CUTANEOUS MANIFESTATIONS IN ENDOCRINAL DISORDERS- AN OBSERVATIONAL STUDY

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ABSTRACT

BACKGROUND

Endocrinology is the term used for the study of glands, the hormones produced by them and their ultimate effect on target organs. These glands communicate with target organs through impulses (the nervous system), chemicals (hormones), chemical mediators (cytokines) and other molecules. Some skin disorders are due to direct effect of hormones or its imbalance, while some are associated with it, whereas, some skin manifestations are only part of general metabolic change. So, examination of cutaneous system should be routinely done in all endocrinal disorders. The objectives of our study were- to observe the prevalence of cutaneous manifestations in individuals having endocrinal disorders, to observe the pattern and type of cutaneous manifestations in patients having endocrinal disorders, and to observe the effect of endocrine disorders on existing skin conditions.

METHODS

150 patients having endocrinal disorders were studied. Detailed history was noted, and physical examination was done in each patient. Patients were regularly followed up and findings were recorded in predesigned proforma. Investigations were done as needed, and patients were treated accordingly and referred to endocrinology department for further management of endocrine disorders.

RESULTS

Out of 150 patients, maximum number of patients (46) were having diabetes mellitus, followed by 37 patients having hypothyroidism.

CONCLUSIONS

Out of 150 patients, 113 patients (75.3%) showed some or other cutaneous manifestation. Maximum cutaneous changes were observed in diabetic patients (44/46). Infection was the commonest (21 patients) and all of them were diabetic. Dry skin was next to infection.

KEYWORDS

Cutaneous Manifestations, Endocrinal Disorders.

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BACKGROUND

Skin is the largest organ of the body. It behaves like mirror for various systemic disorders-endocrinopathy is one of them. Endocrinology is the term used for the study of glands, the hormones they produce and the ultimate effect on target organs. Endocrine glands are pituitary, thyroid, parathyroid, pancreatic islets, adrenals and gonads. These glands communicate with target organs through impulses (the nervous system), chemicals (hormones), chemical mediators (cytokines) and other molecules. Some skin disorders are due to direct effect of hormones or its imbalance, while some are associated with it. Whereas some skin manifestations are only part of general metabolic change. In this way, many hormonal changes are reflected directly or indirectly on the skin. So it seems that detailed clinical examination of cutaneous system should be routine in all endocrinal disorders.

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Endocrinology

Secretion of Hormones

Hypothalamus is the gland which controls the secretion of hormones from pituitary gland. Hypothalamic neural cells synthesize specific releasing and inhibiting hormones that are secreted directly into the portal vessels of pituitary stalk. Pituitary gland is called as "master gland". It consists of anterior and posterior lobes which secrete different hormones. Anterior pituitary secretes GH, ACTH, TSH, MSH, FSH, LH and prolactin. While posterior pituitary secretes vasopressin and oxytocin. These hormones act upon the concerned target organs. Thyroid gland produces thyroxin (T4) and triiodothyronine (T3). Parathyroid gland secretes parathyroid hormone (PTH).

Adrenal gland has two parts. Outer cortex secretes steroid hormones. Functionally it is divided into three zones:

1. Zona glomerulosa-produces mineralocorticoids.
2. Zona fasciculata-produces glucocorticoids.
3. Zona reticularis-produces sex hormones.

Inner medulla secretes adrenaline, noradrenaline.

High level of corticosteroids causes decrease in mitotic activity and vice versa.[1,2,3] They decrease synthesis and accumulation of glycosaminoglycans[4] and collagen.[5]

Pancreas secretes hormones like insulin and glucagon.

Testes consist of two components-clusters of interstitial or Leydig cells, where androgenic steroids are synthesized, and a system of spermatogenic tubules for the production and transport of sperm.

Ovaries cortex contains ovarian follicles which contain ova and secretes oestrogen. After ovulation, follicle gets converted into corpus luteum which secretes progesterone. Ovarian hormones play significant role in puberty, menstruation, fertility etc.

Hormones are transported either as free hormone or in association with serum binding proteins. But only free hormones elicit biological response. Each of the major HPA axis is governed by negative feedback.

Other factors like seasons, diurnal variation, good sleep, meals, and stress like events also affect hormonal rhythms/secretion. Many peptide hormones are secreted in discrete bursts every few hours like LH, FSH. Secretions are exquisitely sensitive to GnRH pulse frequency.[6]

Aim and Objectives

1. To observe the prevalence of cutaneous manifestations in individuals having endocrinal disorders.
2. To observe the pattern and type of cutaneous manifestations in patients having endocrinal disorders.
3. To observe the effect of endocrine disorders on existing skin conditions.

METHODS

Study was done of 150 patients having endocrinal disorders for the period of 18 months. Patients on oral contraceptive pills, patients on steroids for long time, pregnant women were excluded from the study.

Detail history was noted, and physical examination was done in each patient. Patients were regularly followed up and findings were recorded in predesigned proforma. Investigations were done if needed including routine blood investigations, urine examination, blood sugar, x-ray, USG, CT scan, MRI, skin biopsy, KOH examination, fungal culture, slit skin smear, chromosomal study, thyroid scan, hormonal profile, radio-isotope uptake, FNAC etc. Patients were treated accordingly and were referred to endocrine department for further management of endocrine disorders.

RESULTS

Total 150 patients (65 males and 85 females) having endocrinal disorders were studied within 18 months duration. Out of 150, 113 patients (75.3%) had skin manifestations at the time of study which included 51 (45.13%) males and 62 (54.86%) females.

Age (Years)	Male	Female	No. of Cases
Less than 10-10	3	3	6
11-20	10	13	23
21-30	6	16	22
31-40	9	23	32
41-50	15	13	28
51-60	16	10	26
More than 60	7	6	13
Total	65	85	150

Table 1. Age/Sex Distribution

Gland Having Disorder	No. of Pts	Patients with Cuta. Mani.	%
Pituitary	19	14	73.68%
Thyroid	67	42	62.69%
Parathyroid	8	1	12.50%
Adrenals	5	3	60.0%
Pancreatic islets	46	44	95.65%
Gonads	14	9	64.28%

Table 2. Cutaneous Manifestations & Endocrinal Disorders

4 patients with pituitary disorders were also having hyper-prolactinoma and galactorrhoea. 3 patients were found to have hypothyroidism and DM both. 3 other patients of hypothyroidism were having disorders of gonads and pituitary adenoma. While 1 patient was having thyrotoxicosis and DM. So, some patients were having more than one endocrine disorders.

No.	Skin Manifestations	Male	Female	N	%
1	Fungal infection: Superficial (Dermatophytosis)	8	5	13	11.50%
	Deep	1	-	1	0.88%
	Other	4	-	4	3.54%
2	Bacterial infection Folliculitis	1	-	1	0.88%
	Intertrigo	3	1	4	3.54%
3	Pruritus Generalized	2	11	13	11.50%
	Localized	2	3	5	4.42%
4	Thinning of eyebrows	6	10	16	14.16%
5	Thick skin, ↑ skin markings, enlarged pores	6	8	14	12.38%
6	Dry skin	6	8	14	12.38%
7	Eczema	6	7	13	11.50%
8	Thinning of hair	5	7	12	10.61%
9	Increase skin temperature & increase sweating	3	7	10	8.85%
10	Acne	4	6	10	8.85%
11	Pigmentary disorders Hyper pigmentary	4	3	7	6.20%
	Hypo pigmentary	1	-	1	0.88%
	De pigmentary (vitiligo)	1	1	2	1.77%
12	Diffuse alopecia	4	3	7	6.20%
13	Skin tags	1	6	7	6.20%
14	Palmoplantar dyskeratosis	4	2	6	5.31%
15	Hirsutism	-	5	5	4.42%
16	Urticaria	2	2	4	3.54%
17	Acanthosis nigricans	-	4	4	3.54%
18	Ichthyosis	1	1	2	1.77%
19	Purpura	1	1	2	1.77%
20	Miliaria	1	1	2	1.77%
21	LSA/Kraurosis Vulva	-	2	2	1.77%
22	Plane warts	1	1	2	1.77%
23	Seborrhoeic keratosis	-	1	1	0.88%
24	Telangiectasia	1	-	1	0.88%
25	Diabetic bulla	1	-	1	0.88%
26	Perforating disorders	1	-	1	0.88%
27	Alopecia areata	-	1	1	0.88%
28	Psoriasis	1	-	1	0.88%
29	Leprosy	1	-	1	0.88%

Table 3. Skin Manifestations

Other manifestations which have been observed are absence of secondary sex characteristics, discharge from nipple, abnormal breast development, small genitals, increased size of hands and feet, thickened lips, coarsening of facial features, short stature, short webbed neck, oedema

over body parts etc. Oral ulcer, secondary infection, herpes simplex infection, pustular eruptions, palmar erythema, pityriasis capitis, burning sensation on soles, striae were also observed. Each of these manifestations was seen in 1-2 patients.

Disease	No. of Pts. (N)	No. of Pts. With Cuta. Mani. (N)	%
Pituitary adenoma	11 (6M+5F)	8	72.72%
Acromegaly	5 (2M+3F)	4	80.0%
Gigantism	1 (1M)	1	100%
Cushing's disease	1 (1F)	1	100%
Sheehan's syndrome	1 (1F)	-	0.00%

Table 4. Disorders of Pituitary Gland

Out of 19 patients of pituitary disorders, 14 patients showed cutaneous changes. Acromegaly was found in 3 females without finding pituitary adenoma. Hyper prolactinoma was found with galactorrhoea in 3 females and 1 male.

Skin changes observed in pituitary disorders were thick skin with increased skin markings and enlarged skin pores (in 14 patients), acne (8 patients), skin tags (2 pts), thick protruded lower lips, purpura, seborrhoea keratosis, hyperpigmentation on exposed parts of the body etc.

Disease	No. of Pts. (N=)	Pts. With Cutaneous Manifestations	%
Hypothyroidism	37(10M+27F)	27	72.97%
Hyperthyroidism	18(7M+11F)	10	55.55%
Goiter	4(4F)	3	25%
Hashimoto's thyroiditis	3(3F)	1	33.3%3
Thyroid cyst	2(1M+1F)	1	50%
Cretinism	1(1M)	-	-
Myxedema	1(1F)	1	100%
Grave's disease	1(1F)	-	-
Total	67(19M+48F)	42	62.69%

Table 5. Disorders of Thyroid Gland

Majority of patients were having hypothyroidism (that is 37/67) out of which 27 showed cutaneous manifestations. Thinning of eyebrows was observed maximally. Other features were dry skin, thinning of hair, pruritus, skin tags, vitiligo, urticaria etc.

Out of 18 patients of hyperthyroidism, 10 patients had cutaneous manifestations. All 10 patients were having increased skin temperature and excessive sweating, 7 patients had diffuse alopecia and 5 had palmar dyskeratosis. While 1 patient showed characteristic Plummer's nail.

Disease	No. of Pts. (N=)	Pts. With Cutaneous Manifestations	%
Hyperparathyroidism	7(2M+5F)	1	14.28%
Hypoparathyroidism	1(1M)	-	-
Total	8(3M+5F)	1	12.50%

Table 6. Disorders of Parathyroid Gland

Figure 1

Figure 2

Only one patient with congenital X-linked recessive ichthyosis was found to have hyperparathyroidism.

Disease	No. of Pts. (N=)	Pts. With Cutaneous Manifestations	%
Cushing's syndrome	3(1M+2F)	3	100%
Pheochromocytoma	2(1M+1F)	-	-
Total	5(2M+3F)	3	60%

Table 7. Disorders of Adrenal Gland

Cutaneous manifestations observed in 3 patients were puffiness of face, buffalo hump, purpura, hyperpigmentation.

Figure 3

Disease	No. of Pts. (N=)	Pts. With Cutaneous Manifestations	%
Diabetes Mellitus	46(29M+17F)	44	95.65%

Table 8. Disorders of Pancreatic Islets

Skin Changes	No. of Patients (N=)
Dermatophytosis	13(8M+5F)
Candidiasis	3(3M)
Bacterial infection	4(2M+2F)
Eczema	7(5M+2F)
Pruritus	4(4F)
Skin tags	2(1M+1F)
Others	11(9M+2F)
Total	44(28M+16F)

Table 9. Skin Changes in Diabetes Mellitus

Other skin changes observed in diabetic patients were diabetic bulla, acanthosis nigricans, urticaria, leprosy, psoriasis, perforating disorder, mucormycosis etc.

Infection was the commonest cutaneous manifestation which was seen in 21 cases totally (dermatophytic infection being the most common among them).

Figure 4

Disease	No. of Pts. (N=)	Pts. With Cutaneous Manifestations	%
PCOS	6 (6F)	5	83.33%
Hypo gonadotrophic hypogonadism	5 (3M+2F)	4	80%
Turner's syndrome	2 (2F)	-	-
Klinefelter's syndrome	1 (1M)	-	-
Total	14(4M+10F)	9	64.28%

Table 10. Disorders of Gonads and Sexual Differentiation

Out of 14 patients of disorders of gonads and sexual differentiation, 9 were having cutaneous manifestations.

Out of 6 females with polycystic ovarian disease, cutaneous manifestations were found in 5 cases. Hirsutism was seen in 5 patients, acne in 2 patients, acanthosis nigricans in 2 patients, and enlargement of ovaries in 1 patient.

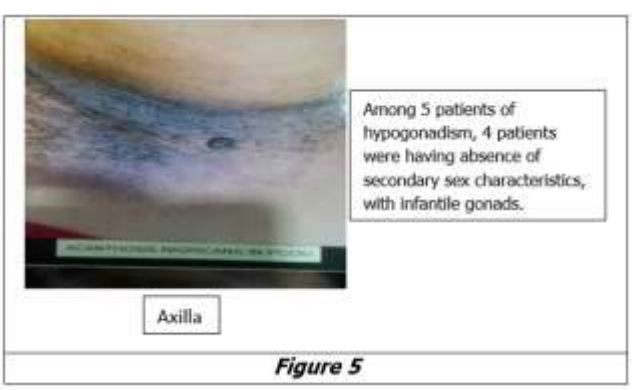

Figure 5

DISCUSSION

Hormones have major role in various physiological functions including growth, metabolism of various nutritive substances, maintenance of balance of various minerals and electrolytes in the body, as well as also have identified role in the attainment of mature sexual functions. Effects of hormones are reflected directly or indirectly on skin in form of various cutaneous manifestations.

Present study was done during the period of 18 months which included 150 patients attending OPD with various endocrinal disorders. Most of them were on treatment.

Out of them, 65 were males and 85 were females with M:F ratio of 1:1.30 which is similar to the ratio of 1:1.38 in the study done by Mahajan S et al.[7] Majority of patients-21.3% (32 patients) were seen in the 4th decade. While Mahajan S et al reported majority patients in 41-50 years age group (33%).[7]

Maximum number of patients (46) were having diabetes mellitus, followed by 37 patients having hypothyroidism.

Out of total 150 patients, 113 patients (75.3%) showed some or other cutaneous manifestation. Maximum cutaneous changes were observed in diabetic patients (44/46).

Among the individual cutaneous manifestation, highest number of patients-18 patients was of pruritus[8] and fungal infection each. Study done by Apra Sood et al also reported diabetes mellitus, thyroid disorders as systemic cause of pruritus.[8] Other skin lesions observed were thinning of eyebrows (16 patients), dry skin (14 patients), eczema (13 patients), skin tags (7 patients), palmoplantar dyskeratosis (6 patients), bacterial infection (5 patients), urticaria (4 patients) etc.

14 out of 19 patients of pituitary disorders showed cutaneous manifestations in form of thick skin, increased skin markings, enlarged skin pores, acne, purpura, skin tags.[9] Hyperpigmentation was also found which was seen in study done by Lang PG et al[10] and in the study done by Michael L et al[11] too. Mhijazy et al also reported skin tags, acne, purpura as common manifestations of pituitary disorders.[9]

Among thyroid disorders, 62.7% patients (42/67), showed cutaneous changes.[12] Excessive sweating, pruritus, diffuse alopecia,[13] palmar dyskeratosis, Plummer's nail were seen in hyperthyroidism. Hair loss in patients of hyperthyroidism was also noted by Jabbour SA.[14] Pruritus was reported as prominent manifestation of hyperthyroidism in study done by Barrow MV et al.[13]

Thinning of eyebrows, dry skin,[8] thin hair, and pruritus were common in patients of hypothyroidism. Mhijazy et al also reported similar cutaneous manifestations in thyroid disorders.[9]

Only 1 patient of parathyroid gland disorder was having skin changes.

Generalized hyperpigmentation on exposed parts and purpura were seen in 3 out of 5 patients of adrenal gland disorders. Generalized hyperpigmentation was also reported as common manifestation in study done by Mhijazy et al[9] and the study done by Jabbour SA.[14]

Out of 46 patients of diabetes mellitus, 44 were having cutaneous manifestations (95%), while Mahajan S et al reported cutaneous manifestations in 64% patients of diabetes mellitus[7] and Nigam PK et al reported cutaneous

manifestations in 70% of diabetic individuals.[15] Among them, infection was the commonest finding (48%) which was comparable with the study done by Mahajan S et al (54%).[7]

Among the disorders of gonads and sexual differentiation, 64.28% patients (9/14) showed cutaneous manifestations in form of hirsutism, acne, acanthosis nigricans, absence of secondary sex characteristics, infantile gonads etc. Similar findings were seen in study done by Keen MA et al.[16]

No significant change was observed in already existing skin conditions in patients having endocrinal disorders.

CONCLUSIONS

Out of 150, 113 patients (75.3%) were found to have cutaneous manifestations with female predominance (85/150). Commonest age group was 4th decade. Commonest endocrine disorder was diabetes mellitus, seen in 46 patients (30.66%) followed by hypothyroidism in 37 patients (24.66%). Commonest cutaneous manifestation observed was infection, seen in a total of 21 patients who were diabetic. Pruritus was next to infection.

Reasonable importance should be given to dermatological examination in patients of endocrinal disorders, in view of 75% of the patients showing cutaneous manifestations in the present study which helps further in detecting and diagnosing endocrine disorders.

Improvement in cutaneous lesion may be considered as index of assessment of control of endocrine disorder. For this, routine cutaneous examination is necessary.

Creating the awareness among the patients and minor preventive measures, at the same time better control of endocrinal disorders help to relieve the cutaneous symptoms in major patients.

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