Research Article

Serum Fibroblast Growth Factors 23, Chemerin, and Vitamin D Levels in Patients with Psoriasis

Shatha N. Tawfeeq¹, Moayad M. Al Anzy², Entedhar R. Sarhat³

¹Department of Medical Microbiology, Cihan University-Erbil, Kurdistan Region, Iraq, ²Department of Pharmaceutical Sciences, Tikrit University, Tikrit, Iraq, ³Department of Basic Science, Faculty of Medicine, Tikrit University, Tikrit, Iraq

ABSTRACT

The aim of the study was to compare the levels of fibroblast growth factor 23 (FGF23) and chemerin, as well as Vitamin D in psoriasis sufferers and healthy controls. From 2021 to 2022, ninety subjects were studied. The study comprised 45 individuals with psoriasis and 45 healthy controls. Serum fasting FGF23 and chemerin levels of the study group were examined by sandwich enzyme-linked immunosorbent assay. The results demonstrate that the mean serum FGF23 and chemerin quantities in psoriasis patients were greater than in controls, with a statistically significant. Patients with psoriasis, on the other hand, had considerably lower blood Vitamin D levels than healthy controls. These findings demonstrate that psoriatic patients have lower Vitamin D levels than healthy controls, and they add to the growing body of data linking FGF23, chemerin Vitamin D levels, and the course of psoriasis.

Keywords: Serum fibroblast, psoriasis, fibroblast growth factor 23, chemerin, 1,25 (OH)2D

INTRODUCTION

Psoriasis is now recognized as a chronic immune-mediated inflammatory dermatosis with an unknown etiology. It is caused by a variety of external and endogenous causes, related with a range of biochemical and immunological abnormalities,[1] affecting approximately 2% of the global population.[2] Despite the fact that it does not affect just one tissue, it is linked to autoimmune reactions all over the body. Sharply defined dull red spots with scales, particularly in the scalp and on extensor prominences, are used to categorize psoriasis.[3] Dendritic cells and T-cells multiply in the immune system, releasing a range of inflammatory precursors cytokines and chemokines, as well as growth factors, which all have a role in the pathogenesis of psoriasis.[4]

In contrast to most other fibroblast growth factors (FGFs), which do not behave as traditional hormones, the FGF23 gene is located on chromosome 12p13 and characterized by endocrine and paracrine effects.[5] It is a phosphaturic proteohormone produced mostly by osteoblasts/osteocytes in the bone that is plays a function in phosphate reabsorption and 1,25 (OH) 2D3 synthesis in the kidney. Metabolism of FGF23 included the cleavage of bioactive intact FGF23 (iFGF23, 30 kD) into C-terminal (cFGF23, 12 kD) and N-terminal (18 kD) fragments. FGF23 could be cleared by kidneys through filtration and catabolism.[6,7] IfGF23 a protein with classical endocrine, but also paracrine effects. Klotho, a transmembrane protein, is required for FGF23-mediated regulation of the renal phosphate transporter NapiIla and CYP27B1, the major enzyme in the production of 1,25(OH)2D3.[8]

Adipose tissue is a metabolic and endocrine organ that is complicated, critical, and highly active. Chemerin is one of the metabolically active peptide hormones, cytokines, chemokines, and adipokines released by this gland.[9-11] Chemerin (16 kDa), also known as TIG2 or RARRES2, is a newly discovered adipocyte-secreted factor that has both pro and anti-inflammatory properties. It is made as an inactive prochemerin that is transformed to its active state by serine proteases. Not just in WAT, it can even be found in the skin, intestines, and airways, chemerin is secreted in enormous levels. ChemR23, GPR-1, and CCRL2 are the three kinds of receptors that chemerin interacts to. Chemerin inhibits neutrophil transepithelial migratory process and increases apical neutrophil evacuation when CHEmR23 is activated.[12,13]
Vitamin D is also known as vitamin that excreted in the body after sun exposure. It refers to a group of fat-soluble biologically active compounds, which is connected with the metabolism of bone and skeletal integrity and generated in the skin by the action of UV irradiation from the sun.

It has historically been known as a hormone that maintains calcium-phosphorus balance and protects the musculoskeletal system's structure. Vitamin D modulates immunity by transforming 25(OH)D (Vitamin D's hormonally-active form) into tissue-specific, locally produced 1,25(OH)2D (Vitamin D's hormonally-active component). Macrophages, T-cells, keratinocytes, and dendritic cells involved in psoriasis pathogenesis can produce and respond to 1,25 (OH)2D in a paracrine and autocrine way when 25 (OH)2D is directly accessible for cellular absorption. A 25(OH)D level of <20 ng/mL indicates Vitamin D insufficiency. Our study's purpose is to compare the concentrations of serum FGF23, chemerin, and Vitamin D in psoriasis patients to those of a healthy population of similar age and gender.

MATERIALS AND METHODS

Patients and Controls
Forty-five patients of psoriasis (18 males [40%] and 27 females [60%]) with a mean age of 38.6 ± 11.2 were included in the study. Forty-five age- and sex-matched normal healthy controls (16 males [35.5%] and 29 females [64.5%]) with a mean age of 37.3 ± 11.21 year as shown in Table 1.

Patients were collected from the Biochemistry department of Tikrit Teaching Hospital in Tikrit city during the period from April 18, 2021, to January 17, 2022. Pregnancy, diabetes, hypertension, and inflammatory diseases other than psoriasis comprised the criterion of exclusion. The study was authorized by the Local Ethics Committee, and all patients and volunteers in the control group gave their informed permission.

Measurement of FGF23, and Chemerin in Serum
After an overnight fast, blood was drawn from patients and controls. After clotting, serum was extracted and kept in aliquots at −70ºC until needed. The enzyme-linked immunosorbent assay was used to assess FGF23 and chemerin (MyBioSource, USA).

Statistical Analysis
Statistical analysis was done using t-test. Correlation between continuous variables was estimated by Pearson's correlation coefficients. A value of P < 0.05 was considered statistically significant for each test.

RESULTS
The study revealed that, in comparison to the healthy control group, psoriatic cases had the highest mean of FGF23 enzyme level (109.93 pg/mL). As demonstrated in Figure 1 and Table 2, the difference was extremely significant (P = 0.0001).

The study showed that psoriatic patients had a greater mean of serum chemerin (328.6 ± 25.2 ng/mL) than the healthy control group, (229.1 ± 15.4 ng/mL according to the research). While S. Vitamin D (21.68 ± 1.79 ng/mL) was significantly reduced in psoriatic patients (45.19 ± 4.31 pg/mL) comparing with the control group (29.92 ± 1.55 ng/mL). Furthermore, parathyroid hormone (PTH) was significantly higher among patients' group (45.19 ± 4.31 pg/mL) compared to the control group (20.78 ± 1.50 pg/mL). as shown in Figures 1-4 and Table 2.

DISCUSSION
The kidneys maintain phosphorus homeostasis in healthy humans by proximal tubular active absorption or filtered phosphorus pass-through. 25-dihydroxyvitamin D (1,25 (OH)2D, parathyroid hormone and fibroblast growth factor-23) are hormones and factors that help kidneys regulate phosphorus (FGF-23). The parathyroid gland's main cells

| Table 1: Demographic characteristics of patients (n=45) and controls (n=45) |
|--------------------------|--------------------------|
| **Patients**             | **Control**              |
| Age                      | 38.6±11.2                | 37.3±11.21               |
| Gender                   |                          |                          |
| Male                     | 18                       | 16                       |
| Female                   | 27                       | 29                       |

Figure 1: Serum FGF23 in patients with psoriasis and the controls

Figure 2: Serum chemerin in patients with psoriasis and the controls
Tawfeeq, et al.: Role of Fibroblast Growth Factors 23, Chemerin, and Vitamin D in Psoriasis

PARATHYROID HORMONE (PTH) is a critical regulator of bone and mineral metabolic process, and its biosynthesis is influenced by changes in blood calcium levels, which trigger responses in several pathways. PTH levels in relation to 25(OH)D levels are often used to determine Vitamin D insufficiency levels. Vitamin D insufficiency appears to lower serum calcium levels, resulting in elevated PTH levels. Vitamin D is required for calcium absorption in the intestines in humans. Furthermore, the 25(OH)D concentration, which begins to climb or no longer falls as the PTH concentration lowers, may indicate Vitamin D inadequacy. PTH is elevated when calcium levels are low, or phosphate levels are high. High levels of parathyroid hormone damage bones and cause phosphate and calcium levels in the bones to fluctuate. PTH-rp is only found typical skin’s basal lamina and acts as a powerful epidermal cell proliferation inhibitor. PTH-rp is prevalent in keratinocytes, and 1,25 (OH)2 D3 regulates it. In psoriatic lesions, PTH is not present. PTH-rp expression was recovered in psoriatic skin when lesions were medicated with 1,25 (OH)2D3.

Inflammation is one of the main causes that leads to an increase in FGF23 transcription. Nuclear factor-kb, a critical component of the inflammatory signaling pathway, affects the expression of target genes, including FGF23, through transcriptional regulation. NFAT was first discovered as a nuclear factor that can bind to the interleukin-2 promoter in activated T cells. NFAT also has a role in innate immunological and inflammatory responses, according to research. FGF23 promotes hepatocytes to secrete inflammatory markers including IL6 and TNF, as well as fibrinogen, C-reactive protein, and vascular cell adhesion molecule-1. Increased FGF23 has the ability to trigger the inflammatory response by suppressing of 1,25-dihydroxyvitamin D, a strong inhibitor of inflammatory cytokine release.

Chemerin was validated to play as an inflammatory intermediary to production of proinflammatory cytokines and encourage the relocation of immature dendritic cells and macrophages. Chemerin concentrations in serum samples were observed to be greater in psoriatic patients than in the control group in this investigation. In a similar manner, Gisondi et al. and Lora et al. discovered elevated levels of chemerin in psoriasis patients having high disease activity. Xue et al. found that patients with psoriasis had considerably lower amounts of circulating chemerin than healthy controls. It is unclear what mechanism could explain these findings. We hypothesized that the mechanism was linked to chemerin’s angiogenic properties. Chemerin is a protein produced mostly by keratinocytes and endothelial cells, as well as white adipose tissue. IL1 and TNF both boost its production. Chemerin increases angiogenesis in psoriatic skin through stimulating adipocytes and endothelial cells. In psoriasis patients’ growing skin lesions, chemerin can stimulate chemotaxis of immature myeloid DCs and plasmatoid dendritic cells. Chemerin may be implicated in psoriasis pathophysiological processes. Chemerin expression was shown to be higher in psoriatic skin biopsies. The enhanced migration of dendritic cells and NK cells to the inflammation may be due to an increase in the concentration of this protein in mast cells, dermal fibroblasts, and endothelial cells throughout early phases of psoriasis. The stimulation of angiogenesis may also play a role in the evolution of psoriatic inflammation. Chemerin’s ability to induce the development of new vasculature could indicate a role for this adipokine in psoriasis. Physiologically, 1,25-dihydroxyvitamin D and Vitamin D receptor directly regulates the proliferation and growth of keratinocytes through Vitamin D receptors. There are several pathways for the effect of Vitamin D deficiency in psoriasis pathogenesis: Loss of antiproliferative, anti-inflammatory, and antiangiogenic activities.
Psoriasis is an autoimmune inflammatory disease involving both innate and acquired immunity. It is defined as an autoimmune inflammatory sickness with Th1-Th17-Th22 components. Decreased amounts of 25(OH)D have also been linked to a higher risk of developing autoimmune pathologies mediated by Th1.[36] The reason for the lower level of serum 25(OH)D in these patients may be due to inadequate 25(OH)D intake, paucity of sunlight exposure, or usage of medicines (e.g., glucocorticoids and immunosuppressive agents) that interact with 25(OH)D breakdown on a regular basis.[37]

**CONCLUSION**

Based on our observations, we have come to the conclusion that psoriasis suffers' serum FGF23 and chemerin levels are higher than healthy controls. Patients with psoriasis, on the other hand, had considerably lower serum Vitamin D levels than healthy controls. Therefore, FGF23, chemerin, and vitamin D levels may be a novel diagnostic marker in psoriasis and may predict the occurrence of comorbidities in psoriasis patients.

**REFERENCES**


