

Study The Effects Of Chronic Kidney Disease On The Level Of Thyroid Hormones In Iraqi Patients

Ezzate H. Ajeena¹ Shaymaa H. Jabber² Kalil Z.Kalil³

^{1,2} Department of Biology, College of Science, University of Kufa/Iraq.
³ Veterinary College, University of Kufa/Iraq.
E.mail; <u>ezath.abdulkarim@uokufa.edu.iq</u>

Abstract

Chronic kidney disease is consider to be a major health issue which affecting high percent of population worldwide. This study attempted to determine the effects of chronic kidney disease on the function of thyroid gland by measuring its hormones levels . There were 70 subjects included in this study their age between 20 to 70 years divided into two groups, patients and control groups each one contain 35 persons. Blood was obtained from the all subjects for measuring the levels of thyroid hormones . There was increasing in the incidence of chronic kidney disease in the fifties of age as the results of this study revealed. The levels of thyroid hormones recorded significantly $P \le 0.05$ decreasing in patients with chronic kidney disease when compared with healthy persons. For conclude, chronic kidney disease leads to significant changes in the levels of thyr oid hormones that need to be carefully interpreted in these patients.

Key words: chronic kidney disease (CKD), Thyroid hormones, blood pressure.

Introduction

Chronic kidney disease (CKD), which is now recognized as a major public health p rimacy worldwide due to the high prevalence of acute disease with noticeable harm ful effects on prognosis and lifestyle and on economic resources(1). Specifically, in the 2010 Global Burden Disease Study(2). Over the last 10 years ,CKD mortality has increased by 31.7%, making it one of the fastest growing major reason of death, beside dementia diabetes and In the samestudy,CKD is listed as the 17th leading cause of universal years of death, an incr ease of 18.4 percent since 2005, and the third major increase of any major cause of death(3).

It has knew for years that there are interactions between kidney and thyroid functions where the various categories of kidney diseases can be related with several defects of thyroid performs (4) and different endocrine diseases (e.g.insulin resistance, secondary hyperparathyroidism) have been diagnosed as extra-renal complexities of CKD, and as potential predictors of morbidity and mortality in this people(5).

The human body synthesizes thyroid hormones accurately according to the change of energy that it's needs(6), where thyroid hormones (TH) are acutal for an sufficient growth and development of the kidney. reciprocally, the kidney is not only an organ for metabolism and removal of TH, however as well as target tissue of some of the iodothyronines activities(7). Where CKD influences together TH peripheral metabolism and hypothalamus–pituitary–thyroid axis (8).



URL: http://www.uokufa.edu.id/journals/index.php/ajb/index http://iasj.net/iasj?func=issues&jld=129&uiLanguage=en Email: biomgzn.sci@uokufa.edu.iq



Materials and methods

Blood specimens were collected from 35 patients with chronic renal failure (CRF) who were treated in the artificial kidney section at Al-Seder teaching City in Al-Najaf Governorate . The identification of the disease was cured by clinical data and biochemical tests such as (serum creatinine , blood urea and creatinine clearance). The type of dialysis for patients was exclusively of hemodialysis type; the sex of patients varied between 16 males and 19 females their ages between 20 to 70 years. The investigation also included 35 healthy persons who did not have any renal disease, high blood pressure, diabetes mellitus and heart disease, where they represented the control group. The serum was isolated from the blood which was drawn from both the healthy and patients groups to measure the rank of thyroid hormones(T3 and T4) by using Monobind ELISA kit (USA). Clinical history and other patients information obtained from medical records within the hospital after obtaining approvals from them or their relatives.

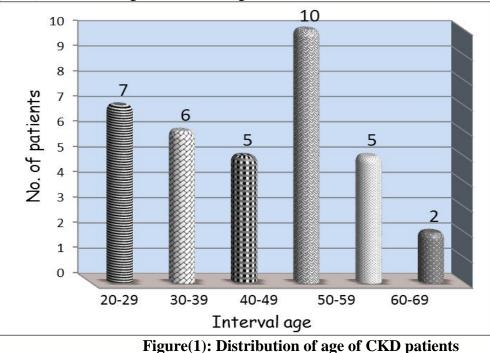
Statistical Analysis

The statistical analysis of this research is based on the SPSS system (Versi on 17.0) and the statistical methods used were Means, Standard Deviations, One Way ANOVA and Chi Square.

Results

1. Age

There were 10 patients (28.5%) in the fifties of age in patients group which act the highest incidence percentage of CKD in this study while there was only 2 cases (5.7%) in sixties of age as shown in figure below.



2. Gender

This study elucidated in figure 2 that CKD increased in females with 19 cases (54%) while males with 16 cases (46%).

URL: http://www.uokufa.edu.iq/journals/index.php/ajb/index http://iasj.net/iasj?func=issues&jId=129&uiLanguage=en Email: biomgzn.sci@uokufa.edu.iq Al-Kufa University Journal for Biology / VOL.12 / NO.1 / Year: 2020 Print ISSN: 2073-8854 Online ISSN: 2311-6544



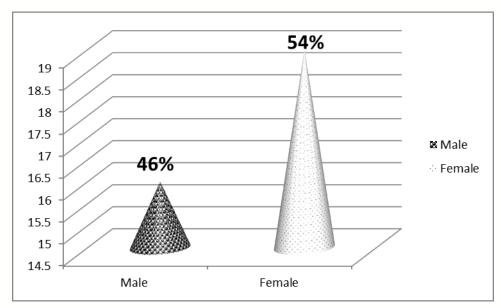


Figure (2) Distribution of patients with (CRD) according to gender

3. Smoking

The number of patients with CRF who smoking were 11 (30%) as figure (3) illustrated while the majority of the patients were nonsmoking with 26 (70%).

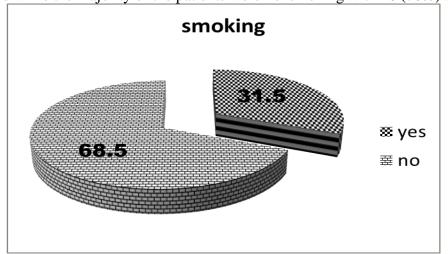


Figure (3) distribution of patients with CRF according to smoking habit.

4. Residence

The residence in this study include rural and urban areas, the patients was distributed as 63% (22 patients) of them live in urban area while 37% (13 patients) of them live in rural area as explained in figure(4) without significant difference when compared with healthy individuals.





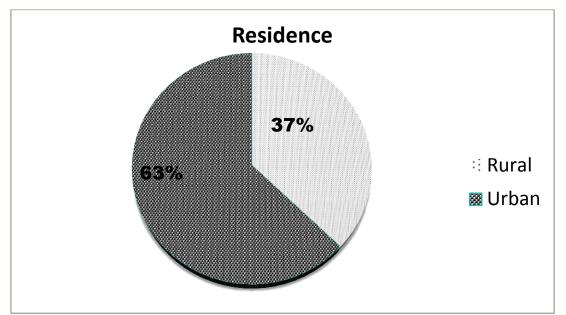


Figure (4) distribution of patients with CRF according to residence .

5. blood pressure

Figure (5) was show that patients with CRF after getting this disease have increased in the levels of blood pressure as comparing with healthy individual. 19 patients (54%) have hypertension while 16 patients (46%) of them didn't undergo of it.

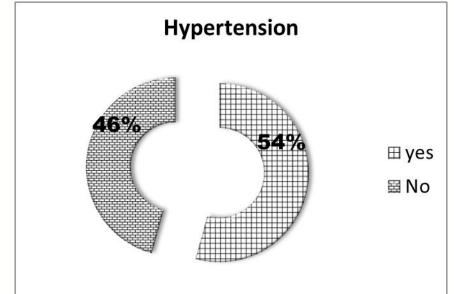


Figure (5): The percentage of patients with CRF who undergo hypertension

6. Triiodothyronine (T3) hormone & thyroxin hormone (T4).

The results of table (1&2) showed that the levels of thyroxin (T4) hormones and triiodothyronine (T3) significantly P<0.05 decreased in patients group $(0.77\pm0.13, 6.25\pm1.36)$ as compared with control group $(0.95\pm0.42, 9.18\pm1.49)$ respectively.





Table (1) Serum Triiodothyronine T3 hormone levels ng/ml in patients and control groups .

groups	No.	Mean±SD	P value
Patients group	35	0.77±0.13	
Control group	35	0.95±0.42	
Total	70	0.86±0.32	

Table (2) Serum Tetraiodothyronine T4 hormone level (ng/ml) in patients and control groups .

groups	No.	Mean±SD	P value
Patients group	35	6.25±1.36	
Control group	35	9.18±1.49	
Total	70	7.72±2.04	

Discussion

This study elucidate that chronic renal failure disease increased in the age of fifties as shown in figure(1). this result has been agreed with (9) who found that the mean age of the patients with CRF was 50 years. (10) also confirm that the disease above increased in interval age (45-54) years in their case-control study. The causes may be as (11) speculated that older patients' kidneys are more vulnerable to proteinuria's nephrotoxic effects due to higher rates of renal fibrosis and ischemia . Rule et al. were estimated their hypothesis from the scientific results of (12) who explained that renal mass decrease between age 30 and 80 years with steepest decline observed after age 50 years.

Nyengaard found that 30% of glomeruli are lost even in normal aging kidneys and display diffuse glomerular sclerosis by 75 years of age. Figure (2) was explained that the incidence of CKD was increased in female than male this is supported by (14) who found in their research in Saudia Arabia the ratio of incidence was male to female 1.00- 1.01. United states renal data system has annual report explained that between 2007 and 2012, the prevalence of CKD was higher among women (15.1%) than among men (12.1%). Women had higher prevalence of high albumin to creatine (9.6% versus 8.1% in men) and higher prevalence of decreased glomerular filtration rate (GFR).(15)

There was no association between smoking habit and increased risk for CRF in figure (3), this was on agree with (16) who didn't find a significant association between smoking and CRF while recent studies confirm a 3 folds the risk increased for glomerulonephritis in patients with CRF who consider heavy smokers (17). Regarding to the relation of hypertension and CRF diseases there was an increasing in the developing high blood pressure in the patients with CRF after the disease has begun and continue with various periods as shown in figure (4). This result was consistent with Japanese study in 1996 perform by (18) who showed that elevated diastolic blood pressure was strongest predictor of the development of end stage of renal diseases. This is due to Na preservation and activation of the renin-angiotensin system in patents with CKD, which was found to be the most important mechanisms

URL: http://www.uokufa.edu.iq/journals/index.php/ajb/index http://iasj.net/iasj?func=issues&jld=129&uiLanguage=en Email: biomgzn.sci@uokufa.edu.iq



involved in the increased blood pressure in those patients 19). In patients with hypertension; GFR has been reported to decline faster compared to those without hypertension(20).

There was a decreasing in the levels of triiodothyronine T3 and tetraiodothronine T4 hormones in the patients with CRF as compared with healthy people as both table (1 &2) illustrated. This result was supported by (21) who found that thyroid abnormalities were very common in end-stage renal disease (ESRD) patients and also reported the most common abnormalities were low in T3 and T4 in (45.5% & 44.3%) of cases respectively. The decreasing in the levels of the hormones above in (ESRD) patients may serve as a warning sign of poor prognosis within the coming months (22).

In 2013 (Balaji, *et. al.*) confirm that the levels of thyroid hormones were significantly reduced when compared with control. reducing levels of T3 (low T3 syndrome) is the most commonly observed thyroid modifications in these patients (24). CRF affects thyroid function in multiple ways including low circulating thyroid hormones levels, altered the metabolism of peripheral hormones , disturpted binding to carrier proteins, possible reduction of thyroid content in the tissue and increased thyroid glands iodine accumulation (25).

Impaired conversion of T4 to T3 may be associated with malnutrition and humoral f actors, including cytokines commonly associated with CKD (26). In 2006 there was a study (27)**showed 75%** of undialyzed CKD patients have diminished T4 levels. This low levels of thyroid hormones due to defective release in response to TSH. CKD affects the hypothalamus- pituitary- thyroid axis.

In uremia, the response of the pituitary receptors to TRH is blunted, causing a reducti on in the release of TSH. The response of receptors on thyrotrops is delayed due to reduced clearance with TSH's half-life increase (28).

References

1- Couser, W. G., Remuzzi, G., Mendis, S., & Tonelli, M. (2011). The contribution of chronic kidney disease to the global burden of major noncommunicable diseases. *Kidney international*, *80*(12), 1258-1270.

2- Lozano, R., Naghavi, M., Foreman, K., Lim, S., Shibuya, K., Aboyans, V., ... & AlMazroa, M. A. (2012). Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *The lancet*, *380*(9859), 2095-2128.

3- Wang, H., Naghavi, M., Allen, C., Barber, R. M., Bhutta, Z. A., Carter, A., ... & Coggeshall, M. (2016). Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980–2015: a systematic analysis for the Global Burden of Disease Study 2015. *The lancet*, 388(10053), 1459-1544.

4-Kaptein EM.(1986) Thyroid function in renal failure. Contributions to Nephrology .50 64–72.

5-Pham, H., Robinson-Cohen, C., Biggs, M. L., Ix, J. H., Mukamal, K. J., Fried, L. F., ... & de Boer, I. H. (2012). Chronic kidney disease, insulin resistance, and incident diabetes in older adults. *Clinical Journal of the American Society of Nephrology*, 7(4), 588-594.



Al-Kufa University Journal for Biology / VOL.12 / NO.1 / Year: 2020 Print ISSN: 2073-8854 Online ISSN: 2311-6544



6-Yen, P. M. (2001). Physiological and molecular basis of thyroid hormone action. *Physiological reviews*, 81(3), 1097-1142.

7- Iglesias, P., & Diez, J. J. (2009). Thyroid dysfunction and kidney disease. *European journal of endocrinology*, *160*(4), 503-515.

8- Singh, P. A., Bobby, Z., Selvaraj, N., & Vinayagamoorthi, R. (2006). An evaluation of thyroid hormone status and oxidative stress in undialyzed chronic renal failure patients. *Indian journal of physiology and pharmacology*, *50*(3), 279.

9- G. Chinnapu Reddy, Ramakrishna Devaki, Pragna Rao.(2013). iron indices in patients with functional anemia in chronic kidney disease. *The Journal of the International Federation of Clinical Chemistry and Laboratory Medicine*.vol.24, no.3-4

10 - Elisabeth Ejerblad, C. Michael Fored, Per Lindblad, Jon Fryzek, Paul W. Dickman, Carl-Gustaf Elinder, Joseph K. Mclaughlin, and Olof Nyre'N. (2004). association between smoking and chronic renal failure in a nationwide population-based case-control study. *J Am Soc Nephrol 15: 2178–2185*

11 - Rule AD, Amer H, Cornell LD et al.(2010). The association between age and nephrosclerosis on renal biopsy among healthy adults. *Ann Intern Med; 152: 561–567.*

12 - Epstein M.(1996). Aging and the Kidney. J Am Soc Nephrol;7:1106-1122.

13 - Nyengaard JR, Bendtsen TF.(1992). Glomerular number and size in relation to age, kidney weight, and body surface in normal man. *Anat Rec*;232:194-201.

14- Ibrahim Abdelmajeed Ginawi, Hussain Gadelkarim Ahmed, Awdah M. Alhazimi.(2014). Assessment of Risk Factors for Chronic Kidney Disease in Saudi Arabia. *International Journal of Science and Research, Volume 3 Issue 7.*

15- United States Renal Data System. 2015 USRDS annual data report: Epidemiology of kidney disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases.

16- Nuyts GD, Van Vlem E, Thys J, De Leersnijder D, D'Haese PC, Elseviers MM, De Broe ME. (1995). New occupational risk factors for chronic renal failure. *Lancet* 346: 7–11,

17- Stengel B, Couchoud C, Cenee S, Hemon D. (2000). Age, blood pressure and smoking effects on chronic renal failure in primary glomerular nephropathies. *Kidney Int* 57: 2519–2526,

18- Iseki K, Ikemiya Y, Fukiyama K. (1996). Blood pressure and risk of end-stage renal disease in a screened cohort. *Kidney Int Suppl 55: S69–S71*,

19- Guyton AC, Coleman TG, Wilcox CS.(1999). Quantitative analysis of the pathophysiology of hypertension. *J Am Soc Nephrol; 10: 2248–2249*.



URL: http://www.uokufa.edu.iq/journals/index.php/ajb/index http://iasj.net/iasj?func=issues&jld=129&uiLanguage=en Email: biomgzn.sci@uokufa.edu.iq



20- Hanratty R, Chonchol M, Miriam Dickinson L, Beaty BL, Estacio RO, Mackenzie TD, Hurley LP, Linas SL, Steiner JF, Havranek EP.(2010). Incident chronic kidney disease and the rate of kidney function decline in individuals with hypertension. *Nephrol Dial Transplant*, *25*(*3*):801-807.

21- J. Horáček1, S. Dusilová Sulková, M. Kubišová, R. Šafránek, E. Malířová, M. Kalousová, I. Svilias1, J. Malý, L. Sobotka, P. Žák. (2012). Thyroid Hormone Abnormalities in Hemodialyzed Patients: Low Triiodothyronine As Well As High Reverse Triiodothyronine Are Associated With Increased Mortality. *Physiol. Res.* 61: 495-501,

22- Carrero Jj, Qureshi Ar, Axelsson J, Yilmaz Mi, Rehnmark S, Witt Mr, Bárány P, Heimbürger O, Suliman Me, Alvestrand A, Lindholm B, Stenvinkel P.(2007). Clinical and biochemical implications of low thyroid hormone levels (total and free forms) in euthyroid patients with chronic kidney disease. *J Intern Med* 262: 690-701,

23- Balaji Rajagopalan, Pragna B. Dolia, Veerendra Kumar Arumalla and Seshadri Reddy V.(2013). Renal function markers and thyroid hormone status in undialyzed chronic kidney disease. *Al Ameen J Med Sci*; 6(1):70-74

24- Lo JC, Chertow GM, Go AS, Hsu CY.(2005). Increased prevalence of subclinical and clinical hypothyroidism in persons with chronic kidney disease. *Kidney International; 67: 1047–1052*.

25- Lim VS.(2001). Thyroid function in patients with chronic renal failure. *American Journal of Kidney Diseases ; 38: S80–S84*.

26- Dudani RA, Desai KB, Mehta MN, Mani LS, ACharya VN.(1981). Thyroid dysfunction in uremia. *J Assoc Phys India*; 29: 1038–1040.

27- Singh PA, Bobby Z, Selvaraj N, Vinayagamoorthi R.(2006). An evaluation of thyroid hormone status and oxidative stress in undialyzed chronic renal failure patients. *Indian Journal of Physiology and Pharmacology; 50: 279–284.*

28- G. Basu and A. Mohapatra. (2012). "Interactions between thyroid disorders and kidney disease," *Indian Journal of Endocrinology and Metabolism, vol. 16, no. 2, pp. 204–213,*

URL: http://www.uokufa.edu.iq/journals/index.php/ajb/index http://iasj.net/iasj?func=issues&jld=129&uiLanguage=en Email: biomgzn.sci@uokufa.edu.iq