Detection of Anti-nuclear Antibodies in Women with Hyperprolactinaemia

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Abstract

Background: Autoimmune disorders are more frequent in females, among other possible factors hormonal make up is thought to play important roles. Prolactin is found in the core of this debate.

Aim: This study aimed to investigate women with hyperprolactinemia (HPRL) for antinuclear antibodies.

Methods: Thirty three hyperprolactinemic women with a mean age of 28.8± 6.5years were involved in this study, also another age-matched thirty women with normal prolactin levels were involved as a control group, demographic data were collected. Besides Immunoblotting antinuclear antibodies profile test, total and differential blood counts were carried out.

Results: Antinuclear antibodies were detected in 3/33 women with HPRL (9%). The detected antinuclear antibodies were anti-scl70 antibodies (Enzyme DNA topoisomerase 1 antibodies) in one case, and anti-CENP B antibodies (centromeres antibodies) in two other cases. No antinuclear antibodies were detected in any of the thirty control individuals (0%). Blood picture detection revealed relatively inflated parameters among the HPRL women.

Conclusions: This study finding indicates a possible commitment of prolactin in immune stimulation activities; this is hoped, with further studies to open promising windows in to the possibility of utilizing prolactin as a biomarker for autoimmunity and as a fair target for therapeutic interventions.

Keywords: Prolactin, Autoimmunity, Hyperprolactinemia, Antinuclear antibodies, Women

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Introduction

Autoimmune disorders arise from an abnormal immune response of the body against substances and tissues normally present in the body. A large number of autoimmune diseases are recognized, a major understanding of the underlying pathophysiology of autoimmune diseases has been the application of genome wide association scans that have identified a striking degree of genetic sharing among autoimmune diseases [(1)]. It has been estimated that autoimmune diseases are among the number one leading causes of death among women in all age groups up to 65 years [(2)]. The relationship between prolactin and the immune system has been demonstrated in the last two decades, opening new windows in the field of the immunoendocrinology. PRL is a peptide hormone secreted from the anterior pituitary gland under tonic inhibition of the hypothalamus, via dopamine and a stimulatory signal by the thyrotropin-releasing Hormone (TRH). The cytokines interleukin 1 (IL-1), interleukin 2 (IL-2) and interleukin 6 (IL-6) stimulate PRL secretion, while interferon γ (INFγ) and endothelin-3 are inhibitory cytokines [(3)]. Prolactin has an important role in the innate and adaptive immune response. Increased prolactin levels have been described in autoimmune diseases such as systemic lupus erythematosus, rheumatoid arthritis, Sjögren syndrome, and systemic sclerosis among others [(4)]. Hyperprolactinemia is associated with active disease and organ involvement in systemic lupus erythematosus. Therefore, prolactin is an integral member of the immunoneuroendocrinology network and seems to have a role in pathogenesis of autoimmune diseases. Few controlled studies of

dopamine agonist treatment in humans with autoimmune disease have been conducted only in systemic lupus erythematosus patients, which support the potential efficacy of such agents even during pregnancy and postpartum [4]. This study aimed to spot the commitment of prolactin by investigating HPRL women for a profile of antinuclear antibodies to detect or highlight part of the prolactin's autoimmune activities.

Methods

Thirty three HPRL women attended TOTAL LAB CARE group laboratories and ASIA hospital in Khartoum, from June to August 2014, with a mean age of 28.8± 6.5years were involved in this study, and another thirty women with normal prolactin levels were involved as a control group, demographic data were collected in a pre-designed sheet. The antinuclear antibodies profile test was performed using Immunoblotting strips (EUROLINE test strips, provides a qualitative invitro assay for human autoantibodies of the IgG class to 14 different antigens {n-RNP, Sm, SS-A native and RO52, SS-B, Scl70, PM-Scl, JO-1, CENP B, PCNA, dsDNA, nucleosomes, histones, ribosomal-P-protein, and AMA M2}, EUROIMMUN, Germany). Beside these a total and differential blood counts were carried out.

Results

This study involved 33 women with a prolactin levels above 500 MIU/ml (normal values for women is 102-496 MIU/ml). The mean age of the selected women was 28.8±6.5 years (Figure. 1).

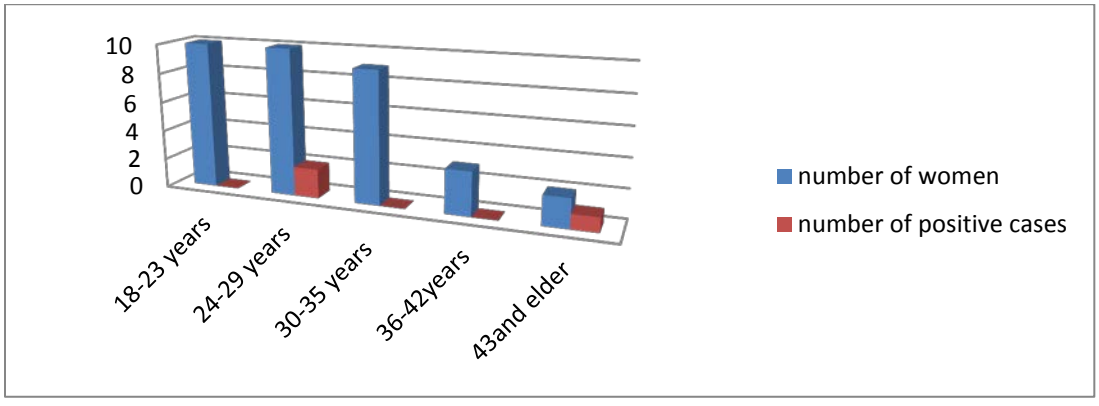

Fig 1: Age distribution of the studied women and the positive cases for ANA.

Antinuclear antibodies were detected in 3/33 women with HPRL (9%). The detected antinuclear antibodies were anti-scl70 antibodies (Enzyme DNA topoisomerase 1 antibodies) in one case, and anti-CENP B antibodies (centromeres antibodies) in two other cases. No antinuclear antibodies were detected in any of the thirty control individuals (0%) (Figure. 2).

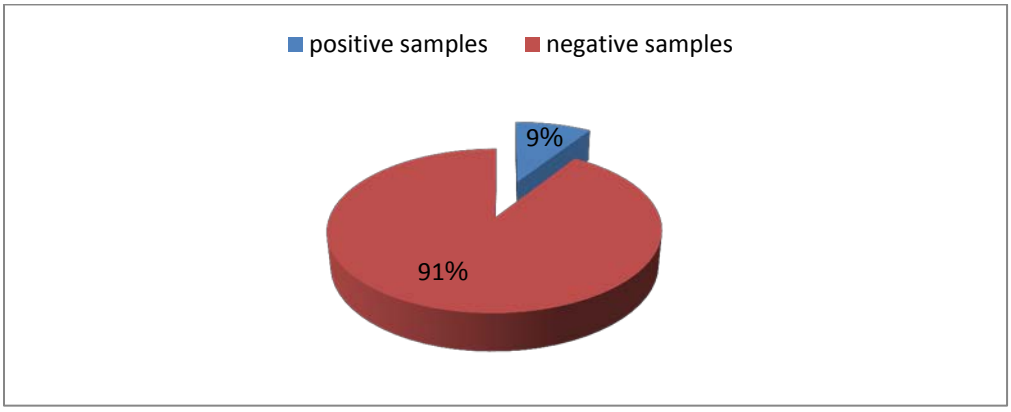

Fig 2: Percentage of HPRL women in whom ANAs were detected from the total number of HPRL women.

On the blood picture aspects the mean of the TWBCs count (TWBC) was $7.2\pm2 \times 10^3$ /UI for the women with HPRL while it was $7.0\pm3\times 10^3$ /UI for the control group, the mean of the lymphocytes count, the monocytes count neutrophils count and the platelets was $2.4\pm0.5\times 10^3$ /UI, $0.4\pm0.2\times 10^3$ /Ul,$4.1\pm2\times 10^3$ /UI and $277\pm45\times 10^3$ /UI respectively while it scored $2.2\pm0.7\times 10^3$ /UI, $0.34\pm0.2\times 10^3$ /UI, $3.4\pm1.4\times 10^3$ /UI and $274\pm51\times 10^3$ /UI respectively for the control group (Figures. 3 and 4).

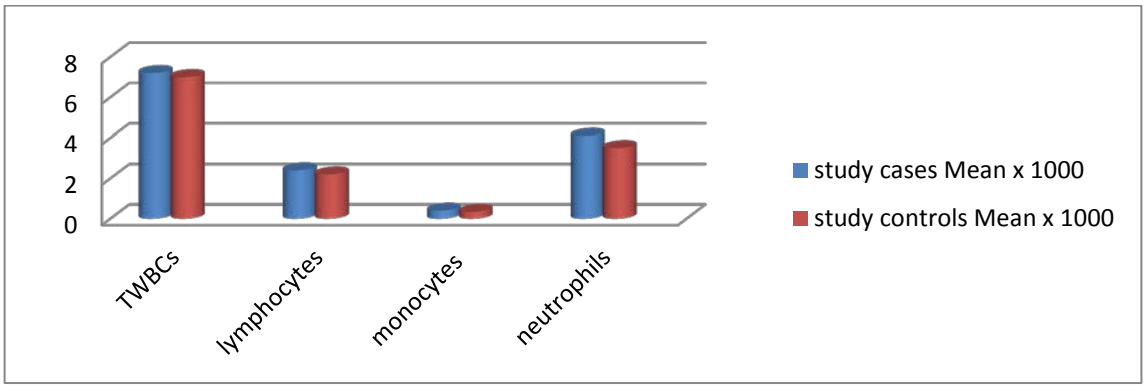

Fig 3: Blood picture specified by mean of TWBCs and differential blood cells count of the study women compared to the controls.

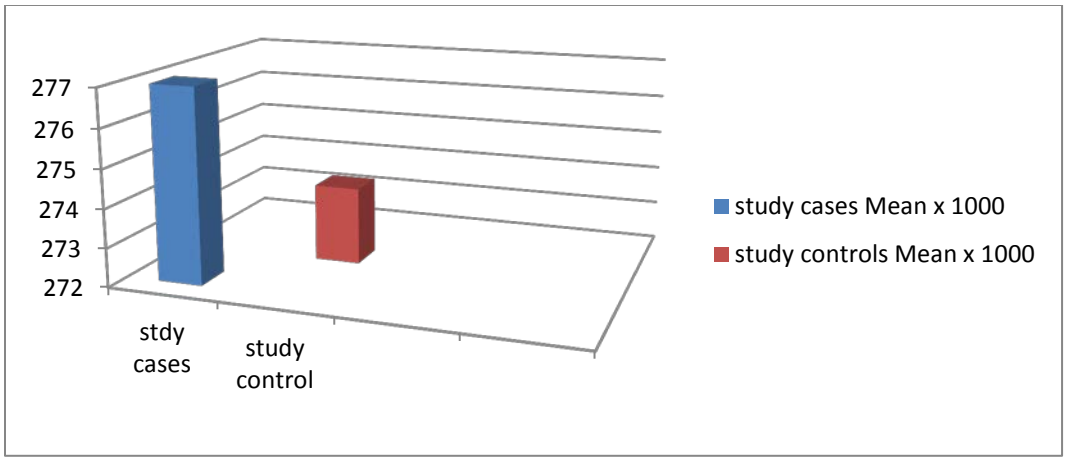

Fig 4: The mean of platelets count of the HPRL women compared to the control group mean.

Discussion

Prolactin has been shown to have immunomodulatory as well as lactogenic effects. Generally less well known is that prolactin may also play a role in the activity of autoimmune diseases such as systemic lupus erythematosus and rheumatoid arthritis. Studies have shown decreasing prolactin production to be beneficial in animal models of autoimmune disease. Thus far, double-blinded, placebo-controlled studies of dopamine agonist treatment in humans with autoimmune disease have been done only in lupus patients, and support the potential efficacy of such agents. Small, open-label trials have also suggested potential benefit in patients with rheumatoid arthritis, Reiter's syndrome, and psoriasis. More studies are required to further delineate the mechanisms by which prolactin affects autoimmune disease activity, to determine in which specific diseases prolactin plays a significant role, and to test the efficacy of prolactin-lowering agents as therapy for such diseases [(5)].

In this study the anti-nuclear antibodies detected were only slightly higher than that in the control group. This might not be enough to shape out a clear image, but the findings are in agreement with that of Miedany [(6)] demonstrated that prolactin level in SjÖgrens syndrome patients was 1.3 to 2.4 higher than controls. Moreover, increased prolactin level was reported from patients

suffering from rheumatoid arthritis [7]. Mild to moderate HPRL was demonstrated in 15%-33% of systemic lupus erythematousus patient of both genders [8].

The study revealed the presence of autoantibodies in patients with HPRL without any clinical signs of autoimmune disorders. A similar studies reported detection of anticardiolipin antibodies in 5/23 HPRL patients and multiple autoantibodies were also detected in sera from HPRL women but the subject did not have clinical evidence of autoimmune disease [8].

In the current study the detected ANAs were CENP B antibodies presented in 2 samples and Scl70 antibodies presented in the third one. The clinical significance of the two detected ANAs (CENPB antibodies and SCl70 antibodies) is associated with systemic sclerosis (SSc) which can manifest itself in two forms, the diffuse cutaneous and the limited cutaneous form.

According to Leroy [9] antibodies against Scl70 are found in 25%-75% of patient with (SSc) where the prevalence is 40%-65% in the diffuse form and 5%-15% in the limited form. While antibodies against centromeres CENP are associated with the limited form (SSc) and can be found in 80%-95%of patients. They are detected only in 8% of patients with the diffuse form, but also occur in 10%-30% of patients with primary biliary cirrhosis. In the study cases however there were not any such clinical sigs, this may be explained by the fact that autoantibodies detection does not necessitate the presence of active autoimmune disease however it may precede the disease.

By looking into the blood picture of the studied women that revealed an inflated parameters compared to the control group but these could not be entirely attributed to the prolactin as the gap between some items is very close, but prolactin might played a role in this relative increase as the biological effects of prolactin suggest. The relatively inflated lymphocytes count agreed with other studies which claimed a correlation between the prolactin level and the number of B and T lymphocytes [10].

Conclusion

This study concluded that prolactin has an immune stimulatory roles and might be important factor on the background of autoimmune gender bias, HPRL is more common among elder and

married women, as this study finding suggests a possible hand of prolactin in immune stimulation activities, this is hoped to open a promising windows in to the possibility of utilizing prolactin as a biomarker for autoimmunity and as a fair target for therapeutic interventions.

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