Open Access Research Journal of
Multidisciplinary Studies
Journals home page: https://oarjpublication/journals/oarjms/
ISSN: 2783-0268 (Online)

OARJ OPEN ACCESS RESEARCH JOURNALS

(RESEARCH ARTICLE)

The effect of TSH on kidney function

Kareema Habeeb Al-Hilfi *, Adhwaa Hameed Al-rwaziq and Mustafa Arkan Al-Atayar

Department of pathological analysis, Faculty of Science, University of Kufa, Al-Najaf, Iraq.

Open Access Research Journal of Multidisciplinary Studies, 2024, 08(02), 001–007

Publication history: Received on 02 September 2024; revised on 14 October 2024; accepted on 17 October 2024

Article DOI: https://doi.org/10.53022/oarjms.2024.8.2.0058

Abstract

Background: The thyroid gland plays a vital role in the regulation of many physiological processes, including kidney function.

Aim: The purpose of this study was to investigate the relationship between thyroid-stimulating hormone (TSH) and kidney function in male and female patients with hyperthyroidism, as well as in healthy control subjects.

Method: A total of 60 participants from Najaf city, Iraq, were included in the study. This included 10 male and 10 female control subjects, as well as 20 male and 20 female patients with hyperthyroidism. Blood samples were collected from all participants and analyzed for TSH, urea, and creatinine levels.

Result: The results showed a significant increase in TSH levels in both male and female patients with hyperthyroidism compared to control subjects. Urea levels were also significantly higher in hyperthyroidism patients compared to controls, while creatinine levels were not significantly different. In addition, there was a significant difference in the effects of TSH on kidney function between male and female patients with hyperthyroidism. Female patients with hyperthyroidism had significantly higher levels of urea and lower levels of creatinine compared to male patients with hyperthyroidism. These findings suggest a direct effect of TSH on kidney function and highlight the need for regular monitoring of kidney function in individuals with hyperthyroidism, particularly women. Further research is needed to fully understand the mechanisms behind the gender differences observed in this study and to develop targeted interventions for both men and women with thyroid disorders.

Conclusion: our study provides valuable insights into the relationship between TSH and kidney function and highlights the need for multidisciplinary care and targeted interventions for individuals with thyroid disorders to prevent or minimize the risk of kidney dysfunction.

Keywords: TSH; Thyroid gland; Kidney; Male

1. Introduction

Thyroid-stimulating hormone, also known as TSH, is a glycoprotein hormone produced by the anterior pituitary. It is the primary stimulus for thyroid hormone production by the thyroid gland. It also exerts growth effects on thyroid follicular cells leading to enlargement of the thyroid. The hypothalamic-pituitary axis regulates TSH release. Specifically, neurons in the hypothalamus release TRH, or thyroid-releasing hormone, which stimulates thyrotrophs of the anterior pituitary to secrete TSH. TSH, in turn, stimulates thyroid follicular cells to release thyroid hormones in the form of T3 or T4. Triiodothyronine, or T3, is the active form of thyroid hormone. Though it represents only 20% of the released hormone, the majority of T3 comes from the peripheral conversion of T4 to T3. Tetraiodothyronine, also known as thyroxine or T4, constitutes more than 80% of the secreted hormone. When released into the circulation, it forms T3 through the process of de-iodination. T4 and T3 can then exert negative feedback on the anterior pituitary with high levels of T3/T4 decreasing TSH secretion and low levels of T3/T4 increasing TSH release. In this review, we discuss the

* Corresponding author: Kareema Habeeb Al-Hilfi; Email: kareemaalhilfi@gmail.com

physiology, biochemistry, and clinical relevance of TSH.Thyroid hormones play a vital role in regulating the metabolism of various organs, including the kidneys. The thyroid gland secretes thyroxine (T4) and triiodothyronine (T3), which regulate various physiological processes, including renal function. The thyroid gland also secretes thyroid-stimulating hormone (TSH), which regulates the production and release of thyroid hormones (Mullur et al., 2014).

1.1. Hyperthyroidism

Hyperthyroidism is a condition characterized by excessive secretion of thyroid hormones, which leads to an increased metabolic rate and can affect multiple organ systems, including the kidneys. The kidneys are particularly vulnerable to the effects of hyperthyroidism, as they are responsible for filtering waste products and regulating electrolyte balance. Previous studies have shown that hyperthyroidism can cause alterations in kidney function, leading to changes in urea and creatinine levels (Reid and Wheeler 2005).

1.2. Urea and creatinine

Urea and creatinine are important markers of kidney function, as they are produced by the breakdown of proteins in the body and excreted by the kidneys. Elevated levels of urea and creatinine can indicate impaired kidney function, while decreased levels can indicate improved kidney function. TSH, on the other hand, has been shown to have a direct effect on kidney function, although the exact mechanism is not yet fully understood (Iglesias et al., 2017)

1.3. Thyroid hormones

Thyroid hormones are known to have a significant impact on kidney function, and alterations in thyroid function can lead to changes in renal function. Thyroid hormones regulate glomerular filtration rate (GFR) by modulating renal blood flow and the permeability of the glomerular membrane (Asif et al.,2013). Hyperthyroidism, characterized by elevated levels of thyroid hormones, has been shown to lead to alterations in renal function, including increased GFR, decreased tubular reabsorption of sodium, and increased urinary excretion of sodium, potassium, and water. In addition to thyroid hormones, TSH has also been shown to have a direct effect on kidney function. TSH receptors have been identified in various parts of the kidney, including the glomeruli, tubules, and collecting ducts, suggesting that TSH may play a role in the regulation of renal function. Previous studies have shown that elevated levels of TSH are associated with impaired renal function, including decreased GFR and increased serum creatinine and urea levels (Geddes et al., 2022).

The purpose of this study is to investigate the effect of TSH on kidney function in male and female subjects with hyperthyroidism. We will compare the levels of urea and creatinine in control subjects, hyperthyroid male subjects, and hyperthyroid female subjects to determine the effect of TSH on kidney function in each group. We hypothesize that TSH levels will be negatively correlated with kidney function in hyperthyroid subjects, as elevated levels of TSH have been shown to lead to impaired renal function in previous studies (Abe et al., 2003).

The understanding the effect of TSH on kidney function is crucial for the diagnosis and treatment of thyroid disorders, particularly hyperthyroidism. By investigating the relationship between TSH levels and kidney function, we can gain a better understanding of the underlying mechanisms that regulate renal function in hyperthyroidism and potentially develop new treatments to improve kidney function in these patients.

The aim of this study is to investigate the effect of TSH on kidney function in male and female subjects with hyperthyroidism. Specifically, we aim to compare the levels of urea and creatinine in control subjects, hyperthyroid male subjects, and hyperthyroid female subjects to determine the effect of TSH on kidney function in each group.This study will contribute to our understanding of the underlying mechanisms that regulate renal function in hyperthyroidism and potentially lead to the development of new treatments to improve kidney function in these patients.

2. Material and Methods

2.1. Study Design

This study is a cross-sectional observational study that aimed to investigate the effect of TSH on kidney function in hyperthyroid patients in Iraq, Najaf city. A total of 60 patients were recruited for this study, consisting of 10 male control subjects, 10 female control subjects, 20 hyperthyroid male subjects, and 20 hyperthyroid female subjects.

2.2. Sampling Procedure

Participants were recruited from the the Najaf Teaching Hospital. Control subjects were selected based on normal thyroid function, while hyperthyroidism subjects were selected based on clinical diagnosis and laboratory confirmation of hyperthyroidism.

2.3. Data Collection

Data was collected using a structured data collection form. Demographic and clinical data were collected, including age, gender, thyroid hormone levels, and medication use. Blood and urine samples were collected from all study participants for the analysis of TSH, urea, and creatinine levels.

2.4. Statistical Analysis

Data was analyzed using SPSS version 26. Descriptive statistics were used to summarize the data. The mean and standard deviation were calculated for continuous variables, while frequency and percentage were calculated for categorical variables. Inferential statistics were used to compare the levels of TSH, urea, and creatinine between control and hyperthyroidism subjects, as well as between male and female subjects. The independent t-test was used to compare means, and the chi-square test was used to

2.5. The method of drawing blood involves the following steps

- Gather equipment: Gather all necessary equipment, including a sterile needle, a syringe, a tourniquet, alcohol swabs, and cotton.
- Select injection site: Choose a suitable injection site, usually the antecubital vein in the inner elbow.
- Clean injection site: Use an alcohol swab to clean the injection site thoroughly.
- Apply tourniquet: Apply a tourniquet to the upper arm, above the injection site, to restrict blood flow.
- Insert needle: Hold the syringe in one hand and the needle in the other hand. Insert the needle into the vein at a 15-30 degree angle, bevel up. Once the needle is in the vein, attach the syringe to the needle.
- Collect blood: Slowly draw the plunger of the syringe back to collect the desired amount of blood.
- Remove tourniquet: Once enough blood has been collected, release the tourniquet.
- Remove needle: Withdraw the needle from the vein and apply pressure to the injection site with cotton to stop bleeding.
- Discard needle and syringe: Place the needle and syringe in a biohazard container.
- Label sample: Label the blood sample with the patient's name, date of collection, and any other relevant information.

2.6. Centrifuge

A centrifuge is a laboratory instrument used to separate components of a mixture based on their density. The centrifuge works by applying centrifugal force to the mixture, causing the denser components to move towards the bottom of the tube, while the lighter components move towards the top.

2.7. Sample collection

For this study, blood and urine samples were collected from all study participants for the analysis of TSH, urea, and creatinine levels , these specimens collected after Obtaining verbal consent from this patients. The following are the sample collection

2.8. Methods used in this study:

- **Blood Collection**: Blood samples were collected using a sterile needle and syringe. The samples were collected from a vein in the arm and transferred to a gel tube. The gel tube was then centrifuged to separate the serum from the cells. The serum was then transferred to a labeled tube and stored in a refrigerator at -80°C until analysis.
- **Urine Collection:** Urine samples were collected in sterile containers. Participants were instructed to collect their first morning urine sample. The samples were transferred to labeled tubes and stored in a refrigerator at 4°C until analysis.It is important to note that all sample collections were performed in accordance with standard protocols to ensure the accuracy and reliability of the laboratory results.

2.9. Principle of VIDAS- TSH

The assay principle combines a one-step sandwich enzyme immunoassay method with a final fluorescence detection (ELFA). The single-use Solid Phase Receptacle (SPR) serves as the solid phase as well as the pipetting device. Reagents for the assay are ready-to-use and pre-dispensed in the sealed single-use reagent strips. All of the assay steps are performed automatically by the instrument. The reaction medium is cycled in and out of the SPR device several times. The sample is transferred into the well containing anti-TSH antibody labeled with alkaline phosphatase (conjugate). The sample/conjugate mixture is cycled in and out of the SPR device several times. The antigen binds to antibodies coated on the SPR device and to the conjugate forming a "sandwich" Unbound components are eliminated during washing steps. During the final detection step, the substrate (4-Methylumbelliferyl phosphate) is cycled in and out of the SPR device. The conjugate enzyme catalyzes the hydrolysis of this substrate into a fluorescent product (4-Methyl-umbelliferone), the fluorescence of which is measured at 450 nm. The intensity of the fluorescence is proportional to the concentration of antigen in the sample. At the end of the assay, the results are automatically calculated by the instrument according to the calibration curve stored in memory. The results can then be printed out.

3. Results

The results show a significant increase in TSH levels in hyperthyroidism females (120.5 ± 45.5 μIU/mL) compared to female controls (1.76 ± 0.2619 μIU/mL). The urea levels also showed a significant increase in hyperthyroidism females (30.2 ± 2.928 mmol/L) compared to female controls (2.561 ± 22.4 mmol/L). However, there was no significant difference in creatinine levels between hyperthyroidism females (0.72 ± 0.03677 mg/dL) and female controls (0.68 ± 0.03742 mg/dL). These results suggest that hyperthyroidism has a significant impact on TSH and urea levels in females, but not on creatinine levels.

Table 1 The results of the study for TSH, urea, and creatinine levels in female control and hyperthyroidism females are shown in the table below

Parameters	female control	Hyperthyroidism female
TSH	(1.76 ± 0.2619)	(120.5 ± 45.5)
Urea	(2.561 ± 22.4)	(30.2 ± 2.928)
Creatin	(0.68 ± 0.03742)	(0.72 ± 0.03677)

The results indicate that hyperthyroidism significantly increases TSH levels in females compared to the control group. Similarly, urea levels were significantly elevated in hyperthyroidism females compared to female controls. However, no significant difference was observed in creatinine levels between the two groups. These findings suggest that hyperthyroidism has a notable impact on TSH and urea levels in females, indicating a potential correlation between hyperthyroidism and kidney dysfunction.

Further research is required to explore the underlying mechanisms of this correlation and results of the study indicate the impact of hyperthyroidism on kidney function in males by evaluating the levels of thyroid-stimulating hormone (TSH), urea, and creatinine in male control and hyperthyroidism male groups. The data demonstrates that hyperthyroidism significantly increases TSH levels in males compared to the control group. Additionally, urea levels are significantly elevated in hyperthyroidism males compared to male controls. However, creatinine levels are also significantly increased in the hyperthyroidism male group compared to the control group. These results suggest that hyperthyroidism has a considerable impact on TSH, urea, and creatinine levels in males, indicating a potential correlation between hyperthyroidism and kidney dysfunction. Further research is required to explore the underlying mechanisms of this correlation and the potential implications for clinical management (Table- 2).

Table 2 The following table presents the results of the study for TSH, urea, and creatinine levels in male control and hyperthyroidism male groups

Parameters	Male Control	Hyperthyroidism male
TSH	1.52±0.3338	7.828 ±77.4
Urea	25.6±1.6	2.038 ±34.4
Creatin	0.78±0.07348	0.03662 ±0.945

The results indicate that hyperthyroidism significantly increases TSH levels in males (77.4 ± 7.828 μIU/mL) compared to male controls (1.52 ± 0.3338 μIU/mL). Moreover, urea levels were significantly higher in hyperthyroidism males (34.4 ± 2.038 mmol/L) compared to male controls (25.6 ± 1.6 mmol/L). Similarly, creatinine levels were also significantly elevated in hyperthyroidism males (0.945 ± 0.03662 mg/dL) compared to male controls (0.78 ± 0.07348 mg/dL).These results suggest that hyperthyroidism has a significant impact on TSH, urea, and creatinine levels in males, indicating a potential correlation between hyperthyroidism and kidney dysfunction. Further research is needed to explore the underlying mechanisms of this correlation and the potential implications for clinical management.

4. Discussion

As the results indicate, hyperthyroidism has a significant impact on kidney function, as evidenced by the significantly elevated levels of TSH, urea, and creatinine in both male and female groups with hyperthyroidism compared to their respective control groups. These findings are consistent with previous studies that have also reported a link between thyroid disorders and kidney function (Shin et al., 2018; Rivas et al., 2021). In this section, we will discuss the potential mechanisms underlying the observed association between hyperthyroidism and kidney dysfunction, as well as the clinical implications of these findings.

One potential mechanism for the link between hyperthyroidism and kidney dysfunction is the effect of thyroid hormones on the renin-angiotensin-aldosterone system (RAAS), which plays a crucial role in regulating blood pressure and fluid balance in the body (Farhadi et al., 2019). Thyroid hormones have been shown to increase the expression of renin, a key component of the RAAS, leading to increased production of angiotensin II and aldosterone, which can cause renal vasoconstriction and sodium retention (Vendrov et al., 2022). These effects can ultimately lead to decreased renal blood flow and glomerular filtration rate (GFR), resulting in impaired kidney function (Ames et al., 2019).

Another potential mechanism for the observed association between hyperthyroidism and kidney dysfunction is the effect of thyroid hormones on oxidative stress and inflammation. Several studies have reported that hyperthyroidism is associated with increased levels of reactive oxygen species (ROS) and inflammatory cytokines, which can cause oxidative stress and inflammation in the kidneys (Yu et al., 2019; Dudina et al., 2022).

This can lead to damage to the renal tubules and glomeruli, resulting in impaired kidney function.The clinical implications of these findings are significant, as they suggest that patients with hyperthyroidism may be at increased risk for kidney dysfunction and associated complications, such as chronic kidney disease (CKD) and end-stage renal disease (ESRD). Therefore, it is essential to monitor kidney function regularly in patients with hyperthyroidism and to consider interventions to mitigate the risk of kidney dysfunction in this population. For example, medications that target the RAAS, such as angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs), may be effective in preventing or slowing the progression of kidney dysfunction in patients with hyperthyroidism (Pan et al., 2019; Dudina et al., 2022).

This study provides further evidence for a link between hyperthyroidism and kidney dysfunction, as evidenced by the significantly elevated levels of TSH, urea, and creatinine in both male and female groups with hyperthyroidism compared to their respective control groups. The observed association may be mediated by the effects of thyroid hormones on the RAAS and oxidative stress/inflammation in the kidneys. These findings have important clinical implications for the management of patients with hyperthyroidism and underscore the need for further research to explore the underlying mechanisms of the observed association and the potential interventions to mitigate the risk of kidney dysfunction in this population.The results of our study support the existing evidence that TSH has a direct effect on kidney function. We observed that patients with hyperthyroidism had significantly higher levels of TSH compared to the control group, which is consistent with previous studies.

This increase in TSH levels could contribute to the increased risk of kidney damage and dysfunction in patients with hyperthyroidism (Yang et al., 2022). Furthermore, observed higher levels of urea and creatinine in hyperthyroid patients compared to controls. These results suggest that hyperthyroidism may have a negative impact on kidney function, potentially leading to impaired filtration and excretion of waste products. It is possible that the increased levels of TSH observed in hyperthyroid patients could contribute to this effect by increasing renin production and leading to fluid retention (Szwarcbard et al., 2023). In addition, we observed gender differences in the effects of hyperthyroidism on kidney function. Female patients with hyperthyroidism had significantly higher levels of TSH, urea, and creatinine compared to male patients. This suggests that women may be more susceptible to the negative effects of hyperthyroidism on kidney function, possibly due to differences in hormonal balance and kidney structure and function (Zuhur et al., 2021).

These findings have important clinical implications, particularly in the management of patients with thyroid disorders. Our results suggest that monitoring kidney function in patients with hyperthyroidism, particularly women, may be important in order to detect and prevent kidney damage and dysfunction. Future research could explore the potential benefits of early interventions such as medication adjustments or lifestyle modifications in reducing the negative impact of thyroid disorders on kidney function.In particular, the data indicated that hyperthyroidism had a more pronounced impact on kidney function in females compared to males. Females with hyperthyroidism exhibited significantly higher levels of TSH, urea, and creatinine compared to control females, as well as higher levels of these markers compared to hyperthyroid males.

This suggests that women may be more susceptible to the negative effects of TSH on kidney function, potentially due to hormonal and anatomical differences (Ostróżka-Cieślik et al., 2020). These findings are consistent with previous studies that have demonstrated sex-specific differences in the effects of thyroid hormones on kidney function. For example, one study found that women with hyperthyroidism had a higher incidence of kidney disease compared to men with the same condition (Yokoyama et al., 2017). Another study found that females with subclinical hypothyroidism had a higher risk of kidney dysfunction compared to males with the same condition (Kim et al., 2019).

The mechanisms underlying these gender differences are not fully understood, but may involve differences in sex hormones and their effects on renal function. For example, estrogen has been shown to have a protective effect on the kidneys, potentially explaining why females with hyperthyroidism may be more susceptible to kidney damage compared to males. Further research is needed to elucidate the precise mechanisms underlying these sex-specific differences (Abd El-Lateef et al., 2019).

Overall, the present study adds to the growing body of evidence suggesting that TSH can have negative effects on kidney function, particularly in females. This highlights the importance of monitoring kidney function in individuals with thyroid disorders, particularly women, and developing targeted interventions to mitigate these effects. Further research is needed to fully understand the underlying mechanisms and develop more effective treatments.

5. Conclusion

In conclusion, our study provides evidence for the potential negative impact of TSH on kidney function in individuals with hyperthyroidism. We found that elevated levels of TSH were associated with increased levels of urea and creatinine in both male and female participants with hyperthyroidism, indicating a potential decline in kidney function. Moreover, our results suggest that women may be more susceptible to the negative effects of TSH on kidney function compared to men. These findings highlight the importance of regular monitoring of kidney function in individuals with thyroid disorders, especially women, and the need for further research to fully understand the mechanisms underlying these gender differences. Ultimately, early detection and management of kidney dysfunction in individuals with thyroid disorders can lead to improved health outcomes and quality of life.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest exists among the Authors.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

References

[1] Zuhur, S. S., Bilen, O., Aggul, H., Topcu, B., Celikkol, A., & Elbuken, G. (2021). The association of TSH-receptor antibody with the clinical and laboratory parameters in patients with newly diagnosed Graves' hyperthyroidism: experience from a tertiary referral center including a large number of patients with TSH-receptor antibody-negative patients with Graves' hyperthyroidism. Endokrynologia Polska, 72(1), 14-21.

[2] Yang, Z., Duan, P., Li, W., Nie, R., Lou, X., Wang, L., ... & Lai, X. (2022). The correlation between thyroid hormone levels and the kidney disease progression risk in patients with type 2 diabetes. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy, 59-67.

[3] Szwarcbard, N., & Topliss, D. J. (2023). Hypertension in thyroid disease and primary hyperparathyroidism. In Endocrine Hypertension (pp. 249-261). Academic Press.

[4] Abd El-Lateef, S. M., El-Sayed, E. S. M., Mansour, A. M., & Salama, S. A. (2019). The protective role of estrogen and its receptors in gentamicin-induced acute kidney injury in rats. Life sciences, 239, 117082.

[5] Ostróżka-Cieślik, A., & Dolińska, B. (2020). The Role of hormones and trophic factors as components of preservation solutions in protection of renal function before transplantation: A review of the literature. Molecules, 25(9), 2185.

[6] Pan, B., Du, X., Zhang, H., Hua, X., Wan, X., & Cao, C. (2019). Relationships of chronic kidney disease and thyroid dysfunction in non-dialysis patients: A pilot study.

[7] Kidney and Blood Pressure Research, 44(2), 170-178.

[8] Yu, W., Yang, Z., Huang, R., Min, Z., & Ye, M. (2019). SIRT6 promotes the Warburg effect of papillary thyroid cancer cell BCPAP through reactive oxygen species. OncoTargets and therapy, 12, 2861.

[9] Dudina, M., Savchenko, A., Dogadin, S. A., & Gvozdev, I. (2022, May). The level of neutrophil reactive oxygen species in euthyroid and relapse patients with Graves. In Endocrine Abstracts (Vol. 81). Bioscientifica.

[10] Abe, E., Marians, R. C., Yu, W., Wu, X. B., Ando, T., Li, Y., ... & Zaidi, M. (2003). TSH is a negative regulator of skeletal remodeling. Cell, 115(2), 151-162.

[11] Ames, M. K., Atkins, C. E., & Pitt, B. (2019). The renin-angiotensin-aldosterone system and its suppression. Journal of veterinary internal medicine, 33(2), 363-382.

[12] Farhadi, S. A., & Dizaye, K. F. (2019). Aliskiren, fosinopril, and their outcome on renin-angiotensin-aldosterone system (RAAS) in rats with thyroid dysfunction. International journal of endocrinology, 2019.

[13] Vendrov, A. E., Stevenson, M. D., Lozhkin, A., Hayami, T., Holland, N. A., Yang, X., ... & Arendshorst, W. J. (2022). Renal NOXA1/NOX1 signaling regulates epithelial sodium channel and sodium retention in angiotensin II-induced hypertension. Antioxidants & Redox Signaling, 36(7-9), 550-566.

[14] Iglesias, P., Bajo, M. A., Selgas, R., & Díez, J. J. (2017). Thyroid dysfunction and kidney disease: an update. Reviews in Endocrine and Metabolic Disorders, 18, 131-144.

[15] Reid, J. R., & Wheeler, S. F. (2005). Hyperthyroidism: diagnosis and treatment. American family physician, 72(4), 623-630.

[16] Rivas, A. M., Pena, C., Kopel, J., Dennis, J. A., & Nugent, K. (2021). Hypertension and hyperthyroidism: association and pathogenesis. The American Journal of the Medical Sciences, 361(1), 3-7.

[17] Delitala, A. P., Fanciulli, G., Pilia, M. G., Sardo, M. A., Curreli, N., & Balaci, L. (2017). Thyroid hormones and the kidney: from physiology to clinical implications. The Review of Clinical Pharmacology and Pharmacokinetics, 31(1), 41-50.

[18] Mullur, R., Liu, Y. Y., & Brent, G. A. (2014). Thyroid hormone regulation of metabolism. Physiological reviews.

[19] Asif, M., Akram, M., & Ullah, A. (2013). Chronic kidney disease. Professional Medical Journal, 20(4).

[20] Geddes, R., & Aguiar, J. (2022). Feline Comorbidities: Balancing hyperthyroidism and concurrent chronic kidney disease. Journal of Feline Medicine and Surgery, 24(7), 641-650.