Nail Changes Associated With Thyroid Disease

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PRACTICE POINTS
• Koilonychia is associated with hyperthyroidism.
• Clubbing is a manifestation of thyroid acropachy in Graves disease and also affects other patients with hyperthyroidism.
• Onycholysis improves in patients with hypothyroidism treated with thyroid hormone replacement therapy.

Nail changes with thyroid disease have not been well studied. Nail findings are helpful in early diagnosis of thyroid disorders and therefore are important for dermatologist education. We reviewed the literature on nail changes in thyroid patients and found that onycholysis and slow-growing, thin nails are associated with hypothyroidism and that onycholysis, koilonychia, and brittle nails changes are associated with hyperthyroidism.

The major classifications of thyroid disease include hyperthyroidism, which is seen in Graves disease, and hypothyroidism due to iodine deficiency and Hashimoto thyroiditis, which have potentially devastating health consequences. The prevalence of hyperthyroidism ranges from 0.2% to 1.3% in iodine-sufficient parts of the world, and the prevalence of hypothyroidism in the general population is 5.3% in Europe and 3.7% in the United States. Thyroid hormones physiologically potentiate α- and β-adrenergic receptors by increasing their sensitivity to catecholamines. Excess thyroid hormones manifest as tachycardia, increased cardiac output, increased body temperature, hyperhidrosis, and warm moist skin. Reduced sensitivity of adrenergic receptors to catecholamines from insufficient thyroid hormones results in a lower metabolic rate and decreases response to the sympathetic nervous system. Nail changes in thyroid patients have not been well studied. Our objectives were to characterize nail findings in patients with thyroid disease. Early diagnosis of thyroid disease and prompt referral for treatment may be instrumental in preventing serious morbidities and permanent sequelae.

Methods
PubMed, Scopus, Web of Science, and Google Scholar were searched for the terms nail + thyroid, nail + hyperthyroid, nail + hypothyroid, nail + Graves, and nail + Hashimoto on June 10, 2020, and then updated on November 18, 2020. All English-language articles were included. Non–English-language articles and those that did not describe clinical trials of nail changes in patients with thyroid disease were excluded. One study that utilized survey-based data for nail changes without corroboration with physical examination findings was excluded. Hypothyroidism/hyperthyroidism was defined by all authors as measurement of serum thyroid hormones triiodothyronine, thyroxine, and thyroid-stimulating hormone outside of the normal range. Eight studies were included in the final analysis. Patient demographics, thyroid disease type, physical examination findings, nail clinical findings, age at diagnosis, age at onset of nail changes, treatments/medications, and comorbidities were recorded and analyzed.

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NAIL CHANGES IN THYROID DISEASE

Results

Nail changes in patients with thyroid disease were reported in 8 studies (7 cross-sectional, 1 retrospective cohort) and are summarized in the Table.4-11 The mean age was 41.2 years (range, 5–80 years), with a higher representation of females (range, 70%–94% female). The most common nail changes in thyroid patients were koilonychia, clubbing, and nail brittleness. Other changes included onycholysis, thin nails, dryness, and changes in nail growth rate. Frequent physical findings were xerosis, pruritus, and alopecia.

Both koilonychia and clubbing were reported in patients with hyperthyroidism. In a study of 32 patients with koilonychia, 22 (68.8%) were diagnosed with hyperthyroidism.10 Nail clubbing affected 7.3% of Graves disease patients (n=150) and 5.0% of hyperthyroid patients (n=120).7 Dermopathy presented more than 1 year after diagnosis of Graves disease in 99 (66%) of 150 patients as a late manifestation of thyrotoxicosis.8 Additional physical features in patients with Graves disease (n=150) were pretibial myxedema (100%), ophthalmopathy (99.0%), and proptosis (88.0%). Non–Graves hyperthyroid patients showed physical features of soft hair (83.3%) and soft skin (66.0%).7

Nail brittleness was a frequently reported nail change in thyroid patients (4/8 studies, 50%), most often seen in 22% of autoimmune patients, 19.6% of nonautoimmune patients, 13.9% of hypothyroid patients, and 9.2% of hyperthyroid patients.5,8 For comparison, brittle nails presented in 10.8% of participants in a control group.5 Brittle nails in thyroid patients often are accompanied by other nail findings such as thinning, onycholysis, and pitting.

Among hypothyroid patients, nail changes included fragility (70%; n=50), slow growth (48%; n=50), thinning (40%; n=50), onycholysis (38%; n=50),7 and brittleness (13.9%; n=173).8 Less common nail changes in hypothyroid patients were leukonychia (9.4%; n=32), striped nails (6%; n=50), and pitting (1.2%; n=173).5,7,11 Among hyperthyroid patients, the most common nail changes were koilonychia (100%; n=22), softening (83%; n=120), onycholysis (29%; n=14), and brittleness (9.2%; n=173).5,7 Less common nail changes in hyperthyroid patients were clubbing (5%; n=120), thinning (4.6%; n=173), and leukonychia (3%; n=120).5,7

Additional cutaneous findings of thyroid disorder included xerosis, alopecia, pruritus, and weight change. Xerosis was most common in hypothyroid disease (57.2%; n=460).8 In 2 studies,6,9 alopecia affected approximately 70% of autoimmune, nonautoimmune, and hyperthyroid patients. Hair loss was reported in 42.6% (n=460) and 33.0% (n=36) of hypothyroid patients. Additionally, pruritus affected up to 28% (n=32) of hypothyroid and 16.0% (n=120) of hyperthyroid patients and was more common in autoimmune (41%) vs nonautoimmune (32%) thyroid patients.8 Weight gain was seen in 72% of hypothyroid patients (n=32),13 and soft hair and skin were reported in 83.3% and 66% of hyperthyroid patients (n=120), respectively.7 Flushing was a less common physical finding in thyroid patients (usually affecting <10%); however, it also was reported in 17.1% of autoimmune and 57.1% of hyperthyroid patients from 2 separate studies.8,9

Comment

There are limited data describing nail changes with thyroid disease. Singal and Arora3 reported in their clinical review of nail changes in systemic disease that koilonychia, onycholysis, and melanonychia are associated with thyroid disorders. We similarly found that koilonychia and onycholysis are associated with thyroid disorders without an association with melanonychia.

In his clinical review of thyroid hormone action on the skin, Safer12 described hypothyroid patients having coarse, dull, thin, and brittle nails, whereas in thyrotoxicosis, patients had shiny, soft, and concave nails with onycholysis; however, the author commented that there were limited data on the clinical findings in thyroid disorders. These nail findings are consistent with our results, but onycholysis was more common in hypothyroid patients than in hyperthyroid patients in our review. Fox13 reported on 30 cases of onycholysis, stating that it affected patients with hypothyroidism and improved with thyroid treatment. In a clinical review of 8 commonly seen nail abnormalities, Fowler et al14 reported that hypothyroidism was associated with nail findings in 5% of cases and may result in onycholysis of the fourth and fifth nails or all nails. They also reported that onychorrhexis may be seen in patients with hypothyroidism, a finding that differed from our results.14

The mechanism of nail changes in thyroid disease has not been well studied. A protein/amino acid–deficiency state may contribute to the development of koilonychia. Hyperthyroid patients, who have high metabolic activity, may have hypoalbuminemia, leading to koilonychia.15 Hypothyroidism causes hypothermia from decreased metabolic rate and secondary compensatory vasoconstriction. Vasoconstriction decreases blood flow of nutrients and oxygen to cutaneous structures and may cause slow-growing, brittle nails. In hyperthyroidism, vasodilation alternatively may contribute to the fast-growing nails. Anti–thyroid-stimulating hormone receptor antibodies in Graves disease may increase the synthesis of hyaluronic acid and glycosaminoglycans from fibroblasts, keratinocytes, adipocytes, or endothelial cells in the dermis and may contribute to the development of clubbing.16

Our review is subject to several limitations. We recorded nail findings as they were described in the original studies; however, we could not confirm the accuracy of these descriptions. In addition, some specific nail changes were not described in sufficient detail. In all but 1 study, dermatologists performed the physical examination. In the study by Al-Dabbagh and Al-Abachi,10 the physical examinations were performed by general medicine physicians, but they selected only for patients with...
### Summary of Studies Reporting Nail Changes in Patients With Thyroid Disorders

<table>
<thead>
<tr>
<th>Reference (year)</th>
<th>Study type</th>
<th>Method</th>
<th>No. of patients</th>
<th>Disease diagnosis</th>
<th>Mean age (SD/range, y)</th>
<th>Sex</th>
<th>Nationality</th>
<th>Nail change (patients affected, %)</th>
<th>Other physical findings (patients affected, %)</th>
<th>Duration (SD), y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Keen et al (2013)</td>
<td>Cross-sectional</td>
<td>Physical examination</td>
<td>460</td>
<td>Hypothyroid</td>
<td>38.42 (11.02)/5–72</td>
<td>90% F</td>
<td>Indian</td>
<td>Britleness (2.0), slow growth (0.7)</td>
<td>Xerosis (57.2), hair loss (42.6), edema (38.5), pruritus (17.2)</td>
<td>NA</td>
</tr>
<tr>
<td>Takir et al (2017)</td>
<td>Cross-sectional</td>
<td>Physical examination</td>
<td>100</td>
<td>Control</td>
<td>40.0 (13.0)/NA</td>
<td>90% F</td>
<td>Turkish</td>
<td>Britleness (10.8), thinning (17.0)</td>
<td>Xerosis (10.6), alopecia (9.3), hyperhidrosis (7.0), pruritus (2.4), flushing (2.3)</td>
<td>NA</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Autoimmune thyroid/hyperthyroid</td>
<td>173</td>
<td>94% F</td>
<td></td>
<td>Britleness (9.2), thinning (4.6), onycholysis (1.2)</td>
<td>Alopecia (12.7), hyperhidrosis (8.7), xerosis (6.9), pruritus (5.8), flushing (4.6)</td>
<td>NA</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Autoimmune thyroid/hypothyroid</td>
<td>127</td>
<td>88% F</td>
<td></td>
<td>Britleness (1.6), thinning (1.6), pitting (1.6)</td>
<td>Xerosis (7.1), pruritus (3.9), hyperhidrosis (3.9), alopecia (3.1), flushing (3.1)</td>
<td>NA</td>
</tr>
<tr>
<td>Fatourechi et al (1994)</td>
<td>Retrospective cohort</td>
<td>Medical record review</td>
<td>6</td>
<td>Graves disease</td>
<td>51.2 (NA)/18–80</td>
<td>78% F</td>
<td>NA</td>
<td>Thyroid acropachy/clubbing (7.3)</td>
<td>Pretibial myxedema (100), ophthalmopathy (99.0), proptosis (88.0), pitting edema (83.0)</td>
<td>1.5 (0.50) a</td>
</tr>
<tr>
<td>Razí et al (2013)</td>
<td>Cross-sectional</td>
<td>Physical examination and questionnaire</td>
<td>120</td>
<td>Hyperthyroid</td>
<td>25.86 (14.69)/ NA</td>
<td>74% F</td>
<td>Iranian</td>
<td>Nail softening (83.0), onycholysis (16.6), clubbing (5.0), leukonychia (3.0)</td>
<td>Soft hair (83.3), soft skin (66.0), pruritus (16.0), hyperpigmented (12.5), myxedema (6.5)</td>
<td>NA</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Hypothyroid</td>
<td>50</td>
<td>70% F</td>
<td></td>
<td>Fragileness (70.0), slow growth (45.0), thinning (40.0), onycholysis (39.0), striped nails (6.0)</td>
<td>Dry, course skin (70.0), myxedema (18.0), purpura ecchymosis (8.0), telangiectasia (6.0)</td>
<td>NA</td>
</tr>
</tbody>
</table>

Abbreviations: F, female; NA, not available.

a Dermopathy 1.5 years after diagnosis in 99 Graves disease patients.

b Additional patients in study included: 2 chronic renal failure, 2 dilated cardiomyopathy, 2 bronchiectasis, 1 thyroid cancer, 1 asthma, 1 liver cirrhosis, and 1 ischemic heart disease.
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<tr>
<th>Reference (year)</th>
<th>Study type</th>
<th>Method</th>
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<th>Mean age (SD/range, y)</th>
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<th>Duration (SD, y)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acer et al (2019)</td>
<td>Cross-sectional</td>
<td>Physical examination</td>
<td>41</td>
<td>Autoimmune thyroid</td>
<td>52.23 (12.52)/NA</td>
<td>85% F Turkish</td>
<td>Brittleness (22.0), longitudinal streak (14.6), fine (12.2), dry (7.3), soft (7.3)</td>
<td>Alopecia (70.7), xerosis (43.9), pruritus (41.5), facial erythema (22.0), flushing (17.1), periorbital edema (4.9)</td>
<td>7.84 (2.14)</td>
<td></td>
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<tr>
<td>56</td>
<td>Nonautoimmune thyroid</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Brittleness (19.6), fine (10.7), dry (10.7), longitudinal streak (8.9), onycholysis (3.6), soft (3.6)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Dogra et al (2006)</td>
<td>Cross-sectional</td>
<td>Physical examination</td>
<td>32</td>
<td>Hypothyroid</td>
<td>39 (NA)/6–60</td>
<td>87% F Indian</td>
<td>Leukonychia (9.4), brittleness (3.1)</td>
<td>Weight gain (72.0), xerosis (59.4), telogen effluvium (40.6), pigmentary disorders (37.5), pruritus (28.0)</td>
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</tr>
</tbody>
</table>

Abbreviations: F, female; NA, not available.

*Dermopathy 1.5 years after diagnosis in 99 Graves disease patients.

+Additional patients in study included: 2 chronic renal failure, 2 dilated cardiomyopathy, 2 bronchiectasis, 1 thyroid cancer, 1 asthma, 1 liver cirrhosis, and 1 ischemic heart disease.
koilonychia and did not assess for other skin findings. Fragile nails and brittle nails were described in hypothyroid and hyperthyroid patients, but these nail changes were not described in detail. There also were studies describing nail changes in thyroid patients; some studies had small numbers of patients, and many did not have a control group.

Conclusion
Nail changes may be early clinical presenting signs of thyroid disorders and may be the clue to prompt diagnosis of thyroid disease. Dermatologists should be mindful that fragile, slow-growing, thin nails and onycholysis are associated with hypothyroidism and that koilonychia, softening, onycholysis, and brittle nail changes may be seen in hyperthyroidism. Our review aimed to describe nail changes associated with thyroid disease to guide dermatologists on diagnosis and promote future research on dermatologic manifestations of thyroid disease. Future research is necessary to explore the association between koilonychia and hyperthyroidism as well as the association of nail changes with thyroid disease duration and severity.

REFERENCES