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Research Paper

Comparative Study of Cystatin C in Hypothyroidism Patients in the Indian Subpopulation

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ABSTRACT

Hypothyroidism is a very serious and common health issue that results from a deficiency of thyroid hormone. The prevalence of hypothyroidism increases with an increase in age. There is a mutual relationship between the thyroid gland and the kidney. Cystatin C (Cys-C) is well known reliable and specific parameter commonly used for the assessment of kidney function in general people but this test is prejudiced by thyroid status. For this study, we performed serum Cys-C test and TSH test in a group of patients who are suffering from hypothyroidism. For this study, thirty hypothyroid patients and 30 normal individuals were recruited. Serum Cys-C was measured by Latex Enhanced immunoturbidometric method and TSH was measured by electrochemiluminescent technology for the comparative study. High concentrations of serum Cystatin C were found in hypothyroid patients when compared to normal healthy individuals. This indicates that thyroid dysfunction affects serum Cystatin C concentration and there might be a mechanism, possibly the increased production rate of the protein which causes an increase in Cystatin C level in case of hypothyroidism. This limits the use of Cystatin C as a marker for renal dysfunction.

KEYWORDS: : Cystatin C, Hypothyroidism, Kidney diseases

INTRODUCTION

The thyroid gland is one of the important endocrine glands that normally lies in the lower front of the neck. Production of thyroid hormone is the prime function of thyroid hormone, which is then transported to the different tissue via bloodstream for different metabolic and physiological processes[1,2]. The thyroid hormone helps in the healthy functioning of the different body systems such as the nervous system, cardiovascular system and muscular system; it maintains the body temperature and helps the body to utilize energy. There are two main hormones namely thyroxin or tetra-iodothyronine (T4) and tri-iodothyronine (T3) that control the speed of a variety of metabolism occurring inside the human body[3]. Though, Thyroxin (T4) accounts for more than 80% and tri-iodothyronine (T3) accounts for about 10%. Tri-iodothyronine (T3) is more biologically active than Thyroxin (T4)[4]. These hormones are collectively called thyroid hormones and are released by the thyroid gland of human beings. Iodine is an essential micronutrient required for the synthesis of thyroid hormones. Thyroid-stimulating hormone (TSH) stimulates the thyroid gland to trap iodine from iodine-rich supplements and produce thyroid hormone

by the process of iodination of tyrosine residues of thyroglobulin molecules. Thyroid follicles store the thyroid hormone as colloid for several months[4,5,6]. Thyrotropin-releasing hormone (TRH), a secretion from the hypothalamus controls the production of thyroid hormone by activating the production and secretion of Thyroid-Stimulating Hormone (TSH) from the pituitary gland. The activated Thyroid-Stimulating Hormone (TSH) stimulates the secretion of tetra-iodothyronine (T4) and tri-iodothyronine (T3).

If the thyroid gland fails to synthesize and secrete an abundant amount of thyroid hormone, it leads to a condition called hypothyroidism. Many conditions are directly or indirectly associated with hypothyroidism, including Hashimoto thyroiditis. Iodine deficiency, thyroid surgery over anti-thyroid medication, and pituitary tumours are the most common cause of hypothyroidism. Common symptoms of hypothyroidism include a decrease in basal metabolic rate (BMR), loss of appetite, reduced cardiac output, mental retardation, myxoedema, and goitre. In the case of primary hypothyroidism such as Hashimoto thyroiditis, TSH secretion increases whereas TSH levels decrease in case of secondary hypothyroidism such as in pituitary gland tumours[7,8]. The production and secretion of insufficient thyroid hormone have widespread consequences for the human body due to its significant effects on the growth and development of the human body. The function of the thyroid gland and pituitary gland to secrete their respective hormones are regulated by a feedback mechanism in which the pituitary gland regulates the

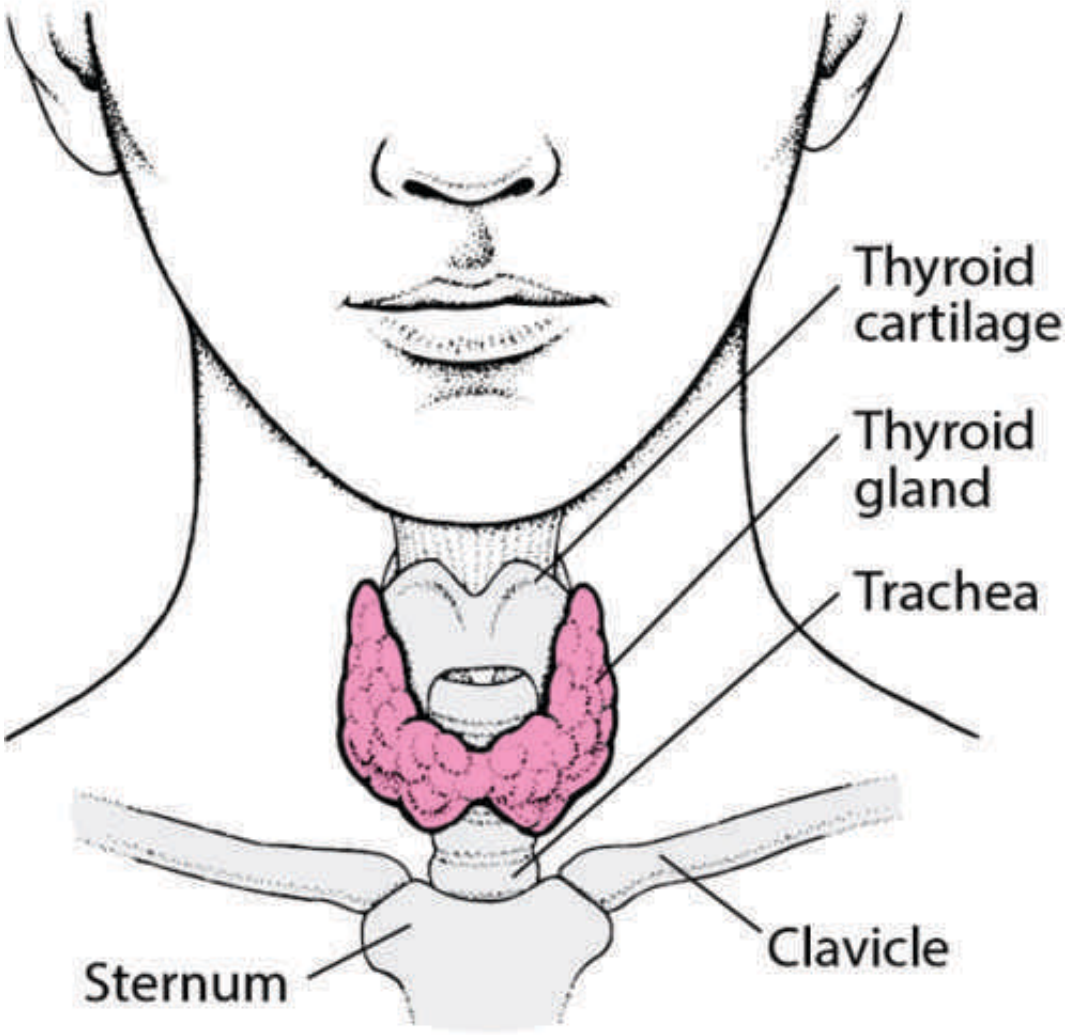

Figure 1: Thyroid Gland[7]

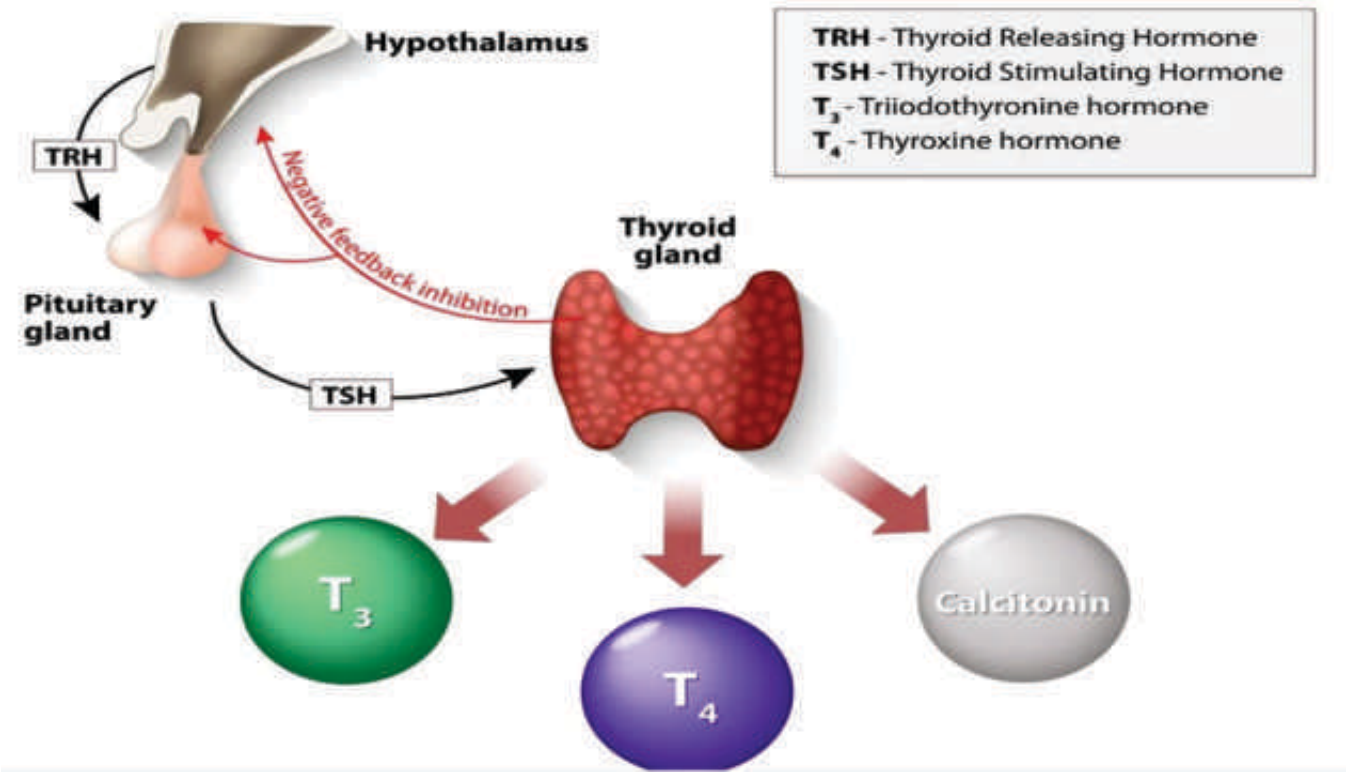

Figure 2: Regulation of Thyroid Hormone Secretion[9]

thyroid gland to produce thyroid hormones and the thyroid hormones along with thyrotropin-releasing hormone (TRH) regulate the pituitary gland to produce TSH. Thyrotropin-releasing hormone (TRH) is a peptide hormone produced by the hypothalamus autogenously to trigger the secretion of thyroid-stimulating hormone (TSH) from the pituitary gland. Finally, the thyroid gland releases the thyroid hormones in response to the thyroid-stimulating hormone (TSH). Any disturbance occurring in this process by any means affects the productivity of the thyroid gland to produce thyroid hormones that ultimately result in hypothyroidism. Secretion of TSH from the pituitary gland increases to trigger the increased production of thyroid hormone from the thyroid gland only when the serum concentration of thyroid hormones falls below it normal level for the normal functioning of the body. But the level of TSH goes down to decrease the excessive production of thyroid hormone when there is excess secretion of thyroid hormones. Therefore, low serum concentrations of thyroid hormones can be seen frequently in individuals who are suffering from hypothyroidism.

Hypothyroidism is the most common pathological condition among people which can be quickly diagnosed and managed but it may affect health directly or indirectly and may be fatal if left untreated.

Prevalence of Hypothyroidism

Approximately, about 3% to 5% of the general inhabitants are badly affected by some form of hypothyroidism, and about 95% to 99% of such individuals are reported to be suffering from primary hypothyroidism[10,11]. The prevalence of hypothyroidism is very common in people of age between 30 to 50 years and females are 10 times more susceptible to hypothyroidism than males[12,13,14]. It has been also reported that white people are more sensitive to hypothyroidism than black or Hispanic people[15].

Cause of Hypothyroidism

An inadequate supply of iodine to the body is the prime cause of thyroid disorder because iodine is the main component for the production of thyroid hormones. Further, iodine makes the thyroid gland more antigenic[16,17,18]. "U-shaped" relationship between iodine intake and hypothyroidism indicates that the prevalence of hypothyroidism decreases in the population with moderate iodine deficiency than those with acute iodine deficiency, while autoimmune hypothyroidism increases the frequency of prevalence as a population of iodine intake increases to adequacy[17]. Other common cause of hypothyroidism includes Hashimoto's thyroiditis, lymphocytic

thyroiditis that occurs after hyperthyroidism, thyroid destruction from radioactive iodine or surgery, pituitary diseases such as pituitary-dependent Cushing syndrome, corticotroph pituitary adenoma, hypothalamic disorder, overmedications, and severe iodine insufficiency.

Symptoms of Hypothyroidism

The symptoms of hypothyroidism vary from person to person because hypothyroidism develops slowly and the symptoms present late with the progress of the disorder. In general, symptoms are non-specific and the most common symptoms include depression, fatigue, increased body weight, hypersensitive to cold temperature, hypersomnia, dry hair, hair loss, constipation, myxoedema, muscle cramp, hypercholesterolemia, leg swelling, irregular periods, loss of libido, hoarseness, and anemia[19].

Hypothyroidism is greatly associated with chronic kidney diseases (CKD) that affect the physiology and development of the urinary system. It has been suggested that hypothyroidism has a relationship with the functioning of kidneys and CKD[20]. A pair of kidney and urinary tract composes the urinary system. The urinary system produces urine as a result of glomerular filtration by the kidney which is then eliminated from the body. It filters the blood to remove metabolic waste products and maintain acid-base balance, electrolyte, and blood pressure homeostasis of the body.

End-stage kidney disease (ESKD) is almost serious and well-established health complication interrelated with high risk of cardiovascular diseases, impaired physical functions, infections, rapid development in impaired kidney function, and mortality. Assessment of glomerular filtration rate (GFR) is therefore highly recommended for the diagnosis, staging, and management of kidney diseases[21-23]. The bi-directional and multi-layered relationship between hypothyroidism and kidney diseases has been demonstrated by several studies in which it has been discussed how both organs affect each other by several mechanisms but yet there are gaps in knowledge in the management and the treatment of chronic kidney disease patient with hypothyroidism[24,25].

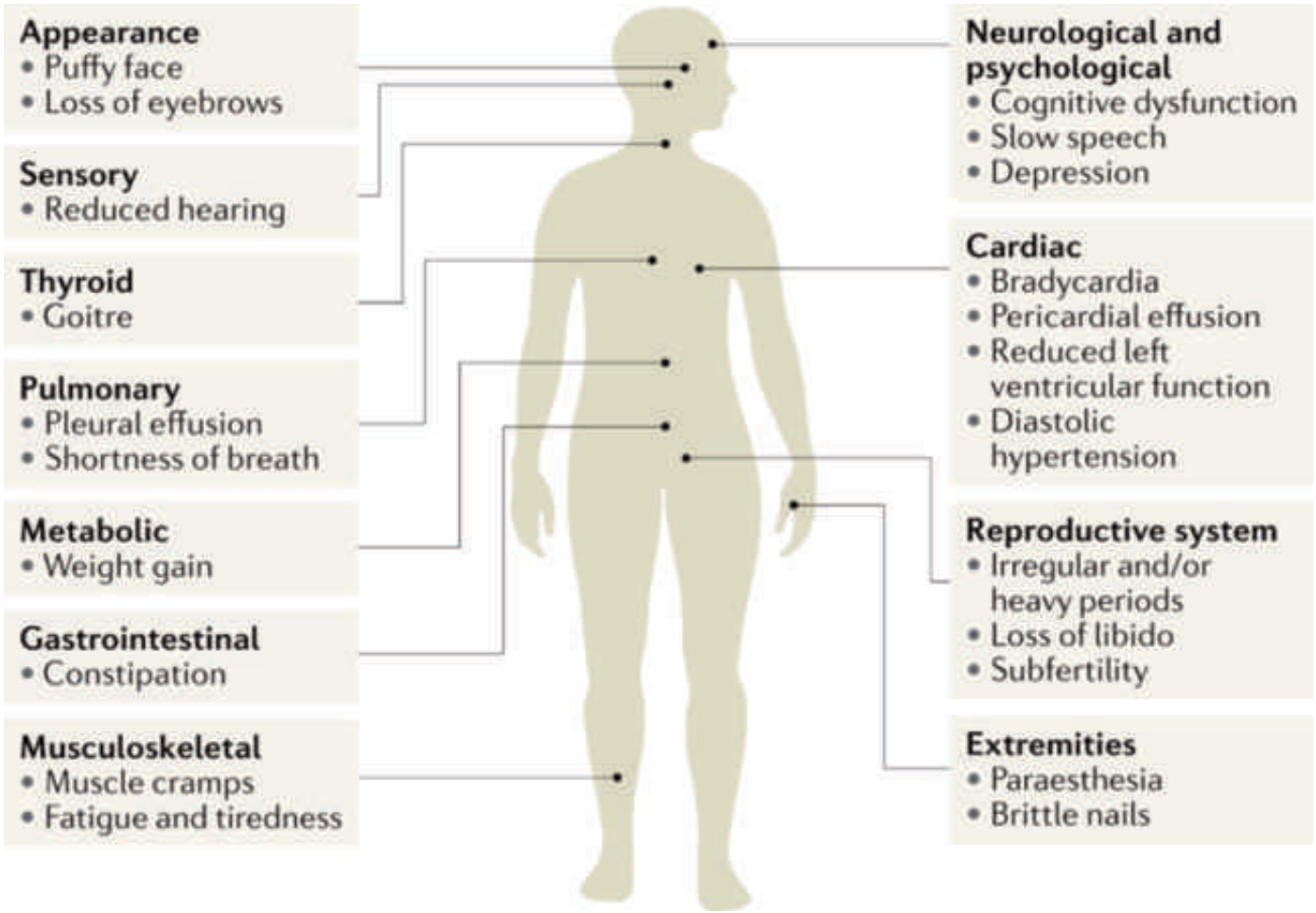

Figure 3: Symptoms of Hypothyroidism[19]

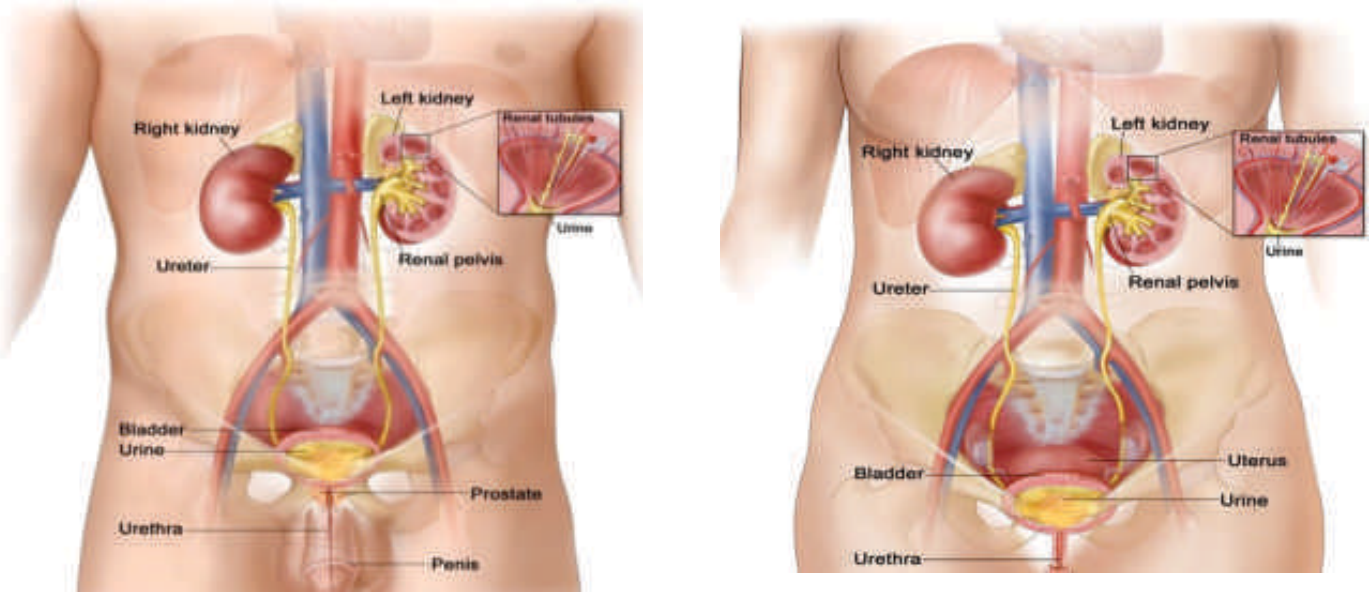

Figure 4: Male and Female Urinary System[21]

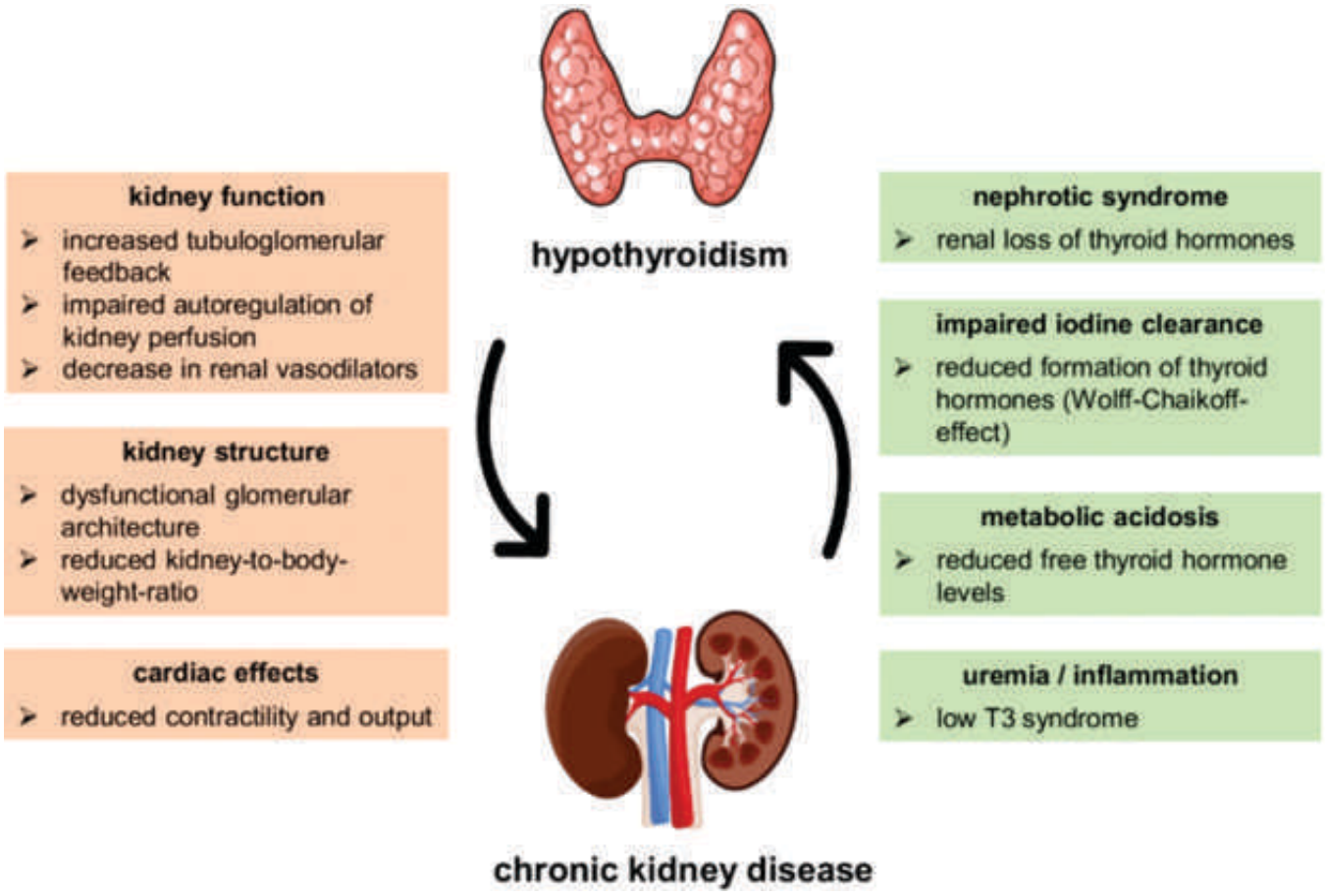

Figure 5: The Relationship between Hypothyroidism and Chronic Kidney Diseases[25]

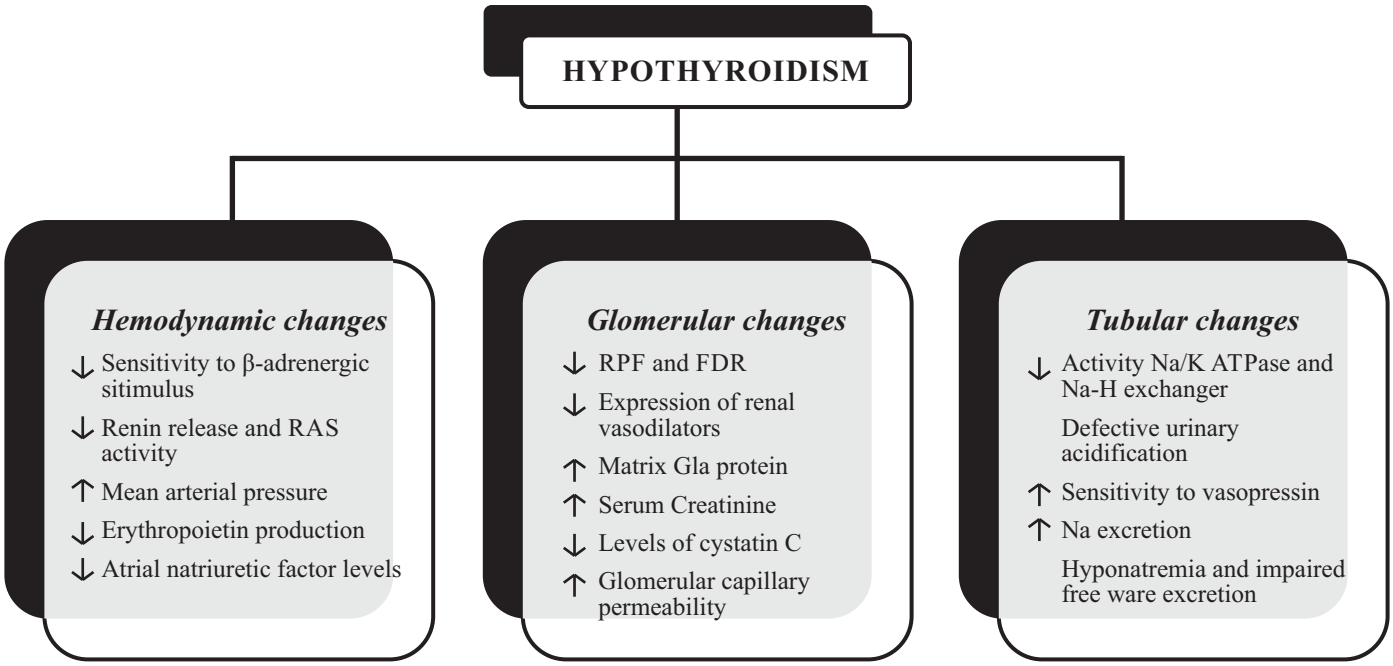

Figure 6: Changes in the Kidney due to Hypothyroidism[26]

CYSTATIN C

Cystatin C (Cys-C) is a non-glycosylated cationic protein with low molecular weight from the Cystatin super family of endogenous cysteine proteinase inhibitors. Cystatin C (Cys-C) contains 120 amino acids and is constantly synthesized by nucleated cells at a constant rate, filtered through the glomerulus, and regained by the proximal tubule. Therefore, Cystatin-C possesses affirmative properties for a renal biomarker such as free filtration by the glomerulus without reabsorption into the blood. Estimation of serum creatinine concentration is mostly preferred to assess the proper functioning of the renal system. But serum concentration of Cys-C is a better marker of glomerular filtration rate (GFR) in all age groups than creatinine because creatinine is an inaccurate marker of glomerular filtration rate (GFR)[27,28]. Unlike creatinine, the rate of production of Cys-C is unaffected by various factors such as malignancy, inflammation, muscle mass, gender, or age. The Cys-C is constant from the age of 1 year onwards and therefore it offers a reasonable supremacy in the accurate estimation of GFR due to its reliability, sensitivity, and specificity than that of classical creatinine–derived parameters[28]. The present studies try to explore the Cystatin C values in hypothyroid patients by comparing and correlating Cystatin C levels in hypothyroid patients and healthy subjects.

MATERIALS AND METHODS

Specimen Collection, Preparation, Handling, and Analysis:

The hypothyroid patients who come to Padmashree Diagnostic Center, Vijaynagar, Bangalore for general check-ups were conscripted to conduct this study. Written consent was obtained from the participating patients after a complete oral explanation of this study to them. The whole blood sample was obtained in a plain vacutainer from the patients under aseptic condition. The labelled clotted blood sample was then received in the laboratory and centrifuged at 4000 rpm for 15 min. Cell-free serum obtained from centrifugation was processed for the analysis of routine biochemical parameters which were recommended by the treating clinicians. The samples were then labelled and stored at -20°C until it was used for further analysis. Aliquot of specimens once thawed were used for the analysis on the same day. Repeated freezing and thawing of specimens were not allowed to avoid pre-analytical errors in this study.

Method:

Latex Enhanced immunoturbidometric Method

The Cystatin C test system is a device intended for the in-vitro quantitative determination of Cystatin C in serum or plasma.

Assay Principle

The pre-incubation of the sample with a buffer and anti-Cystatin C-coated latex undergoes in a chemical reaction to a form an antigen-antibody complex. The formation of the antigen-antibody complex increases the turbidity of the test solution which is measured at 570 nm. By constructing a standard curve from the absorbance of the standards, the Cystatin C concentration of the sample is determined.

Source of Data

Available literature information from recent publications was updated and used as a source of data for this study. The available analytical technique was standardized and modified according to the demand of the situation before applying for the sample analysis. Information for the clinical diagnosis was proceeding from the normal individual and the clinical expertise opinion was sought before the outcome of this study. The physician's clinical diagnosis based on the well-defined criteria was taken into consideration for relating the findings to the clinical status.

Statistical Analysis

The obtained data was discussed with a Biostatistician and SPSS Ver19 Data analysis package was applied to analyze the obtained data. All the obtained values were expressed in mean ± SD. Student t-test was used for statistical comparison. The student's 't' test *p< 0.05; **p< 0.01; ***p< 0.001 was considered as significant.

Assay Protocols

The analyte of interest, Serum Cystatin C was assayed by pre-incubating the test serum sample with Tris-buffer solution and a suspension of latex particles coated with rabbit-anti human Cystatin C polyclonal antibody. Turbidity produced by the antigen-antibody reaction in the test solution was measured at 570 nm. The concentration of serum Cystatin C in the test samples was determined by constructing a standard curve from the absorbance of standard solutions.

Stability and Preparation of Reagents:

All reagents were ready to use and were stable up to the expiry date when stored at 2-8°C

Assay Procedure for Serum Cystatin C:

Assay Mode: 2-point rate 19-34

Procedure:

Reagent blank, standard, control, and test samples were prepared as given in Table 1 and incubated at 37 degrees for 30 seconds. Then, the value was taken after 10 minutes at 570nm in a semi-auto analyzer.

Table 1: Composition of Reagent

Contents	Concentration of Solutions
Reagent 1	Tris-buffer solution.
Reagent 2	Suspension of latex particles coated with rabbit anti-human Cystatin C polyclonal antibody.

Table 2: Test Procedure for Cys-C

	RB	S1	S2	S3	S4	S5	C1	C2	T1
Tris buffer R1(µl)	-	180	180	180	180	180	180	180	180
D/W (µl)	183	-	-	-	-	-	-	-	-
Std (µl)	-	3	3	3	3	3	3	3	3
Latex reagent/R2 µl(µl)	60	60	60	60	60	60	60	60	60

Calibration:

The assay was calibrated using the Gcell calibrator (Cat.no.GC-CystC-L) provided in the kit.

Calculation:

A standard curve was constructed from the absorbance of the standard to calculate Cys-C concentration in the test samples.

Quality Control for Cystatin C:

A commercial QC serum was used.

Table 3: Concentration of Normal and Abnormal Control

Controls	Concentration (mg/L)
C1 (Normal control)	0.85 ± 0.13
C2 (Abnormal control)	1.70 ± 0.25

Biological Reference Intervals for Serum Cystatin C

Age: 1- 60 yrs.: < 1.03mg/L

Age :> 60 Yrs.: <1.26mg/L

Specific Performance Characteristics

Linearity

The method is linear up to 8.0mg/l. A sample with a concentration of more than 8.0mg/l was subjected to dilution with 0.9% NaCl and the assay procedure was repeated. And the result was multiplied by diluting factor.

Assay Method for Thyroid Stimulating Hormone

An immunoassay using electrochemiluminescent technology was used to measure the TSH level. Electro-chemiluminescent technology is based on the sandwich principle which employs two incubation periods. In 1st incubation: 50µl of a test sample was incubated with a biotinylated monoclonal TSH specific-antibody and a monoclonal TSH-specific antibody coated with a ruthenium complex. Sandwich complexes were formed in the 1st incubation which was mixed with streptavidin-coated micro particles and subjected for 2nd incubation. In 2nd incubation period: Sandwich complexes that formed in the 1st incubation reacted with biotin and streptavidin, and become bound to the solid phase. The reaction mixture was taken in a measuring cell so that micro particles can be captured on the electrode surface. Unbound particles were removed with Pro Cell/Pro Cell M. An electric field was applied to the electrode to induce chemiluminescent emission.

The emission of chemiluminescence was measured by a photomultiplier. Results were determined by using a calibration curve and master curve obtained from 2-point calibration, provided by instrument and reagent barcode respectively.

Performance Characteristics of the TSH Test:

i) Performance specifications: Linearity: 100mIU/L

ii) Sensitivity and detection limit: 0.005-10mIU/L

Analytical Specificity:

Luteinizing hormone (LH) 0.038% and Follicle - Stimulating Hormone (FSH) 0.008% were found as interfering factors for the monoclonal antibodies that are used.

Functional Sensitivity:

0.014µIU/mL

The functional sensitivity is the lowest analyte concentration that can be reproducibly measured with an intermediate precision CV of ⩽20.

Calibration Procedures of Instrument for TSH:

Traceability: this method was standardized against the 2nd IRP WHO reference standard 80/558.Every reagent provided with a barcode label containing specific information for calibration of the particular reagent lot supplied by the supplier was used. The pre-defined master curve was adapted to the analyser using the relevant CalSet.

Calibration Frequency:

The fresh reagent was used to carry out calibration because the reagent kit was registered on the analyser. Calibration was carried out once per reagent lot.

Quality Control Procedures:

For quality control, pre-control universal or precicontrol TSH was applied. Controls for the different concentration ranges were run individually at once every 24 hours when the test was in use, once per reagent kit, and following each calibration. The control intervals and limits were adapted to establish correct measurements for the obtained values that fall outside the defined limits.

Quality Control Procedures:

Timing: Morning 9 AM

No of levels: 2 levels

Internal QC: Aliquots of clinical biochemistry QC level 2 and level 3 was taken and brought to room temperature. TSH reagent was loaded and the start bottom was pressed. Once QC results were released, values within the 2SD range were checked.

Biological Reference Intervals for TSH:

1-5 days: 0.72 - 15.2µIu/ml

6D-3 M: 0.72 - 11.0µIu/ml

4M - 11M: 0.73 - 8.35µIu/ml

13M - 6years:0.72 - 5.97µIu/ml

12-20 yrs: 0.51 - 4.30µIu/ml

Male 21 and above: 0.27 - 4.20µIu/ml

Hypothyroidism is a most common and major health issue in the world that results from the deficiency of thyroid hormone. Two types of hypothyroidism, primary hypothyroidism, and central (secondary) hypothyroidism have been defined. Primary hypothyroidism is the most common form of hypothyroidism that mainly results either from an inadequate supply of iodine to the body or due to autoimmune thyroiditis such as Hashimoto's thyroiditis. Other causes of primary hypothyroidism include congenital thyroid dysgenesis, thyroidectomy, treatment with radioiodine, and regional radiotherapy. Whereas, central hypothyroidism results from inadequate secretion of either TRH or TSH due to pituitary disease, pituitary surgery, and infection or ischemic disorders[29].

Various aspects of the mutual interaction between the thyroid gland and the renal have been investigated. Studies have suggested that thyroid hormones are actively required to maintain physiology, morphology, growth, development, and healthy functioning of the renal. Adversely, kidneys contribute a significant role in maintaining the metabolism and concentration of iodine and thyroid hormones[30,31]. Therefore, estimating the glomerular filtration rate (GFR) is an essential tool for the diagnosis and management of different stages of CKD[32,33]. It is demonstrated that analysing the concentration of serum Cystatin C is a more reliable, sensitive, and specific index of glomerular filtration rate than that of serum creatinine for the estimation of glomerular filtration rate (GFR) because Cystatin C is not influenced that much as creatinine by interfering factor such as body muscle mass, diet, etc. muscle[34,35].

A mature Cystatin C is a low molecular weight polypeptide that consists of 120 amino acids. Almost all body fluids contain a significant amount of mature and active forms of Cystatin C but the methods for its measurement were not developed till 1979. The introduction of enzyme-amplified immunoassay became a landmark for the assessment of several diseases by estimating the concentration of Cystatin C as a marker in all body fluids[36]. In this study marked label of serum Cystatin C was observed in the patient suffering from hypothyroidism. The serum concentration of Cystatin C varies according to the age of an individual. Normally, the concentration of serum Cystatin C in adult people ranges from 0.8mg/l to 1.2 mg/l whereas in babies the concentration is considerably higher than adult.

It has been proposed that an altered concentration of serum Cystatin C is an index of renal function; increased serum concentration of serum Cystatin C is closely associated with a reduced glomerular filtration rate. Cystatin C concentration is not much more affected in stored serum samples. The report says that Cystatin C protein remains stable for about 6 months when plasma/serum samples are stored at −80◦C and for up to 24 hours when whole blood samples are not centrifuged[37]. Physiologically, urine concentration of Cystatin C is very low than that of serum because freely filtered Cystatin C are reabsorbed by proximal tubular cells of the kidney. The normal value of urine Cystatin C lies between 0.03 to 0.30 mg/l36.

Change in the normal concentration of urine Cystatin C can be seen if there is a defect in Glomerular Filtration Rate (GFR). Hence normal renal functioning can be ruled by measuring GFR in several ways. Measuring 51Cr-EDTA, creatinine or Cystatin C precisely determines the function of the kidney. Creatinine serves as the most commonly used marker in estimating the GFR because creatinine is synthesized by muscle cells removed from the body through glomerular filtration. But, in case of reduced renal function, the rate of clearance of creatinine is influenced by tubular secretion. In addition, medicines, foodstuffs, and muscle mass greatly affect the concentration of plasma creatinine in the blood[38].

Morphology and physiology of renal are influenced by abnormal functioning of the thyroid gland. Any defect in the thyroid gland not only affects cardiac output but individually affects the structure of the kidney, renal blood flow, GFR, tubular transport, as well as water and electrolyte balance[31,37]. Loss of inotropic and chronotropic effects of thyroid hormones leads to reduce cardiac output in case of hypothyroidism which ultimately decreases renal blood flow and GFR. It has been reported that thyroid dysfunction may result in an altered rate of glomerular filtration of creatinine that is present in the blood[37,39].

Both hypothyroidism and hyperthyroidism are associated with changes in creatinine concentration in the blood due to thyroid dysfunction. In hypothyroidism, rhabdomyolysis and myopathy change the plasma creatinine whereas in hyperthyroidism diminished muscle mass brings about changes in the plasma creatinine[40,41]. Initially, interrelationships between thyroid and kidney diseases were clinically understated. But to date, several studies have reported that the concentration of serum creatinine is increased in patients with hypothyroidism, and hypothyroidism increases the risk of chronic kidney diseases that may be fatal if not managed in time[41,42].

A study carried out by using 51CrEDTA-clearance for the estimation of GFR reported that hypothyroidism may have a connection with diminished GFR but the method is found to be independent on creatinine to estimate GFR of[43]. Our study focuses on the changes in Cystatin C in the hypothyroid patient. To carry out this study, 30 patient samples were obtained from the patients with hypothyroidism after a complete explanation of this study and written informed consent was obtained to participate in the study. Several interfering factors such as BMI, qualification, addiction to alcohol and smoking, nutritional habits, culture and family history were considered prior to selecting the patients. The demographic data like sex, age, weight, etc of the participants were recorded. A male and female patient (Aged between 25-45 years) with high TSH value (with a clinical history of hypothyroidism) was recruited in the study. And patients with any clinical history of any disease other than hypothyroidism, ages below 25 years and above 45 years, individuals under medication or alcohol/ drug abuse were excluded from this study. The study was submitted and approved by the institutional review board. The study population consisted of 30 participants with Hypothyroidism (n=30) and normal subjects (n=30), with a mean age of 38.11 ± 4.3 and 54.40 ± 4.6 respectively suspected to be suffering from hypothyroidism.

The Individuals with normal TSH levels were used as control samples for this study. Cystatin C elevation is one of the common complications at Hypothyroidism. Consequently, with an emphasis on the required sensitivity of the assay methods, this study was carried out on Hypothyroidism by a validated available analytical method for serum analysis that is often used in laboratory medicine.

Methodological Investigations:

Biochemical investigations such as Cystatin C and TSH have been carried out. Because establish the normative data for patients suffering from Hypothyroidism, Cystatin C level was adopted from the available reference interval from literature.

TSH Study

TSH estimation plays a vital role in the diagnosis of hyper and hypothyroidism since this diseased status is linked with much health risks and due to lifestyle changes hyper and hypothyroidism is becoming a very commonly countered health problem in India. So estimation should be done in every individual before it leads to major health problems for the individual. It has been noted that a comparative study of Cystatin C with hypothyroidism patients shows an increase in the level of serum Cystatin C.

Cystatin C Study

As a part of this study, Cystatin C levels were assessed in normal and hypothyroidism subjects. It is found that the levels of Cystatin C are significantly higher in Hypothyroidism patients compared to normal subjects (P: <0.001).

SUMMARY & CONCLUSION

Serum Cystatin C is a modern marker of kidney function. The marked effect of mild thyroid dysfunction on serum Cys - C has not been explored. Thyroid hormones (TH) are essential for the adequate growth and development of the renal as well as to balance water and electrolyte homeostasis. Similarly, the

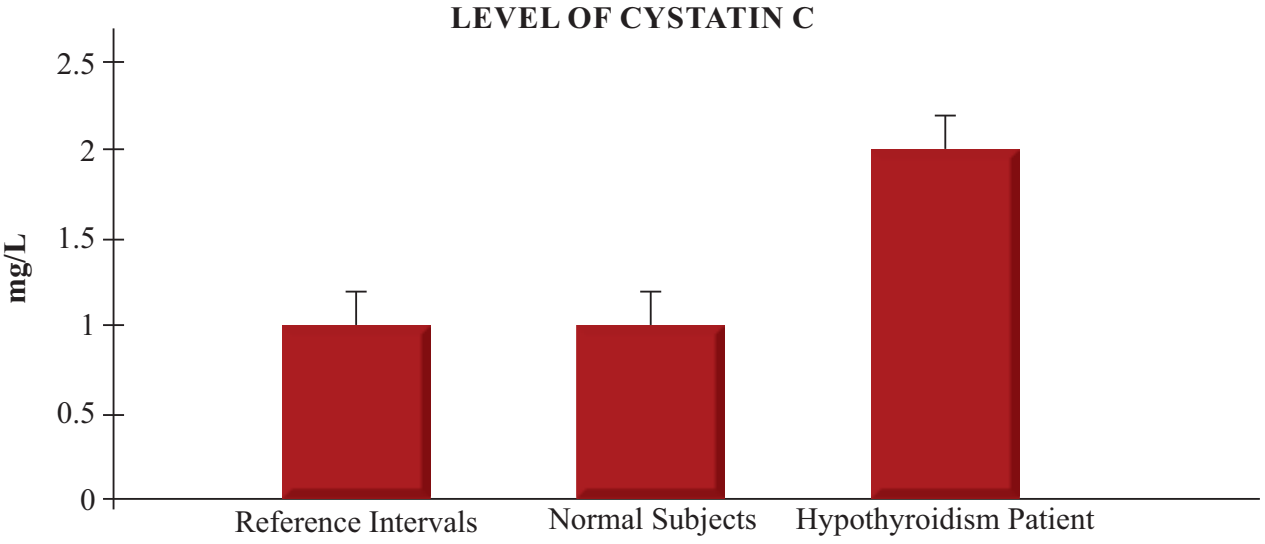

Figure 7: Histogram representing the Serum Cystatin C of Normal and Hypothyroidism subjects. Values expressed as Mean ± SD. Students" test: *: $p < 0.05$; **: $p < 0.01$: ***: $p < 0.001$

kidneys actively participate in the metabolism and removal of thyroid hormones.

From a clinical perspective, it should be noted that thyroid dysfunctions are escorted by remarkable changes in the cardiovascular system and the metabolism of water and electrolyte. All these changes alter the water and electrolyte homeostasis of the renal system. However, the alteration in the production, release, metabolism, and removal of thyroid hormone represents kidney dysfunction. The present study aimed at the Estimation of Cystatin C values in hypothyroid patients and the comparison and correlation of Cystatin C levels in hypothyroid patients and healthy subjects. In a study conducted by Krishnan S et al, Cystatin C values of >1 mg/l and 1.3 mg/dl in males were defined as "elevated levels, same was seen in our study in both males and females. In another study done by L Manetti et al, hypothyroid individuals showed a decrease in Cystatin C levels whereas in our study it showed increased Cystatin C concentrations. Similarly, Manuel Fricker shows that in hypothyroid patients, Cystatin C levels were increased without any renal impairment which is in line with our study.

In the present study when compared to normal healthy individuals, hypothyroid subjects had high levels of Cystatin C concentration. This suggests that there is an unknown mechanism that causes an increase in Cystatin C in hypothyroid patients even though there are no signs of kidney dysfunction.

CONCLUSION

In conclusion, hypothyroidism alters the concentration of serum Cystatin C most probably by influencing the production rate of the protein. However, increased level of serum Cystatin C observed in patients with hypothyroidism limits the use of Cystatin C as an index of kidney function.

CONFLICT OF INTEREST: None

FINANCIAL SUPPORT: None

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