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# CORRELATION OF AGE AND SEX IN RELATION TO SERUM CALCITONIN, CREATININE AND URIC ACID ON CKD PATIENTS WITH THYROID ABNORMALITY COMPLICATION

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***Abstract:*** **This study evaluated the serum calcitonin, creatinine and uric acid levels in chronic kidney diseases (CKD) complicated by dysthyroidism. A total of 119 participants were recruited in this study, majority of who were males. Majority of the participants in this study were between the ages of 30 to 68 years with a median of 49 years. The high prevalence of CKD among this age group can be attributed to underlying pathologies such as hypertension, diabetes or both. The level of serum calcitonin, $T_3$, $T_4$, TSH, creatinine and uric acid of study participants according to age range, for age < 20 years, Calcitonin(126±23.9), $T_3$ (0.800±0.0741), $T_4$ (6.79±0.296), TSH (8.41±1.48), Creatinine (11.1±1.29), Uric Acid (21.1±2.55), for age 21 - 40 years, Calcitonin(145±42.0), $T_3$ (0.763±0.0565), $T_4$ (7.75±0.701), TSH (8.64±1.43), Creatinine (7.91±1.29), Uric Acid (14.0±1.77). for age > 41 years, Calcitonin(71.2±11.3), $T_3$ (0.765±0.0396), $T_4$ (7.45±0.255), TSH (8.11±0.529), Creatinine (7.01±0.66), Uric Acid (13.4±0.801).from the result of this study calcitonin, creatinine and uric acid proved to be statistically significant ($p \leq 0.05$), however $T_3$, $T_4$, TSH showed no statistical significance.**

***Keywords:*** **serum calcitonin, uric acid levels, chronic kidney diseases (CKD).**

## 1. INTRODUCTION

The mutual interactions between kidney and thyroid functions are known for years (Wu *et al*.,2022). Maintenance of homeostasis of metabolic functions in all body organs is important in the human body. This balance is achieved by actions of hormones or vital regulatory organs. Thyroid hormones have effects on cellular growth and differentiation and also regulate important physiological functions in virtually every human tissue (Priest *et al*., 2019). On the other hand, the kidney

is involved in metabolic waste excretion, maintenance of fluid and acid base balance by regulating the concentration of hydrogen, sodium, potassium, phosphate and other ions in the extracellular fluid, secretion and metabolism of hormones which are involved in haemodynamic control, red blood cell production and mineral metabolism (Hall *et al*., 2020).

Thyroid hormones are important in cellular growth and differentiation, and modulation of physiological functions in all human tissues including the kidney. They also play a role in maintenance of water and electrolyte homeostasis. Therefore, thyroid dysfunction, either hypothyroidism or hyperthyroidism is accompanied by alterations in the metabolism of water and electrolytes, as well as cardiovascular function (Liu *et al*., 2019). On the other hand, the kidney is an important target organ for thyroid hormone actions and for the metabolism of the thyroid hormones. Decline in kidney function is proportionally associated with abnormalities in the thyroid hormone physiology. Chronic kidney disease affects both hypothalamus-pituitary-thyroidal axis and thyroid hormone peripheral metabolism (Lossow *et al*., 2021). The effects of impaired kidney function may lead to hypothyroidism, hyperthyroidism and non-thyroidal illness which are associated with deranged cardiovascular function which will adversely affect the prognosis of CKD. A local study done 20 years ago in CKD patients on haemodialysis and conservative management showed biochemical features of hypothyroidism. This study sought to describe the nature and magnitude of thyroid hormone derangements in CKD patients, given the global increase in CKD prevalence. The information can provide evidence on the value of including thyroid hormone estimations in CKD patients (Kumar *et al*., 2018).

The proportion of older people in the general population is steadily increasing worldwide, with the most rapid growth in low- and middle-income countries. This demographic change is to be celebrated, because it is the consequence of socioeconomic development and better life expectancy. However, population aging also has important implications for society, in diverse areas including health systems, labor markets, public policy, social programs, and family dynamics (Lee *et al*., 2020). Despite the large population size of Nigeria with 180million people, little is known about the epidemiology of CKD in the general population. There is no national data on prevalence of CKD, and only few community-based studies were done in some regions of the country (Imtiaz *et al*., 2018).

## 2. MATERIALS AND METHOD

**Study Area:** This study was carried out at the Irrua specialist Teaching Hospital, Edo State.

**Study Population:** The study population for this research are renal unit patients attending clinic at the Irrua Specialist Teaching Hospital, Benin City, Edo state, Nigeria.

**Inclusion Criteria: (Test Group)**

Adult male and female subjects with renal insufficiency

**Exclusion Criteria:** Male and Female subjects without renal insufficiency

**Control Group**: Apparently healthy male and female subjects

**Sample Size:** The sample size (N) was calculated using prevalence from previous studies done on prevalence of chronic Kidney diseases among civil servants in Bayelsa ,Nigeria, which was 7.8% (Ugege *et al*., 2022). The sample size for this study was obtained using the formula described by Saputra *et al*., (2018).

**Sample Collection:** 5ml of blood sample was collected from the cubital fossa of each subject by an experienced Phlebotomist using aseptic collection procedure as described by **Sonmez *et al*.,** (2020), dispensed into plain sample container and allowed to clot.

**LABORATORY ANALYSIS**

**Determination of Thyroid Stimulating Hormone Using ELISA Method (Beitollahi *et al*., 2018)**

All reagents and clinical specimen were allowed to attain room temperature ($18^0$-$22^0$).A known volume, 50µl each of standards, specimens and controls were dispensed into appropriate microplate wells. 100µl of Enzyme Conjugate Reagent was dispensed into each wells and then mixed thoroughly for 30 seconds. The strip was then covered with a lid and then Incubate at room temperature (18-22$^o$C) for about 60minutes.The wells were washed 5 times with 300ul of working washing solution. The plate was firmly tapped against absorbent paper to remove all the residual water droplets. 100ul of TMB solution was then added into each of the wells and mixed gently for 5 seconds. It was later incubated at room temperature for 20 minutes in a dark place. The reaction was stopped by adding 100ul of stop solution to each well, mixed and then read. The optical density was read at 450nm with a microtiter well reader.

**Determination of Total Thyroxine ($T_4$) Using ELISA Method (Bowerbank *et al.*, 2019)**

All reagents and clinical specimen were allowed to attain room temperature ($18^0$-$22^0$).A known volume, 50µl each of standards, specimens and controls were dispensed into appropriate microplate wells. 100µl of Enzyme Conjugate Reagent was dispensed into each wells and then mixed thoroughly for 30 seconds. The strip was then covered with a lid and then Incubate at room temperature (18-22ºC) for about 60minutes.The wells were washed 5 times with 300ul of working washing solution. The plate was firmly tapped against absorbent paper to remove all the residual water droplets. 100ul of TMB solution was then added into each of the wells and mixed gently for 5 seconds. It was later incubated at room temperature for 20 minutes in a dark place. The reaction was stopped by adding 100ul of stop solution to each well, mixed and then read. The optical density was read at 450nm with a microtiter well reader.

**Determination of total triiodothyronine ($T_3$) using ELISA Method (Bowerbank *et al.*, 2019)**

In the $T_3$ EIA, a certain amount of anti-$T_3$ antibody is coated on microtiter wells. A measured amount of patient serum, and a constant of T3 conjugated with horseradish peroxidase are added to the microtiter wells. During incubation, the anti-$T_3$antidody is bound to the second antibody on the wells, and T3 and conjugated $T_3$ compete for the limited binding sites on the anti-T3 antibody. After incubation at room temperature, the wells are washed to remove unbound $T_3$ conjugate. Addition of TMB solution results in the development of blue colour. The colour development is stopped with the addition of 2 N HCL, and the absorbance is measured spectrophotometrically at 450nm. The intensity of the colour formed is proportional to the amount of enzyme present and is inversely related to the amount of unlabeled T3 in the sample.

**Assay procedure for total triiodothyronine ($T_3$)**

All reagents and clinical specimen were allowed to attain room temperature ($18^0$-$22^0$).A known volume, 50µl each of standards, specimens and controls were dispensed into appropriate microplate wells and mixed for 10 seconds. 100µl of Enzyme Conjugate Reagent was dispensed into each wells and then mixed thoroughly for 30 seconds. The strip was then covered with a lid and then Incubated at room temperature (18-22ºC) for about 60minutes.The wells were washed 5 times with 300ul of working washing solution. The plate was firmly tapped against absorbent paper to remove all the residual water droplets. 100ul of TMB solution was then added into each of the wells and mixed gently for 5 seconds. It was later incubated at room temperature for 20 minutes in a dark place. The reaction was stopped by adding 100ul of stop solution to each well, mixed gently for about 15 seconds and then read. The optical density was read at 450nm with a microtiter well reader.

**Calcitonin Estimation**

- Wells for diluted standard, blank and sample were determined. 5 wells for standard point prepared, I well for blank. Add 50PL each of dilutions of standard, blank and samples into the appropriate wells, respectively. And then 50 microlitre of detection reagent A were added to each well immediately shake the plate gently using a microplate shaker. It was covered with a plate sealer. Solution was incubated for 1 hour at $37^0$C. Detection reagent A may appear cloudy. Allow to assume room temperature and allow to mine gently until solution appear uniform.

- Solution was aspirated and washed with 350 microlitre of IX wash solution to each well using a squirt bottle, multi channel pipette manifold dispenser or auto washer, and it is allowed to slit for 2 minutes. Remaining liquid from all wells are removed by snapping the plate onto absorbent paper. This is repeated thrice after the last wash, all remaining wash buffer are removed by decanting plate is inverted and blotted using absorbent paper.

- 100 microlitre of detection reagent B is added to each well solution is incubated for 30 minutes at $37^0$C after covering it with plate sealer.

- The aspiration / wash process is repeated for 5 times as conducted in step 2.

- 90 microlitre of substrate solution is added to each well, after which it is covered with a plate sealer incubation for 20 minutes at $37^0$c is carried out protect against light. The liquid will turn blue by the addition of substrate solution.

- 50 microlitre of stop solution was added to each well. The liquid turned yellow by addition of stop solution liquid was thoroughly mixed by tapping the side of the plate. if colour change does not appear uniform, side of plate will be tappeds to ensure thorough mixing.

- Ensure no drop of water and finger print on the bottom of the plate and no bubble present on the surface of liquid then run microplate reader and conduct measurement at 450 nanometers immediately.

**Estimation of Uric Acid (Liu *et al*., 2018)**

- 20 microlitre of sample pipetted into sample test tube
- 20 microlitre of uric acid standard was pipetted into test tube labeled standard
- 1 Millilitre of reagent pitetted into both tubes containing both sample and standard.
- 1 Millilitre of reagent pipetted into a third test tube to at as reagent blank
- It was mixed and incubated for 5 mins at $37^0$C and absorbance was read at 520 nm against a reagent blank within 30 minutes.

**Assay for Creatinine by Jaffe Reaction (Küme *et al*., 2018)**

- 100 microlitre of sample pipetted into sample test tube
- 100 microlitre of creatinime standard pipetted into the test tube labeled standard.
- A third test tube derived of sample or creatinine standard is labeled Reagent blank
- 1 Millilitre of picric acid is added to respective test tubes
- 1 Millilitre of sodium hydroxide is added to the three test tubes
- It was mixed and incubated at room temperature for 10minutes, and read at 500nm.

**Data Analysis**

Data was collected, screened for completeness and entered into the SPSS version 20 for analysis. The mean, standard error of mean, and probability value (p-value) was gotten using chi-square, also correlation analysis will be done using the Pearson's correlation and data will be presented as tables and bar graphs. Differences will be considered statistically significant at an error probability (P) of less than or equal to 0.05 ($p \leq 0.05$) and not significant at $p \geq 0.05$.

## 3. RESULT

**TABLE 1 SERUM CALCITONIN, T3, T4, TSH LEVELS OF STUDY PARTICIPANTS ACCORDING TO AGE RANGE**

| Age Range | Calcitonin (pg/l) | T3 (ng/ml) | T4 (mµg/dl) | TSH (miu/ml) | Creatinine (mg/dl) | Uric Acid (mg/dl) |
|---|---|---|---|---|---|---|
| < 20 years | 126±23.9 | 0.800±0.0741 | 6.79±0.296 | 8.41±1.48 | 11.1±1.29 | 21.1±2.55 |
| 21 - 40 years | 145±42.0 | 0.763±0.0565 | 7.75±0.701 | 8.64±1.43 | 7.91±1.29 | 14.0±1.77 |
| > 41 years | 71.2±11.3 | 0.765±0.0396 | 7.45±0.255 | 8.11±0.529 | 7.01±0.661 | 13.4±0.801 |
| F value | 4.04 | 0.117 | 1.38 | 0.0635 | 5.06 | 7.63 |
| Anova P value | 0.022 | 0.89 | 0.26 | 0.939 | 0.009 | 0.001 |

T3: Triiodothyronine

T4: Tetraiodothyronine

TSH: Thyroid Stimulating hormone

**TABLE 2: SERUM CALCITONIN, T3, T4, TSH, CREATININE AND URIC ACID LEVELS FOR FEMALE CONTROLS AND CKD SUBJECTS**

| Parameters | Normal Range | Control Subjects (n = 32) | CKD Subjects (n = 13) | t value | p value |
|---|---|---|---|---|---|
| Calcitonin (pg/L) | ≤10 | 44.8±11.1 | 88.8±11.3 | 2.48 | 0.017 |
| T3 (ng/mL) | 0.6 - 2.0 | 1.47±0.0610 | 0.792±0.0720 | 6.36 | 0.001 |
| T4 (mµg/dL) | 6.0 - 12 | 8.95±0.325 | 6.92±0.326 | 3.7 | 0.001 |
| TSH (miu/mL) | 0.4 - 4.2 | 2.22±0.251 | 9.00±1.69 | 6 | 0.001 |
| Creatinine (mg/dL) | 0.7 - 1.4 | 0.756±0.0442 | 5.98±1.49 | 5.57 | 0.001 |
| Uric Acid (mg/dL) | 3.4 - 6.5 | 4.86±0.219 | 11.6±1.46 | 6.89 | 0.001 |

T3: Triiodothyronine

T4: Tetraiodothyronine

TSH: Thyroid Stimulating hormone

**Table 3: CALCITONIN, T3, T4, TSH CREATININE, URIC ACID, LEVELS FOR MALES CONTROL AND CKD SUBJECTS**

| Parameters | Normal Range | Control Subjects (n = 18) | CKD Subjects (n = 56) | t value | p value |
|---|---|---|---|---|---|
| Calcitonin (pg/L) | ≤10 | 44.8±11.1 | 98.8±12.4 | 2.37 | 0.02 |
| T3 (ng/ml) | 0.6 - 2.0 | 1.54±0.0875 | 0.770±0.0356 | 9.64 | 0.001 |
| T4 (mμg/dl) | 6.0 - 12 | 9.18±0.425 | 7.40±0.228 | 3.79 | 0.001 |
| TSH (miu/ml) | 0.4 - 4.2 | 2.48±0.418 | 8.07±0.523 | 5.86 | 0.001 |
| Creatinine (mg/dl) | 0.7 - 1.4 | 0.761±0.0705 | 8.70±0.618 | 7.24 | 0.001 |
| Uric Acid (mg/dl) | 3.4 - 6.5 | 5.19±0.359 | 16.3±1.07 | 5.85 | 0.001 |

T3: Triiodothyronine

T4: Tetraiodothyronine

TSH: Thyroid Stimulating hormone

**TABLE 4: CORRELATION OF AGE AGAINST MEASURED VARIABLES**

| Correlation | r value | p value |
|---|---|---|
| Age (years) vs Creatinine (mg/dl) | -0.28 | 0.019 |
| Age (years) vs Uric Acid (mg/dl) | -0.28 | 0.017 |
| Age (years) vs Calcitonin (pg/L) | -0.23 | 0.05 |
| Creatinine (mg/dl) vs Uric Acid (mg/dl) | 0.74 | 0.0001 |
| Creatinine (mg/dl) vs Calcitonin (pg/L) | 0.59 | 0.0001 |

## 4. DISCUSSION

The result of this present study on the correlation of age and sex in relation to serum calcitonin, creatinine and uric acid on CKD patients with thyroid abnormality complication is represented in table 4.1, 4.2,4.3 and 4.4. Table 4.1 shows the level of serum calcitonin, $T_3$, $T_4$, TSH,creatinine and uric acid of study participants according to age range, for age < 20 years, Calcitonin(126±23.9), $T_3$ (0.800±0.0741), $T_4$ (6.79±0.296), TSH (8.41±1.48), Creatinine (11.1±1.29), Uric Acid (21.1±2.55), for age 21 - 40 years, Calcitonin(145±42.0), $T_3$ (0.763±0.0565), $T_4$ (7.75±0.701), TSH (8.64±1.43), Creatinine (7.91±1.29), Uric Acid (14.0±1.77). for age > 41 years, Calcitonin(71.2±11.3), $T_3$ (0.765±0.0396), $T_4$ (7.45±0.255), TSH (8.11±0.529), Creatinine (7.01±0.66), Uric Acid (13.4±0.801).from the result of this study calcitonin, creatinine and uric acid proved to be statistically significant ($p \leq 0.05$), however $T_3$, $T_4$, TSH showed no statistical significance.

CKD prevalence For sub-Saharan Africa (SSA), recent systematic reviews reported a prevalence of 13.9%, and 10.1% respectively (Olanrewaju *et al*., 2020). The pooled prevalence for CKD was 16% in West Africa, the highest in the continent. The prevalence of CKD among females in the Chinese general population increases from 7.4% among those aged 18–39 years to 18.0% and 24.2% among those aged 60–69 and 70 years, respectively (Abd ElHafeez *et al*., 2018).

A recent systematic review identified 7 population-based studies, 5 from the Southern part and 2 from the Northern part (Chukwuonye *et al*., 2018); in this study, the prevalence of CKD ranged from 2.5 to 26%. Oluyombo, 2010 previously reported the prevalence of CKD of 18% in a rural community in South-Western Nigeria. Similar study in the South-East Nigeria found a prevalence of 11.4% in rural, and 11.7% in semi-urban dwellers (Akokuwebe *et al*., 2022). In addition, a study from North-West Nigeria in the recent review documented CKD prevalence of 26%, suggesting overall high prevalence of CKD and indicating a need for more studies to understand the true burden of CKD in Nigerian population (Chukwuonye *et al*., 2018).

A study was carried out by Jouda *et al*., 2020 on patients within the age of 20-50years with hypothyroidism and chronic kidney disease and the relationship between them, in his study TSH hormone levels increase significantly in the hypothyroidism group while $T_4$ hormone level decrease significantly in both patients groups but there was no significantly different in $T_3$ among these groups. Serum Creatinine levels are significantly higher in CKD and hypothyroidism group. However, there was no significant different in the Uric acid levels among these groups, Jouda *et al*., 2020 further postulated that the significant increased observed in serum creatinine levels observed in his study was due to the underlying chronic kidney disease. However the findings of Jouda *et al*., 2020 are in contrast with the findings of this study. Nielsen *et al*.,1979 in his study on serum calcitonin levels in patients with chronic kidney diseases discovered a significantly elevated levels of

serum calcitonin among chronic kidney disease patients, the increase in serum calcitonin could be due to elevated C-cell production or by calcitonin retention due to a decrease in renal function . Fereira *et al*., 1991 in his study of Serum concentration of calcium and calcitonin in hyperthyroidism caused by Graves' disease discovered a significant increase in serum calcitonin levels and stated that the increase in calcitonin levels could be due to increase level of calcium (hypercalcemias) as calcitonin is released by thyroid gland in response to calcium levels in the body. These increase in calcitonin level in chronic kidney disease and case of thyroid abnormalities confirms or is in support with the findings of this study.

Table 4.2 shows the Serum Calcitonin, T3, T4, Tsh, Creatinine And Uric Acid Levels For Female Controls And Chronic kidney diseases Subjects. For control subjects, Calcitonin(110±10.9), $T_3$ (1.47±0.0610), $T_4$ (8.95±0.325), TSH (2.22±0.251), Creatinine (0.756±0.0442), Uric Acid (4.86±0.219), Chronic kidney diseases Subjects values are Calcitonin(126±23.9), $T_3$ (0.792±0.0720), $T_4$ (6.92±0.326), TSH (9.00±1.69), Creatinine (5.98±1.49), Uric Acid (11.6±1.46). from the result of this study calcitonin, creatinine, $T_3$, $T_4$, TSH and uric acid proved to be statistically significant ($p \leq 0.05$) when compared with the control subjects of females.

Increased female levels of calcitonin was discovered in the research of Sabia *et al*., 2019, it was by assumed by Sabia *et al*., 2019 that an increased C-cell hormone secretion results from disturbance in mineral metabolism due to renal failure, this supports the findings of this present study.

Chronic kidney disease affect the pituitary-thyroid axis which is the main control axis of thyroid hormones and metabolism of thyroid hormones. Primary hypothyroidism is common in female CKD patients who have decline in (eGFR. The most common thyroid dysfunction in CKD patients is a “low T3 syndrome”. However, the T4 levels also affected because of impaired protein binding of T4 (Pan *et al*.,2019). Other factors that associated with T3 reduction in female patients with CKD such as systemic acidosis, endothelial damage markers, and inflammation. The most commonly thyroid dysfunction that seen in CKD patients is low T3, this is due to decreased peripheral deiodinase conversion of T4 to T3 this happen because of by chronic metabolic acidosis and malnutrition of proteins that seen in CKD (Choi *et al*., 2020).in similarity to this study, the study of Iglesias and Diez, 2009 discovered an increase in the TSH levels of female patients with CKD and stated that thyroid hormones urinary loss associated with stimulation of hypothalamus–pituitary–thyroid axis led to increase in TSH concentration.

Female Creatinine level is influenced by diet and muscle mass it’s filtered and not re-absorbed and cleared by the kidneys (Peterson *et al*., 2018). The reason behind creatinine elevation is the lowering in GFR and also protein. The creatinine which derived from phosphocreatinine catabolism in the muscles it should be cleared by the glomerulus but in case of CKD its get higher in inverse relationship with GFR (Balestrino *et al*., 2019). A previous study that measured creatinine in female patient with CKD agreed these results (Yoo *et al*., 2019). Elevation in creatinine levels happened because of reduction in body mass and reduction in nephron number that happened as a result of aging (Yokota *et al*., 2018).

Renal excretion, tubular secretion and creatinine degradation are declines in female CKD patient and cause creatinine elevation also meat intake and protein supplement lead to increase of serum creatinine. Another reason of high level of creatinine is the medication that inhibit tubular creatinine secretion and decrease the breakdown of creatinase by the gut (Post *et al*., 2019).

This increase in uric acid in females is associated with defects in transport of nephron. Uric acid may participate in the development of interstitial lesions which leads to inflammation in the renal parenchyma that is observed in CKD patients (Dos *et al*., 2020).

Table 4.3 shows the calcitonin, $T_3$, $T_4$, TSH creatinine, uric acid, levels for males control and ckd subjects. For control subjects, Calcitonin (44.8±11.1), $T_3$ (1.54±0.0875), $T_4$ (9.18±0.425), TSH (2.48±0.418), Creatinine (0.761±0.0705), Uric Acid (5.19±0.359), Chronic kidney diseases Subjects values are Calcitonin(98.8±12.4), $T_3$ (0.770±0.0356), $T_4$ (7.40±0.228), TSH (8.07±0.523), Creatinine (8.70±0.618), Uric Acid (16.3±1.07). from the result of this study calcitonin, creatinine, $T_3$, $T_4$, TSH and uric acid proved to be statistically significant ($p \leq 0.05$) when compared with the control subjects of males.

Renal failure is an increasing problem representing a great health challenge regarding the gender difference, it has been stated that chronic renal failure affects males more than females in all adult ages with more incidence in youths than in old ages (García *et al*., 2022). Its prevalence is two times higher in males than females. Its incidence is also higher in blacks three to four times more than found in white races. Some authors attributed the gender difference in renal failure incidence to the influence of sex hormones (Baio *et al*., 2018).

The mean value of calcitonin level was significantly increased in male patients of CKD as compared to controls (patients of CKD 98.8±12.4, controls 44.8±11.1), the aforementioned findings are similar to the findings Mulder *et al*., 1982 who observed enhanced calcitonin release levels in male patients with chronic kidney damages, he stipulated the the increase release of calcitonin in the system could be as result of the underlying kidney damage, due to smoking or high body weight.

The mean value of serum T3 level was significantly less in patients of CKD as compared to controls (patients of CKD 0.770±0.0356, controls 1.54±0.0875), Similarly mean serum T4 value was significantly less in patients of CKD as compared to controls (serum T4 in CKD 7.40±0.228, controls 9.18±0.425. Serum mean TSH level was significantly increased in patients of CKD as compare to controls (CKD 8.07±0.523, Controls 2.48±0.418). A large number of hormonal systems are affected by CKD, yet it remains unclear to what extent these changes are responsible for manifestations of CKD. Patients with CKD often have signs & symptoms suggestive of thyroid dysfuction & hence the diagnosis of thyroid hormones in these patients have obvious prognostic implications. The data reported deals primarily with the clinical symptoms sign index & biochemical parameters. In CKD the mean values of both serum T3 & T4 were significantly reduced when compared to their respective controls. This is comparable to various studies done earlier by aqualini *et al*., 1991 and Pagliacci *et al*., 1987. The likely explanations for low levels of both T3 & T4 could be defective release in response to TSH. The increase in TSH levels can be explained by the normal negative feedback regulation of the pituitary thyroid axis.

In contrast to our study, Spector *et al*., 1976 and Ramirez *et al*., 1976 reported normal levels of serum TSH in patients of CKD inspite of low serum T3 levels. They demonstrated abnormality in the hypophyseal mechanism of TSH release in uraemic patients as the TSH response to the administration of thyotropin releasing hormone (TRH) was blunted.

Our results are comparable with Joseph *et al*., 1993 who had low T3,T4 but had high TSH levels suggesting maintenance of pituitary-thyroidaxis. Serum Creatinine (SCr) is commonly used among clinicians to determine renal function. the outcome of this study is similar showed an elevated level of serum Creatinine of male subjects with Chronic kidney diseases when compared with the control, these findings are in accordance with the findings of Janice *et al*., 2017 who also observed a significant increase in serum creatinine level and stated further that Possible causes of high creatinine level in the male subjects could be as a result of kidney damage, high protein consumption, diabetes or heart disease

In the study of Tamaki *et al*.,2011, the author examined male applicants undergoing routine checkup after analysis, it was observed that the serum uric acid concentration was elevated and stated that the increase in uric acid concentration could be due to underlying renal failure.

Table 4.4 shows the correlation of age against measured variables, of such variables include Creatinine Uric Acid and Calcitonin. At the end of the study it was observed that age has a statistically significant effect on these variables

Serum creatinine concentrations are widely used clinically as an index of renal function. In stable normal or reduced renal function they are determined by the rate of creatinine production and the endogenous creatinine clearance, and, during changing renal function, also by the apparent volume of distribution of creatinine. These determinants of serum creatinine concentrations, however, are affected by age, sex and body weight. The rate of creatinine production is proportional to body weight, and it decreases with age and is slower in females than in males (Bjornsson, 1979). The research of Bjornsson, 1979 was supported by the study of James *et al*., 1988. However contrary to the study of Bjornsson, 1979 and James *et al*., 1988, Jim *et al*., 2002 stated in his research on The effect of age on serum creatinine levels in an aging population that Serum creatinine concentration increased steadily with age; in females from the age of 40 years and 60 years for males.

The serum level of uric acid is affected by aging and genetic and environmental factors. There was a clear increase in SUA level with age in French men between the ages of 20 and 55, based on a survey conducted between 1967 and 1970. The study conducted in the United States from 1959 to 1960 reported that the SUA values in men rose rapidly to a peak level at 20 to 24 years, after which they declined slightly, and then reached a plateau, except for a slight later rise at 55 to 59 years (Kuzuya *et al*., 2002).

In women from the same study, however, SUA levels rose to a minor peak at 15 to 19 years, after which they declined slightly, and levelled out to about age 40. From about 40 to 54 years, the curves rose slowly again to peak levels at 50 to 54, and later at 60 to 64 years. In the Framingham Heart Study, no significant age-related changes of SUA levels were observed between ages 20 and 80 in men. In women, the SUA levels gradually increased from the fourth to the seventh decades of life (Culleton *et al*., 1999).

Calcitonin (CT) is a peptide hormone which is produced by the C-cells of the thyroid gland. The release of CT is stimulated by an acute rise in serum calcium (Ca) levels (Sonntag *et al*., 2020). Cooper *et al*., 1967 discovered a more pronounced

level of CT in rats 5 weeks old compared to older rats. Moreover, an indirect clue for an age-dependent functional role of CT was the observation of a 5-fold decrease in serum CT from the neonatal period to adolescence by Body *et al*., 1993. As published recently by Eckelt *et al*., 2019, CT levels showed a clear age and gender dependence with maximal levels in the first year of life and significantly higher values in boys ($p < 0.01$). An accelerated decline of CT levels from newborns to children at the age of 4 and 5 years was observed for both sexes.

In the study of Nishida, 1992 significant positive correlation between 24 hour urinary creatinine and uric acid excretion was observed. In the steady state urinary excretion of uric acid over 24 hours is thought to represent the urate production over the same period. Although 24 hour urinary excretion of creatinine may be affected by the dietary creatinine content, it seems that there is a close association between creatinine and uric acid synthesis.( Komori *et al*., 2018)

One possible mechanism for this associationis the increased supply of creatinine from the diet. This exogenous creatinine is subsequently metabolised to creatinine phosphate, then creatinine. The phosphate donor is ATP. Increased degradation of ATP has been shown to cause accelerated urate synthesis.( Zhang *et al*., 2020)

Another possible mechanism for the association between creatinine and uric acid synthesis is endogenous creatinine synthesis, by methylation of guanidinoacetic acid. In this reaction S-adenosylmethionine is converted to S-adeno syl homocysteine, which is then catalysed to adenosine. Accelerated creatinine synthesis may cause increased synthesis of adenosine, which is degraded subsequently to inosine, hypox- anthine, xanthine, and uric acid (Aziz *et al*., 2020). Christensen *et al*., 1979 studied the relationship between serum calcitonin and serum creatinine in chronic renal failure and a highly significant inverse correlation was found between serum calcitonin and creatinine clearance in patients with chronic renal failure.

## 5. CONCLUSION

In conclusion, it was observed at the end of this study that age and sex plays a significant role in the alteration of Serum Calcitonin, T3, T4, TSH, Creatinine And Uric Acid Levels in individuals.

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