Thyroid disorders in the aged

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Abstract: A review of current information related to the likely incidences of thyroid diseases in the aged population of Malaysia, raising issues such as the need for further epidemiological studies of iodine intake in relation to thyroid diseases within different geographical regions and population subtypes, the need for general country-wide iodization of salt, and the screening of elderly Malaysians for so-called "occult" thyroid diseases.

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"Nobody ever said that growing old would be easy. Just having to hold the newspaper out in your forties and then hair growing out of unusual parts of your body in your fifties. It's tough on the ego." Geoffrey Roy Rush (born 6 July 1951), a distinguished actor, named the Australian of the Year in 2012.

As a car ages, more and more parts of it wear out or no longer function optimally. Sometimes when an old car breaks down, it is difficult to work out exactly where the problem lies and what should be repaired. So it is with the human condition. Old age is characterized by multiple co-existent diseases. This paper will review diseases of the thyroid in the elderly of relevance to the Malaysian situation. Thyroid diseases are of substantially greater prevalence in old age than in those of younger age and are often covert, being masked by co-morbidities. Thus in an Australian population (n = 4489) aged > 49 the prevalence of recognized (10%) and unrecognized (3.6%) thyroid disease (as determined from an abnormal level of plasma TSH, greater or lesser than the euthyroid range of 0.1–4.5 mIU/L) was 13.6%.[1] Similar figures have been presented from many other studies, but tend to differ according to the means of detection of disease (ultrasound *vs* TSH *vs* thyroid antibody levels *vs* free T3 *vs* T4). Regardless of the absolute level of thyroid disease, there is a greater incidence in females. Thus in a questionnaire of inhabitants aged over 20 (n = 94009) carried out in an area of mid-Norway where adequate levels of iodine are present in food, the overall prevalence of hypothyroidism within the population was 0.9% for males and 4.8% for females (sex ratio females : males = 5.4). The corresponding figures for hyperthyroidism were 0.6% for males and 2.5% for females (sex ratio of females : males = 4.2).[2]

The long-term iodine intake status of the study population is of paramount importance in determining the spectrum of thyroid-related diseases in older populations. According to 2005 report of the Technical Working Group on Nutritional Guidelines, Ministry of Health Malaysia[3], "Currently there is no available data on the intake of iodine in Malaysia". Consequently, there is a dearth of information related to the relationship between iodine intake and the prevalence of different thyroid diseases in different population sub-groups in Malaysia. Iodine intakes tend to be much lower in regions where the soil content of iodine is low. This relates in particular to rural, mountainous areas of Malaysia, in which the iodine has been washed out of the soil by heavy tropical rainfall, and where the study population does not have adequate access to marine fish as a significant dietary source.

There is widespread acceptance of measuring the spot concentration of iodine in urine as a means of assessing the iodine intake in populations, as 90% of dietary iodine intake ends up eventually being excreted into urine.[4] By this criterion, the median urinary iodine concentration of Malaysian children aged 8-10 years old (n = 15,600) in Peninsular Malaysia (where salt is not iodized by law) was 104 μg/L in a survey reported in 2010.[5] As would be expected, the median urinary iodine concentration in children throughout the whole of Malaysia (Peninsular and Borneo states and Federal Territories together) was found to be significantly higher among urban children (121 μg/L) than among rural children (94 μg/L, p=<0.01), most likely because of the much greater availability of marine fish in the former group. As noted by the authors of this study, these

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figures suggest that the iodine intake status in Malaysia as a whole is of "borderline adequacy", based on current WHO criteria.[6] Generally urinary iodine levels are higher in children than in the rest of the population, for example being 50% higher in Canadian 6-11-year-olds than in adults from the same areas.[7] Hence it is likely that the Malaysian data in children considerably over-represent the urinary iodine level of the Malaysian population as a whole, suggesting that iodine deficiency may be moderately severe in Peninsular Malaysia, particularly amongst the rural population.

The short-term consequences of severe iodine deficiency, those of endemic goiter, are well characterized. They include severe impairment of fetal growth during pregnancy that involves irreversible inhibition of normal neuro-development and subsequently, cretinism, involving reduced somatic growth and cognitive and motor functions.[8] However, in circumstances of relatively marginal iodine deficiency, the resulting TSH-induced changes in the thyroid and elsewhere can generally compensate in the short-term for the deficiency and maintain T3 levels within an adequately functional range. In a 1997 study, thyroid disorders in elderly nursing home subjects from different areas of the Carpathian basin ethnographical region were compared by a standardised methodology.[9] Clinical and subclinical hypothyroidism were found to occur frequently in an Eastern Hungarian area of abundant iodine intake and in a nearby region of Slovakia where obligatory iodinated salt prophylaxis had been undertaken since the 1950s. On the other hand hyperthyroidism, as manifest as increased thyroid volume and goiter, was of greater prevalence in iodine-deficient Northern Hungary than in the other two areas. Essentially the same conclusions have emerged from a substantial number of similar studies. Representative papers of relevance to iodine-deficient areas include references[10,11,12].

A comparative study of elderly subjects from Jutland, Denmark, (with chronically low iodine intake of 40-60 μg/day for many years) and from Iceland (with high iodine intake estimated as 300–350 μg/day) was undertaken in 1998.[13] This revealed that 14% of subjects from Jutland and 19% from Iceland had serum TSH values outside the reference range of 0.40 – 4.0 mU/L. However, in Jutland, serum TSH was generally low, indicating thyroid hyperactivity, whereas in Iceland, TSH values were generally high, indicating impaired secretion of T4/T3, i.e. occult hypothyroidism. In Jutland, despite the average iodine intake being chronically low, there was no evidence of excessive rates of goiter in school children. As a consequence, an iodine supplementation program had not been initiated. However, this study indicated that the group mostly at risk at this low level of iodine intake was not predominantly the young, but elderly females, who were suffering from undiagnosed, often occult, hyperthyroidism. In the elderly, this is commonly the result of multinodular toxic goiter, which is responsible for a considerable incidence of atrial fibrillation.[14] As discussed by these authors, the pathophysiology of toxic goiter in the elderly seems to be as follows: chronically low iodine intake, and therefore T4/T3 deficiency, stimulate TSH secretion from the anterior pituitary. High TSH stimulates replication of follicular thyroid cells and eventually causes activating mutations of the TSH receptor. These activating mutations induce functional autonomy of the thyroid, and result in a nodular-type of thyroid growth, sometimes euthyroid, but often resulting eventually in toxic hyperthyroidism.

Unfortunately there is a dearth of studies of the epidemiology of thyroid diseases within Malaysia, and how these change with population age, gender and geographical location. However, it would be predicted, by comparison with the studies discussed above that the incidence of multinodular goiter in elderly females in particular would be relatively high, because the rural areas of West Malaysia, which have no iodine supplementation, are regions of borderline iodine adequacy and a high proportion of the population is rural (72%), rather than urban (28%).[15] Indeed, the suggestion that nodular goiter is relatively common in Malaysia is reinforced by a 2009 study of thyroid

hospitalizations in the state of Kelantan.[16] The authors concluded "This study suggests that malignant thyroid lesions arising from multi-nodular goiter are high in a population living in an iodine-deficiency area."

If these considerations are borne out by comprehensive, well-designed clinical and epidemiological studies, it raises the question of whether apparently well elderly subjects should be periodically and routinely assessed for thyroid function, as has been suggested for other relatively iodine-deficient regions such as Italy.[17]

A secondary question is whether iodine supplementation should be undertaken in West Malaysia, as it is in most of East Malaysia. A recent 4-week study of iodine supplementation in a previously iodine-adequate but euthyroid population of Chinese students[18] has indicated that a total iodine intake of >700 μg/day (i.e. 400 μg/day supplementation), was associated with subclinical hypothyroidism, as assessed from an increase in serum TSH concentrations above the normal range (which was set at 0.3–5.0 mIU/L for that study). This suggests that there is a modification of "normal" thyroid function by high doses of dietary iodine, This concept is in accordance with the well-established fact that grossly excessive iodine intake above WHO recommendations will induce goiter.[19] This appears to arise from an autoimmune response in which stimulating anti-thyroid antibodies are initially induced by thyroid iodide swamping, causing thyroid hyperplasia.[20] It appears that these are subsequently largely replaced by non-stimulating antibodies, inducing the classical long-term hypothyroidism seen in populations exposed to iodine excess.[21] It might be anticipated that a marginally iodine-deficient population that was physiologically adjusted to the deficiency might initially respond in a similar manner to a sudden increase in iodine intake following the introduction of iodization of salt. However, a study in which iodine-deficient Moroccan schoolchildren (n = 323) received iodised salt (25 μg/g) suggests otherwise. The resulting increase in iodine intake caused a rise in the childrens' plasma T4 levels and a significant reduction in their initial hypothyroidism. The anticipated increase in anti-thyroid antibodies was transient and had returned to baseline by 1 year. TSH concentrations were not elevated. The authors concluded that "rapid introduction of iodized salt does not provoke significant thyroid autoimmunity in severely iodine-deficient children followed for 1 year".[22] It is therefore likely that iodine supplementation in West Malaysia would not be followed by any serious adverse long-term consequences for thyroid function.

This brief review will conclude with a comment from where it started. Old age is characterized by multiple co-morbidities. In this context, both occult hypothyroidism and hyperthyroidism have received general attention. Thus in 1994, the difficulties associated with diagnosing sub-clinical hypothyroidism in the elderly from clinical signs alone were noted.[23] Similarly, in 1989, so-called "idiopathic" atrial fibrillation in the elderly was suggested to occur as a result of occult hyperthyroidism, which is "not readily identifiable clinically or through routine thyroid function tests".[24] Hence there may be a case for regular periodic screening for occult hyperthyroidism and hypothyroidism as individuals within the Malaysian population grow old. Indeed, the New York Times, has very recently canvasses this option in the U.S.A.[25]

It is beyond the scope of this present review to address these latter questions, which relate to funding and public health issues, but they have been raised in this brief review to stimulate discussion and further in-depth research into this problem, which undoubtedly will become of more importance as the Malaysian population ages in the future.[26]

REFERENCES

1. Empson M, Flood V, Ma G, Eastman CJ, Mitchell P. Prevalence of thyroid disease in an older Australian population. Intern Med J 2007; 37: 448-55.
2. Bjoro T, Holmen J, Kruger O, Midthjell K, Hunstad K, Schreiner T, Sandnes L, Brochmann H. Prevalence of thyroid disease, thyroid dysfunction and thyroid peroxidase antibodies in a large, unselected population. The Health Study of Nord-Trondelag (HUNT). European J Endocrin 2000; 143: 639-47.

3. Recommended Nutrient Intakes for Malaysia. A Report of the Technical Working Group on Nutritional Guidelines. National Coordinating Committee on Food and Nutrition, Ministry of Health Malaysia, Putrajaya, 2005.
4. Offie Porat Soldin (2002) Review: controversies in urinary iodine determinations. Clin Biochem 2002; 35: 575–9.
5. Selamat R, Mohamud WNW, Zainuddin AA, Rahim NSCA, Ghaffar SA, Aris T. Iodine deficiency status and iodised salt consumption in Malaysia: findings from a national iodine deficiency disorders survey. Asia Pacific J Clin Nutr 2010; 19: 578-85.
6. World Health Organization. Assessment of iodine deficiency disorders and monitoring their elimination. A guide for programme managers. Second edition, 2001.
7. Statistics Canada (2012)Iodine status of Canadians, 2009 to 2011. http://www.statcan.gc.ca/pub/82-625-x/2012001/article/11733-eng.htm.
8. Zimmermann MB. Iodine deficiency. Endocr Rev 2009; 30: 376–408.
9. SzabolcsI, Podoba J, Feldkamp J, Dohan O, Farkas I, Sajgo M, Takats KI, Goth M, Kovacs L, Kressinszky K, Hnilica P, Szilagyi G. Comparative screening for thyroid disorders in old age in areas of iodine deficiency, long-term iodine prophylaxis and abundant iodine intake. Clin Endocrin 1997; 47: 87–92.
10. Ozbakir O, Doğukan A, Kelestimur F. The prevalence of thyroid dysfunction among elderly subjects in an endemic goiter area of Central Anatolia. Endocrin J 1995; 42: 713-6.
11. Andersen S, Iversen F, Terpling S, Pedersen KM, Gustenhoff P, Laurberg P. More hypothyroidism and less hyperthyroidism with sufficient iodine nutrition compared to mild iodine deficiency - a comparative population-based study of older people. Maturitas 2009; 64: 126-31.
12. Ceresini G, Ceda GP, Lauretani F, Maggio M, Usberti E, Marina M, Bandinelli S, Guralnik JM, Valenti G, Ferrucci L. Thyroid status and 6-year mortality in elderly people living in a mildly iodine-deficient area: the aging in the chianti area study. J Amer Geriat Soc 2013; 61: 868-74.
13. Laurberg P, Pedersen KM, Hreidarsson A, Sigfusson N, Iversen E, Knudsen AR. Iodine intake and the pattern of thyroid disorders: a comparative epidemiological study of thyroid abnormalities in the elderly in Iceland and in Jutland, Denmark. J Clin Endocrin Metab 1998; 83: 765–9.
14. Vitti P, Rago T, Tonacchera M, Pinchera A. (2002).Toxic multinodular goiter in the elderly. J Endocrin Investig 2002; 25: 16-8.
15. Geohive (2010) http://www.geohive.com/earth/pop_urban.aspx.
16. Othman NH, Omar E, Naing NN. Spectrum of thyroid lesions in hospital Universiti Sains Malaysia over 11 years and a review of thyroid cancers in Malaysia. Asian Pacific J Cancer Prev 2009; 10: 87-90.
17. Faggiano A, Del Prete M, Marciello F, Marotta V, Ramundo V, Colao A. Thyroid diseases in elderly . Minerva Endocrinoogica 2100; 36: 211-31.
18. Sang Z, Wang PP, Yao Z, Shen J, Halfyard B, Tan L, Zhao N, Wu Y, Gao S, Tan J, Liu J, Chen Z, Zhang W (2012) Exploration of the safe upper level of iodine intake in euthyroid Chinese adults: a randomized double-blind trial. Amer J Clin Nutr 2012; 95: 367-73.
19. Zhao J, Wang P, Shang Li, Sullivan KM, van der Haar F, Glen Maberly G. Endemic Goiter Associated With High Iodine Intake. Amer J Pub Hlth 2000; 90: 1633–5.
20. Henjum S, Barikmo I, Gjerlaug AK, Mohamed-Lehabib AI, Oshaug A,Strand TA,Torheim LE. Endemic goitre and excessive iodine in urine and drinking water among Saharawi refugee children. Pub Hlth Nutr 2010; 13: 1472-7.
21. Nuovo JA and Wortofsky L. Adverse effects of iodine. In Principles and Practice of Endocrinology and Metabolism, 3rd Edition pp 360-366, edited by Kenneth L. Becker. Lipincott William Wilkins Baltimore, Maryland USA, 2001.
22. Zimmermann MB, Moretti D, Chaouki N, Torresani T. Introduction of iodized salt to severely iodine-deficient children does not provoke thyroid autoimmunity: a one-year prospective trial in northern Morocco. Thyroid 2003; 13: 199-203.
23. Bemben DA, Hamm RM, Morgan L, Winn P, Davis A, Barton E. Thyroid disease in the elderly. Part 2. Predictability of subclinical hypothyroidism. J Family Practice 1994; 38: 583-8.
24. Sulimani RA. Diagnostic algorithm for atrial fibrillation caused by occult hyperthyroidism. Geriatrics 1989; 44: 61-4.
25. New York Times Tuesday, July 9, 2013. Health Guide In-Depth Report: Diagnosis Hypothyroidism. Review Date: 5/31/2012. Reviewed By: Harvey Simon, MD, Editor-in-Chief, Associate Professor of Medicine, Harvard Medical School; Physician, Massachusetts General Hospital. Also reviewed by David Zieve, MD, MHA, Medical Director, A.D.A.M., Inc.
26. Barling PM. Editorial - osteoporosis – an increasingly important issue for both young and aging citizens of Malaysia. IeJSME 2013; 7: 1-3.