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BIOCHEMICAL MARKERS OF THYROID DYSFUNCTION AND ASSOCIATED OCULAR CHANGES IN CHILDREN

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ABSTRACT

Background: Thyroid problems in children often develop quietly, and the earliest signs may appear in the eyes long before parents or clinicians suspect an endocrine disorder. Many young patients do not complain of visual discomfort, making it easy for thyroid-related eye changes to go unnoticed. Recognizing how hormonal disturbances relate to specific ocular patterns may help clinicians detect thyroid disease earlier.

Methodology: A cross-sectional study was carried out between January 2024 and January 2025 at HBS Medical and Dental College, Islamabad. Sixty-two children aged 5–15 years who were being evaluated for possible thyroid dysfunction were enrolled. Each child underwent a structured clinical assessment, thyroid profile testing, and a detailed ophthalmic examination that included eyelid assessment, tear film evaluation, measurements of proptosis, extraocular movements, and visual acuity. All laboratory and clinical data were analyzed using SPSS (version 20).

Results: Eye changes were noticeably more common among children with abnormal thyroid hormone levels. Eyelid retraction, forward displacement of the eyeball, and mild motility restriction showed the clearest association with biochemical dysfunction. Children who had proptosis also tended to show higher TSH values and reduced FT4 levels. Tear film instability and conjunctival redness were seen frequently but were not statistically decisive in every comparison. Autoantibody positivity appeared more prominent among those with orbital involvement.

Conclusion: The study shows that children with thyroid abnormalities display a range of ocular signs, some of which emerge early in the course of the disease. Features such as proptosis and eyelid changes appear to have the strongest link with disturbed thyroid hormone levels. Routine

examination of the eyes in children being assessed for thyroid disorders may improve early detection and help prevent long-term visual problems.

Key Words: Thyroid dysfunction, pediatric ophthalmology, proptosis, eyelid changes, TSH, autoimmune thyroid disease, ocular involvement

INTRODUCTION

Thyroid disorders in children can occur and be overlooked easily due to the clinical features being very subtle and diverse in the early stages. Children are primarily in focus during the early stages as growth and metabolic related symptoms are most important. Another area that can show early signs and changes are the eyes. Children have difficulty in verbalizing their discomfort and visual symptoms. Caregivers see these ocular symptoms as something trivial which can further lead to a delay in diagnosis. Therefore, visual symptoms are a critical part of the assessment of children with potential thyroid dysfunction [1-3].

There are a variety of mechanisms through which changes in the eye associated with the thyroid develop. Hormonal shifts can cause complex changes in the metabolism of various tissues, retention of bodily fluids, change in the behavior of connective tissues, while autoimmune phenomena can cause inflammation of the orbit and surrounding eye tissues. Well-known signs in adults are prominent eyes, inability to fully close the eye, and inflammation of the eye tissues, although exhibiting these symptoms in children may be quite different. In children these signs are often more mild and the disease more of a mixed picture, although the published literature indicates that changes in the eyes of children with thyroid dysfunction are not uncommon. With good clinical examination, these changes can be diagnosed early [4-6].

Biochemical markers are fundamental to the assessment of the thyroid. TSH, FT4, and FT3 are the primary markers reflecting thyroid function abnormalities, while the presence of antibodies reflects autoimmune processes, e.g. Hashimoto thyroiditis and Graves' disease. The linkage of these markers with specific ocular findings (especially in children who cannot verbalize the presence of visual symptoms or discomfort) may provide clinicians with helpful guidance [7-9].

Given the importance of early identification, this study was conducted to explore how biochemical thyroid abnormalities relate to ocular changes in children. By examining both hormonal markers and detailed eye findings within the same group of patients, the study aims to improve understanding of how thyroid dysfunction manifests ophthalmologically in younger age groups and to support more comprehensive clinical assessment in routine practice.

METHODOLOGY

This research was done using an observational cross-sectional approach, examining the correlation between specific biochemical indicators of thyroid disruption and the effects in the eyes of the affected children. The research was conducted from January 2024 to January 2025 and took place at HBS Medical and Dental College Islamabad. The study concerned children with symptoms of potential thyroid disharmony and children who were directed to endocrine or eye specialists within the period the research data was collated.

The study culminated with a total of 62 children. Each eligible child visiting the facility from the study start date and the end date were allowed to take part in the study as participants. Each of 5 – 15 years of age were registered. Those with systemic disorders not related to thyroid disease, prior eye trauma, congenital eye disease, and those on drugs that may affect thyroid function were excluded from the study. Parents or guardians were informed about the study and their procedures and provided informed consent and older children were asked to provide assent when appropriate.

Participants went through a structured process that included some demographic questions, a clinical examination, some clinical/biochemical tests, and an eye exam. Specifically, demographic details included age, sex, symptoms duration and family history of thyroid disease as well as some nutritional parameters like height, weight, and age-appropriate BMI. The clinical examination looked for signs suggestive of hypothyroidism or hyperthyroidism including pulse irregularities,

presence of goiter and its grade, and a range of physical characteristics that can be associated with thyroid disease in pediatrics.

The analysis included measuring TSH, FT4, and FT3 from serum samples. Blood specimens were drawn for analysis of the autoimmune markers, TPO-Ab and Tg-Ab. Blood was drawn under standard condi- tions and analyzed at the hospital laboratory by trained hospital personnel under standard procedures, calibrating the tools, and validated methods for assay measurement.

Each child had a full ophthalmic assessment performed in the same manner. Eyelid position, eyelid lag, swelling of the eyelids, swelling around the eyes, and the conjunctiva were all recorded. Assessments of the tear film stability were done using the tear breakup time. Proptosis was assessed with a Hertel exophthalmometer and all measurements were done by the same examiner for consistency. The extraocular motility of both eyes were assessed in all positions of gaze to check for any restrictions. Age-appropriate charts were used to measure visual acuity, and the fundus was examined to assess for changes in the optic disc or retina.

Data were entered and analyzed using SPSS (version 20). Categorical variables were summarized as frequencies and percentages, while continuous variables were reported as means with standard deviations. Group comparisons were performed using the chi-square test or Fisher's exact test for categorical variables. Independent sample t-tests or Mann–Whitney U tests were used for continuous variables depending on distribution. Correlation analysis was conducted to explore the association between biochemical markers and ocular findings. A p-value of ≤ 0.05 was considered statistically significant.

RESULTS

This study's participants were children of a particular age, most of whom were in the middle childhood developmental stage. The average age of the participants in the cohort was just under ten years, while in the group participants Clinical, overt hypothyroidism was the most prevalent condition, while hyperthyroidism was the second most prevalent condition. Some were asymptomatic and had subclinical disturbances, while others had normal thyroid function and no disturbances at the time of evaluation.

Table 1. Baseline Demographic and Clinical Characteristics of the Children (n = 62)

Variable	Frequency (%) / Mean ± SD
Age (years)	9.8 ± 2.7
Sex (Male/Female)	31 (50%) / 31 (50%)
Duration of symptoms (months)	5.2 ± 3.1
Family history of thyroid disease	14 (22.6%)
BMI category	Underweight 11 (17.7%), Normal 39 (62.9%), Overweight 12 (19.4%)
Goiter present	18 (29.0%)
Tachycardia/Bradycardia	13 (21.0%)
Clinical diagnosis	Hypothyroidism 22 (35.5%), Hyperthyroidism 17 (27.4%), Subclinical dysfunction 9 (14.5%), Euthyroid 14 (22.6%)

Thyroid function among the children in the study's sample was found to be varied in its biochemical profile. Children in the sample that were found to have high TSH levels hypothyroid showed more variability. Most of the children had Free T4 levels that were at the lower end of the range, and that were within range, and Free T3 levels were actually quite good. The children also had thyroid autoimmunity. One-third of the children had TPO antibody positivity. Slightly less than one-quarter of the children with a positive thyroglobulin antibody, suggesting that a considerable portion had autoimmunity.

Table 2. Biochemical Markers among Study Participants (n = 62)

Marker	Mean ± SD	Normal Range
TSH (mIU/L)	6.82 ± 4.97	0.5–4.5
Free T4 (ng/dL)	1.01 ± 0.39	0.8–2.0
Free T3 (pg/mL)	3.72 ± 0.91	2.3–4.2
TPO antibodies positive	21 (33.9%)	—
Tg antibodies positive	15 (24.2%)	—

When looking at eye-related symptoms in children with normal thyroid function and in children whose thyroid function was biochemical or clinically abnormal, a distinct pattern began to become apparent. Recessive eyelids and eye proptosis were much more frequent and there was a significant association with extraocular muscle restriction in children with thyroid malfunctions. These results indicate that periocular tissues suffer minor thyroid-related inflammatory changes disturbances. A greater rate of ocular abnormality findings such as lower tear breakup time and conjunctival injection were more common again in the dysfunction group; however, results were not statistically significant. There were mild changes to visual acuity and were not strongly connected to the thyroid levels of the subjects.

Table 3. Ocular Findings in Children with Thyroid Dysfunction (n = 62)

Ocular Variable	Normal Thyroid (n=14)	Thyroid Dysfunction (n=48)	p-value
Eyelid retraction	0 (0%)	12 (25%)	**0.018**
Eyelid lag	1 (7.1%)	9 (18.8%)	0.287
Periorbital edema	2 (14.3%)	14 (29.2%)	0.225
Conjunctival injection	1 (7.1%)	11 (22.9%)	0.161
Tear film breakup time <10 sec	3 (21.4%)	19 (39.6%)	0.194
Proptosis present	0 (0%)	10 (20.8%)	**0.031**
Restriction of eye movements	0 (0%)	7 (14.6%)	**0.049**
Visual acuity reduction	2 (14.3%)	13 (27.1%)	0.308

A noticeable pattern was found when analyzing the levels of hormones in children with proptosis and those without proptosis. Children with proptosis had considerably more subcutaneous tissue. As such proptosis was also associated with biochemical derangements. The proptosis group had more elevated TPO antibody positivity suggesting an association with autoimmunity and orbital inflammation. Free T3 levels also showed a non-significant increase in the proptosis group.

Table 4. Association between Thyroid Hormone Levels and Proptosis Severity (n = 62)

Variable	No Proptosis (n=52)	Proptosis (n=10)	p-value
Mean TSH (mIU/L)	5.91 ± 4.32	10.84 ± 5.11	**0.004**
Mean Free T4 (ng/dL)	1.06 ± 0.33	0.78 ± 0.29	**0.012**
Mean Free T3 (pg/mL)	3.61 ± 0.88	4.21 ± 0.97	0.065
TPO-Ab positivity	26.9%	60.0%	**0.041**

as the children were classified by their first thyroid diagnosis, ocular comorbidity varied by group. Children with hyperthyroid disease were the most likely to have ocular changes, followed by children with overt hypothyroidism, and subclinical hypothyroidism had milder manifestations largely and the most euthyroid children had no ocular abnormalities. While such trends were clear, the small sample size of each subgroup likely explains why the differences were not statistically significant.

Table 5. Thyroid Dysfunction Categories and Ocular Involvement (n = 62)

Thyroid Category	Ocular Involvement Present	No Ocular Changes	p-value
Hypothyroidism (n=22)	10 (45.5%)	12 (54.5%)	0.211
Hyperthyroidism (n=17)	9 (52.9%)	8 (47.1%)	0.142
Subclinical dysfunction (n=9)	3 (33.3%)	6 (66.7%)	0.622
Euthyroid (n=14)	4 (28.6%)	10 (71.4%)	—

Correlation analysis data strengthened the initial associations. TSH levels moderate correlation with the proptosis severity. This reinforces the association with the biochemical imbalance and the orbital tissue involvement. Free T4 levels negative correlate with the visual acuity which suggests that a greater hormonal deficiency may inhibit visual acuity. Free T4, which shows some association with the extraocular muscle restriction, suggests that the association is quite negligible. This strengthens the association with biochemical markers and points to the early involvement of the eyes in children with thyroid disease.

Table 6. Correlation between Biochemical Markers and Ocular Parameters (n = 62)

Correlation Pair	r-value	p-value
TSH vs. Proptosis (mm)	**0.42**	**0.002**
TSH vs. TBUT	-0.19	0.143
Free T4 vs. Visual acuity	-0.28	**0.032**
Free T3 vs. EOM restriction	0.21	0.094

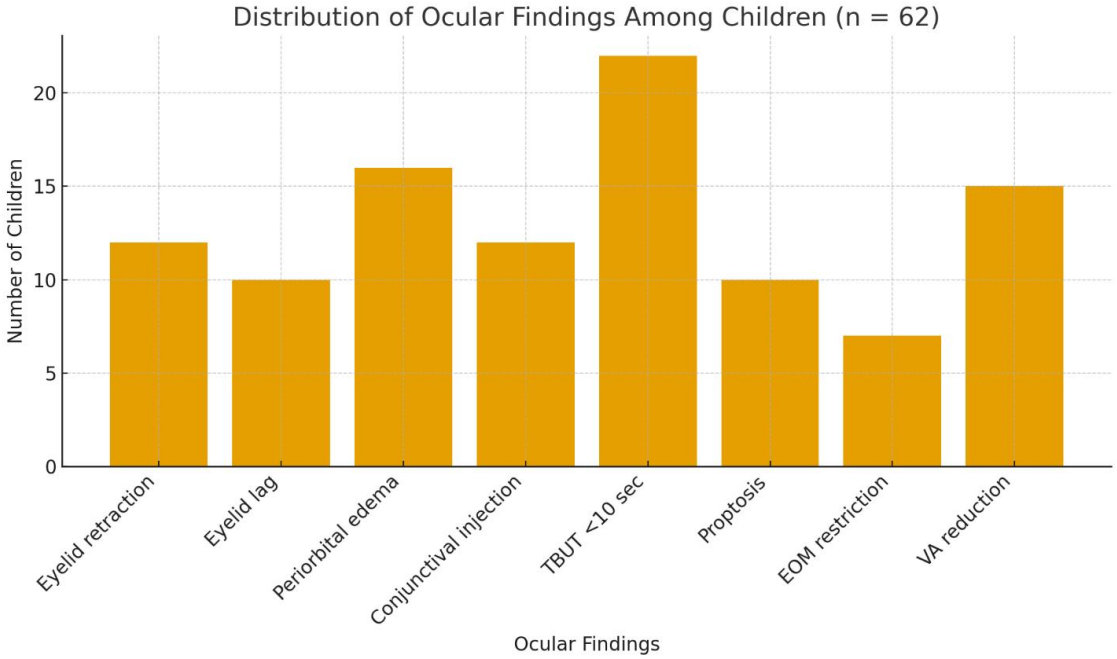


Figure 1. Distribution of ocular findings among children with suspected thyroid dysfunction (n = 62)

The bar chart illustrates the frequency of various ocular changes observed in the study population. Tear film instability (TBUT <10 seconds) and peri-orbital edema appeared most frequently, while extraocular muscle restriction was the least common finding. The pattern indicates that surface-related and soft-tissue changes were more prominent compared to motility deficits.

DISCUSSION

The results of this study suggest that there are several ocular symptoms that accompany thyroid dysfunction during childhood, some of which arise during the very early stages of hormonal changes. The children whose biochemistry showed abnormalities and who had achalasia of the eyelids, proptosis, and restriction of the extraocular muscles, represent the clinical picture of the most common thyroid orbitopathy. Other changes, such as new formation of conjunctival hyperemia and decreased breakup time of the tear film, perhaps indicate that the ocular symptoms in the initial stage of the disease in children are less pronounced and, perhaps, more complex, and will manifest in the future as more severe symptoms. This is consistent with the opinion of some authors in pediatric ophthalmology, who studied the symptoms of the disease in children and described them as changes in different stages of development, rather than a consistent symptom complex [10-12].

The connection made in this dataset between high TSH levels and proptosis adds great value to existing studies. In the previous studies, TSH levels were high. Researchers found that untreated or advanced hypothyroid states may act on the orbital tissues through high fluid retention and glycosaminoglycan deposition. The increased proptosis rate in pediatric cases with elevated TSH and decreased FT4 levels may indicate orbital soft tissue minimal inflammatory changes, unlike the more tissue inflammatory responses characterized in adult thyroid eye disease. This finding is supported in the pediatric endocrinology literature, where the thyroid dysfunctional state in children is noted to demonstrate a milder or more insidious inflammatory orbital sign [13-15].

The impact of autoimmunity on the findings of the eye disabilities was of great importance. A much greater number of children with proptosis had their TPO antibodies showing positivity. This indicates that there is influence on the immunology of the orbital reinforcing the findings of the eye disabilities. As indicated with other older cohorts, children with Hashimoto disease hypothyroidism or with Graves disease at the early stages of the condition demonstrate the multifaceted connections that are present with autoimmune conditions. As such, autoimmune conditions with antibodies demonstrate inflammation of the periorbital area that can occur before other autoimmune conditions demonstrate their systemic signs [16, 17].

Eyelid lag and conjunctival injection are some of the ocular features that did not significantly differ between children with normal and abnormal thyroid function, which may represent the smaller sample size within the groups, or that these signs may be governed by a host of other explanations, thyroid hormones not included. Some other variability has been documented in pediatric populations, as the ocular features are less consistent than in adult thyroid eye disease and are also subject to environmental or allergic factors [18, 19].

Hypothyroidism and hyperthyroidism and their related ocular complications seem to fall under the same clinical umbrella. In the literature, this same trend also suggests less severe complications in the ocular region in children, and also subclinical forms of thyroid disease, regulating clinical monitoring and pilytos as the disease progresses. Perhaps this is because the milder expression in the this group still suggests cases of subclinical disease [20].

Recognizing thyroid abnormalities in a child has certainly implied the need for ocular assessment. Pediatric patients cannot always articulate changes in their visual fields, visual discomfort, and super fine changes in the eyes like inflammation and mechanical changes. Thus, the data suggests that an ocular assessment to the baseline ophthalmic evaluation to the standard assessment of thyroid abnormalities in a child will facilitate the early detection of changes in the eyes that may otherwise go unrecognized.

The results pertain to the correlation of the thyroid's hormone levels with particular eye manifestations. Despite there being some incongruity with respect to the eye signs of pediatrics with thyroid disease, the dataset corroborates the presence of eye signs in children. With respect to the thyroid, the disease, and the age, and illness duration, paired with autoimmune disease processes, there is a huge difference. Biochemical par understudies the complete contrast to the subtle thyroid. This is how the clinic and delicate hand should address the patients' signs.

CONCLUSION

The patterns observed in this research indicate that thyroid dysfunction in children is commonly accompanied by ocular changes, particularly those involving eyelid position, tear film stability, and early soft-tissue involvement. Elevated TSH and reduced FT4 levels showed clear associations with proptosis and other orbital findings, while antibody positivity appeared to increase the likelihood of ocular involvement. Although some features were not statistically significant, the overall trend supports the view that ocular manifestations may develop early in the course of pediatric thyroid disorders. These observations reinforce the value of incorporating routine ocular screening into the evaluation of children with suspected or confirmed thyroid dysfunction, as early identification may help prevent progression of visual or ocular complications.

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