ELEVATED TSH LEVELS IN ELDERLY- PHYSIOLOGIC OR PATHOLOGIC?

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Biochemical profiling of Thyroid hormones and TSH, is the cornerstone in confirming the diagnosis of Thyroid disorders. Of these the most important and depended test is the third generation TSH assay which gives the clue to the thyroid problem. During the last decade the technological aspect of TSH assay has improved, so that that we will be able to measure a change of 0.001mIU of TSH in majority of available assays. But the interpretation of these TSH values, especially in elderly persons is still not well settled to the satisfaction of every body. Large studies are equivocal in stating that TSH levels remain either stable during aging or go up or down. A rising TSH is a clue that the thyroid function is declining, and it may antedate fall in free hormones and frank hypothyroidism.

Hypothyroidism is more common in elderly, especially among women, and it may be due to rising incidence and prevalence of auto-immune thyroiditis in the older population. Estimates of hypothyroidism in the elderly have varied rates depending upon the population studied and the criteria used to define the condition. Recent community surveys of populations of healthy adults have found that 7-14% of elderly subjects have serum TSH levels above the upper limit of normal range. A screening study that evaluated more than 25,000 persons attending an exhibition and fair, revealed that 10% of men and 16% of women between the ages of 64 to 74 had TSH levels that were increased above the upper limit of reference range. Also in the same study 16% of men and 21% of women above the age of 75 and older had increased TSH level. The recent National Health and Nutrition Examination Survey (NHANES) found higher TSH levels in women compared to men in the older age group and also higher TSH in Whites and Mexican Americans compared to blacks.

The estimates of prevalence of hypothyroidism in the elderly at the present time are getting complicated as the normal TSH distribution in elderly appear to be shifted towards higher values. Age specific analysis of TSH levels measured as part of recent NHANES study showed that 12% of subjects aged 80 years and older with out any evidence of autoimmune thyroid disease had TSH above 4.5 mIU/L. This is graphically shown in figure 1.

As from the data above elderly patients can have an elevated TSH as a physiological event as
evidenced by the recent NHANES study. But elderly patients have a higher chance of having hypothyroidism compared to youngsters as evident from many population studies. So elevated TSH in elderly could also be pathological as a laboratory evidence of hypothyroidism. The higher incidence of hypothyroidism in the elderly is due to higher prevalence of autoimmune thyroiditis, higher incidence of post surgical hypothyroidism and post radio-iodine hypothyroidism. Another cause for hypothyroidism in the elderly people, is head and neck radiation given for malignancies. The risk of developing hypothyroidism in this setting increases with advancing age.

It is the usual teaching that biochemical diagnosis of thyroid diseases in the elderly must take into consideration the age related changes in thyroid function, especially the low T3, slightly higher T4 and TSH in the elderly population. But other studies have shown that the low T3 is found only in institutionalized elderly persons and that the age related low T3 reported earlier were due to effects of nonthyroidal illness. Two recent studies also came with the data against the existence of “low T3 Syndrome” associated with aging.

Blunted circadian fluctuations of TSH and diminished TSH response to TRH stimulation were noted in elderly males, the aetiology of which is unclear. There is no histological or immunoreactive differences of thyrotropes from elderly persons compared to youngsters. However in one study showed decrease in deiodinase activity with increasing age which was paralleled by a decrease in selenium levels. Also selenium supplementation restored the serum levels of selenium, serum deiodinase activity and T3 /T4 ratios in elderly patients to normal range.

The interpretation of T3, T4 and TSH in hospitalized elderly patients, must take into consideration the effect of nonthyroidal disease in thyroid hormone levels. Studies have shown that early in the course of severe illnesses, TSH in the euthyroid patients may decline to levels that fall below the lower limit of the normal, which may be associated with a parallel decline in T3 and T4 levels. One study has demonstrated that the decline in T3 correlated with the severity of illness rather than with advancing age. The current thinking is that the low or normal TSH found in the presence of low T3 and T4 are due to combined effect of central hypothyroidism and reduced peripheral conversion of T4 to T3. When the patient survives from the nonthyroidal illness, TSH start rising transiently above the upper limit of reference ranges and precedes the increase in low T3 and T4 levels. At this stage there will be confusion whether the patient has hypothyroidism requiring thyroxine therapy. In one study which looked at these patients recovering from nonthyroidal illnesses, 14% showed thyroid hormone profile suggestive of hypothyroidism, where as when they were retested after 6 weeks, only 2% were proved to be having hypothyroidism.

In conclusion the elevated TSH seen in an elderly patient can be both physiological and pathological. A thorough look at the history, nutritional status, associated nonthyroidal illness and judicious use of TSH measurement will help to differentiate between those who require only observation and those who require thyroxine therapy. Leaving a minimally raised TSH untreated, but keeping under observation will not produce any harm. Indeed there was one study which showed that elderly persons with a higher than normal TSH had lived longer. So your aim is to differentiate between physiological and pathological TSH elevation using your knowledge, clinical skills and wise interpretation.

REFERENCES