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The Relationship of Serum Osteoprotegerin Level with Disease Severity in Iraqi Females with Lupus Erythematosus

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Abstract

Systemic Lupus Erythematosus (SLE) is a complex autoimmune condition that frequently presents with symptoms affecting the joints, such as inflammation, swelling due to fluid accumulation, or ongoing discomfort. A key diagnostic indicator of SLE is morning joint stiffness or pain, which typically persists for at least half an hour. Musculoskeletal complications, including arthritis and chronic joint pain, rank among the most common clinical manifestations of SLE, with studies indicating these symptoms are observed in nearly 90% of cases throughout the progression of the disease. The study aims to assess the relationship between the serum level of Osteoprotegerin (OPG) and the severity of SLE disease. Over four months, from November 2022 to March 2023, 131 women with systemic lupus erythematosus (SLE) and 50 healthy women participated in the case-control observational study. According to the Roma Helper program, a consultant physician conducted clinical examinations and divided the severity of the condition into patient groups (Intense, Mild, Moderate, and Dormant). Dormant SLE patients had greater OPG levels, although mild and moderate patients had higher OPG levels than the Dormant group. The Intense group had the highest OPG level of all the groups. Additionally, the group of healthy people had the lowest values. The levels of OPG were significantly increased in SLE patients, the OPG levels were of increased with disease activity.

Keyword: Systemic lupus erythematosus 1, Osteoprotegerin 2

1. Introduction

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that primarily impacts women and involves multiple organ systems. It is marked by heterogeneous clinical manifestations, ranging from mild to severe, reflecting its complex and systemic nature [1]. Immune system abnormalities are a hallmark of SLE [2]. While genetic and environmental risk factors have been implicated, the precise causes of SLE remain unknown. These factors have triggered substantial shifts in the immune landscape, often marked by elevated effector T-cell activity, diminished regulatory T-cell [3], [4].

Because SLE is brought on by exposure to environmental variables like UV radiation, infections, and chemicals, genetically predisposed people lose their immunological tolerance and

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experience abnormal autoimmune system activation [3]. Swollen and painful joints, fever, chest pain, mouth ulcers, hair loss, enlarged lymph nodes, fatigue, and a red rash, commonly on the face, are all common signs of SLE [2]. There are frequently flare-ups, or episodes of disease, and remissions, or times when symptoms are minimal [4].

Osteoprotegerin (OPG), a glycoprotein classified under the tumor necrosis factor superfamily (TNFSF), consists of 401 amino acid residues and exhibits a molecular mass of approximately 60 kDa. Functionally, it serves as a pivotal regulator of bone remodeling dynamics, modulating skeletal turnover across diverse physiological states and disease processes [5]. OPG synthesis occurs in a variety of organ systems and tissue types [6]. OPG suppresses the RANKL-RANK interaction by acting as a receptor activator of the nuclear factor-κB ligand (RANKL) decoy receptor [7]. Beyond its role as a secreted decoy receptor for RANKL, emerging evidence suggests OPG may directly modulate osteoclast activity. This glycoprotein exerts its effects by competitively binding to RANK receptors, thereby inhibiting RANKL-mediated signaling pathways critical for osteoclast differentiation and activation [8]. Numerous investigations revealed that SLE patients' serum OPG was higher than that of healthy controls [9], [10].

2. Methods

Study Design: In this case-control study, 131 women with SLE took part during a four-month period, from November 2023 to March 2024. The study cohort comprised female participants diagnosed with SLE, who were enrolled from the Baghdad Teaching Hospital—a tertiary care center located in Medical City, Baghdad. Biochemical analyses for diagnostic and research purposes were performed at the International Centre for Research and Development, specifically within its dedicated research laboratories in Kadhimiya City. Inclusion criteria included every woman with SLE who was between the ages of 15 and 65, who had a clinical examination conducted by a consultant physician. Exclusion criteria included the following criteria were excluded: cyclophosphamide treatment, chronic conditions like asthma or Crohn's disease, thyroid disease, pregnancy, other inflammatory diseases like RA, OA, myositis, vasculitis, a history of hypersensitivity, and any patients with tumors who were taking nutritional supplements.

This study adhered to ethical guidelines and received formal approval from the Institutional Higher Scientific and Ethical Committee. Prior to enrolment, all participants were provided with detailed information about the research and required to submit written informed consent.

To determine the distribution of the data, a one-sample Kolmogorov-Smirnov test was employed with the Statistical Package for Social Science (SPSS 16 IBM, Armonk, USA). The Mann-Whitney test should be applied if the values were not regularly distributed, and the t-test should be applied if they were. The means of the variables in the control and patient groups (Dormant, moderate, and Intense SLE groups) were compared using an analysis of variance (one-way ANOVA) test. The mean ± standard deviation (SD) was used to represent the results. P-values less than 0.05 were considered statistically significant.

3. Results and Discussion Section

The results in Fig. 1 show that the mean OPG level for the Dormant SLE patient was high at (1.79 ± 0.58), whereas the mean OPG level for the mild and moderate patients was higher at (2 ± 0.51)

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than for the Dormant group. The Intense group had the highest OPG level among the groups, with a mean of (2.12±0.51), and the group of healthy people had the lowest values (0.51+0.07). When compared to the mild categories, the SLE patient group showed significant differences ($p < 0.05$), but when compared to the healthy group, showed a very highly significant ($p < 0.001$). However, there was a substantial rise ($p < 0.05$) in the groups that were compared to the Dormant group.

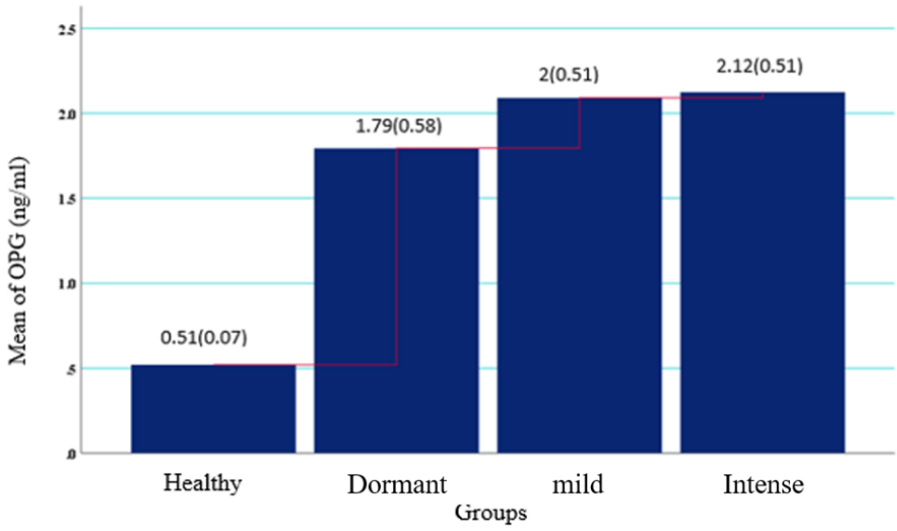

Fig. 1 OPG in groups of healthy people and patients (Dormant, mild, moderate, and Intense)

The analysis revealed a statistically significant elevation in osteoprotegerin (OPG) levels among individuals with systemic lupus erythematosus (SLE) compared to healthy controls. These findings align with prior research documenting markedly increased OPG concentrations in SLE patients relative to the general population [9]. Additionally, the authors in [10] found that OPG was considerably higher in patients compared to persons in good health, as well as [6], [11]. B cells, which produce 64% of OPG, may be more active, which could explain the rise in OPG.

It has been demonstrated that CD40 has a role in SLE disease, either directly or indirectly, and that SLE patients have elevated CD40 levels [12]. CD40 plays a part in the creation of OPG, and as B cell activity rises during the disease, so does CD40 production and activity. CD40 activation receptors cause B cells to produce more OPG [13].

Leptin levels are elevated in SLE patients [14], OPG suppresses osteoclast formation via the RANK/RANKL/OPG signaling axis, a key mechanism underlying bone regulation. Functionally, OPG acts as a secreted decoy receptor for RANKL, competitively binding to RANKL and blocking its interaction with RANK, a receptor expressed on osteoclast precursors and dendritic cells. By sequestering RANKL, OPG prevents RANKL-RANK binding, thereby halting the molecular cascade required for osteoclast differentiation and activation [15]. OPG expression may be stimulated by estrogen, according to in vitro research. Results from in vitro experiments demonstrate that 17-estradiol increases osteoblastic cells' production of OPG [16].

4. Conclusion

A marked elevation in Osteoprotegerin concentrations was observed in individuals diagnosed with systemic lupus erythematosus compared to healthy controls. Furthermore, this rise in OPG levels

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exhibited a direct correlation with the severity of SLE manifestations, suggesting a proportional relationship between OPG expression and the progression of disease activity.

Conflict of Interest

There is no conflict of Interest

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