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**ORIGINAL ARTICLE**

# Prevalence of Hypothyroidism in Chronic Kidney Patients Under Different Treatment modalities

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## ABSTRACT

**Background** Many studies were performed for thyroid dysfunction in CKD patients and had very variable prevalence**.** This study aimed to determine the most significant predictors of hypothyroidism in patients with CKD under various treatment methods in our area and to estimate the prevalence of hypothyroidism in such patients.

**Methods**: 200 CKD patients were included in this study, subdivided into 2 groups; 120 conservatively treated and 80 hemodialysed patients. All patients underwent a clinical examination, detailed history, routine investigations, and the MDRD equation was used to estimate their eGFR. The enzyme-linked immunosorbent assay (ELISA) was used to quantify thyroid stimulating hormone (TSH), free T3, and free T4.

**Results:** Among 200 patients**;** 10.5% had subclinical hypothyroidism , and 2% had overt hypothyroidism, with no significant prevalent difference between the two modality of treatment, Significant positive correlation was found between TSH versus CKD duration and age of CKD patient's in the two modality of treatment, and between TSH versus serum phosphorus in conservatively treated group binary regression analysis revealed that increasing serum phosphorus and CKD duration increase risk of hypothyroid dysfunction by 1.471 and 1.442 fold in conservatively treated and by 1.826 and 1.542 fold in hemodialysed patients respectively.

**Conclusions:** Hypothyroidism is common in CKD patients in our locality with no significant difference between the two modalities of treatment. Serum phosphorus and the age of CKD patients could be independent predictors of hypothyroidism in those patients.

**Keywords:** Hypothyroidism; Chronic kidney disease; ESRD.

## INTRODUCTION

The definition of chronic kidney disease (CKD) has changed over time, but current international guidelines define it as a reduction in kidney function, regardless of the underlying cause, as demonstrated by a glomerular filtration rate (GFR) of less than 60 mL/min per 1•73 m2 or the presence of kidney damage markers, or both, for at least three months. In many low-income nations as well as all high- and middle-income countries, diabetes and hypertension are the primary causes of chronic kidney disease (CKD). Additionally, CKD incidence, prevalence, and progression differ throughout nations [1].

Thyroid dysfunction and goiter are more common with end-stage renal disease (ESRD). There is a suggestion that hypothyroidism is more prevalent in individuals with ESRD. Thyroid hormone abnormalities have also been reported in patients with end-stage renal disease (ESRD) [1].

Thyroid disease leads to alterations in renal function. Reproductive blood flow, glomerular filtration rate (GFR), tubular function, electrolyte balance, the process of electrolyte pumps, and kidney architecture are all impacted by hypothyroidism and hyperthyroidism. The main renal dysfunctions associated with hypothyroidism are elevated blood creatinine levels, reduced renal plasma flow (RPF) and

glomerular filtration rate (GFR), a compromised capacity to excrete excess water, and hyponatremia [2].

The absence of these abnormalities in patients with central hypothyroidism can be attributed to the concurrent presence of other pituitary hormone deficits, which might directly or indirectly impact kidney function [2].

Thyroid hormone metabolism, breakdown, and excretion are all very much under the kidneys' regulatory influence. Hormone transport, synthesis, and excretion are all impacted by impaired kidney function. Data suggests that hypothyroidism is common in chronic kidney disease (CKD) patients who have not yet begun dialysis.

Hypothyroidism exhibits similar symptoms as CKD, including pallor, hypothermia, and asthenia [3]. It is typically treated by replacing thyroid hormones, which not only reduces the symptoms of hypothyroidism but also helps improve kidney and heart function. Furthermore, it facilitates the restoration of normal renal plasma flow (RPF) and glomerular filtration rate (GFR) [4].

The relationship between thyroid problems and disorders of the kidneys has become a major concern in the last several years. The development and growth of the kidneys depend on thyroid hormones. Furthermore, the kidney is crucial for the metabolism, deterioration, and excretion of thyroid hormones [5].

Thyroid problems are significantly more common in kidney disorders. The precise explanation of this correlation is not fully comprehended, and certain hypotheses propose that the correlation arises from an increase in iodine reserves resulting from a reduction in renal iodine excretion, leading to iodine retention and subsequent development of hypo- and hyperthyroidism [5].

Numerous research has been conducted about the severity of thyroid dysfunction in patients with chronic kidney disease (CKD) with varying prevalence. However, to the best of our knowledge, very few studies have been conducted in Egypt and the Arab World regarding the prevalence of thyroid dysfunction in patients with CKD under various treatment modalities.

## METHODS

This cross-sectional study was conducted at nephrology and dialysis units of Internal Medicine Departments of Zagazig university And Alahrar Teaching hospitals (Egypt) in the period between September 2022 and February 2023. Written informed consent was obtained from all participants, the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University (IRB number 9114). The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

This study includes 200 patients with CKD which were diagnosed according to KEDOKI (2011) and they were divided into two groups according to the estimated GFR to Two groups as follows:

***Group A:*** CKD with estimated GFR less than 90 ml/dL up to 15 ml/dL who were under conservative treatment including 120 patients with 64 of them were female and 56 of them were male, their ages ranged from 18 years to 78 years , with mean age of 45 years, 45 of them had hypertension controlled on anti-hypertensive treatment and 29 of them had diabetes mellitus on anti-diabetic treatment, their BMI ranged from 17 kg/m2 to 33 kg/m2, with mean of 31 kg/m2 .

***Group B:*** Including 80 patients with ESRD with estimated GFR less than 15 ml/dL under regular HD, three times per week their age ranged from 21 years to 75 years, 29 of them had hypertension controlled on anti-hypertensive treatment and 19 of them had diabetes on regular anti-diabetic treatment, their BMI ranged from 17 kg/m2 to 30 kg/m2, with a mean of 23.5 kg/m2. With duration of dialysis ranged from 1 year to 10 years.

***Inclusion criteria***:

Adult patients of both sexes over the age of 18 were receiving conservative or routine dialysis treatment for chronic renal disease.

***Exclusion criteria***:

Patients with other renal diseases other than CKD, patients with hyperthyroidism, patients < 18 years old.، medications that alter thyroid hormone function as: (Amiodarone, lithium, phenytoin, glucocorticoids dose more than 50 mg), family history of thyroid disorders، thyroid dysfunctions before the appearance of CKD, recent contrast imaging, patients who had thyroidectomy, patients who are receiving thyroid medication, and uncooperative patients refused to give the consent of sharing in the study.

The following procedures were applied to each patient in this study: full history and comprehensive clinical examination, which includes an abdominal and general examination with a focus on blood pressure and body mass index (BMI). Standard lab tests such as serum electrolytes, liver function test (KFT), kidney function test (KFT), ABG, complete blood count

(CBC), RBS, HBA1c, and urine examination. in addition to using the MDRD equation to estimate eGFR, an ECG, and pelvic abdominal ultrasonography.

Specific inquiries, such as: thyroid stimulating hormone (TSH), free T3, and free T4, proteins produced from cells are detected using the enzyme-linked immunosorbent test (ELISA). A calometric reaction based on avidin-horseradish peroxidase activity on a particular substrate (such as ABTS, SuperAqua Blue, or TMB) is used to quantify the proteins. Using a spectrophotometer, the final product's optical density is determined. evaluated using LC-MS/MS methods and serum-based immunoassays.

***Statistical analysis:***

Microsoft Excel software is used to code, enter, and analyze historical data as well as basic clinical examination, laboratory tests, and outcome measurements. The program known as the Statistical Package for the Social Sciences (SPSS v28, IBM©, Chicago, IL, USA). was then used to import data and analyze it. The Kolmogorov-Smirnov test was used to verify the normality of distribution. The following tests were performed to determine if differences were significant: the Chi square test (X2) was used to determine the difference and association of the qualitative variable, and the numbers and percentages of the quantitative group were represented by mean ± SD. P values were established at <0.05 and <0.001, respectively, for significant and very significant outcomes.

## RESULTS

There were 200 participants in this trial, 120 of whom had CKD and 80 of whom had ESRD. Table 1 listed the demographic statistics for both groups. Patients with CKD receiving conservative treatment had a significantly higher BMI than those with ESRD receiving hemodialysis (Table 1).

Among the total 200 studied patients**;** twenty-one patients had subclinical hypothyroidism and four patients had overt hypothyroidism while one hundred and seventy-five patients had euthyroid state. The frequency of overt and subclinical hypothyroidism did not differ significantly between CKD patients under conservative and ESRD patients under dialysis (Table 2).

The disease duration was higher among hypothyroid CKD patients under conservative treatment between (euthyroid CKD patients under conservative treatment and ESRD patients under hemodialysis) (Table 3).

The body mass index was higher among CKD patients under conservative treatment, Within CKD group under conservative treatment, age was significantly higher in euthyroid patients. Both ESRD patients receiving regular hemodialysis and hypothyroid CKD patients receiving conservative therapy showed a substantial drop in serum calcium and increase in serum phosphorus, while there was a significant increase in both hemoglobin and WBCs level among hypothyroid ESRD patients under regular hemodialysis in comparison to euthyroid ESRD patients under regular hemodialysis (Table 4).

There was a strong negative correlation found between free T4 and HbA1c. Additionally, there was a statistically significant positive link found between TSH and the age, disease duration, and blood phosphate levels in patients with CKD and those with ESRD. WBCs and free T3 exhibited a negative association. (Table 5).

The probability of subclinical hypothyroidism increases by 1.442 and 1.471 times, respectively, with an increase of disease duration. On the other hand, younger age and lower serum calcium reduce the likelihood of subclinical hypothyroidism. Reduced serum calcium levels in ESRD patients reduce the probability of subclinical hypothyroidism. However, the incidence of subclinical hypothyroidism is increased by 1.542 and 1.826 times, respectively, by greater serum phosphorus and WBC levels (Table 6).

Linear regression analysis revealed that increasing serum phosphorus and CKD duration increase risk of hypothyroid dysfunction by 1.471 and 1.442-fold in conservatively treated and by 1.826 and 1.542-fold in hemodialysed patients respectively. Within ESRD patients, serum calcium and age of patients independently associated with TSH levels (Table 7).

**Table (1):** Comparison between studied groups of CKD under conservative treatment and ESRD regarding demographic, clinical vital data, routine lab investigations and regarding thyroid function test.

| | CKD group N=120 (%) | ESRD group N=80 (%) | $\chi^2$ | p |
|---|---|---|---|---|
| **Gender:** Female Male | 41 (34.2%) 79 (65.8%) | 23 (38.7%) 57 (71.3%) | 0.647 | 0.421 |
| | **Mean ± SD** | **Mean ± SD** | **t** | **p** |
| **Age (year)** | 57.03 ± 15.36 | 56.7 ± 15.19 | 0.147 | 0.883 |
| **Body mass index (kg/m$^2$)** | 25.38 ± 3.89 | 23.12 ± 3.56 | 4.177 | <0.001** |
| **Systolic blood pressure (mmHg)** | 133.75 ± 26.41 | 133.38 ± 25.9 | 0.099 | 0.921 |
| **Diastolic blood pressure (mmHg)** | 80.75 ± 17.45 | 81.5 ± 17.07 | -0.3 | 0.764 |
| **Hemoglobin (g/dl)** | 9.87 ± 1.33 | 8.88 ± 1.55 | 4.654 | <0.001** |
| **WBCs (10$^3$/mm$^3$)** | 4.68 ± 1.88 | 4.51 ± 2.05 | 0.601 | 0.549 |
| **Platelet count (10$^3$/mm$^3$)** | 170.19 ± 46.53 | 166.91 ± 50.36 | 0.472 | 0.637 |
| **ALT (U/L)** | 20.83 ± 7.79 | 21.43 ± 7.38 | -0.545 | 0.586 |
| **AST (U/L)** | 20.98 ± 8.17 | 21.6 ± 7.79 | -0.533 | 0.595 |
| **Creatinine (mg/dl)** | 7.62 ± 2.6 | 9.4 ± 2.24 | -5.16 | <0.001** |
| **Urea (mg/dl)** | 85.78 ± 28.32 | 84.26 ± 28.05 | 0.371 | 0.711 |
| **HbA1c (%)** | 5.84 ± 1.07 | 5.72 ± 0.99 | 0.799 | 0.4254 |
| **Serum calcium (mg/dl)** | 8.6 ± 1.16 | 7.52 ± 1.84 | 4.712 | <0.001** |
| **Serum phosphorus(mg/dl)** | 4.75 ± 1.63 | 5.26 ± 1.89 | -2.051 | 0.042* |
| | **Median (IQR)** | **Median (IQR)** | **Z** | **p** |
| **TSH (mlU/mL)** | 2.15(1.63 – 2.9) | 2.1(1.6 – 2.8) | -0.514 | 0.607 |
| **Free T3(ng/dL)** | 2.1(1.9 – 2.4) | 2.1(1.9 – 2.3) | -0.319 | 0.749 |
| **Free T4(ng/dL)** | 1.4(1.13 – 1.7) | 1.4(1.1 – 1.7) | -0.88 | 0.379 |

WBCs: white blood cells, ALT: alanine transaminase, AST: aspartate aminotransferase, HbA1c: Hemoglobin A1c, TSH: thyroid stimulating hormone, T3: Triiodothyronine, T4: Thyroxine.
$\chi^2$chi square test t independent sample t test,
**p≤0.001 is statistically highly significant
**p≤0.001 is statistically highly significant
*p<0.05 is statistically significant t independent sample t test
Z Mann Whitney test IQR interquartile range

**Table (2):** Prevalence of hypothyroidism (subclinical and overt) in all CKD patients and in between CKD under conservative treatment and ESRD under regular hemodialysis.

| | All CKD =200(%) | CKD group N=120(%) | ESRD group N=80(%) | $\chi^2$ | p |
|---|---|---|---|---|---|
| **Thyroid function:** | | | | | |
| Euthyroid | 175 (87.5%) | 104 (86.7%) | 71 (88.9%) | 0.046 | 0.831 |
| Subclinical hypothyroidism | 21 (10.5%) | 14 (11.7%) | 7 (8.8%) | | |
| Overt hypothyroidism | 4 (2%) | 2 (1.7%) | 2 (2.5%) | | |

$\chi^2$Chi square test

**Table (3):** Comparison of the grades, etiology and duration between all CKD patients in subclinical, overt hypothyroidism versus Euthyroidism.

| | **Hypothyroidism (Subclinical + Overt)** | **Euthyroidism** | $\chi^2$ | **p** |
|---|---|---|---|---|
| | **N=25(%)** | **N=175(%)** | | |
| **1- Grade:** | | | | |
| Grade 2 | 3 (12%) | 14 (8%) | | |
| Grade 3a | 7 (28%) | 46 (26.3%) | 0.92 | 0.337 |
| Grade 3b | 6 (24%) | 25 (14.3%) | | |
| Grade 4 | 0 (0%) | 19 (10.9%) | | |
| Grade 5 | 9 (36%) | 71 (40.6%) | | |
| **2- Etiology** | | | | |
| Congenital polycystic kidney | 1 (4%) | 22 (12.6%) | | |
| Diabetes mellitus | 11 (44%) | 41 (23.4%) | MC | 0.325 |
| Hypertension | 9 (36%) | 66 (37.7%) | | |
| Obstructive uropathy | 2 (8%) | 22 (12.6%) | | |
| Recurrent UTI | 1 (4%) | 6 (3.4%) | | |
| **SLE** | 1 (4%) | 18 (10.3%) | | |
| **3- Disease duration ( years )** | **Median** (IQR) | **Median (IQR)** | **Z** | **p** |
| **CKD** under conservative treatment | 8 (6.25 – 11) | 6(3 – 8) | 2.941 | 0.003* |
| **ESRD** under dialysis | 8 (4.5 – 10) | 6(3 – 9) | 2.278 | 0.008* |
| **$Z^{\infty}$** | **-0.713** | -0.165 | | |
| **P** | **0.476** | 0.869 | | |

UTI: urinary tract infection, SLE: Systemic lupus erythematosus, CKD: Chronic kidney disease, ESRD: End-Stage Renal Disease

$\chi^2$Chi square for trend test MC Monte Carlo test Z MannWhitney test

**Table (4):** Comparison of the demographic, clinical data and routine lab parameters between hypothyroid and euthyroid patients within CKD under conservative treatment and ESRD patients under regular hemodialysis.

| | **CKD** | | **t§** | **P** | **ESRD** | | **t§** | **p** |
|---|---|---|---|---|---|---|---|---|
| | **Hypothyroidism** | **Euthyroidism** | | | **Hypothyroidism** | **Euthyroidism** | | |
| | **N=16(%)** | **N=104(%)** | | | **N=25(%)** | **N=175(%)** | | |
| **Age (year)** | 47.13 ± 18.11 | 58.55 ± 14.39 | -2.852 | 0.005* | 51.0 ± 15.6 | 57.42 ± 15.1 | 1.198 | 0.234 |
| **BMI ( Kg/m2 )** | 25.06 ± 3.95 | 25.43 ± 3.9 | -0.354 | 0.724 | 23.26 ± 4.01 | 23.1 ± 3.53 | 0.124 | 0.902 |
| **Systolic blood Pressure (mmHg )** | 130.0 ± 26.83 | 134.33 ± 26.43 | -0.608 | 0.544 | 143.33 ± 33.17 | 132.11 ± 24.84 | 1.128 | 0.223 |
| **Diastolic blood Pressure (mmHg )** | 78.75 ± 17.46 | 81.06 ± 17.51 | -0.491 | 0.624 | 85.56 ± 17.4 | 80.99 ± 17.08 | 0.755 | 0.453 |
| **Female** | 8 (50%) | 33 (31.7%) | **2.058** | **0.151** | 4 (44.4%) | 19 (26.8%) | **1.219** | **0.269** |
| **Hemoglobin (g/dl)** | 9.79 ± 0.76 | 9.88 ± 1.4 | -0.368 | 0.715 | 9.78 ± 0.97 | 8.77 ± 1.58 | 2.697 | 0.017* |
| **WBCs ($10^3$/$mm^3$)** | 4.74 ± 1.86 | 4.67 ± 1.89 | 0.137 | 0.891 | 5.8 ± 1.89 | 4.35 ± 2.02 | 2.051 | 0.044* |
| **Platelet ($10^3$/$mm^3$)** | 169.5 ± 50.15 | 170.3 ± 46.21 | -0.064 | 0.949 | 166.44 ± 43.01 | 166.97 ± 51.49 | 0.029 | 0.977 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **ALT (U/l)** | 20.38 ± 9.39 | 20.89 ± 7.56 | -0.247 | 0.805 | 24.67 ± 4.3 | 21.01 ± 7.6 | -1.408 | 0.163 |
| **AST (U/l)** | 20.81 ± 10.1 | 21.01 ± 7.89 | -0.089 | 0.929 | 24.56 ± 6.06 | 21.23 ± 7.94 | 1.211 | 0.229 |
| **Creatinine (mg/dl)** | 7.34 ± 2.24 | 7.66 ± 2.66 | -0.466 | 0.6422 | 9.17 ± 2.54 | 9.43 ± 2.22 | -0.322 | 0.741 |
| **Urea (mg/dl)** | 83.38 ± 28.6 | 86.14 ± 28.4 | **-0.363** | **0.717** | 83.89 ± 31.89 | 84.31 ± 27.77 | **0.042** | **0.966** |
| **HbA1c (%)** | 6.24 ± 1.01 | 5.77 ± 1.07 | **1.629** | **0.106** | 5.92 ± 1.07 | 5.69 ± 0.98 | **0.661** | **0.511** |
| **Calcium (mg/dl)** | 7.47 ± 1.21 | 8.69 ± 1.03 | **-4.292** | **<0.001**** | 6.01 ± 0.56 | 7.74 ± 1.8 | **-6.069** | **0.006*** |
| **Phosphorus (mg/dl)** | 5.27 ± 0.93 | 4.23 ± 1.43 | **2.797** | **0.006*** | 7.0 ± 0.96 | 5.13 ± 1.75 | **3.116** | **0.003*** |

BMI: body mass index, WBCs: white blood cells, ALT: alanine transaminase, AST: aspartate aminotransferase, HbA1c: Hemoglobin A1c.
Independent sample t test between hypothyroid and euthyroid patients within each group t independent sample t test **p≤0.001 is statistically highly significant $\chi^{2¥}$ Chi square test between hypothyroid and euthyroid patients within each group
all groups are compared by independent sample t test **p≤0.001 is statistically highly significant

**Table (5):** Correlation each of the age, BMI, duration of the disease and routine lab investigations versus thyroid profile among CKD patients group under conservative treatment and ESRD patients under regular hemodialysis.

| **CKD** | **Free T3** | | **Free T4** | | **TSH** | |
|---|---|---|---|---|---|---|
| | **R** | **p** | **r** | **P** | **R** | **p** |
| **Age (year)** | 0.062 | 0.499 | -0.001 | 0.992 | **0.205*** | **0.025*** |
| **BMI (kg/m$^2$)** | 0.018 | 0.849 | 0.029 | 0.749 | 0.041 | 0.656 |
| **Disease duration (year)** | -0.077 | 0.405 | -0.093 | 0.311 | **0.209*** | **0.038*** |
| **SBP (mmHg)** | -0.033 | 0.723 | -0.056 | 0.544 | 0.032 | 0.725 |
| **DBP (mmHg)** | -0.064 | 0.488 | -0.026 | 0.781 | -0.041 | 0.657 |
| **Hemoglobin (g/dl)** | -0.158 | 0.085 | -0.101 | 0.272 | -0.061 | 0.51 |
| **WBCs (10$^3$/mm$^3$)** | 0.015 | 0.873 | -0.103 | 0.263 | -0.07 | 0.447 |
| **Platelet count (10$^3$/mm$^3$)** | -0.022 | 0.809 | -0.125 | 0.172 | 0.174 | 0.058 |
| **ALT (U/L)** | -0.157 | 0.088 | -0.112 | 0.222 | -0.064 | 0.488 |
| **AST (U/L)** | -0.147 | 0.109 | -0.119 | 0.195 | 0.082 | 0.374 |
| **Serum urea (mg/dl)** | 0.145 | 0.114 | -0.011 | 0.904 | 0.08 | 0.384 |
| **Serum creatinine (mg/dl)** | -0.083 | 0.366 | 0.003 | 0.978 | -0.028 | 0.768 |
| **HbA1c (%)** | -0.04 | 0.622 | **-0.255*** | **0.005*** | -0.006 | 0.949 |
| **Serum calcium (mg/dl)** | -0.213 | 0.02 | 0.097 | 0.293 | 0.005 | 0.956 |
| **Serum phosphate (mg/dl)** | -0.08 | 0.385 | -0.022 | 0.814 | **0.213*** | **0.02*** |
| **ESRD** | **Free T3** | | **Free T4** | | **TSH** | |
| | **R** | **p** | **r** | **P** | **R** | **P** |
| **Age (year)** | 0.107 | 0.345 | -0.009 | 0.938 | **0.305*** | **0.025*** |
| **BMI (kg/m$^2$)** | -0.125 | 0.268 | 0.193 | 0.087 | 0.078 | 0.494 |
| **Disease duration (year)** | -0.003 | 0.978 | 0.045 | 0.693 | **0.282*** | **0.837*** |
| **SBP (mmHg)** | -0.125 | 0.268 | 0.193 | 0.08 | 0.1 | 0.377 |
| **DBP (mmHg)** | -0.149 | 0.187 | 0.064 | 0.57 | 0.139 | 0.218 |
| **Hemoglobin (g/dl)** | 0.011 | 0.919 | -0.088 | 0.438 | 0.115 | 0.31 |
| **WBCs (10$^3$/mm$^3$)** | **-0.236*** | **0.035*** | -0.052 | 0.644 | 0.018 | 0.876 |
| **Platelet count (10$^3$/mm$^3$)** | -0.053 | 0.638 | -0.164 | 0.145 | 0.054 | 0.636 |
| **ALT (U/L)** | -0.012 | 0.918 | -0.031 | 0.783 | 0.037 | 0.742 |
| **AST (U/L)** | 0.039 | 0.733 | -0.081 | 0.474 | 0.033 | 0.772 |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Serum urea (mg/dl)** | 0.116 | 0.308 | -0.122 | 0.282 | -0.107 | 0.347 |
| **Serum creatinine (mg/dl)** | -0.083 | 0.366 | 0.003 | 0.978 | -0.063 | 0.576 |
| **HbA1c (%)** | 0.026 | 0.819 | 0.083 | 0.463 | 0.047 | 0.68 |
| **Serum calcium (mg/dl)** | 0.094 | 0.408 | 0.097 | 0.392 | -0.087 | 0.441 |
| **Serum phosphate (mg/dl)** | 0.06 | 0.597 | -0.024 | 0.833 | **0.227*** | **0.013*** |

BMI: body mass index, SBP: Systolic blood pressure, DBP: diastolic blood pressure, WBCs: white blood cells, ALT: alanine transaminase, AST: aspartate aminotransferase, HbA1c: Hemoglobin A1c.
r Spearman rank correlation coefficient *p<0.05 is statistically significant

**Table (6):** Binary regression analysis of Calcium, Phosphorus, duration of the disease and age of patients among CKD patients under conservative treatment and ESRD patients under regular hemodialysis with clinical and subclinical hypothyroidism.

| **CKD** | | | | | |
|---|---|---|---|---|---|
| | **B** | **P** | **AOR** | **95% C.I.** | |
| | | | | **Lower** | **Upper** |
| Calcium (mg/dL) | 0.386 | 0.082 | 0.396 | 0.223 | 0.701 |
| Phosphorus (mg/dL) | 0.927 | 0.001** | 1.471 | 0.952 | 2.271 |
| Duration of disease (years) | 0.366 | 0.007* | 1.442 | 1.107 | 1.880 |
| Age (years) | -0.041 | 0.071 | 0.959 | 0.917 | 1.004 |
| **ESRD** | | | | | |
| | **B** | **P** | **AOR** | **95% C.I.** | |
| | | | | **Lower** | **Upper** |
| Calcium (mg/dL) | -0.846 | 0.062 | 0.429 | .176 | 1.044 |
| Phosphorus (mg/dL) | 0.602 | 0.025* | 1.826 | 1.079 | 3.088 |
| Duration of disease (years) | 0.433 | 0.050* | 1.542 | 1.001 | 2.376 |

AOR adjusted odds ratio CI confidence interval **p≤0.001 is statistically highly significant *p<0.05 is statistically significant

**Table (7):** Linear stepwise regression analysis of serum phosphorus and age associated with TSH level among CKD patients under conservative treatment and ESRD patients under regular hemodialysis.

| **CKD** | | | | | | | |
|---|---|---|---|---|---|---|---|
| | **Unstandardized Coefficients** | | **Standardized Coefficients** | **t** | **P** | **95.0% Confidence Interval** | |
| | **B** | **Std. Error** | **Beta** | | | **Lower Bound** | **Upper Bound** |
| **(Constant)** | 9.251 | 1.802 | | 5.132 | <0.001** | 5.681 | 12.820 |
| **Serum phosphorus (mg/dl)** | 0.507 | 0.207 | 0.219 | 2.450 | 0.016* | -0.916 | 0.097 |
| **Age (year)** | 0.034 | 0.015 | 0.202 | 2.257 | 0.026* | -0.065 | 0.004 |
| **ESRD** | | | | | | | |
| | **Unstandardized Coefficients** | | **Standardized Coefficients** | **t** | **P** | **95.0% C.I** | |
| | **B** | **Std. Error** | **Beta** | | | **Lower Bound** | **Upper Bound** |
| **(Constant)** | 5.754 | 1.287 | | 4.471 | <0.001** | 3.191 | 8.316 |
| **Age (years)** | 0.313 | 0.017 | 0.286 | 2.061 | 0.044* | 0.066 | 0.021 |
| **Serum phosphorus (mg/dl)** | 0.305 | 0.143 | 0.241 | 2.133 | 0.036* | -0.59 | -0.02 |

**p≤0.001 is statistically higher significant *p<0.05 is statistically significant

## DISCUSSION

Our current findings regarding prevalence of hypothyroidism clearly revealed that twenty-one patients had subclinical hypothyroidism (10.5%) and four patients had overt hypothyroidism (2%), while one hundred and seventy-five patients had euthyroid state (87.5 %). The prevalence of overt and subclinical hypothyroidism did not differ significantly (11.7% versus 8.8%, 1.7% versus 2.5% respectively between CKD patients under conservative and ESRD patients under dialysis.

In accordance with our study, Saudi Arabian researchers Alshammari *et al.* [6] reported that 255 individuals had chronic kidney disease, 166 had euthyroidism, 43 had subclinical hypothyroidism, and 46 had hypothyroidism. After exclusion, the proportion of hypothyroidism in CKD patients was 17.66%. According to Nazzal *et al.* [5], there was a 16.3% prevalence of hypothyroidism in Palestine, with 9.6% of cases being overt hypothyroidism and 6.7% being subclinical hypothyroidism.

On the other hand, higher prevalence than our study was reported by Kamal *et al.* [7] who reported a high statistically significant increase (88 %) between both groups as regards freeT3, free T4, and TSH. Additionally, Adani *et al.* [8] reported that 28% of the sample under study had hypothyroidism among hemodialysis patients. Furthermore, they reported that 42.2% of people had overt hypothyroidism and 57.8% had subclinical hypothyroidism.

Moreover, research from Pakistan by Memon *et al.* [9] found that 37.9% of 140 patients receiving maintenance hemodialysis had hypothyroidism.

Chaker *et al.* [10] examined 10318 CKD patients older than 45 years, showed low prevalence in contrast to our findings, stating that the prevalence of subclinical hypothyroidism was 9.1% compared to overt hypothyroidism's 0.8%.

In addition to, Sinjari *et al.* [11] showed that 2.9% and 1.9% of CKD patients had overt and subclinical hypothyroidism, respectively. They found that among CKD subjects with greater BMI, there was no rise in the prevalence of hypothyroidism. There are several reasons for this disparity in prevalence, including differences in locality, ethnicity, environment, culture, and nutritional status among various groups.

According to the results of the current investigation, patients with hemodialysis-treated ESRD had a significantly lower BMI than those with conservatively treated CKD. While there was no significant difference between the two study groups in terms of gender, age, systolic or diastolic blood pressure, TSH, or free T3 or free T4 levels.

These results were compatible with Kamal *et al.* [7] who reported that there was high statistically significant decrease in each of BMI, diabetes mellitus (DM) and thyroid disorder in ESRD patients under hemodialysis compared to CKD patients under conservative treatment, with no statistically significant differences as regards age and sex. They reported that the reason was in the ultrafiltration with lowering the dry weight of the patients, bad nutrition of ESRD patients and muscle breakdown due to each of hyperparathyroidism and disturbed Calcium level.

In ESRD patients receiving regular hemodialysis, the current study revealed a significant decrease in hemoglobin and a rise in serum creatinine. in comparison to CKD patients under conservative treatment. This was in accordance with Kamal et al. [7] who reported that there was a highly significant increase as regards to serum creatinine in ESRD under hemodialysis compared to CKD under conservative treatment, while there was significant increase in Hemoglobin level (Hb) in CKD under conservative treatment compared to ESRD.

In the current study, both ESRD patients receiving regular hemodialysis and hypothyroid CKD patients receiving conservative therapy showed a substantial drop in serum calcium and increase in serum phosphorus, While there was a significant increase in both Hemoglobin and WBCs level among hypothyroid ESRD patients under regular hemodialysis in comparison to euthyroid ESRD patients under regular hemodialysis. This may be explained as dialysis wash out and decrease serum calcium level as well as hemoglobin due to blood loss in dialysis lines also the non- functioning kidneys do not generate erythropoietin hormone causing anemia, so we recommend those patients under regular hemodialysis a strict follow up on calcium intake and erythropoietin injection.

In contrast to our results in which there was no significant difference regarding blood urea between both studied groups, when comparing CKD patients receiving conservative treatment to ESRD receiving regular hemodialysis, Fawzy *et al.* [12] showed a highly significant decrease in urea. It was explained that the kidneys in the CKD group can still eliminate waste products such creatinine and urea, although to varying degrees depending on the CKD grade.

Our current study showed no significant increase in TSH level and decrease in free T3 in both CKD patients and ESRD patients. This disagrees with Fawzy *et al.* [12] who showed significant increase as regards TSH that a highly significant decrease in free T3 was found among both CKD patients under conservative treatment and ESRD patients under regular hemodialysis. They proposed several methods of disrupting thyroid function, such as lowering thyroid hormone levels in the blood, altering protein binding, upsetting the thyroid gland's iodine storage, and upsetting the hypothalamic-pituitary thyroid axis. Additionally, uremia is associated with a decrease in T4 conversion to T3, disrupted T4 binding to thyroid binding globulin by heparin, and elevated levels of free fatty acids in the blood; these effects are more pronounced in the ESRD group. Additionally, in ESRD euthyroid individuals, hemodynamics and malnutrition have an impact on the blood's content of thyroid hormones. This difference may be due to different severity and duration of disease.

In the current study there was a significant increase in serum phosphorus and decrease in serum calcium among both hypothyroid CKD patients under conservative treatment and ESRD patients under regular hemodialysis. This was explained as renal impairment decrease calcium level by disturbed metabolism of vitamin-D increase (hyper-parathyroidism) also blood urea level increase serum phosphorus level. While there was a significant increase in both hemoglobin and WBCs level among hypothyroid ESRD patients under regular hemodialysis in comparison to euthyroid ESRD patients under regular hemodialysis which was explained by many causes such as dialysis may cause some blood loss as well as hemolysis of RBCs causing anemia, also hemodialysis itself might be a source of infection as ESRD patients are immune compromised.

The present study revealed there was positive correlation between TSH and each of serum phosphorus and the disease duration as increasing serum phosphorus and CKD duration increase risk of hypothyroid dysfunction by 1.471 and 1.442-fold in conservatively treated and by 1.826 and 1.542-fold in hemodialysed patients respectively. On the contrary of the results of our study, according to Fawzy *et al.* [12], there was a highly significant positive association between FT3, and the amount of urea and creatinine produced following hemodialysis, as well as the duration of hemodialysis. Additionally, a noteworthy inverse link was observed between TSH and the length of hemodialysis as well as the urea produced after hemodialysis, whereas FT3, TSH, and Hb showed a positive correlation. Moreover, they demonstrated that FT4 and each of age, urea, creatinine, hemoglobin, SGOT, and SGPT had negligible relationships in the CKD group receiving conservative treatment.

However, Sanai *et al.* [13] discovered a negative association and found a progressive decrease in TSH as the time of dialysis increased.

In our current findings, by binary regression analysis we found that revealed that increasing serum phosphorus and CKD duration increase risk of hypothyroid dysfunction by 1.471 and 1.442-fold in conservatively treated and by 1.826 and 1.542-fold in hemodialysed patients respectively. Shortly, by linear regression analysis it was found that increase each of serum phosphorus and age of the patients were independent predictors for hypothyroidism among CKD patients under conservative treatment and ESRD patients under regular hemodialysis.

In agreement with our findings, increasing age of the CKD patients increases the risk of hypothyroidism, according to Adani *et al.* [8], a larger chance of developing subclinical hypothyroidism was associated with advancing age. They failed to discover a statistically significant link between overt hypothyroidism and age. Also, Sinjari *et al.* [11] who reported that hypothyroid patients tended to be older, which agreed with previous reports, including a large observational study conducted by Rhee *et al.* [14]. However, they recommend that more studies are needed to be performed to prove the correlation between their results.

Our study had the following limitations: small sample size and short duration of follow up, so, we recommend that further studies must be done in large scales with long term follow up in multiple centers to analyze all aspects of this issue.

## CONCLUSIONS

There is no significant difference in the prevalence of hypothyroid dysfunction between hemodialysis on a regular basis for ESRD patients receiving conservative treatment and CKD patients receiving conservative treatment. Moreover, there was a correlation observed between the length of renal impairment and the results of thyroid function testing. Furthermore, older patients with CKD and elevated serum phosphorus may independently predict hypothyroidism in those individuals.

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## Citation

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