



## The Relationship of Prolactin Hormone with Rheumatoid Arthritis Patient

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### Abstract

Rheumatoid arthritis is the most common inflammatory arthritis that can cause irreversible joint deformities and functional impairment. The current study was designed to assess the relationship between prolactin levels and rheumatoid arthritis in women and men patients with hyperprolactinemia, which included healthy samples (males 9, females 211) and samples of patients with arthritis (males 6, female 32), for studying the relationship of prolactin hormone with rheumatoid arthritis patient. There is an increase in the level of prolactin in the blood of RA patients ( $36.76 \pm 4.54$ ) compared to the group of healthy controls ( $26.08 \pm 4.59$ ), but this increase did not reach to a significant level ( $p < 0.05$ ). Our study indicates that there is a possible association between prolactin and development of rheumatoid arthritis

### Keywords

Prolactin, Rheumatoid arthritis, hyperprolactinemia

### 1-Introduction

Prolactin (PRL) is one of the hormones that may play a role in regulating immune function. It is mainly produced in the anterior pituitary gland and consists of a single peptide chain of 198 amino acids, with a molecular weight of 23,500 Da [1]. Prolactin secretion is stimulated by thyrotropin releasing hormone (TRH), oxytocin, serotonin, and vasoactive intestinal peptide. Cytokines probably also participate in this regulation. In vitro studies have shown that IL-1, IL-2 and IL-6 are able to stimulate prolactin production, IFN-gamma can inhibit prolactin production, while TNF- $\alpha$  has been found to increase as well as to decrease secretion of prolactin [2,3].

A recent study shows an increase of prolactin in serum and synovial fluid from subjects affected with RA perhaps indicating that cytokines acts as a proinflammatory factor to increase disease. It is interesting to note that giving antiprolactin drugs to the

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patient of rheumatoid arthritis has improved the disease condition. In a study carried out by, Prolactin levels are higher in women than in men, though there is a considerable overlap in the ranges, prolactin levels rise in response to stress. It has been suggested that prolactin enhance inflammatory responses [4,5]. In human, raised levels of prolactin have been reported in some autoimmune diseases such as Rheumatoid arthritis (RA). Systemic lupus erythematosus (SLE), multiple sclerosis (MS), Sjogern syndrome(SS) [6,7].

Rheumatoid arthritis is a chronic, autoimmune inflammatory disease with a worldwide prevalence of 1% to 2% autoimmunity followed by the articular infiltration of leukocytes and hyperplasia of synovial cells lead to the development of an invasive inflammatory pannus that destroys the adjacent cartilage and bone. Locally produced cytokines are crucial for initiating the inflammatory process and destroying articular tissue, among these cytokines, TNF- $\alpha$ , IL-1 $\beta$ , and IFN-gamma stimulate both chondrocyte apoptosis and cartilage extracellular matrix degradation, and their inhibition ameliorates joint destruction [8,9,10].

Prolactin acts both as a circulating hormone and a cytokine to regulate the function of a wide variety of tissues, including cartilage [11]. PRL and the PRL receptor are expressed in chondrocytes where this hormone can promote differentiation and survival [12]. Fuxe K. first reported the prolactin immuno-reactivity in hypothalamic axon terminals. Prolactin immuno-Prolactin in arthritis reactivity was subsequently found in the telencephalon, hippocampus, amygdala, septum [13].

This fact was accepted based on various feasible studies, Prolactin was found in immune competent cells from thymus and spleen as well as peripheral lymphocytes, Prolactin stimulates the synthesis of proteoglycans and type II collagen by bone marrow-derived chondrocytic mesenchymal cells, and it inhibits the apoptosis of articular chondrocytes that induced by serum deprivation, suggesting the action of PRL on chondrocyte survival may be relevant in RA [14].

Prolactin is present in RA synovial fluid which produced by RA synovial cells, and can influence cartilage survival by exerting immuno regulatory effects. The PRL receptor is a member of the hematopoietin/cytokine receptor superfamily and is expressed in a variety of immune cells, in which this hormone can be pro inflammatory or anti-inflammatory by regulating proliferation, survival, and the release of inflammatory mediators [15,16]. The current study aims to determine the relationship of rheumatoid arthritis in women and men patients with hyperprolactinemia.

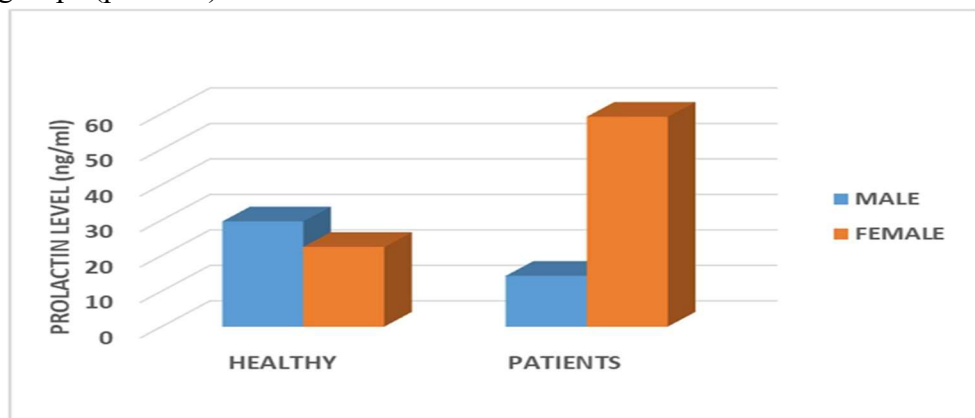
## 2-Methods

The total sample will collected was (58) sera sample, which include (43) patients women with hyper prolactinemia of ages (20-45) years from AL-Basra hospital for women and obstetrics, private laboratory, and (15) patients men with normal prolactin of ages (20-45) years from AL Basra hospital for women and obstetrics, private laboratory on 1/11/2016 - 1/2/2017.

Serum prolactin concentrations were measured under basal conditions and all blood samples were collected in dry tubes, blood samples were centrifuged at 3000 rpm for 5 minutes and serum was stored in freeze at  $-20^{\circ}\text{C}$  until analysis. hormonal assay was done in the patient of rheumatoid arthritis. The patient had active synovitis with tender swollen joints, early morning stiffness. Serum prolactin concentrations were measured by using Mini vidas device for hormonal test. All the study groups carried out to measure Prolactin and RF by using Mini vidas device for hormonal test and using RF latex test for RF test, as shown in the leaflet of the kit [17]. The statistical analysis are performed by using SPSS version 15 with  $P < 0.05$ ,  $P \leq 0.01$  at a significant [18].

### 3-Results

The results shown in Table (1) and Figure (1) show that there is a significant difference in the average level of serum prolactin between females ( $40.84 \pm 3.57$ ) and males ( $22.00 \pm 5.38$ ) at a significant level ( $p < 0.05$ ), when comparing gender. There is an increase in the level of prolactin in the blood of RA patients ( $36.76 \pm 4.54$ ) compared to the group of healthy controls ( $26.08 \pm 4.59$ ), but this increase did not reach to a significant level ( $p < 0.05$ ). Overall, the level of prolactin for males was higher in the control group ( $29.67 \pm 6.80$ ), while in females, the level of prolactin in patients with arthritis was much higher ( $59.19 \pm 3.61$ ) than in the healthy, that is, there is a significant difference between the two groups ( $p < 0.05$ ).



**Fig. 1- Comparison between RA patients and healthy controls according to PRL concentrations.**

**Table 1- Comparison between RA patients and healthy controls according to PRL concentrations.**

Gender	Group		Mean
	Healthy	Patients	
Male	b 29.67 ± .80	c 14.33 ± 8.33	22.00 ± 5.38
Female	b 22.48 ± .16	a 59.19 ± 3.61	40.84±3.57
Mean	B26.08 ±4.59	A 36.76 ± 4.54	

#### 4-Discussion

It is suggested that production of PRL by lymphocytes can play a role in the pathogenesis of some autoimmune diseases; some researchers found increased level of PRL has been described in serum of patients suffering from (SLE) [19]. In humans, rheumatoid synovial T- cells produce PRL. Also PRL receptors are found on T,B, fibroblast and like synovial cells. Addition of PRL to rheumatoid synovial cells in rats causes increased production of proteolytic enzymes causing cartilage destruction and increased production cytokines which indicates that PRL injected in joints caused inflammation [20].

This study shows that the level of serum prolactin concentration is higher in the female group ( $p < 0.05$ ) than in males because the female prolactin secretion is higher. The results are consistent with [21].

There is an increase in the level of prolactin in the blood of RA patients compared to the group of healthy controls, but this increase did not reach to a significant level ( $p < 0.05$ ). These results were consistent with [22] ,

found raised serum PRL levels up to  $40.20 \pm 5.6$  ( $p < 0.01$ ) in women with RA than the healthy adults, Other studies have reported increased serum PRL levels in RA patients in correlation with some parameters like duration of RA , however explore the hormonal status and the efficacy of anti-prolactin drugs in remission of rheumatoid arthritis which may contribute for the treatment strategy. Severity and joint damage in RA, while others studies demonstrates that prolactin inhibits cytokine and arthritis-driven chondrocyte apoptosis. This effect involves the reduced expression of pro-inflammatory cytokines in joints tissue and the blockage of their proapoptotic effect at the chondrocyte level [23].

Our results were not consistent with [24] found serum PRL levels between  $(5.49 \pm 5.47 \text{ } 8.76 \pm 10.5)$  ( $p < 0.05$ ) in RA patients. In females, the level of prolactin in patients with arthritis was much higher than in the healthy . The results are consistent with several studies reported higher serum prolactin concentration in women with

rheumatoid arthritis compared with control [25].

Other research showed there is an increased level of prolactin in patient with RA and an abnormal increase of prolactin level after surgery [26]. Nonsteroid anti-inflammatory drugs (NSAIDs) can also influence prolactin secretion has not been studied extensively, but one study in humans showed a decrease in plasma prolactin levels during prostaglandin E2 PGE2 infusion and an increase after use of NSAIDs , more clearly after the use of indomethacin than after naproxen[27].

Furthermore, a higher incidence of RA development has been found in the post-partum period, particularly when the mother breast feeds, another indication of a role of prolactin in the post- partum flare of RA comes from a study in mice, in which bromocriptine, a prolactin secretion inhibitor, administered shortly after parturition, led to a reduction of the post-partum flare of arthritis, however, during pregnancy and after delivery, there are many hormonal changes also involving hormones of the hypothalamus pituitary -axis, which makes it very difficult to clearly show a relation of RA activity with one of these, if enhanced levels of prolactin are a pro-inflammatory factor in RA, reduction of prolactin levels might improve disease outcome in RA, reduction normal levels of prolactin could still be beneficial in arthritis as it was shown in animal studies that normal levels were necessary to induce autoimmune arthritis[28,29].

Prolactin has a role in immunomodulation and it has been proposed that prolactin is a risk factor for development of autoimmunity, however it remain unclear whether the higher prolactin concentration are the cause or consequence of RA.[30].

Although the role of endogenous prolactin in autoimmune diseases has generated controversies, some study reveals that elevating serum prolactin levels significantly attenuates cartilage death and joint inflammation in inflammatory arthritis, this strategy may be comparable to the well- established use of glucocorticoid in patients with rheumatoid arthritis in which levels of the endogenous hormones appear insufficient to control the disease, While prolactin is not essential for normal immune system development and function, it is a major stress-related hormone balancing immune system homeostasis in the context of stress, trauma, and inflammation [31, 32, 33].

Previous studies of prolactin concentration in patients with rheumatoid arthritis have had inconsistent results the values being either increased, decreased, or unchanged, there could be several explanation for the contradictory reports; first, it is possible that non-steroidal anti- inflammatory drugs(NSAIDS) may influence prolactin levels, second, treatment with glucocorticoid may influence prolactin concentrations, third, disease modifying anti rheumatic drugs (DMARDS) may influence prolactin levels [34,35].

## 5- Conclusion

Our study indicates that there is a possible association between prolactin and development of rheumatoid arthritis. We are, however interested to explore the

hormonal status and the efficacy of anti-prolactin drugs in remission of rheumatoid arthritis which may contribute for the treatment strategy.

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