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To Study Prevalence of Thyroid Disorders in Chronic Kidney Disease Patients and Its Association with Dyslipidaemia and Cardiovascular Diseases

[1]Anil Jadav, Department of General Medicine, Dr. Vithalrao Vikhe Patil Foundation's Medical College and Hospital, Ahilyanagar

[1]Sonawane T C, Department of General Medicine, Dr. Vithalrao Vikhe Patil Foundation's Medical College and Hospital, Ahilyanagar

[1]Sanjay Warude, Department of General Medicine, Dr. Vithalrao Vikhe Patil Foundation's Medical College and Hospital, Ahilyanagar

Corresponding Author: Anil Jadav, Department of General Medicine, Dr. Vithalrao Vikhe Patil Foundation's Medical College and Hospital, Ahilyanagar

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Abstract

Background: Thyroid dysfunction is frequently observed in patients with chronic kidney disease (CKD), particularly in its advanced stages. The altered thyroid hormone metabolism in CKD contributes to subclinical or overt hypothyroidism and is often associated with dyslipidemia and cardiovascular disease (CVD), compounding morbidity and mortality.

Objectives: To assess the prevalence and patterns of thyroid dysfunction in CKD stages 3 to 5 and to evaluate its association with dyslipidemia and cardiovascular comorbidities.

Methods: A cross-sectional observational study was conducted over 18 months at a tertiary care center involving 200 adult CKD patients (stage 3–5). Patients with acute kidney injury, pregnancy, or medications affecting thyroid function were excluded. Thyroid function tests (T3, T4, TSH), serum lipid profiles, and cardiovascular evaluations (history, ECG, echocardiography) were performed. CKD staging followed KDIGO guidelines. Thyroid disorders were classified as euthyroid, low T3/T4 syndrome, subclinical or clinical hypothyroidism.

Results: Among 200 patients, thyroid dysfunction was present in 82%: low T3 syndrome (40%), subclinical hypothyroidism (22%), low T4 syndrome (14.5%), and clinical hypothyroidism (5.5%). No cases of hyperthyroidism were reported. Most patients were female (61%) and obese (58%). Stage 4 CKD was most common (54.5%), followed by stage 5 (36.5%) and stage 3 (9%). Symptoms included breathlessness (69%) and pedal edema (41.5%). Dyslipidemia and prior cardiovascular events were notably more frequent in patients with thyroid abnormalities.

Conclusion: Thyroid dysfunction, especially low T3 syndrome and subclinical hypothyroidism, is highly

prevalent in advanced CKD. These dysfunctions are significantly associated with dyslipidemia and increased cardiovascular risk. Routine thyroid screening in CKD patients may aid in early detection and holistic management, potentially improving cardiovascular outcomes.

Keywords: Chronic Kidney Disease, Hypothyroidism, Low T3 Syndrome, Thyroid Function, Dyslipidemia, Cardiovascular Disease

Introduction

Thyroid disorders are prevalent among patients with chronic kidney disease (CKD), significantly impacting their health outcomes. CKD patients frequently experience alterations in thyroid hormone levels due to impaired renal function, leading to hypothyroidism or, less commonly, hyperthyroidism. These thyroid dysfunctions are closely associated with dyslipidemia, characterized by abnormal lipid profiles, which further exacerbates cardiovascular disease (CVD) risk. The interplay between thyroid disorders, dyslipidemia, and CVD creates a complex clinical challenge, necessitating comprehensive management strategies to mitigate adverse health effects and improve overall patient prognosis. Understanding these associations is crucial for optimizing treatment and preventing cardiovascular complications in CKD patients.

Methodology

Study Design

Type of Study: Cross-sectional observational study.

Location: Conducted at a tertiary care center.

Duration: The study will span 18 months.

Inclusion Criteria

1. Age >18 years
2. Patients ready to give consent and answer relevant questions for the study
3. Patients fulfilling criteria of chronic kidney Disease
   - Raised serum creatinine levels
   - Reduced GFR

That is Patients with CKD stage 3-5

Exclusion Criteria

1. Age <18 years
2. Patients with Acute Kidney Injury
3. Pregnant women (Given potential pregnancy related changes in thyroid function
4. Subjects receiving concurrent treatment with drugs that could affect thyroid function (Lithium, Amiodarone, Iodine, methimazole, etc)

Chronic Kidney Disease is defined by evidence of renal damage including

1. raised serum creatinine levels
2. reduced GFR <90ml/min/1.73m2 (as calculated by Cockcroft-Gault formula)

Divided into stages

- Stage 1: Kidney damage with normal or increased GFR(>90ml/min/1.73m2)
- Stage 2: mild reduction in GFR (60-89 ml/min/1.73m2)
- Stage 3a: moderate reduction in GFR (45-59 ml/min/1.73m2)
- Stage 3b: moderate reduction in GFR (30-44ml/min/1.73m2)
- Stage 4: severe reduction in GFR (15-29 ml/min/1.73m2)
- Stage 5: kidney failure (GFR <15ml/min1.73m2 or dialysis)

3. Renal imaging studies (USG) showing bilateral contracted kidneys(<9cm) with thinned parenchyma and reduced corticomedullary differentiation

Routine investigations done including CBC RFT Serum electrolytes, ECG, Chest X-ray. Staging of CKD done according to KIDGO guidelines

Thyroid Function Test including T3 T4 and TSH done in every selected CKD patient to look for subclinical or clinical hypothyroidism

Clinical Hypothyroidism: It is defined as increased serum TSH levels with decreased free Thyroxine (FT3) levels

Subclinical Hypothyroidism: It is defined as TSH> 5mIU/L and free T3 and T4 within reference range.

Reference range - FT3 4-8.3 pmol/L, FT4 9-20 pmol/L, TSH 0.25-5 mIU/L

Serum Lipid Profile including cholesterol and triglycerides done to look for dyslipidaemia

Evidence of cardiovascular event noted by the past history of myocardial infarction or angina pectoris, congestive heart failure, peripheral arterial disease or stroke.

1. Detailed history taken regarding diabetes mellitus /hypertension / IHD / heart failure

2. Selected 200 CKD patients (stage 3-5)

3. Free T3/T4/TSH, Serum lipids, serum creatinine and routine investigations done.

Imaging modalities done include ECG, USG abdomen and pelvis to look for renal sizes and

CMD and 2D echocardiography to look for regional wall motion abnormality and IHD.

Following parameters studied

1. Prevalence of thyroid disorder in CKD patients

2. Prevalence of thyroid disorders as per stages of CKD

3. Prevalence of hypothyroidism versus hyperthyroidism

4. Prevalence of overt versus subclinical disease

5. Association of cardiovascular disease and dyslipidemia with thyroid dysfunction.

Approval and Ethical Considerations

Ethical Approval: The study protocol will be reviewed and approved by the Ethical Committee for Approval of Research Projects (ECARP).

Informed Consent: Proper informed consent will be obtained from all participants prior to their inclusion in the study.

Data Collection

Patient Recruitment: Cases will be selected from those admitted in the wards during the 18 months duration of the study.

Data Sources

- Medical records of patients.
- Laboratory results.
- Clinical assessments.

Variables

- Independent Variables:
- Presence of chronic kidney disease.
- Dependent Variables:
- Prevalence of thyroid disorders.
- Presence of dyslipidemia.
- Presence of cardiovascular diseases (CVD).

Data Collection Procedure

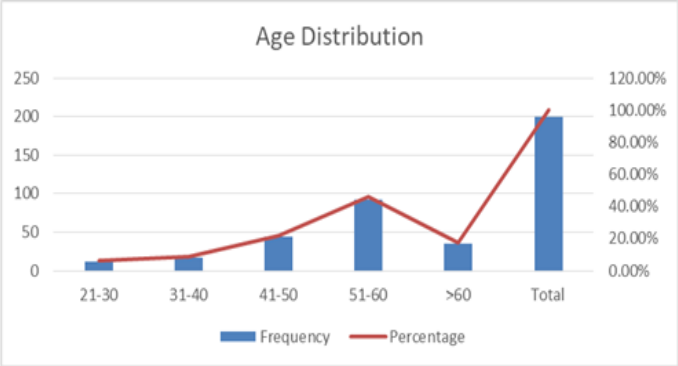
1. Identification and Recruitment:
- Screen admitted patients for CKD.
- Approach eligible patients to explain the study and obtain informed consent.
2. Data Extraction:
- Collected demographic data (age, gender, etc.).
- Reviewed medical records for thyroid function tests.
- Recorded lipid profiles and cardiovascular assessments.
- Noted any history of dyslipidemia and cardiovascular diseases.
3. Laboratory Tests:
- Thyroid function tests (T3, T4, TSH).
- Lipid profile (total cholesterol, HDL, LDL, triglycerides).
4. Clinical Assessments:

- Detailed history and physical examination focusing on cardiovascular symptoms.
- Echocardiography and other relevant cardiovascular tests done.

Data Management

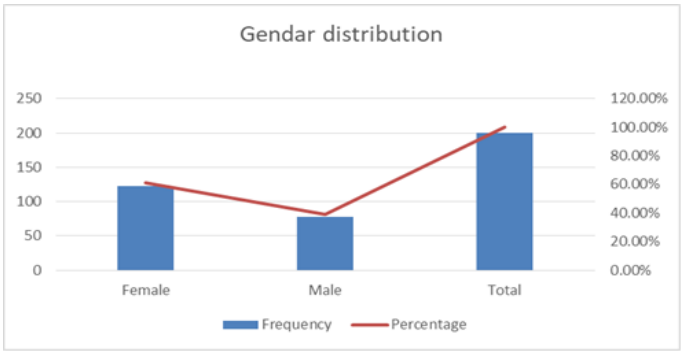
- Confidentiality: Patient confidentiality was maintained at all stages of the study.

Result



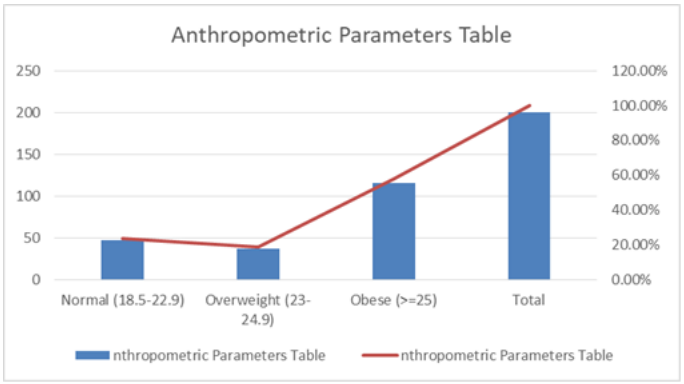
Graph 1:

The study highlights several key observations about the age distribution. The 21-30 age range has the lowest frequency of individuals, indicated by the smallest blue bar. The frequency increases gradually in the 31-40 and 41-50 age ranges. The highest frequency is found in the 51-60 age range, which has the tallest blue bar, signifying that the majority of individuals belong to this age group. There is a notable decline in frequency for individuals aged over 60.



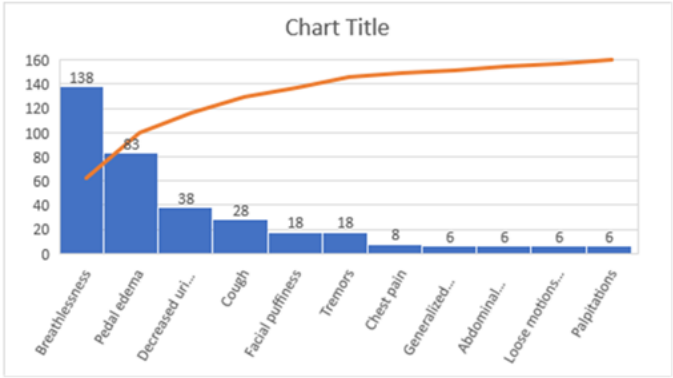
Graph 2:

The "Gender Distribution" shows that provides insights into the frequency and cumulative percentage of individuals based on gender. The blue bars represent the frequency of females and males, while the orange line represents the cumulative percentage. Observing that, it is evident there are more females than males, as indicated by the taller blue bar for females. The frequency for females is higher, with the bar reaching above the 100 mark, whereas the frequency for males is lower, with the bar around the 50 mark. The cumulative percentage line starts higher for females, showing a significant initial proportion, then drops for males, reflecting their lower frequency.



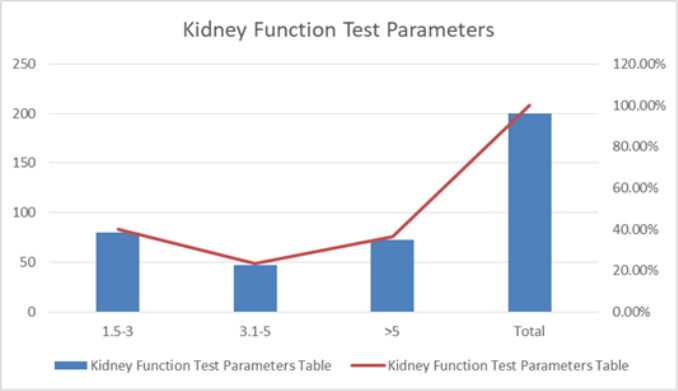
Graph 3:

Body mass index(kg/m²) of 116(58.00%) cases was >=25 kg/m² {Obese}, 47(23.50%) cases was 18.5 to 22.9kg/m² {Normal BMI} and 37(18.50%) cases was 23 to 24.9 kg/m² {Overweight}. Mean value of body mass index(kg/m²) of study subjects was 25.22 ± 3.14 with median (25th-75th percentile) of 26(24-27).



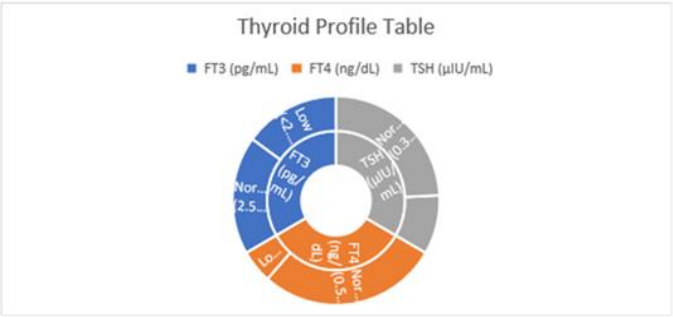
Graph 4:

In present study, 138(69.00%) cases had breathlessness, 83(41.50%) cases had pedal edema, 38(19.00%) cases had decreased urine output, 28(14.00%) cases had cough, 18(9.00%) cases had facial puffiness, 18(9.00%) cases had tremors, 8(4.00%) cases had chest pain and 6(3.00%) cases had generalized body swelling and pain, abdominal distension, loose motions and vomiting and palpitations each.



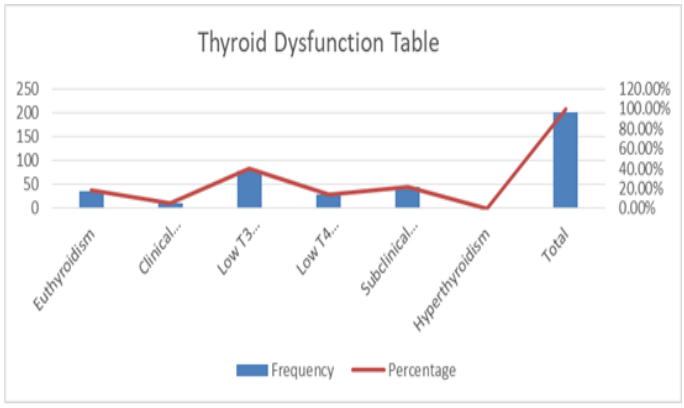
Graph 5:

Serum creatinine (mg/dL) of 80(40.00%) cases was 1.5-3 mg/dL, 73(36.50%) cases was >5 mg/dL and 47(23.50%) cases was 3.1-5 mg/dL. Mean value of serum creatinine (mg/dL) of study subjects was 4.53 ± 2.18 with median(25th-75th percentile) of 4.3(2.8-6.4).



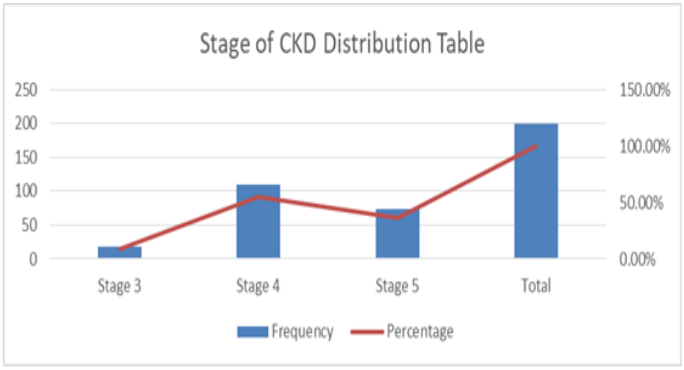
Graph 6:

It shows the reference ranges for three thyroid hormones: Free Triiodothyronine (FT3), Free Thyroxine (FT4), and Thyroid Stimulating Hormone (TSH). low, normal, and high. Each section shows the reference range for each hormone. For example, the normal reference range for FT3 is 2.5 to 5.0 pg/mL. FT3: Low (<2.0 pg/mL), Normal (2.5-5.0 pg/mL), High (>5.0 pg/mL) , FT4: Low (<0.5 ng/dL), Normal (0.5-1.2 ng/dL), High (>1.2 ng/dL) , TSH: Low (<0.3 uIU/mL), Normal (0.3-5.0 uIU/mL), High (>5.0 uIU/mL)



Graph 7:

In the study, 80(40.00%) cases had low T3 syndrome, 44(22.00%) cases had subclinical hypothyroidism, 36(18.00%) cases were euthyroid, 29(14.50%) cases had low T4 syndrome and 11(5.50%) cases had clinical hypothyroidism. None of patient had hyperthyroidism.



Graph 8:

In the study, 109(54.50%) cases had stage 4, 73(36.50%) cases had stage 5 and 18(9.00%) cases had stage 3.

Discussion

This study investigates thyroid dysfunction and its association with the severity of renal disease, dyslipidemia, and cardiovascular diseases in patients with chronic kidney disease (CKD). Conducted at a tertiary care center, the study included 200 patients over 18 years of age diagnosed with CKD.

Age and Gender Distribution

In this study, the majority of patients (46%) were aged between 51 and 60 years, with a mean age of 52.6 ± 12.4 years and a median age of 54 years (25th-75th percentile: 49-58). This age distribution is consistent with other studies, such as Khatiwada et al[1], who reported a mean age of 44.1 ± 16.4 years. The study population had a higher female predominance (61%) compared to males (39%), aligning with findings from Kampmann et al[2]. and other studies indicating a higher prevalence of CKD in women[1].

Study by Kampmann JD et al (Prevalence and incidence of chronic kidney disease stage 3-5 results from KidDico gave results as predominantly women suffered from CKD group (60.4%) [2].

Body Mass Index (BMI)

The majority of patients (58%) were classified as obese (BMI ≥ 25 kg/m²) according to Asian BMI classification standards, with a mean BMI of 25.22 ± 3.14 kg/m² and a median of 26 kg/m² (25th-75th percentile: 24-27). This suggests that obesity is a significant comorbidity in CKD patients, which may influence disease progression and complications.

Goldberg et al[3] in study, the role of gender in chronic kidney disease in Israel. Descriptive statistics of weight(kg), height(cm) and body mass index(kg/m²). Body mass index(kg/m²) of 116(58.00%) cases was >=25 kg/m² {Obese}, 47(23.50%) cases was 18.5 to 22.9 kg/m² {Normal BMI} and 37(18.50%) cases was 23 to 24.9 kg/m² {Overweight}. As per Asian classification of BMI. Mean value of body mass index(kg/m²) of study subjects was 25.22 ± 3.14 with median (25th-75th percentile) of 26(24-27). Mean value of weight(kg) and height(cm) of study subjects was 65.44 ± 8.09 and 160.04 ± 4.74 with median (25th-75th percentile) of 67(60-70) and 159(156-163) respectively.

Clinical Presentations and Symptoms

The most common symptoms observed were breathlessness (69%), pedal edema (41.5%), and decreased urine output (19%). These findings are comparable to other studies, where dyspnea was reported in 63% of cases, and Sathyan et al[4]., who reported dyspnea and oliguria as chief complaints. Anemia (pallor) was the most common physical finding, present in 97% of cases, consistent with other studies highlighting anemia as a frequent complication in CKD patients.

In a study by Dr Amar Prakash Arvind, et al most common symptom was easy fatiguability (60%) followed by pedal edema (38%)[5].

Thyroid Dysfunction in CKD Patients

In this study, thyroid dysfunction was present in 55 (27.5%) of the cases. The distribution of thyroid disorders was as follows: low T3 syndrome in 40% of cases, subclinical hypothyroidism in 22%, euthyroid state in 18%, low T4 syndrome in 14.5%, and clinical hypothyroidism in 5.5%. These findings are consistent with studies, which reported similar prevalences of low T3 and T4 syndromes. The study by Saroj et al. also supports these findings, reporting subclinical hypothyroidism in 27% and overt hypothyroidism in 8.1% of CKD patients.

Severity of CKD

The study categorized CKD stages among the patients, with 54.5% in stage 4, 36.5% in stage 5, and 9% in stage 3. This distribution underscores the severity of renal impairment in the study cohort, with the majority of patients being in the advanced stages of CKD. These findings are consistent with Khatiwada et al[1]., who reported a significant proportion of patients in stages 4 and 5 CKD.

Conclusion

The study highlights the significant prevalence of thyroid dysfunction in CKD patients, particularly subclinical and overt hypothyroidism. The demographic data, symptomatology, and severity of CKD stages observed in this study align well with other reported studies, reinforcing the need for regular thyroid function monitoring in CKD patients to manage potential complications effectively. Further research with larger sample sizes and diverse populations is recommended to strengthen these findings and explore the underlying mechanisms linking thyroid dysfunction with CKD progression.

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