Original Article

Ocular Manifestations in Thyroid Disorders in Karachi

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ABSTRACT

Objective: To analyze the ocular findings in thyroid disorders presented in Karachi.
Study Design: A Cross-sectional study
Place and Duration of Study: This study was conducted at the outpatients departments of two tertiary care hospitals of Karachi, Liaquat National Hospital and Dow University of Health Sciences Ojha Campus, Karachi in the department of Endocrinology and Ophthalmology from June, 2018 to June, 2019.
Materials and Methods: Inclusion criteria of thyroid disorder patients were; age between 12-60 years, known hypothyroidism or hyperthyroidism, finding of thyroid abnormalities and visible goiter or exophthalmos. The exclusion criteria were, known diabetic or hypertensive, on iodine containing drugs, pulsatile exophthalmos, poly glandular autoimmune diseases and lens/corneal/retinal abnormalities. One hundred and eleven patients were selected according to the inclusion criteria. After consent recent detailed history, clinical examination and ophthalmic examinations were done. Required laboratory and radiological investigations were done and analyzed. The data were entered in SPSS version 20 for descriptive and other relevant statistical analysis. Each patient was examined with slit lamp for anterior segment, snellen chart for measurement of visual acuity, ophthalmoscope for fundoscopy, Goldmann Applanation Tonometer for intraocular pressure measurement, Torch for examination of pupil and extraocular movements and Hertel exophthalmometer to measure amount of exophthalmos. CT and (Hertel) MRI in selected cases were done.
Results: The mean age of involvement was 39+/- 15 years and there was female preponderance 2.6:1. Out of 111 patients 70% were hyperthyroid and 30% were fixed with the diagnosis of hypothyroidism. Almost 20% had bilateral proptosis while unilateral exophthalmos was 5.5%. Goiter was visible among 28%. Around 20% had family history of thyroid disorders and habitual usage of iodized salt was 17%. Addiction to smoking was 26%. The main ocular sign in hyperthyroidism was ocular pressure and increased myopia and while xerosis of eyes and loss of hairs in eyebrows were main ocular presentation among hypothyroidism. The most elicited sign in hyperthyroidism was lid lagging and eye protrusion while congested eye lids, dry eyes and weak ocular movements were main signs among hypothyroidism. Marcus Gunn pupil and papilledema were present in 2 patients. Optic neuropathy was present in one patient. The latter signs were red flag signs of oculopathies in hyperthyroidism.
Conclusion: Eyes are good representative of thyroid disorders if examined according to the standard protocol. Hyperthyroidism has sine qua non ocular markers while in hypothyroidism the slow basal metabolic rate represents in eyes as xerosis and loss of eyebrows.
Key Words: Ocular manifestations, thyroid eye diseases

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INTRODUCTION

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Thyroid disorders are one of the diseases which have specific peripheral stigmata or target organ involvement.[1] Thyroid dysfunction has specific changes in whole eye including adjacent structures that is thyroid orbitopathy.[2] It is said that if these ocular signs are present in euthyroid status, the patients in future ultimately develop the clinical features of thyrotoxicosis with biochemical evidence.[3] This is an interesting fact that hypo and hyper function of thyroid gland, both can involve the specific changes in eye[4.] Incidence of thyroid eye disease (TED) in hyperthyroidism is 77% and less frequently in euthyroid 20% and 3% among hypothyroidism in most of the studies conducted around the world.[5] In Pakistan the ocular manifestations associated with thyroid disorders varies between 27%-46% in different

locations of the country.[6] TED is one of the mysterious disease in which pathogenesis is arguable since many decades. Exact pathology is yet not known however different theories are suggested[7.] Infact the pathogenesis is multifactorial.[8] The most important pathogenesis effect detected is increased TSH, T_3, T_4 and increment of receptors in the orbit.[9]The other important role is after the initiation of inflammation intraorbitally the influx of neutrophils followed by lymphocytes and fibroblasts.[10]Other factor postulated is release of long acting thyroid stimulating hormone and exophthalmos producing substance.[11] Another view widely accepted is the production of antibodies against different constituents of orbit especially intra ocular muscles.[12] Histopathology in cadavers had shown excessive deposition of muccopolysaccharides inside the orbit.[12]

MATERIALS AND METHODS

This is an observational cross-sectional study conducted at Liaquat National Hospital and Dow University of Health Sciences Ojha Campus, Karachi in the department of Endocrinology and Ophthalmology from June 30th, 2018 to June 30th, 2019. The study was approved by Institutional and Ethical Review Committees of both institutions. Verbal consent was taken from each patient included and recorded. Inclusion criteria were, (a) known patient of thyroid disorders for at least 6 months, (b) known or detected unilateral or bilateral exophthalmos, (c) goiter clinically visible or palpable, (d) biochemical evidence of thyroid hyper or hypo function, (e) age between 12-60 years to exclude genetic disorders and degenerative impact on eyes.Exclusion criteria were, (a) known case of diabetes and hypertension, (b) those who took iodinated compounds for more than 6 months, (c) polyglandular autoimmune diseases, (d) those who had bilateral cataracts and retinal/corneal abnormalities, (d) pulsatile exophthalmos. The patients were selected from the Outpatient Departments and indoors of the hospitals fulfilling the inclusion criteria. The detailed history and clinical examination were done by the consultants and full ophthalmological reviews were done by the ophthalmologists for ocular findings. The investigations were also analyzed by the consultants including thyroid function tests, thyroid scan, and MRIs of the orbits where indicated. Autoimmune profile was also obtained in the indicated patients. All the informations were recorded in patients profile and then entered in SPSS, version 20 for data analysis. Chi square statistical test is applied where indicated and p value of <0.05 was taken as statistically significant**.**

RESULTS

One hundred and eleven patients were enrolled in the study as per inclusion criteria. Their ages range between 12-60 years and the mean age was 39±15 years. The proportion of females was 78/111 that becomes 70.2% and females to males ratio was 2.3:1. Overall as per thyroid function tests, 78/111 or 70.2% had hyperthyroidism and 33/111(29.7%) had hypothyroidism. Twenty two patients, 22/111 or 20% had bilateral proptosis while 6/111(5.4%) had unilateral exophthalmos. Thirty one patients 31/111 or 27.9% had clinical goiter and 23/111 that is 20.7% had positive family history of thyroid disorders. Forty one patients 41/111 belonged to rural areas of Sindh. Habitual use of iodized salt were present in 19/111 patients that is 17.1% and all belonged to urban areas. Twenty nine patients or 26.1% (24 males and 5 females) were addicted to cigarette smoking or huqqa. Sixty eight patients that is 68/111 or 61.2% were already on anti-thyroid drugs/thyroxine. Clinical presentation in hyperthyroidism and hypothyroid patients are shown in table 1 and the specific ocular changes /signs of comparison between hypothyroidism and hyperthyroidism is depicted in table No 2.

Table no.1 Occular clinical presentations of hyperthyroidism and hypothyroidism

S. No	**Symptoms / Hyperthyroidism (78) Patients**		**Symptoms / hypothyroidism (33) patients**	
	Clinical presentations	**No of patients**	**No of patients**	**Total Count**
1	Dry eyes	63	31	94(85%)
2	Puffiness of eyelids	41	24	65(59%)
3	Gazing eyes	79	2	81(73%)
4	Reduction in visual acuity	54	7	61(55%)
5	Vision loss	3	0	3(2.7%)
6	Disturbance in color vision	2	0	2(1.8%)
7	Proptosis	3	0	3(2.7%)
8	Ocular pressure (pain)	78	0	78(70.27%)

Table No.2: Comparison of ocular signs in hyper/hypothyroidism

S.No	Signs in Thyroid Disorders	Variants of Hyperthyroidism (78/111)							Variants of Hypothyroidism (33/111)			
		Grave's Diseases	Thyrotoxicosis	Toxic Nodular rGoitre	CA-Thyroid	Auto immuneThyroiditis	Drug induced	Secondary	Auto Immuno Thyroiditis	Nutritional	Subclinical (MTF)	Secondary
1	Number of Patients	38	24	7	1	2	3	2	17	7	8	1
2	Visual Acquity disturbed	24	7	2	0	2	2	2	10	5	7	1
3	Color vision	5	0	0	0	0	0	0	0	0	0	0
4	Disturbance in field of vision	15	2	3	0	0	0	0	0	0	0	1
5	Conjunctiva red	33	17	3	1	1	1	1	3	1	1	0
6	cornea normal	33	17	3	1	2	3	2	17	7	8	1
7	Eye lashes/ loss of hair	0	0	1	0	0	0	0	8	2	0	1
8	RAPD	2	0	0	0	0	0	0	0	0	0	1
9	Vongraffe sign	38	21	5	1	2	2	0	0	0	0	1
10	Proptosis unilateral	5	1	0	0	0	0	0	0	0	0	0
11	Proptosis bilateral	18	2	0	0	0	0	1	0	0	0	1
12	Restricted eye movements	11	3	1	0	0	0	0	0	0	0	1
13	Optic neruropathy	4	0	0	0	0	0	0	0	0	0	0
14	Pappiloedema	2	0	0	0	0	0	0	0	0	0	0
15	Xerosis of eyes	0	0	0	0	0	0	0	24	3	1	1

ABBV…RAPD…Relative afferent pupillary defect. MTF..mild thyroid failure.

DISCUSSION

It is known from ancient times that swelling of eyes is related to thyroid glands.[15] Inspite of the disputed pathogenesis of ocular manifestations related to thyroid disorders specific eye changes are seen in both hyper and hypothyroidism.[16] Overall, females are more involved than males in this research article supported by many researchers.[17] The female preponderance is most probably due to the sensitivity to estrogen, pregnancy and lactation.[18] In this study the prevalence of hyperthyroidism is more than hypothyroidism which is against the study done by Knuden and co-workers.[19] In year 2000 in Denmark and surrounding temperate zones were hypothyroidism more seen. Probably in our areas sufficient iodine in water and food cause Weil-Cheikoff effect which cause enhancement for hyperactivity of gland, twenty five percent in our study showed exophthalmos among them almost 5% was unilateral. As compared to American and European countries where proptosis is more than 42-45% among overall hyperthyroid patients but this figure is lower because of genetic, racial and environmental factors.[20] In our study the family history was present in 20.7% while study done by Medgalchi and his co-workers found the higher association that is > 60.5% in the areas near Turkey border.[21] This difference is probably due to higher rate of consanguineous marriages and iodine content in water and soil. Indigenous usage of iodine salts in diet and food, very low/high in iodine content has positive and negative influence on thyroid eye diseases. In our study the habitual use of iodized salt was 17.1% supporting the study done by Rati and Uberti in 2004.[22]Smoking has linear relationship found in this study supported by work done by Kim and co-researchers in 2019.[23] The major ocular symptoms in hyperthyroid in this study was xerosis of eyes with puffiness and gazing stance, increase in myopic error and ocular pressure while in hypothyroidism, dryness of eyes with grittiness, puffy eyelids and reduced visual acuity. These observations are supported by Perroz and coworkers in 2009[23.]

The main etiology of hyperthyroidism in this study was Graves' disease, thyrotoxicosis, toxic multinodular goiter and toxic solitary nodular goiters among the majority of cases while the cause of hypothyroidism in this study was Hashimoto's thyroiditis (autoimmune) and nutritional and sub-clinical hypothyroidism. There was one case of secondary hypothyroidism and two were detected as secondary hyperthyroidism. These facts are supported by many studies done in the last 4 decades especially elaborated in a study done by Kurian and colleagues in 2008.[24] The major signs in ophthalmology of hyperthyroidism were reduction of visual acuity plus increased myopia, congested conjunctiva, fullness of eyes, infrequent blinking, limited upward gaze, vongraffe sign, relative afferent pupillary defect (RAPD) and papilledema while 4 cases of optic neuropathy were detected. These signs are supported by the study done by Satli and Gunduz in 2017[25]. The major ocular signs in hypothyroidism in this study were xerosis of eyes, loss of hairs of eyelashes and lateral one third of eyebrows and only one patient who had primary hyperthyroidism demonstrated proptosis. These observations are supported by the study done by Mahto in 1972[26].

CONCLUSION

Thyroid disorders either manifest as hyper or hypothyroidism has specific ocular changes. In majority of cases in hyperthyroidism, decrease in visual acuity, conjunctival injection, propotosis, lid lagging, gazing stance and weakness of extra ocular muscles are major manifestations. On the other hand, in hypothyroidism, xerosis of eyes and loss of hair of eye lashes and brows are common presentations. Blindness can occur due to optic neuropathy in severe untreated cases. The impact of genetics, smoking and indigenous use of iodized salts on thyroid functions and associated ocular changes are also highlighted.

Author's Contribution:

Concept & Design of Study:	Abdul Hameed Siddique
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Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Jafran K, Sandhegi A, Minaee A, Amen N, Anvari A, Mahmoodi FA, et al. Ocular movements disorders and extra ocular muscles involvement in Iranian Grave's Opthalmopathy. Binocul Vis Strabismus Q 2010; 25: 217-30.
2. Mathur C, Singh S, Sharma S. Prevalence and risk factors of thyroid associated opthalmopathy among Indians. Int J Adv Med 2016;3: 662-5.
3. Sofro O, Safro FS, Anash BO, Yorke E, Akpalu J, BC Nkum et al. Frequency and determinants of thyroid autoimmunity in Ghanian type 2 diabetes patients: a case control study. BMC Endocrinol disorder 2017; 17: 2-5.
4. Tani J, Wall JR. Autoimmunity against eye muscle antigens may explain thyroid – associated opthalmopathy. CMAJ 2006; 175:239-41.
5. Tom C, Paul M, Donald O. Recent developments in thyroid eye disease. BMJ 2004; 329(7462): 385-90.
6. Zoofishan B. Kabir A, Amir S, Faryal R. Relationship of symptoms with demographic features in case of thyroid disorders in Pakistani population. As J Bio + Pharma Sci 2012;2(12): 40-41.
7. Kumari R, Chandra S. Advances in management of thyroid eye diseases: An overview. Int Optholomol 2018;38(5):2247-55.
8. Ayabe R, Rootman DB, Hawang CJ. Adalimumab as steroid sparing treatment of inflammatory stage thyroid eye disease. Opthal Plast Reconsir Surg 2014;30:415-19.
9. Shan SJ, Douglas RS. The pathophysiology of thyroid eye disease. Neuro-opthalmol 2014;34(2): 177-85.
10. Shivani G, Raymard D. The pathophysiology of thyroid eye disease: Implications for immunotherapy. Curr Opin opthalmol 2011;22(5): 385-90.
11. Khong JJ, McNab AA. Ebeling PR. Pathogenesis of thyroid eye disease: review and update on molecular mechanisms. Br J opthalmol 2016; 100: 142-150.
12. Wang Y, Smith T. Current concepts in molecular pathogenesis of thyroid associated opthalmolpathy. Invest opthalmol Vis Sci 2014;55:1735-48.
13. Moreiras JVP, Alverz A, Gomez EC. Treatment of active corticosteroid resistant Grave's opthalmolpathy. Opthal Plast Reconstruct Surg 2014;30:162-7.
14. Shoon JS, Raymard S. The pathophysiology of Thyroid Eye Disease. J Neuro Opthalmol 2014; 34(2):177-185.
15. Woo K, Kim YD, Lee SY. Prevalence and risk factors for steroid eye diseases among Korean dysthyroid patients. Kor J Opthalmol 2013; 27:397-404.
16. Ackuaku EM, Akpalu J, Abaidoo B. Epidemiology and clinical features of thyroid associated orbitopathy in Accra. Middle East. Afr J Opthalmol 2017;24:183-9.

17. Colm M. An overview of thyroid eye disease. Eye vision (London) 2014; 1:9-10.
18. Kavaussi CS, Glacometti NJ, Servat JJ, Levin F. The relationship between sex and symmetry in thyroid eye disease. Clin. Opthalmol 2014;8: 1295-1300.
19. Knuden N, Bulow I, Jorgewen T, Laurberg P, Ovesen L, Perrild H. Comparative study of thyroid functions and types of thyroid dysfunctions in two areas of Denmark with slightly different iodine status. E J Endo 2000;143:485-491.
20. Reddy SV, Jain A, Yadav SB, Sharma K, Bhattia E. Prevalence of Grave's opthalmopathy in patients with Grave's disease presenting to referral centre in North India. Ind J Med Res 2014;139(1):99-104.
21. Roti E, Uberti ED. Iodine excess and hyperthyroidism. Thyroid 2001;11(5):462-66.
22. Kim S, Kim J, Yoon SB, Myong JP, Yu HW, Chai WJ, Choi YC, et al. Impact of smoking on thyroid gland: due related effect of continue levels on thyroid function and thyroid autoimmunity. Scientific Reports 2019;9:4213.
23. Perros P, Neoh C, Dickison J. Thyroid eye diseases BMJ 2009;338:646-50.
24. Kuriyon AE, Phillipes RP, Feldon SE. The eye and thyroid disease. Curr Opin Opthalmol 2008; 19(6):49-506.
25. Sohli E, Gunduz K. Thyroid associated opthalmopathy. Turk J Optholmol 2017;7(2): 94-105.
26. Mahto RS. Ocular features of hypothyroidism. Brit J Opthalmol 1972;56:546-47.