

Cutaneous Manifestations of Hypothyroidism amongst Gynecological consultations

Zaheera Saadia, M.D.⁽¹⁾, Abdullateef A. Alzolibani, M.D.⁽²⁾, Ahmad Al Robaee, M.D.⁽²⁾, Hani A. Al Shobaili M.D.⁽²⁾, Ahmad A Settin, M.D.⁽³⁾

Department of Obstetrics and Gynecology⁽¹⁾

Department of Dermatology⁽²⁾

Department of Pediatrics⁽³⁾

College of Medicine, Qassim University

Saudi Arabia

Abstract

Objectives: Many of the signs of hypothyroidism, affect the skin as well as the genital system of affected female cases. The aim of this study is to highlight the presenting dermatologic and gynecologic manifestations of firstly-diagnosed hypothyroid females.

Patients and Methods: This is a case control study that included 150 patients presenting for gynecological consultation. Out of them, 60 were affected with hypothyroidism and 90 were euthyroid based on clinical and laboratory investigation backgrounds. Their gynecologic and dermatologic findings were analyzed and compared statistically.

Results. Compared to euthyroid cases, hypothyroid ones were presenting mostly with amenorrhea (OR=7.76). Other gynecologic manifestations that were prominent in hypothyroid cases were dyspareunia, PCO, PMS and Breast tenderness. On the other hand, rate of menstrual irregularities and infertility were non-significantly different in both groups.

Hypothyroid women showed also significantly higher frequency of urticaria and puffiness of hands and feet (both were present in 16.7% in hypothyroid vs. 3.3% of euthyroid cases, $p = 0.007$, OR=5.8). Hypothyroid cases showed also significantly higher frequency of yellow ivory skin (OR=5.4) and coarse rough dry skin (OR=3.8). On the other hand, alopecia and periorbital edema were observed only among cases of hypothyroidism and none of euthyroid cases.

Conclusion. A great index of suspicion should be always exerted to the diagnosis of disorders manifesting with subtle manifestations as hypothyroidism in female cases particularly having gynecologic and dermatologic disorders.

Key words: dermatologic manifestations, hypothyroidism, gynecologic problems

Corresponding Author:

Zaheera Saadia, M.D.P.O.Box 30109

Buraidah 51477 Qassim, Saudi Arabia

Tel: +966-6-3800050 Ext. 2862

Fax: +966-6-3801228

Email: zaheerasaadia@hotmail.com

Introduction

Hypothyroidism is a clinical state resulting from an insufficient amount of circulating thyroid hormone to support a normal body function. The prevalence of unsuspected overt hypothyroidism ranges from 1-18 cases per thousand persons. The female to male ratio in hypothyroidism ranges from 2:1 to 8:1 in various epidemiological surveys^{1,2}.

Dermopathies associated with thyroid disease includes melasma, vitiligo, alopecia, premenstrual acne, myxedema, dry skin, yellowish discoloration and onychodystrophy. Frequently, a high degree of suspicion is required in order to appreciate the clinical manifestations of hypothyroid disorders particularly related to the skin and genital tract of affected female cases to reach a diagnosis. Unfortunately, there is very little information available on this subject from

Qassim region, the central area of Saudi Arabia. Therefore, this work was planned in order to highlight the possible dermatologic as well as gynecologic features of hypothyroidism among female cases from this locality.

Patients and methods

This was a case control study, carried out at the Qassim University affiliated Clinics, Buraydah, Saudi Arabia. All the patients holding Saudi nationality coming to Gynecological Clinic for their Gynecological consultations from January to October 2009 were screened for thyroid disease by laboratory test and examined by a group of trained physicians for any skin problems after obtaining a verbal consent. Both the doctors and the patients were unaware of the thyroid status of the patients at the time of interview and examination. The diagnosis of

hypothyroidism was established after the availability of results of laboratory investigations on the basis of both clinical judgment and the laboratory investigations. The laboratory tests comprised of serum T₃, T₄ and TSH by radioimmunoassay. TSH >4.20 IU/ml, T₃<3.9 pm/it and T₄<12.0 pm/it were considered as hypothyroid. Exclusion criteria included all patients with already established diagnosis of hypothyroidism, thyroid ablation or thyroidectomy, co-existing infections, thyroid or other malignancies, other systemic illnesses like, diabetes mellitus, cardiac, renal and liver failure etc., hyperthyroidism, sub-clinical hypothyroidism, pregnancy and those already on thyroid hormone replacement therapy were excluded from the study. There was no age limit specified for inclusion in the study. On these bases, 60 of these cases were found to have hypothyroidism. Their age mean \pm SD was 33.9 ± 10.1 years. They were compared to

other 90 euthyroid cases with an age mean \pm SD of 34.6 ± 11.2 years. In terms of their dermatologic and gynecologic manifestations.

Statistical analysis

The data were entered and analyzed using SPSS statistical software package, version 16.0 for Windows (Vista premium). Both gynecologic and dermatologic manifestations in both studied groups of women with hypothyroidism or controls were compared using Fisher exact test and odds ratio with 95% confidence intervals. Probability (p) value less than 0.05 was considered as significant.

Results

Regarding the gynecologic manifestations, hypothyroid cases were presenting mostly with amenorrhea compared to the euthyroid ones (OR=7.76). Interestingly, vulvovaginal infections were found significantly lower in hypothyroid

cases than euthyroid ones (OR=0.12). Other gynecologic manifestations that were prominent in hypothyroid cases were dysparunia, PCO and PMS and Breast tenderness. On the other hand, rate of menstrual irregularities and infertility were non-significantly different in both groups. (Table 1.)

Compared to euthyroid cases, hypothyroid women showed significantly higher frequency of urticaria and puffiness of hands and feet (both were present in 16.7% in hypothyroid vs. 3.3% of euthyroid cases, $p=0.007$, OR=5.8). Hypothyroid cases showed also significantly higher frequency of yellow ivory skin (OR=5.4) and coarse rough dry skin (OR=3.8). On the other hand, alopecia and periorbital edema were observed only among cases of hypothyroidism and none of euthyroid cases. Other cutaneous manifestations were also detected in higher proportion among hypothyroid cases but statistically nonsignificant from the

euthyroid ones included vitiligo, brittle thick nails and eczema (Table 2.).

Discussion

Hypothyroidism may form a relatively diagnostic problem as its manifestations are usually subtle and can be easily overlooked. This was well apparent in the results of the survey carried out in County Durham, England, in which hypothyroidism was detected in 1.9% of women and was overt in 1.4%. The prevalence in men was less than 0.1 percent². Moreover, recent surveys indicated hypothyroidism to be more prevalent in elderly population, reaching as high as 20%³. Another study among Framingham population showed that 5.9% of the women and 2.4% of men above the age of sixty had serum TSH levels more than 10mU/L⁴. In Ireland the prevalence of primary hypothyroidism has been stated as 8.6% in the women above the age of fifty years as compared to only 0.9% in younger females⁵. The incidence of congenital

hypothyroidism was reported to be 1 in 2,640 in a study from India⁶. In iodine-replete areas, autoimmune thyroid disease and thyroablative therapy are the major reasons of hypothyroidism. Even in children and adolescents autoimmune thyroiditis is the commonest cause of non-endemic thyromegaly and acquired hypothyroidism⁷. However, worldwide, iodine deficiency is the leading cause of hypothyroidism⁸.

Many authors reports that hypothyroidism have non specific clinical presentation and high degree of clinical suspicion is required before going for biochemical markers¹¹. The clinical manifestations of hypo-thyroidism are variable, depending upon its cause, duration, and severity. The spectrum extends from sub-clinical to overt hypothyroidism to myxedema coma. The characteristic pathological finding in a hypothyroid patient is the accumulation of hyaluronic acid and other glycosaminoglycans in the interstitial

tissues.⁹

Skin and cutaneous appendages are target organs for thyroid hormones. Thus, a variety of changes of skin, hair and nails occurs in association with thyroid diseases. Most of these cutaneous changes are unspecific, but in their entirety they may nonetheless be indicative of thyroid diseases¹⁰. The diagnosis of thyroid disease can often first be identified by recognizing various cutaneous manifestations associated with an imbalance of circulating thyroid hormone.

In this study most of the cases coming with gynecologic problems particularly amenorrhea, dysparunia, PCO and PMS and Breast tenderness had also hypothyroidism. In the meantime they were found also to have evident skin manifestations mostly with urticaria and puffiness of hands and feet. They also showed higher frequency of yellow ivory skin and coarse rough dry skin along with other manifestations like alopecia

and periorbital edema, vitiligo, brittle thick nails and eczema. These manifestations are mainly due to the accumulation of glycosaminoglycans in the interstitial space is responsible for coarse skin, puffy face and rough hair ¹².

Our results are consistent with that of Jabbour who reported that in patients with hypothyroidism there is hair loss and the skin was cold and pale, with myxedema changes in the hands and periorbital region ¹³. Lenzoff and Sussman evaluated 624 cases with urticaria found 90 to have thyroid disease ¹⁴. Heymann has stated that the mechanism by which thyroid autoimmunity is associated with urticaria is unknown they have stated that there is a clustering of thyroid microsomal antibodies in patients with a positive autologous serum test ¹⁵. Thyroid dermopathy is said to be the most characteristic cutaneous sign of hypothyroidism which is characterized by generalized myxedema caused by deposition

of dermal acid mucopolysaccharide especially hyaluronic acid and chondroitin sulphate ¹⁶.

Although we excluded all pregnant ladies in our study while reviewing literature we noticed a study from Iran revealed that when thyroid status of mother was checked who have given birth to hypothyroid babies Subclinical hypothyroidism was diagnosed ¹⁷. This further strengthens our opinion that obstetricians and gynaecologists should be vigilant to look for any sign of thyroid disease in females.

This work stressed the strong association between cutaneous signs and symptoms with hypothyroidism especially among females with gynecologic problems. Gynecologists may commonly miss skin lesions while concentrating on the gynecological complaint only. Therefore, 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.

References

1. Helfand M, Crapo L. Screening for thyroid disease. *Ann Intern Med* 1990; 112(11):840-849.
2. Tunbridge WM, Evered DC, Hall R, Appleton D, Brewis M, Clark F, et al. The spectrum of thyroid disease in a community: the Whickham survey. *Clin Endocrinology (Oxf)* 1977 Dec; 7(6):481-93.
3. Sawin CT, Chopra D, Azizi F, Mannix JE, Bacharach P. The aging thyroid: increased prevalence of elevated serum thyrotropin levels in the elderly. *JAMA* 1979; 242(3): 247-50.
4. Sawin CT, Castelli WP, Hershman JM, McNamara P, Bacharach P. The aging thyroid: Thyroid deficiency in the Framingham study. *Arch Intern Med* 1985; 145(8):1386-88.
5. Bonar BD, McColgan B, Smith DF, Darke C, Guttridge MG, Williams H, et al. Hypothyroidism and aging: the Rosses' survey. *Thyroid* 2000; 10(9): 821-7.
6. Desai MP. Disorders of thyroid gland in India. *Indian J Pediatr* 1997; 64(1):11-20.
7. Doeker B, Reinehr T, Andler W. Autoimmune thyroiditis in the children and adolescents: clinical and laboratory findings in 34 patients. *Klin Padiatrie* 2000; 212(3):103-107.
8. Chiu AC, Sherman SI. Clinical manifestations and differential diagnosis of hypothyroidism. In: Falk SA, ed. *Thyroid disease: Endocrinology, Surgery, Nuclear Medicine, and Radiotherapy*. 2nd ed. Philadelphia, Lippincott-Raven, 1997, pp379.
9. Smith TJ, Balin RS, Gorman CA. Connective tissue, glycosaminoglycans and diseases of the thyroid. *Endocr Rev* 1989; 10(3): 366-391.
10. Irfan M Khurram, Kiran S Choudhry, Khan Muhammad, Najmul Islam. Clinical presentation of hypothyroidism: A case control study. *J Ayub Med Coll*. Jan - Mar 2003; 15(1):45-9.
11. Ali Jabbari, Sima Besharat, Nasrin Razayianzadeh, Mansour Moetabar. Common signs and symptoms in hypothyroidism in central part of Iran. *PakJMedSci*. Jan-Mar2008; 24(1):44-7.

12. Smith, TJ, Bahn,RS,Goman. C.Connective tissue, glycosaminoglycans, and diseases of the thyroid. *Endocr Rev* 1989; 10:366.
13. Jabbour SA. Cutaneous manifestations of endocrine disorders: a guide for dermatologists. *Am J Clin Dermatol.* 2003;4(5):315-31.
14. Leznoff A, Sussman GL. Syndrome of Idiopathic chronic urticaria and angioedema with thyroid autoimmunity: A study of 90 patients. *J Allergy Clin Immunol* 1989; 84:66-
15. Rumbly JS, Katz JL, Schock AL . Resolution of chronic urticaria in patients with thyroid autoimmunity. *J Allergy Clin Immunol* 1995; 96:901-5.
16. Heymann WR. Cutaneous manifestation of thyroid disease. *J Am Acad Dermatol* 1992; 26:85-902.
17. Gholamreza Asadi Karam, Hamid Hakimi, Mohsen Rezaeian, Abdollah Gafarzadeh, Hamidreza Rashidinejad, Mohammad Khaksari. Thyroid function in mothers who gave birth to neonates with transient congenital hypothyroidism. *Pak J Med Sci Jul - Sep 2009;25(4):568-72.*

Table 1. Gynecologic manifestations of hypothyroid female cases compared to euthyroid controls

Gynecologic manifestations	Hypothyroid n=60 n (%)	Euthyroid n=90 n (%)	Fisher exact (p)	Odds ratio (95% CI)
Menstrual irregularities	21(35.0)	36 (40.0)	0.61	0.8 (0.14- 1.59)
Amenorrhea	9 (15.0)	2 (2.2)	0.004*	7.76 (1.61- 37.34)
Infertility	7 (11.7)	11(12.2)	1	0.95 (0.35- 2.6)
recurrent miscarriages	5 (8.3)	7 (7.8)	1	1.1 (0.31- 3.57)
Dysparunia	4 (6.7)	0 (0)	0.024*	-
##PMS and Breast tenderness	6 (10.0)	6 (6.7)	0.544	1.6 (0.477-5.07)
PCOS	6 (10.0)	8 (8.9)	1	1.14 (0.37- 3.47)
Vulvovaginal infections	2 (3.3)	20 (22.2)	0.002*	0.12 (0.027- 0.54)

*significant $p < 0.05$ ** $p < 0.001$

Table 2. Dermatologic manifestations of hypothyroid female cases compared to euthyroid controls

##Dermatologic manifestations	Hypothyroid n=60 n (%)	Euthyroid n=90 n (%)	###Fisher exact (p)	Odds ratio (95% CI)
Normal skin	1 (1.7)	69 (76.7)	00.00**	0.005 (0.0007-0.04)
Yellow ivory skin	7 (11.7)	2 (2.2)	0.030*	5.44 (1.10- 27.05)
Puffy hands and feet	10 (16.7)	3 (3.3)	0.007*	5.8 (1.52- 22.07)
Brittle thick nails	2 (3.3)	1 (1.1)	0.564	3.1 (0.3- 34.62)
Eczema	10 (16.7)	6 (6.7)	0.062	2.8 (0.96- 8.17)
Vitiligo	2 (3.3)	2 (2.2)	1	1.5 (0.21- 11.1)
Urticaria	10 (16.7)	3 (3.3)	0.007*	5.8 (1.52- 22.07)
Alopecia	5 (8.3)	0 (0.0)	0.009*	-
Coarse rough dry skin	9 (15.0)	4 (4.4)	0.036*	3.8 (1.11- 12.95)
Periorbital edema	4 (6.7)	0 (0.0)	0.024*	-

*significant $p < 0.05$ ** $p < 0.001$