ORIGINAL RESEARCH PAPER

Dermatology

THYROID FUNCTION IN PSORIATIC PATIENTS - AN OUTPATIENT REVIEW FROM KARAIKAL

KEY WORDS: Psoriasis, Thyroid disorders.

Dr. Sivakumar Sivasubramaniam Department Of Dermatology, Venerology & Leprosy,vinayaka Mission's Medical College And Hospital, Vinayaka Mission Research Foundation (Deemed to be University), Karaikal.

Dr. Ambujam Govindasamy Department Of General Surgery, - Vinayaka Mission's Medical College And Hospital, Vinayaka Mission Research Foundation (Deemed to be University), Karaikal.

Dr.Tony Kuncheria* Department Of Dermatology, Venerology & Leprosy,vinayaka Mission's Medical College And Hospital, Vinayaka Mission Research Foundation (Deemed to be University), Karaikal. *Corresponding Author

Dr. S.S.arulvasan Department Of Dermatology, Venerology & Leprosy,vinayaka Mission's Medical College And Hospital, Vinayaka Mission Research Foundation (Deemed to be University), Karaikal.

ABSTRACT

INTRODUCTION: Psoriasis is a chronic papulosquamous disorder with remissions and exacerbations. The disease is believed to be multifactorial with both genetic and environmental factors playing a role in its development. It is associated with several comorbidities, endocrine abnormalities have been shown to play an important role in the pathogenetic mechanisms as well as progression of psoriasis.

AIM: To study the association between incidence and thyroid hormone levels in psoriasis patients.

MATERIALS AND METHODS: Total 135 psoriatic patients (62 males and 73 females) and 100 age and sex matched healthy controls were selected for the study. Free T3, Free T4 and TSH were evaluated by chemiluminescence assays.

RESULTS: Mean age of the control was 47±2 years and the psoriatic patients was 48±1.5 years. Incidence of the disease was higher in females as compared to males. In males 6 were hypothyroid, 55 were euthyroid and 1 was hyperthyroid whereas, in females 7 were hypothyroid, 63 were euthyroid and 3 were hyperthyroid

CONCLUSION: Thyroid disorders are very common in psoriasis patients. Several hormones like thyroid hormones and Corticotropin-Releasing factor are involved in the pathophysiology of psoriasis. Evaluation of thyroid function tests at the earliest and initiation of pharmacological intervention as soon as possible may prevent worsening of the disease and its associated comorbidity.

INTRODUCTION

Psoriasis is undoubtedly one of the most long standing and intriguing skin disease known to mankind. Psoriasis is a T-cell mediated disease characterized by activation of Antigen Presenting Cells along with activation and expansion of Th-1 and Th-17 cells. The worldwide prevalence is about 2%, but varies according to regions [1]. It shows a lower prevalence in Asian and some African populations, and up to 11% in Caucasian and Scandinavian populations [2]. Psoriasis has been associated with insulin resistance, thyroid dysfunction, cardiovascular disease, atherosclerosis, Crohn's disease, depression, skin cancer and non-alcoholic fatty liver disease (NAFLD) [3-5]. Skin is one of the most important site of synthesis and metabolism of several neuropeptides including components of the Hypothalamic-Pituitar y-Adrenal (HPA) and Hypothalamic-Pituitary-Thyroid (HPT) axis and also a source of vitamin D [6]. Any derangement of these axis may lead to or may be an indicator of various skin diseases.

Neuropeptides and hormones synthesized in the skin not only act locally in paracrine or autocrine fashion but may also diffuse to the blood or activate dermal nerve endings and thereby influence central organs including the brain. Since, thyroid hormone receptors are expressed in human skin, and the hormones exert their effects on epidermal proliferation and differentiation, they have been hypothesized to play a role in the pathogenesis of psoriasis [7]. Hormomal factors, Genetic, environmental and immune defect take part in the pathogenesis of autoimmune diseases. Various hormones like thyroid stimulating hormone, cortisol, prolactin and thyroid hormones in pathogenesis of psoriasis has been studied previously [8,9]. The severity of the disease correlated with levels of thyroid hormones, since like prolactin, the thyroid hormone receptors are expressed in the skin [10] and their levels change during the active phase of disease and alleviation of the disease by anti-thyroid therapy [11]. Cortisol is involved in the mediation of psycho-emotional stress, and cortisol response to stress is diminished in psoriasis as shown by Evers and colleagues [12]. In this study, we have investigated the prevalence of thyroid disorders in patients who are suffering from psoriasis.

MATERIALS AND METHODS

In our hospital based cross-sectional study, a total of 152 people in the age group 18-60 years were included after obtaining ethical clearance from the Institutional Ethical Committee. Individuals attending the Out-patient Department of Dermatology,Venereology and Leprosy at Vinayaka Missions Medical College, Karaikal, Puducherry, India, were selected within the time period from June 2019 to June 2021. Written informed consent was obtained from all participants of the study. Total 135patients (62 males and 73 females) diagnosed mild psoriasis (defined as percentage of body surface area (BSA) ≤10), were selected as study group(Fig:1) and 100 age and sex matched healthy individuals (38 females and 62 males) were selected as controls. Exclusion criteria for participants of the study consisted of the following conditions: consumption of drugs that affected thyroid hormone levels (phenothiazines, H2 blockers, anti-depressants, butyrophenones, antipsychotics, oestrogens, reserpine, methyldopa, metoclopramide, verapamil, etc.,), pregnancy or lactation, menstrual abnormalities, any condition that could interfere with the evaluated hormone levels like pituitary, hypothalamic, adrenal or renal diseases, head trauma, and any malignancy or psychiatric or physical condition that could hamper participation in the study.

Five milliliters of fasting blood sample was collected under aseptic conditions from the individuals, centrifuged and immediately analysed or stored at -20°C. All estimations were

carried out on auto-analyser (Siemens dimension RxL Max). Thyroid profile consisting of free tri-iodothyronine (FT3), free thyroxine (FT4) and Thyroid-Stimulating Hormone (TSH) was estimated by chemiluminescence assay on Siemens Centaur CP.

According to the serum TSH levels, participants were classified as having hypothyroidism (>5.5 mIU/L), euthyroid status (0.4–5.5 mIU/L) and hyperthyroidism (<0.4 mIU/L). Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) Software, Version 20. Student-unpaired t-test was calculated to determine significance of the results obtained.

The level of significance based on p-value is as follows:
p > 0.05 – Non-significant
p < 0.05 – Significant
p < 0.01 – Highly significant

RESULTS

The demographic data of the study population is depicted in [Table-1]. In our study population, the mean age of control group was 47±2.0 years and the psoriatic group was 48±1.5 years. Incidence of the disease was more in females as compared to males [Table-2]. [Table-2] also shows the distribution of cases according to TSH levels into hypothyroid, euthyroid and hyperthyroid groups. The relationship between thyroid hormones and psoriasis is shown in [Table-3]. In males 6 were found to be hypothyroid, 55 euthyroid and 1 with hyperthyroid whereas in females 7 were found to be hypothyroid, 63 euthyroid and 3 were hyperthyroid. There was no significant differences in the values of FT3, FT4 and TSH hormones among the control group and patient group.

Table-1 : Demographic data of study population

	Cases	Controls
Age(years)	48±1.5	47±2.0
Males	62	38
Females	73	62
SBP (mmhg)	126±1.2	128±1.1
DBP (mmhg)	90±0.9	88±1.1

Table-2: Prevalence of thyroid disorders in psoriasis patients.

	Hypothyroid	Euthyroid	Hyperthyroid
Males(n=62)	6(9.6%)	55(88.7%)	1(1.6%)
Females(n=73)	7(9.5%)	63(86.3%)	3(4.1%)

Table-3 :Thyroid hormone levels in euthyroid psoriatic patients.

	Controls	Euthyroid Cases	p-value
FT3 (pg/ml)	2.97±0.69	3.12±0.98	0.30
FT4 (ng/ml)	1.1±0.24	1.3±0.4	0.07
TSH	3.5±1.3	2.6±1.1	0.52

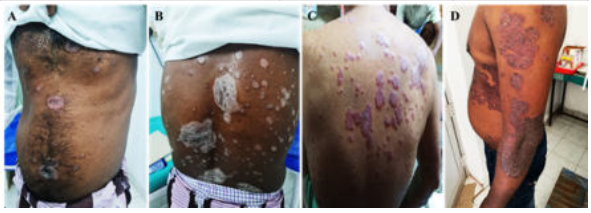

Figure 1(A,B,C,D) – Multiple erythematous to hyperpigmented plaques present over the anterior and posterior aspects of trunk, forearms with silvery white or micaceous scales.

DISCUSSION

Our objective was to evaluate the relationship between the disease and thyroid hormone levels in patients diagnosed with psoriasis. Incidence in females was higher compared to males. In males 6 were found to be hypothyroid, 55 euthyroid and 1 with hyperthyroid whereas in females 7 were found to be hypothyroid, 63 euthyroid and 3 were hyperthyroid. There was no significant differences in the values of FT3, FT4 and TSH hormones among the control group and patient group. It can be due to the small sample size. These findings are similar to a study by Robati RM et al., who did not observe any statistically significant difference in the mean T3, T4 and TSH levels between psoriatic patients and controls [7]. Arican O et al., also observed no differences in serum levels of total T3, free T4 and TSH between cases and controls [8]. Even though there are few studies shown to have high prevalence of thyroid autoimmunity in patients with psoriatic arthritis, Gul U et al., did not find any statistically significant differences in the levels of anti-thyroglobulin and anti-thyroid peroxidase antibodies [13]. T3 has a major role in the regulation of cell growth and differentiation [14]. Propylthiouracil, an anti-thyroid drug, may interfere with keratin synthesis by binding to nuclear T3 receptors [15]. One of the factors for the induction of autoantibodies in psoriasis might be the unique neo-epitopes generated by structural alterations in albumin and thyroid antigens by Reactive Oxygen Species (ROS) [16].In a similar study conducted, compared to patients with mild psoriasis, patients with severe psoriasis demonstrated increased TSH levels and positive autoantibody titres [17]. A significantly higher prevalence of thyroid autoimmunity (positive AbTPO, hypoechoic thyroid) was observed in men and women with psoriatic arthritis and of sub-clinical hypothyroidism in women with psoriatic arthritis than in the general population [4]. The diabetes characteristics when studied in psoriasis patients were clearly worse compared to patients without psoriasis. Prevalence of comorbid conditions and depression were higher and more aggressive diabetes therapy was required [18]. The analysis of the U.S. National Health and Nutrition Examination Survey database [19] revealed that patients with thyroid diseases had a significantly increased risk of having psoriasis. But after adjusting for confounding variables, this association was not significant. Levels of TSH in patients with active psoriasis were significantly lower than those without active disease. Physiological response to stress in healthy individuals is different from that in patients with psoriasis, as demonstrated by alterations in the HPA axis and sympathetic– adrenal–medullary system function. Psychological stress plays an important role by redistribution of leucocytes with increased trafficking of inflammatory cells into the skin, which may exacerbate psoriasis [20]. Chronic inflammatory property of psoriasis can predispose to an association with other inflammatory diseases like cardiovascular diseases and metabolic disorders. The cardiovascular comorbidities and cardiovascular risk according to the Framingham risk score were both increased in patients with psoriasis [21].The risk of metabolic syndrome and obesity was increased in psoriasis but there was no consistency across studies for diabetes, hypertension and dyslipidaemia [22]. Acute stress leads to increased skin vascular permeability and inflammation through mast cell activation by Corticotropin-Releasing Hormone (CRH) both in rodents and humans as shown by Crompton and colleagues [23]. Hormones like Corticotropin-Releasing Hormone are hypothesized to be involved in the pathophysiology of skin diseases since CRH and CRHR-1 are both expressed in human skin [24]. Several other hormones influence the clinical manifestations of psoriasis, including glucocorticoids, epinephrine, thyroid hormones, and insulin although sex hormones and prolactin have a major role in psoriasis pathogenicity [25]. A change in thyroid hormone levels has been reported during the active phase of psoriasis and an improvement in psoriasis was seen in patients with hyperthyroidism [7,8]. Propylthiouracil have been proven to be effective in treating psoriasis stating that there may be an association between psoriasis and thyroid function [26]. The study can be done on a large sample size and the levels of Total T3 and Total T4 can be studied along with anti TPO antibodies.

CONCLUSION

Psoriasis is a chronic papulosquamous disorder that has believed to be multifactorial with both genetic and environmental factors playing a role in its development and

its associated with various endocrine dysfunctions. From our interpretation, we conclude that the prevalence of thyroid disorders in psoriatic patients is high although there was no statistically significant difference was noted in the levels of thyroid hormones between healthy individuals and patients with psoriasis. Patients have to be screened for thyroid abnormalities and thus prevent worsening of the disease course. Further studies are required to be carried out on a larger population to establish statistical significance.

ACKNOWLEDGEMENT

We sincerely thank the dean and staffs of tertiary care centre, Karaikal for their immense support in the completion of this study.

Conflict Of Interest

None

REFERENCES

[1] Christophers E. Psoriasis—Epidemiology and clinical spectrum. *Clin. Exp. Dermatol.* 2001;26:314–320. doi: 10.1046/j.1365-2230.2001.00832.x.
[2] Parisi R., Symmons D.P., Griffiths C.E., Ashcroft D.M. Global epidemiology of psoriasis: A systematic review of incidence and prevalence. *J. Investig. Dermatol.* 2013;133:377–385. doi: 10.1038/jid.2012.339.
[3] Gyldenlove M, Storgaard H, Holst JJ, Vilsboll T, Knop FK, Skov L. Patients with psoriasis are insulin resistant. J Am Acad Dermatol. 2015;72(4):599-605.
[4] Antonelli A, Sedie AD, Fallahi P, Ferrari SM, Maccheroni M, Ferrannini E, et al. High prevalence of thyroid autoimmunity and hypothyroidism in patients with psoriatic arthritis. J Rheumatol. 2006;33(10):2026-28.
[5] Isabela GRB, Flávia VB, Bernardo G, Eugênio MAG. Comorbidities and cardiovascular risk factors in patients with psoriasis. An Bras Dermatol. 2014;89(5):735-44.
[6] Zmijewski MA, Slominski AT. Neuroendocrinology of the skin. An overview and selective analysis. Dermatoendocrinol. 2011;3(1):03-10.
[7] Robati RM, Toossi P, Rahmati-Roodsari M, Khalilazar S, Abolhasani E, Namazi N, et al. Association of psoriasis severity with serum prolactin, thyroid hormones, and cortisol before and after treatment. Scientific World Journal. 2013;2013:921819.
[8] Arican O, Bilgic K, Koc K. The effect of thyroid hormones in psoriasis vulgaris. Indian J Dermatol Venereol Leprol. 2004;70(6): 354-56.
[9] Zangeneh FZ, Fazeli A. The significance of stress hormones in psoriasis. Acta Medica Iranica. 2008;46(6):485-88.
[10] Ribeiro RCJ, Apriletti JW, West BL, Wagner RL, Fletterick RJ, Schaufele F, et al. The molecular biology of thyroid hormone action. Annals of the New York Academy of Sciences. 1995; 758:366-89.
[11] Elias AN, Dangaran K, Barr RJ, Rohan MK, Goodman MM. A controlled trial of topical propylthiouracil in the treatment of patients with psoriasis. Journal of the American Academy of Dermatology. 1994;31(3):455–58.
[12] Evers AW, Verhoeven EW, Kraaimaat FW, Jong EM, Brouwer SJ, Schalkwijk J, et al. How stress gets under the skin: cortisol and stress reactivity in psoriasis. Br J Dermatol. 2010;163(5): 986-91.
[13] Gul U, Gonul M, Kaya I, Aslan E. Autoimmune thyroid disorders in patients with psoriasis. Eur J Dermatol. 2009;19:221-23.
[14] Wagner RL, Apriletti JW, McGrath ME, West BL, Baxter JD, Fletterick RJ. A structural role for hormone in the thyroid hormone receptor. Nature. 1995;378:690-97.
[15] Takagi S, Hummel BC, Walfish PG. Thionamides and arsenite inhibit T3 binding to hepatic nuclear receptor. Biochem Cell Biol. 1990;68:616-21.
[16] Al-Shobaili HA, Ahmed AA, Rasheed Z. Recognition of oxidized albumin and thyroid antigens by psoriasis autoantibodies - A possible role of reactive-oxygen-species induced epitopes in chronic plaque psoriasis. Saudi Med J. 2015;36(12):1408-19.
[17] Zoabi A, Ziv M, Rozenman D, Lovoshitski R. Prevalence of thyroid abnormalities among psoriatic patients. Harefauh. 2012;151(10):566-69,605-06. HYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/23316662" \o "Harefuah."Harefuah.
[18] Schwandt A, Bergis D, Dapp A, Ebner S, Jehle PM, Köppen S, et al. Psoriasis and diabetes: a multicenter study in 222078 type 2 diabetes patients reveals high levels of depression. Journal of Diabetes Research. 2015, Article ID 792968 DOI:10.1155/2015/792968.
[19] Lai YC, Yew YW. Psoriasis and thyroid profile: Analysis of the U.S. National Health and Nutrition Examination Survey database. Indian J Dermatol Venereol Leprol. 2016;82 (3):310-12.
[20] Hunter HJ, Griffiths CE, Kleyn CE. Does psychosocial stress play a role in the exacerbation of psoriasis? Br J Dermatol. 2013;169(5):965-74.
[21] Baeta IGR, Bittencourt FV, Gontijo B, Goulart EMA. Comorbidities and cardiovascular risk factors in patients with psoriasis. An Bras Dermatol. 2014; 89(5):735-44.
[22] Paul C, Gourraud PA, Bronsard V, Prey S, Puzenat E, Aractingi S, et al. Evidence-based recommendations to assess psoriasis severity: systematic literature review and expert opinion of a panel of dermatologists. J Eur Acad Dermatol Venereol. 2010;24(2):02-09.
[23] Crompton R, Clifton VL, Bisits AT, Read MA, Smith R, Wright IM. Corticotropin-releasing hormone causes vasodilation in human skin via mast cell dependent pathways. J Clin Endocrinol Metab. 2003;88:5427-32.
[24] Slominski A. On the role of the corticotropin-releasing hormone signalling system in the aetiology of inflammatory skin disorders. Br J Dermatol. 2009;160(2):229-32.
[25] Iulia IR, Anne MC, Mihaela EM, Remus IO. The role of hormones in the pathogenesis of psoriasis vulgaris. Clujul Medical. 2016;89(1):11-18.
[26] Chowdhury MM, Marks R. Oral propylthiouracil for the treatment of resistant plaque psoriasis. J Dermatolog Treat. 2001; 12:81-85.