Influence of Thyroid Dysfunction on Electrolyte Levels of Outdoor Patients of Tertiary Care Hospitals

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Abstract

The study aimed to evaluate the impact of thyroid dysfunction on serum electrolyte levels in individuals visiting outpatient departments of tertiary care institutes. The study included 88 participants who were divided into five groups: NTF, Hypo-TF, Hyper-TF, NTFT, and HC. The thyroid hormones T_3, T_4, and TSH and electrolyte levels, were analyzed in the sera obtained from the control and study groups. The results showed a statistically significant variation in thyroid hormone levels among the different study groups of both genders. The Hyper-TF group had higher levels of T_3 and T_4, while the TSH level was higher in the Hypo-TF group of both genders. The age of the patients and duration of treatment did not significantly affect the thyroid hormones and electrolyte levels of the study groups. The Na^+ level was positively correlated with T_3 and T_4 levels of the control and Hypo-TF groups and TSH of the Hyper-TF group. The K^+ level was negatively correlated with the thyroid hormone levels of each group except TSH of the Hyper-TF group. The study found that thyroid dysfunction significantly affected the thyroid hormone levels in male and female patients, which were positively correlated with Na^+ level and negatively correlated with K^+ level.

Keywords: Thyroid dysfunction, Electrolyte balance, Hypothyroidism, Hyperthyroidism, Thyroid-stimulating hormone, Triiodothyronine

1. Introduction

Thyroid hormones including thyroxin (T_3) and triiodothyronine (T_4) are secreted in the human body from thyroid glands. These are tyrosine-based hormones that stimulate protein synthesis at the transcriptional level (Klein & Ojamaa, 2001; Satyanarayana & Chakrapani, 2006). Thyroid hormones also facilitate growth by improving the nitrogen balance and stimulate lipid metabolism (Smith et al., 2002; Unnikrishnan & Menon, 2011). They act on the central nervous system (CNS) and are essential for the normal growth of the brain (Bernal, 2005; Schiera et al., 2021; Smith et al., 2002). Thyroid hormones also control the growth of the lungs and enhance the velocity of respiration (Fisher, 1996). These are also involved in the mineral metabolism, development of bone, and maturation of skeletal muscles (Cardoso et al., 2014; Dhanwal, 2011).

The abnormalities associated with thyroid functions are Goiter (irregular rise in the size of the thyroid gland), hyperthyroidism (an increased production of T_3, T_4 by the thyroid gland), and Hypothyroidism (an underproduction of T_3, T_4 by the thyroid gland) (Braverman, 2002; Cappola &

Ladenson, 2003; Roti & Uberti, 2001; Stanbury et al., 2013). Abnormally increased T_3 and T_4 levels and decreased levels of TSH lead to Graves' disease (Brent, 2008).

Since iodine is vital for the biosynthesis of thyroid hormones, its deficiency is the most frequent cause of hypothyroidism (Zimmermann & Boelaert, 2015). The incidence of thyroid dysfunction may disturb diabetes control. Hyperthyroidism is usually related to falling glycemic control and increased requirement of insulin. There is rapid gastrointestinal (GI) absorption of glucose and perhaps increased resistance to insulin (Kumar et al., 2018). As thyroid hormones increase the heart rate or cardiac output, any alteration in the concentration of T3 and T4 may lead to heart failure (Klein & Ojamaa, 2001).

Previous studies report controversies in the serum sodium ion level of hypothyroid patients. In most of the studies, relatively lower serum sodium and potassium ion levels have been reported in hypothyroid patients (Abuzaid & Birch, 2015; Hanna & Scanlon, 1997; Murgod & Soans, 2012; Schwarz et al., 2012). However, no relationship has been reported between low serum sodium ions and high TSH levels.

There have been no reports on the prevalence and effects of thyroid abnormalities in individuals visiting outpatient departments of Tertiary Care Institutes in Pakistan. This study aimed to investigate the impact of thyroid dysfunction on electrolyte balance in individuals visiting the Outpatient Department of Multan Institute of Nuclear Medicine and Radiotherapy, Multan, Pakistan. Additionally, the study examined the relationship between age, duration of treatment, thyroid dysfunction, and electrolyte balance.

2. Materials and Methods

Overall 88 participants were included in the study that was distributed in two major groups: a healthy control group consisting of 16 healthy individuals without any signs or complaint of thyroid dysfunction and thyroid dysfunction (TDF) group consisting of 72 individuals who approached the outpatient department (OPD) of Multan Institute of Nuclear Medicine and radiotherapy (MINAR) Multan with a complaint of some thyroid problem during October 2019 to April 2020. The TDF group was subdivided into four groups based on thyroid function: 1) An NTF group consisting of 21 outdoor patients with normal thyroid function, 2) Hypo-TF consisting of 15 outdoor patients with hypothyroid function, 3) Hyper-TF consisting of 15 outdoor patients with hyperthyroid function, and 4) NTFT group consisting of 21 outdoor patients recovered to normal thyroid function after treatment. The study was approved by the Advanced Studies and Research Board and Institutional Ethical Committee of Bahauddin Zakariya University, Multan (No. Biochem./12/2019, Dated 10.10.2019). The participants were informed about the purpose of the research project, written consent was taken and a questionnaire based on the patient's history was filled by each participant. The individuals with a history of renal, hepatic or cardiovascular abnormalities were excluded from the study. The blood samples were collected from the participants, the blood plasma and the sera were analyzed for thyroid function and electrolyte balance respectively. The data were statistically analyzed by one-way ANOVA (analysis of variance) to find out the variation in the level of thyroid hormones and electrolytes.

The blood sample (5 mL) was collected from each participant in EDTA containing plasma tubes and heparin containing serum tubes and centrifuged at 3000 × g for 20 min to obtain plasma and serum respectively. The plasma was subjected to analysis of thyroid hormones and the sera were analyzed for electrolyte level immediately after centrifugation.

Thyroid hormone level was determined by chemiluminescent immunoassay based on the Ag-Ab complex using the standard protocols given in the commercially available diagnostic kit (Thyroid hormone kit, Roche Diagnostics, Switzerland) (Zhao et al., 2009). The sample was added to a solid

stationary phase coated with antigen. After incubation at room temperature for 15 min, the substrate was added and the thyroid hormone level was measured in terms of the relative light units by measuring the intensity of light produced by the formed complex using a Chemiluminescent analyzer (COBAS e411 Analyzer, Hoffmann-La Roche Ltd., Switzerland).

The levels of serum electrolytes including Na^+ and K^+ were estimated by the Ion-Selective Electrode technique (ISE) (Pungor, 1998). This technique uses the ion-selective probe which is used to identify and quantify every single ion, dissolved in the solution. It is based on the principle of the Nernst Equation. It measures both positive and negative ions without the interference of other dissolved components in the sample. The tests were performed using the standard operating procedures given with the an ISE analyzer (Roche Diagnostics, Cat. AVLGD-5043, Thermo Fisher Scientific Inc. UK).

Statistical analysis

The results were presented as mean± S.D. The statistical software (SPSS version 24) One-way analysis of variance (ANOVA) was used to determine the significance of variance among the study groups.

3. Results and Discussion

The experimental values of the studied thyroid hormones and serum electrolytes of the control and study groups of male and female individuals are presented in Table 1.

Table 1. Experimental values of thyroid hormones in normal individuals and thyroid patients

Sr. No	Healthy control n=16 Male: 18% Female: 81%			*Hypo-TF n=15 Male: 20% Female: 80%			Hyper-TF n=15 Male: 20% Female: 80%			NTF n=21 Male: 14% Female: 86%			NTFT n=21 Male:14% Female: 86%		
	T_3 (nmol/L)	T_4 (nmol/L)	TSH (µlU/ml)	T_3 (nmol/L)	T_4 (nmol/L)	TSH (µlU/ml)	T_3 (nmol/L)	T_4 (nmol/L)	TSH (µlU/ml)	T_3 (nmol/L)	T_4 (nmol/L)	TSH (µlU/ml)	T_3 (nmol/L)	T_4 (nmol/L)	TSH (µlU/ml)
1	1.1	170	0.4	0.4	35	59.1	5.9	177	0.01	2.3	93	0.2	2.1	112	2.2
2	2.4	110	0.6	0.1	55	56.1	9.9	240	0.01	2.4	145	1.9	2.2	108	0.5
3	1.6	127	1.2	0.8	35	53.3	3.7	209	0.07	1.8	101	2.4	1.4	112	0.4
4	2.2	113	0.2	0.8	40	46.3	4.9	360	0.05	1.8	98	0.8	1.3	130	0.3
5	2.0	102	1.5	0.5	60	39.4	4.6	221	0.01	1.6	102	0.2	1.4	91	0.4
6	1.9	121	1.8	0.2	41	57.0	4.1	220	0.06	1.7	123	0.8	1.4	66	0.5
7	1.9	138	1.3	0.5	31	52.0	4.7	290	0.04	1.8	72	4.0	1.1	93	2.0
8	1.9	124	2.2	0.7	36	45.0	4.2	240	0.02	1.7	82	0.9	1.8	126	0.2
9	2.1	129	0.6	0.9	43	48.0	4.7	300	0.05	1.8	80	0.2	1.5	111	2.5
10	1.3	121	1.3	0.6	32	55.0	3.8	210	0.08	2.6	77	3.6	1.9	95	1.4
11	1.7	160	0.5	0.3	39	53.0	4.5	289	0.07	1.6	109	0.6	1.4	103	0.7
12	1.5	122	2.1	1.0	39	23.0	3.6	204	0.06	2.3	110	3.1	1.3	68	2.8
13	2.2	120	0.5	0.9	37	34.8	6.1	189	0.03	1.9	102	0.2	1.8	101	0.3
14	1.7	123	0.8	0.5	35	55.0	5.1	200	0.05	1.6	113	1.1	1.8	148	0.1
15	1.8	72	4.0	0.6	51	29.5	8.6	200	0.02	1.5	69	2.3	2.0	129	2.6
16	1.5	120	3.0							1.9	73	1.8	2.2	127	0.3
17										2.3	103	1.2	3.0	96	0.1
18										1.8	125	0.5	1.4	75	0.8
19										1.7	87	0.4	2.2	125	0.3
20										1.6	87	0.9	2.1	167	0.2
21										1.8	85	1.5	2.1	115	2.1
Mean ±SD	1.8±0.34	123.2±21.89	1.37 ±1.044	0.58 ±0.26	40.6 ±8.44	47.1 ±10.8	5.22 ±1.80	236.6 ±51.0	0.04 ±0.02	1.88 ±0.3	97 ±19.6	1.36 ±1.14	1.78 ±0.45	109.4 ±24.8	0.98 ±0.95

*Hypo-TF: Outdoor patients with hypothyroid function, Hyper-TF: Outdoor patients with hyperthyroid function, NTF: Outdoor patients with normal thyroid function, NTFT: Outdoor patients recovered to normal thyroid function after treatment

The levels of T_3, T_4, and TSH in the healthy control and thyroid dysfunction groups range from 0.59±0.26 to 5.23±1.81, 40.60±8.44-236.60±51.0 nmol/L, and 0.05±0.023-47.10±10.8 µlU/ml respectively. A statistically significant variation ($p<0.05$) was observed in the studied hormone levels of various study groups. Comparatively higher levels of T_3 and T_4 were observed in the individuals of the Hyper-TF group while that of TSH was found to be higher in the Hypo-TF group of both male (Figure 1a-c) and female (Figure 1f-h) individuals.

The levels of Na^+ and K^+ of the control and thyroid dysfunction groups ranged from 126.7±7.90 to 141.4±2.79 and 4.11±0.18-5.86±0.66 mmol/L respectively. The Na^+ levels of the study groups were statistically similar to that of the healthy control group except those of the Hypo-TF group that were comparatively lower than other groups of both male (Figure 1d) and female (Figure 1i) individuals. The serum levels of K^+ of the healthy control group were found to be statistically different from the thyroid dysfunction groups with comparatively higher values in Hyper-TF groups of both male (Figure 1e) and female individuals (Figure 1 j).

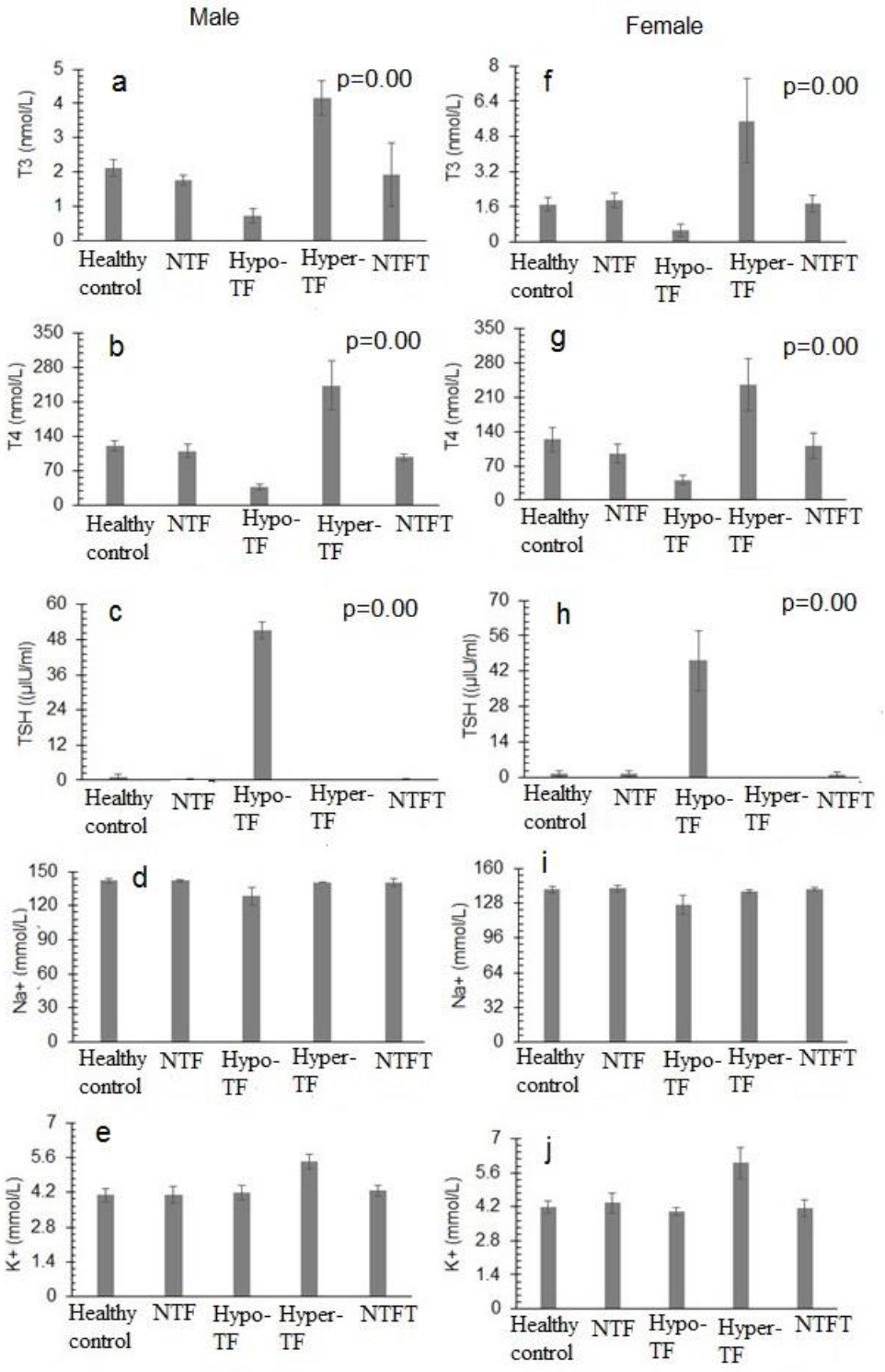

Figure 1. The levels of thyroid hormones including T_3, T_4 and TSH and electrolytes including Na^+ and K^+ in male a-e), female individuals f-j)

The age-dependent response of the studied thyroid hormones and serum electrolytes of the control and study groups are presented in Figure 2a-e.

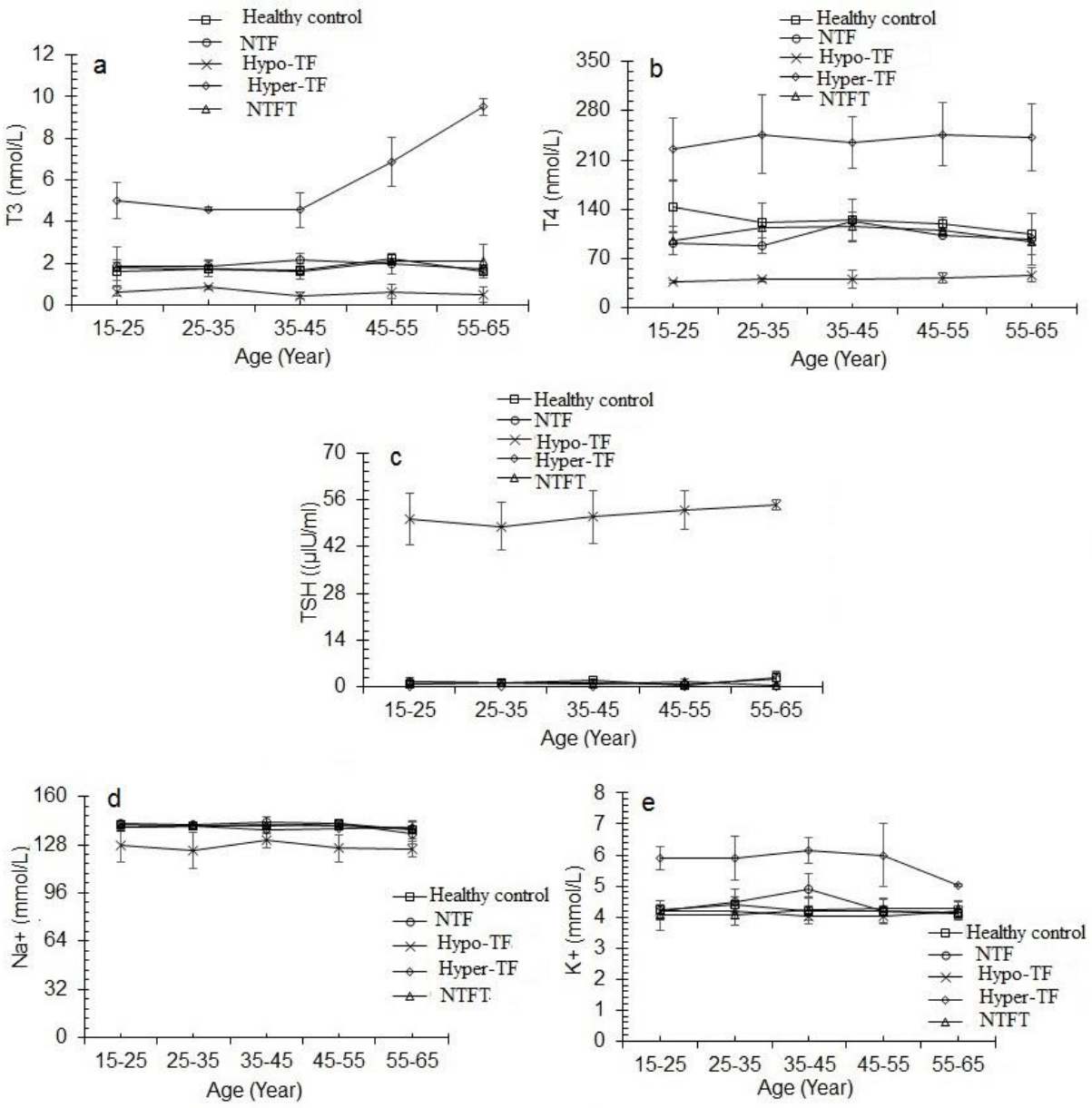

Figure 2. The levels of thyroid hormones including T_3, T_4, and TSH, and electrolytes including Na^+ and K^+ in normal individuals and thyroid patients with different age group

a) T_3, b) T_4, c) TSH, d) Na^+ and e) K^+

No significant age-dependent variation ($p>0.05$) in the levels of the studied thyroid hormones and serum electrolytes was observed in the control and thyroid dysfunction groups except the T_3 level of the Hyper-TF group that was raised to 10 nmol/L after the age of 35 years. However, the serum K^+ level of the Hyper-TF group was decreased to 5 mmol/L after the age of 45 years.

The levels of the studied thyroid hormones and serum electrolytes of the thyroid dysfunction groups under different durations of treatment are presented in Figure 3a-e.

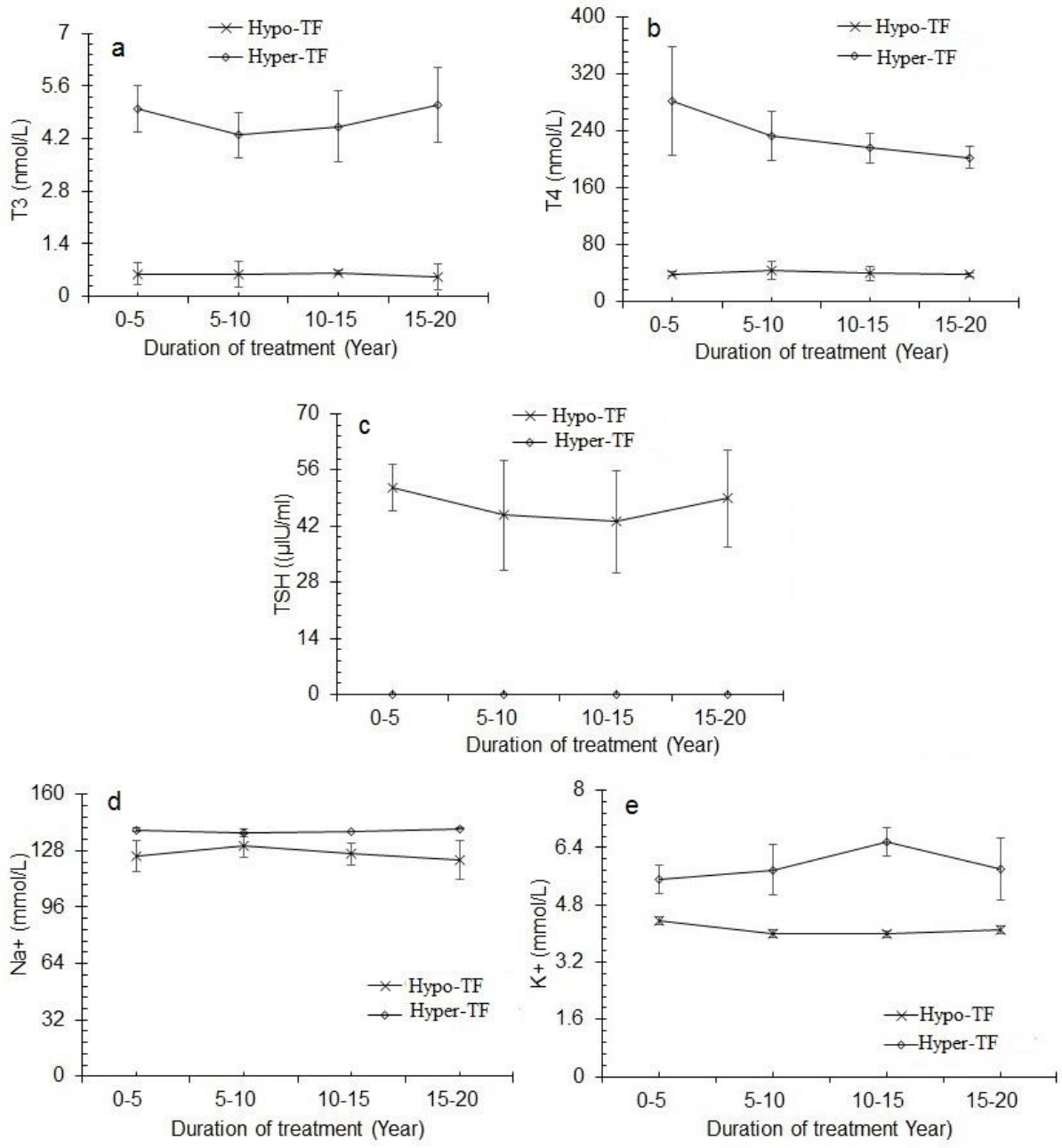

Figure 3. The levels of thyroid hormones including T_3, T_4, and TSH and electrolytes including Na^+ and K^+ in thyroid patients in the various duration of treatment a) T_3, b) T_4, c) TSH, d) Na^+ and e) K^+

The results showed a non-significant effect of duration of treatment on the studied thyroid hormones and serum electrolyte levels of both the Hypo-TF and Hyper TF groups. A slight decrease was observed in T_3 and T_4 levels of the Hyper-TF group, and TSH and K^+ levels of the Hypo-TF group under treatment for 5-10 years.

The correlation between the thyroid hormones and serum electrolytes of healthy control and thyroid dysfunction groups is presented in Figure 4a-i.

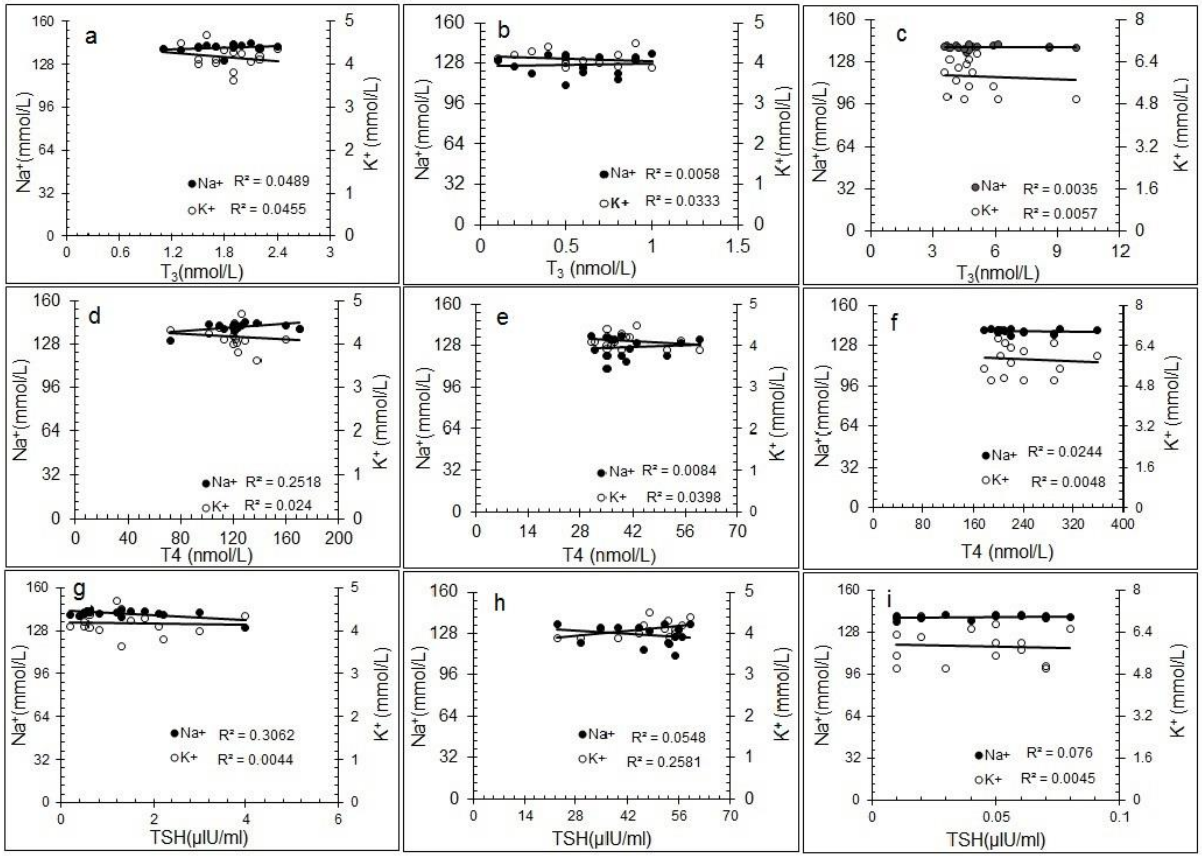

Figure 4. Correlation of electrolytes levels including Na^+ and K^+ with thyroid hormones levels of healthy control individuals and study groups a, b, c: T_3, d, e, f: T_4 and g, h, i: TSH of control, Hypo-TF, and Hyper-TF respectively.

The healthy control and Hypo-TF groups showed a positive correlation of Na^+ with T_3 and T_4 levels and a negative correlation of K^+ with T_3 and T_4 levels. The individuals of the Hyper-TF group showed a negative correlation between the studied serum electrolytes and thyroid hormone levels. However, the TSH level of both groups was negatively correlated with the Na^+ levels but positively correlated with and K^+ level.

The results showed significantly elevated levels of T_3 and T_4 and decreased levels of TSH in male and female individuals of the Hyper-TF group than those of the healthy control group. The hypo-TF group showed comparatively lower levels of T_3 and T_4 and elevated levels of TSH in individuals of both genders. The Elevation in T_3 and T_4 levels of hyperthyroid patients may be due to excessive synthesis and secretion of these hormones from thyroid glands. However, the elevated levels of TSH in hypothyroid patients may be attributed to the excessive excretion of this hormone from the hypothalamus to stimulate the synthesis of T_3 and T_4 from the thyroid gland to compensate for the hypothyroid condition. An elevation in T_3 level and decline in K^+ level of Hyper-TF group after the age of above 35 years may be attributed to the age-dependent dysfunction of thyroid glands. The slight decrease in T_3 and T_4 levels of the Hyper-TF group, and TSH and K^+ levels of the Hypo-TF group under treatment for 5-10 year may be due to the recovery of thyroid function after treatment.

Relatively, higher levels of serum Na^+ and K^+ in hyperthyroid patients of both genders indicate an association between thyroid dysfunction and serum electrolyte level. However, the exact mechanism of thyroid-dependent variation in electrolyte levels is not clear. Hypothyroidism is the most prevalent

thyroid dysfunction in females that causes a range of clinical complications. Previously it has been reported that hypothyroidism is more frequent in females than males, and its prevalence increases with age (Vanderpump, 2011). Our results showed almost similar trends of thyroid hormones in both male and female patients with thyroid dysfunction. Our research work is in agreement with the previous studies that reported an inverse correlation between serum sodium levels and TSH levels and a positive correlation between K^+ and TSH levels (Bharti et al., 2015; Murgod & Soans, 2012a; Schwarz et al., 2012). Hyponatremia has been directly associated with hypothyroidism. It has been hypothesized that in the majority of tissues the action of Na-K ATPase is synchronized by T_3, T_4, and TSH levels. In hypothyroidism, this enzyme is affected due to decrease potassium levels that result in water accumulation into the cells leading to edema (Hanna & Scanlon, 1997; Murgod & Soans, 2012). The results were also in agreement with the previous findings that females exhibit a higher susceptibility to hypothyroidism and inverse correlation between serum sodium level and TSH levels and positive correlation between K^+ and TSH level (Kataraki 2019, Karmacharya, Bhattarai et al. 2022, Namani and Laxmi Narayana Sripuram 2022).

4. Conclusion

Thyroid dysfunction was more frequent in females than male individuals with almost similar trends of thyroid hormones and serum electrolytes. Comparatively elevated levels of TSH and low levels of T_3 and T_4 were observed in hypothyroid patients and vice versa in hyperthyroid patients. Serum Na^+ and K^+ levels were directly correlated with T_3 and T_4 inversely correlated with TSH levels. An age-dependent elevation in T_3 level was observed in hyperthyroid patients while no significant variation in thyroid hormones and serum electrolyte levels was found with an increase in the duration of treatment of both hyperthyroid and hypothyroid o patients. The data would be a significant contribution to the literature regarding the physiological association of thyroid dysfunction with other abnormalities.

5. Acknowledgments

The authors are grateful to The Department of Biochemistry, Bahauddin Zakariya University, Multan, and Multan Institute of Nuclear Medicine and Radiotherapy, Multan, Pakistan for providing the facilities to conduct this study.

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