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Systemic Inflammatory Markers in Patients with Combined Otitis Media and Rhinosinusitis

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Abstract: Background: Otitis media and rhinosinusitis are common inflammatory disorders of the upper airway that frequently coexist due to shared anatomical and immunological pathways. Increasing evidence supports the concept of a unified airway, suggesting that inflammation of the nasal cavity and paranasal sinuses may extend to the middle ear. **Objective:** To evaluate systemic inflammatory markers in patients with combined otitis media and rhinosinusitis and compare them with healthy controls. **Methods:** This hospital-based case–control study was conducted at the Department of Otolaryngology, Al-Kindy Teaching Hospital, Baghdad, Iraq, between March 1, 2025, and December 30, 2026. A total of 140 participants were enrolled, including 70 patients diagnosed with combined otitis media and rhinosinusitis and 70 age- and sex-matched healthy controls. Clinical diagnosis was confirmed through otoscopic examination, nasal endoscopy, and radiological assessment when indicated. Venous blood samples were collected to measure systemic inflammatory markers including white blood cell count (WBC), neutrophil count, lymphocyte count, neutrophil-to-lymphocyte ratio (NLR), platelet count, platelet-to-lymphocyte ratio (PLR), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and hemoglobin levels. **Results:** No significant differences were observed between groups regarding age or sex distribution ($p>0.05$). Patients with combined OM and RS demonstrated significantly elevated WBC (9.80±2.10 vs. 6.70±1.50 $\times 10^9$/L), neutrophil count (6.50±1.90 vs. 3.80±1.20 $\times 10^9$/L), NLR (3.50±1.20 vs. 1.40±0.60), platelet count (320.00±60.00 vs. 260.00±50.00 $\times 10^9$/L), PLR (160.00±40.00 vs. 95.00±30.00), CRP (12.40±5.60 vs. 3.20±1.80 mg/L), and ESR (28.60±10.20 vs. 12.30±5.40 mm/hr) compared with controls (all $p < 0.001$). Lymphocyte count was significantly reduced in cases (2.10±0.70 vs. 2.80±0.80 $\times 10^9$/L, $p < 0.001$). Hemoglobin was mildly but significantly lower in cases (12.60±1.40 vs. 13.20±1.30 g/dL, $p = 0.02$). Correlation analysis demonstrated significant associations among inflammatory indices, particularly between NLR and CRP, ESR, and neutrophil count ($p<0.001$). **Conclusion:** Combined otitis media and rhinosinusitis are associated with significant systemic inflammatory response. Hematological inflammatory indices such as NLR, PLR, CRP, and ESR may serve as accessible and cost-effective markers reflecting disease burden and inflammatory severity. Incorporating systemic inflammatory markers into clinical evaluation may enhance patient stratification and management strategies.

Keywords: Otitis Media, Rhinosinusitis, Neutrophil-To-Lymphocyte Ratio, Platelet-To-Lymphocyte Ratio

INTRODUCTION

Occurring worldwide, otitis media (OM) and rhinosinusitis (RS) are among the most prevalent inflammatory disorders in otolaryngology practice [1-2]. These conditions have a fundamental effect on quality of life as well as healthcare utilization and resources since they are recurrent and chronic in nature [3]. The "unified airway" theory is increasingly being supported by evidence suggesting a pathiophysiological correlation between inflammatory processes occurring within the nasal cavity, paranasal sinuses, and middle ear [4-5]. The Eustachian tube is a major anatomical and functional link between the nasopharynx and middle ear, permitting bidirectional propagation of inflammatory mediators and pathogens [6-7]. Chronic rhinosinusitis has frequently been associated with Eustachian tube dysfunction and

middle ear effusion [8-9]. Similarly, otitis media is often comorbid with sinonasal inflammatory disease, more so in patients with allergic or chronic inflammatory phenotypes [10-11]. Systemic inflammation underpins the common theme in upper airway diseases [12]. These studies may move away from only mucosal inflammation to pick up on some systemic signs of inflammation driving the acute and chronic conditions of ENT [13-14]. Circulatory markers like total WBC (white blood cell) count, NLR, PLR, CRP, and ESR are showing promise as indicators of systemic immune activation [15-18]. Elevated NLR has been associated with chronic rhinosinusitis and associated with increased disease severity and recurrence risk [19-20]. High PLR has also been associated with otitis media with effusion and chronic inflammatory otologic conditions [21-22]. CRP was raised in both acute otitis media infections and bacterial rhinosinusitis because CRP is an index of a systemic acute-phase response [23-24]. It may, in fact, have further implications in the increased inflammatory response seen in patients with concomitant diseases of OM and RS compared to those presenting with solitary ailments [25]. However, limited reports exist on the assessment of these systemic inflammatory markers in this combined phenotype, particularly in adults [26-27]. An appreciation of the systemic inflammatory pattern in this patient group could help in risk stratification and therapeutic decision-making. Therefore, this study is aimed at exploring the systemic inflammatory biomarkers in patients with combined otitis media and rhinosinusitis in comparison to healthy controls and to evaluate their potential significance in clinical practice.

MATERIALS AND METHODS

Patients and Methods

This hospital-based case-control study was conducted at the Department of Otolaryngology, of the Al-Kindy Teaching Hospital, Baghdad, Iraq, during the period between March 1, 2015, and December 30, 2016. The study has been performed by consultants in otolaryngology with specialists in clinical laboratory. The institutional scientific board provided ethical approval following written informed consent secured from each participant before recruitment commenced.

Overall, there were 140 adult participants in the study, divided equally into two groups. The case group was comprised of 70 patients who were diagnosed with otitis media combined with rhinosinusitis, while the control group was made up of 70 healthy people of either sex who were matched for age and without signs of an ENT inflammatory disease on clinical examination. The cases underwent consecutive recruitment over the course of interactions in the ENT outpatient clinic. Controls were selectees at the help of hospital staff and relatives of patients who were included in the study and found free of any otologic or sinonasal pathologies.

Inclusion criteria for the case group included a clinically confirmed diagnosis of otitis media whose diagnosis was based on otoscopic findings of congestion, effusion, and retraction of the tympanic membrane, along with radiological and/or endoscopic confirmation of rhinosinusitis. Recruited cases were patients at least 18 years of age.

Participants that had autoimmune disorders, malignancy, systemic inflammatory disorders, had undergone recent systemic corticosteroid or immune-suppressive therapy, were in systemic infections, or have known hematologic problems were excluded, with the objective of decreasing confounding elements that could affect systemic inflammatory markers.

All patients were assessed by experienced ENT specialists using a standardized protocol, which began with the taking of a detailed medical history focused on the onset and recurrence of symptoms, allergy history, smoking status, and prior treatments received. Otoscopy using a high-definition otoscope was employed to inspect the health status of the middle ear. Nasal endoscopy was performed to visualize mucosal edema, purulent discharge, nasal polyps, and ostiomeatal complex occlusion. When clinically warranted, computed tomography (CT) of the paranasal sinuses was carried out for confirmation of sinus involvement and assessment of disease extent.

Under carefully controlled morning conditions, venous blood samples were taken to ensure harmony in laboratory parameters. Samples were then taken to the central laboratory for processing following established procedures. Inflammatory markers from the systemic bloodstream were measured as total WBC count, absolute neutrophil count, absolute lymphocyte count, NLR, platelet count, platelet-to-lymphocyte ratio (PLR), CRP, ESR, and hemoglobin. CBC was analyzed through automation hematology analyzers, while CRP was assessed through a high-sensitivity immunoturbidimetric means. ESR was measured with the Westergren method.

Continuous variables followed by descriptive statistics are Means±SD, while categorical variables are given as n (%). These authenticated (by the chi-square test) the distribution. Pearson correlation analysis was used for determining the associations between markers. Factors were considered statistically significant when $p<0.05$.

RESULTS

The study intimated that there was no dissimilarity between the cases and the controls with regards to their age means, which were 38.40 years (SD = 12.60) and 37.90 years (SD = 11.80) respectively, as per Mann-Whitney U test ($p = 0.81$). This is further deducible from the distribution of male components with cases making 57.14% (40 males) and female components with 54.29% (38 male cases), with a p-Value of 0.72 (Table 1).

Table 1: Demographic Characteristics

Variable	Cases (n = 70)	Controls (n = 70)	p-Value
Age (years)	38.40±12.60	37.90±11.80	0.81
Male	40 (57.14%)	38 (54.29%)	0.72
Female	30 (42.86%)	32 (45.71%)	-

Table 2: White Blood Cell Count

Variable	Cases	Controls	p-Value
WBC ($\times 10^9$/L)	9.80±2.10	6.70±1.50	<0.001

Table 3: Neutrophil Count

Variable	Cases	Controls	p-Value
Neutrophils ($\times 10^9$/L)	6.50±1.90	3.80±1.20	<0.001

Table 4: Lymphocyte Count

Variable	Cases	Controls	p-Value
Lymphocytes ($\times 10^9$/L)	2.10±0.70	2.80±0.80	<0.001

Table 5: Neutrophil-to-Lymphocyte Ratio

Variable	Cases	Controls	p-Value
NLR	3.50±1.20	1.40±0.60	<0.001

Table 6: Platelet Count

Variable	Cases	Controls	P-Value
Platelets ($\times 10^9$/L)	320.00±60.00	260.00±50.00	<0.001

Table 7: Platelet-to-Lymphocyte Ratio

Variable	Cases	Controls	p-Value
PLR	160.00±40.00	95.00±30.00	<0.001

Table 8: C-Reactive Protein

Variable	Cases	Controls	p-Value
CRP (mg/L)	12.40±5.60	3.20±1.80	<0.001

Table 9: Erythrocyte Sedimentation Rate

Variable	Cases	Controls	p-Value
ESR (mm/hr)	28.60±10.20	12.30±5.40	<0.001

Table 10: Hemoglobin Level

Variable	Cases	Controls	P-Value
Hemoglobin (g/dL)	12.60±1.40	13.20±1.30	0.02

Table 11:Correlation between Systemic Inflammatory Markers in Cases (n = 70)

Variable	NLR (r)	PLR (r)	CRP (r)	ESR (r)	p-Value
Lymphocytes ($\times 10^9$/L)	−0.68	−0.54	−0.49	−0.46	<0.001
Neutrophils ($\times 10^9$/L)	0.72	0.51	0.58	0.53	<0.001
Platelets ($\times 10^9$/L)	0.44	0.61	0.47	0.42	<0.001
CRP (mg/L)	0.59	0.52	—	0.63	<0.001
ESR (mm/hr)	0.55	0.49	0.63	—	<0.001
Hemoglobin (g/dL)	−0.31	−0.27	−0.29	−0.25	0.01

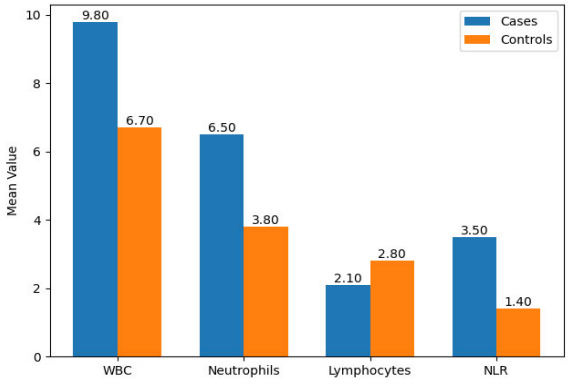

Figure 1: Comparison of Systemic Inflammatory Markers between Cases and Controls

The study showed significantly elevated total WBC count in cases (9.80±2.10 $\times 10^9$/L) compared with controls (6.70±1.50 $\times 10^9$/L), $p < 0.001$, indicating systemic inflammatory activation (Table 2).

Neutrophil count was significantly higher among cases (6.50±1.90 $\times 10^9$/L) compared to controls (3.80±1.20 $\times 10^9$/L), p<0.001 (Table 3).

Lymphocyte count was significantly reduced in cases (2.10±0.70 $\times 10^9$/L) compared with controls (2.80±0.80 $\times 10^9$/L), p<0.001 (Table 4).

The neutrophil-to-lymphocyte ratio (NLR) was significantly elevated in cases (3.50±1.20) versus controls (1.40±0.60), p<0.001 (Table 5).

Platelet count was significantly increased in cases (320.00±60.00 $\times 10^9$/L) compared to controls (260.00±50.00 $\times 10^9$/L), p<0.001 (Table 6).

PLR was significantly higher in cases (160.00±40.00) compared to controls (95.00±30.00), p<0.001 Table 7.

CRP levels were markedly elevated in cases (12.40±5.60 mg/L) versus controls (3.20±1.80 mg/L), p<0.001 Table 8.

ESR was significantly increased in cases (28.60±10.20 mm/hr) compared to controls (12.30±5.40 mm/hr), p<0.001 (Table 9).

Hemoglobin was slightly lower in cases (12.60±1.40 g/dL) compared to controls (13.20±1.30 g/dL), with statistical significance ($p = 0.02$) (Table 10).

Pearson correlation analysis demonstrated that lymphocyte count was significantly negatively correlated with NLR ($r = -0.68$, $p < 0.001$). Platelet count showed a moderate positive correlation with PLR ($r = 0.61$, p<0.001). CRP and ESR demonstrated strong positive correlations with NLR ($r = 0.59$ and $r = 0.55$, respectively; both p<0.001). Hemoglobin showed a mild negative correlation with CRP ($r = -0.29$, $p = 0.01$). These findings confirm that elevated systemic inflammatory markers are interrelated and reflect overall inflammatory burden in patients with combined otitis media and rhinosinusitis Table 11 (Figure 1).

DISCUSSION

This study underscores elevated systemic inflammatory markers in patients suffering from combined otitis media and rhinosinusitis compared to controls. These escalated values of WBC, absolute neutrophils, neutrophil-lymphocyte ratio, platelet-lymphocyte ratio, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR) suggest that systemic immune activation is present with current concurrent inflammation of the middle ear and sinonasal cavity. The concept of a united airway could explain the results of our study [4-5]. Cytokines released in the nose and nasal tissues might reach the middle ears via continuity of the mucosa and thereby the systemic circulation and may enhance inflammation in the middle ear [6,28]. Earlier studies have also suggested that middle ear effusion and Eustachian tube dysfunction have heights in patients with chronic rhinosinusitis [8,9,29]. Conclusively, the finding of significantly raised WBC and neutrophils (p<0.001) fits with earlier reports where neutrophils get to behave in predominance in bacterial rhinosinusitis and otitis media [12-13]. Neutrophil-

inspired tissue harm can be linked to reactive oxygen species and proteases [30]. The increase in NLR is consistent with other studies done which also describe the same in various ENT diseases [15,19-20]. Elevations in PLR are consistent with an individual-level increase in platelet activation, enhancing the supposition of inflammasome and endothelial disgracing [16,21]. Platelets have the capability to recruit immune cells and excessively release cytokines for the so-called reinforcement of inflammatory mechanisms in upper airway diseases [31]. CRP and ESR were markedly elevated in cases ($p < 0.001$) in line with systemic inflammation and acute-phase response [17,23]. Increased cartilage-binding CRP has been associated with bacterial cleansing capacity and disease extent in cases of otitis media and rhinosinusitis [24,32]. Raising ESR portrays a long-standing burden of inflammation [18]. In declined hemoglobin values (though discrete), further evidence may exist quantifying restrictions to erythropoiesis by inflammation in a variety of chronic inflammatory states [33]. Inflammatory cytokine-rich chronic sinonasal inflammation links hemorrhage-systemic cytokine mediated hematological changes [34]. The combined spectrum of OM and RS may have a more serious inflammatory phenotype when compared with singular disease [25,27]. What is found in the literature regarding proinflammatory mediators in ME effusion implies that raised ILs and tumor necrosis factors are seen with concurrent sinonasal disease [35]. Clinically, systemic inflammatory markers, if abnormal, can also act as adjunctive tools in identifying patients at risk for persistent/recurrent disease. The recognition of systemic inflammation is vital for the initiation of intensified close follow-up or more aggressive therapy. The study is strong as it leverages the case–control design and universally useful laboratory evaluations, yet it is subject to narrowness due to being a single-center study, with the lack of cytokine profiling. Future works focused on the molecular markers of inflammation would be welcomed.

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