



Cutaneous Manifestations of Hypothyroidism: A Clinical Study

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Abstract

Hypothyroidism commonly has dermatologic manifestations. The endocrinopathies that may have cutaneous findings, in hypothyroidism the physician most likely see the skin reflect the functional capacity of the thyroid gland. The aim of the study was to find out the cutaneous manifestations of the hypothyroid patients in tertiary care hospital of Bangladesh. The descriptive type of cross-sectional study was conducted in the Department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University, Dhaka, during the period of July 2017 to June 2018. In this study, 100 patients were enrolled who have skin complaints and symptoms of hypothyroidism and parameters were noted regarding history, cutaneous symptoms and signs. Among the 100 patients, 22% were male and 78% were female with mean age 41 yrs. Most common cutaneous symptom was pruritus (76%), followed by dry skin (72%), diffuse hair loss (44%), course/rough skin (32%), puffy oedema (27%), nail changes (23%), decrease sweating (6%) and delayed wound healing (4%). The most usual cutaneous sign was xerosis (72%), followed by hair changes (56%), alteration in skin texture (53%), pigmentary changes (32%), oedematous changes (29%) and keratoderma (24%). The most conventional pigmentary change was vitiliginous change (19%), followed by melasma (6%), periocular pigmentation (4%) and diffuse hyperpigmentation (3%). Present study also assessed nail and hair changes in those patients. Common nail change was onycholysis (14%), followed by leuconychia (11%), brittle nail (9%), cuticle loss (6%) and vertical striations (1%). And usual hair change was diffuse hair loss (29%), followed by thin scalp hair (19%), both thin scalp hair and hair loss (11%), madarosis (6%) and canitis (2%). Considering high prevalence of skin, hair and nail changes in patients with hypothyroidism, early diagnosis and treatment can be helpful to reduce disease burden in Bangladesh.

Introduction

Thyroxine (T4) and Tri-iodothyronine (T3) which are secreted from thyroid gland; in which Thyroxine is inactive and is converted into tri-iodothyronine by the tissues or organs that need it. Insufficient amount of thyroid hormone slows down the body's metabolism and this is manifested by changes in various tissues. Around 80% of tri-iodothyronine is derived from thyroxine in the tissues and the remainder coming directly from the thyroid gland [1,2]. Usually thyroid hormone in the blood is bind with proteins. The free fraction of T4 and T3 in the blood is therefore a more useful measure of thyroid hormone levels and specified as free T4 (FT4) and free tri-iodothyronine (FT3) [3].

Hypothyroidism is defined as insufficient levels of thyroid hormone or target cell inhibition of the hormone activity. It is classified as congenital, primary, secondary and tertiary hypothyroidism [4]. Hypothyroidism is identified by TSH (thyroid stimulating hormone) levels <4.2 IU/ml, T3 <3.95 pmol/l and T4 <12 pmol/l [5].

Thyroid Hormone Disorder (THD) is associated with a wide range of diseases in human body. It affects all organic systems of the body including the skin. Thyroid hormones are instrumental in regulating the health of skin. When it becomes underactive or overactive a variety of skin problems have occurred. Hypothyroidism affects

all age groups and causes different symptoms and its cutaneous manifestations are often varied among patients. These cutaneous manifestations may occur due to the decreased thyroid hormone levels or the presence of thyroid autoantibodies that interact with skin components [6]. Cutaneous manifestations may include dry coarse skin, hair loss, pruritus, hypohydrosis, yellow skin, brittle nails, loss of cuticle, vertical striations, etc. [7]. The cutaneous changes seen in hypothyroidism are due to slow metabolism or due to dermal accumulation of mucopolysaccharides which bind water in the tissue, leading to myxedematous appearance. About 25-40% patients show an atypical presentation that prevents early diagnosis and treatment [8].

In Primary Autoimmune Hypothyroidism (PAIH) skin manifestations commonly associated with a number of skin diseases (presence of autoantibodies even in a euthyroid state) and others directly dependent on thyroid function. In the former group, the frequency of thyroid dysfunction is variable, occurring in 40-70% of patients with melanin spots in Centro-facial location, in 42% of males and 62% of females with vitiligo, in 50% of patients with chronic mucocutaneous candidiasis, in 34% with herpetiform dermatitis, in 8% of delayed hypersensitivity reactions, and in 8% of patients with alopecia areata. Autoimmune thyroid disease is commonly associated with pemphigus and other bullous diseases, systemic lupus erythematosus, scleroderma, reticular erythematous mucinosis, anemia, herpes gestationis, dermatomyositis, polymyositis etc and atopic manifestations such as urticaria, dermatographism and angioedema [9].

Skin Changes Directly Dependent on Thyroid Function Include

- a) Typically dry, pale, and cold skin due to decreased capillary flow, sweating, and thermogenesis; palmoplantar keratoderma, which may become generalized and convert into xeroderma, but dramatically responds to replacement therapy [10].
- b) Keratosis pilaris of follicles leading to permanent alopecia, thinned hair, and lateral loss of eyebrows. It may be associated with livedo reticularis in the limbs.
- c) Generalized myxedema or cutaneous mucinosis, due to the accumulation of hyaluronic acid and glycosaminoglycans in the skin. This causes the characteristic hypothyroid facies: thick skin, periorbital edema, and mucosal thickening with dysphonia. There may be periocular hyperpigmentation (Jellinek's sign) and hypercarotenemia due to the lack of hepatic metabolism of carotene, which accumulates in the corneal layer, is excreted in sweat, and becomes deposited in areas rich in sebaceous glands [11].
- d) An uncommon lesion related to primary hypothyroidism and autoimmune polyglandular syndrome type I, erythema annulare centrifugum, consists of a ring-shaped eruption with central clearing occurring in the buttocks, thighs, and proximal part of the arms. Histological examination shows a perivascular lymphocyte infiltrate in the middle and deep dermis.

- e) Sometimes hypothyroidism associated with Granuloma annulare and oral lichen planus. So, the skin presents important external markers associated with thyroid disease and gives signal to dermatologists to investigate and diagnose thyroid disorder [11]. But the cutaneous manifestations of the thyroid disorders remain under-diagnosed in the rural part of the country due to illiteracy, lack of access to medical care, poverty, negligence among the patients [12].

Iodine is the most important element for the production of thyroid hormone. Almost one-third of the world's population lives in the iodine deficiency areas, where the prevalence rate can be as high as 80% [13]. Populations live in mountainous areas in South- East Asia, Latin America and Central Africa have high risk to develop this disease [7,14]. Bangladesh lies in an iodine deficiency belt where the prevalence of THD was too high [15,16]. From a report it was observed that more than 50 million Bangladeshis are suffering from thyroid disease, with 30 million not even aware of their condition. Female's faces 10 times higher and more risk to develop this disease than males. In Bangladesh around 20-30% of women suffered from some form of thyroid disease and the situation is worse in rural part of the country [17].

Some skin diseases may be the first symptoms of thyroid diseases but there is no available data till date. Therefore this study had been planned to find out the cutaneous manifestation in patients with hypothyroidism in a tertiary care hospital of Bangladesh.

Material and Methods

Ethical Considerations

Ethical issues were carefully followed in this study. The research protocol was approved by the IRB (Institutional Review Board) of BSMMU, Dhaka before starting the study. In this study, provision was taken to protect the confidentiality of the participants. Verbal and informed agreement was acquired from the participants by maintaining strict privacy.

Study Populations

This hospital based descriptive clinical study was conducted in collaboration with the Department of Endocrinology of Bangabandhu Sheikh Mujib Medical University. A total of 100 patients were enrolled in the study with age ranged from 14 to 62 years with mean age 41 years. Out of 100 patients 22 (22%) were male and 78 (78%) were female. These patients were evaluated due to presence of any cutaneous manifestation. There was no age limit for inclusion of patients in this study. A detailed medical history regarding to hypothyroidism was exhaled in each case for cutaneous complaints including duration, history of evolution and progression. An informed consent was taken from each patient and the relevant details were recorded and tabulated. A thorough clinical examination i.e. general physical examination, systemic examination and a detailed dermatological examination on regarding site of lesion, type of lesion, number, color, distribution, hair changes, nail changes were carried out in all patients in

adequate daylight. Weight and height of the patients were also measured. The interview included socio-demographic information (age, sex, family status, residence, religion, socio-economic condition, educational level and occupation). Apart from routine laboratory investigations, thyroid function tests (TSH, T3 and T4) were also done and diagnosis result was compared according to normal reference value. Other relevant investigations were done if required and the final diagnosis of dermatological manifestations was made clinically.

Statistical Analysis

Frequencies & percentages were calculated for categorical variables. Mean was calculated for continuous variable age. The prevalence rates of all cutaneous manifestations were calculated. Statistical analysis of the data was performed by appropriate statistical methods using Statistical Package for Social Sciences (SPSS Version 20) and inferences were drawn.

Results

Table 1: Socio-demographic characteristics of the study population (n=100).

Characteristics	Number of respondents	Percentage (%)
Age (Years)		
11-20	3	3
21-30	16	16
31-40	28	28
41-50	37	37
≥50	16	16
Range	(14-62) years	Mean: 41 years
Sex		
Male	22	22
Female	78	78
Male: Female ratio	0.000734954	
Family status		
Nuclear	85	85
Joint	15	15
Socioeconomic condition		
Upper	21	21
Middle	77	77
Lower	2	2
Residence		
Urban	91	91
Rural	9	9
Religion		
Muslim	84	84
Hindu	9	9
Others	7	7
Level of education		
Illiterate	4	4
Primary	26	26
Secondary	26	26
Higher secondary	14	14
Graduate and above	30	30

Table 1 shows the socio-demographic characteristics of the study population. A total of 100 subjects were enrolled in the study. Age ranged from 14 to 62 years. Majority of the subjects were in 41-50 age group, constitute 37% of the study population; followed by 28% in 31-40 age group. Minimum respondents (3%) were in 11-20 age groups. Out of 100 persons there were 22 (22%) male and 78 (78%) female. Male to female ratio was 1:3.5.

Most of the respondents i.e. 85% came from nuclear family and 15% came from joint family. It was found that 91 (91%) respondents

came from urban background and 9 (9%) from rural background. There were 84 (84%) Muslim persons, 9 (9%) hindu and 7(7%) from other religions. This table also shows the educational status of the respondents. Educational status of 26 (26%) respondents were at primary level, 26 (26%) at secondary level, 14 (14%) at higher secondary level and 30 (30%) at graduate and above level. Only 4 (4%) persons were illiterate. Among the 100 respondents, 21 (21%) persons came from upper socioeconomic condition, 77 (77%) from middle and 2 (2%) persons from lower socioeconomic class.

Table 2: Cutaneous symptoms, signs and pigmentary nail & hair change.

Symptoms	≤20 years (n=3)(%)	21-40 (n=44) (%)	41-50 (n=37) (%)	≥50 (n=16) (%)	Total (n=100)
Cutaneous symptoms					
Dry Skin	2(66.6)	32(72.7)	27(73)	11(68.7)	72
Diffuse Hair Loss	1(33.3)	22(50)	13(35.1)	8(50)	44
Puffy Oedema	0(0)	11(25)	9(24.3)	7(43.7)	27
Decrease Sweating	0(0)	2(4.5)	2(5.4)	2(12.5)	6
Course/Rough skin	0(0)	16(36.6)	11(29.7)	5(31.2)	32
Pruritus	1(33.3)	35(79.5)	30(81.1)	10(62.5)	76
Delayed wound healing	0(0)	1(2.3)	3(8.1)	0(0)	4
Nail changes	0(0)	13(29.5)	8(21.6)	2(12.5)	23
Total	4	132	103	45	284
Cutaneous signs					
Xerosis	2(66.6)	32(72.7)	29(78.3)	9(56.2)	72
Alteration in skin texture	3(66.6)	24(54.4)	19(51.3)	7(43.7)	53
Keratoderma	1(33.3)	13(29.5)	10(27)	0(0)	24
Pigmentary changes	0(0)	20(45.5)	9(24.3)	3(18.7)	32
Hair Changes	1(33.3)	29(65.9)	18(48.6)	8(50)	56
Oedematous changes	0(0)	15(34)	9(24.3)	5(31.3)	29
a) Puffy oedema	0(0)	9(20.4)	7(18.9)	4(25)	20
b) Leg oedema (Myxedema)	0(0)	6(13.6)	2(5.4)	1(6.3)	9
Total	7	148	103	37	295
Pigmentary changes					
Melasma	0(0)	2(4.5)	3(8.1)	1(6.3)	6
Diffuse hyperpigmentation	0(0)	1(2.2)	0(0)	2(12.5)	3
Periocular pigmentation	0(0)	3(6.8)	1(2.7)	0(0)	4
Vitiligenous change	0(0)	5(11.4)	5(13.5)	9(56.3)	19
Total	0	11	9	12	32
Nail change					
Brittle nail	0(0)	3(6.8)	5(11.4)	1(6.3)	9
Onycholysis	0(0)	8(18.1)	3(8.1)	3(18.7)	14
Cuticle loss	0(0)	2(4.5)	3(8.1)	1(6.3)	6
Vertical striations	0(0)	0(0)	0(0)	1(6.3)	1
Leuconychia	0(0)	6(13.6)	2(5.4)	3(18.7)	11
Total	0	19	13	9	41

Hair change					
Diffuse hair loss	2(66.6)	8(18.1)	10(27)	9(56.2)	29
Thin scalp hair	0(0)	11(25)	6(16.2)	2(12.5)	19
Both thin scalp and hair loss	0(0)	4(9)	3(8.1)	4(25)	11
Madarosis	0(0)	2(4.5)	3(8.1)	1(6.3)	6
Canitis	0(0)	2(13.6)	0(0)	0(0)	2
Total	2	27	22	16	67

Table 2 shows cutaneous symptoms, cutaneous signs, pigmentary change, nail change and hair change among the hypothyroidism patients in each age group. The most common cutaneous symptom was pruritus (76%), followed by dry skin (72%), diffuse hair loss (44%), course/rough skin (32%), puffy oedema (27%), nail changes (23%), decrease sweating (6%) and delayed wound healing (4%) as depicted in the table. Almost all of the symptoms were found high among 21-40 years age group. The most usual cutaneous signs were xerosis (72%), followed by hair changes (56%), alteration in skin texture (53%), pigmentary changes (32%), oedematous changes (29%) and keratoderma (24%). Xerosis were found 32% and 29% in 21-40 and 41-50 age groups respectively and hair changes were found 29% and 18% in 21-40 and 41-50 age groups respectively. Pigmentary changes were observed among 32% hypothyroid patients. The most occurring pigmentary change was vitiliginous change (19%), followed by melasma (6%), periocular pigmentation (4%) and diffuse hyperpigmentation (3%). Most of the vitiliginous change (9%) was found in ≥ 50 age group. Pigmentary changes were not found in ≤ 20 age group. Nail changes were found among the total of 41% hypothyroid patients. The most usual nail change was onycholysis (14%), followed by leuconychia (11%), brittle nail (9%), cuticle loss (6%) and vertical striations (1%). Most of the nail changes (19% and 13% respectively) were found in 21-40 and 41-50 age groups. Nail changes were absent in ≤ 20 age group of patients. Hair changes were observed among 67% hypothyroid patients. The most common hair change was diffuse hair loss (29%), followed by thin scalp hair (19%), both thin scalp hair and hair loss (11%), madarosis (6%) and canitis (2%). Most of the hair changes were found in 21-40 and 41-50 age groups respectively.

Discussion

Hypothyroidism is a common endocrine disorder which affects people of both sexes and all ages and sometimes associated with cutaneous manifestations. It is a hot topic of dermato-endocrinology that "long-recognized hypothyroid skin problems encircle many layers of complication". Thyroid disorders are involved with all organic systems of the body as well as the skin. Cutaneous manifestations generally noticeable following the development of thyroid disease, but may be the first presenting sign or even precede the diagnosis by many years. Of all the endocrinopathies that may have cutaneous findings, hypothyroidism is probably the one most likely to be seen by the practicing physician since the skin readily reflect the functional capacity of the thyroid gland. It was

the aim of our study to investigate the cutaneous manifestations in patients with hypothyroidism.

The result showed that the most common cutaneous symptom was pruritus (76%), followed by dry skin (72%), diffuse hair loss (44%), course or rough skin (32%), puffy oedema (27%), nail changes (23%), decrease sweating (6%) and delayed wound healing (4%). Dryness of skin is due to diminished eccrine and sebaceous gland activity and also because of decreased sweating due to cytological changes in the sweat glands in hypothyroidism. Hypothyroidism causes increase in number of telogen hair, explaining increased hair loss, facial puffiness and non-pitting oedema of hands and feet. The most common cutaneous sign was xerosis (72%), followed by hair changes (56%), alteration in skin texture (53%), pigmentary changes (32%), oedematous changes (29%) and keratoderma (24%). Xerosis was found highest in 21-40 and 41-50 age groups and hair changes also found highest in 21-40 and 41-50 age groups.

Thyroid disorders are associated with deflected human skin and hair structure as well as function [18]. Thyroid hormone plays a central role in primary development of mammalian skin as well as in maintenance of normal cutaneous function. Thyroid hormonal action has been exhibited cutaneous symptoms; such as epidermis, dermis and hair. It also maintains epidermic oxygen consumption, protein synthesis, mitosis and epidermal thickness [19]. In addition, investigators have found hypothalamic-pituitary-thyroid hormones are in human skin and have determined that thyroid hormone receptors negotiate skin proliferation and inflammation along with skin response to retinoids [20].

The characteristic of hypothyroidism patient skin is cold, xerotic and pale. The coldness of skin occurs due to reduced core temperature and cutaneous vasoconstriction. Decreased skin perfusion has been recorded with nail fold capillaroscopy [21]. Decreased skin perfusion is the reflex vasoconstriction compensatory to reduced core temperature which may be secondary to reduced thermogenesis. Occasionally, purpura may be noted in hypothyroid patients as a result of reduced levels of clotting factors and the loss of vascular support for dermal mucin [22]. The dullness of hypothyroid skin results from diminished eccrine gland secretion. The accurate reason for decreased sweating is not clear although the hypothyroid glands are atrophic on histologic examination. Xerosis is the most prevalent manifestation in the skin involvement in hypothyroidism and occurs in 57-59% of

hypothyroid patients [23,24]. Xerosis occurs because of change in skin texture and poor hydration of the stratum corneum. The skin of palms and soles may be quite dry. The epidermis is hyperkeratotic, and there is follicular plugging. Hypothyroidism also may affect the expansion of the lamellar granules (Odland bodies), which plays an essential role in the establishment of a normal stratum corneum [25]. In hypothyroidism, the skin becomes pale because of the dermal mucopolysaccharides and water content which change the refraction of light [26]. Myxedema is caused by increased glycosaminoglycan deposition in the skin which is the classic cutaneous sign of hypothyroidism. Generally, myxedema is diffuse, but focal mucinous papules have been described and the skin may appear swollen, dry, pale, waxy, and firm to the touch [26]. Sometimes candidal folliculitis is observed among hypothyroid patients [26]. High level of dermal carotene may turn up as a prominent yellow stain on the palms, soles and nasolabial folds [27]. The hypothyroid skin heals slowly, which is proportional to the level of hormone deficiency. Most recent data suggest that wound healing rate may be accelerated by topical thyroid [28].

Different skin cells of the body may be affected not only by variation in thyroid hormone levels but also by the presence of thyroid-specific auto antibodies for autoimmune thyroid diseases [29]. For autoimmune thyroid disease, skin findings may be obvious and these may reflect associated autoimmune disease [30]. Graves' disease and Hashimoto's thyroiditis are common autoimmune diseases and the skin manifestations may be related to either thyroid hormone levels or to associated with T and/or B cell abnormalities for those diseases [30]. A list of autoimmune conditions that become apparent when examining the skin includes: vitiligo, alopecia areata, chronic urticaria, bullous disorders and connective tissue diseases. Most commonly reported cutaneous disorders related with thyroid disease are: vitiligo and alopecia areata [31]. In addition, vitiligo and alopecia areata often lead thyroid dysfunction by many years [32].

Pretibial skin thickness was increased in 33% of patients with autoimmune thyroid disease, indicating that infiltrative dermatopathy is likely to have a higher subclinical prevalence [33]. Pretibial fibroblasts are the target for antithyroid antibodies. After stimulation by thyroid auto antibodies, fibroblasts may produce excess glucosaminoglycans [10]. T cells are the primary effectors of dermatopathy. Interaction of T-cells with an auto antigen is either identical or cross-reactive with a thyroid auto antigen in the dermis [26]. From the clinical perspective, thyroglobulin antibodies are more prevalent in patients with different skin diseases [34]. Both dermatologist and endocrinologists have to investigate their patients about the family history of autoimmune diseases and associated autoimmune disorders. Clarifying these associations further, will create a new light on the pathogenesis of autoimmune diseases and obviously guide to new therapeutic approaches.

The present study showed that the most common pigmentary change was vitiliginous change (19%), followed by melasma (6%), periocular pigmentation (4%) and diffuse hyperpigmentation

(3%). Most of the vitiliginous change (9%) was found in ≥ 50 age group. Any pigmentary changes were not found in ≤ 20 age group. Pigmentary change on skin is very common for hypothyroidism disease [35,36].

The most common hair change was diffuse hair loss (29%), followed by thin scalp hair (19%), both thin scalp hair and hair loss (11%), madarosis (6%) and canitis (2%). Hair loss can be attributed to inhibition of initiation and duration of the actively growing phase of hair cycle. Hence the percentage of hair in telogen increases leading to telogen effluvium. The hair growth is also slowed with decreased length due to the duration of anagen.

In addition, thyroid hormone is essential for both the initiation and maintenance of hair growth and normal secretion of sebum. Thyroid hormone acts on skin directly and is negotiated by Thyroid Hormone Receptor (TR) [37]. TRs have been observed in hair arrector pili muscle cells, skin fibroblasts, epidermal keratinocytes, vascular endothelial cells, and cell which made hair follicle [38]. The interaction of tri-iodothyronine (T3) with its receptors (TR α and TR β) affects epidermal differentiation and enhances its responsiveness to growth factors [39]. T3 plays an important role for the function of sebaceous, eccrine, and apocrine glands, growth of hair follicles and synthesis of proteo-glycosaminoglycans by dermal fibroblasts [40]. The growth of both epidermal keratinocytes and dermal fibroblasts are stimulated by T3 and proliferation of hair follicle keratinocytes are stimulated by thyroxine (T4) [41]. Hair follicle stem cells may also be affected by thyroid hormones, since T3 and T4 were found to avert clonal growth of hair follicle epithelial stem cells. According to the TR expression in hair follicle cells, it is argued that thyroid hormone can affect hair growth directly, rather than through an intermediate mechanism such as a general metabolic status [32].

In hypothyroidism, hair can be dry, frieze, fragile and slow growing. Some symptoms of hair loss are also found such as; unbalanced and diffuse loss of scalp hair, loss of the eyebrow (madarosis), diminished body hair, sparse pubic and axillary hair. The alopecia may be mediated by hormone effects on the initiation as well as the duration of hair growth [26]. Massive telogen effluvium may occur due to unexpected onset of hypothyroidism, and the percentage of scalp hairs in telogen is generally increased [27]. From a study, it was observed that cell proliferation indices were diminished in hair bulbs of hypothyroid subjects and increased in hyperthyroidism compared with normal values [42]. A tendency to develop frequently long and lanugo-type hair on the back, shoulders, and extremities were observed among the hypothyroid patients, especially children [27]. Sometimes, hair loss is the only symptom of hypothyroidism and the dermatologist needs to diagnosis first to treat the condition [26].

The most common nail change was onycholysis (14%), followed by leuconychia (11%), brittle nail (9%), cuticle loss (6%). and vertical striations (1%). 19% and 13% the nail changes were found in 21-40 and 41-50 age groups respectively. Nail changes were

absent in ≤ 20 age group. In hypothyroidism patients, nails grow slowly, thick, striated and brittle. Onycholysis is also associated with hypothyroidism [43].

Thyroid disorders may affect all the organs of the body as well as associated with various skin disorders. Although cutaneous manifestations of thyroid diseases are well mentioned, a better understanding of these processes is needed for further research. A lot of hypothesis has been proposed to clarify the pathogenesis of skin manifestations of thyroid disease and more than one mechanism is accountable for these clinical manifestations. It is conjecturable but unproven that cellular immunity induced in the thyroid gland could trigger development of the skin lesions.

Limitations of the Study

This study had some limitations. Those are as follows:

- a) Reconfirmation of serum level of TSH, FT₄ and FT₃ were done but there associations with skin changes with the level of that hormone were not evaluated,
- b) Biopsy of skin was not done,
- c) Sample size should be large for the clarification of skin problem with hypothyroidism,
- d) Sample should be taken throughout the year which helps us to find out the association of seasonal changes of skin with hypothyroidism.

Conclusion

This was the first study in Bangladesh to explore the cutaneous manifestations of hypothyroidism. The findings of this study revealed that various symptoms and signs of skin, hair and nail changes related to hypothyroidism such as xerosis, course/rough skin, pruritus, pigmentary changes, vitiliginous change, onycholysis, leuconychia, thin scalp hair, diffuse hair loss. This skin, hair and nails changes may remain unrecognized and most of them are not evaluated properly. In our study, we observed that hypothyroidism was closely associated with such cutaneous changes. So it is our recommendation to evaluate various cutaneous symptoms and signs associated with hypothyroidism for its early detection and treatment in Bangladesh context.

Conflict of Interest

Authors have no conflict of interest.

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Author's Contribution

Siddique MR, Islam M and Sikder MS formulated the research questions, developed the study concepts. Islam M analyzed the data and drafted the manuscript. Finally, all authors have read and approved the final version of the manuscript.

References

1. Angell TE, Huang SA, Alexander EK (2014) The Thyroid. Principles of Endocrinology and Hormone Action 353-366.
2. Peeters RP, Visser TJ (2017) Metabolism of thyroid hormone. Endotext.
3. Sheehan MT (2016) Biochemical testing of the thyroid: TSH is the best and, oftentimes, only test needed—a review for primary care. Clin Med Res 14: 83-92.
4. Paswett F, Devi B, Santa N, Syiemlieh AJ (2016) Cutaneous Manifestations of Hypothyroidism: A Clinical Study. International Journal of Advanced Research 4: 109-113.
5. Kambil SM (2018) Clinical study of skin manifestations of hypothyroidism at a tertiary hospital in North Kerala. IntJResDerm 4: 298.
6. Keen MA, Bhat MH, Hassan I (2016) A clinical study of the cutaneous manifestations of hyperthyroidism in Kashmir valley-India. Indian J Dermatol 58: 326.
7. Sijapati KS, Rijal A, Agrawal S, Khadka DK, Maskey R (2019) Cutaneous Manifestations of Thyroid Hormone Disorder. Nepal Journal of Dermatology, Venereology & Leprology 17: 42-48.
8. Heymann WR (1992) Cutaneous manifestations of thyroid disease. J Am Acad Dermatol 26: 885-899.
9. Burman KD, McKinley-Grant L (2006) Dermatologic aspects of thyroid disease. Clin Dermatol 24: 247-255.
10. Leonhardt JM, Heymann WR (2002) Thyroid disease and the skin. Dermatol Clin 20: 473-481.
11. Diven DG, Gwinup G, Newton RC (1989) The thyroid. Dermatol Clin 7: 547-558.
12. Srujana B, Reddy BN, Prasad GK (2016) Clinical spectrum of cutaneous manifestations of thyroid disorders in patients attending MediCiti Institute of Medical Sciences. Indian Journal of Clinical and Experimental Dermatology 2: 146-152.
13. Zimmermann MB (2009) Iodine deficiency. Endocr Rev 30: 376-408.
14. Vanderpump MPJ (2005) The epidemiology of thyroid diseases. In: Braverman LE, Utiger RD (eds). Werner and Ingbar's The Thyroid: A Fundamental and Clinical Text, (9th edn). JB Lippincott-Raven: Philadelphia 398-496.
15. Sayeed MA, Mohsena M, Haq T, Morshed AH, Afroz S, et al. (2019) Prevalence of hypothyroidism in different occupational groups of Bangladeshi population. IMC Journal of Medical Science 13: 9-17.
16. Rabeya R, Zaman S, Chowdhury AB, Nabi MH, Hawlader MD (2019) Magnitude and Determinants of Hypothyroidism among Dyslipidemic Patients in Bangladesh: A Hospital-Based Cross-Sectional Study. International Journal of Diabetes and Metabolism 25: 19-25.
17. Dhaka tribunes, 2018-Experts: 50 million people suffer from thyroid disease in Bangladesh.
18. Bodó E, Kromminga A, Bíró T, Borbíró I, Gáspár E, et al. (2009) Human female hair follicles are a direct, nonclassical target for thyroid-stimulating hormone. J Invest Dermatol 129: 1126-1139.
19. Mullin GE, Eastern JS (1986) Cutaneous consequences of accelerated thyroid function. Cutis 37: 109-114.

20. Bodó E, Kany B, Gáspár E, Knüver J, Kromminga A, et al. (2010) Thyroid-stimulating hormone, a novel, locally produced modulator of human epidermal functions, is regulated by thyrotropin-releasing hormone and thyroid hormones. *Endocrinology* 151: 1633-1642.
21. Pazos-Moura CC, Moura EG, Breitenbach MM, Bouskela E (1998) Nailfold capillaroscopy in hypothyroidism and hyperthyroidism: Blood flow velocity during rest and postocclusive reactive hyperemia. *Angiology* 49: 471-476.
22. Christianson HB (1976) Cutaneous manifestations of hypothyroidism including purpura and ecchymoses. *Cutis* 17: 45-52.
23. Keen MA, Hassan I, Bhat MH (2013) A clinical study of the cutaneous manifestations of hypothyroidism in Kashmir valley. *Indian J Dermatol* 58: 326.
24. Dogra A, Dua A, Singh P (2006) Thyroid and skin. *Indian Journal of Dermatology* 51: 96-99.
25. Hanley K, Devaskar UP, Hicks SJ, Jiang Y, Crumrine D, et al. (1997) Hypothyroidism delays fetal stratum corneum development in mice. *Pediatric research* 42: 610-614.
26. Kasumagic-Halilovic E, Begovic B (2012) Thyroid autoimmunity in patients with skin disorders. 18: 297.
27. Freinkel RK (1993) Cutaneous manifestation of endocrine disease. *Dermatology in general medicine*.
28. Safer JD (2013) Thyroid hormone and wound healing. *Journal of thyroid research*.
29. Cianfarani F, Baldini E, Cavalli A, Marchioni E, Lembo L, et al. (2010) TSH receptor and thyroid-specific gene expression in human skin. *J Invest Dermatol* 130: 93-101.
30. Ai J, Leonhardt JM, Heymann WR (2003) Autoimmune thyroid diseases: Etiology, pathogenesis, and dermatologic manifestations. *J Am Acad Dermatol* 48: 641-662.
31. Baldini E, Odorisio T, Sorrenti S, Catania A, Tartaglia F, et al. (2017) Vitiligo and autoimmune thyroid disorders. *Front in Endocrinol* 8: 290.
32. Kasumagic-Halilovic E (2014) Thyroid disease and the skin. *Annals Thyroid Res* 1: 27-31.
33. Salvi M, De Chiara F, Gardini E, Minelli R, Bianconi L, et al. (1994) Echographic diagnosis of pretibial myxedema in patients with autoimmune thyroid disease. *Eur J Endocrinol* Aug 131: 113-119.
34. Baric A, Brcic L, Gracan S, Skrabic V, Brekalo M, et al. (2019) Thyroglobulin antibodies are associated with symptom burden in patients with Hashimoto's thyroiditis: a cross-sectional study. *Immunol Invest* 48: 198-209.
35. Banba K, Tanaka N, Fujioka A, Tajima S (1999) Hyperpigmentation caused by hyperthyroidism: differences from the pigmentation of Addison's disease. *Clin Exp Dermatol* 24: 196-198.
36. Song X, Shen Y, Zhou Y, Lou Q, Han L, et al. (2018) General Hyperpigmentation induced by Grave's disease. *Medicine* 97(49): 13279.
37. Billoni N, Buan B, Gautier B, Gaillard O, Mahe YF, et al. (2000) Thyroid hormone receptor β 1 is expressed in the human hair follicle. *Br J Dermatol* 142: 645-652.
38. Yousef H, Miao JH, Alhaji M, Badri T (2020) Histology, skin appendages. *Stat Pearls*.
39. Slominski A, Wortsman J (2000) Neuroendocrinology of the skin. *Endocr Rev* 21: 457-487.
40. Slominski AT, Zmijewski MA, Skobowiat C, Zbytek B, Slominski RM, et al. (2012) Sensing the environment: Regulation of local and global homeostasis by the skin neuroendocrine system. *Adv Anat Embryol Cell Biol* 212: 1-115.
41. Van Beek N, Bodo E, Kromminga A, Gáspár E, Meyer K, et al. (2008) Thyroid hormones directly alter human hair follicle functions: anagen prolongation and stimulation of both hair matrix keratinocyte proliferation and hair pigmentation. *J Clin Endocrinol Metab* 93: 4381-4388.
42. Schell H, Kiesewetter F, Seidel C, Hintzenstern JV (1991) Cell cycle kinetics of human anagen scalp hair bulbs in thyroid disorders determined by DNA flow cytometry. *Dermatology* 182: 23-26.
43. Cooper DS, Halpern R, Wood LC, Levin AA, Ridgway EC (1984) L-thyroxine therapy in subclinical hypothyroidism: a double-blind, placebo-controlled trial. *Ann Intern Med* 101: 18-24.



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