

Thyroglobulin: a promising biomarker of iodine status

Excerpted from: **Ma, ZF and Skeaff, SA. Thyroglobulin as a biomarker of iodine deficiency: a review.**

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Background

Iodine deficiency is assessed by measuring urinary iodine concentration (UIC). But due to large intra- and inter-individual variation, UIC is only appropriate for groups. Thyroglobulin (Tg) is a thyroid storage protein and is a precursor for the synthesis of T3 and T4. In iodine deficiency, an increased amount of Tg is released into the blood, which is positively correlated with thyroid volume. In their paper, Ma and Skeaff reviewed the evidence on the usefulness of Tg to assess iodine status.

Measuring Tg concentration

Tg can be measured using either radioimmunoassay (RIA) or a variety of immunometric assays (IMA). Tg measurements are method dependent, which means that it may be difficult to compare studies. But the considerable interassay variation (43–65% in healthy adults) can be reduced by 14–27% by standardizing the assays against a certified reference material (CRM-457) (1). Yet, not many studies have performed standardization, and the authors encourage greater use of CRM-457.

The results of Tg assays may be altered by Tg antibodies (TgAb), present in 3–13% of adults. The authors recommend that adults are screened for TgAb prior to measuring Tg. In children, the prevalence of TgAb is lower, and so screening for TgAb in this age group is likely not necessary.

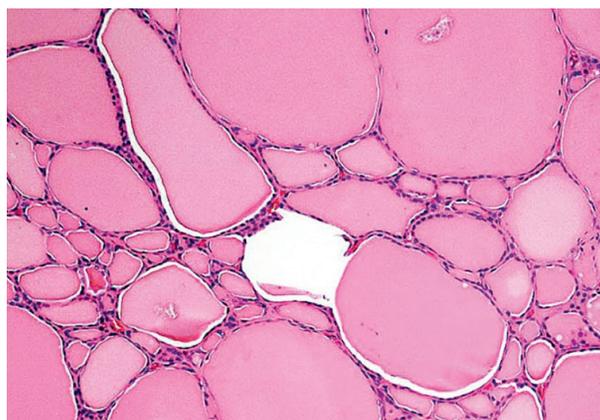
The reference range for Tg in adults (3–40 µg/L) has been determined using both RIA and IMA methods. For healthy children aged 5–14 years, a similar reference range of 4–40 µg/L was established by a dried blood-spot fluorimmunoassay (FIA) (2). There appears to be no consistent effect of age or sex on Tg. An international study of children (n=2512) with varying iodine status suggested that a median Tg <13 µg/L and/or a prevalence below 3% of Tg values >40 µg/L should be used as a biomarker of adequate iodine status in children (3).

Pregnant women

Pregnant women who are iodine deficient typically have a median Tg ≥ 13 µg/L. Interestingly, iodine supplementation does not consistently decrease Tg below this cutoff either during pregnancy or postpartum, but this may be due to inadequate supplementation. More large trials are needed, measuring both Tg and UIC, before conclusions can be drawn about the usefulness of Tg as a biomarker in pregnancy. It is also unclear whether Tg needs to be trimester specific.

Newborns and children

Measuring Tg may be useful in addition to neonatal TSH, a common biomarker of iodine status in newborns. Newborns whose mothers did not take iodine during pregnancy had Tg concentrations of 62–113 µg/L, while those born to mothers who took iodine supplements had Tg concentrations of 31–65 µg/L. The majority of studies in



Microscopic view of a goiter: thyroid follicles distended with thyroglobulin

school-age children appear to support the 13 µg/L cutoff. However, the relationship between UIC and Tg is not always consistent, suggesting that Tg alone should not be used in this age group.

Adults

Based only on observational studies, it is difficult to conclude whether the Tg cutoff of 13 µg/L can also be used in adults. Importantly, there are no randomized placebo-controlled trials in adults showing an improvement in iodine status (indicated by an increase in UIC from <100 to ≥ 100 µg/L) with a simultaneous fall in Tg concentration from ≥ 13 to <13 µg/L.

Summary

The authors conclude that Tg does hold promise as a biomarker of iodine deficiency. The studies included in this review support the use of Tg as a biomarker of iodine status in school children, using the <13 µg/L cutoff. However, it is not possible to draw conclusions regarding the efficacy of Tg in adults because the data are equivocal. Well-designed randomized placebo-controlled trials are required to investigate further the effect of iodine supplementation on Tg.

References

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