

## EVALUATION OF SERUM CALCITONIN, CREATININE AND URIC ACID ON CKD PATIENTS AT VARIOUS STAGES WITH THYROID ABNORMALITY COMPLICATION

### ABSTRACT

The aim of this study was to evaluate the serum calcitonin, creatinine and uric acid on ckd patients at various stages with thyroid abnormality complication. in the study population for this research are renal unit patients attending clinic at the Irrua Specialist Teaching Hospital, Benin City, Edo state, Nigeria. This study was carried out at the Irrua specialist Teaching Hospital, Edo State. Total Thyroxine ( $T_4$ ), total triiodothyronine ( $T_3$ ), total triiodothyronine ( $T_3$ ) and Calcitonin Estimation were estimated using ELISA Method, Uric acid and Creatinine by Jaffe Reaction were estimated calorimetrically. Data was collected, screened for completeness and entered into the SPSS version 20 for analysis. The result shows the serum levels of Calcitonin,  $T_3$ ,  $T_4$ , TSH, creatinine, uric Acid based on different stages of renal disease patients, calcitonin Stage 3 ( $85.7 \pm 17.3$ ) Stage 4 ( $109 \pm 16.8$ ) Stage 5 ( $74.5 \pm 17.8$ ).  $T_3$  Stage 3 ( $0.773 \pm 0.0771$ ) Stage 4 ( $0.731 \pm 0.0419$ ) Stage 5 ( $0.48 \pm 0.0288$ ).  $T_4$  Stage 3 ( $12.9 \pm 5.45$ ) Stage 4 ( $8.06 \pm 0.255$ ) Stage 5 ( $5.35 \pm 0.2$ ). TSH Stage 3 ( $5.63 \pm 0.620$ ) Stage 4 ( $15.2 \pm 4.72$ ) Stage 5 ( $6.91 \pm 0.644$ ). Creatinine Stage 3 ( $7.04 \pm 0.823$ ) Stage 4 ( $8.33 \pm 0.797$ ) Stage 5 ( $9.11 \pm 1.41$ ). Uric Acid Stage 3 ( $15.6 \pm 1.74$ ) Stage 4 ( $14.1 \pm 0.993$ ) Stage 5 ( $15.7 \pm 2.35$ ). There was no relationship between the serum levels of Calcitonin,  $T_3$ ,  $T_4$ , TSH, creatinine, and uric acid based on different stages of renal disease is that these markers are influenced by different physiological processes, and the changes in these processes that occur in CKD can vary among individuals

Keywords

### INTRODUCTION

Chronic kidney disease (CKD) is a progressive condition that affects the kidneys' ability to filter blood and remove waste products from the body. It is a common complication of various underlying medical conditions, including thyroid abnormalities. Abnormalities in the thyroid gland can affect kidney function and contribute to the development of CKD (Kasbekar and Ambizas, 2021).

**Comment [WU1]:** The first thing in abstract should be a sentence introducing the main study topic, not aim of study.

The sentence is too long and its meaning is unclear.

**Comment [WU2]:** made

**Comment [WU3]:** using calorimetric assays

**Comment [WU4]:** not needed in abstract but under methods

**Comment [WU5]:** acid

**Comment [WU6]:** where are the keywords

**Comment [WU7]:** should take this form

**Comment [WU8]:** wrong referencing style

Serum calcitonin, creatinine, and uric acid are important markers of kidney function that can be used to monitor CKD progression in patients with thyroid abnormalities. These markers can be measured at various stages of CKD to assess the severity of the disease and guide treatment decisions(Sindhu, 2018).

Comment [WU9]: referencing style

Calcitonin is a hormone produced by the thyroid gland that regulates calcium levels in the body. Elevated levels of calcitonin can indicate thyroid abnormalities, such as thyroid cancer or hyperthyroidism, which can contribute to the development of CKD. Creatinine is a waste product produced by muscle metabolism that is excreted by the kidneys. Elevated levels of creatinine in the blood indicate impaired kidney function, which is a hallmark of CKD. Uric acid is another waste product that is excreted by the kidneys. Elevated levels of uric acid can contribute to the development of CKD and can also be a sign of gout or other metabolic disorders(Giannetta *et al.*, 2020).

In patients with thyroid abnormalities, serum calcitonin, creatinine, and uric acid levels can be used to monitor CKD progression and guide treatment decisions. For example, if calcitonin levels are elevated, further testing may be needed to rule out thyroid cancer. If creatinine levels are elevated, interventions may be needed to slow the progression of CKD, such as blood pressure control, dietary changes, or medication adjustments. If uric acid levels are elevated, treatments may be needed to reduce the risk of gout and metabolic complications(Bahtiyar *et al.*, 2020).

Monitoring serum calcitonin, creatinine, and uric acid levels can provide important insights into the progression of CKD in patients with thyroid abnormalities. Early detection and

intervention can help to slow the progression of CKD and improve overall outcomes for these patients(van der Wijst *et al.*, 2019).

**Comment [WU10]:** The last paragraph of introduction should highlight the challenges that prompted the study, and what the study is all about.

## METHODS

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

**Comment [WU11]:** Add this

**Study Population:** The study population is made up of patients with CKD stage.....tostage.....for this research are renal unit patients attending clinic at the Irrua Specialist Teaching Hospital, Benin City, Edo state, Nigeria.

**Comment [WU12]:** Rephrase accordingly

### Inclusion Criteria: (Test Group)

Adult male and female subjects with renal insufficiency

**Comment [WU13]:** With CKD

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

**Comment [WU14]:** What was your diagnostic cut- off criteria?

**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).

**Comment [WU15]:** the prevalence from a similar study conducted in Bayelsa, Nigeria

**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

Total Thyroxine (T<sub>4</sub>), total triiodothyronine (T<sub>3</sub>) and Calcitonin

Estimation were estimated using ELISA Method (Beitollahi *et al.*, 2018). Uric acid (Liu *et al.*, 2018) and Creatinine by Jaffe Reaction (Küme *et al.*, 2018) were estimated calorimetrically

### Data Analysis

Data was collected, screened for completeness and entered into the SPSS version 20 for analysis. 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  $p \geq 0.05$ .

**Comment [WU16]:** pls what is the difference in these two T3

**Comment [WU17]:** were.....  
Is this a proposal or manuscript?

## RESULT

**TABLE 1: COMPARISON OF SERUM LEVELS OF CALCITONIN, THYROID HORMONES, CREATININE AND URIC ACID AMONG CONTROLS AND CKD SUBJECTS**

Parameters	Normal Range	Control Subjects (n = 50)	CKD Subjects (n = 70)	t value	p value
Calcitonin (pg/L)	Males= $\leq$ 19ng/L Females=14ng/L	15.4 $\pm$ 0.22	23.9 $\pm$ 0.40	4.29	0.001
T3 (ng/mL)	0.6 - 2.0	1.49 $\pm$ 0.0498	0.774 $\pm$ 0.0317	12.8	0.001
T4 (m $\mu$ g/dL)	6.0 - 12	9.03 $\pm$ 0.256	7.31 $\pm$ 0.195	5.43	0.001
TSH (miu/mL)	0.4 - 4.2	2.31 $\pm$ 0.218	8.25 $\pm$ 0.525	9.2	0.001
Creatinine (mg/dL)	0.7 - 1.4	0.758 $\pm$ 0.0376	8.19 $\pm$ 0.585	10.8	0.001
Uric Acid (mg/dL)	3.4 - 6.5	4.98 $\pm$ 0.190	15.4 $\pm$ 0.935	9.42	0.001

**TABLE 2: THE SERUM LEVELS OF MEASURED PARAMETERS BASED ON STAGES OF RENAL DISEASE AMONG STUDY PARTICIPANTS.**

Parameters	Normal Range	Stage 3	Stage 4	Stage 5	F value	p value
Calcitonin (pg/L)	≤10	85.7±17.3	109±16.8	74.5±17.8	1.02	0.367
T3 (ng/ml)	0.6 - 2.0	0.773±0.0771	0.731±0.0419	0.48±0.0288	3.02	0.056
T4 (mµg/dl)	6.0 – 12	12.9±5.45	8.06±0.255	5.35±0.299	2.38	0.101
TSH (miu/ml)	0.4 - 4.2	5.63±0.620	15.2±4.72	6.91±0.644	1.56	0.217
Creatinine (mg/dl)	0.7 - 1.4	7.04±0.823	8.33±0.797	9.11±1.41	0.758	0.473
Uric Acid (mg/dl)	3.4 - 6.5	15.6±1.74	14.1±0.993	15.7±2.35	0.401	0.671

Comment [WU18]: Meaning???

UNDER PEER REVIEW

## DISCUSSION

Table 1 shows the comparison of Serum Calcitonin, thyroid hormones, Creatinine and Uric Acid Levels among Controls and Chronic kidney diseases Subjects. For control subjects, Calcitonin(15.4±0.22), T<sub>3</sub> (1.49±0.0498), T<sub>4</sub> (9.03±0.256), TSH (2.31±0.218), Creatinine (0.758±0.0376), Uric Acid (4.98±0.190), Chronic kidney diseases Subjects values are Calcitonin(23.9±0.40), T<sub>3</sub> (0.774±0.0317), T<sub>4</sub> (7.31±0.195), TSH (8.25±0.525), Creatinine (8.19±0.585), Uric Acid (15.4±0.935). from the result of this study calcitonin, creatinine, T<sub>3</sub>, T<sub>4</sub>, TSH and uric acid proved to be statistically significant ( $p \leq 0.05$ ) when compared with the control subjects of females. This increase levels of calcitonin could be due to the fact that In CKD, elevated levels of phosphorus in the blood can stimulate the secretion of fibroblast growth factor 23 (FGF23), a hormone that regulates phosphorus metabolism. FGF23 can stimulate the production of calcitriol, the active form of vitamin D, in the kidneys (Bhattarai *et al.*, 2020). Calcitriol can increase the absorption of calcium from the gut and bones, leading to increased calcium levels in the blood. High levels of calcium in the blood can stimulate the release of calcitonin from the thyroid gland. Calcitonin can help to reduce calcium levels in the blood by inhibiting the release of calcium from bones and increasing the excretion of calcium by the kidneys (Babić Leko *et al.*, 2021). This observation is in similarity with the studies of Roza *et al.*, 2019.

The mean value of serum T3 level was significantly less in patients of CKD as compared to controls, similarly mean serum T4 value was significantly less in patients of CKD as compared to controls. Serum mean TSH level was significantly increased in patients of CKD as compare to controls. This could be due to reduced conversion of T4 to T3 as in CKD patients, the conversion of T4 (thyroxine) to T3 (triiodothyronine) can be impaired, leading

**Comment [WU19]:** This is quite very wrong. The first paragraph in discussion should summarize the essential findings in the study not referring to tables nor giving numbers. This should be in the result session

**Comment [WU20]:** References should not be dated in the main text

to lower levels of T3. This is because the enzyme responsible for this conversion, called type 1 iodothyronine deiodinase (D1), is primarily located in the liver and kidney. In CKD, the reduced renal function can result in decreased D1 activity and hence lower T3 levels (Kumar *et al.*, 2018). It could also be due to decreased production of T4 as in CKD patients with thyroid dysfunction may have reduced production of T4 due to decreased thyroid gland function or reduced TSH secretion (Narasaki *et al.*, 2021). Increased clearance of T4 and T3 due to reduced protein binding or increased urinary excretion may also be another cause (Bartalena *et al.*, 2022). This results were in similarity with Aqualini *et al.*, 1991 and Pagliacci *et al.*, 1987 who observed altered feedback mechanism between the hypothalamus, pituitary gland, and thyroid gland may be altered, resulting in reduced TSH secretion.

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. However, our results are comparable with Joseph *et al.*, 1993 who had low T3,T4 but had high TSH levels suggesting maintenance of pituitary-thyroidaxis.

Comment [WU21]: Thyroidal axis

Table 2 shows the serum levels of Calcitonin,T3,T4,TSH , creatinine,uric Acid based on different stages of renal disease patients, calcitonin Stage 3 (85.7±17.3)Stage 4 (109±16.8)Stage 5 (74.5±17.8). T3 Stage 3 (0.773±0.0771)Stage 4 (0.731±0.0419)Stage 5 (0.48±0.0288). T4 Stage 3 (12.9±5.45)Stage 4 (8.06±0.255) Stage 5 (5.35±0.2). TSH Stage 3 (5.63±0.620)Stage 4 (15.2±4.72) Stage 5 (6.91±0.644). Creatinine Stage 3 (7.04±0.823)Stage 4 (8.33±0.797) Stage 5 (9.11±1.41). Uric Acid Stage 3 (15.6±1.74)Stage 4 (14.1±0.993) Stage 5 (15.7±2.35).

Comment [WU22]: Remove this

The reason why there may be no relationship between the serum levels of Calcitonin, T3, T4, TSH, creatinine, and uric acid based on different stages of renal disease is that these markers are influenced by different physiological processes, and the changes in these processes that occur in CKD can vary among individuals (Ma *et al.*, 2020).

**Comment [WU23]:** Not a strong enough reason. Revise this and rephrase

For example, Calcitonin is a hormone produced by the thyroid gland, and its levels are not directly affected by kidney function. Similarly, T3, T4, and TSH are primarily regulated by the thyroid gland, and although there may be some indirect effects of CKD on thyroid function, the relationship is not straightforward and may vary among individuals (Kim *et al.*, 2020). On the other hand, creatinine and uric acid are markers of kidney function and metabolism, respectively, and their levels are directly affected by the degree of kidney dysfunction (Borghi *et al.*, 2020). However, the relationship between the levels of these markers and the severity of CKD may not always be linear, as other factors such as age, sex, muscle mass, and comorbidities can also affect their levels. Moreover, the progression of CKD can be influenced by various factors, such as underlying causes of kidney disease, medication use, blood pressure control, and comorbidities, which can also affect the levels of these markers in unpredictable ways (Anders *et al.*, 2018). Therefore, the lack of a consistent relationship between the serum levels of Calcitonin, T3, T4, TSH, creatinine, and uric acid in different stages of renal disease may reflect the complexity of CKD pathophysiology and the heterogeneity of CKD patients.

**Comment [WU24]:** These are not scientifically proven facts but generalized assumptions. Why didn't the author discuss why the levels of thyroid function indexes seem to be non-predictable in patients with stage 4 CKD as opposed to stages 3 and 5.

## CONCLUSION

There was no relationship between the serum levels of Calcitonin, T3, T4, TSH, creatinine, and uric acid based on different stages of renal disease is that these markers are influenced by different physiological processes, and the changes in these processes that occur in CKD can vary among individuals (Ugege *et al.*, 2022).

Comment [WU25]: Not true.

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