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ORIGINAL ARTICLE

Determining Thyroid Disorders in Younger Age Group (pre-Pubertal, Peri-Pubertal & Pubertal) Individuals: An Observational Study

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ABSTRACT

Objective: Determine thyroid disorders in younger age group (pre-Pubertal, Peri-Pubertal & Pubertal) individuals.

Method: : Blood samples were obtained from patients advised assessment of thyroid hormone levels, during an eight month period spanning from May to December 2010. Only those subjects were included for this study, which had been evaluated for all three parameters of thyroid function (T3, T4, and TSH). The assessment of free fraction of T3 and T4 was carried out keeping in view their diagnostic advantage over the total hormones. Serum thyroid hormones from patients' serum were estimated by using the Roche Elecsys 2010 immunoassay analyzer installed at the Reproductive Physiology department of the National Institute of` Health, Islamabad. It is an automated analyzer with inbuilt software system, and is based on electrochemiluminiscence. Data of all subjects were expressed as Mean±SD, and compared statistically by correlation, and student's "t" test.

Result: Serum samples of 12 pre-pubertal (6-9 years) subjects were evaluated for their thyroid functions. Results of 8 subjects showed normal thyroid hormone levels, and 3 different patterns of abnormal activity were observed. In peri-pubertal subjects (10-15 years) Serum of 28 (19 female and 9 male) subjects in this age group (10-15 years) were evaluated for thyroid function, and 19 subjects showed normal results constituting 14 female and 5 males. In pubertal subjects serum samples of 37 individuals of this age group (16-19 years) were evaluated for thyroid function. Out of which 25 individuals showed normal thyroid activity, and FT4 and TSH had significant ($p<0.05$) negative correlation ($r= -0.3799$) with them.

Conclusion: About 200 million people in the world have some form of thyroid disease. Thyroid disorders are common endocrine disorders encountered in Pakistan. This disease can't be prevented but early diagnosis can reduce complications that can be life threatening.

Keywords: Endocrine disorders, thyroid, hyperthyroidism, Graves's disease, hypothyroidism, pubertal, and antithyroglobulin antibodies, hyperthyroxinemia.

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INTRODUCTION

Lodine plays a key role in synthesis of thyroid hormones. For the maintenance of proper thyroid activity, about 50 mg per year or one mg per week ingested iodine is required. Excessive ingestion of iodine causes the production of thyroid hormones which is more than requirement, whereas insufficient accumulation of iodine leads to suppressed production of these hormones. According to a report there was 94 percent prevalence of iodine deficiency within school going children of Pakistan [1,2]. Many factors have been found responsible for abnormal T3 and T4 levels. Slightly elevated T3 level may occur in pregnancy, while depressed levels may occur during severe illness, malnutrition and in renal failure [3]. Preventable brain damage worldwide is commonly caused by iodine deficiency. Due to iodine deficiency about 800 million people are affected by deficiency disorders that include

goiter, hypothyroidism, mental retardation, and a wide spectrum of other growth and developmental abnormalities. Iodine supplementation, in the form of iodized salt and iodized vegetable oil, produced dramatic improvements in many areas, even though iodine deficiency is still a problem for developed countries as well, and not only for developing countries alone [4].

Graves disease is a common cause of hyperthyroidism, which is a diffuse toxic goiter in which enlargement of thyroid gland occurs, as a result of the thyroid glands' overproduction of T3 and T4.

Measurement of serum TSH is generally considered the best screening test for thyroid disease. Subclinical hypothyroidism is caused by the same disorders of the thyroid gland as those that cause overt hypothyroidism. Chief among these is chronic autoimmune thyroiditis (Hashimoto's disease), which is commonly associated with increased titers of antithyroid antibodies, such as antithyroid microsomal antibodies (antithyroid peroxidase) and antithyroglobulin antibodies. Another common cause of hypothyroidism is the treatment of Graves' disease.

Exercise affects the activity of many glands and the production of their hormones, and thyroid is one of the affected glands. When exercise is repeated at certain intervals, there is a pituitary-thyroid interaction that is properly coordinated by increasing turnover of thyroid hormones. Thyroxin turnover and related hormonal action increase can lead to hyperthyroidism [5]. Sub clinical hyperthyroidism has been linked with increased risk of cardiovascular disease, and at least in some cases, it could be related with sub clinical thyroid dysfunction [6].

Presence of abnormal levels of T4 in blood circulation is called thyroxinemia. If serum level of T4 is lower than normal range condition is called hypothyroxinemia, and if values are more than normal range condition is called hyperthyroxinemia. Hypothyroxinemia during pregnancy is common. Different studies demonstrated the pivotal role exerted by maternal thyroxin on fetal brain development and the negative impact of hypothyroxinemia on neurobehavioral performance in offspring [7]. Hyperthyroxinemia is defined as a condition in which the serum total or, free thyroxine (T4) concentrations are abnormal without evidence of clinical thyroid disease. These changes may be transient or persistent [8].T4 and T3 circulate in the blood bound to 3 different binding proteins, ie, thyroxine-binding globulin (TBG), thyroxine-binding prealbumin (TBPA, or transthyretin (TTR), and albumin [9].

Most of the conditions resulting in hyperthyroxinemia do not have any adverse clinical outcomes. An exception to this is the syndrome of thyroid hormone resistance; children with this disorder may have learning difficulties [10].

MATERIALS AND METHODS

Blood samples were obtained from patients advised assessment of thyroid hormone levels, during an eight month period spanning from May to December 2010. Only those subjects were included for this study, which had been evaluated for all three parameters of thyroid function (T3, T4, and TSH). The assessment of free fraction of T3 and T4 was carried out keeping in view their diagnostic advantage over the total hormones.

Collection of blood samples

Venous blood samples were collected from patients, visiting Reproductive Physiology Department (RP/RH) of the National Institute of` Health (NIH), Islamabad referred by different hospitals and clinics of Rawalpindi and Islamabad for assessment of thyroid hormones. Using a tourniquet applied to the upper arm of the patient, skin of patient at venipuncture site was cleaned with 70 percent alcohol and allowed to dry. Afterwards 3 cc of blood was drawn from a suitable vein in the arm, using a dry, sterile needle and syringe. The blood was slowly ejected into a clean, dry, sterile centrifuge tube, and placed in water bath at 37°C to clot. After clot formation, blood was centrifuged at 3,000 revolutions per minute for ten minutes in a centrifuge to obtain serum, which was transferred to a sterile Eppendorf tube and stored at -20°C.

Determination of serum thyroid hormones

Serum thyroid hormones from patients' serum were estimated by using the Roche Elecsys 2010 immunoassay analyzer installed at the Reproductive Physiology department of the National Institute of` Health, Islamabad. It is an automated analyzer with inbuilt software system, and is based on electrochemiluminiscence.

Reagents

Elecsys reagent kits, purchased from Roche (Pakistan) Ltd, for FT3, FT4 and TSH (200 tests each) were used.

Test principle

Elecsys 2010 immunoassay analyzer works on the sandwich principle. In first incubation 15 micro liter (µL) sample for FT3, and FT4, and 50 micro liter (µL) for TSH, is incubated with anti-Analyte-Specific antibody labelled with ruthenium complex. In the second incubation after addition of biotinylated analyte

and streptavidin labelled micro particles, the free binding sites of labelled antibody become occupied with the formation of antibody-heptain complex. The entire complex produced is bound to the solid phase via biotin-streptavidin interaction. The reaction mixture is aspirated into the measuring cell where the micro particles are magnetically captured onto the surface of the electrode. Unbound substances are then removed using ProCell. Application of a voltage to the electrode then induces chemiluminescense, which is measured by a photomultiplier. Results are determined via a calibration curve specifically generated by the instrument.

Testing procedure

Patients' samples, calibrators and controls were brought at room temperature (20-25 0C) before measurement. The reagents were placed on the reagent disk of the analyzer avoiding formation of foam. The system automatically maintains the temperature of the reagents and the opening/closing of the bottles.

Quality Control

Quality control samples representing the lower and upper range of the assay were used for the quality control of the results. Results ±1SD of the target value were considered acceptable. Only the batches with all the controls being within permissible limits were accepted.

Calculation and measuring range

The Elecsys 2010 determines the hormonal concentration of FT3 and FT4 in pico mole per liter (pmol/L), and micro international unit per milliliter (µIU/ml) for TSH. The measuring range of the system for the studied parameters, as well as their reference range is given in Table 1.

Table 1. Measuring and reference ranges for thyroid hormone assays

Analyte	Measuring Range	Reference Range	
FT (pmol/L)	0.4-50	1-6Yr: 3.8-8.2	7-12Yr :3.8-8.6
		13-17Yr: 3.7-7.7	Adults: 2.8-7.1
FT4 (pmol/L)	0.3-100	1-6Yr: 12.1-22.0	7-12Yr :13.9-22.1
		13-17Yr: 13.6-23.2	Adults: 12.-22.0
TSH (µIU/ml)	0.005-100	1-6Yr: 0.85-6.5	7-12Yr : 0.28-4.3
		Adults: 0.27-4.2	

Statistical analysis

Data of all subjects are expressed as Mean±SD, and compared statistically by correlation, and student's "t" test as described earlier (Steel and Torrie, 1960).

RESULTS

Serum of 312 subjects was obtained at National Institute of Health (NIH) during May, 2010 to December 2010. Subjects were distributed in pre-pubertal, peri-pubertal, pubertal and adult groups according to age (Table 2). Out of these 248 were female subjects and 64 were male. Samples were taken only from those subjects who required results of all three parameters i.e. FT3, FT4 and TSH. Results of 186 individuals (59.6%) showed normal thyroid activity and constituted 152 (47.8%) female and 37 (11.8%) male, the remaining had disturbance in thyroid activity (Table 2).

In normal subjects FT3 showed significant ($p<0.05$) negative correlation ($r= -0.2681$) with age (Fig-01), other parameters correlated non-significantly with each other. Individuals with disturbed thyroid hormones showed 14 different abnormal conditions (Table 4). The first condition showed hypothyroidism where, FT3 and FT4 were below normal range while TSH levels were higher than normal limit. All hormonal parameters varied highly significantly ($p<0.001$), while age varied non-significantly. FT3 showed significant ($p<0.05$) positive correlation ($r= 0.7964$) with FT4 (Figure 2), while TSH showed significant ($p<0.05$) negative correlation ($r= -0.7340$) with age (Figure 3), other parameters had non-significant

correlation between them. In the second condition again, FT3 and FT4 were below permissible range while TSH was normal. All parameters differed highly significantly ($p<0.001$), age (was higher) also showed highly significant ($p<0.001$) variation from normal subjects. The third condition revealed that the FT3 and TSH levels were below normal values, while levels of FT4 were above normal, indicating primary hyperthyroidism. All hormonal parameters varied highly significantly ($p<0.001$) from the mean of normal group. Age (was lower) showed highly significant ($p<0.001$) differences from normal individuals' age.

The fourth condition had normal FT3, elevated FT4 and decreased TSH levels, also indicative of primary hyperthyroidism. All parameters, including age (was higher), showed highly significant variation from normal subjects. Hormone levels in the fifth condition indicated FT3 toxicosis. In this condition, only FT3 levels were pathological, while FT4 and TSH levels were within normal range. FT4 and age differed non-significantly, FT3 showed highly significant ($p<0.001$) variation from normal group. The sixth abnormal condition revealed normal FT3 and FT4 levels, while TSH levels were increased, indicating sub-clinical hypothyroidism. FT3 and TSH showed more-significant ($p<0.01$) variation, FT4 and age varied non-significantly in this condition. FT3 showed significant ($p<0.05$) positive correlation ($r= 0.3756$) with FT4 (Figure 4). The seventh condition showed hypothroxinemia, this condition had normal FT3, and TSH levels, and FT4 levels in this condition were below normal. FT3 and TSH, along with age, showed non-significant variation, FT4 showed highly significant ($p<0.001$) variation from normal subjects. In the eighth condition, results indicated hyperthyroxinemia where, FT3 and TSH values were within permissible range, while FT4 values were disturbed, and were above normal. FT3, TSH and age showed non-significant variation and FT4 had highly significant ($p<0.001$) variation from normal group. Significant ($p<0.05$) negative correlation ($r= -0.8770$) was seen in this group between FT3 and TSH (Figure 5).

The ninth condition had primary hypothyroidism where, FT3 levels within normal range, and levels of FT4 were below normal while TSH exhibited higher values than those of normal range, age was (higher) significantly ($p<0.05$) in this condition. FT4 showed significant ($p<0.05$) negative correlation ($r= -0.6557$) with TSH (Figure 6), and TSH in this group had significant ($p<0.05$) negative correlation ($r= -0.4580$) with age (Figure 7). In the tenth abnormal condition FT3 and FT4 were within normal range and TSH was less than permissible levels (sub-clinical hyperthyroidism). In this condition, TSH showed highly significant ($p<0.001$) variation along with age while FT3 showed more significant ($p<0.01$) variation and FT4 differed non-significantly from normal subjects. Additionally, FT3 and TSH showed significant ($p<0.05$) negative correlation ($r= -0.5840$) with each other (Figure 8), FT4 also had significant ($p<0.05$) negative correlation ($r= -0.6835$) with TSH in this condition (Figure 9) and there was no significant relationship between other parameters in this group.

Eleventh group showed that levels of FT3 were higher than normal values, and FT4 remained below normal limit, while TSH levels were within permissible range. Although TSH levels were within normal range but due to disturbance in other two parameters, they varied significantly ($p<0.01$) from normal group. In the twelfth condition, results indicated primary hyperthyroidism where, FT3 levels were higher than normal and TSH exhibited lower levels, but FT4 in this condition was within normal permissible range, but varied significantly ($p<0.01$), age varied non-significantly. In this condition FT3 and FT4 demonstrated significant ($p<0.05$) negative correlation ($r= -0.9877$) between them (Figure 10), and all other parameters showed non-significant correlation. In the thirteenth condition, FT3 values were high while the other two parameters (FT4, TSH) were within normal range, indicating FT3 toxicosis. TSH in this condition differed non-significantly. FT4, although was within normal limits but was towards the higher side, showing significant ($p<0.01$) variation, FT3 showed highly significant ($p<0.001$) variations from normal group, age was (lower) highly significantly ($p<0.001$). Age and FT4 had significant ($p<0.05$) negative relationship ($r= -0.9920$) between them (Figure 11), other parameters correlated non-significantly with each other. The Fourteenth group had high FT3, FT4 and low TSH values (hyperthyroidism), and all three parameters showed highly significant ($p<0.001$) variation from the normal group while age was (higher) significantly ($p<0.05$). In this group FT3 had significant ($p<0.05$) positive correlation ($r= 0.9314$) with FT4 (Figure 12), while, all other parameters showed non-significant correlation.

Table 2. Distribution of Different Abnormal conditions in All Subjects (High:↓, Low: ↓, Normal:↓, Significant: a (p<0.05), More significant: b (p<0.01), Highly significant: c (p<0.001), Non-significant:d)

Pathological Conditions	Group	n	Age	FT3	FT4	TSH
	Normal	186	29.45 ±1.07	4.74 ±0.06	15.33 ±0.14	1.76 ±0.07
01	↓ FT3, ↓ FT4, ↓TSH	9	37.89 ±5.87 d	1.33 ±0.21 c	2.7 ±0.81 c	80.06 ±8.70 c
02	↓ FT3, ↓ FT4, ↓TSH	1	35.00 ±0.00 c	2.47 ±0.00c	11.87 ±0.00 c	2.71 ±0.00 c
03	↓ FT3, ↓FT4, ↓ TSH	1	17.00 ±0.00 c	2.13 ±0.00 c	34.95 ±0.00 c	0.01 ±0.00 c
04	↓FT3, ↓FT4, ↓ TSH	1	52.00 ±0.00 c	4.64 ±0.00 d	27.1 ±0.00 c	0.024 ±0.00 c
05	↓ FT3, ↓FT4, ↓TSH	3	26.33 ±9.33 d	2.32 ±0.14 c	14.23 ±0.79 d	1.908 ±0.86 d
06	↓FT3, ↓ FT4, ↓TSH	22	28.33 ±12.81 d	4.134 ±0.18 b	15.45 ±0.53 d	8.68 ±2.13 b
07	↓FT3, ↓ FT4, ↓TSH	34	32.62 ±2.50 d	4.46 ±0.139 d	10.90 ±0.19 c	1.63 ±0.15d
08	↓FT3, ↓FT4, ↓TSH	5	29.00 ±8.08 d	5.60 ±0.50 d	24.12 ±0.59 c	1.64 ±0.55 d
09	↓FT3, ↓ FT4, ↓TSH	22	36.14 ±2.37 a	4.15 ±0.114 c	9.85 ±0.39 c	22.72 ±5.34 c
10	↓FT3, ↓FT4, ↓ TSH	9	32.22 ±4.37 c	5.656 ±0.30 b	15.88 ±0.623 d	0.09 ±0.03 c
11	↓FT3, ↓FT4, ↓TSH	1	6.00 ±0.00 c	7.14 ±0.00 c	11.72 ±0.00 c	3.64 ±0.00 c
12	↓FT3, ↓FT4, ↓TSH	3	30.67 ±7.51 d	7.91 ±0.492 c	19.85 ±0.599 c	0.01 ±0.01 c
13	↓FT3, ↓FT4, ↓TSH	3	17.67 ±2.96 c	7.97 ±0.241 c	18.25 ±1.329 a	1.78 ±0.198 d
14	↓FT3, ↓FT4, ↓TSH	12	38.33 ±3.74 a	29.13 ±4.07 c	71.37 ±8.70 c	0.007 ±0.01 c

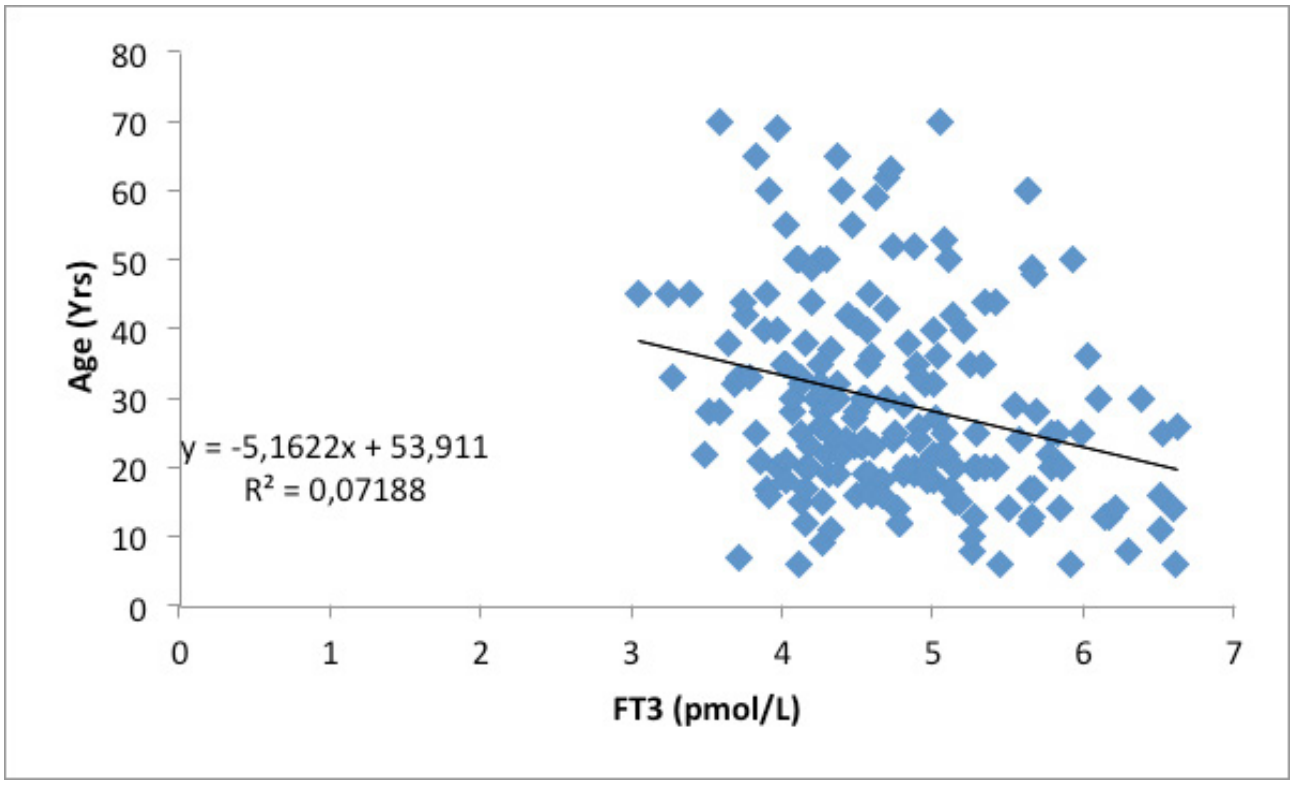

Figure 1. Significant negative correlation (p=<0.05) between FT3 and Age (normal subjects).

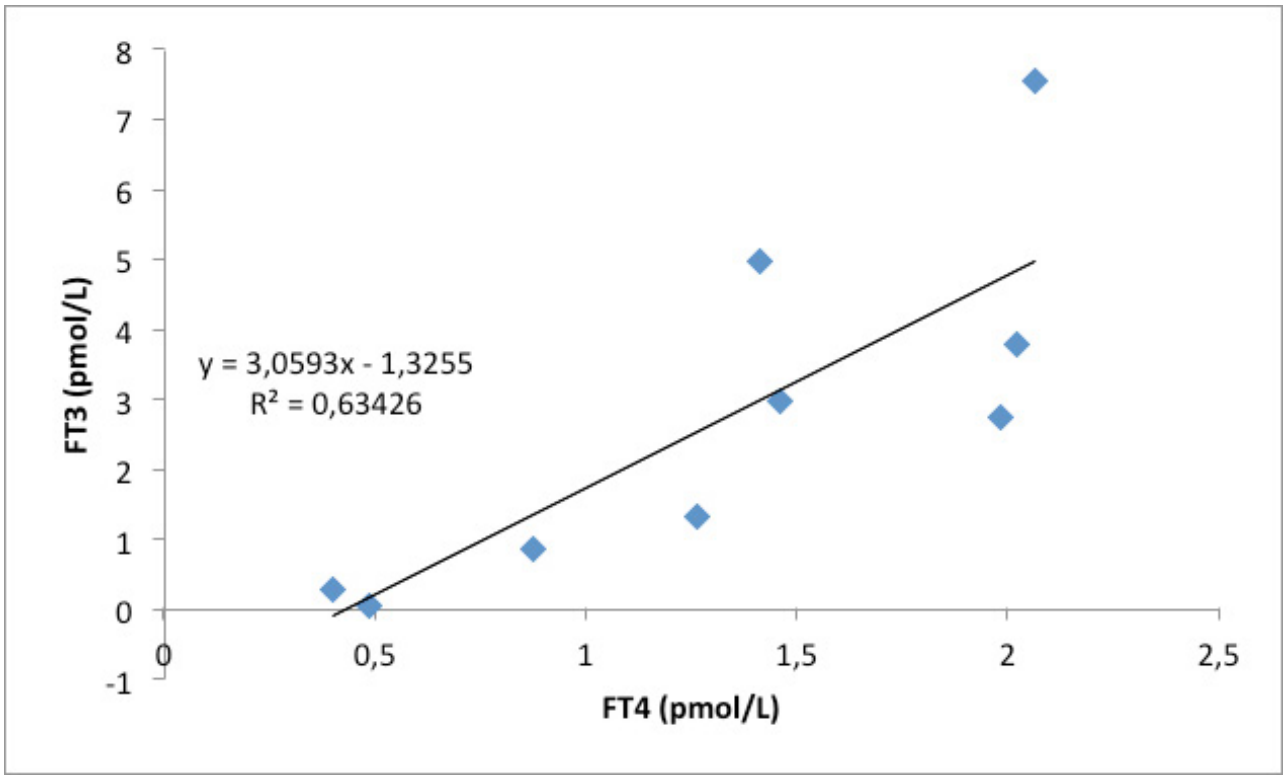

Figure 2. Significant positive correlation (p=<0.05) between FT3 and FT4 (Where FT3, FT4 were low and TSH was high).

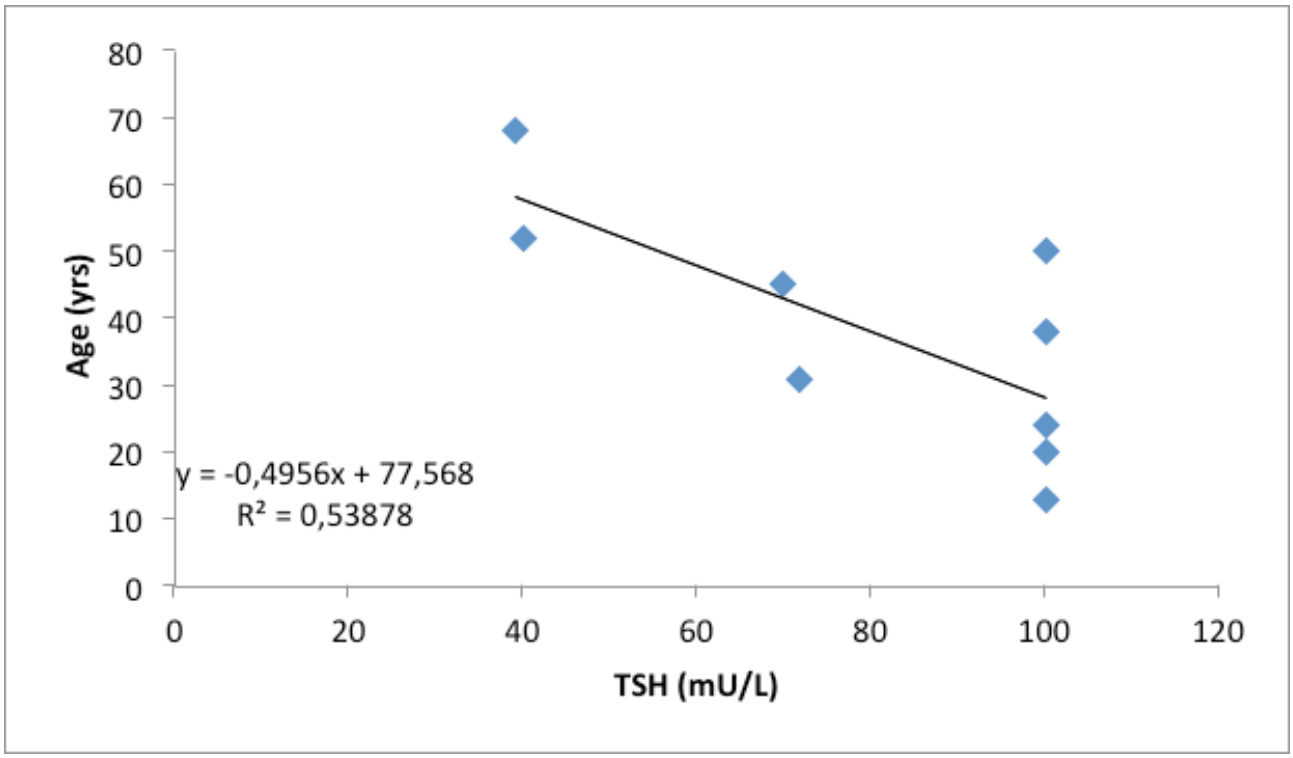

Figure 3. Significant negative correlation (p=<0.05) between TSH and Age (FT3, FT4 low and TSH high).

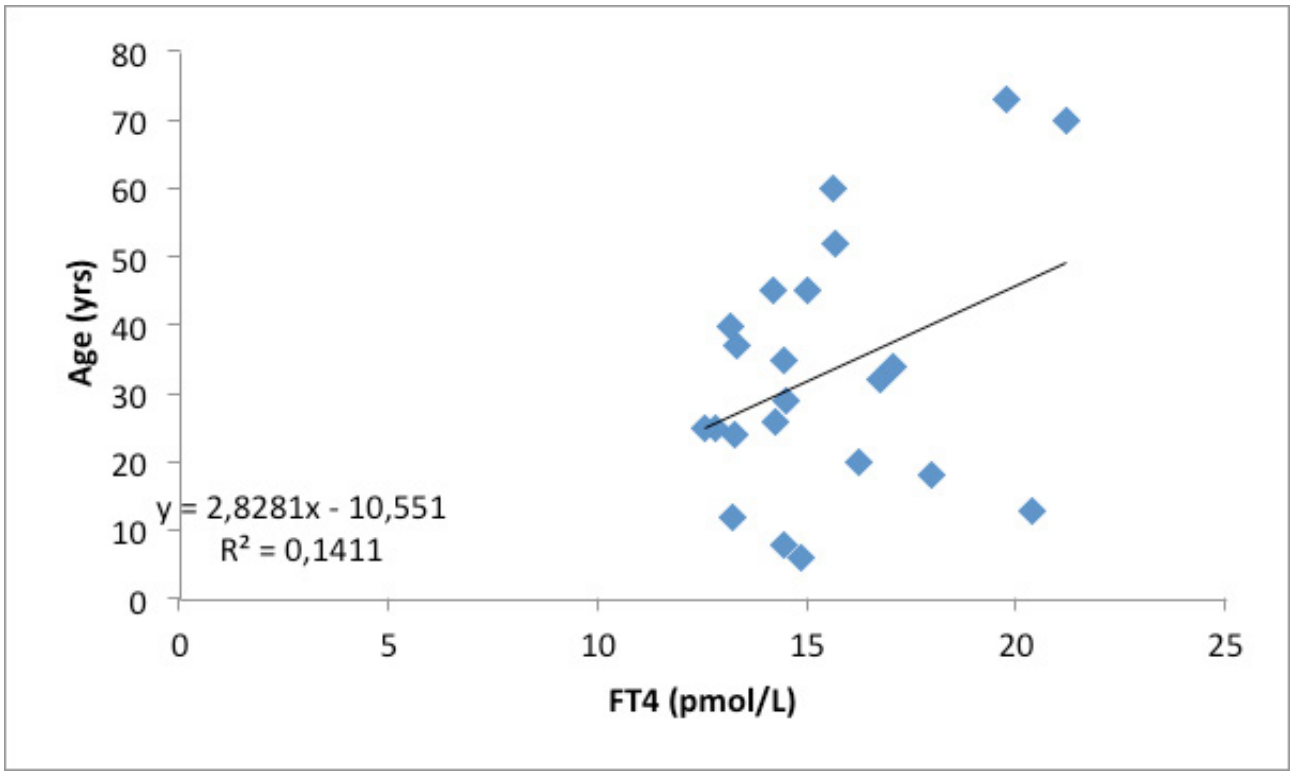

Figure 4. Significant positive correlation (p=<0.05) between FT4 and Age (FT3, FT4 normal and TSH high).

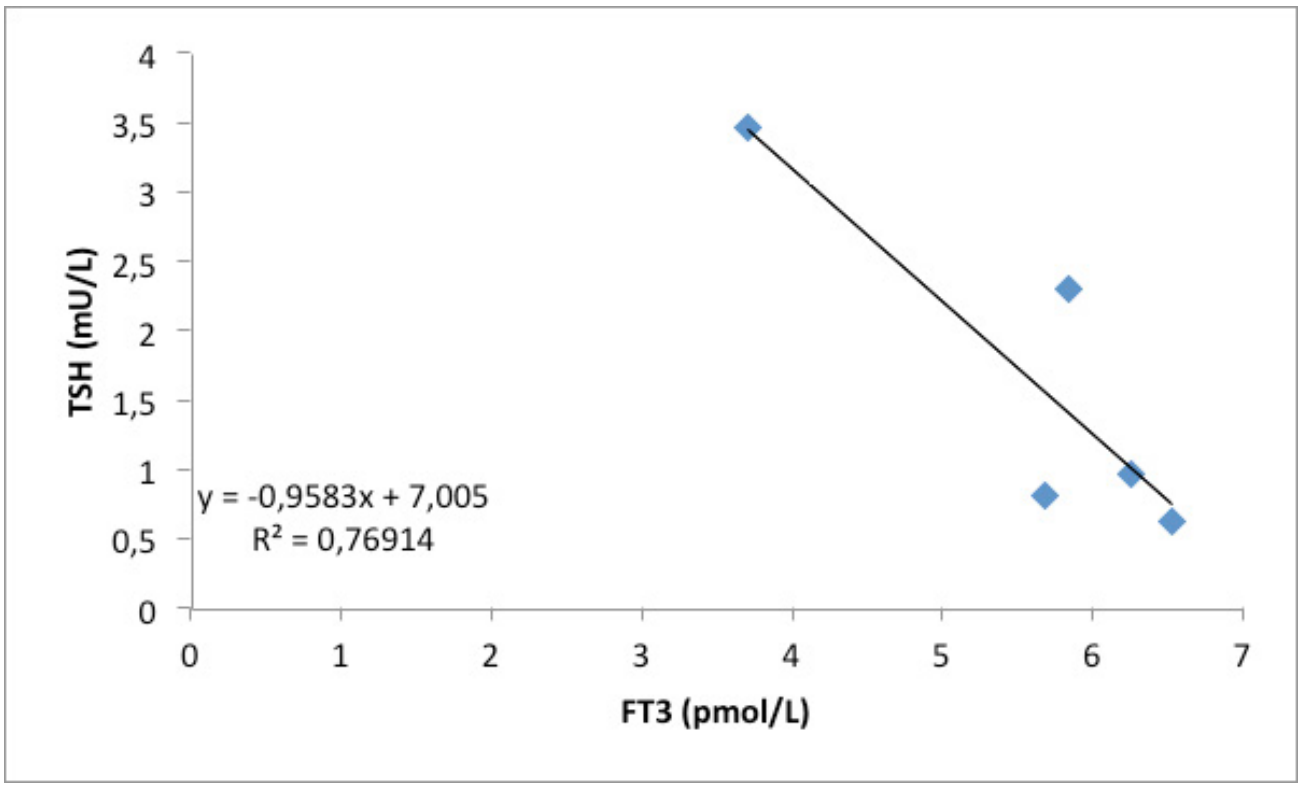

Figure 5. Significant negative correlation (p=<0.05) between FT3 and TSH (FT3 normal, FT4 high and TSH normal).

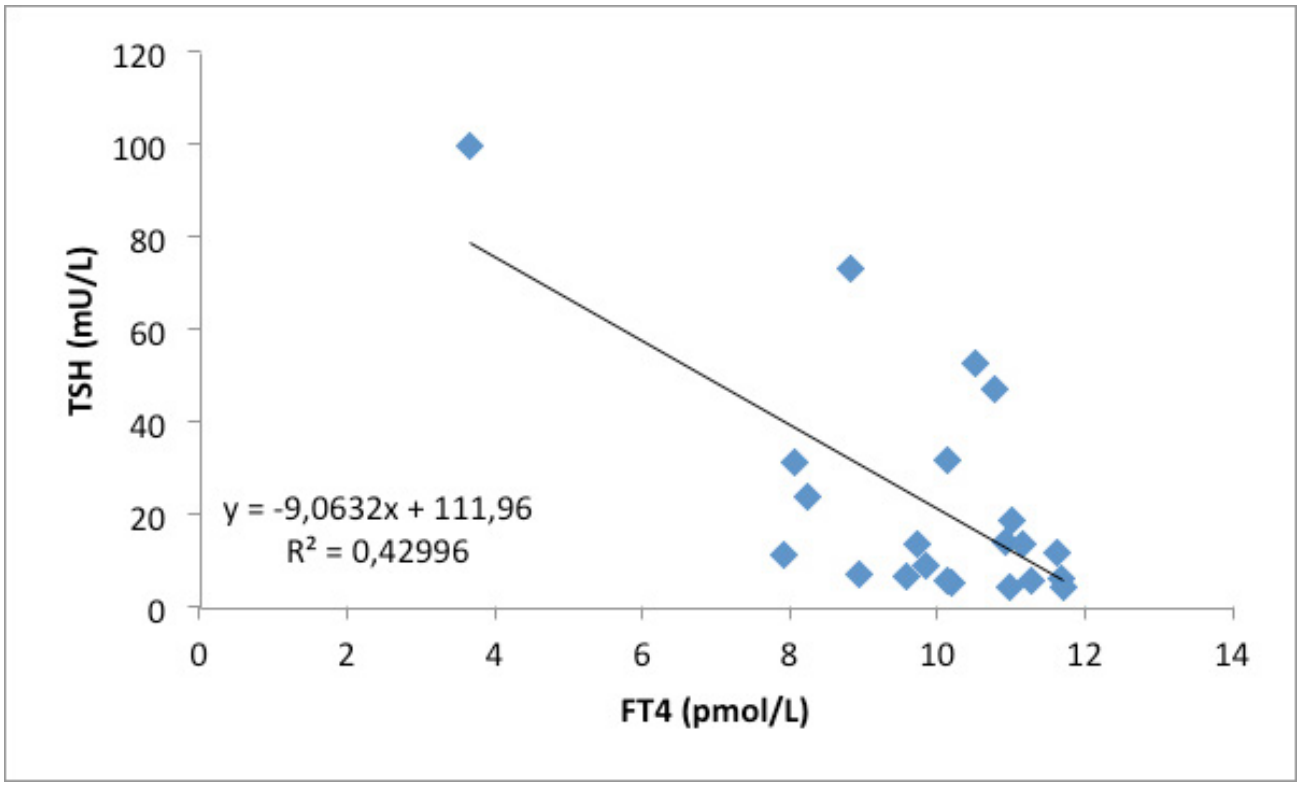

Figure 6. Significant negative correlation (p=<0.05) between FT4 and TSH (FT3 normal, FT4 low and TSH normal).

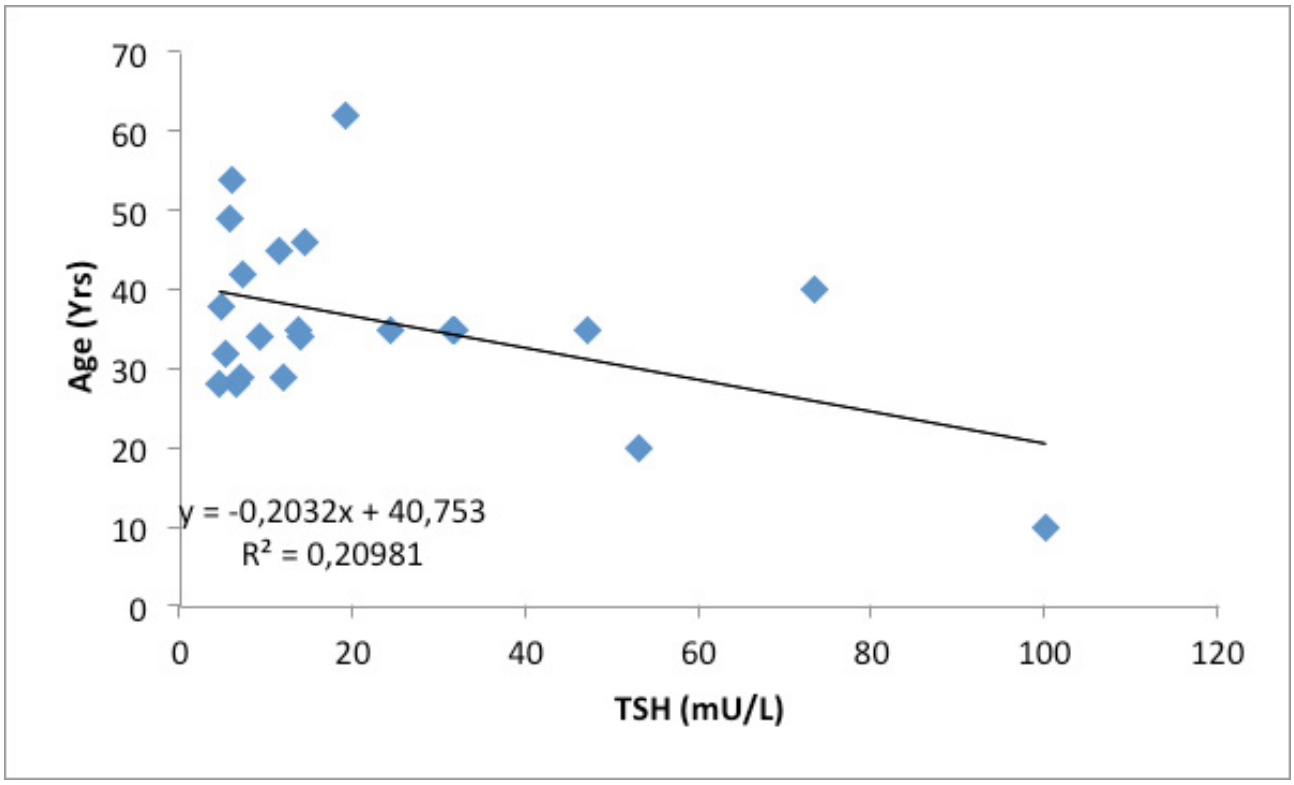

Figure 7. Significant negative correlation (p=<0.05) between TSH and Age (FT3 normal, FT4 low and high TSH).

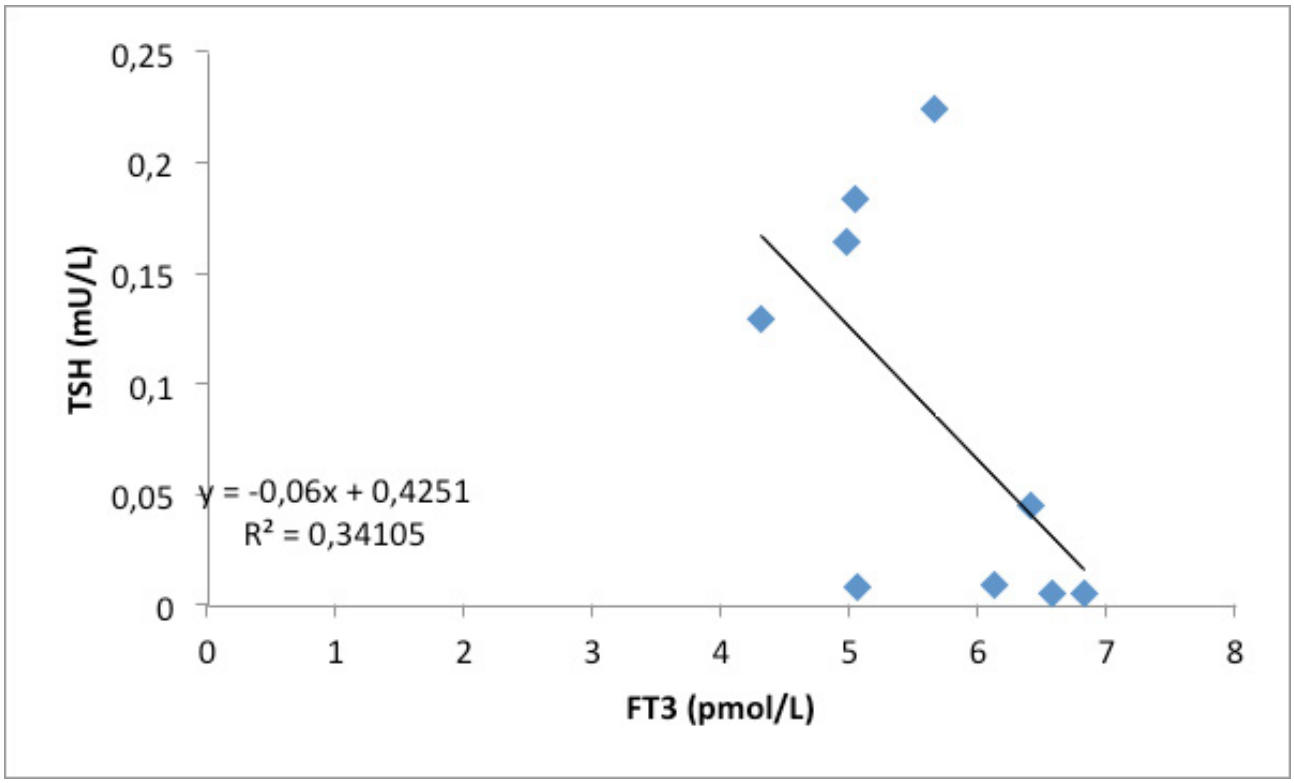

Figure 8. Significant negative correlation (p=<0.05) between FT3 and TSH (FT3, FT4 normal and TSH low).

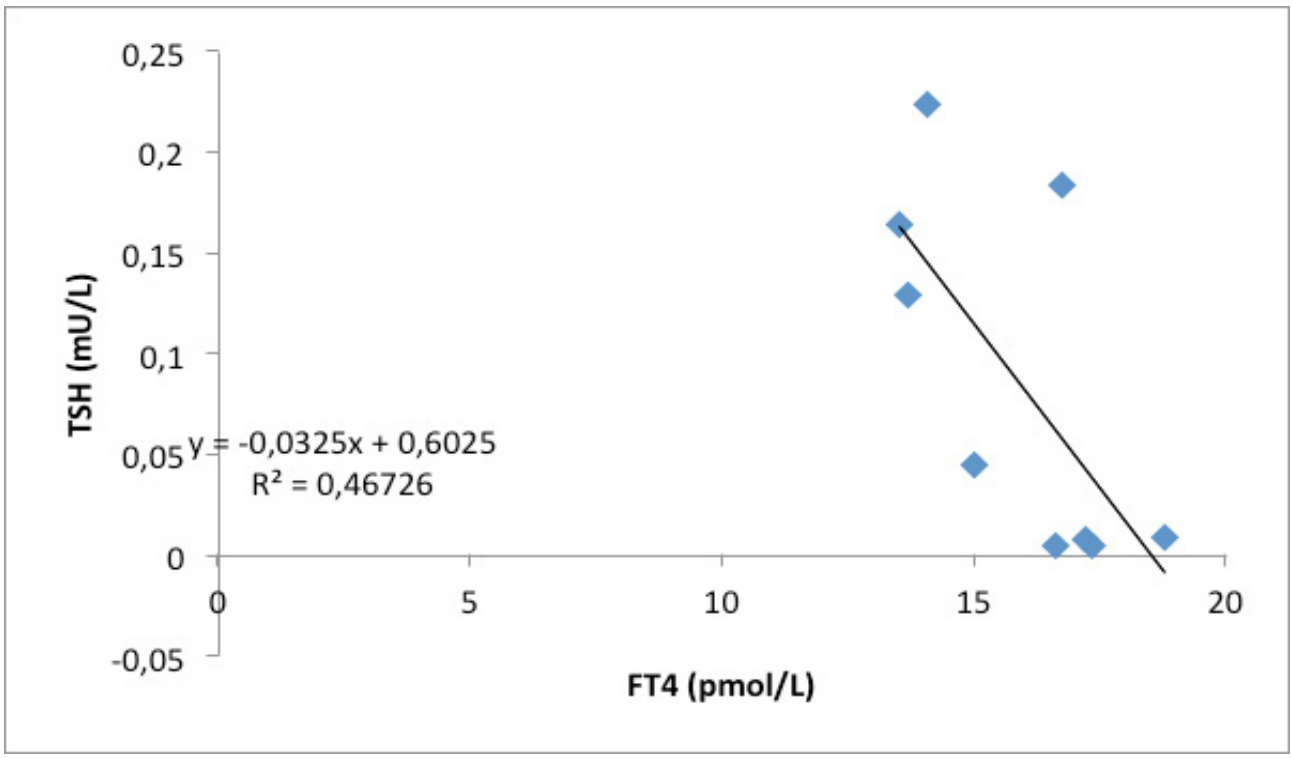

Figure 9. Significant negative correlation (p=<0.05) between FT4 and TSH (FT3, FT4 normal, TSH low).

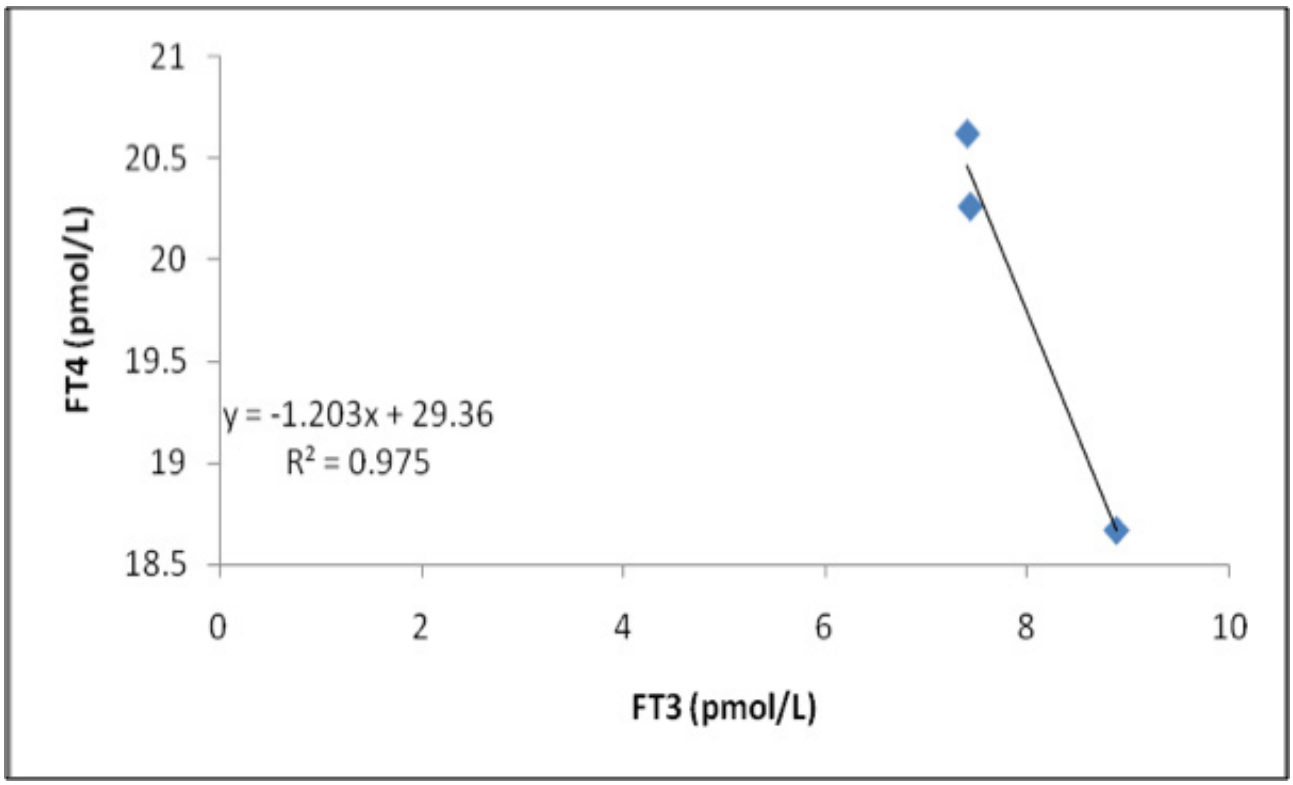

Figure 10. Significant negative correlation (p=<0.05) between FT3 and FT4 (FT3 high, FT4 normal and TSH low).

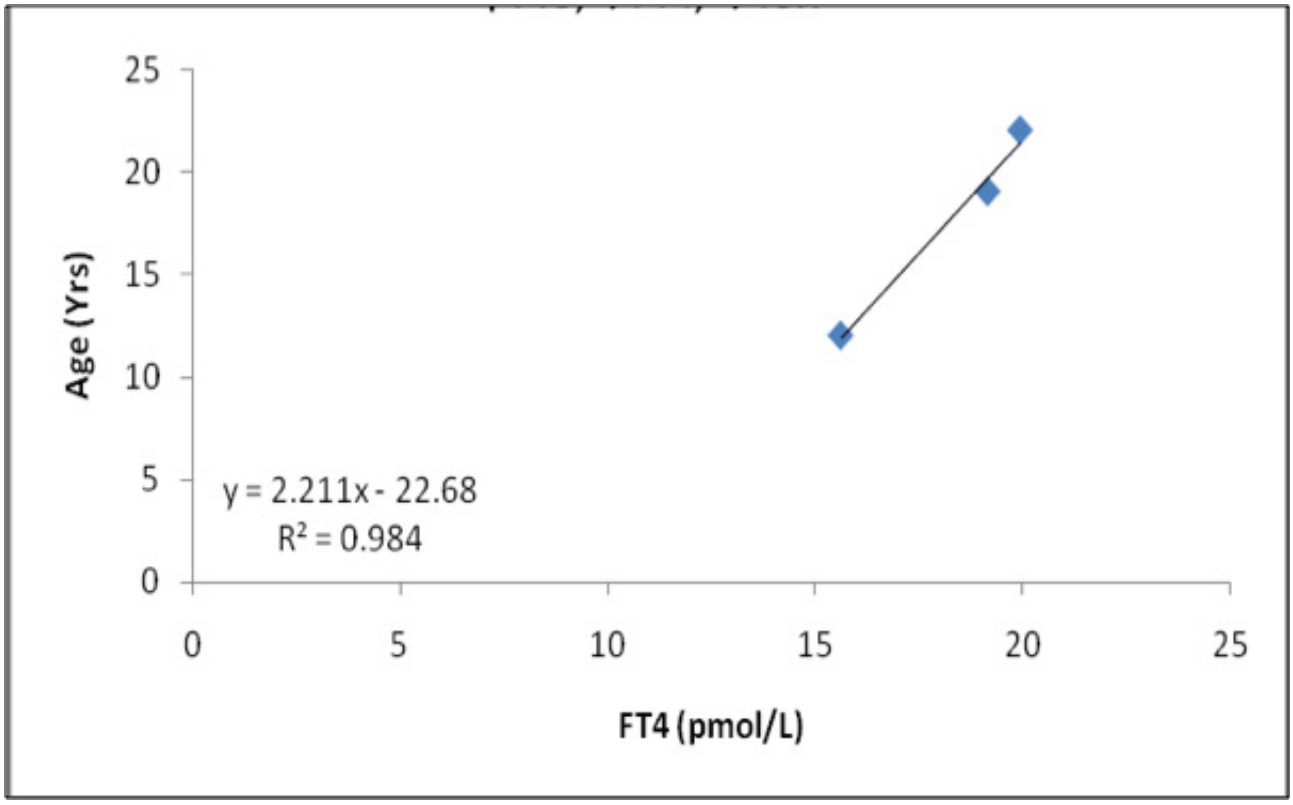

Figure 11. Significant positive correlation (p=<0.05) between FT4 and Age (FT3 raised, FT4 and TSH normal).

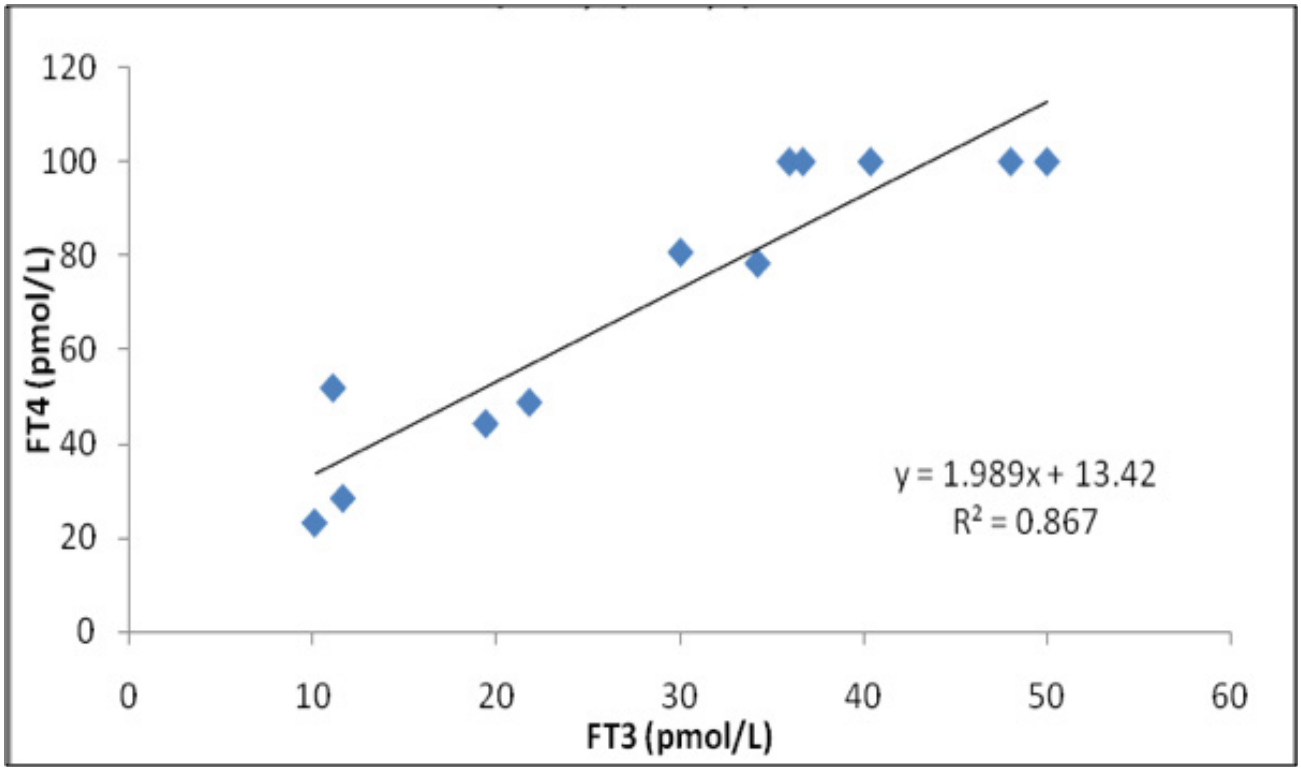

Figure 12. Significant positive correlation (p=<0.05) between FT3 and FT4 (FT3, FT4 high and TSH low).

Pre-pubertal subjects

Serum samples of 12 pre-pubertal (6-9 years) subjects were evaluated for their thyroid functions. Results of 08 subjects showed normal thyroid hormone levels, and 03 different patterns of abnormal activity were observed (Table 3). In the first condition FT3 and FT4 were normal while, TSH was below normal giving picture of sub-clinical hyperthyroidism. FT3 showed more significant ($p<0.01$) variation, FT4 had significant ($p<0.05$) variation, and TSH varied highly significantly ($p<0.001$). In another condition, FT3 was raised while FT4 was below normal and TSH was normal. FT3 had more significant ($p<0.01$) variation, while FT4 and TSH showed highly significant variation ($p<0.001$). Although TSH was normal but due to disturbance in other two hormones, it also varied significantly ($p<0.05$). In the last condition, FT3 and FT4 were normal, and TSH was more than normal. All hormonal parameters along with age varied non-significantly in this condition.

Table 3. Distribution of different abnormal conditions in Pre-pubertal Subjects (High: ↓, Low: ↓, Normal:↓, Significant: a ($p<0.05$), More significant: b ($p<0.01$), Highly significant: c ($p<0.001$), Non-significant: d).

Pathological Conditions	Group	n	Age	FT3	FT4	TSH
	Normal	8	7.00 ±0.42	5.19 ±0.38	15.67 ±0.653	1.97 ±0.26
01	↓FT3, ↓FT4, ↓ TSH	1	6.00 ±0.00 d	6.56 ±0.00 b	17.33 ±0.00 a	0.01 ±0.00 c
02	↓FT3, ↓FT4, ↓TSH	1	6.00 ±0.00 d	7.14 ±0.00 b	11.72 ±0.00 c	3.64 ±0.00 c
03	↓FT3, ↓ FT4, ↓TSH	2	7.00 ±1.00 d	5.28 ±0.50 d	14.63 ±.0.22 d	28.71 ±21.37 d

Peri-pubertal subjects

Serum of 28 (19 female and 9 male) subjects in this age group (10-15 years) were evaluated for thyroid function, and 19 subjects showed normal results constituting 14 female and 5 males. Six different conditions were observed showing different patterns of thyroid abnormalities (Table 4). In the first condition FT3 and FT4 were low, while TSH values was higher than normal (hypothyroidism), all three hormonal parameters varied highly significantly ($p<0.001$). The second condition had normal FT3 and FT4 was low, while TSH was more than normal, indicating primary hypothyroidism. All three parameters had highly significant ($p<0.001$) variation as compared with normal subjects. The third condition revealed normal FT3, FT4 and high TSH, also indicating sub-clinical hypothyroidism. All hormonal parameters as well as age varied non-significantly. In the fourth condition FT3 was more than normal, FT4 and TSH on the other hand were normal. FT3 was high and varied highly significantly ($p<0.001$), while FT4 and TSH showed non-significant variation. The fifth condition revealed normal FT3, TSH and low FT4 (hypothyroxinemia). FT3 and TSH had non-significant variation, while FT4 varied highly significantly ($p<0.001$). FT3 and TSH had significant ($p<0.05$) positive correlation ($r= 0.9944$) with them (Figure 13), FT3 and age exhibited significant ($p<0.05$) positive correlation ($r= 0.9990$) with them (Figure 14), while a significant ($p<0.05$) positive correlation ($r= 0.9999$) was observed between TSH and age (Figure 15). In the last group of this age group FT3 and TSH were within normal limit and FT4 were abnormal but in this condition levels of FT4 were above normal values (hyperthyroxinemia). In this condition all three parameter varied highly significantly. Although FT3 and TSH were within normal limits, but there values, but varied significantly as compared with normal group.

Table 4: Distribution of different abnormal conditions in Peri-pubertal Subjects(High: ↓, Low: ↓, Normal:↓, Significant: a (p<0.05), More significant: b (p<0.01), Highly significant: c (p<0.001), Non-significant: d).

Condition	Group	n	Age	FT3	FT4	TSH
	Normal	19	13.00 ±0.33	5.31 ±0.18	15.67 ±0.57	2.16 ±0.20
01	↓ FT3, ↓ FT4, ↓TSH	1	13.00 ±0.00 d	1.98 ±0.00 c	2.74 ±0.00 c	100.00 ±0.00 c
02	↓FT3, ↓ FT4, ↓TSH	1	10.00 ± 0.00 c	4.52 ±0.00 c	3.64 ±0.00 c	100.00 ±0.00 c
03	↓FT3, ↓ FT4, ↓TSH	2	12.50 ±0.50 d	4.67 ±0.70 d	16.76 ±3.58 d	9.00 ±4.45 d
04	↓FT3, ↓FT4, ↓TSH	1	12.00 ±0.00 b	7.85 ±0.00 c	15.63 ±0.00 d	1.98 ±0.00 d
05	↓FT3, ↓ FT4, ↓TSH	3	13.00 ±1.53 d	5.94 ±0.44 d	9.94 ±0.99 c	1.59 ±0.28 d
06	↓FT3, ↓FT4, ↓TSH	1	15.00 ±0.00 c	6.53 ±0.00 c	23.25 ±0.00 c	0.63 ±0.00 c

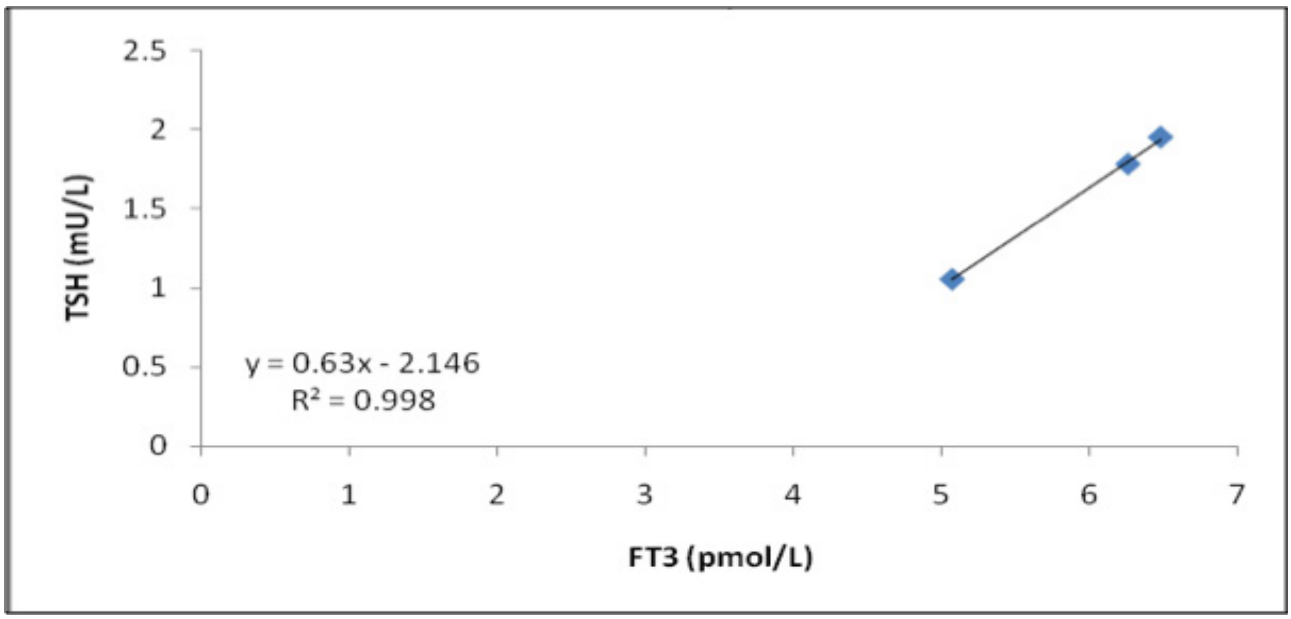

Figure 13. Significant positive correlation (p=<0.05) between FT3 and TSH (where FT3 was normal, FT4 decreased and TSH levels normal in peri-pubertal subjects).

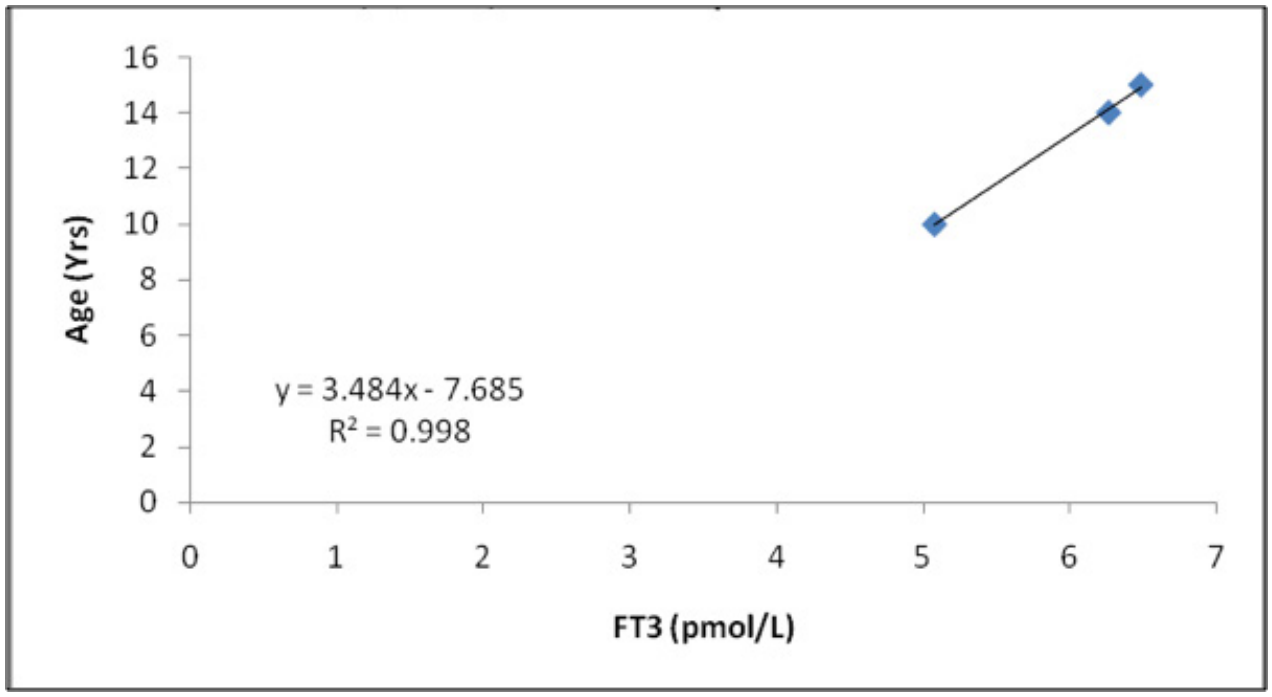

Figure 14. Significant positive correlation (p=<0.05) between FT3 and Age (where FT3 was normal, FT4 decreased and TSH levels normal in peri-pubertal subjects).

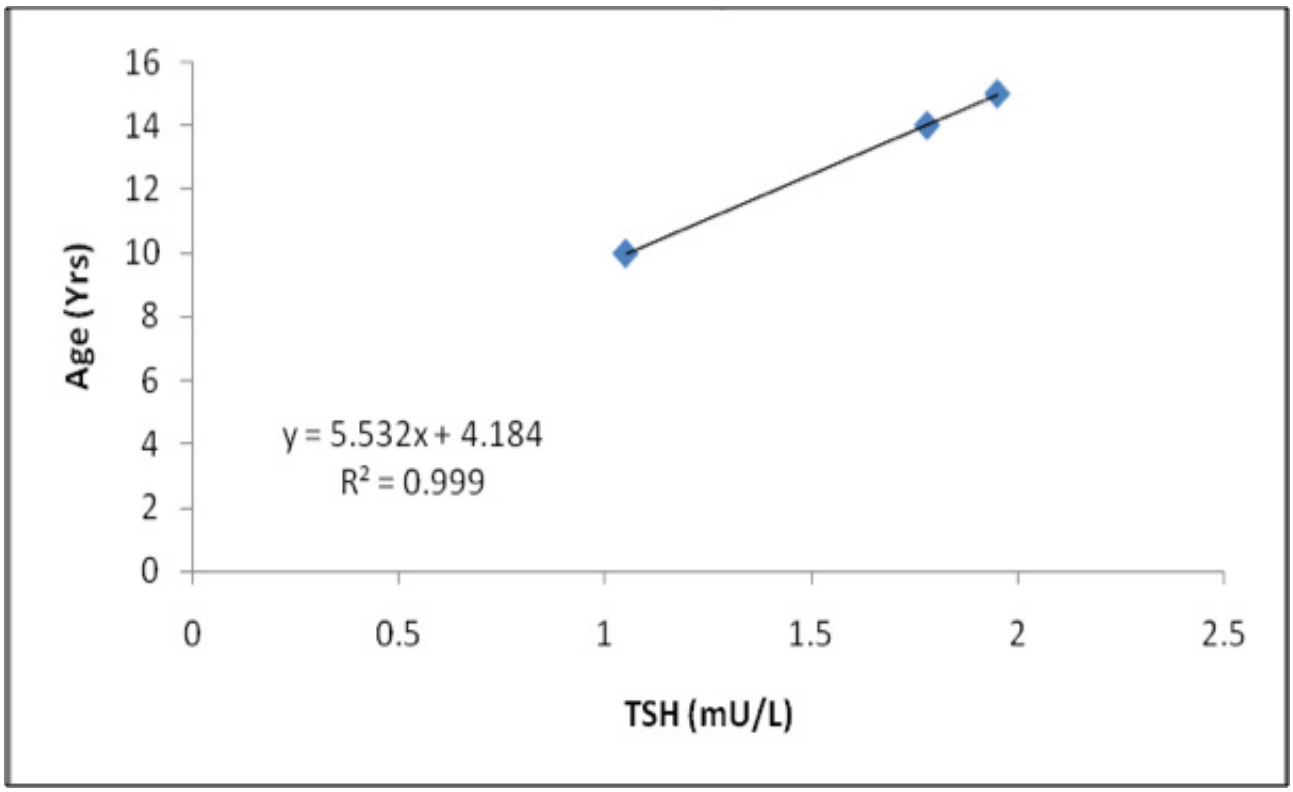

Figure 15. Significant positive correlation (p=<0.05) between TSH and Age (where FT3, TSH were normal while FT4 levels were low).

Pubertal subjects

Serum samples of 37 individuals of this age group (16-19 years) were evaluated for thyroid function. Out of which 25 individuals showed normal thyroid activity, and FT4 and TSH had significant ($p<0.05$) negative correlation ($r= -0.3799$) with them (Figure 16), there was no significant correlation between other parameters. With respect to thyroid dysfunction 08 different patterns of disturbance were found (Table5). In the first condition, results indicated sub-clinical hypothyroidism where, FT3 and FT4 were normal while TSH was high and had highly significant ($p<0.001$) variation, although FT3 and FT4 were normal but they also showed highly significant variation ($p<0.001$). The second condition revealed FT3 toxicosis with high FT3 and normal FT4 and TSH. As FT3 was high thus varied highly significantly ($p<0.001$), FT4 varied highly significantly ($p<0.001$), while TSH had more significant ($p<0.01$) variation. In the third abnormal condition FT3 and TSH were normal, while FT4 was low (hypothyroxinemia). FT3 and TSH varied non-significantly while FT4 varied highly significantly ($p<0.001$) from normal subjects. In the fourth condition FT3 and TSH were normal FT4 was higher than normal range indicating hyperthyroxinemia. All three hormonal parameters showed varied from normal, FT3 and FT4 varied highly significantly ($p<0.001$) where TSH had a significant variation ($p<0.05$). The fifth condition exhibited all three parameter low FT3 and TSH, whereas FT4 was more than normal. Highly significant ($p<0.001$) variations were seen in all three hormonal parameters. In the sixth condition, FT3 was below normal and FT4 and TSH were within normal limits. All three hormonal parameters differed highly significantly ($p<0.001$) from normal group. The seventh condition had FT3 elevated more than normal, FT4 was normal and TSH was below normal limits (primary hyperthyroidism), all three parameters had highly significant differences from normal group. The final condition revealed FT3 and FT4 more than normal and TSH was below normal (hyperthyroidism). In this case as all three hormonal parameters showed highly significant ($p<0.001$) variation from normal group.

Table5. Distribution of different abnormal conditions in pubertal subjects (High: ↓, Low: ↓, Normal:↓, Significant: a (p<0.05), More significant: b (p<0.01), Highly significant: c (p<0.001), Non-significant: d).

Pathological Conditions	Group	n	Age	FT3	FT4	TSH
	Normal	25	17.12 ±0.29	4.72 ±0.12	15.76 ±0.38	1.95 ±0.16
01	↓FT3, ↓ FT4, ↓TSH	1	18.00 ±0.00 b	4.25 ±0.00 c	17.93 ±0.00 c	4.85 ±0.00 c
02	↓FT3, ↓FT4, ↓TSH	1	19.00 ±0.00 c	7.62 ±0.00 c	19.17 ±0.00 c	1.38 ±0.00 b
03	↓FT3, ↓ FT4, ↓TSH	4	17.00 ±0.71 d	4.29 ±0.32 d	11.09 ±0.37 c	1.79 ±0.42 d
04	↓FT3, ↓FT4, ↓TSH	1	16.00 ±0.00 c	5.84 ±0.00 c	22.34 ±0.00 c	2.30 ±0.00 a
05	↓ FT3, ↓FT4, ↓ TSH	1	17.00 ±0.00 d	2.13 ±0.00 c	34.95 ±0.00 c	0.01 ±0.00 c
06	↓ FT3, ↓FT4, ↓TSH	2	17.00 ±0.00 d	2.37 ±0.22 c	13.71 ±1.04 c	1.19 ±0.80 c

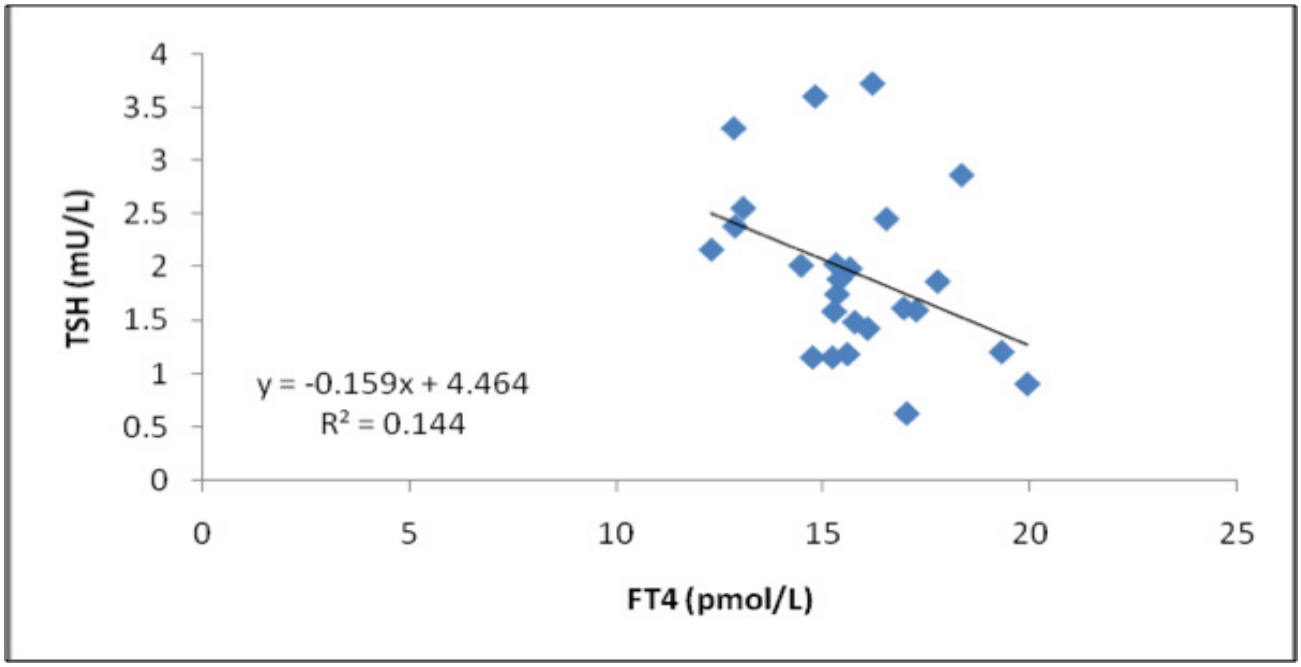

Figure 16. Significant negative correlation (p=<0.05) between FT4 and TSH (pubertal normal subjects).

DISCUSSION

In the study under discussion, hypothyroidism was 2.88%, and hyperthyroidism was to be 3.84%. An earlier study reported an overall 40.18 % prevalence of thyroid disorders in Rawalpindi Islamabad, which is consistent with results of the current study (40.4%) [11]. Hypothyroidism was found in all age groups, except in pre-pubertal stage. Furthermore, no male individual from any age group in this study showed hypothyroidism. In another study in America it was found that, 8.9% people were hypothyroid and 1.1% hyperthyroid [12]. Sub-clinical hypothyroidism was found in almost all age groups, and at a quite high frequency. The present study showed sub-clinical hypothyroidism to be 7.05%. Sub-clinical hypothyroidism is more prevalent over sub-clinical hyperthyroidism [11]. The prevalence of sub-clinical hypothyroidism ranges up to 10% [13]. In a recent Indian study, the prevalence of sub-clinical hypothyroidism was reported to be 9.5% [14]. The risk of developing sub-clinical hypothyroidism into hypothyroidism is 2.6% to 4% per year [15]. The sub-clinical hyperthyroidism in this study was 2.88%, and was

distributed in almost all age groups, whereas in an Indian study it was 1.2%. Primary hyperthyroidism was found in 1.92% subjects, and was not present in younger subjects, with over all more prevalence in males (3.62%). Distribution of this condition started from pubertal subjects and found in almost all age groups, with highest frequency in pubertal subjects (5.40%). Primary hypothyroidism and primary hyperthyroidism were found to be 7.05% and 1.92% respectively primary hypothyroidism had distribution in all age groups, and prevailed at higher levels in 31-40 year age group. In earlier studies, it was found that people of 30-45 year were most affected [16]. Low iodine intake enhances the TSH sensitivity and positive influence of growth factors was involved in the physiological regulation of thyroid growth. The outcome of such stimulation may be substantial in girls with mild iodine deficiency leading to the development of goiter during mid to late puberty [17]. Epidemiological studies have shown that pattern of thyroid dysfunction in a community is largely determined by iodine intake level [18]. In iodine deficient communities, incidence of hypothyroidism is low while nontoxic goiter, and hyperthyroidism due to toxic nodular goiter, is common and increases with age. Reported that iodine deficiency, thyroid autoimmunity, infection and previous irradiation are the common etiological factors of thyroid disorders.

CONCLUSION

About 200 million people in the world have some form of thyroid disease. Thyroid disorders are common endocrine disorders encountered in Pakistan. This disease can't be prevented but early diagnosis can reduce complications that can be life threatening. Thyroid patients require life-long monitoring. Further thyroid research is necessary to continue the progress that has been made in diagnosis and treatment. Although there are effective treatments for most thyroid disorders, the underlying causes require further investigation. The continued study of the thyroid may yield important knowledge in other areas of medical science. The role of new treatments for thyroid cancer has to be defined and improved. To achieve these goals, public support of thyroid research is vital.

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