Chronic otitis media (COM) is a common disease with some severe complications that result from long-standing damage to the middle ear by inflammation or infection [1]. Although the etiopathogenesis of COM has not been fully elucidated to date, genetic, inflammatory, autoimmune, and infectious factors, including cytokines, endotoxins, and oxidative stress, have been implicated [2].

Blood chemicals and trace elements play important roles in the establishment of vital chemical responses [3]. However, some immunological and inflammatory responses may alter the distribution of these chemicals in the body. In contrast, the status of blood chemicals may influence lymphocyte and granulocyte function as well as the immune response [4]. Moreover, trace elements play various vital roles as important constituents of vitamins, enzymes, and other proteins.

Some data in the literature support the immunological function of various blood chemicals. Serum iron (Fe) and zinc (Zn) levels are reduced during infection and inflammation [5]. Manganese (Mn) is an important cofactor for several enzymes that maintain DNA integrity. In addition, Mn is an important antioxidant. Cobalt (Co) is a critical fragment of vitamin B12 that is crucial in folate and fatty acid metabolism [6]. Lead (Pb) down-regulates nitric oxide production and induces oxidative stress and inflammation. Copper (Cu), magnesium (Mg), Zn, and Fe have been previously studied in some acute and chronic infections, including tuberculosis, Helicobacter pylori (H. pylori) infection, sepsis, and viral hepatitis [7-9].

OBJECTIVE: To determine the serum iron (Fe), zinc (Zn), manganese (Mn), copper (Cu), magnesium (Mg), cobalt (Co), and lead (Pb) levels in patients with chronic otitis media (COM) and to evaluate the association of the serum levels of these elements with treatment outcomes.

MATERIALS and METHODS: Thirty-one healthy volunteers and 31 patients with COM were prospectively included in this study. Serum levels of Fe, Zn, Mn, Mg, Cu, Co, and Pb were determined by an atomic absorption UNICAM-929 spectrophotometer.

RESULTS: Serum Co, Pb, and Fe levels were significantly increased (p<0.001) and serum Cu, Zn, Mg, and Mn levels were significantly reduced in patients with COM compared with controls (p<0.001). Serum Co and Mn levels were significantly decreased (p<0.001 and p<0.005, respectively) and serum Cu levels were significantly increased after surgery (p<0.005). The other evaluated blood chemicals and heavy metals did not exhibit significant differences (p>0.05).

CONCLUSION: Significant alterations in the serum chemical composition of patients with COM were observed. Moreover, with surgical treatment, serum levels of some of these chemicals were significantly altered. Further prospective studies are warranted to elucidate the exact association of these alterations in the etiopathogenesis of COM.

KEYWORDS: Chronic otitis media, trace elements, heavy metals
However, data regarding alterations of blood chemicals in patients with COM are limited. In this study, we aimed to determine the serum Fe, Zn, Mn, Cu, Mg, Co, and Pb levels in patients with COM and to evaluate the associations of the serum levels of these elements with treatment outcomes.

**MATERIALS and METHODS**

**Study Design**

The local institutional review board approved the study, and informed consent was obtained from all participants. In this prospective study, 31 patients with COM and 31 healthy volunteers were evaluated.

Patients were diagnosed based on their medical histories and routine otomicroscopic evaluations. Patients with a history of diabetes mellitus, hypertension, rheumatoid arthritis, liver disease, renal disease, and coronary artery disease as well as those who received immunosuppressive treatments were excluded from the study. However, all participants in the control group were asymptomatic nonsmokers with normal physical examination and otomicroscopic evaluations. None of the participants were taking antioxidant vitamin supplements.

**Outcome Parameters**

Prior to treatment, blood samples were obtained and stored at 4°C. Serum was isolated by centrifugation (3,000 rpm, 10 min) and stored at -80°C. The Fe, Zn, Mn, Mg, Cu, Co, and Pb levels were determined using a UNICAM-929 atomic absorption spectrophotometer (Unicam Ltd, York Street, Cambridge, UK).

**Statistical Analysis**

Data were analyzed using the IBM Statistical Package for Social Sciences version 11 (SPSS Inc.; Chicago, IL, USA). Qualitative variables were assessed using the Chi-square test. To compare patients and healthy controls, Student’s t-test was used. To compare values before and after treatment, a paired t-test was used. A p value of 0.05 or less was considered significant.

**RESULTS**

The study group included 31 patients (16 females and 15 males) with a mean age of 41±6 years (Table 1). No significant differences regarding age or gender were noted between groups.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Controls (n=31)</th>
<th>COM (n=31)</th>
<th>p</th>
</tr>
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<tr>
<td>Age (years)</td>
<td>39±7</td>
<td>41±6</td>
<td>0.237</td>
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<tr>
<td>Sex (female/male)</td>
<td>14/17</td>
<td>16/15</td>
<td>0.611</td>
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</table>

**Table 1. Demographic characteristics of the two groups in this study**

COM: chronic otitis media; SD: standard deviation

Values are the mean±SD

Comparred with healthy controls, serum Co, Pb, and Fe levels were significantly increased in the COM group (p<0.001), whereas serum Cu, Zn, Mg, and Mn levels were significantly reduced (p<0.001; Table 2, Figure 1).

After surgery, serum Co and Mn levels decreased significantly (p<0.001 and p<0.005, respectively), whereas serum Cu levels increased significantly (p<0.005). Other serum chemicals did not exhibit any significant alterations after surgery (Table 3, Figure 2).

**DISCUSSION**

In this study, we aimed to determine the levels of serum chemicals and heavy metals in patients with COM before and after surgery and compare the results with healthy volunteers. To the best of our knowledge, this is one of the foremost studies regarding blood chemicals in patients with COM. We determined that patients with COM exhibit increased serum Zn, Mn, Mg, and Cu levels and reduced Co, Pb, and Fe levels compared with healthy subjects. Moreover, after surgery, serum Co and Mn levels decreased, whereas serum Cu levels significantly increased.

Considering that blood chemicals and trace elements are essential for immune system function via the integration into regulatory pathways or control of oxidative stress, their deficiencies may result in infectious diseases. Data regarding blood chemicals in COM are limited. Elemraid et al. investigated the nutritional factors associated with chronic suppurative otitis media in children and reported that children with this disease were more undernourished compared with controls, with lower mean serum Zn, selenium (Se), and calcium (Ca) concentrations.

Previous studies have revealed that trace elements, such as Zn, Fe, Cu, and Mg, may play a role in infectious diseases, such as tuberculosis, *H. pylori* infection, sepsis, and viral hepatitis. Zn is an important micro-nutrient in the body with numerous functions, including growth, nerve impulse transmission, hormone release, and activation of immune-enhancing T-cells. In an experimental study, Prasad et al. stated that a significant decrease in Zn concentrations was associated with a decrease in interferon-gamma and interleukin (IL)-2 production as well as the nat-
Zn and Cu are required to maintain a proper immune response and antioxidative protection in the body as they are the cofactors of metalloenzymes [17, 18]. Superoxide dismutase, one of the most important enzymatic antioxidants, also contains Zn and Cu [18]. Serum Cu levels are increased in some infections and inflammatory processes, as previously noted [19,20]. Recently, the serum Cu/Zn ratio was defined as an important inflammatory marker [21]. However, in the present study, we revealed that serum Cu levels were reduced in COM patients compared with control subjects. In patients with COM, serum Cu levels were significantly increased after the surgical treatment. The lower serum Cu and Zn levels determined in this study may be associated with defects in the immune response and antioxidative mechanisms.

Mn is a trace element that is related to the transport and absorption of Fe, and the levels of these two elements exhibit a positive correlation [22]. Mn also plays a significant role in the immune system, interacting with neutrophils and macrophages and protecting the body against oxidative stress [23]. To the best of our knowledge, no studies have evaluated serum Mn levels in COM patients. In the present study, we found that serum Mn levels were reduced in COM patients compared with controls. Interestingly, after surgical treatment, serum Mn levels were significantly further reduced. The role of Mn in the etiopathogenesis and treatment of COM warrants further studies.

Mg is a vital element for the function of numerous enzymes that are involved in DNA and RNA synthesis [24]. Some antibacterial effects of Mg have also been previously reported [25, 26]. Yue et al. [27] reported higher Mg levels in the middle ear fluids of patients with otitis media. In the present study, we revealed that serum Mg levels were significantly reduced in COM patients compared with controls. This finding may be attributed to the utilization of Mg in this inflammatory response. After surgical treatment, serum Mg levels were not altered in patients.

Fe is crucial for cell growth and numerous metabolic processes, and Fe deficiency is associated with several diseases and oxidative DNA damage [28]. Based on its function in cell proliferation and bacterial activity, low levels of Fe can also result in an impaired immune response. Moreover, Fe is essential for the growth and virulence of numerous microbial pathogens [29]. In the present study, serum Fe levels were significantly increased in COM patients compared with control subjects. Increased serum Fe levels may cause susceptibility to infections by providing an appropriate media for microorganisms. After surgical treatment, serum Fe levels were not altered in patients.

Heavy metals, such as Pb and Co, may accumulate in different organs of the body and inhibit vital enzymes. Pb affects endothelial function and alters the inflammatory response [30]. Based on its function in cell proliferation and bactericidal activity, low levels of Fe can also result in an impaired immune response. Moreover, Fe is essential for the growth and virulence of numerous microbial pathogens [29]. In the present study, we demonstrated that serum Pb levels were significantly increased in COM patients compared with control subjects. Increased serum Pb levels may cause susceptibility to infections by providing an appropriate media for microorganisms. After surgical treatment, serum Pb levels were not altered in patients.

Although this is the first study in the literature evaluating blood chemicals in patients with COM, it has some limitations that should be mentioned. First, due to the cross-sectional design of this study, we cannot address causal relationships. Second, we assessed serum levels of blood chemicals, and these values may not always correlate with definite functions at the tissue level.

In conclusion, we determined that there were significant alterations in serum chemicals in COM patients. Moreover, upon surgical treatment, the serum levels of some of these chemicals were also significantly altered. Further prospective studies are warranted to elucidate the exact association of these alterations in the etiopathogenesis of COM.


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