



Determination of Serum Thyroid Hormones and Electrolytes in Hypothyroid and Hyperthyroid Females-A Case Control Study in Lahore, Pakistan

Hipotiroid ve Hipertiroid Kadınlarda Serum Tiroid Hormonları ve Elektrolitlerinin Belirlenmesi-Lahor, Pakistan'da Bir Vaka Kontrol Çalışması

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Abstract

Objective: This study aimed to determine the correlation between serum electrolytes and TSH in patients with hypothyroidism and hyperthyroidism.

Material and Methods: A total of 160 (80 hypothyroid and 80 hyperthyroid) patients and 80 age and gender matched controls were enrolled in this study, which was performed between September 2017-February 2018. Of the venous blood, 3 mL was collected from each study participant, for measurement of thyroid hormones (T3, T4, and TSH) and electrolytes (Na, K and Ca).

Results: Serum calcium was observed to be significantly high in hyperthyroid patients as compared to their controls. Serum sodium and potassium levels were not found to differ significantly among hyperthyroid and hypothyroid patients compared to that in their controls. Patients with hyperthyroidism showed significant negative correlation of TSH with calcium and a non-significant positive correlation with sodium and potassium. The correlation of TSH with calcium was positive while that with potassium and sodium was negative in hypothyroid patients, though this co-relation was statistically non-significant.

Conclusion: This study found high serum calcium levels in hyperthyroid patients. A significantly negative correlation was found between TSH and calcium level in hyperthyroidism.

Keywords: Hyperthyroidism; hypothyroidism; thyroxine; calcium; potassium

Özet

Amaç: Bu çalışmada, hipotiroidi ve hipertiroidi hastalarında serum elektrolitleri ve TSH arasındaki korelasyonun belirlenmesi amaçlanmıştır.

Gereç ve Yöntemler: Eylül 2017-Şubat 2018 tarihleri arasında yapılan bu çalışmaya, toplam 160 (80 hipotiroidi ve 80 hipertiroidi) hasta ile yaş ve cinsiyeti eşleştirilmiş 80 kontrol dâhil edildi. Tiroid hormonlarının (T3, T4 ve TSH) ve elektrolitlerinin (Na, K ve Ca) ölçümü için her bir katılımcıdan 3 mL venöz kan alındı.

Bulgular: Hipertiroidili hastalarda serum kalsiyumun kontrollerine göre anlamlı derecede yüksek olduğu gözlemlendi. Serum sodyum ve potasyum düzeylerinin, hipertiroidi ve hipotiroidi hastaları arasında kontrollerine göre anlamlı derecede farklı olmadığı bulundu. Hipertiroidi hastalarında TSH ile kalsiyum arasında anlamlı negatif korelasyon, sodyum ve potasyum ile anlamlı olmayan pozitif korelasyon saptandı. Hipotiroidi hastalarında TSH'nin kalsiyum ile korelasyonu pozitif, potasyum ve sodyum ile korelasyonu negatif idi ama bu korelasyonlar istatistiksel olarak anlamlı değildi.

Sonuç: Bu çalışmada, hipertiroidili hastalarda serum kalsiyum seviyelerinin yüksek olduğu bulundu. Hipertiroidizmde TSH ile kalsiyum düzeyi arasında anlamlı bir negatif korelasyon olduğu görüldü.

Anahtar kelimeler: Hipertiroidi; hipotiroidi; tiroksin; kalsiyum; potasyum

Introduction

Thyroid hormones are essential for body temperature regulation, hemodynamics,

metabolic functions, protein synthesis, and maintenance of electrolyte balance (1,2). About 3-10% of the population, globally, are

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Received: 31/10/2018 **Received in revised form:** 20/12/2018 **Accepted:** 29/12/2018 **Available online:** 20/03/2019

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Turkish Journal of Endocrinology and Metabolism published by Türkiye Klinikleri

affected by hypothyroidism; the rate of prevalence is higher in females (3,4,13). In Pakistan, the frequency of hypothyroidism is 2% higher than that of hypothyroidism (5). Thyroid diseases are among the most common health problems in northern Pakistan, with the frequency being higher in the females (5.1%) than in males (6).

Electrolytes play an essential role in many functions of the body like control of fluid level, pH balance, and blood coagulation. Electrolyte balance is very important for normal functioning of cells and organs in the human body (7). Sodium (Na), calcium (Ca), and potassium (K) are the common electrolytes analyzed in blood (8,9).

Thyroid hormones affect the structure, development, and hemodynamics of kidney, along with the GFR, the transport along the nephron, as well as Na and water homeostasis, though renal failure may lead to thyroid disorders (10). Hypothyroidism decreases the renal size and weight, tubule length, and diameter and to some level, glomerular volume (11). Conversely, in patients with hyperthyroidism, renal to body weight ratios raise to as high as 30% (12). Although the exact mechanism of changes in the kidney is unknown, there is evidence of direct activation of the renin-angiotensin-aldosterone system by thyroid hormones (2). Thyroid hormones directly elevate serum Ca and phosphorus (P) levels by stimulating bone resorption. Low levels of thyroid hormone in hypothyroidism lead to hypocalcemia (13). Increased renal water retention, mediated by vasopressin, is an adverse effect of hypothyroidism (14). The activity of Na-K pump is also regulated by thyroid hormones in most of the tissues (2). Renal dysfunction and electrolyte imbalance may be associated with thyroid disorders (15,16).

Begic-Karup et al. (17) observed an increase in serum Ca in subjects with hyperthyroidism. Thyroid dysfunction results in increased levels of phosphate and calcium (18). Hypothyroidism forms one of the reasons for decreased Na levels. Assessment of patients with hyponatremia requires the measurement of Thyroid Stimulating Hormone (TSH) (19). On the other side, hypokalemia is observed in patients with thyrotoxicosis (20). Although the association between thyroid hormones and kidney func-

tions is well established, but the relationship between thyroid hormones and electrolytes has not been widely studied in the Pakistani population. Therefore, this study was designed to determine the serum Ca, Na, and K levels and to correlate the levels of these electrolytes with TSH in patients with hypothyroidism and hyperthyroidism.

Material and Methods

This is a case-control study conducted in the Department of Chemical Pathology in Jinnah Hospital, Lahore between September 2017 and February 2018. One hundred and sixty female patients (80 hypothyroid and 80 hyperthyroid) attending the outpatient department of Jinnah Hospital and 80 apparently healthy females from same population acting as controls, were enrolled in this study. The clinical history of participants was recorded on a structured questionnaire. The study was done in accordance with the "Principles of the Helsinki Declaration". Ethical approval from the Institutional Review Board (IRB Faculty of Allied Health Sciences, University of Lahore) was taken on 16th August, 2017 (Approval number: IRB-UOL-FAHS/266-IA).

Selection Criteria

Subjects between 18-60 years of age, recently diagnosed with hypothyroidism (TSH >5.6 mIU/mL, T3 <2.5 pg/mL and T4 <0.61 ng/dL) and hyperthyroidism (TSH <0.3 mIU/mL, T3 >3.9 pg/mL and T4 >1.12 ng/dL) were included in this study as patients. Patients with subclinical thyroid disorder; kidney, liver and bone diseases; diabetes mellitus; children; and subjects who were on medication or mineral supplements that might change the levels of serum electrolyte, were excluded from the study.

Sample Collection

After obtaining written informed consent, 3 mL of blood samples was collected from the cubital vein and stored in a gel vacutainer. After clotting, the vial was centrifuged at 3000 revolutions per min (rpm) for 10-15 min at 25 °C. Serum T3, T4, and TSH levels were analyzed by enzyme-linked immunosorbent assay (ELISA) technique. Serum levels of Na, K, and Ca were measured by RANDOX manufacturer kit (Antrim,

Northern Ireland) using chemistry analyzer strip reader (huma Reader H) from Germany.

Data Analysis

Results were presented as mean±SD for quantitative variables. One way ANOVA was applied to find the difference of mean in quantitative variables between cases (hypothyroid and hyperthyroid) and controls. Tukey's post-hoc test was used to confirm where the difference existed between groups. All correlation data were analyzed by spearman correlation test using statistical software SPSS Version 25. A p-value of less than 0.05 was considered statistically significant.

Results

The mean age of the studied subjects was 40.02±11.3 years. The mean age of hypothyroid, hyperthyroid cases, and controls were 38.13±10.6, 40.53±12.1 and 41.37±10.9 years, respectively. There was no statistically significant age difference between the cases and controls (p>0.05).

Thyroid and electrolyte profile in cases and healthy controls

The mean level of TSH in healthy controls, hyperthyroid, and hypothyroid patients was 2.54±1.6, 0.32±0.6, and 6.67±0.9 mIU/l, respectively. Serum T3 levels were found to be 3.05±0.4, 5.11±1.1, and 1.85±0.5 pg/mL in the controls, hyperthyroid, and hypothyroid patients, respectively. Mean T4 levels were 0.90±0.1, 2.08±0.7 and 0.49±0.1 ng/dL in controls, hyperthyroid, and hypothyroid patients, respectively. Among the measured electrolytes, the Na and K levels in serum were observed to be non-significantly different among hypothyroid, hyperthyroid, and control subjects (p>0.05) (Figure 1). There was a statisti-

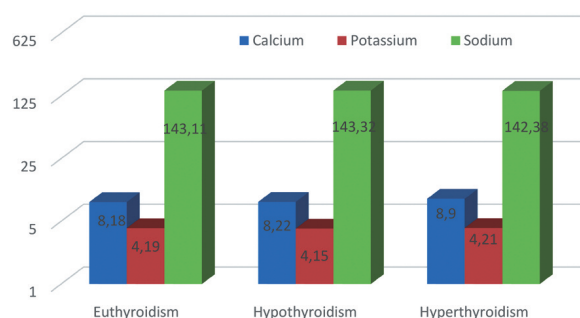


Figure 1: Comparison of electrolyte profile in hyperthyroid, hypothyroid patients and controls.

cally significant difference between the mean Ca levels among the groups (p=0.004). Tukey's post-hoc test revealed that the mean Ca was statistically significantly higher in hyperthyroid (8.90±1.4 mg/dL) patients as compared to that in the hypothyroid patients (8.22±1.6 mg/dL p=0.015) and healthy controls (8.18±1.6 mg/dL p=0.009). There was no statistically significant difference between the hypothyroid and control groups (p=0.983). The results are summarized in Table 1 and Figure 2.

Correlation of TSH with electrolyte profile in hypothyroid and hyperthyroid patients

TSH levels in patients were studied in relation to serum Ca, Na, and K levels. A statistically significant negative relationship was found between serum Ca and TSH levels (r=-0.185, p<0.05) although a non-significant positive correlation was seen between TSH and the levels of Na (r=0.017) and K (r=0.143, p>0.05) in hyperthyroid patients. Serum TSH and Ca levels showed a non-significant positive correlation in hypothyroid patients (r=0.047, p>0.05). A negative but non-significant correlation was found between serum TSH and Na (r=-0.143), and K levels (r=-0.119, p>0.05).

Table 1. Comparison of age and electrolyte profile between the cases and controls (n=240).

Parameters	Hypothyroid (n=80)	Controls (n=80)	Hyperthyroid (n=80)	p-value
Age (years)	38.13±10.6	41.37±10.9	40.54±12.1	0.17
Calcium (Ca) mg/dL	8.22±1.6	8.18±1.6	8.90±1.4	0.004
Sodium (Na) mmol/l	143.32±8.9	143.11±9.0	142.38±8.8	0.78
Potassium (K) mmol/l	4.15±0.8	4.19±0.8	4.21±0.7	0.87

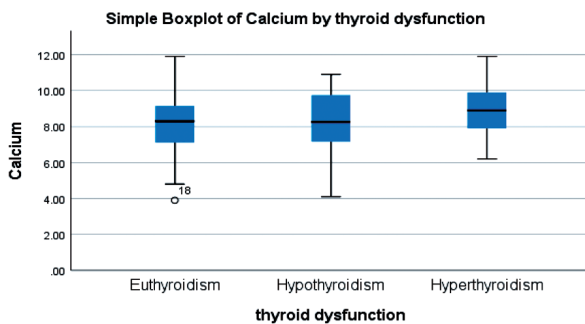


Figure 2: Mean calcium level in cases (hypothyroid and hyperthyroid) and controls.

Discussion

This case control study was designed to investigate the association between thyroid and serum electrolyte levels in patients with hypothyroidism and hyperthyroid and their controls. Thyroid diseases are one of the most common health problems in Pakistan, with higher frequency in females as compared to that in males (19). The correlation between thyroid disorder and electrolyte imbalance has been revealed in different studies. In the present study, serum Ca was found to be high in hypothyroid patients, as compared to the control group, although the difference was not significant. Serum Na and K levels were not statistically different between hypothyroid patients and control subjects. These findings were similar to those of Abebe et al. (21) (2016) wherein the Ca and K levels were not different between the hypothyroid patients and control.

This study was, however, in contrast to the studies carried out by Amrut (22) in 2016 and Arvind et al. (7) in 2015, where decreased levels of Na, K, and Ca were reported in hypothyroid cases as compared to that in the controls. Jaskiran et al. (23) 2014 and Murgod et al. (8) 2012 reported significantly decreased Ca and Na levels in hypothyroid patients which were in contrast to the present study; however, K levels were not statistically different between hypothyroid patients and controls in Jaskiran study which was in accordance with findings of the current study.

The authors of the present study also correlated serum levels of Ca, Na, and K with TSH. In the case of hypothyroidism, serum Na and K levels were found to be negatively

correlated while Ca level was observed to be positively linked with TSH, though the correlation was not statistically significant. These results are supported by those of Arvind et al. (7) (2015) who reported that TSH and serum electrolytes are not statistically correlated. Similarly, Alaeldin et al. (24) documented a significant positive correlation between TSH and Ca in hypothyroid patients. Murgod et al. (8) showed a significant negative correlation between TSH, serum Na, K and Ca in hypothyroid patients. The present study is also in concordance with research done by Amrut (22) and Kumara et al. (25) who demonstrated a non-significant correlation between electrolyte levels and TSH.

This research revealed a significant high serum Ca level in hyperthyroid patients, though there were non-significant differences in Na and K levels between the hyperthyroid patients and controls. The results of the present study are different from the findings of Abebe (21) (2016) and Arvind et al. (7) (2015) where Ca level was non-significantly different and Na level was significantly different between the patient and controls. The results of studies by Abebe et al. (21) and Arvind et al. (7) are also in accordance with that of the present study in terms of K that was not statistically significantly different between hyperthyroid and control groups. Kumara et al. (25) reported that there was no association between Na with hyperthyroidism. Schwarz et al. (20) documented similar finding for Ca but contrasting results for Na and K.

A significant negative correlation was found between serum levels of TSH and Ca in hyperthyroid patients in this study. This finding is in agreement with that of Jasim et al. (26) in 2015. Kumara et al. (25) documented a non-significant correlation of TSH with K in hyperthyroidism, which is in agreement with the present study.

Conclusion

This study demonstrated the significant effect of thyroid hormones on the levels of serum Ca in hyperthyroid patients. The present study indicated increased levels of serum Ca and Na, but low levels of serum K in patients with hypothyroidism as com-

pared to that in the controls, although the difference was not statistically significant. The present study also demonstrates a significant increase in Ca and a non-significant decrease in Na level in hyperthyroid patients. A significant negative correlation has been observed between TSH and Ca in hyperthyroid patients.

Study limitations

Due to financial and time constraint, the power of the study is weak. Owing to the small sample size of this study, it may not be suitable to mention that the variations in Ca levels are appropriate to influence patient condition.

Recommendations

Further studies with a sample size larger than this study are required to conclude whether regular measurement of serum electrolytes can improve the symptoms of patients with thyroid disorders.

Data Availability

The data used to support the findings of this study can be sent by the corresponding author (Ms. Bushra Mubarak; Bushra.mubarik@yahoo.com) on request to the reviewers and researchers who wish to reproduce the results.

Ethical Considerations

Ethical clearance from the Institutional Ethical review committee was obtained. The study objectives are explained to all study subjects. Informed consent was received from all study participants before venipuncture.

Acknowledgement

We are thankful to the University Institute of Medical Laboratory Department, the University of Lahore for being helpful and supportive and express our deepest gratitude to Prof. Dr. Nazar Ullah Raja (Head of Department of University Institute of Medical Lab Technology) and Dr. Kashaf Junaid.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from

a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: Sohail Ashraf, Bushra Mubarak; Design: Bushra Mubarak; Control/Supervision: Bushra Mubarak; Data Collection and/or Processing: Sohail Ashraf, Raheela Aslam; Analysis and/or Interpretation: Bushra Mubarak; Literature Review: Raheela Aslam; Writing the Article: Raheela Aslam; Critical Review: Bushra Mubarak; References and Fundings: Bushra Mubarak, Sohail Ashraf; Materials: Sohail Ashraf.

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