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Prevalence of Hypothyroidism in Peri-/Post-Menopausal Thai Women

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ABSTRACT

Objectives: This study aimed to determine the prevalence of hypothyroidism and its association with menopausal symptoms and evaluated the diagnostic performance of Zulewski's clinical score for predicting hypothyroidism in peri-/post-menopausal Thai women.

Materials and Methods: This hospital-based cross-sectional study was conducted between June 2015 and April 2016 in Srinagarind Hospital, Khon Kaen, Thailand. We enrolled 305 peri-/post-menopausal women 45-65 years of age without previous history of thyroid diseases, radiation exposure at the neck, or concurrent use of lithium. The participants were interviewed by two research assistants' vis-à-vis symptoms of menopause and hypothyroidism, current medications and menstrual characteristics. Blood samples were taken for TSH and FT4 levels. Main outcomes were prevalence of hypothyroidism, the Menopause-Specific Quality of Life (MENQOL) score, and diagnostic performance of Zulewski's clinical score .

Results: Mean age was 56 ± 4.7 years. The prevalence of hypothyroidism was 6.2% (95%CI 3.5% to 8.9%). The sensitivity of Zulewski's clinical score at the cutoff point ≥ 3 was 70%. Neither the MENQOL domain score nor the composite score was associated with hypothyroidism.

Conclusion: The prevalence of hypothyroidism in peri-/post-menopausal Thai women is low. There is no association between MENQOL score and hypothyroidism. Zulewski's clinical score is not a good screening test for hypothyroidism in this group.

Keywords: menopausal women, hypothyroidism, Zulewski's clinical score, MENQOL

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ภาวะขาดไทรอยด์ฮอร์โมนในสตรีวัยหมดประจำเดือน: การวิจัยแบบตัดขวาง และวิเคราะห์

กนกพร บุตรมารศรี, วรลักษณ์ สมบูรณ์พร, สุกรี สุนทราภา, ศรีนารี แก้วฤดี, จรูญศักดิ์ สมบูรณ์พร

บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาหาความชุกของภาวะฮอร์โมนไทรอยด์ต่ำ และศึกษาอาการที่สามารถบ่งชี้ภาวะฮอร์โมนไทรอยด์ต่ำในสตรีวัยหมดระดู*

วัสดุและวิธีการ: *ทำการศึกษาเชิงพรรณนาแบบตัดขวางในโรงพยาบาลศรีนครินทร์ จังหวัดขอนแก่น ตั้งแต่เดือนมิถุนายน พ.ศ. 2558 ถึง เดือน เมษายน พ.ศ. 2559 ในสตรีวัยหมดระดูอายุระหว่าง 45-65 ปี จำนวน 305 คน ที่ไม่เคยได้รับการวินิจฉัยว่าเป็นโรคไทรอยด์มาก่อน ไม่เคยได้รับการฉายรังสีที่บริเวณคอ และไม่ได้ใช้ยาลิเธียม สตรีวัยหมดระดูจะได้รับการสอบถามข้อมูลทั่วไป รวมไปถึงอาการของวัยหมดระดู ยาที่ใช้ ลักษณะของรอบเดือน อาการต่างๆ ของภาวะไทรอยด์ทำงานบกพร่อง และตอบแบบสอบถามอาการแสดงของฮอร์โมนไทรอยด์ต่ำ (Zulewski clinical score) และแบบวัดคุณภาพชีวิต (MENQOL) พร้อมเจาะเลือดเพื่อส่งตรวจ TSH, ฮอร์โมน T4 ชนิดอิสระ (FT4)*

ผลการศึกษา: *อายุเฉลี่ยของสตรีวัยหมดระดูคือ 56 ± 4.7 ปี ความชุกของภาวะไทรอยด์ฮอร์โมนต่ำแบบไม่แสดงอาการคิดเป็นร้อยละ 6.2 (95%CI 3.5% to 8.9%). Zulewski's clinical score ที่คะแนนมากกว่าหรือเท่ากับ 3 พบว่ามีความไวร้อยละ 70 และไม่พบความสัมพันธ์ระหว่างคะแนน MENQOL กับอาการและอาการแสดงของภาวะพร่องไทรอยด์*

สรุป: *ภาวะไทรอยด์ฮอร์โมนต่ำแบบไม่แสดงอาการในกลุ่มสตรีไทยวัยหมดระดูมีความชุกน้อย ไม่พบความสัมพันธ์ระหว่างคะแนน MENQOL กับอาการและอาการแสดงของภาวะพร่องไทรอยด์ Zulewski's clinical score ไม่ใช่เครื่องมือที่ดีในการตรวจคัดกรองภาวะฮอร์โมนไทรอยด์ต่ำ*

คำสำคัญ: *สตรีวัยหมดระดู, ภาวะฮอร์โมนไทรอยด์ต่ำ, แบบสอบถามอาการแสดงของฮอร์โมนไทรอยด์ต่ำ, แบบวัดคุณภาพชีวิต*

Introduction

Thyroid function and the female gonadal axes are related throughout the reproductive years[1], moreover, thyroid dysfunctions are more prevalent in women than men[2,3]. Notwithstanding, based on a limited number of studies about thyroid dysfunction, in particular hypothyroidism, is unlikely to relate to menopausal status. In the Study of Women's Health Across the Nation (SWAN), a community-based multi-ethnic study of the natural history of the menopausal transition, there was no significant difference in thyroid-stimulating hormone (TSH) concentrations among SWAN enrollees classified as pre-menopausal vs. early peri-menopausal[4]. This finding is consistent with the results from Massoudi et al[5].

Hypothyroidism has an insidious onset with a range of non-specific symptoms that can delay the diagnosis for months or even years[6]. Some menopausal symptoms are similar to the symptoms of hypothyroidism. In the SWAN study, frequency of feeling fearful in the 2 weeks prior to interview was associated with TSH concentrations ($p<0.008$)[4], i.e. women who reported feeling fearful were disproportionately represented in the group with TSH < 0.5 mIU/L ($p < 0.02$)[4]. Likewise, women who self-reported less sexual interest had a slightly lower adjusted mean TSH concentration than women who had a sustained level of sexual interest (2.03 vs. 2.16 mIU/L; $p<0.03$)[4]. Undiagnosed or untreated subclinical hypothyroidism is likely to have an impact on some serious health problem. In a systematic review, subclinical hypothyroidism was associated with an increased risk of coronary heart disease (CHD) events and CHD mortality in those with higher TSH levels[7].

Iodine deficiency is considered an important risk factor for hypothyroidism[8]. According to the report in 2001, the prevalence of iodine-deficiency in Europe was 44.2% compared to 31.7% in South-East Asia[9]. So universal fortification of tablet salt has been introduced for the prevention and control of iodine deficiency[10]. Recently, the relationship between universal salt iodization (USI) and iodine excess has attracted more attention. Results from a systematic review have shown that iodine excess can lead to hypothyroidism and autoimmune thyroiditis, especially for susceptible populations with recurring thyroid disease, the elderly, fetuses, and neonates[11].

As iodine intake may be changed by universal salt iodization program, we were interested to evaluate the existing prevalence of hypothyroidism in menopausal women in our region. In addition, we also aimed to explore the association between various menopausal symptoms and hypothyroidism as well as the diagnostic performance of Zulewski's clinical score as a screening tool for hypothyroidism.

Materials and Methods

This study was conducted between June 2015 and April 2016 at Srinagarind Hospital, Khon Kaen, Thailand. This project proceeded in accordance with international guidelines of Good Epidemiology Practice. The Khon Kaen University Ethics Committee for Human Research reviewed and approved the study protocol. Research assistants informed the participants with regard to the purposes, procedures, risks and benefits of the study as specified in the participant information package. All included participants signed consent forms. Fundamental data on medical history, and reproductive factors were collected through questionnaires (including age, parity, age at menarche, and duration after the last menstrual period, history of contraceptive use, cigarette smoking, alcohol consumption, body weight and height).

Population

The recruitment was taken at outpatient department. Menopausal women between 45 and 65 years of age were included. We excluded women having a history of thyroid disorders, radiation exposure at the neck, or lithium consumption. A peri-menopausal woman was defined as a woman being 45 or older with irregular menstrual cycles over the last 12 months while a post-menopausal woman was defined as a woman 45 or older who had not had a menstrual period for 12 months or more.

Clinical assessment of hypothyroidism and menopausal symptoms

Two well-trained research assistants administered questionnaires to evaluate menopausal symptoms and clinical hypothyroidism by using the Menopause-Specific Quality of Life (MENQOL) questionnaire and Zulewski's clinical score, respectively. The MENQOL comprises 32 questions covering 4 domains (physical, vasomotor, psychosocial and sexual)[12].

Pongpatiroj et al translated the MENQOL questionnaire into Thai language and reported the Cronbach alpha of reliability 0.89[13]. For Zulewski's clinical score (max 12), the twelve symptoms and signs of hypothyroidism were evaluated. A score more than 5, 3-5, and less than 3 defined hypothyroidism, borderline hypothyroidism and euthyroidism, respectively[14].

Assays for TSH and FT4

A blood sample was taken and TSH and FT4 concentrations assessed by radioimmunoassay. The respective inter- and intra-assay coefficient of variations (CVs) for the TSH were 5.4% and 5.7%. The respective inter- and intra-assay coefficient of variations (CVs) for the FT4 were 8.3% and 4.4%. The normal range of TSH concentration for normal thyroid function is 0.25-4 mIU/L. Hypothyroidism was diagnosed if the TSH level was 5 or more mIU/L and further classified as clinical if the FT4 was low or subclinical if the FT4 was normal. If the FT4 was below normal and the TSH was normal or depressed, this case was classified as secondary hypothyroidism.
Sample size calculation

As per previous study[15],we used a prevalence of hypothyroidism of 4.8%. Thus, 305 menopausal women were adequate to estimate prevalence with a 95% confidence interval and a desired precision of ±2.4%.

Data analysis

Data management and analysis were done using Stata version 10.0. We reported means (±SD), medians (interquartile range, IQR), percentages or 95% confidence intervals as appropriate. We also calculated the relative risk to determine if menopausal status was a risk for thyroid disorders, using a multinomial logistic regression analysis. The two-sample Wilcoxon rank-sum or Mann-Whitney U test was used to test for differences in the composite vs. other domains of the MENQOL score between the euthyroid group and the subclinical hypothyroid group. The diagnostic performance of Zulewski's clinical score for hypothyroidism was calculated according to the cut-off levels ≥ 3 and > 5. Post hoc analysis was conducted to assess the correlation between body weight and TSH levels by using Sperman's Rho. The association between BMI and thyroid status (euthyroidism and hypothyroidism) was evaluated using Pearson Chi-square. To determine whether hypothyroidism was the risk for BMI > 23 kg/m^2, matched case-control analyses by age (within 1 year) and time since last menstrual cycle (within 1 year) were computed.

Results

Between June 2015 and April 2016, 305 menopausal women were included in the study. The respective mean age (SD) at recruitment and mean time since last menstrual period was 56.1 (4.7) and 7.2 years (5.6). Of these recruited, 31 and 274 were peri-menopausal and post-menopausal, respectively. The respective median (IQR) of TSH concentration in the included menopausal women was 1.9 mIU/L(1.3–2.8 IQR). The respective median (IQR) of MENQOL score for the vasomotor, psychosocial, physical and sexual domain was 0 (0-3), 1 (0-5), 9 (4-18) and 0 (0-2), respectively. Hormonal replacement therapy (HRT) was used in only 3.3% of women in both groups.

The prevalence of subclinical hypothyroidism was 6.2% (95%CI 3.5% to 8.9%) (n=19). When we classified the women into a peri-menopausal or post-menopausal group, the respective prevalence was 12.9% (95%CI 0.4% to 25.4%)(n=4) and 5.5% (95%CI 2.8% to 8.2%) (n=15). There was no overt

hypothyroidism. The prevalence of euthyroidism and hyperthyroidism are presented in Table 1.

When assessing the peri-menopausal group using logistic regression analysis, the relative risk of subclinical hypothyroidism was not significantly different vis-à-vis the post-menopausal group whereas the relative risk of hyperthyroidism was significantly lower in the post-menopausal group. After the age-adjusted analysis, however, there was no longer any significant difference in the relative risk for hyperthyroidism (Table 2).

According to the two-sample Wilcoxon rank-sum (Mann-Whitney U) test, neither composite nor other domains of MENQOL score showed any statistically significant differences between the euthyroidism group and the subclinical hypothyroidism group (data not shown).

Table 1. Prevalence of thyroid disorders and menopausal status.

Thyroid function	Perimenopause (n = 31)		Postmenopause (n = 274)		Total (n = 305)	
	%	95%CI	%	95%CI	%	95%CI
Euthyroidism	74.2	57.9, 90.5	89.4	85.7, 93.1	87.9	84.2, 91.6
Hypothyroidism						
Subclinical	12.9	0.4, 25.4	5.5	2.8, 8.2	6.2	3.5, 8.9
Overt	0	N/A	0	N/A	0	N/A
Secondary	0	N/A	0.4	0.0, 1.1	0.3	0.0, 1.0
Hyperthyroidism						
Hyperthyroidism	3.2	0.0, 9.8	0.7	0.0, 1.7	1.0	0.0, 2.1
Subclinical	9.7	0.0, 20.7	2.2	0.4, 3.9	3.0	1.0, 4.8
Secondary	0	N/A	1.8	0.2, 3.4	1.6	0.2, 3.1

N/A: Not Applicable

Table 2. Relative risk (RR) of menopausal status for thyroid disorders.

Thyroid status	RR (95% CI)	RR after age-adjusted analysis (95% CI)
Hypothyroidism		
Perimenopausal	Reference	
Postmenopausal	0.6 (0.1, 2.1)	0.9 (0.8, 1.0)
Hyperthyroidism		
Perimenopausal	Reference	
Postmenopausal	0.2 (0.0, 0.9)	1.0 (0.9, 1.1)

When using Zulewski's clinical score for hypothyroidism, the sensitivity at a cut-off of > 3 and > 5 were 70.0% (95%CI 45.7% to 88.1%) and 10.0% (95%CI 1.2% to 31.7%), respectively. (Table 3)

When we used Sperman's Rho to test the hypothesis that body weight and TSH levels were independent, the p value was 0.54. This indicated that there was no association between body weight and TSH levels (Fig. 1)

Table 3. Diagnostic Performance of Various Cut-off Points for Hypothyroidism.

Diagnostic Performance	Zulewski's Clinical Score			
	> 3	95%CI	> 5	95%CI
Sensitivity	70.0%	(45.7, 88.1)	10.0%	(1.2, 31.7)
Specificity	32.6%	(27.2, 38.4)	65.6%	(59.8, 71.1)
Positive predictive value	6.8%	(3.77, 11.1)	2.0%	(0.2, 7.0)
Negative predictive value	93.9%	(87.3, 97.7)	91.2%	(86.5, 94.7)
Positive likelihood ratio	1.0	(0.7, 1.4)	0.3	(0.0, 1.1)
Negative likelihood ratio	0.9	(0.5, 1.8)	1.4	(1.2, 1.6)

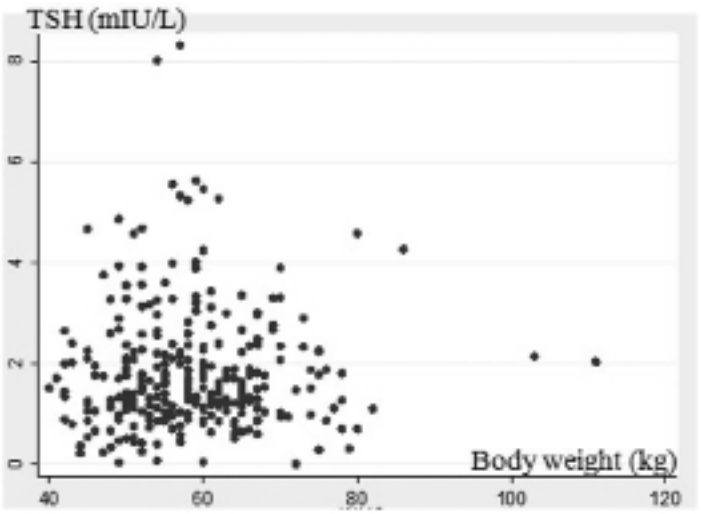

Fig. 1. a) Ethyl chloride spray application b) Lidocaine injection

Table 4. Thyroid Status and BMI Classification.

Classification	Thyroid Status	
BMI (kg/m^2)	Euthyroidism (n=264)	Hypothyroidism (n=18)
<23	43.56% (115)	33.33% (6)
>23	56.44% (149)	66.67% (12)

P value=0.396

According to the BMI cut-offs for determining overweight and obesity in Asian populations(16), we classified the included menopausal women into two groups (i.e., BMI < 23 kg/m2 and ≥ 23 kg/m2). Post hoc analysis—to determine the correlation between the two BMI groups and thyroid status (i.e., euthyroidism and hypothyroidism) using Pearson Chi-square—showed that there was no significant correlation between the two (Table 4).

Discussion

After more than a decade of the published studies regarding to hypothyroidism in menopausal women, this study shows the persistent prevalence of hypothyroidism among menopausal women (i.e., 6.2% (95%CI 3.5% to 8.9%)). This is consistent with other studies published more than 10 years ago. In a study published in 2002 by Suchartwatnachai et al., the prevalence of subclinical hypothyroidism was 4.2%[15]. In 2003, the SWAN study also reported a prevalence of 6.2% for women in mid-life with TSH >5.0 mIU/L[4]. This suggests that the prevalence is steady across countries and over time.

We also found that when comparing the prevalence of subclinical hypothyroidism in peri-menopausal women with that of postmenopausal women, prevalence did not differ. This is in line with results of the SWAN study and that of Massoudi et al. and Cooper[4,5]. In the SWAN study, there was no significant difference in TSH concentrations among SWAN enrollees classified as pre-menopausal vs. early peri-menopausal[4]. In the study by Massoudi et al., the included women were classified into 3groups (viz., pre-menopausal, post-menopausal not on HRT, and post-menopausal using HRT)[5]. They reported that the TSH levels did not differ according to menopausal status[5]. The respective age of the included women in the SWAN study, the study by Massoudi et al. and our own was 42–52, 42–50, and 45–65 years.

In the current study, the sensitivity and the specificity of Zulewski's clinical score at a cut-off of >5 were 10.0% and 65.6%, respectively; however, the positive likelihood ratio was 0.3 (95%CI 0.0, 1.1) and negative likelihood ratio was 1.4 (95%CI 1.2, 1.6). This suggests that Zulewski's clinical score may not change the likelihood of disease when applied to healthy Thai menopausal women. In the other study, sensitivity and specificity were 62% and 99% for the cut-off points 5; however, likelihood ratio was not reported[14]. The differences between these diagnostic performances may be explained by the different population.

In the SWAN study, self-report of less sexual interest had a slightly lower adjusted mean TSH concentration than women who reported a sustained level of sexual interest (2.03 vs. 2.16 mIU/L; $p < 0.03$)[4]. In our study, neither domains nor symptoms of MENQOL score were associated with hypothyroidism. The explanation for the different results may be that in the SWAN study, the authors did not classify the included women into euthyroid vs. hypothyroid groups as we did; so, the analytical methods differed according to the types of variables themselves. In our post hoc analyses, body weight and body mass index were not associated with TSH levels even after adjusting the analyses for age and time since last menstrual period. The findings are in line with the findings of the Cardiovascular Health Study—a cross-sectional analysis of 1276 participants, ≥65 years of age[17]. The results from a cross-sectional study in Japan were also comparable[18]. By contrast, results from the Solanki's study showed a significant relationship between serum TSH and BMI[19]. Mean TSH increased as BMI increased[19]. In the latter study, the authors included participants of a wide age range (i.e., 18–60) which differs from our own as well as that of the Cardiovascular Health Study. In addition, they did not adjust for other covariates in their analyses[19]. In 3 large longitudinal studies, the results were that weight gain is significantly associated with increasing TSH[20,20-22], these 3 trials included women with a wide age range: (a) the DanThyr study included women aged 18-65 years old[20], (b) the Framingham Offspring Study included women of all ages[21], and (c) the HUNT study included women 20 years or older[22].

As our primary aim was to establish the prevalence of hypothyroidism in menopausal women, the sample size was inadequate to clearly indicate the lack of association between hypothyroidism and other variables (such as: menopausal symptoms, body weight, and BMI). A larger number of participants in a further study would, therefore, be needed to determine if there is any association between hypothyroidism and these variables or not.

As we claim that all hypothyroid cases in our study were subclinical, this will be questioned since we

did not measure FT3; however, clinical guidelines suggest that TSH and FT4 are clinically useful for measuring indicators for detecting hypothyroidism[23]. Li et al. conducted a study to clarify the clinical value of serum total triiodothyronine (TT3), total thyroxine (TT4), FT3, and FT4 to assess thyroid function. They suggest that TSH and FT4 are the most valuable indicators in assessing thyroid function in a healthy population[24].

In clinical practice, controversy persists regarding TSH screening of the general population[23]. The Royal College of Physicians of London has stated that screening of the healthy adult population is unjustified whereas all American organizations have suggested to have TSH screening—starting at a particular age—differs across organizations[23]. American organizations do, however, agree on TSH screening in the ageing population (> 60)[23]. In light of our results, TSH screening in every menopausal woman would be excessive due to the low prevalence of hypothyroidism. However, further research regarding the impact of undiagnosed or untreated subclinical hypothyroidism would be valuable for making clearer decision on TSH screening in peri-/post-menopausal women.

Conclusion

The prevalence of hypothyroidism in peri-/post-menopausal Thai women was low. There was no association between MENQOL score and hypothyroidism. Zulewski's clinical score was not a good screening test for hypothyroidism in this group.

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Potential conflicts of interest

The authors declare no conflict of interest.

References

1. Krassas GE. Thyroid disease and female reproduction. Fertil Steril 2000;74:1063-70.
2. Canaris GJ, Manowitz NR, Mayor G, Ridgway EC. The Colorado thyroid disease prevalence study. Arch Intern Med 2000;160:526-34.
3. Vanderpump MP, Tunbridge WM. Epidemiology and prevention of clinical and subclinical hypothyroidism. Thyroid 2002;12:839-47.
4. Sowers M, Luborsky J, Perdue C, Araujo KL, Goldman MB, Harlow SD. Thyroid stimulating hormone (TSH) concentrations and menopausal status in women at the mid-life: SWAN. Clin Endocrinol (Oxf) 2003;58:340-7.
5. Massoudi MS, Meilahn EN, Orchard TJ, Foley TP, Jr., Kuller LH, Costantino JP, et al. Thyroid function and perimenopausal lipid and weight changes: the Thyroid Study in Healthy Women (TSH-W). J Womens Health 1997;6:553-8.
6. Schindler AE. Thyroid function and postmenopause. Gynecol Endocrinol 2003;17:79-85.
7. Rodondi N, den Elzen WP, Bauer DC, Cappola AR, Razvi S, Walsh JP, et al. Subclinical hypothyroidism and the risk of coronary heart disease and mortality. JAMA 2010;304:1365-74.
8. Zimmermann MB, Andersson M. Assessment of iodine nutrition in populations: past, present, and future. Nutr Rev 2012;70:553-70.
9. Andersson M, Karumbunathan V, Zimmermann MB. Global iodine status in 2011 and trends over the past decade. J Nutr 2012;142:744-50.
10. World Health Organization (WHO). Iodine and Health: Eliminating Iodine Deficiency Disorders Safely throughSalt Iodization. Geneva, Switzerland: World Health Organization 1994.
11. Zhao W, Han C, Shi X, Xiong C, Sun J, Shan Z, et al. Prevalence of goiter and thyroid nodules before and after implementation of the universal salt iodization program in mainland China from 1985 to 2014: a systematic review and meta-analysis. PLoS One 2014;9:e109549.
12. Hilditch JR, Lewis J, Peter A, van MB, Ross A, Franssen E, et al. A menopause-specific quality of life questionnaire: development and psychometric properties. Maturitas 1996;24:161-75.
13. Pongpatiroj A, Sripramote M, Wanitwanathong G. Effects of hormone replacement therapy on the quality of life in postmenopausal women. Vajira Med J 2001;45:1-11.
14. Zulewski H, Muller B, Exer P, Miserez AR, Staub JJ. Estimation of tissue hypothyroidism by a new clinical score: evaluation of patients with various grades of hypothyroidism and controls. J Clin Endocrinol Metab

1997;82:771-6.
15. Suchartwatnachai C, Thepppisai U, Jirapinyo M. Screening for hypothyroidism at a menopause clinic. Int J Gynaecol Obstet 2002;77:39-40.
16. WHO Expert Consultant. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet 2004;363:157-63.
17. Garin MC, Arnold AM, Lee JS, Tracy RP, Cappola AR. Subclinical hypothyroidism, weight change, and body composition in the elderly: the Cardiovascular Health Study. J Clin Endocrinol Metab 2014;99:1220-6.
18. Sakurai M, Nakamura K, Miura K, Yoshita K, Takamura T, Nagasawa SY, et al. Association between a serum thyroid-stimulating hormone concentration within the normal range and indices of obesity in Japanese men and women. Intern Med 2014;53:669-74.
19) Solanki A, Bansal S, Jindal S, Saxena V, Shukla US. Relationship of serum thyroid stimulating hormone with body mass index in healthy adults. Indian J Endocrinol Metab 2013;17(Suppl 1):S167-S169.
(20) Bjergved L, Jorgensen T, Perrild H, Laurberg P, Krejbjerg A, Ovesen L, et al. Thyroid function and body weight: a community-based longitudinal study. PLoS One 2014;9:e93515.
21. Fox CS, Pencina MJ, D'Agostino RB, Murabito JM, Seely EW, Pearce EN, et al. Relations of thyroid function to body weight: cross-sectional and longitudinal observations in a community-based sample. Arch Intern Med 2008;168:587-92.
22. Svare A, Nilsen TI, Bjoro T, Asvold BO, Langhammer A. Serum TSH related to measures of body mass: longitudinal data from the HUNT Study, Norway. Clin Endocrinol (Oxf) 2011;74:769-75.
23. Garber JR, Cobin RH, Gharib H, Hennessey JV, Klein I, Mechanick JI, et al. Clinical practice guidelines for hypothyroidism in adults: cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association. Endocr Pract 2012;18:988-1028.
24. Li H, Yuan X, Liu L, Zhou J, Li C, Yang P, et al. Clinical evaluation of various thyroid hormones on thyroid function. Int J Endocrinol 2014;2014:618572.