 10 patients (90.9%), Hypertension (HT) in 6 patients (54.5%), and Chronic Kidney Disease (CKD) in 3 patients (27.3%).

Cranial nerve involvement was observed in 5 patients (45.4%), with the 7th cranial nerve affected in 4 patients (36.6%), and both the 10th and 7th cranial nerves affected in 1 patient (9.1%).

Microbiological analysis revealed Pseudomonas aeruginosa in 4 patients (36.4%), Enterobacter cloacae in 1 patient (9.1%), Candida tropicalis in 1 patient (9.1%), skin flora in 3 patients (27.3%), and Corynebacterium spp. in 1 patient (9.1%).

When classified according to Tengku's radiological classification, the distribution of CT phases was as follows: Phase 1 in 2 patients (18.2%), Phase 2 in 3 patients (27.3%), Phase 3 in 3 patients (27.3%), Phase 4 in 1 patient (9.1%), and Phase 5 in 2 patients (18.2%). The

demographic features and clinical findings of the patients are given Table 1.

The mean Systemic Inflammatory Index (SII) value was 1337.19±1006.954, with the mean HbA1c level at 8.08±2.2, and the mean CT phase at 2.9±1.4. These findings suggest a significant association between higher SII values and advanced CT phases, as well as comorbid conditions such as DM and CKD. Various comorbid conditions and their effects on SII values were examined. Comorbidities such as Chronic Kidney Disease (CKD), Diabetes Mellitus (DM), and Hypertension (HT) were associated with higher SII values. CKD was found to have the highest average SII value among the comorbidities. Comorbidities and SII values are given Figure 1. The relationship between CT phases and SII values was examined. Phase 1 had the lowest SII value, while phase 4 had the highest SII value. The chi-square test results showed no statistically significant relationship

Table 1. The demographic features and clinical findings of the patients

Patient	Age	Gender	HbA1c	Comorbidities	Cranial Nerve Involvement	Microbiology	CT Phases	SII	Treatment
1	71	M	9.11	DM	7	Pseudomonas a.	Phase 3	1232.89	Meropenem, Metronidazole
2	78	M	8.20	DM, HT, CRF	None	Enterobacter cloacae	Phase 2	2001.95	Ceftazidime, Metronidazole
3	62	M	10.50	DM, HT, CRF, CHF	None	Pseudomonas a.	Phase 2	1058.14	Cefepime
4	62	F	8.20	DM, HT, CRF, CAD	7	Pseudomonas a.	Phase 5	1713.32	Imipenem, Amikacin, Piperacillin Tazobactam
5	76	M	12.00	DM	10,7	Candida tropicalis	Phase 5	1923.27	Meropenem, Linezolid, Caspofungin
6	62	M	8.70	DM	None	None	Phase 1	563.18	Ciprofloxacin
7	84	M	5.90	DM, CHF, COPD, Parkinson,	None	Skin flora	Phase 2	229.93	Piperaslin Tazobactam, Ciprofloxacin
8	78	M	6.60	HT	7	Skin flora	Phase 1	109.13	Meropenem, Teicoplanin, Ciprofloxacin
9	75	M	8.80	DM, HT,CAD	7	Skin flora	Phase 3	759.85	Meropenem, Metronidazole
10	83	F	6.50	DM, HT, AF	None	Pseudomonas a.	Phase 3	1020.70	Meropenem
11	72	F	4.80	HT, DM	None	Corynbacterium spp.	Phase 4	3331.25	Meropenem, Teicoplanin

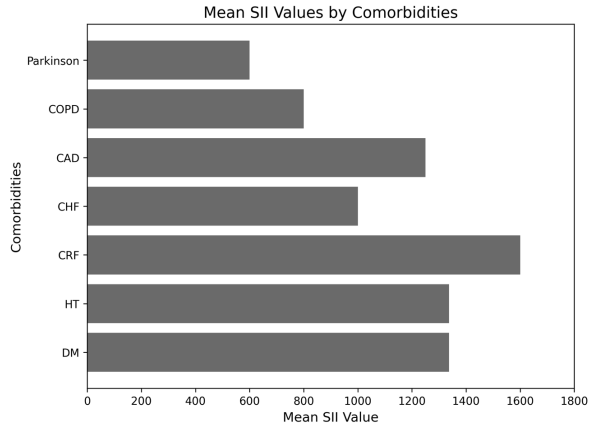

Figure 1. Comorbidities and systemic inflammatory index (SII) values. Comorbid diseases accompanying malignant otitis externa and SII values are shown. (SII: Systemic Inflammatory Index, CKD: Chronic Kidney Disease, DM: Diabetes Mellitus, HT: Hypertension, CRF: chronic Renal Failure, CHF: Congestive Heart Failure, CAD: Coronary Artery Disease, COPD: Chronic Obstructive Pulmonary Disease)

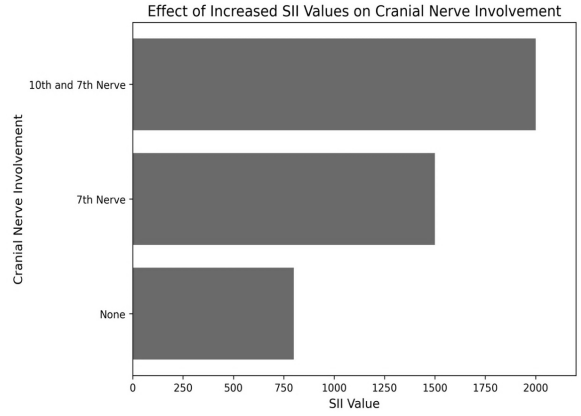

Figure 2. Cranial nerve involvement and systemic inflammatory index (SII) values (SII: Systemic Inflammatory Index)

between CT phases and SII categories ($p > 0.05$). However, higher CT phases were generally associated with higher SII values.

The relationship between increased SII values and cranial nerve involvement was evaluated. The mean and median SII values of patients with cranial nerve involvement were higher than those without. However, the t-test results showed that this difference was not statistically significant ($p > 0.05$). Cranial nerve involvement and SII values are given Figure 2.

The correlation between HbA1c values and SII was examined. The correlation coefficient was indicating a very weak negative correlation between HbA1c and SII, suggesting that HbA1c values do not have a significant effect on SII ($r = -0.053$, $p > 0.05$).

The relationship between microbiological findings, CT phases, and SII values was analyzed. Pseudomonas aeruginosa was the most isolated microorganism and was associated with high SII values. Additionally, microorganisms such as Corynebacterium spp. and Candida tropicalis were also associated with high SII values.

DISCUSSION

Comorbidities such as Chronic Kidney Disease (CKD), Diabetes Mellitus (DM), and Hypertension (HT) may lead to an increased inflammatory response and consequently higher SII values (1). These patients require more careful monitoring and treatment approaches. Particularly, DM is a common condition in MOE patients due to its effects on inflammation and immune response and the inflammatory response is generally more severe in diabetic patients, making close monitoring crucial in MOE management. While HbA1c levels reflect the overall health status and effectiveness of diabetes management, the direct impact on the inflammatory response may be more complex (2,12).

The findings demonstrate that SII is an important biomarker in MOE patients, and various clinical and microbiological factors can affect SII. The impact of comorbidities on SII may influence the severity of the inflammatory response. Association of high SII values with CT phases and cranial nerve involvement may provide information on the progression and severity of the disease. This highlights the need for careful interpretation when using inflammatory biomarkers in clinical assessments.

The higher SII values in patients with cranial nerve involvement highlight the impact of the inflammatory response on the central nervous system. Early diagnosis and regular monitoring are critical in managing these patients. Cranial nerve involvement is considered a serious complication of MOE, and patients in this condition require more aggressive treatment (17,18). In this study, the SII values of the patients were measured when they were first examined. Repeat measurements can be made with blood counts performed during the clinical follow-up of the patient and can provide useful information in terms of prognosis.

The association of higher CT phases with higher SII values provides information on the extent and severity of the disease. In our study, observing the

highest SII values in phase 4 indicates a severe inflammatory response at this stage. This finding is based on Kamalden et al.'s Tengku's radiological classification in MOE (6). CT phases play a crucial role in determining the clinical course and treatment strategies of the disease. Similarly, Yiğider et al. proposed a classification system based on clinical and radiological findings in monitoring MOE disease (19). Özer et al. also proposed a classification based on MRI that could help clinicians predict prognosis (14).

Microorganisms such as Pseudomonas aeruginosa and Candida tropicalis were associated with high SII values. These pathogens can increase the severity of the disease and complicate the treatment process. Microbiological examinations are critical in determining the etiology of the infection and guiding appropriate antibiotic treatment (4). In the treatment of MOE, broad-spectrum antibiotics and antifungal agents should be used to effectively control pathogens (15). Orji et al. noted that some pathogens might develop resistance to antibiotic treatment, which could lead to misleading inflammatory markers (16).

The relationships between SII and other clinical parameters should also be evaluated, and more research should be conducted on this subject. For example, the treatment duration, comparison of CT phases at the end of treatment, and their relationship with SII values. Additionally, the impact of different treatment methods and drug regimens on SII values should be investigated. These findings can contribute to the development of more personalized treatment strategies in managing MOE.

A multidisciplinary approach is crucial in managing MOE. Close collaboration between otolaryngologists, neurologists, and infectious disease specialists should be ensured. Additionally, patients should be regularly monitored, and early detection of cranial nerve involvement symptoms is necessary. New treatment methods and protocols should be researched and developed for these patients.

Our small number of patients may be the reason why our results were not statistically significant. This situation constitutes the limitation of our study.

CONCLUSION

In this study, the relationships between systemic inflammatory index (SII) values and various clinical and microbiological factors in patients with malignant otitis externa (MOE) were examined. Although some of the findings were not statistically significant, notable trends were observed demonstrate that comorbidities, especially diseases such as Diabetes Mellitus (DM) and Chronic Kidney Disease (CKD), significantly affect SII values. CT phases and cranial nerve involvement were also associated with high SII values. SII can be used as an important biomarker in evaluating the prognosis and response to treatment in MOE. Further studies involving larger patient groups will contribute to validating these relationships and improving treatment processes.

Acknowledgements: None.

Authors contributions; AFB contributed by designing the analysis and interpreting the data. BÇ contributed by data collection, providing the intervention, writing the paper, and interpreting the results. MMD contributed to writing the manuscript and interpreting the data. All authors read and approved the final manuscript.

Conflift of interest: The authors have no conflict of interest.

Ethical approval; Ethical approval for the study was received from Izmir Katip Celebi University Non-Invasive Clinical Research Ethics Committee (Date: 21.03.2024, Decision No:0143).

Funding: None.

Peer-review: Externally peer-reviewed.

REFERENCES

1. Treviño González JL, Reyes Suárez LL, Hernández de León JE. Malignant otitis externa: An updated review. Am J Otolaryngol 2021;42(2):102894.
2. Karaman E, Yilmaz M, Ibrahimov M, Haciyev Y, Enver O. Malignant otitis externa. J Craniofac Surg 2012;23(6):1748-51.
3. Chen CN, Chen YS, Yeh TH, Hsu CJ, Tseng FY. Outcomes of malignant external otitis: survival vs mortality. Acta Otolaryngol 2010;130(1):89-94.
4. Afzalzadeh M. Antimicrobial agents in malignant otitis externa: A systematic review. Rev Clin Med 2021;8(4):145-159.
5. Hollis S, Evans K. Management of malignant (necrotising) otitis externa. J Laryngol Otol 2011;125(12):1212-7.
6. Kamalden TMIT and Misron K. A 10-year review of malignant otitis externa: A new insight. Eur Arch Otorhinolaryngol 2022;279(6):2837-2844.
7. Sudhoff H, Rajagopal S, Mani N, Moumoulidis I, Axon PR, Moffat D. Usefulness of CT scans in malignant external otitis: effective tool for the diagnosis, but of limited value in predicting outcome. Eur Arch Otorhinolaryngol 2008;265(1):53-6.
8. Dziedzic EA, Gąsior JS, Tuzimek A, et all. Investigation of the Associations of Novel

Inflammatory Biomarkers-Systemic Inflammatory Index (SII) and Systemic Inflammatory Response Index (SIRI)-With the Severity of Coronary Artery Disease and Acute Coronary Syndrome Occurrence. Int J Mol Sci 2022;23(17):9553.
9. Islam MM, Satici MO, Eroglu SE. Unraveling the clinical significance and prognostic value of the neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, systemic immune-inflammation index, systemic inflammation response index, and delta neutrophil index: An extensive literature review. Turk J Emerg Med 2024;24(1):8-19.
10. Templeton AJ, McNamara MG, Šeruga B, et all. Prognostic role of neutrophil-to-lymphocyte ratio in solid tumors: a systematic review and meta-analysis. J Natl Cancer Inst 2014;106(6):dju124.
11. Stevens SM, Lambert PR, Baker AB, Meyer TA. Malignant Otitis Externa: A Novel Stratification Protocol for Predicting Treatment Outcomes. Otol Neurotol 2015;36(9):1492-8.
12. Sideris G, Latzonis J, Avgeri C, Malamas V, Delides A, Nikolopoulos T. A Different Era for Malignant Otitis Externa: The Non-Diabetic and Non-Immunocompromised Patients. J Int Adv Otol 2022;18(1):20-24.
13. Arsovic N, Radivojevic N, Jesic S, Babac S, Cvorovic L, Dudvarski Z. Malignant Otitis Externa: Causes for Various Treatment Responses. J Int Adv Otol 2020;16(1):98-103.
14. Özer F, Pamuk AE, Atay G, Parlak Ş, Yücel T. Skull base osteomyelitis: Comprehensive analysis and a new clinicoradiological classification system. Auris Nasus Larynx 2021;48(5):999-1006.
15. Long DA, Koyfman A, Long B. An emergency medicine-focused review of malignant otitis externa. Am J Emerg Med 2020;38(8):1671-1678.
16. Foster, T. Orji, James, O. Akpeh, Onyinyechi, C. Ukaegbe. Malignant otitis externa: An assessment of emerging pathogens and the prognostic factors. International Journal of Medicine and Medical Sciences 2017;9(7):86-91.
17. Freeman MH, Perkins EL, Tawfik KO, O'Malley MR, Labadie RF, Haynes DS, Bennett ML. Facial Paralysis in Skull Base Osteomyelitis - Comparison of Surgical and Nonsurgical Management. Laryngoscope 2023;133(1):179-183.
18. Marina S, Goutham MK, Rajeshwary A, Vadisha B, Devika T. A retrospective review of 14 cases of malignant otitis externa. J Otol 2019;14(2):63-66.
19. Yigider AP, Ovunc O, Arslan E, Sunter AV, Cermik TF, Yigit O. Malignant Otitis Externa: How to Monitor the Disease in Outcome Estimation? Medeni Med J 2021;36(1):23-29.