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ORIGINAL RESEARCH OPEN ACCESS

A study of serum prolactin in dermatological diseases in a tertiary care hospital of Assam

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Abstract

Background: Prolactin functions as a neuroendocrine modulator of the skin immune system and epithelial cell proliferation. Prolactin and the immune system inter relationship have been studied extensively and opened new avenues in the field of immunoendocrinology. Prolactin may have an important role in some dermatological diseases like psoriasis, alopecia areata, and vitiligo. We aim to estimate serum prolactin values in patients of psoriasis, alopecia areata and vitiligo and compare it with healthy controls and also evaluate the correlation between serum prolactin levels and severity of the diseases.

Methods: We performed a case–control study on 200 subjects which include 150 patients; suffering from psoriasis, alopecia areata and vitiligo; 50 patients in each group and 50 age- and sex-matched healthy controls. The serum prolactin level was measured in patients and control groups using enzyme linked immunosorbent assay (ELISA).

Results: Serum prolactin levels were significantly high in all three dermatological diseases in comparison with the control group ($P < 0.05$). The mean ± SD of the serum prolactin levels was 19.2 ± 6.7 ng/ml, 20.6± 6.9 ng/ml, and 16.4 ± 6.2 ng/ml in patients with psoriasis, alopecia areata, and vitiligo respectively. Moreover the serum prolactin levels in patients with psoriasis and alopecia areata were significantly correlated with disease severity ($P < 0.05$).

Conclusions: Prolactin may play a role in the pathogenesis of psoriasis, alopecia areata, and vitiligo; and may serve as a biochemical marker of disease severity in patients with psoriasis and alopecia areata.

Keywords: dermatological diseases; psoriasis; alopecia areata; vitiligo; ELISA; Assam

Introduction

Prolactin is a neuropeptide hormone consisting of 199 amino acids, secreted by the lactotroph cells in the anterior pituitary gland that functions systemically as a hormone, and locally as a cytokine [1]. It is known for its main role as lactogenic and mammotropic hormone. But in addition to its primary role it also acts as a part of a neuroendocrine-immune network by stimulating the release of specific cytokines [2] by forming a 'prolactin circuit' between the central nervous system and the skin [3, 4]. Thus it plays an important role in the immune reactions and exerts a proliferative effect on human keratinocytes by binding some specific sites. It stimulates the synthesis of IFN-gamma and IL-2 by Th1 lymphocytes and also activates Th2 lymphocytes with autoantibody production [5]. Hyperprolactinemia has been linked to NK cell activation and Th1-type cytokine induction in chronic inflammation [6].

Psoriasis is a chronic inflammatory skin disease which is characterized by well-defined red, scaly plaques and these plaques are typically located on the scalp, knee, or elbows [7]. The main pathological features of these skin lesions are keratinocyte hyperproliferation and loss of differentiation, inflammatory cell infiltration, and vascular changes [8, 9]. Looking into the important

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fact that keratinocyte hyperproliferation is a prominent feature of psoriasis, and prolactin has proliferative effect on human keratinocytes, it can be stated that this hormone may play some role in the pathogenesis of the disease [10].

Vitiligo is a chronic acquired depigmenting disorder resulting from the lack of melanocytes from the basal epidermal layer, has a prevalence of 1% in the world population. It is multifactorial in its etiology. Several theories have been proposed in a trial to explain this complex disease, including the autoimmune and the neuroendocrine theories [11].

Alopecia areata is a T-cell-mediated autoimmune disease which is triggered or exacerbated by stress in patients with a genetic predisposition [12–14]. Prolactin acts on skin, and specially scalp hair follicles as these are both its direct extramammary targets and extrapituitary sources [15]. Most important cytokine here is the IFN-c whose expression is altered in alopecia areata through Th1 mediated response.

Several studies showed the clinical significance of prolactin in various skin diseases with different results [16]. Therefore, in this study, we aim for further investigations to determine the proper role of serum prolactin in the pathogenesis of psoriasis, vitiligo and alopecia areata.

We aim to estimate serum prolactin values in patients of psoriasis, alopecia areata and vitiligo and compare it with healthy controls and also evaluate the correlation between serum prolactin levels and severity of the diseases.

Materials and methods

This case–control study was conducted at the Biochemistry department in coordination with Dermatology department at Gauhati Medical College and Hospital, Guwahati, Assam from the time period of 1st February, 2022 to 31st August 2023. The study protocol was approved by the Institutional ethical committee. 200 subjects were enrolled in the study having age group from 15 to 47 years. Among them 150 are patients, suffering from psoriasis, vitiligo and alopecia areata, 50 in each group and 50 age and gender-matched healthy controls. All study participants including all patients and healthy subjects gave their written informed consent after explaining the nature and purpose of the study to them.

Inclusion criteria: Our patients were selected among who attended the Dermatological OPD of a tertiary care hospital and were clinically diagnosed of psoriasis, vitiligo and alopecia areata by a consultant Dermatologist based on clinical findings. From healthy volunteers controls were randomly selected who were matched with the patients in terms of gender and age. All the participants gave the written informed consent and filled up a questionnaire about their demographic data and dermatological and medical history.

Exclusion criteria: Those patients who have some other autoimmune or inflammatory disorders, who were on either topical or systemic treatment for one month prior to blood collection which could alter the levels of prolactin (e.g., psychotropic drugs, antidepressants, thyroid hormones, glucocorticoids, and estrogens or contraceptives) were excluded from study. Also pregnant and lactating women and patients having other medical conditions such as thyroid disorders, renal and/or hepatic failure are excluded.

Sample collection and testing

The 5 ml venous blood samples were taken in the morning hours, between 08:00 and 09:00 am from each patient and controls in a clot vial. Avoidance of exercise before sample collection was assured. The blood sample was centrifuged at 3000g for 10 min, and then serum was taken and stored at temperature −20°C.

Using a standard kit (Prolactin ELISA kit 96Test/Box—BeneSphera™), serum prolactin levels were estimated in all the samples by using direct ELISA (Enzyme linked immunosorbent assay) method.

Psoriasis was graded for severity based on the PASI (Psoriasis area and severity score) score, as the patients presented at the time of blood collection. The patients were divided into three groups based on the severity of the disease as 1) Mild (PASI 0-5) 2) Moderate (PASI 6 - 10) 3) Severe (PASI >10). Vitiligo patients were divided into two groups as 1) Active disease and 2) Stable disease depending on the progression of the lesions and the appearance of new lesions in the last three months. The severity of alopecia areata was determined by severity of alopecia tool (SALT) score. The patients are divided into three groups as 1) Mild (SALT score of 1-20) 2) Moderate (SALT score of 21-49) and 3) Severe (SALT score of 50 to 94). Comparative analyses were carried out between age, gender, severity and serum prolactin levels. All data were analyzed by the online tool Open epi [17]. t test, ANOVA and Chi square tests are done for various comparison. A p value ≤0.05 was considered significant.

Results

Among the 50 patients of psoriasis, 24 are female and

26 are male patients. Average age of these patients is 35.6 ± 10 years. Among total 50 patients of vitiligo, 27 are females and 23 are male patients. Their average age is 34.5±8 years. Similarly, among 50 patients of alopecia, 26 are females and 24 are males. Average age of these patients is 32.1 ± 7 years. Among 50 controls, 28 are females and 22 are males. Their average age is 34.9 ± 8 years. ANOVA and chi square tests are done to evaluate any statistical significance among the parameters. No significant difference is seen in patients age and gender when compared to control group (p value >0.05) (Table1).

Table 1: The demographic characteristics of patients and controls.

Age and gender of different groups	*Psoriasis (n=50)*	*Vitiligo (n=50)*	*Alopecia areata (n=50)*	*Control subjects (n=50)*	*Statistics*
Age+ SD	35.6 +10 years	34.5+8 years	32.1+7 years	34.9+8 years	ANOVA values F=1.6673 d.f=199 p value=0.1753
Female gender no	24	27	26	28	Chi-square value Chi Square=0.7018 d.f=3 p value=0.8728
Male gender no	26	23	24	22	

As shown in Table 2, the mean serum prolactin of control subjects was 11.1± 4.5 ng/ml. The mean serum prolactin of psoriasis patients was 19.2 ± 6.7 ng/ml which was statistically significantly higher than serum prolactin of control subjects (p value <0.05). Patients with vitiligo had a mean serum prolactin of 16.4 ± 6.2 ng/ml which was significantly higher than the serum prolactin value of the control subjects (p value <0.05). The mean serum prolactin of Alopecia areata was 20.6 ± 6.9 ng/ml which was significantly higher than the serum prolactin of the control subjects (p value <0.05).

Table 2: Serum prolactin in patients and control groups.

Subjects	*Psoriasis*	*Vitiligo*	*Alopecia*	*Control*
Serum prolactin	19.2 ± 6.7 ng/ml	16.4 ± 6.2 ng/ml	20.6 ± 6.9 ng/ml	11.1 ± 4.5 ng/ml
p value	0.006	0.03	0.003	

Psoriasis patients are divided into three groups depending on the severity of disease as mild (18 no), moderate (10) and severe (22) psoriasis. The average prolactin value of mild, moderate and severe psoriasis is 12.39 ± 2.95 ng/ml, 20.6 ± 1.53 ng/ml and 23.99 ± 5.06 ng/ml respectively. ANOVA statistics are done. As shown in Table 3, prolactin value is increased across the severity grades of psoriasis which is statistically significant (F=45.1898, d.f.=49, p value <0.0001) (Table 3).

Table 3: Serum prolactin value in different grades of severity of psoriasis.

Types of psoriasis (depending on PASI score)	*No of patients*	*Serum prolactin value (mean ±SD)*	*ANOVA values*
Mild psoriasis	18	12.39 ± 2.95 ng/ml	F value=45.1898 p value <0.0001 d.f. =49
Moderate psoriasis	10	20.6 ± 1.53 ng/ml	
Severe psoriasis	22	23.99 ± 5.06 ng/ml	

Vitiligo patients are divided into active disease and stable disease depending on the activity of disease. 26 no of patients (52%) had active disease and 24 (48%) number of patients had stable disease. Average prolactin value of active and stable disease group are 21.23 ± 3.16 ng/ml and 11.19 ± 3.94 ng/ml respectively. Prolactin value is increased in active disease group when compared to stable disease group but it is not statistically significant (p value >0.05) (Table 4).

Alopecia areata patients are divided into three groups as mild (15 no), moderate (17 no), and severe (18 no) depending on severity of the disease. Average prolactin value of mild, moderate and severe groups are 11.22 ± 0.64 ng/ml, 21.66 ± 2.51 ng/ml and 27.49 ± 1.49 ng/ml respectively. As shown in table 5, prolactin value is increased across the severity grades of Alopecia areata which is statistically significant (F=357.25, d.f.=49, p value <0.0001) (Table 5).

Table 4: Serum prolactin value in different groups of vitiligo according to severity.

Types of vitiligo	*No. of patients*	*Serum prolactin value (mean ±SD)*	*p value*
Active disease	26	21.23 ± 3.16 ng/ml	0.28
Stable disease	24	11.19 ± 3.94 ng/ml	

Table 5: Serum prolactin value in different grades of severity of alopecia areata.

Types of alopecia areata (depending on SALT score)	*No. of patients*	*Serum prolactin value (mean ±SD)*	*ANOVA values*
Mild	15	11.22 ± 0.64 ng/ml	F= 357.25 d.f = 49 p value <0.0001
Moderate	17	21.66 ± 2.51 ng/ml	
Severe	18	27.49 ± 1.49 ng/ml	

Discussion

Although prolactin is basically known for its lactogenic properties, it is also an immunomodulatory hormone [18]. Prolactin functions as a neuroendocrine modulator of the skin immune system and epithelial cell proliferation by forming a "prolactin-circuit" between the the skin and central nervous system [3, 4]. Prolactin binds to some specific receptors in the skin which modulate release of cytokine in the skin and also stimulate mesenchymal cells to secret somatomedin. So, its increased level in serum may play an important role in the hyper proliferation of keratinocytes, which is the hallmark of the pathophysiological process of psoriasis [19]. Also, for proper functioning of immunocompetent T and B lymphocytes, normal levels of prolactin are necessary. Psoriasis is a T-cell-mediated autoimmune skin disease which is characterized by abnormal differentiation and hyperproliferation of keratinocytes, changes to the dermal capillaries and presence of some inflammatory cell infiltrate [20]. There is evidence from literature that an association between psychological stress and initiation and/or exacerbation of psoriasis exists, which has recently been the focus of systemic reviews and one meta-analysis [21-23]. Much of the existing literature points towards the involvement of interleukin 6 (IL-6) along the brain–skin axis [21, 24]. Therefore, taking prolactin's role as a stress hormone [21, 25], it may be stated that prolactin acts as an important mediator of the effect of stress on psoriasis. Lee et al. [26] stated that circulating prolactin levels are higher in patients with psoriasis, and also confirmed that prolactin levels may correlate with psoriasis severity. In our study serum prolactin is significantly increased in psoriatic patients when compared to controls. But in contrast, some studies like Gorpelioglu et al. did not find any association between serum prolactin levels and psoriasis along with its activity [20].

Alopecia areata is a disease characterized by some areas of hair loss which is nonscarring and ranging from a single oval patch to multiple patches. High serum prolactin levels are observed in alopecia areata patients [27]. In our study, serum prolactin levels were significantly higher in patients when compared with controls (P <0.05). This agrees with the results of Elsherief et al. [28] and Ganzetti et al. [29] and Shawky et al [30]. Gilhar et al. [12], found that there was no statistically significant difference in prolactin level between patients and control. Similarly Burak et al. [31] and El Tahlawi et al [32] subsequently showed same finding. The expression of the PRLR (Prolactin receptor) was significantly increased in patients with alopecia areata, and its expression also correlated with disease severity. The PRLR belongs to the type I cytokine receptor family. The PRLR dimerized following prolactin binding and signals via the JAK2/STAT5, Ras-Raf-MAPK and PI3K/Akt/mTOR pathways. Interestingly, several JAK inhibitors, have also shown promise in the treatment of alopecia areata [33]. Vitiligo is a chronic acquired depigmenting disorder which results from the loss of melanocytes from the basal epidermal layer of skin, with a prevalence of ?1% in the world population. It is characterized by milky white macules and patches [34]. Previous studies assessed the serum level of prolactin, and results were contradictory [35-37]. Local production of prolactin was suggested to have a higher correlation with the disease [36]. Prolactin promotes autoimmunity and it also has multiple immunostimulatory effects [6], which plays an important role in vitiligo. Prolactin improves the survival and also mediate proliferation and differentiation of T lymphocytes [38]. Prolactin stimulates both humoral and cell-mediated immune responses. In vitiligo antigen specific CD8+ T cells promote the destruction of melanocytes in skin [39]. In addition, prolactin increases the synthesis of IL-6 and IL-2, which play a crucial role in melanocytic cytotoxicity in patients with vitiligo [40]. Moreover, prolactin increases the synthesis of tumor necrosis factor alpha (TNF-α), which stimulates nuclear factor kappa B and TNF apoptosis-inducing ligand (TRAIL), which induces melanocyte apoptosis. Bozkurt et al stated that prolactin has no role in the disease process of vitiligo [41]. Also Sanad et al found no correlation between prolactin value and pathogenesis of vitiligo [42]. In our study, serum prolactin levels in patients with vitiligo were significantly higher than that of the control subjects, with no significant association with disease activity.

Limitation of the study: This study was conducted in a tertiary care hospital of Assam, in a limited number of patients. Therefore, data from the study do not precisely represent the disease profile of the community and is inadequate to provide conclusive data. Further studies with a larger sample size and a multicentric approach may be helpful in elucidating the proper role of Prolactin in dermatological diseases.

Conclusion

We can conclude that there are significantly increased levels of prolactin in patients with psoriasis, alopecia areata and vitiligo when compared to controls. Moreover, the levels of prolactin were correlated with the severity of psoriasis and alopecia areata. This leads to the assumption that prolactin may play an important role in the pathogenesis of these diseases; also prolactin may serve as a biochemical marker for disease severity and activity.

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Conflicts of interest

Authors declare no conflicts of interest.

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