

Age- and Gender-Specific Changes in Thyroid Size and Thyroid Function Test Values of Euthyroid Subjects

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Abstract

Background: The thyroid status is evaluated by two clinical diagnostic tests which are thyroid ultrasonography and thyroid function tests. The objective of this research is to critically analyze the age and gender based variations of thyroid volume and thyroid hormone levels in the hospital based euthyroid subjects. **Methodology:** A total of 221 euthyroid subjects aged 1 - 86 years were selected to observe the normal thyroid size by ultrasonography at Department of Radiology and the thyroid function test values (FT3, FT4 and TSH) of 2413 euthyroid subjects aged (<1)-93 years were observed at Department of Biochemistry, Tribhuvan University Teaching Hospital, Kathmandu, Nepal during January 2017 to February 2018. The observed data were analyzed graphically and statistically to check the cross-correlations among the variables. **Results:** The best fitted equations with significant correlation coefficients and $p < 0.05$ provide the empirical relations between any two of the observed variables: age, thyroid lobe volumes, FT3, FT4 and TSH. The mean \pm SD ($p < 0.0001$) of thyroid volume, FT3, FT4 and TSH are 4.74 ± 2.30 mL, 5.46 ± 0.82 pmol/L, 14.09 ± 2.71 pmol/L and 2.30 ± 0.98 mIU/L, respectively. **Conclusion:** The thyroid size first increases and then decreases whereas the thyroxin level first decreases and then increases with aging. Left lobe volume is almost same for both genders and right lobe volume is higher in males. The thyroid size in menarche and menopause periods of females is larger than that of males. Such age- and gender-specific changes recommend the new reference ranges for the normal thyroid functions.

Keywords

Euthyroid Subject, Thyroid Function Test, Thyroid Hormone Levels, Thyroid

1. Introduction

Thyroid hormones (TH) play the important role in the development and the maintenance of homeostasis through the interactions with autonomic nervous system and the regulations of cardiovascular and metabolic functions [1] [2]. The disorders seen in thyroid hormone regulations during embryonal and early postnatal stages can persist into adulthood also. Thyroid stimulating hormone (TSH) is an important marker to diagnose thyroid status clinically. Many studies related to the age and gender based variations of serum free thyroid hormones (TH: FT3 and FT4) and TSH have uncertainties [3] [4] [5]. As reported in [3] [5], TSH distributes in higher concentration with aging regardless the status of thyroid antibodies and the increased TSH makes impact on lipid profile influenced by age in both genders. There is log-linear relationship among FT3, FT4 and TSH based on age- and gender-specific responses [6].

The routine assessment of thyroid status basically relies on ultrasonographic (USG) examinations and thyroid function tests (TFT) determining the serum concentrations of FT3, FT4 and TSH. More precise and accurate parameters are to be prescribed in defining a patient's thyroid status. There is a regional influence of iodine supply on establishing the reference ranges for the normal thyroid functioning [7]. Even a mild alteration in thyroid functioning causes psychiatric problem, weight gain or loss, atrial fibrillation and osteoporosis [8]. So, the thyroid clinical diagnosis seems to be historically sensitive. The biologically active life stages of females make differences in studying the working mechanism of their endocrine system. The thyroid function test report as well as thyroid size normally changes in menarche, pregnancy and menopause periods. More critically saying that the differential genetic mechanisms are potentially associated with the thyroid function regulation in both genders. In euthyroid subjects, the TFT values lie within a narrow range suggesting a unique hypothalamus-pituitary-thyroid (HPT) axis working under the controlled way by negative feedback mechanism of thyroid cycle for each individual.

Iodine deficiency is still present in mild levels in Nepal leading to the prevalence of subclinical hypothyroidism in all age groups of both genders. The nutritional iodine intake makes changes on thyroid hormone levels in the blood stream, then on TSH production and even on thyroid size. The neonatal thyroid is sensitive to maternal iodine intake and its impact can persist lifelong. Age, gender, body mass index, living status, thinking and feeding habits, genetics, environmental factors, and non-thyroid illness and associated medications influence normal thyroid status [9] [10]. A number of earlier studies [11] [12] [13] [14] [15] have analyzed factors that affect thyroid size and they have also reported the reference intervals for the normal thyroid volume with different un-

certainties.

There are seasonal and diurnal as well as nocturnal variations of TH-levels even in normal thyroid conditions. The serum free T3 decreases in winter season due to the accelerating disposal of thyroid hormones in cold described as the polar T3 syndrome [16]. Without any change observed in thyroid status, about 20% variation in TSH level is found [17]. The reference levels of TSH, FT3 and FT4 are slightly varying for the different constrained groups of healthy people as reported in [4] [18] [19] [20]. In a hospital based study performed at central Nepal, out of 5230 subjects ranging from early infant to elderly age, 71% of them have euthyroidism with serum FT3 = 2.3 ± 0.6 pg/mL, FT4 = 11.5 ± 2.0 pg/mL and TSH = 2.3 ± 1.1 mIU/L [20]. In another hospital based study performed in hilly region of Nepal, 76.7% of 3136 subjects have clinically diagnosed euthyroidism [21]. In the studies of age-based variations of serum FT4 in normal thyroid subjects, its concentration trends to decrease slightly with aging having the smaller values for males than for females in younger age below 60 years [4] [22] [23] [24]. As the functioning of thyroid gland is influenced by secretion and regulation of TSH, T3 and T4 hormones, our study is designed to analyze the correlation between thyroid gland volume and TFT values of euthyroid subjects along with age and gender based variations.

2. Materials and Methods

The thyroid USG of hospital based euthyroid subjects was performed at the Department of Radiology and the TFT values were observed at the Department of Biochemistry, Tribhuvan University Teaching Hospital (TUTH), Kathmandu, Nepal during January 2017 to February 2018. This study was carried out by the informed consent under the guidelines of and taking authority from the Institutional Review Board (IRB), TUTH.

A total of 90 males and 131 females aged 1 - 86 years were selected as euthyroid subjects after the USG observations. The USG machine, SAMSUNG UGEO H60 with 7.5 MHz linear transducer was used in brightness mode (B-mode) to produce good quality image by adjusting actual frequency of ultrasound, emission time, sonation angle, size and curvature of the transducer and by minimizing effects of reverberation, enhancement, edge and mirror artifacts [25] [26] [27]. The included subjects were examined in the supine position with the neck hyperextended and transverse as well as longitudinal sections of thyroid lobes were scanned to measure the appropriate volumes and to confirm the normal status of the thyroid gland. The subjects having abnormal thyroid with nodules, vascularity, thyroiditis, hyper- and hypoechogenicity, and heterogeneous extextures were excluded in this study. The thyroid volume was obtained by using ellipsoid formula ($V = \text{length} \times \text{width} \times \text{thickness} \times 0.52$) for each lobe [12] [13] [14]. Multiple USG measurements were done in case of imaging problems due to the body composition differences such as short neck, and kyphosis. Age, sex, family history of thyroid problems, demographic locations, thinking, sleeping

and feeding habits, and USG results: antero posterior length, craniocaudal length and width or transverse and mediolateral length, echogenicity, and disease related findings of both thyroid lobes of all individuals were recorded in the pre-designed data collection sheet for further analysis.

The TFT values of 2413 clinically euthyroid subjects including 1748 females and 665 males of early infant age (<1 years) to elderly age (93 years) were observed to analyze the normal levels of serum free T3, T4 and TSH varying with age and sex. About 2 - 3 mL blood sample was taken from antecubital vein in a plain vial. The sample was allowed to clot and then it was centrifuged at 4000 rpm for 10 minutes to separate serum. The measurements of FT3, FT4 and TSH were done using the technique of enhanced chemiluminescence immunoassay (ECI) [28] [29] with Vitros 3600 machine. The normal reference ranges of TFT values used at the laboratory were 4.26 - 8.10 pmol/L for FT3, 10.20 - 28.20 pmol/L for FT4 and 0.46 - 4.68 mIU/L for TSH.

The statistical as well as graphical analysis was performed among the age and gender based variables such as thyroid lobe volumes, FT3, FT4 and TSH using the softwares: Origin-2017 and MS Excel-2007. The standard deviations and/or standard errors were calculated in each of the mean values. The possible linear and second order polynomials were fitted providing the related equations with standard errors in their coefficients. The degrees of correlation among the variables were evaluated with Pearson's correlation test and the results with $p < 0.05$ were accepted as statistically significant.

3. Results and Discussion

The results from observed data and analysis are classified into three categories: ultrasonographic (USG) results, thyroid function test (TFT) results and USG & TFT cross-sectional analysis of the hospital based euthyroid subjects to explain the possible correlations among the variables such as age, thyroid lobe volumes, FT3, FT4 and TSH of males and females.

3.1. Thyroid Ultrasonographic Results

From the USG reports of euthyroid subjects having mean age 32 ± 17.18 years ranging 1 to 86 years, the mean \pm SD of left lobe volume (LLV), right lobe volume (RLV) and thyroid gland volume (TGV) are 2.12 ± 1.07 mL, 2.61 ± 1.40 mL and 4.74 ± 2.30 mL, respectively with $p < 0.0001$. Here, RLV has been found to be greater than LLV. The results with the range of normal thyroid size are listed in **Table 1**. The graph (**Figure 1(a)**) for $y(\text{TGV})$ vs. $x(\text{age})$ of the people satisfies the trendline of second order polynomial with $R^2 = 0.197$ whose equation is

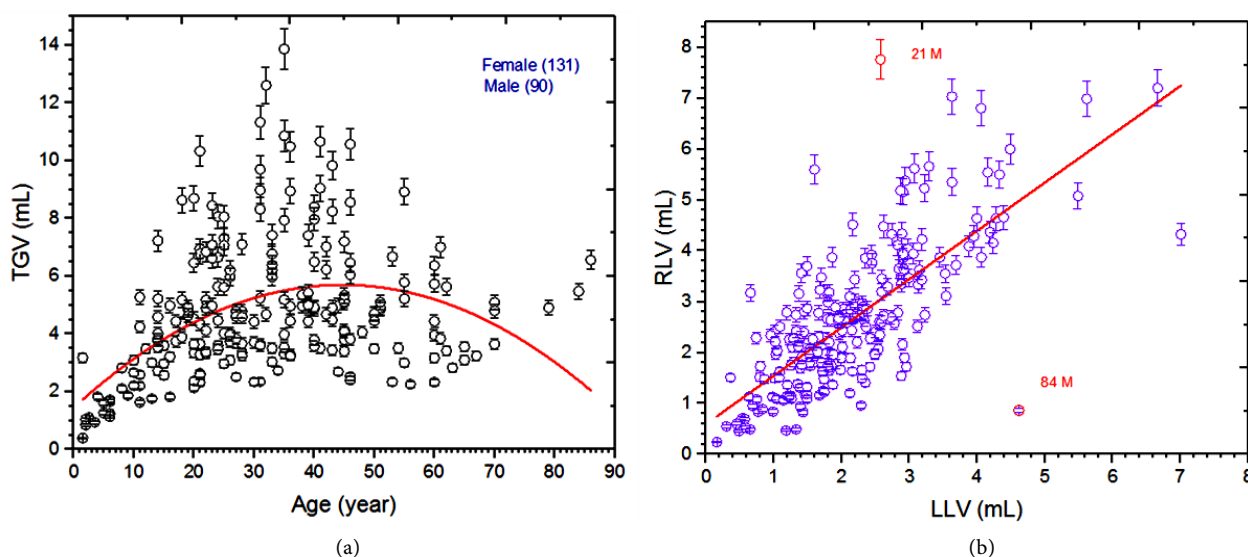
$$y = (-0.002 \pm 0.0004)x^2 + (0.19 \pm 0.03)x + (1.45 \pm 0.47) \quad (1)$$

where the included errors indicate the standard errors in the related coefficients.

The volume of normal thyroid gland is greater for adults than for early pubertal

Table 1. Normal thyroid size ($p < 0.0001$) of the euthyroid subjects.

Variables	Age (yr)	LLV (mL)	RLV (mL)	TGV (mL)
Mean	32.02	2.12	2.61	4.74
SE	1.16	0.07	0.09	0.15
SD	17.18	1.07	1.40	2.30
Min.	1.50	0.16	0.24	0.40
Max.	86.00	7.01	7.76	13.87

**Figure 1.** (a) Thyroid size with aging, and (b) positive correlation between right lobe and left lobe volumes. The error-bars indicate 5% of the measured value.

and elderly which is in agreement with the results in [13] [14] [30]. However, the mean thyroid volume excluding isthmus in our study is found to be smaller for both genders than that reported by [13] [14] [30]. Seker *et al.* (2010) reported the mean thyroid volume as 13.00 ± 6.27 mL for the age range of 15 - 78 years [30]. Our result for the normal thyroid size is still smaller than 6.63 ± 2.50 mL as studied by Kayastha *et al.* (2010) for the age range of 1-83 years [10].

There is a linear correlation between LLV and RLV as demonstrated in **Figure 1(b)**. The equation of linear fit with Pearson's $r = 0.727$ and $p < 0.001$ for $y(\text{LLV})$ vs. $x(\text{RLV})$ is

$$y = (0.95 \pm 0.06)x + (0.60 \pm 0.14) \quad (2)$$

This means that RLV can be estimated by knowing LLV.

Taking average values ($p < 0.05$) for both genders from **Table 2**, the thyroid size is maximum, *i.e.* 6.09 ± 2.78 mL in the age group of 31 - 40 years. Its value is the least, *i.e.* 1.73 ± 0.17 mL in the childhood range of 1 - 10 years. This variation of thyroid size is due to the various reasons including the change in body mass index and body surface area. If we analyze the gender based variations of thyroid volume, it is maximum, *i.e.* 7.84 ± 3.18 mL for males in the age group of 31 - 40

years and 5.62 ± 2.49 mL for females in the age group of 41 - 50 years as depicted in **Table 2** and compared by the column plots in **Figure 2(a)**. Here, the thyroid volume is greater for females than for males in the age groups of 11 - 20 and 41 - 50 years and otherwise, it is greater for males. It is to be noted that the age groups of 11 - 20 and 41 - 50 years for females include the periods of menarche and menopause respectively. The thyroid of healthy Nepalese people has smaller size in both genders than that reported in [30] [31]. Seker *et al.* (2010) reported the mean thyroid volume as 15.87 ± 7.18 mL for males and 10.94 ± 4.53 mL for females [30]. In the study of 500 healthy adults performed by Oberhofer *et al.* (1989), the mean TGV of males is 14.94 mL and that of females is 12.09 mL [31]. The main cause behind such variation of thyroid size is the demographic status of subjects under study.

In this study, the mean \pm SD ($p < 0.0001$) of LLV and RLV are 2.12 ± 0.98 mL and 2.54 ± 1.29 mL, respectively for females aged 33.46 ± 15.10 years. Similarly, for males of age 29.92 ± 19.72 years, LLV is 2.13 ± 1.20 mL and RLV is 2.73 ± 1.55 mL. The gender based minimum and maximum range of the thyroid lobe volumes with the standard errors are listed in **Table 3**. The variations of LLV

Table 2. Normal thyroid size ($p < 0.05$) averaged over different age groups.

Age (yr)	Female			Male		
	TGV (mL)	SE	N	TGV (mL)	SE	N
01 - 10	1.53	0.22	8	1.86	0.25	12
11 - 20	4.27	0.43	17	3.88	0.35	21
21 - 30	4.41	0.23	32	5.54	0.52	20
31 - 40	5.31	0.40	31	7.84	0.85	14
41 - 50	5.62	0.48	27	4.74	0.19	7
51 - 60	4.40	0.73	9	4.91	0.41	9
61 - 90	4.09	0.42	7	4.93	0.56	7

Table 3. Normal ranges of thyroid lobe volumes ($p < 0.0001$) in males and females.

Gender	Values	Age (yr)	LLV (mL)	RLV (mL)	TGV (mL)
Female	Mean	33.46	2.12	2.54	4.66
	SE	1.32	0.09	0.11	0.19
	SD	15.10	0.98	1.29	2.12
	Min.	1.50	0.16	0.24	0.40
	Max.	79.00	5.62	7.03	12.61
Male	Mean	29.92	2.13	2.73	4.85
	SE	2.08	0.13	0.16	0.27
	SD	19.72	1.20	1.55	2.56
	Min.	1.50	0.30	0.49	0.85
	Max.	86.00	7.01	7.76	13.87

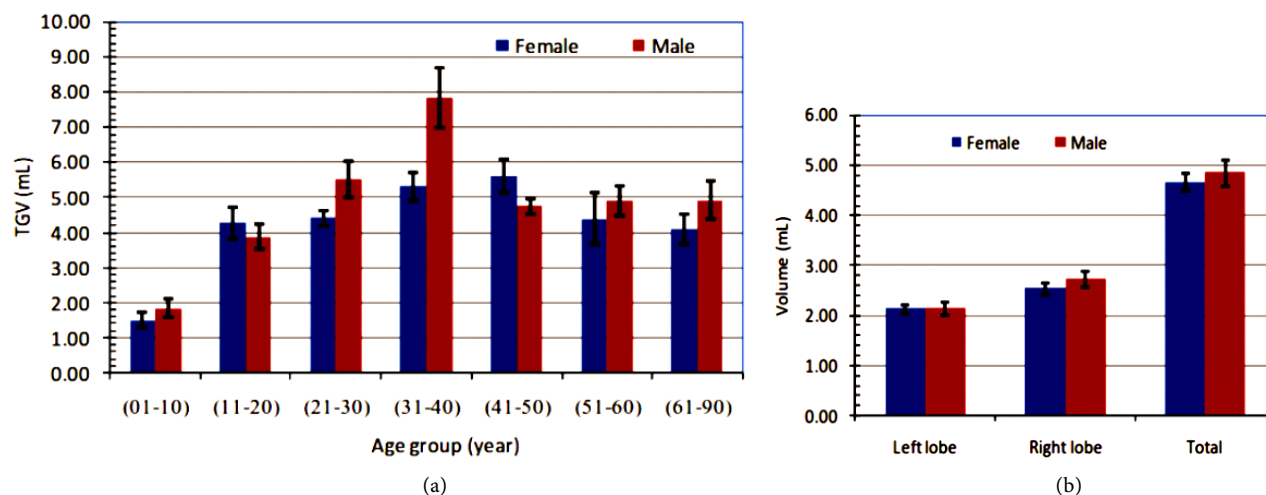


Figure 2. (a) Normal thyroid size related to the gender based age groups including standard error bars, and (b) gender-specific changes in the normal thyroid size with the standard error bars.

and RLV are shown by the column plots in **Figure 2(b)**. Here, LLV is almost same for both genders whereas RLV is higher for males than for females. In general, RLV is greater than LLV. The right handed subjects have significantly larger volume of right thyroid lobe as explained by Ying *et al.* (2009) [32]. Lewinisky *et al.* (1982) and Gerendai *et al.* (2001) suggest that there is unilateral differentiation of hypothalamus to enlarge the right lobe of thyroid gland [33] [34].

3.2. Thyroid Function Test Results

From the TFT reports of 1737 female and 634 male euthyroid subjects aged 1 - 93 years, the mean values with the standard deviations ($p < 0.0001$) of serum TSH, FT4 and FT3 are observed to be 2.30 ± 0.98 mIU/L, 14.09 ± 2.71 pmol/L and 5.46 ± 0.82 pmol/L respectively. The observed ranges of normal TFT values are listed in **Table 4**. These results are not much deviated from the TFT values of euthyroid subjects reported in Mahato *et al.* (2015) [20]. However, the mean value of FT4 in this study is less than that in Rohil *et al.* (2010) [35]. To analyze the correlations of FT3 with FT4 and that of FT3 or FT4 with TSH, the linear fits of the corresponding data are performed as shown in **Figure 3**. Here, the linear equation of the best fit between y_1 (FT3) and x_1 (FT4) with Pearson's $r = 0.095$, p -value < 0.001 and the standard errors in the slope and intercept (**Figure 3(a)**) is

$$y_1 = (0.03 \pm 0.006)x_1 + (5.05 \pm 0.088) \quad (3)$$

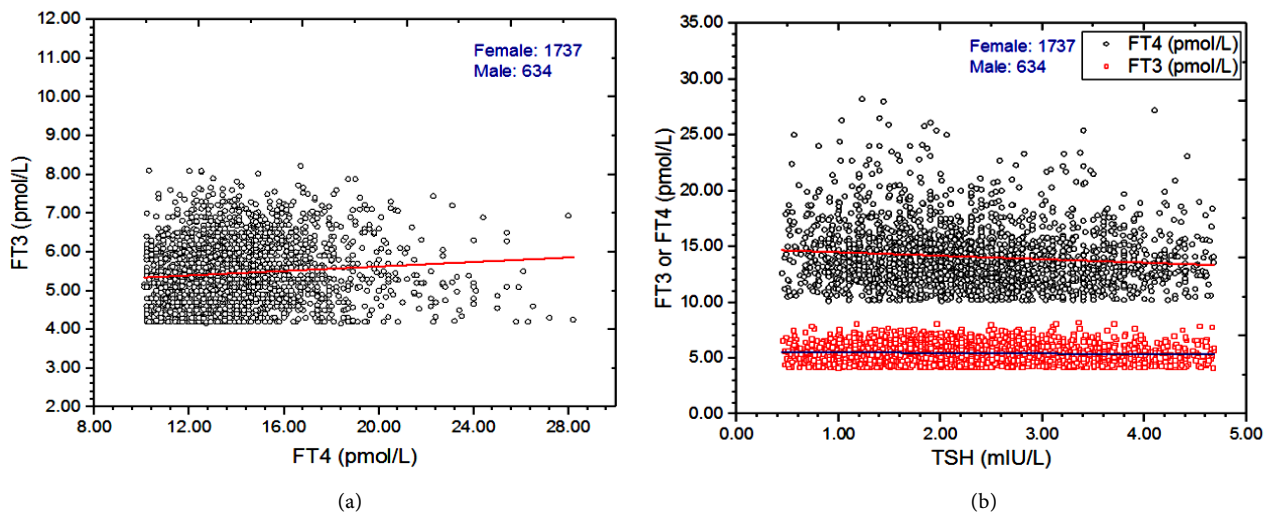
Also, the linear fit between y_2 (FT3) and x_2 (TSH) shown in **Figure 3(b)** obtains the equation of a straight line (3) with the standard errors in slope and intercept, Pearson's $r = -0.061$ and p -value < 0.001 .

$$y_2 = (-0.05 \pm 0.017)x_2 + (5.58 \pm 0.04) \quad (4)$$

Similarly, the equation of linear fit between y_3 (FT4) and x_3 (TSH) as in **Figure 3(b)** with Pearson's $r = -0.113$ and p -value = 0.002 is

Table 4. TFT values ($p < 0.0001$) of the clinically euthyroid subjects.

Variables	TSH (mIU/L)	FT4 (pmol/L)	FT3 (pmol/L)
Mean	2.30	14.09	5.46
SE	0.02	0.06	0.02
SD	0.98	2.71	0.82
Min.	0.46	10.20	4.26
Max.	4.68	28.20	8.10

**Figure 3.** Linear correlations between (a) FT3 & FT4 and (b) FT3 or FT4 & TSH of the euthyroid subjects.

$$y_3 = (-0.31 \pm 0.056)x_3 + (14.81 \pm 0.14) \quad (5)$$

There is a positive correlation between FT3 & FT4 whereas negative correlations between FT3 or FT4 & TSH. This signifies that T3 and T4 are fed back to hypothalamus and pituitary through the blood stream and under the controlled mechanism on HPT-axis, T3 and T4 are produced by thyroid gland. Finally, the thyroid cycle completes under with the regulation of thyroid hormones.

In the infant age (<1 years), TSH, FT3 and FT4 all are higher than in the adults. The serum free TH levels are observed to be decreased and then increased slowly in advancing from child to adult and then to elderly age for both genders (**Figure 4**). However, TSH is the highest, *i.e.* 2.57 ± 0.89 pmol/L in the early childhood < 1 years and it is the lowest, *i.e.* 2.05 ± 0.93 pmol/L ($p < 0.0001$) in the elderly of 71 - 100 years. If we analyze the results depicted in **Table 5** & **Table 6**, we see the almost negative correlations between FT3 or FT4 and TSH along each age group of male as well as female adults. This is the fact behind negative feedback mechanism of thyroid hormones in the thyroid cycle. In many researches [22] [23] [24], serum FT4 is observed to be low in the middle age subjects. Fontes *et al.* (2013) reported that TSH increases and conversely, FT4 decreases with aging [22]. In a study performed by Chaurasia *et al.* (2011) at

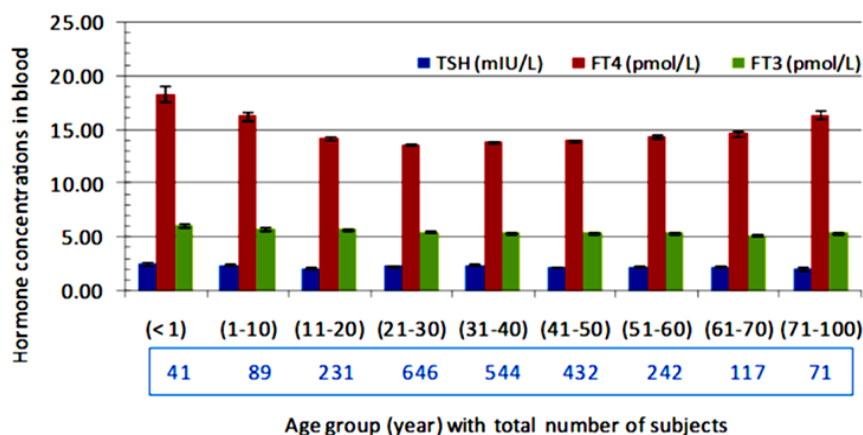


Figure 4. Age-specific changes in the normal TFT values with the standard error bars.

Table 5. TFT values averaged in the different age groups of 1748 female euthyroid subjects.

	Age (yr)	(<1)	(1 - 10)	(11 - 20)	(21 - 30)	(31 - 40)	(41 - 50)	(51 - 60)	(61 - 70)	(71 - 80)	(81 - 100)
TSH (mIU/L)	Mean	2.58	2.30	2.11	2.34	2.50	2.29	2.35	2.31	2.12	2.55
	SD	0.91	0.89	1.00	0.94	0.92	0.95	1.07	1.21	0.88	1.32
FT4 (pmol/L)	Mean	19.87	16.73	13.99	13.49	13.76	13.98	14.50	14.58	16.75	17.90
	SD	5.63	2.82	2.74	2.13	2.49	2.42	2.65	2.49	3.84	4.15
FT3 (pmol/L)	Mean	5.59	5.65*	5.62	5.46	5.32	5.33	5.40	5.04	5.19	5.64
	SD	1.13	0.95	0.80	0.81	0.80	0.76	0.81	0.68	0.83	0.94
	N	11	39	162	511	408	332	175	72	31	7

*The ANOVA-single factor $p < 0.0001$ for all of the TFT values averaged over the age groups except for FT3 = 5.67 ± 0.95 ($p = 0.57$) in the age group 1 - 10 years.

Table 6. TFT values averaged in the different age groups of 665 male euthyroid subjects.

	Age (yr)	(<1)	(1 - 10)	(11 - 20)	(21 - 30)	(31 - 40)	(41 - 50)	(51 - 60)	(61 - 70)	(71 - 80)	(81 - 100)
TSH (mIU/L)	Mean	2.56	2.56	2.11	2.22	2.28	2.03	2.12	2.15	1.88	1.88
	SD	0.88	1.17	0.91	0.97	0.91	0.90	1.05	1.30	0.92	0.74
FT4 (pmol/L)	Mean	17.78	15.91	14.81	13.90	14.02	14.10	14.19	14.69	15.14	17.46
	SD	4.03	3.84	3.47	2.58	2.88	2.70	3.12	3.86	2.93	3.71
FT3 (pmol/L)	Mean	6.20	5.88*	5.96	5.69	5.54	5.64	5.45	5.41	5.36	6.07
	SD	0.94	1.01	0.87	0.79	0.80	0.82	0.84	0.77	0.77	0.92
	N	30	50	69	135	136	100	67	45	26	7

*The ANOVA-single factor $p < 0.0001$ for all of the TFT values averaged over the age groups except for FT3 = 5.88 ± 1.01 ($p = 0.86$) in the age group 1 - 10 years.

Gujarat, India, T4 levels are found to be lower in 20 - 40 years than other age groups [23]. Lipson *et al.* 1979 interprets that TSH has significant positive correlation and T3 has weak negative correlation with aging of the euthyroid adults [24]. The variation of TH levels with aging is associated with brain development, autonomous tissues, nutritional status, gender based biological activities and en-

vironmental factors.

The age and gender based variations of TFT reports are depicted in **Table 5** & **Table 6** where the concentrations of the serum free TH remain almost same from 11 to 60 years in both male and female euthyroid subjects. If we draw the column plots of age dependent TH levels separately for the both genders, they follow almost same pattern as in the given **Figure 4**. The pattern of change in TSH is more distinct which is 2.34 ± 1.1 mIU/L for males and 1.88 ± 0.81 mIU/L for females in the age > 71 years than in other age groups. In the infant age group < 1 years, TSH as well as T3/T4 are higher in both genders. According to Franklyn *et al.* (1985), the age based changes in serum free TH are not much evident but FT3 is lower in females than in males aged 16 - 29 years [36]. In the study of Sujuky *et al.* (2012), FT3 or FT4 has negative correlation with aging of males, but no correlation in females, and TSH increases with aging in both genders [6].

3.3. USG and TFT Cross-Sectional Analysis

In a cross-sectional study of USG and TFT values of 34 euthyroid adults (18 - 50 years), the mean \pm SD ($p < 0.0001$) of age, thyroid volume, FT3, FT4 and TSH are 33.56 ± 11.13 years, 5.05 ± 2.06 mL, 5.62 ± 0.80 pmol/L, 14.89 ± 3.38 pmol/L and 2.31 ± 0.89 mIU/L, respectively. The cross-correlations among TSH, FT3 and FT4 have been demonstrated in **Figure 5(a)**. Here, FT4 is exceptionally high near to the upper boundary of the given reference level without fall in TSH of 16th subject which may be related to the undiagnosed non-thyroid illness. Otherwise, the serum free thyroxin (FT4) lies within the small range. In many subjects, the values of TSH lying below its average line are associated with the values of FT3 and/or FT4 lying above their average lines and vice versa. This is due to the negative feedback mechanism of TH to hypothalamus and pituitary to

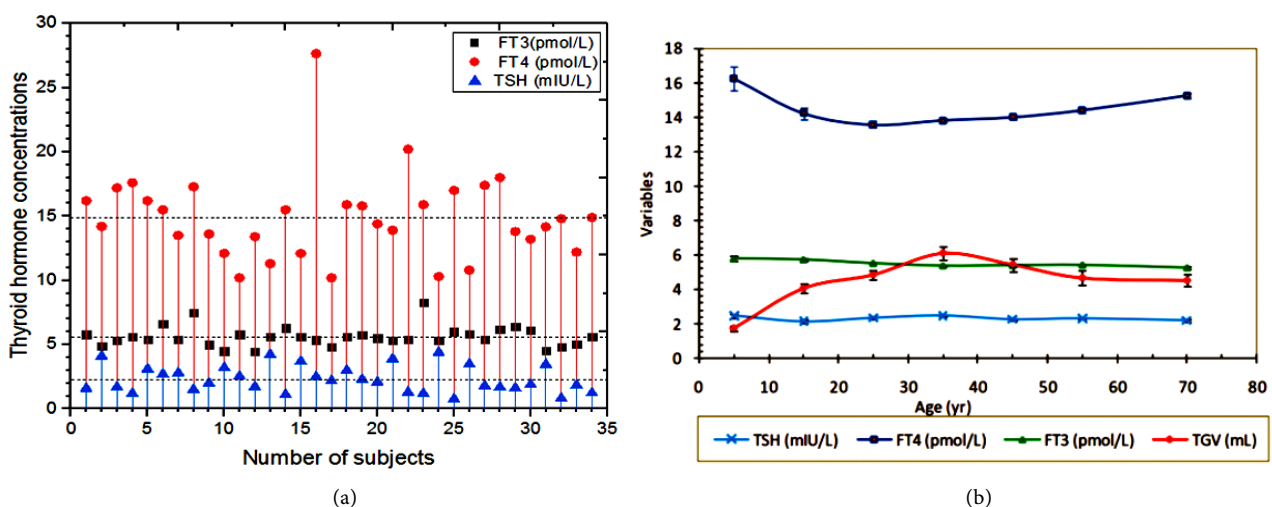


Figure 5. (a) Fluctuations in TFT values in 34 adults having normal thyroid where the horizontal dotted lines represent the observed mean values, and (b) healthy thyroid status with aging where the markers indicate the mean values in the age groups of 10 years interval.

trigger the production of thyrotropin (TSH) by means of which they are produced in a controlled way from the thyroid gland.

The thyroid size and the TFT values varying with different age groups of euthyroid subjects are plotted in **Figure 5(b)**. The results in this study show that FT3 and TSH remain almost constant, but FT4 decreases and then increases with aging. Conversely, the normal thyroid size increases and then decreases with aging.

Age, gender, thyroid size, FT3, FT4 and TSH are included as covariates. Lack of health awareness in rural areas, urbanization with increased environmental pollutants and reduced physical activity, socio-economic conditions, nutritional status, biologically activated life stages, mental and physical stress, and genetics play the crucial role in the thyroid malfunction and the development of metabolic syndrome. The alterations in thyroid functions and prevalence of thyroid diseases are higher in women than in men due to the change in lipid profile, hyperinsulinemia, android obesity, and hypertension [37]. The aging results the increased thyroid dysfunction and prevalence of metabolic syndrome. Along with the adverse changes in TFT values by estrogenic protective defects, women have higher inclination towards thyroid dysfunction than men. Moreover, the gender based changes in thyroid size can also be observed distinctly in menarche and menopause periods.

4. Conclusions

In this study, the thyroid gland of the euthyroid subjects has mean \pm SD ($p < 0.001$) of LLV and RLV as 2.12 ± 1.07 mL, 2.61 ± 1.40 mL, respectively. RLV with higher value has significant positive linear correlation with LLV ($r = 0.727$, $p < 0.001$). TGV increases and then decreases with aging having larger value for adults than that for children and elderly. LLV of both genders is almost same, but RLV and TGV of males are larger than that of females. In the age groups including periods of menarche (11 - 20 years) and menopause (41 - 50 years) of females, the size of their thyroid gland is larger than that of males. TGV is maximum in the age group of 31 - 40 years for males and it is maximum in the age group of 41 - 50 years for females.

The TFT values of the hospital based euthyroid subjects have mean \pm SD ($p < 0.0001$) of FT3, FT4 and TSH as 5.46 ± 0.82 pmol/L, 14.09 ± 2.71 pmol/L and 2.30 ± 0.98 mIU/L, respectively. FT3 has a weak positive linear correlation ($r = 0.095$, $p < 0.001$) with FT4. FT4 has a small degree of negative linear correlation ($r = -0.113$, $p = 0.002$) with TSH. The TFT values are higher for the early infant age group (< 1 years). FT3 and TSH are not significantly changed, but FT4 decreases from children to adults and then increases slightly to elderly in the similar way for the both genders.

The thyroid size increases and then decreases, but conversely, FT4 decreases and then increases with aging by means of increased thyroid dysfunction and prevalence of metabolic syndrome in the elderly. In this normal thyroid analysis,

FT3 and FT4 have negative correlations with TSH supporting the principle of negative feedback mechanism in the thyroid cycle.

Ethical Consent and Approval

This research work has been performed under the ethical guidelines provided by and taking authority from Institutional Review Board (IRB), Institute of Medicine (IOM), Tribhuvan University Teaching Hospital (TUTH), Maharajgunj, Kathmandu, Nepal.

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Authors' Contributions

All authors were involved in the research and they read and approved the final manuscript.

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Conflicts of Interest

The authors declare that they have no conflict of interest.

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Abbreviations

USG: Ultrasonography

TFT: Thyroid Function Test

LLV: Left Lobe Volume

RLV: Right Lobe Volume

TGV: Thyroid Gland Volume

TH: Thyroid Hormones

FT3: Free Triiodothyronine

FT4: Free Thyroxine

TSH: Thyroid Stimulating Hormone