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ORIGNAL ARTICLE

Age, Gender, and Seasonal Effects on Thyroid Profile in Adults with Normal Thyroid Functions

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ABSTRACT

Background: Thyroid hormone variations have been observed according to age and sex. Seasonal effects also induce variations in thyroid function even in people with normal thyroid levels. The majority of clinical laboratories follow a single reference range without the consideration of age, gender, and especially seasonal variations in thyroid function tests.

Objectives: To evaluate age, gender, and seasonal variations in thyroid function tests in adults with normal thyroid functions.

Methodology: This cross sectional study was carried out at Pathology Department, Quaid-e-Azam Medical College, Bahawalpur. One year data from Jan 2018 to Jan 2019 of thyroid function tests (TSH, T3 and T4) and demographic details were obtained for all those patients whose Thyroid Stimulating Hormone (TSH) was in normal reference range (0.5-4.5mU/L). We found the data of 418 subjects from 16 to 75 years of age, among them 196 were females and 222 were males.

Results: Serum TSH levels were higher in females (2.11mU/L ±1.54) than serum TSH levels of males (1.59mU/L ±1.2) with a p-value of 0.0002. FT4 levels (normal range: 0.89-1.76ng/dL) were significantly lower (p-value 0.0018) in females (1.33ng/dL ±0.50) as compared to males (1.48ng/dL ±0.48). In <20 years of the age group of both genders, serum TSH was at lowest levels, while highest in 20-40 years of the age group of males and >60 years of females. The mean TSH of all subjects was high (2.98mU/L) in winters and it was low (2.4mU/L) in autumn. FT4 was at the lowest level (1.16ng/dL) in winters and it was highest (1.46ng/dL) in summers. FT3 levels in the winter season were higher than in other seasons.

Conclusion: Age, gender, and season affects the thyroid hormones levels, and these factors should be considered while interpreting the lab results of thyroid function tests.

Keywords	*Address of Correspondence	Article info.
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INTRODUCTION

The most important gland in the endocrine system is the thyroid gland. It is situated below the larynx, on both anterior sides of the trachea[1]. The thyroid gland secretes two major hormones; Triiodothyronine (T3) and Thyroxin (T4). The concentration of T3 is 7% and T4 is 93% of total thyroid hormone secretion. Both thyroid hormones circulate in the blood in a free and bound form. About 99% of thyroid hormones are bound forms, and the major carrier

of bound forms of T3 and T4 is thyroid binding globulin, whereas a small amount is carried out by transthyretin and albumin[2]. Free form is the active form of both hormones and free T3 (FT3) is more active than free T4 (FT4)[3]. The FT4 is involved in the control mechanism of thyroid secretion and both FT3 and FT4 are indicators of thyroid health of an individual[4]. These hormones are involved in growth and metabolism of the body, therefore, in the absence of thyroid hormones, the metabolism is decreased and BMR fall to 50% below the range of normal[5]. Thyroid hormones are very important in brain development[6]. Iodine and a protein known as thyroglobulin are required for the synthesis of T3 and T4 from the thyroid gland. Different factors like age, sex, body weight, nutritional, climate and health and disease condition effect the production of T3 and T4[7]. The Thyroid Stimulating Hormone (TSH) which is also called thyrotropin is released from the anterior pituitary. TSH controls the production of T3 and T4 from the thyroid gland through a negative feedback mechanism[7]. TSH itself is regulated by Thyroid Releasing Hormone (TRH) from the hypothalamus, by positive feedback mechanism[8]. TSH measurement can accurately assess the functions of the thyroid gland and it is used as a screening test for thyroid disorders[9].

In patients with normal pituitary function, an accurate inverse association between free FT4 and the logarithm of TSH can be calculated across the range of primary thyroid disorders. According to the logarithmic response in the concentration of TSH to variations in FT4 levels, TSH measurement gives a more accurate estimation of thyroid gland health than thyroid hormones measurement[10]. Reference range for TSH is 0.5-4.5mU/L[11]. The application of this reference normal range for thyroid function of all normal populations has been much discussed over the last 20 years[12]. The normal reference range for FT4 is 0.89-1.76ng/dL and FT3 is 2.3-4.2ng/dL[11]. Age influences T3, T4 and TSH concentrations. It has been observed that the tendency to develop auto-antibodies against the thyroid gland and its components are gradually increased with age, making people more prone to thyroid disorders. Higher incidences of thyroid disorders are observed in people exceeding 40yrs of age[13]. The variations in thyroid hormone levels have also been observed in different genders[14]. Asian women are involved in many activities and they have more domestic responsibilities, therefore malnutrition among poor and illiterate women and in their children are more prevalent. They are at high risk to develop goiter, anaemia and other disorders. The decrease in the concentration of thyroid hormones with age has been observed in both sexes, but the deprivation of thyroid hormone is more in women than men[15, 16]. The seasonal effect on T3, T4 and TSH has also been observed. T3 and T4 levels in autumn and winter were higher than in spring and summer[17]. In common clinical lab practices here in Pakistan, almost a single reference value of thyroid profile is applied for both genders, without the consideration of age and seasonal variations. This study was carried out to analyze age, gender and season related variations in thyroid profile in adults with normal thyroid functions, to provide sound data to a clinician to consider such factors when interpreting the thyroid profile results.

MATERIAL AND METHODS

Required data for this cross sectional study was obtained from Jan 2018 to Jan 2019 from Pathology Department, Quaid-e-Azam Medical College, Bahawalpur. During one year, a total of 1034 patients attended the pathology lab for the thyroid profile (TSH, FT3 and FT4) test. In this study, only data of those patients were collected whose TSH was within the normal reference range (0.5-4.5mU/L)[11]. We found the data of 418 subjects from 16 to 75 years of age, included 196 females and 222 males.

Inclusion Criteria

Data of all patients with TSH in the normal reference range (0.5-4.5mU/L) from Jan 2018 to Jan 2019 were included in this study.

Exclusion Criteria

The patients with hyper or hypothyroidism, those who were on medication for hyper or hypothyroidism, and those less than 16 years were excluded from the study.

Measurements

Acess2, Beckman Coulter, a sophisticated fully automated immunoassay analyzer was used for the measurement of thyroid function tests. Test results of thyroid profile (TSH, FT3 and FT4) of these subjects with age, sex and season were statistically analyzed to explore the age, gender, and seasonal variations. Four seasons were considered in one year cycle, winter from Dec to Feb, spring from March to

May, summer from June to Aug, and the autumn period from Sep to Nov. Therefore, to present the seasonal variations in thyroid profile, the obtained data were distributed into four seasons according to the date of test reports.

RESULTS

In our study, a total of 418 subjects was selected. The frequency distribution according to age and gender is given in Table **1**, and gender wise comparison of the thyroid is given in Table **2**.

Two sample t-test was used to compare TSH, FT3 and FT4 between male and female groups. TSH and FT4 levels were significantly different in both groups with a p-value <0.05. FT3 levels between both groups were not significantly different with a p-value >0.05. Age wise and seasonal variations were presented in charts. Variations in thyroid profile in males in different age groups were presented in Fig. **1**.

TSH levels were comparatively low in <20 years and high in >60 years of age. FT3 levels were high in 20 to 60 years of age, while FT4 levels were at a peak in <20 years of age group and were low in >60 years of age group. Variations in thyroid profile in a female with age groups were presented in Fig. **2**.

Table 1. Frequency Distribution According to Age and Gender.

Gender	<20 year	20-40	41-60	>60	Total
Males	38	48	65	71	222
Females	29	44	55	68	196

Table 2. Gender wise Compression of Thyroid Profile.

Gender	TSH (mU/L)	FT3 (ng/dL)	FT4 (ng/dL)
Male (222)	1.59 ± 1.2	2.4 ± 1.04	1.48 ± 0.48
Female (196)	2.11 ± 1.54	2.48 ± 0.8	1.33 ± 0.50
p- value	0.0002	0.3754	0.0018

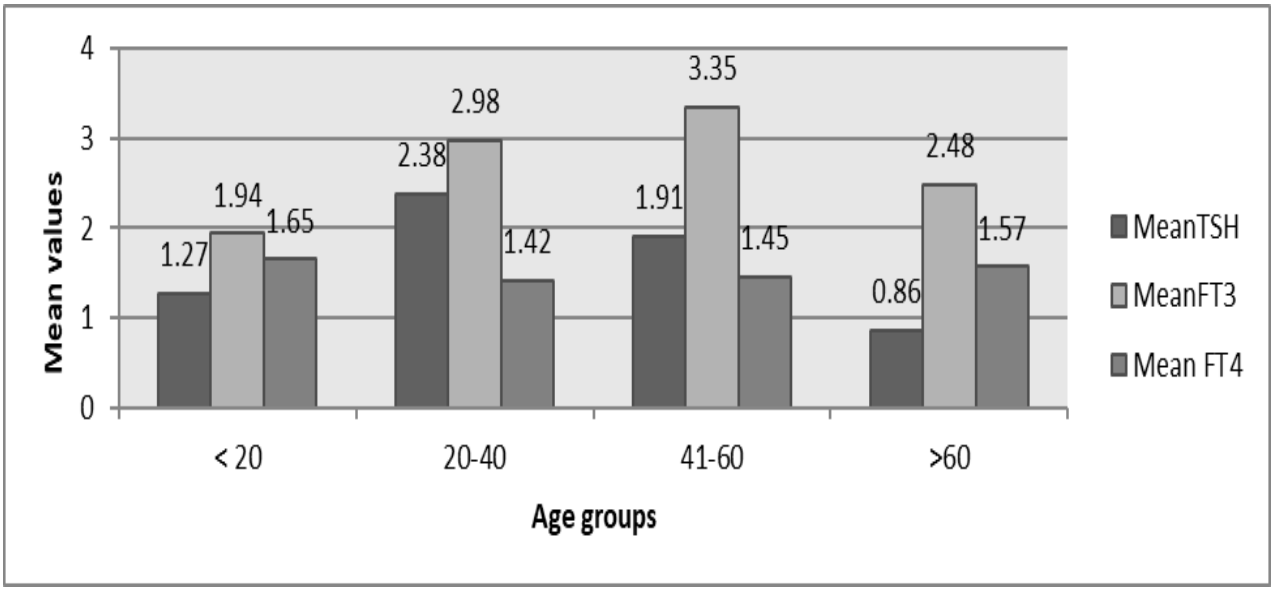

Figure 1. Variations in thyroid profile of males in different age groups.

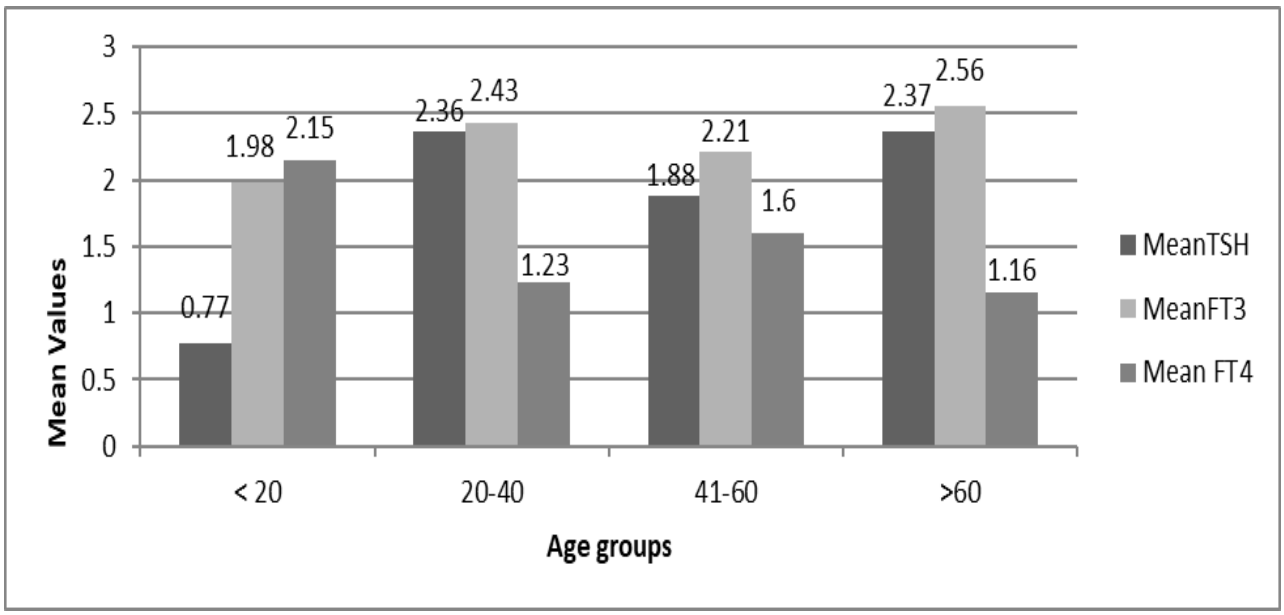

Figure 2. Variations in thyroid profile of females in different age groups.

In females, TSH levels were low in <20 years and high in >60 years age groups, while high levels were observed in 20 to 60 years of age. The highest FT3 levels were seen in the>60 years of age group while there was little difference in other age groups. FT4 mean levels in the <20 year age group were significantly high. We observed a negative relationship between TSH and FT4 in all groups of both genders. Seasonal variations in all participants were presented in Fig. **3**.

Subjects were divided into four groups according to the date of test result reports. TSH mean value was high in winters and low in the summer season. FT3 levels were also high in winters and comparatively low in autumn. FT4 levels in all four seasons were slightly different with considerably low levels in winters.

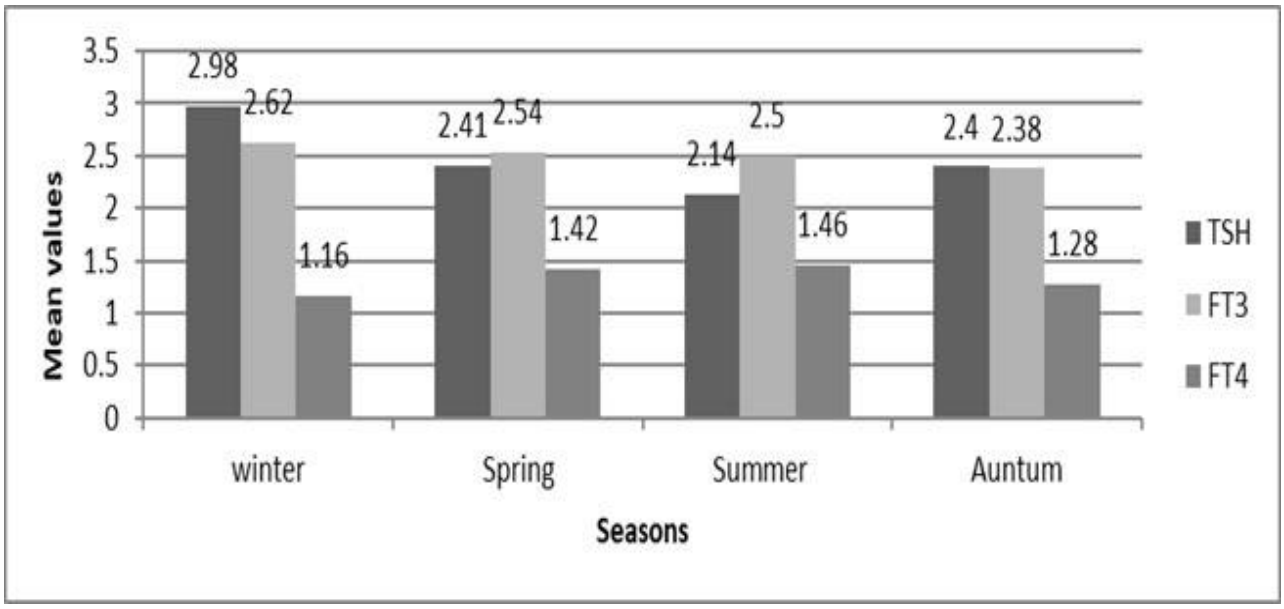

Figure 3. Seasonal variations in thyroid profile.

DISCUSSION

Iodine deficiency disorders (IDDs) are commonly prevalent in developed and less-developed countries[18]. Pakistan has overcome this problem to some extent but still, there are some areas, where the IDDs are present with high frequency. We need some serious steps to improve IDD control program[19]. Iodine deficiency is the main cause of hypothyroidism in both genders as well as in children and elderly people[20]. Thyroid functions are decreased with the increase of age[17]. The present study was conducted to explore the effect of age, gender, and season on thyroid profile. Gender wise comparison of thyroid profile (Table **2**) suggests that TSH levels were significantly higher in females than the males, and FT4 levels were higher in males as compared to females. FT3 in both genders was not statistically different with a p-value of 0.375. Our study presented the picture of slightly decreased thyroid functions in females, similar findings about the variations in thyroid hormone in two sexes were in accordance with previous work by Razzak *et al*[21] and Chaurasia *et al.* 2011[22]. There is already evidence for the decrease of thyroid functions during menstrual abnormalities. Elevated TSH level in one of eight females during child bearing age, high prevalence of hypothyroidism that is 4.8% in females, and higher tendency towards primary hypothyroidism of females with the increase of age support our findings[23-25]. Some other studies also are in favor of our high FT4 results in males, according to the findings of these studies, male sex hormones increases the level of Thyroxin Binding Globulin (TBG), which leads to increase in level of T4[17, 22]. Age-related variations were given in Fig. **1** for the male group and Fig. **2** for females. In <20 years age group of both genders, TSH level was comparatively low, whereas FT4 was higher than all other age groups of both genders except >60 year age group of males, where TSH was low. A study carried out in India during 2011 also reflects similar findings of>60 years male group[22]. In females of >60 years of age group, the TSH level was significantly high with low FT4, which indicates a decrease in the thyroid functions of females after menopause and with an increase of age[26] as well as a high prevalence of subclinical and overt hypothyroidism in females of advance age[27].

Seasonal variations in the concentration of TSH, T3 and T4 is given in Fig. **3**, which presents a higher level of TSH in winters than in summers, while T3 is nearly similar in all seasons but slightly higher in winters and slightly lower in autumn. T4 is similar in all seasons but slightly lower in winters and slightly high in summers. Summer and winter results are comparable with the findings of Chaurasia *et al.* 2011[22] and are in accordance with a study done by Khan *et al.* 2001[28]. The season in which thyroid tests were performed was independently related to the transition from euthyroid status to subclinical hypothyroid status. Seasonal variations in TSH concentration should be taken into account before deciding on treatment for subclinical hypothyroidism, especially in areas with a wide range of annual temperatures[29]. The climatic components contributed to the slight variance in hormone levels during the different seasons and the effect was mainly on the peripheral conversion of FT4 to FT3, rather than on the pituitary-thyroid axis, leading to slightly more FT3 high in winters[30]. Seasonal changes in TSH occurred independently of the changes in peripheral thyroid hormone, gender, age, and environmental temperatures. The underlying physiological mechanism remain uncertain and specific studies are necessary to clarify its impacting role in humans[31].

Serum-free T3 was significantly correlated with the previous month's average outside temperature. Serum TSH did not show any correlation with the average temperature of the month or with free T3. A low level of free T3 serum in winters suggests that the elimination of thyroid hormones is accelerated by the cold, as described in Polar T3 syndrome. Elevations in serum TSH are not taken into account by changes in circulating thyroid hormones, suggesting that other influences, such as photoperiod may mediate this fluctuation[32].

CONCLUSION

From our study, it is concluded that gender, age, and seasons have a significant effect on thyroid profile, and females have high TSH levels as a whole, especially >60 years of age, while TSH is high in both genders during winters. These factors should be observed while interpreting the lab results of the thyroid profile.

CONFLICTS OF INTEREST

None.

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LIST OF ABBREVIATIONS

FT3	Free T3
FT4	Free T4
T3	Triiodothyronine
T4	Thyroxin
TSH	Thyroid Stimulating Hormone
TRH	Thyroid Releasing Hormone

REFERENCES

1. Franjic S. In shortly about thyroid gland. Clin Surg. 2021; 4(9):1-5.
2. Silva JF, Ocarino NM, Serakides R. Thyroid hormones and female reproduction. Biol Reprod. 2018; 99(5):907-21.
3. Wejaphikul K, Groeneweg S, Hilhorst-Hofstee Y, Chatterjee VK, Peeters RP, Meima ME, *et al*. Insight into molecular determinants of T3 vs T4 recognition from mutations in thyroid hormone receptor alpha and beta. J Clin Endocrinol Metab. 2019; 104(8):3491-500.
4. Roef GL, Rietzschel ER, Van Daele CM, Taes YE, De Buyzere ML, Gillebert TC, *et al*. Triiodothyronine and free thyroxine levels are differentially associated with metabolic profile and adiposity-related cardiovascular risk markers in euthyroid middle-aged subjects. J Thyroid Res. 2014; 24(2):223-31.
5. Ettleson MD, Bianco AC. Individualized therapy for hypothyroidism: is T4 enough for everyone?. J Clin Endocrinol Metab. 2020; 105(9): 3090-104.
6. Ahmed RG. Non-genomic actions of thyroid hormones during development. App Clin Pharmacol Toxicol: 2018;10-18.
7. Soundarrajan M, Kopp PA. Thyroid Hormone Biosynthesis and Physiology. Thyroid Dis Reprod. 2019; 1-17.
8. Nillni EA. Regulation of the hypothalamic thyrotropin releasing hormone (TRH) neuron by neuronal and peripheral inputs. Front Neuroendocrinol. 2010; 31(2):134-56.
9. Soldin OP, Chung SH, Colie C. The use of TSH in determining thyroid disease: How does it impact the practice of medicine in pregnancy? J Thyroid Res. 2013; 22-31.
10. Stockigt J. Assessment of thyroid function: Towards an integrated laboratory-clinical approach. Clin Biochem Rev. 2003; 24(4):109-16.
11. Lewandowski K, editor Reference ranges for TSH and thyroid hormones. J Thyroid Res. 2015; 8(1):1-3.
12. Sheehan MT. Biochemical testing of the thyroid: TSH is the best and, oftentimes, only test needed–a review for primary care. Clin Med Res. 2016; 14(2):83-92.
13. Franco J-S, Amaya-Amaya J, Anaya J-M. Thyroid disease and autoimmune diseases. Autoimmunity: From Bench to Bedside: El Rosario University Press; 2013; 18-27.
14. Lamichhane TR, Pant SP, Lamichhane B, Gautam C, Paudel S, Yadav BK, *et al*. Age-and gender-Specific changes in thyroid size and thyroid function test values of euthyroid subjects. JBSM. 2018; 6(11):59-73.
15. Rakov H, Engels K, Hönes GS, Brix K, Köhrle J, Moeller LC, *et al*. Sex-specific phenotypes of hyperthyroidism and hypothyroidism in aged mice. Biol Sex Differ. 2017; 8(1):1-10.
16. Fox EL, Davis C, Downs SM, Schultink W, Fanzo J. Who is the Woman in Women's Nutrition? A Narrative Review of Evidence and Actions to Support Women's Nutrition throughout Life. CDN. 2019; 3(1):76-84.
17. Dabla PK, Sharma S, Sinha N. Effect of age, gender and season on thyroid hormones status in children of east delhi-a hospital based study. Front Endocrinol. Clin Chem Lab Med. 2018; 54-63.
18. Lazarus J. Iodine status in europe in 2014. Eur Thyroid J. 2014; 3(1):3-6.
19. Khattak RM, Khattak MNK, Ittermann T, Völzke H. Factors affecting sustainable iodine deficiency elimination in Pakistan: A global perspective. Int J Epidemiol. 2017; 27(6):249-57.
20. Chung HR. Iodine and thyroid function. Ann Pediatr Endocrinol Metab. 2014; 19(1):8-12.
21. Abdel R. Effect of age and sex on thyroid function tests. Establishment of norms for the Egyptian population. Develop Radioimmunoassay Related Pro. 1992; 353-8.

22. Chaurasia P, Modi B, Mangukiya S, Jadav P, Shah R. Variation in thyroid hormones level among people of different age, gender and seasons, Piparia, Gujarat. J Int Med Res. 2011; 1(2):57-9.
23. Velayutham K, Selvan SSA, Unnikrishnan A. Prevalence of thyroid dysfunction among young females in a South Indian population. Indian J Endocrinol Metab. 2015; 19(6):781-84
24. Li X, Meng Z, Tan J, Liu M, Jia Q, Zhang G, *et al*. Gender impact on the correlation between thyroid function and serum lipids in patients with differentiated thyroid cancer. Exp Ther Med. 2016; 12(5):2873-80.
25. Meng Z, Liu M, Zhang Q, Liu L, Song K, Tan J, *et al*. Gender and age impacts on the association between thyroid function and metabolic syndrome in Chinese. Med. 2015; (94):50-8.
26. Suzuki S, Nishio S-i, Takeda T, Komatsu M. Gender-specific regulation of response to thyroid hormone in aging. J Thyroid Res. 2012; 5(1):1-8.
27. Al Eidan E, Ur Rahman S, Al Qahtani S, Al Farhan AI, Abdulmajeed I. Prevalence of subclinical hypothyroidism in adults visiting primary health-care setting in Riyadh. J Community Hosp Intern Med Perspect. 2018; 8(1):11-5.
28. Khan A, Akhter S, Siddiqui MM, Khan MMA, Nawab G. Effect of age, sex and seasons on the concentration of thyroid and thyroid stimulating hormones. Res J Med Sci. 2001; 1(4):224-37.
29. Kim TH, Kim KW, Ahn HY, Choi HS, Won H, Choi Y, *et al*. Effect of seasonal changes on the transition between subclinical hypothyroid and euthyroid status. J Clin Endocrinol Metab. 2013; 98(8):3420-29.
30. Mahwi TO, Abdulateef DS. Relation of different components of climate with human pituitary-thyroid axis and FT3/FT4 ratio: A study on euthyroid and SCH subjects in two different seasons. Int J Endocrinol. 2019; 12-21.
31. Santi D, Spaggiari G, Brigante G, Setti M, Tagliavini S, Trenti T, *et al*. Semi-annual seasonal pattern of serum thyrotropin in adults. Sci Rep. 2019; 9(1):1-7.
32. Leppäluoto J, Sikkilä K, Hassi J. Seasonal variation of serum TSH and thyroid hormones in males living in subarctic environmental conditions. Int J Circumpolar Health. 1998; 57:383-5.