### A STUDY ON CUTANEOUS MANIFESTATIONS OF HYPOTHYROIDISM IN A TERTIARY HOSPITAL IN SOUTH INDIA

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**ABSTRACT: BACKGROUND:** Endocrinological disorders occasionally present with cutaneous manifestations. Thyroid hormonal abnormalities are frequently associated with abnormalities of the skin, hair and the nails. **AIM:** To study the various dermatological manifestations of hypothyroidism and to identify various associations with hypothyroidism in a tertiary hospital in South India from September 2014 to March 2015. **RESULTS:** In a total of 56 patients studied, cutaneous changes were seen in 83.92 percent of the patients. Male is to female ratio of hypothyroid patients studied was 1:4.6. 17.85 percent of the total patients were males and 66.07 percent of the female patients showed cutaneous features of hypothyroidism. The commonest general symptoms seen in our study were weight gain and fatigue. Xerosis/Ichthyosis, pedal oedema, facial puffiness and hair changes were the common cutaneous features seen in our study. Urticaria, vitiligo, acanthosis nigricans, melasma and pemphigus foliaceous were the few cutaneous associations of hypothyroidism in our study whereas diabetes mellitus, microcytic hypochromic anaemia and hyper-cholesterolaemia were the systemic features associated with hypothyroidism in our study. **CONCLUSION**: Patient with hypothyroidism most commonly present with xerosis/ichthyosis and pedal oedema and more commonly associated with urticaria, vitiligo, acanthosis nigricans ingricans were with urticaria, vitiligo, acanthosis nigricans and melasma.

KEYWORDS: Cutaneous Manifestations, Hypothyroidism.

**INTRODUCTION:** It's a well-known fact skin is referred to as window to the body. Many internal ailments are detected by looking for the various cutaneous signs and symptoms. Dermatologists often see skin lesions that suggest an underlying endocrine disorder. Identifying the endocrine disorder is very important, so that patients can be treated appropriately rather than giving symptomatic treatment. The endocrine system consists of hormone producing glands, including the pituitary, pancreas, thyroid, parathyroids, adrenals, testes and ovaries. A failure in any of these glands may clinically present as an endocrine disorder. Hormones are essential in regulating physiologic processes in each system of the body, including the skin. Endocrine hormones when in excess or deficient result in changes in cutaneous morphology and function.

They act as chemical messengers that serve to regulate growth, metabolism, reproduction, behavior and development. Underlying endocrine disorders which may present as skin diseases are, diabetes mellitus; thyrotoxicosis; hypothyroidism; Cushing syndrome; Addison disease; acromegaly; hyper and rogenism; hypopituitarism; primary hyperparathyroidism; hypoparathyroidism<sup>1</sup>. Like most systemic pathologies, hypothyroidism is expressed in multiple ways through the skin and its adnexa. In some patients, the initial and most prominent complaints are related to alterations in the skin, and hence the dermatologist will at times be the first physician to be consulted. To make a diagnosis of the underlying endocrinopathy is essential, so that patients can receive corrective treatment and prevent morbidity.<sup>1</sup>

Though thyroid hormone has tremendous impact on activity of integuments, its effects are more notable during deficiency or excess status. Cutaneous changes accompanying thyroid disease are neither unique nor pathognomic. However such cutaneous findings and associations often provide important clues in instances of unsuspected and undetected thyroid disease.

Hypothyroidism is defined as the presence of insufficient levels of circulating thyroid hormone or target cell resistance to the hormone. It is classified as congenital, describing a newborn with reduced or very rarely absence of thyroid hormone production; primary, caused by intrinsic defect of thyroid structure; secondary to a pituitary insufficiency; and tertiary from insufficient secretion of hypothalamic thyrotrophic releasing hormone. The most frequent type is the primary type, characterized by the presence of low free plasma T4 (thyroxin), below 0.8 ng/dl and high TSH (Thyrotrophic) above 4.0 mIU/ml. Where TSH exceed 2.5 mIU/ml, we face a subclinical hypothyroidism even though thyrotrophic levels are normal.

According to the degree of this hormone defect, the disease may appear with signs and symptoms of diverse extent. Deficits of thyroid hormone produces cutaneous changes like dryness, ichthyosis, puffiness of face, pedal edema, myxoedema, diffuse hair loss, brittle nails, carotenemias etc.

The present study was undertaken to know the spectrum of dermatological manifestations of hypothyroidism and its various other dermatological associations, which enables to make an early diagnosis of the same. Recognition of hypothyroidism is important in order to ensure that appropriate treatment is provided at the earliest, thus preventing complications.

#### **MATERIALS AND METHODS:**

**Study Period:** The study was conducted during the period of September 2014 to March 2015 in the department of DVL.

### Inclusion Criteria:

- 1. Patients attending DVL and cases referred from Medicine, Surgery and Gynaecology departments to DVL outpatient department with skin complaints suggestive of hypothyroidism were investigated for their thyroid profile (total T4, total T3 and TSH).
- 2. Known cases of hypothyroid referred from medicine, endocrinology and surgery departments and those on treatment for hypothyroidism were also included.
- 3. All ages including children and adults as well as both sexes were included.

### **Exclusion Criteria**:

1. Patients with cutaneous manifestations suggestive of hypothyroidism but with normal values of T3, T4, TSH were excluded from the study.

### **Our Study Included:**

- **1. History:** Personal particulars such as age, sex, occupation, demographic profile of the patient, dietary history (regarding goitrogens), presenting complaints and duration, family history, menstrual and obstetric history (in case of females), any thyroid surgical interventions, any drug history are noted in the proforma.
- **2. Examination:** This includes general examination, cutaneous and systemic examination. All these findings are recorded in the proforma.

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#### 3. Investigations:

- a. Complete Haemogram {Including Peripheral smear (Association with pernicious anemia)}.
- b. Liver function tests: including Serum bilirubin (to differentiate carotenemias from icterus).
- c. Renal function tests: Blood urea, Serum creatinine
- d. Blood sugar levels.

e.	Fasting lipid profile:	Total Triglyceride levels.
		Total cholesterol levels.
		LDL, VLDL, LDL/VLDL ratio.
f.	Thyroid profile:	ТЗ.
		Τ4.
		TSH.
		FT4.

All these investigations were done to find any associations with hypothyroidism and also to rule out coexisting systemic diseases that can present with skin changes which can mimic the skin changes of hypothyroidism.

- g. Skin biopsy: Punch biopsy was done in the relevant cases such as Myxoedema, Systemic scleroderma, Lichen planus, Morphea etc. to see the respective histological changes.
- **4.** Weight and Height measurements: were recorded in every case. Consent of the patient taken in every case.

**OBSERVATION AND RESULTS:** 56 patients fulfilled the inclusion criteria of the study and they were analyzed as follows.

Sl. No.	Gender	Number	Percentage		
1	Males	10	17.85		
2	Females	46	82.14		
3	Total	56	100.00		
Table 1: Distribution of patients according to sex					

Out of 56 cases of hypothyroid cases studied, 17.85 percent were males and 82.14 percent were females. Male to Female ratio was 1:4.6.

Sl. No.	Age group (years)	Number	Percentage	
1	1 - 10	0	0	
2	11 – 20	8	14.28	
3	21 - 30	11	19.64	
4	4 31 - 40		33.92	
5	41 - 50	9	16.07	
6 51 - 60		7	12.50	
7 61 - 70		2	3.57	
Total 56 100.00				
Table 2: Age wise distribution of patients				

Maximum number of patients are in the age group of 31–40 years which constitutes 33.92 percent. This is followed by patients belonging to the age group 19.64 percent.

Sl. No.	General symptoms	No. of patients	Percentage	
1	Weight gain	26	46.42	
2	Fatigue	25	44.64	
3	Neck swelling	11	19.64	
4	Cold intolerance	17	30.35	
5	Slowness to response	8	14.28	
6	Hoarse voice	23	41.07	
7 Constipation		12	21.42	
Table 3: General symptom wise distribution of patients				

Out of total 56 Patients, 46.43 percent patients are having weight gain, 44.64 percent patients are having fatigue, 19.64 percent patients are suffering from neck Swelling, 30.36 percent patients are suffering from cold Intolerance, 14.29 percent patients are slow to respond, 41.07 percent patients are having hoarse voice and 21.43 percent patients are suffering from constipation.

		Number	Percentage	Gender	Total	Percent
Cutaneous manifestations Of hypothyroidism	Present	47	83.93	Males	10	17.85
				Females	37	66.07
	Absent	9	16.07	Males	0	0
				Females	9	16.07
	Total	56	100		56	100
Table 4: Cutaneous manifestations of hypothyroidism						

Out of total 56 patients, cutaneous manifestations of hypothyroidism are present in 83.93 percent of the patients and absent in 16.07 percent of the patients.

Sl. No.	Skin symptoms	No. of patients	Percentage
1	Puffiness of face	23	41.07
2	Oedema of feet	19	33.93
3	Dry skin	21	37.50
4	Itching	9	16.07
5	Hair fall + slow growth of hair	7	12.50
6	Brittle nails	3	5.35
7	Thickening of palms and soles	5	8.92
Table 5: Skin Symptom wise distribution of patients			

Out of total 56 Patients, 41.07 percent of the patients were having puffiness of face, followed by 37.50 percent having dry skin/xerosis. Other symptoms seen were oedema of feet (33.93 percent), itching (16.07 percent), hair fall and slow growth of hair (12.50 percent), thickening of palms and soles (8.92 percent) and brittle nails (5.35 percent).

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Sl. No.	Cutaneous signs	No. of patients	Percentage	
1	Xerosis	30	53.57	
2	Ichthyosis	8	14.28	
3	Fine wrinkling	4	7.14	
4	Pallor	6	10.71	
5	Carotenaemias	3	5.35	
6	Cool skin	10	17.85	
7	Myxoedema	3	5.35	
8	Puffiness of face	33	58.92	
9	Pedal oedema	18	32.14	
10	Palmoplantar keratoderma	5	8.92	
11	Hair changes	15	26.78	
12	Nail changes	5	8.92	
Table 6: Cutaneous signs wise distribution of patients				

Puffiness of face (58.92 percent) was the predominant sign in this study on hypothyroid diseases. This was followed by xerosis (53.57 percent), pedal oedema (32.14 percent) and hair changes (26.78 percent). Other signs in descending order were cool skin (17.85 percent), ichthyosis (14.28 percent), pallor (10.71 percent), palmoplantar keratoderma (8.92 percent), nail changes (8.92 percent), fine wrinkling (7.14 percent), myxedema (5.35 percent) and carotenaemias (5.35 percent).

Sl. No.	Type of hypothyroidism	Number	Percentage	
1	1 Primary		96.42	
2 Secondary		1	1.79	
3 Cretinism		1	1.79	
Total 56 100				
Table 7: Types of hypothyroidism				

Out of total 56 patients, 96.43 percent are having primary hypothyroidism, 1.79 percent patients are having secondary hypothyroidism and 1.79 percent patients are having cretinism.

Sl. No.	Dermatological disorder	No. of patients	Percentage	
1	Urticaria	3	5.35	
2	Vitiligo	3	5.35	
3	Acanthosis nigricans	3	5.35	
4	Melasma	3	5.35	
5	Pemphigus foliaceous	1	1.78	
6	Systemic scleroderma	1	1.78	
7	Xanthalesma palpebrum	1	1.78	
8	Lichen planus	1	1.78	
	Total	16	28.57	
Table 8: Dermatological associations				

Urticaria, vitiligo, acanthosis nigricans and melasma were the common dermatological associations, each seen in 5.35 percent of the patients. The other associations seen were pemphigus foliaceous, systemic scleroderma, xanthalesma palpebrum and lichen planus, each of which were seen in 1.78 percent of the patients.

#### Laboratory parameters were don in all the patients, which showed the following Results:

- 1) Haemogram Microcytic hypochromic anemia was noted in 4 patients.
- 2) Random Blood Sugar was elevated in 4 patients.
- 3) Thyroid profile TSH > 4mIU/ml with elevated T3 and T4 was seen in 26 patients. TSH >2.5 mIU/ml with normal T3 and T4 was seen in 29 patients.
- 4) Lipid profile Hypercholesterolemia was noted in 2 patients.
- 5) Biopsy Myxedematous changes were noticed in 3 patients.

**DISCUSSION:** In our study of 56 patients of hypothyroidism, one was of congenital hypothyroidism (cretinism) and 55 of adult onset.

In our study the maximum cases of hypothyroidism were in the age group 31 - 40 years (33.92 percent) and also the maximum number of females with hypothyroidism were in this same age group. This was similar to the study done by Samson JF et al.,<sup>2</sup> which showed that the maximum number of hypothyroid cases were in the age group of 30-39 years (34.37 percent).

The male to female ratio was 1:4.6 in our study, which is almost the same as reported in study done by Samson JF et al. (M:F – 1:4.2)  $^{2}$  In a study by Keen MA et al, $^{3}$  the male to female ratio was 1:9.45.

In our study out of 56 patients, cutaneous changes were seen in 47 patients (83.92 percent). Keen MA et al<sup>3</sup> found that cutaneous changes were seen in 83.26 percent of the patients. In a study by Haritha S et al,<sup>4</sup> cutaneous changes were seen in 63.00 percent of the study population. In our study cutaneous changes were seen in 100 percent of men who had hypothyroidism and only in 80.41 percent of women. This was in contrast to the studies of Veeranna SK et al,<sup>5</sup> who recorded cutaneous changes only in 5 percent of men and 15 percent of women with thyroid dysfunction.

In our study, weight gain was the main presenting complaint in majority of the patients (46.42 percent), as evidenced in other study done by Dogra A et al., <sup>6</sup> in which majority of the patients presented with weight gain as a presenting complaint (71.85 percent).

In our study, lethargy and weakness were seen in 44.64 percent of the patients, a feature quite commonly seen in hypothyroidism. In the study by Dogra A et.al, <sup>6</sup> lethargy and weakness were seen in 65.62 percent of the patients.

Cold intolerance was noticed in 30.35 percent of the patients in our study whereas Dogra A et.al<sup>6</sup> noticed in 31.25 percent of their patients. Hypothermia is a result of hypo metabolic state which causes reduced core temperature and reflux cutaneous vasoconstriction.

Out of 56 patients, (Irregular periods, menorrhagia) as the main complaint in our study. Dogra et al<sup>6</sup> found out that in their study, 31.25% presented with menstrual abnormalities.

Menstrual abnormalities are an expected complication seen with thyroid disorders as discussed by Thymas, Bohhnet and Dirolof. No cutaneous manifestations were seen in these patients even though they had biochemically hypothyroid profiles.

The texture of the skin was found to be 'dry and coarse' in 53.57 percent of the patients, which constituted the most common cutaneous sign. The findings (56.25 percent) are similar to those found by Dogra A et al.<sup>6</sup> Keen MA et al found that dry coarse skin was seen in 65.22 percent of all the patients. In a study by Samson JF et al,<sup>2</sup> dry skin was seen in 21.87 percent of the patients. The xerosis was severe in some cases to be considered as an acquired ichthyosis. Hypohidrosis accompanied by cytologic changes within the eccrine apparatus and diminished sebaceous gland secretion are considered potential etiological factors.

Myxedema, the typical feature of hypothyroidism was seen in 5.35 percent in our study. Samson JF et al<sup>2</sup> noticed that myxoedematous changes were present in 25.00 percent of the patients. In the study by Dora A<sup>6</sup> et al, no myxedema cases were reported. Increase in body mass index (BMI) was seen in 46.42 percent of patients, which was in obese (BMI>30) and overweight (BMI 25-29.9) range. Palmoplantar keratoderma (PPK), a common feature of hypothyroidism was seen in 54.68 percent of cases in a study done by Samson JF et al.<sup>2</sup> In a study by Keen MA et al.<sup>3</sup> keratoderma was seen in 19.35 percent of the patients. But in our study palmoplantar keratoderma was seen only in 8.92 percent of the patients.

In our study, telogen effluvium was noticed in 25.00 percent of the patients and 1.78 percent of the patients presented with hirsutism. Haritha et al<sup>4</sup> observed that telogen effluvium was 34.92 percent of the patients in their study. Dogra A et al<sup>6</sup> noticed that telogen effluvium was present in 40.62 percent of patients in their study. Telogen effluvium was observed in 46.09 percent of the patients by Keen MA et al.<sup>3</sup> Alopecia of hypothyroidism is mediated via hormone effect on the initiation as well as duration of hair growth. Normal telogen–anagen hair relationships were restored with thyroid hormone replacement.<sup>4</sup>

The nails are thickened and brittle and grew slowly in 8.92 percent of the patients in our study, as is also evidenced in the study done by Dogra A et al<sup>6</sup> (i.e., 6.25 percent). In another study done by Samson JF et al.<sup>2</sup> brittle nails were seen in 3.12 percent of the patients. Brittle nails were seen in 4.35 percent of the patients and slow growing nails were seen in 0.65 percent of the patients in the study by Keen MA et al.<sup>3</sup>

In our study, it was observed that 98.21 percent of the patients were having adult hypothyroidism while 1.78 percent of the patients were having congenital hypothyroidism. Dogra A et al<sup>6</sup> observed in their study that 96.87 percent of the patients were adult hypothyroidism and 3.12 percent of the patients were having congenital hypothyroidism.

In our study, chronic urticaria was seen in 3 cases (5.35 percent). Dogra A et al<sup>6</sup> study noted that 15.62 percent of her patients had chronic urticaria. Leznoff and Sussman<sup>7</sup> evaluated 624 patients with idiopathic chronic urticaria and angioedma and found 90 patients to have evidence of thyroid disease. Urticaria was found in 13.04 percent of the patients by Keen MA et al in their study.<sup>3</sup>

Heymann has stated that the mechanism by which thyroid autoimmunity is associated with urticaria is poorly understood. They have stated that there is a clustering of thyroid microsomal antibodies in patients with a positive autologous serum test although it is unlikely that thyroid hormone itself has any in vivo effect on the cutaneous vascular response to histamine and on mast cell releasability.

The prevalence of vitiligo in general population is 1.84 percent and in our study it is seen in 3 patients (5.35 percent), it correlated with the study conducted by Samson JF et al.<sup>2</sup> and Haritha S et al,<sup>4</sup> where vitiligo was seen in 4.00 percent and 4.76 percent of study population respectively. 9.37

percent had vitiligo in a study done by Dogra A et al.<sup>6</sup> Keen MA et al found that 1.52 percent of their patients had vitiligo.

5.35 percent of melasma patients were seen in our study. Haritha S et al<sup>4</sup> observed that 14.28 percent of patients were affected by melasma in their study group. In a study by Dogra A et al,<sup>6</sup> melasma was seen in 18.75 percent of cases and diffuse hyperpigmentation was seen in 12.50 percent cases. In a study by Keen MA et al,<sup>3</sup> melasma was seen in 1.30 percent of the patients. Hyperpigmentation in thyroid disorders has been reported mainly in hyperthyroidism.

The explanation of hyperpigmentation in hyperthyroid patients is, increased release of pituitary adrenocorticotropic hormone compensating for accelerated cortical degradation. In hypothyroidism though, the cause of melasma cannot be explained although it has been documented in literature.

One patient (1.78 percent) presented with pemphigus foliaceous in our study. In the study by Dogra A et al,<sup>6</sup> one patient (3.12 percent) presented with pemphigus vulgaris. Wolf and Fewermann have repeatedly found the association of pemphigus group of disorders with thyroid disease.

Xanthalesma palpebrum was found in 1.78 percent of patients in our study which correlated with the percentage of cases in a study by Haritha et al<sup>4</sup> (1.58 percent) and Keen MA et al<sup>3</sup> (1.52 percent). Lichen planus was seen in 1.78 percent of our patients in our study whereas it was seen in 3.17 percent of the patients in a study by Haritha S et al<sup>4</sup> and 0.434 percent in a study by Keen MA et al.<sup>3</sup>

Systemic scleroderma and acanthosis nigricans were seen in 1.78 percent and 5.35 percent respectively, whereas in a study by Keen MA et al, <sup>3</sup> they were seen in 0.43 percent and 0.86 percent. Dogra A et al<sup>5</sup> had other associations in her study, which were alopecia areata (3.12 percent), tinea cruris and corporis (6.25 percent), ecchymosis on forearm (3.12 percent), skin tags (3.12 percent), and cutaneous amyloidosis (3.12 percent). Haritha S et al<sup>4</sup> observed the following other cutaneous changes in their study, namely, generalized pruritus (11.11 percent), tinea corporis (7.93 percent) and alopecia areata (6.34 percent).

Diabetes was found in 7.14 percent of our study group, whereas it was observed in 3.12 percent of the study group by Dogra et al.<sup>6</sup>

Four patients (7.14 percent) were having microcytic hypochromic anemia in our study. This was a finding similar to that of Dogra et al,<sup>6</sup> but which is in contrary to the usual association of hypothyroidism and pernicious anemia.<sup>2</sup> Hypercholesterolemia was noticed in 3.57 percent of patients in our study.

### **CONCLUSIONS:**

- 1. Around 33.92 percent of patients belonged to 31–40 age group.
- 2. Thyroid diseases were more common in females. (82.14 percent)
- 3. Weight gain (26%), lethargy (25%), puffiness of face (23%), dry skin (21%) were the main presenting complaints.
- 4. Xerosis (53%), facial puffiness (33%), icthyosis (14%), hair changes (26%) were the main cutaneous manifestations.
- 5. Cutaneous manifestations like carotenemias, palmoplantar keratoderma, skin pallor and systemic manifestations like bradycardia, neurological manifestations like sluggish deep tendon reflexes were mostly noticed in patients with severe hypothyroidism.

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- 6. Pigmentary disorders like melasma and vitiligo were seen in three patients (5.35 percent) each.
- 7. Chronic urticaria was seen in three patients (5.35 percent).
- 8. Microcytic hypochromic anemia (7.14 percent), diabetes mellitus (7.14 percent), hypercholesterolemia (3.57 percent) were noticed.

With our study, we have reached a conclusion that there definitely exists a strong association between cutaneous signs and symptoms with hypothyroidism. Though we found a varied pattern in form of high incidence of xerosis and low incidence of thyroid dermopathy nonetheless a high degree of suspicion must be kept in mind in patients presenting with such signs and symptoms to rule out an underlying thyroid disorder.

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