

**Research Article**

## **Thyroid Disorders and Biological parameters in chronic kidney disease patients having psychiatric illness**

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**Abstract**

**Background:** Chronic Kidney Disease (CKD) is a public health problem that tends to take dimensions of epidemic and has serious impact on quality of patient's life. Thyroid function disorders are common in patients with chronic kidney disease.

**Aim:** The aim of the present study was to explore the conditions of Thyroid Disorders and Biological parameters in chronic kidney disease patients having psychiatric morbidity undergoing haemodialysis.

**Materials and Methods:** Prospective study included 130 participants undergoing haemodialysis with Psychiatric morbidity. Exclusion criteria were: previous thyroid disorders, systemic illnesses, critically ill patients. Blood samples were taken for standard laboratory analysis, total and free thyroid hormone levels.

**Results:** On comparing patients with and without psychiatric illness and their potassium values, there was a significant association ( $p < 0.05$ ) between abnormal potassium values and psychiatric illness. There was a significant association ( $p < 0.05$ ) between psychiatric illness and total bilirubin values.

The thyroid profile, there was a significant association ( $p < 0.05$ ) between abnormal FT3, FT4 values and psychiatric illness.

**Conclusions:** Our study showed that functional thyroid gland disorders are more common among patients having psychiatric morbidity undergoing haemodialysis compared with healthy subjects and reveal their link with time on dialysis.

**Keywords:** Chronic Kidney Disease, Thyroid Disorder, Biological parameters

### **1. Introduction**

Chronic kidney disease (CKD) influence hypothalamo- pituitary-thyroid axis. Thyroid stimulating hormone (TSH) is disturbed in uraemia and the TSH response to the hypothalamic thyrotrophic releasing hormone (TRH) is reduced<sup>1,2</sup>. CKD affects the thyroid function by lowering levels of circulating the thyroid hormones and interfering with hormones it will bind to the protein carriers, disrupting metabolism and elimination of thyroid hormones<sup>3</sup> and affect the storage of iodine in thyroid gland<sup>4</sup>. The concentration of serum iodine in patients with CKD is higher due to lower iodine clearance caused by reduced glomerular filtration. Elevated levels of serum inorganic iodine in patients with CKD may potentially block thyroid hormone synthesis (Wolf-Chaikoff effect), what can explain higher prevalence of diffuse goitre and hypothyroidism in these patients<sup>5</sup>. More specifically, the prevalence of primary hypothyroidism increases with decreasing glomerular filtration rate (GFR)<sup>6,7</sup>. Chronic Hemodialysis (HD) is associated with abnormal concentrations of circulating thyroid hormones; mainly the reduction of total and free serum thyrotrophin (T3). Total and free T4 can be increased in haemodialysed patients due to lipolytic effects of heparin used in anticoagulant therapy during haemodialysis<sup>8</sup>. The aim of this study was to compare thyroid function among patients on chronic haemodialysis and healthy participants and to assess if there is an association between the dialysis duration and thyroid disorders.

While it is thought that the uremic syndrome may manifest as fatigue, weakness and the association between biochemical markers such as albumin, creatinine, phosphate, calcium and fatigue has been inconsistent<sup>9,10,11</sup>. Uraemia may lead to nausea, and loss of appetite all contribute to fatigue<sup>12</sup>.

A goal in patients with chronic kidney disease is maintenance of optimal quality of life as possible<sup>13,14</sup>. Functional ability and well-being of individuals with chronic kidney disease is related to multiple factors and the complications of chronic kidney disease can affect functioning and well-being in a negative manner. Furthermore, co morbid conditions such as diabetes mellitus, hypertension, and cardiac disease, all of which are common in patients with chronic kidney disease, may impact quality of life.

### **2. Materials and Methods**

All patients who underwent dialysis procedure in Sri Ramachandra Medical Centre during the period January to June 2010.

#### **2.1. Inclusion criteria**

Patients who have been diagnosed to have CKD by the nephrologists and are undergoing dialysis in Sri Ramachandra Medical Centre. Either the patient or his relatives who had given informed consent for the study.

#### **2.2. Exclusion criteria**

Patient previously diagnosed for mental illness prior to the onset of chronic kidney disease. Patients having mental retardation were excluded. Patient or relatives who refused to give consent to the study. Patient who were dangerously ill, previous thyroid disorders and who had very poor medical condition were excluded.

#### **2.3. Materials**

Patients and relatives were interviewed in the dialysis unit of Sri Ramachandra Medical Centre. A semi structured proforma was designed for the purpose of the study. It has been utilized to gather information on the demographic details, duration of CKD, Mental illness.

#### **2.4. Methods**

Sample was collected from Dialysis Unit, Department of Nephrology, Sri Ramachandra medical center, Sri Ramachandra University. Those cases which were diagnosed as Chronic Kidney disease were undergoing haemodialysis were included in the study. Blood samples were taken fasting and

before dialysis treatment and heparin administration. The following biological parameters were assessed: Sodium, Potassium, Chloride, Bicarbonate, SGOT, SGPT, and Alkaline phosphatase, Bilirubin total and Bilirubin direct. T3, T4, and TSH by means of standard laboratory methods<sup>15,16</sup>.

**2.5 Statistics**

All data collected through the proforma and the rating scales were tabulated and analyzed with the help of the university statistician using SPSS (Statistical Package for social Sciences) Statistics 18. Chi square test have been used test the significance of categorical or count data and T-test was used to test the significance of measurement data, Results are presented as mean ± SD throughout the document unless otherwise stated. The default level of significance was set p=0.05.

**3. Results**

Biological parameters such as laboratory values were analysed for relationship with psychiatric diagnosis. Abnormal levels of electrolytes were seen in patient. Patients with psychiatric diagnosis (n=27, 24.1%) had abnormal potassium levels. Among these patients, (

Table 2) moderate depressive episode (n=10, 20.4%) was higher compared to other diagnosis such as delirium (4.08%), undifferentiated schizophrenia (2.04%). On comparing patients with and without psychiatric illness and their potassium values, there was a significant association (p< 0.05) between abnormal potassium values and psychiatric illness. 11 patients (11.57%) had abnormal levels of direct bilirubin. The psychiatric diagnoses amongst these patients were moderate depressive episode (n=9, 23.68%), Adjustment disorders- Prolonged depressive reaction (n=8, 21.05%) delirium (n=1, 2.63%) and dementia (n=2, 5.26%) (

Table 2). Comparing patients with and without psychiatric illness with total bilirubin values, there was a significant association (p< 0.05) between psychiatric illness and direct bilirubin values.

**Table 1: Relationship of different Lab to psychiatric morbidity -1**

Parameters	Result	Psychiatric Illness		Total	Chi Square	p Value
		Present	Absent			
Sodium	Normal	29(25.66%)	37(32.74%)	66(58.4%)	0.006	1.000
	Abnormal	21(18.58%)	26 (23%)	47(41.59%)		
Potassium	Normal	23(20.53%)	44(39.28%)	67(59.82%)	7.179	0.011*
	Abnormal	27 (24.1%)	18(16.07%)	45(40.17%)		
Chloride	Normal	25(24.03%)	40(38.46%)	65 (62.5%)	4.127	0.067
	Abnormal	23(22.11%)	16(15.38%)	39 (37.5%)		
Bicarbonate	Normal	16(15.68%)	13(12.74%)	29(28.43%)	1.071	0.380
	Abnormal	32(31.37%)	41(40.19%)	73(71.56%)		
SGOT	Normal	25 (24.5%)	33(32.35%)	58(56.86%)	0.206	0.650
	Abnormal	17(16.66%)	27(26.47%)	44(43.13%)		
SGPT	Normal	10 (9.8%)	16(15.68%)	26(25.49%)	0.195	0.658
	Abnormal	33(32.35%)	43(42.15%)	76 (74.5%)		
Alkaline Phosphatase	Normal	37(38.14%)	54(55.67%)	91(93.81%)	0.203	0.653
	Abnormal	3 (3.09%)	3 (3.09%)	6 (6.18%)		
Bilirubin Total	Normal	38(28.12%)	53(44.79%)	91(72.91%)	1	1
	Abnormal	1 (12.5%)	4 (14.58%)	5 (27.08%)		
Bilirubin Direct	Normal	28(29.47%)	51(53.68%)	79(83.15%)	6.099	0.024*
	Abnormal	11(11.57%)	5 (5.26%)	16(16.84%)		

**Table 2: Psychiatric diagnosis in relation to abnormal laboratory values**

Psychiatric Diagnosis	Bilirubin Direct	FT3	T4	Potassium
Unspecified dementia	2 (5.26%)	2 (9.09%)	2 (8%)	(0%)
Delirium, not superimposed on dementia	1 (2.63%)	1 (4.54%)	1 (4%)	2 (4.08%)
Undifferentiated schizophrenia	(0%)	1 (4.54%)	1 (4%)	1 (2.04%)
Mild depressive episode	5 (13.15%)	2 (9.09%)	5 (20%)	3 (6.12%)
Moderate depressive episode	9 (23.68%)	3 (13.63%)	9 (36%)	10 (20.4%)
Severe depressive episode without psychotic symptoms	(0%)	(0%)	(0%)	1 (2.04%)
Mixed anxiety and depressive disorder	2 (5.26%)	(0%)	1 (4%)	(0%)
Adjustment disorders- Prolonged depressive reaction	8 (21.05%)	(0%)	5 (20%)	6 (12.24%)

25 patients with a psychiatric diagnosis (59.52%) had abnormal Free thyroxine (FT4) levels. in which majority of the patients had a psychiatric diagnosis of Moderate depressive episode (n=9, 36%). Free Triiodothyronine (FT3) was found to be abnormal in 22 patients with psychiatric diagnosis (56.41%) (Table 3) namely moderate depressive episode (n=3, 13.63%), Unspecified dementia (n=2, 9.09%), Mild depressive episode (n=2, 9.09%), Delirium (n=1, 4.54%) and Undifferentiated schizophrenia (n=1, 4.54%) was found (

Table 2). On comparing patients with and without psychiatric illness and their thyroid profile, there was a significant association (p< 0.05) between abnormal FT3, FT4 values and psychiatric illness (Table 3).

**Table 3: Relationship of different Lab to psychiatric morbidity -2**

Parameters	Psychiatric Illness	N	Mean	Std. Deviation	t value	p Value
FT3	Present	22(56.41%)	1.98	0.56	-2.634	0.012*
	Absent	17(43.59%)	2.61	0.94		
T4	Present	25(59.52%)	1.39	0.80	2.580	0.014*
	Absent	17(40.48%)	0.88	0.22		

TSH	Present	25(59.52%)	4.36	2.76	-0.011	0.991
	Absent	17(40.48%)	4.37	2.61		

#### 4. Discussion

There are so many reasons for thyroid abnormalities in patients with CKD. Due to reduced de iodinase activity, tissue and circulating levels of the active form of T3 are low in kidney failure<sup>17</sup>. On the other hand, accumulation of toxic uremic solutes alters the central (hypothalamic) control of the pituitary gland, and the TSH response to thyrotrophin-releasing hormone is subnormal in these patients<sup>18</sup>. In contrast, the thyroid-pituitary feedback loop seems to remain intact, because steady-state plasma TSH remains substantially normal and TSH undergoes the expected rise after thyroidectomy in these patients<sup>19</sup>. In case of central effects the toxic uremic solutes reject the protein binding of thyroxine<sup>20</sup>. Furthermore, studies in the last decade showed that systemic inflammation<sup>21</sup> and metabolic acidosis<sup>22</sup> might alter thyroid function in CKD patients. Serum iodine concentrations are high in CKD but are not correlated with the degree of kidney failure<sup>23</sup>. Elevation of serum iodine levels result in prolongation of the Wolff-Chaikoff effect<sup>24</sup>. Iodine excess leads to increase prevalence of goitre and hypothyroidism in CKD<sup>25</sup>. A high exposure to iodine facilitates the development of hypothyroidism in CKD patients<sup>26</sup>. Some authors have reported that a restriction of dietary iodine in uraemia patients on HD can correct the hypothyroidism avoiding the need for hormone replacement with levothyroxine<sup>27</sup>. Undiagnosed and untreated hypothyroidism is posing danger on CKD patients in many ways. End stage renal disease patients have a great risk of cardiovascular disease and early in the course of CKD it results in 10-fold cardiovascular mortality after the start of renal replacement therapy<sup>28</sup>. Hypothyroidism itself is also a risk factor for cardiovascular disease<sup>29</sup> thus adding to the existing risks. Hypothyroidism is a modifiable risk factor it should be recognized and treated at proper situation. Second, hypothyroidism impairs myocardial function<sup>30</sup>. In CKD patient's cardiac function can be already challenged by fluid overload, overt hypertension, anaemia, etc., leading to cardiac failure. Hypothyroidism can worsen the situation. Third, certain neurobehavioral and neuromuscular dysfunctions are also associated with hypothyroidism, e.g. depression, memory loss, cognitive impairment and peripheral nerve dysfunction<sup>31-33</sup>. The prevalence of depression in dialysis patients is high<sup>34</sup> and hypothyroidism can contribute to its development. Fourth, hypothyroidism is associated with anaemia; approximately 20-60% of patients with hypothyroidism are also diagnosed with anaemia<sup>35</sup>. It can have various aetiologies, and can manifest as normocytic, microcytic or macrocytic anaemia<sup>36</sup>. Several potential confounding factors influence progression of renal failure. Medical factors such as hypertension<sup>37</sup> and diabetes contributing to CKD and psychiatric factors such as alcohol and substance abuse have obvious interactions with other.

#### 5. Conclusion

Our study showed that functional thyroid gland disorders are more common among patients having psychiatric morbidity undergoing haemodialysis. The function of thyroid hormone and hypokalemia appear to be more common in haemodialysis patients. Further study involving larger sample with cohort study along with additional imaging techniques, genetic studies and CSF studies may unravel the precise causative factors.

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