

## Hypothyroidism: To Screen or not to Screen, that is the Question?

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### Editorial

Hypothyroidism is an entity that we all encounter in clinical practice, some more frequently than others. At times, this may be due to a referral where another physician has already checked a patient's thyroid function and made a biochemical diagnosis. However, very often we are faced with the dilemma of whether we should check the thyroid function of a patient with subtle non-specific complaints. Here, we try to rely on our clinical judgment and strive to appropriately utilize healthcare resources. Scenarios such as this give rise to a host of questions, most importantly, whom do we screen?

There are certain populations around the world that are at a higher risk of having hypothyroidism i.e. those who live in areas of iodine deficiency. This cohort alarmingly accounts for approximately 1/3 of the world's population and resides in areas such as the mountainous regions of Central Africa, Latin-America and South-East Asia. Congenital hypothyroidism itself is present in 1/3500-4000 births. In areas that are iodine-replete, the majority of these cases are due to conditions such as thyroid dysgenesis or athyreosis. A small proportion may also be due to thyroid dysmorphogenesis. In communities that are iodine-replete, the prevalence of hypothyroidism itself has been reported as being 1-2%. Data from Japan, Northern Europe and the United States of America indicates that in investigated individuals, the prevalence of spontaneous hypothyroidism ranged from 0.6 and 12 per 1000 in women, and between 1.3 and 4.0 per 1000 in men (females>males). The elderly seem to be more at risk [1]. For example, a study in Leiden, Netherlands found that overt hypothyroidism was present in 7% of subjects aged between 85-89 years (n=558) [2]. The prevalence of hypothyroidism in India is thought to be around 11%, which are much above the prevalence of less than 5% in the United States and less than 2% in the United Kingdom [3].

Subclinical hypothyroidism, on the other hand, seems to be more common. In the late 1970s, the Whickham survey of Northeast England revealed that 7.5% of women and 2.8% of men had subclinical hypothyroidism (TSH>6 mIU/L) [4]. Later, Vanderpump and Tunbridge reckoned that approximately 5% of different population cohorts have a TSH>6 mIU/L [5]. In terms of ethnic variability, the National Health and Nutrition Examination Survey (NHANES III) noted that not only did serum TSH concentrations increase with age in both men and women; they were lower in African-Americans as opposed to their Caucasian counterparts, regardless of their anti-thyroid antibody titers [6]. Interestingly, virtually all the clinical studies had done in this field document a higher prevalence rate of subclinical hypothyroidism in women and the elderly. The Framingham Study itself demonstrated that 13.6% of women in the United States, older than 60 years, had a TSH>5 mIU/L [5].

In a robust study from Colorado, Canaris et al. screened 25,862 individuals at a health fair. Of these, 2,450 subjects (9.5%) had an

elevated TSH, with the majority of the group falling under the umbrella of subclinical hypothyroidism. Of this subset, 1,799 individuals (74%) had a TSH level between 5.1-10 mIU/L, and 619 individuals (26%) had a value>10 mIU/L. The researchers concluded that if the Colorado experience could be generalized, there may be over 13 million cases of undetected thyroid gland failure in the nation [5]. In India, the data on subclinical hypothyroidism is not as lucid. In one study, Deshmukh et al. screened 237 normal subjects and picked up subclinical hypothyroidism in 11.3% [7].

Nonetheless, the numbers above do provide food for thought and make one ponder as to who should be screened and whether such screening is cost effective. The criteria for population screening include identifying a condition that is prevalent and an important health concern, a condition where an early diagnosis is usually not made, a condition where the diagnosis is straightforward and accurate, and a condition where the treatment is safe and cost effective. Having said this, there continues to be disagreement amongst expert panels with regards to TSH screening of the general population [8], as experts question its cost-effectiveness and benefit. The recommendations from some of the major panels are tabulated in Table 1. Pregnancy and neonatal screening will be discussed separately.

Thus, the issue of whom to screen and when to screen remains unclear. One must consider screening individuals who, for example, have symptoms suspect of thyroid failure, an established autoimmune disease such as type 1 diabetes mellitus or vitiligo, pernicious anemia, a first-degree relative with an autoimmune thyroid disease, a history of thyroid surgery or ablation, an abnormal thyroid exam, a psychiatric disorder, are on drugs like amiodarone or lithium, or have entities like adrenal insufficiency [8].

With regards to neonatal screening for congenital hypothyroidism, the consensus is a lot more concrete. Groups such as the American Academy of Pediatrics and the European Society for Paediatric Endocrinology recommend checking TSH after birth [11,12]. Screening of all newborns has become a part of routine practice in Australia, Canada, Europe, Israel, Japan, New Zealand and the United States. Numerous countries in Africa, Asia, Eastern Europe and South America are currently in the process of developing their own protocols [13].

Lastly, any discussion on this topic would be remiss if the question of screening in pregnancy was not discussed. Again, the issue of universally screening asymptomatic pregnant women is a bone of contention and consequently, there is a wide variation in clinical practice [14,15]. Unfortunately, there is a paucity of data suggesting the cost-effectiveness/benefit of screening versus not screening. In one decision analysis model, the authors assumed a baseline prevalence of 2.5% for subclinical hypothyroidism in pregnant women. They calculated a saving of \$8 million due to better neonatal outcomes, for

every 100,000 pregnant women screened [16,17]. A second analysis compared universal screening to risk-based screening and found that the former method resulted in an incremental cost-effectiveness ratio of \$7,258 per quality-adjusted life-year (QALY). However, both risk-

based screening and universal screening were shown to be relatively more cost effective as opposed to no screening with incremental cost-effectiveness ratios of \$6,753/QALY and \$7,138/QALY, respectively [18].

U.S. Preventive Services Task Force	Insufficient evidence for or against screening
Royal College of Physicians of London	Screening of the healthy adult population unjustified
American Association of Clinical Endocrinologists	Older patients, especially women, should be screened.
American Academy of Family Physicians	Patients $\geq$ 60 years of age should be screened.
American Thyroid Association	Women and men $>$ 35 years of age should be screened every 5 years.
American College of Physicians	Women $\geq$ 50 years of age with an incidental finding suggestive of symptomatic thyroid disease should be evaluated.
American College of Pathologists [9]	Screening recommended for women aged over 50 years who seek medical care and for all geriatric patients upon hospital admission
Australian College of General Practitioners [10]	The routine testing of thyroid function is not recommended in asymptomatic low-risk people

**Table 1:** Recommendations Regarding the Screening of Asymptomatic Adults for Thyroid Dysfunction [8].

Nonetheless, due to insufficient evidence favoring universal TSH screening in the first trimester, most societies such as the American Thyroid Association, the Endocrine Society and the American College of Obstetricians and Gynecologists lean towards targeted case-finding [19-21]. Other institutional bodies such as the National Institute for Health and Clinical Excellence and the Royal Australian and New Zealand College of Obstetricians and Gynecologists follow this view as well. On the other hand, supporters of universal screening put forth the argument that screening at the first antenatal visit is commonly practiced in a lot of areas and appears cost effective. They submit that the case-finding technique misses approximately 30-50% of the cases of thyroid dysfunction [18,22]. In India, some centers opt for universal screening, whilst others target only high-risk individuals [23]. Studies such as that by Dave et al. document that if the high-risk screening approach was applied to pregnant Indian females, we would miss 4.6% of cases. In fact, the Indian Thyroid Society guidelines advocate the screening of all pregnant women at their 1st antenatal visit. These recommendations also emphasize that in an ideal setting, screening should be done during the pre-pregnancy evaluation or as soon as conception is confirmed [24].

Ultimately, when all is said and done, we are still left musing upon whether to screen or not to screen. Unfortunately, the answer may not be that simple. As guidelines continue to vary and debates rage on into the night, an evidence based recommendation continues to elude us. At present, the final decision to screen or not to screen rests with the treating physician and should be based on factors such as a patient's geographic location, past medical history, and perhaps regional treatment patterns. The need of the hour is of larger longitudinal randomized control trials that factor in both maternal and neonatal outcomes, as well as healthcare economics, to give us a true cost-benefit ratio.

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