Prevalence of Hypothyroidism in Diabetic and Non diabetic Chronic Kidney Disease (CKD) and effect of treatment on GFR

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NEED FOR THE STUDY

✓ The interplay between thyroid and the kidney in each other's functions is well known. Thyroid dysfunction affects renal physiology and development, whereas kidney disease could result in thyroid dysfunction.

✓ Increased prevalence of goiter and thyroid gland volume have been reported in patients with end-stage renal disease (ESRD), and it has been suggested that primary hypothyroidism may be more common in patients with ESRD compared with the general population.

✓ The reduced T3 levels without increase in rT3, the reduced free T4 levels along with an elevated TSH, and hypo responsiveness of TSH to TRH question the "euthyroid" state and raise the possibility of benefit from thyroid supplementation in CKD.

✓ A recent study on 113 CKD patients concluded that thyroid hormone replacement therapy (THRT) attenuated the rate of decline in renal function in CKD patients with SH suggesting that THRT may delay reaching end-stage renal disease. Little has been known on whether the prevalence and impact of Hypothyroidism varied between Diabetic and Non diabetic CKD.

OBJECTIVES

✓ Determine the prevalence of subclinical (SH) and overt hypothyroidism (OH) in CKD.

✓ Observe the results after three and six months of treatment of hypothyroidism on progression of CKD in either group.

✓ Comparison of prevalence of hypothyroidism and effect of treatment between Diabetic and Non diabetic CKD.

METHODOLOGY

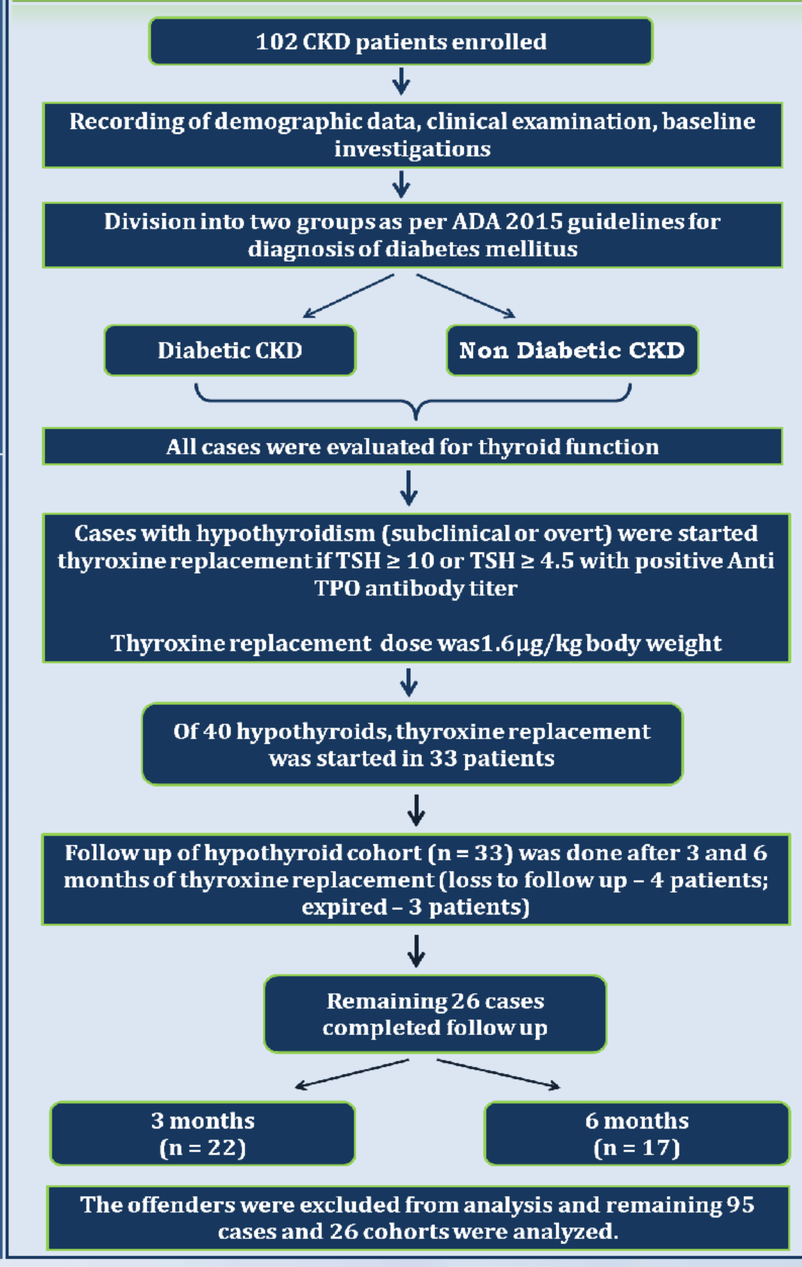
Study Design: Observational prospective cohort study.

Inclusion: CKD patients(as per KDOQI guidelines) aged ≥18 years of either sex.

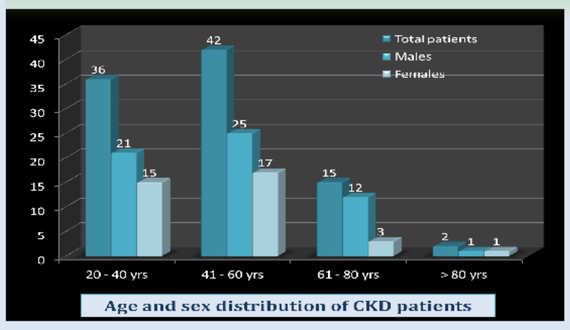
Exclusion: Known cases of thyroid dysfunction or concurrent treatment with drugs (lithium, amiodarone) that may cause hypothyroidism.

Statistics: Graphpad software version 6.0 was used with level of significance being 0.05. Numerical data was analyzed using paired and unpaired student's t test while z test for proportions and chi square test was used for non parametric data. Other tests included Repeated measures ANOVA and Pearson's linear coefficient calculation.

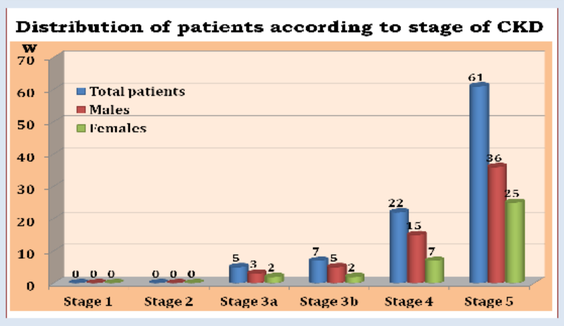
STUDY PROCEDURE



RESULTS



Age and sex distribution of CKD patients



Baseline characteristics of cases

Parameter	Range	Mean ± SD
Age (in yrs.)	20 - 85	46.42 ± 17.49
SBP (in mmHg)	116 - 240	163.97 ± 23.25
DBP (in mmHg)	70 - 130	92.02 ± 11.08
Hemoglobin (in g/dl)	3.3 – 12.7	7.92 ± 1.86
S. Urea (in mg/dl)	21.5 – 417.8	151.66 ± 77.91
S. Creatinine (in mg/dl)	1.13 18.01	5.82 ± 3.59
eGFR at baseline (in ml/min/1.73m²)	2.39 – 58.4	15.97 ± 12.36
FT3 (in pg/dl)	0.78 – 4.02	2.09 ± 0.75
FT4 (in ng/dl)	0.31 – 5.9	1.18 ± 0.56
TSH (in µIU/ml)	0.62 – 26.5	5.02 ± 4.91
Total protein (in g/dl)	4.4 7.94	6.55 ± 0.72
S. Albumin (in g/dl)	1.8 – 4.57	3.21 ± 0.57
iPTH (pg/ml)	78 – 1513	396.09 ± 250.1

Comparison of baseline characteristics between male and female population

Parameter	Males (n = 59)	Females (n = 36)	p value
Age (yrs.)	48.06 ± 18.22	43.75 ± 16.13	0.229
SBP (mmHg)	166.32 ± 23.69	160.11 ± 22.27	0.198
DBP (mmHg)	92.20 ± 10.99	91.72 ± 11.36	0.839
Hemoglobin (g/dl)	8.03 ± 1.88	7.73 ± 1.82	0.441
S. Urea (mg/dl)	162.25 ± 74.2	134.30 ± 81.7	0.094
S. Creatinine (mg/dl)	6.24 ± 3.68	5.12 ± 3.38	0.125
eGFR at baseline (ml/min/1.73m²)	16.28 ± 12.65	15.47 ± 12.03	0.754
FT3 (pg/dl)	1.94 ± 0.72	2.35 ± 0.71	0.006
FT4 (ng/dl)	1.19 ± 0.73	1.16 ± 0.23	0.769
TSH (µIU/ml)	4.61 ± 4.44	5.68 ± 3.87	0.216
Total protein (g/dl)	6.52 ± 0.71	6.60 ± 0.73	0.600
S. Albumin (g/dl)	3.18 ± 0.56	3.23 ± 0.58	0.679
iPTH (pg/ml)	380.67 ± 194.27	421.36 ± 323.12	0.490
Hypothyroid	14	18	0.008
Diabetic	27	8	0.021

Comparison of characteristics of between Diabetic and Non diabetic CKD

Parameter	Diabetic CKD (n = 35)	Non diabetic CKD (n = 60)	p value
Age (yrs.)	54.48 ± 14.92	41.71 ± 17.27	<0.0001
SBP (mmHg)	166.17 ± 21.78	162.68 ± 24.14	0.469
DBP (mmHg)	93.94 ± 11.32	90.9 ± 10.87	0.200
Hemoglobin (g/dl)	8.13 ± 1.70	7.79 ± 1.94	0.270
S. Urea (mg/dl)	142.30 ± 63.9	157.12 ± 85.05	0.335
S. Creatinine (mg/dl)	5.55 ± 3.17	5.97 ± 3.84	0.565
eGFR at baseline (ml/min/1.73m²)	17.24 ± 14.23	15.22 ± 11.18	0.471
FT3 (pg/dl)	1.97 ± 0.71	2.17 ± 0.76	0.197
FT4 (ng/dl)	1.14 ± 0.27	1.20 ± 0.67	0.536
TSH (µIU/ml)	4.94 ± 4.23	5.06 ± 4.76	0.898
Total protein (g/dl)	6.37 ± 0.83	6.65 ± 0.62	0.083
S. Albumin (g/dl)	3.10 ± 0.68	3.27 ± 0.48	0.168
iPTH (pg/ml)	406.28 ± 243.74	390.15 ± 255.59	0.759
Hypothyroid	10	23	0.333

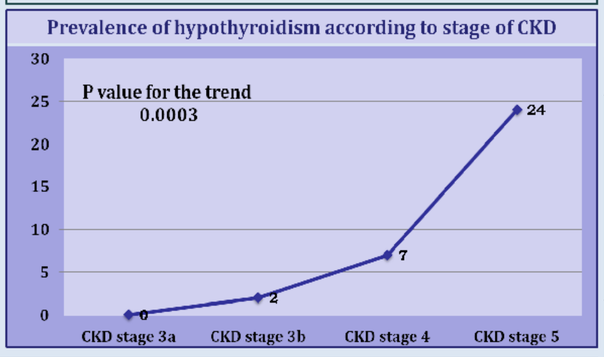
Prevalence of Hypothyroidism in study population

Hypothyroid patients 34.7% (n = 33)

Subclinical Hypothyroidism 31.5% (n = 30)

Overt Hypothyroidism 3.1% (n = 3)

Prevalence of hypothyroidism according to stage of CKD



Comparison of characteristics of between hypothyroid and euthyroid patients

Parameter	Hypothyroid (n = 33)	Euthyroid (n = 62)	p value
Age (yrs.)	37.33 ± 14.73	51.26 ± 17.00	<0.0001
Females	19	17	0.004
SBP (mmHg)	170.45 ± 21.6	160.51 ± 23.50	0.038
DBP (mmHg)	95.5 ± 11.80	90.16 ± 10.29	0.028
Hemoglobin (g/dl)	7.36 ± 2.19	8.21 ± 1.58	0.048
S. Urea (mg/dl)	155.48 ± 74.68	149.62 ± 80.08	0.722
S. Creatinine (mg/dl)	6.57 ± 3.87	5.41 ± 3.40	0.147
eGFR at baseline (ml/min/1.73m²)	13.03 ± 9.69	17.53 ± 13.37	0.060
Total protein (g/dl)	6.52 ± 0.70	6.62 ± 0.72	0.189
S. Albumin (g/dl)	3.17 ± 0.55	3.22 ± 0.50	0.678
iPTH (pg/ml)	388.5 ± 184.25	400.12 ± 280.25	0.808

Comparison of eGFR before and after thyroid hormone replacement therapy(THRT)

	eGFR (ml/min/1.73m²) baseline	eGFR (ml/min/1.73m²) after 3 mnths of THRT	eGFR (ml/min/1.73m²) after 6 mnths of THRT
Mean	12.97	17.14	19.25
SD	10.14	9.84	7.17
N	26	22	17

Comparison of eGFR at baseline and after 3 months of THRT: p = 0.0007

Comparison of eGFR at baseline and after 6 months of THRT: p = <0.0001

Comparison of eGFR after 3 and 6 months of THRT: p = 0.0004

On applying within group ANOVA for 17 patients, p < 0.05

Comparison of eGFR before and after THRT between Diabetic and Non diabetic CKD

	Diabetic CKD (n=35)	Non diabetic CKD(n=60)	p value
eGFR (baseline)	11.19 ± 10.83 (n=8)	13.04 ± 9.81 (n=18)	0.670
eGFR (after 3 mnths of THRT)	17.41 ± 15.32 (n=7)	16.13 ± 7.34 (n=15)	0.790
eGFR (after 6 mnths of THRT)	15.77 ± 5.52 (n=6)	19.89 ± 8.35 (n=11)	0.297

Diabetic CKD

Comparison of eGFR at baseline and after 3 months of THRT: p = 0.026

Comparison of eGFR at baseline and after 6 months of THRT: p = 0.337

Comparison of eGFR after 3 and 6 months of THRT: p = 0.718

On applying within group ANOVA for 6 patients, p > 0.05

Non diabetic CKD

Comparison of eGFR at baseline and after 3 months of THRT: p = 0.037

Comparison of eGFR at baseline and after 6 months of THRT: p = <0.0001

Comparison of eGFR after 3 and 6 months of THRT: p = 0.004

On applying within group ANOVA for 11 patients, p < 0.05

CONCLUSIONS

✓ Patients with Non diabetic CKD were significantly younger in age than Diabetic CKD.

✓ Young patients with CKD have significantly higher prevalence of hypothyroidism.

✓ Anemia and Hypertensiom are more severe in hypothyroid CKD patients as compared to euthyroid CKD patients.

✓ Prevalence of diabetic kidney disease across gender is consistent with higher rates occurring in men than in women.

✓Hypothyroidism (31.5% subclinical and 3.1% overt) is a relatively common occurrence in CKD.

✓ Prevalence of hypothyroidism increases with progressively lower levels of GFR i.e. declining renal function.

✓ THRT significantly improved renal function (evident by increment in GFR) in non Diabetic CKD patients with hypothyroidism after three and six months of THRT. However in Diabetic CKD, though there was improvement in GFR after THRT it was significant at six, but not at three months of THRT.

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