

Incidence and Relationship between Hypothyroidism and Chronic Renal Failure

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ABSTRACT

Aim: To find out incidence and relationship between thyroid diseases with End Stage Renal Disease

Methods: This is a cross-sectional study conducted in Punjab social security hospital Lahore, 45 patients of renal disease is participating along with 15 controls who has disease free stat, patients having diabetes mellitus and hypertension are included in study criteria and patients with acute renal failure and renal stones, cardiovascular diseases were excluded from the study.

Results: Three out of 45 patients are diagnosed as hypothyroid and six patients having enlarged goiter and in euthyroid stat.

Conclusion: Thyroid diseases and ESRD are common conditions present in population of Pakistan. In presence of higher incidence of these diseases it is imperative to judge the relationship between thyroid disorders and chronic kidney disease. The most observing change in patients with chronic kidney disease (CKD) in comparison with thyroid disorder is low serum T3 level, and clinically hypothyroidism, the risk of disease progression in these patients who had decrease in eGFR level which further worsening the renal function.

Keywords: End stage renal disease, estimated glomerular filtration rate, chronic kidney disease

INTRODUCTION

Chronic kidney disease is a progressive loss in renal function over a period of months or years. The symptoms of worsening kidney function are non-specific and might include feeling of unwell and experiencing a reduced appetite. Kidney disease may also be identified when it lead to one of its recognized complications. The CKD is identified by a blood test for creatinine. Higher levels of creatinine indicate a lower glomerular filtration rate and as a result of decreased capability of the kidney to excrete waste products. Serum creatinine level may be normal in early stages of CKD and the condition is discovered if urinalysis (testing of a urine sample) shows that kidney allowing to loss of protein and red blood cells into the urine. The most important risk factors for CKD are diabetes mellitus, hypertension and thyroid diseases. Physiological active thyroid hormones are secreted from cuboidal epithelial cells and follicles of thyroid gland. About 92% of metabolically active hormone of thyroid gland is thyroxin (T₄) and 8% triiodothyronine (T₃) considering both these hormones are functionally and metabolically active. The most important function of thyroid hormone is to increase level of nuclear transcription mechanism of great number of genetic material in almost all the cells of body to produce different kinds of enzymes, structural, and transport type of proteins. Inactive thyroid hormones when it is converted into its active

form which is (T₃) increases anions and cation transport across the cell membrane and it also enhances the rate of growth of brain in fetal life and in growing children's and it also control other hormones effectiveness. Any abnormality in function of thyroid gland influences the rate of synthesis of T₃ and T₄ which can lead to a range of disorders all over body. Extensively essential situation is under research about thyroid hormones concentration that through which mechanism it has an effect on succession of CKD. Abnormality of kidney function is found in association with precise levels of thyroid hormones. Non-autoimmune hypothyroidism is frequently experiential in CKD subjects. The initial and mainly frequent thyroid test irregularity shows in CKD subjects is a low T₃ level (specifically total T₃) probable mechanism results to weaken renal function test are due to decreased thyroid hormone secretion causing decreased metabolism of different systems of body, which leads to an initial step towards organ failure, synthesis of protein in decreased, destabilized contraction of muscles especially of hands and myxedema due to deposition of hyaluronic acid and chondroitin sulfate causing excessive gel like material in the interstitial space. Hypothyroidism individuals may experience lethargy, fatigue and extreme sleeping up to 12 to 14 hours in a day, extreme muscular listlessness, decrease in heart rate, cardiac output & blood volume, sometimes excessive weight gain, constipation, skin and hair abnormality, husky voice (frog like). Thyroid dysfunction leads to hypothyroidism which ultimately affect kidney function in which serum creatinine is

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increased, serum cystatin C decreased, 24 hour urinary protein in increased due to hyperfiltration of glomerulus. All these expressions lead to increase natriuresis and decrease diuresis produce electrolyte imbalance and develop hyponatremia, reduced renal blood flow due to stiffening of glomerular membrane and expansion of mesangial surrounding substance. Decrease renal vasodilator appearance including vascular endothelial growth factor, and somatomedins. eGFR is decreased (about 39%) in 60% of 25-50 years of subjects diagnosed with hypothyroidism due to a number of explanations it follows reduced renin secretion due to reduced compassion to β -adrenergic incentive and impairment in renin-angiotensin system (RAS) functioning all these factors accompanying to worsen kidney function. In hypothyroidism due to renal epithelial abnormalities which leads to inadequate surface area of glomerulus for fluid filtration. In adding together reduced (Na^+) sodium, (Cl^-) chloride and water absorption mainly in proximal tubules, decrease appearance of chloride channels in basolateral membrane, decrease its reabsorption and raise transport of chloride to distal tubule and elicit autoregulatory feedback mechanism which reduces RAS action as a result the GFR decreases.

MATERIAL AND METHODS

This is a cross-sectional study. The present study comprises on a total of 75 subjects in which 45 patients with renal failure with or without obesity and/or metabolic syndrome. The patients included in this study age limitation between (25-50 years) recruited from the (OPD) out-patient departments of the Punjab Social Security Health Management Company Hospital 8km Manga Raiwind Road Lahore voluntary participation of subjects with a written signed well-versed permission (consent). The subjects with acute renal failure, primary renal hemodynamic abnormalities, renal artery stenosis, malignant hypertension, renal immunologic disorder and specific tubular disorders, renal hypoplasia (congenital absence of kidney tissue) or specific cardiovascular disease (CVD) were excluded from this study. Physical parameters include (Blood pressure (BP) was measured from the right or left arm in a sitting position) and biochemical parameters were determined in using standard procedures. Serum creatinine, urea, and 24-hour urinary proteins were determined by biochemical procedures. Thyroid stimulating hormone (TSH) KIA kit concentrations were analyzed by enzyme-linked immunosorbent assay (ELISA) using commercial kits (Cayman Chemical Company, Ann Arbor, MI, U.S.A). Serum Triiodothyronine (T3) and serum Thyroxine (T4) concentrations were analyzed by in vitro competitive

ELISA (Enzyme Linked Immunosorbent Assay (Abcam UK) Samples were processed and analyzed following the manufacturers recommendations for each assay. The subjects were separated in next three groups: Group A: normal subjects (control=C)(n=15; M :8; f: 7), Group B: patients with renal failure(n=15; M :11; F:4) (Renal Disease=RD), Group C: patients with chronic renal failure and metabolic syndrome (MS), Diabetes mellitus (DM), and Hypertension (HTN) (n=15;M:7;F:8)

RESULTS

According to our research total thirty patients of CKD were examined, three out of thirty patients having clinical features of hypothyroidism with age limitation 25-50 years, as compare to control subjects were equivalent in age, gender and physical parameters. All subjects of (group A=Control) were euthyroid. TSH in males subjects as compare to female subjects are significantly higher in patients with renal disease (5.8 ± 0.3) these patients had serum creatinine and urea levels mean (2.8 ± 0.2) (126.3 ± 12.5) are also towards higher sides respectively as compare to control group whose TSH, serum creatinine and urea levels are within normal range. TSH in both males and female subjects diagnosed with metabolic syndrome having DM, HTN towards higher sides, mean TSH (7.3 ± 0.9). No important gender difference is found in patients diagnosed with hypothyroidism and metabolic syndrome. The average mean serum T3 level in patients of renal disease and metabolic syndrome is considerably or significantly lower in three subjects (0.78 ± 0.24 vs. 0.79 ± 0.24) respectively, with clinically diagnosed hypothyroid. The mean serum T4 levels in patients with RD and MS is significantly lower (5.89 ± 1.81 vs. 5.92 ± 1.90) as compared with fifteen subjects of control group (7.56 ± 0.96). The mean of arterial pressure (mean SBP 160 ± 4.0 -DBP 100 ± 0.9) was appreciably higher in patients with MS as they are previously hypertensive compared in the rest of the two groups in which the values were within the normal range (SBP: 115-118, DBP: 70-78 mmHg). No considerable gender dissimilarity was found in Blood Pressures in all three groups. Hypothyroid patients having MS had Mean random blood sugar levels were (272.1 ± 12.9) higher as compared with rest of two groups of RD and control subjects. As predictable, serum creatinine levels were higher in patients with renal disease, metabolic syndrome and in hypothyroidism subjects. The mean serum creatinine levels in RD and MS subjects were significantly higher or different from the control group (2.8 ± 0.2 vs. 0.6 ± 0.0 , mg/dl respectively). The mean urea levels were found higher in subjects with renal disease, MS and hypothyroid. Also, mean serum urea levels in RD and MS subjects were significantly different from control group (152.0 ± 23.4 vs. 27.7 ± 1.1

mg/dl).The mean eGFR levels in RD and MS/hypothyroid pts(35.8±3.0-58.4±16.2)were markedly lower as compare to the control subjects(151.7±13.0).

Physical and Biochemical parameters in both males and females

Each Group(n=15) (Mean±S.E.M)	Group A (Control)	Group B (RD)	Group C (RD-MS)
N	15	215	15
Gender (M/F)	8/7	11/4	7/8
Age Yrs	36±2	36±2	39±2
SBP	118±2.9	115±2	160±4.0
DBP	78±2.0	70±1	100±0.9
BSR(mg/dl)	127.5±3.4	108.6±6.7	272±0.3
Creatinine (mg/dl)	0.6±0.0	2.8±0.2	2.7±0.3
Urea (mg/dl)	27.7±1.1	126.3±12.5	109.8±11.8
eGFR	151.7±13.0	35.8±3.0	58.4±16.2
TSH (mIU/L)	4.0±0.2	5.8±0.3	7.3±0.9
T3ng/ml	1.13±0.18	0.78±0.24	0.79±0.24
T4 ug/dl	7.56±0.96	5.89±1.81	5.92±1.90

“Normal ranges of physical and biochemical parameters”
 Systolic blood pressure (SBP) Diastolic blood pressure (DBP)
 BSR 100-180mg/dl,Creatinine: 0.2-1.3mg/dl, Urea: 15-45mg/dl, TSH: 0.36-6.16miu, T3: 1.4-4.2ng/ml, T4: 4.5-11.2ug/dl

DISCUSSION

Chronic kidney disease may affect a variety of different hormonal functions throughout the body these hormonal abnormalities may lead to organ failure, successive trialsis conducted to evaluate whether the presence of hypothyroidism and CKD can worsen each other. Previous studies evaluate thirty patients clinically diagnosed as CKD out of them thirteen patients (43.33%) biochemically declared having higher serum TSH levels (>5.2uu/ml) there seven patients out of thirteen had lower serum levels of T3 due to negative feedback mechanism of hypothalamic –pituitary thyroid axis(HPT axis). In adding together the four subjects from thirteen having enlarged scatter smooth goiter which indicates higher prevalence.In distinction with our study the mean serum TSH level in three subjects are higher in RD, MS groups as compare to controls. Mean serum T3 and T4 levels are lower as compare to control group. The lower levels of thyroid secretions are likely due to malfunctioning in release of its secretions in response to TSH. Hypothyroidism is frequently commenced by autoimmunity in opposition to the thyroid gland and this immunity destroys the gland instead of stimulates it. This causes progressive worsening and to end with fibrosis of the thyroid gland, with resultant reduce or lackingthyroid hormone secretion. Our results comparison with previous researches of patients with CRF had lower serum levels of T3 and T4 but having higher serum levels of TSH that shows preservation of HPT axis. According to our study when detailed history will be taken from subjects of CRF with goiter, find out that their diet is deficient with iodine.The mean TSH level was highest in RD and MS groups with lower levels in control group. In this enlarge group of adult OPD patients, we find in raised

prevalence of primary hypothyroidism which is sub clinical in subjects with decreased eGFR independent of age, sex. Moreover, if there is decreased eGFR, there was a graded raised chance of subclinical primary hypothyroidism.

CONCLUSION

CKD and thyroid abnormalities (hypothyroidism) are important and self - determining risk factor for health of adult population in Pakistan. In the presence of higher frequency of both disorders the wide spread transformation in CKD patients having low serum T3 level and clinically diagnosed as hypothyroidism the incidence of this disorder is rise continuously in patients having progressive deterioration in kidney function and fall in eGFR. Due to impaired kidney function there is failure of renal excretion of waste products and raised nitrogen preservation these factors accumulate and deteriorates the normal function and metabolism of thyroid gland hormones. The clinically and biochemically diagnosed hyperthyroidism is not linked with CKD but definitely speed up the process of becoming progressively worse. In our cohort of study there is distinctive relationship between CKD and thyroid disorders.

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