Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 4, 2021, Pages. 9064 - 9069
Received 05 March 2021; Accepted 01 April 2021.

Assessing the Potential of Prolactin Hormonein Chronic Kidney Disease Patients

H.M.Al-ajely[1], Khalid Mohammed Khudhur Al-Bofkane[2], Nadwah mohammed Khudhur Al-Bofkane[3] , Shihab A. Al-Bajari [4]

[1]College of science / Mosul university, Mosul, Iraq
[2] College of pharmacy / Ninevah university, Mosul, Iraq
[3,4]Mosul Technical Institute/ Northern Technical University, Mosul, Iraq

Abstract

Prolactin is a protein known as luteotropin, which enables mammals(females) to produce milk.This study evaluated the relationship between increasing prolactin levels and Chronic Kidney Disease (CKD). Blood sampleswere collected from 36patients with CKD and 35healthy people as a control group.Kidney function test was conducted, as the following parameters were calculated for both CKD patients and the control group: serum prolactin, insulin, insulin resistance, creatinine,glucose, uric acid,urea, albumin and total protein. Results showed that high levels of serum prolactin (57±3.21ng/dl) were observed in CKD patients in comparison to the control group (21±2.2 ng/dl). A significant difference ($P<0.05$) was recorded in serum prolactin, insulin, insulin resistance, urea, creatinine and uric acid levelsbetweenCKD patients and the control group. Results also revealed that serum prolactin in CKD patients was higher in females (68±1.21ng/dl) than that recorded in males (47±3.22 ng/dl) in comparison to the control group for both males and females (19±1.2 and 23±2.4 ng/dl) respectively. Insulin resistance recorded nearly the same values in CKD patients for both males and females (5.99±1.12 and 6.39±0.51) respectively but higher than those recorded in the control group (2.79±0.31and3.07±0.31) respectively. Blood urea levels were considerably higher in males (81±3.11 mg/dl) than that recorded in females (72±3.11 mg/dl) for CKD patients in comparison to the control group for both males and females (15.8±2.1 and 14.3±3.1 mg/dl) respectively.

Key words:chronic kidney disease, prolactin, insulin resistance.

Introduction

Prolactinaffects 300 species in vertebrates such as humans. It is secreted from the pituitary gland as a reaction for eat, ovulation, mate, estrogen treatment, and nursing. Prolactin hormone plays an important role in regulating the immune system, metabolism and pancreatic development[1], which may results in cardiovascular consequences among CKD patients.

Chronic kidney disease is anadvanced loss of kidney function over months or years [2,3]. CKD is aglobal health problem that affects 5–10% of the world population [4,5].

Worsening kidney function has no specificsymptoms, butthe patient might feel unwell and experienceloss in appetite. Moreover, CKD is identifiedinpeople who have a potential risk of kidney problems, such as those with diabetes, high blood pressure and a bloodline relative with CKD. This disease could be determined by its certain complications, such as anemia, pericarditis, cardiovascular disease or renal osteodystrophy (renal osteodystrophy is included in chronic kidney disease–mineral and bone disorder CKD-MBD) [3].

Chronic kidney disease is a long-term pattern of kidney disease,therefore, it is recognized from acute kidney disease or acute kidney injury, as the decrease in kidney function should be manifest for over 3 months. CKD is diagnosedwith a blood test for creatinine as a resultof muscle metabolismbreakdown. Previous studies have shown that prolactin may have biological actions, which contributes in atherosclerotic progression and leads to insulin resistance [6]. Insulin is a hormone produced by the β cells of Langerhans, which is exist in Pancreas. Insulin preserves normal blood sugar (glucose) levels by facilitating the uptake of glucose, regulating lipid metabolism, carbohydrate and protein and enhances growth and cell division [7].

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 4, 2021, Pages. 9064 - 9069
Received 05 March 2021; Accepted 01 April 2021.

Insulin resistance occurs when the level of fat exceeds the normal rangein fatty tissues leading to accumulation of fats in the abdomen, muscles, liver as well as intestine [8].In Particularly, Insulinresistance is defined as the elevation of insulin level leading to aweak biological response, which impaired glucose elimination [9].Serious problems that are associated to insulin resistance are high blood pressure and increasing insulin levels, which in turn, leads to cardiovascular disease and Diabetes type 2 [10]. Particularly, insulin resistance is related to Diabetes type 2, however, it is increasing in Diabetes type 1[11].

Materials and Methods

The test sample

The current study was conducted by utilizing 36 patients with CKD and 35 healthy people as a control group. Both groups were from males and females. The characteristics of both groups are shown in Table1.

Table 1 Demographic data of the CKD patients and the control group

Characteristics	Control	CKD Patients
	Mean ± SD	Mean ± SD
Age (year)	35 ± 2.5	36 ± 3.1
Sex (male/female)	5/30	12/24
Duration of CKD (years)	------	3.5

Kidney function tests

Prolactin and insulin were assessed by ELISA using Elabscience and monobind respectively (ELISA is a USA Kit which depends on the high affinity and specificity [18] and [19]). Insulin resistance was determined in blood serum by [20]. Urea and serum creatinine and were determined calorimetrically as described by [12].Serum total protein and albumin were determined by using manual Biuret method [13]and [14]respectively.Uric acid was determined by [15, 16]. Glucose was determined by[17].

Statistical analysis:

Data collected from the experiment was analysed usingt-test, which is a type of statistic used for determining if there is a significant difference between the means of two groups.

Results& Discussion

A number of parameters that is related to kidney function were assessed. Results revealed that prolactin values were 21±2.2 and 57±3.21ng/dl in control group and CKD patients respectively. Insulin recorded 12.89±1.08and 19.31±.2.25 μIU/mL respectively, whereas insulin resistance achieved 2.96±0.55 and 6.56±1.37 respectively. Glucose values were 5.09±0.11 and 7.19±0.11mmol/L for the control and CKD patients respectively. Blood urea recorded 15.3±2.1and 76±3.11mg/dlrespectively. Creatinine values were 0.91±0.11 and 2.1±0.12mg/dl respectively. Uric acid recorded 3.3±0.42 and 8.1±1.2mg/dlfor the control and CKD patients respectively. Total protein achieved 6.5±0.51 and 5.4±1.3 mg/dl respectively. Albumin recorded 4.7±0.22and 3.8±1.1mg/dl respectively as shown in Table 2.

Table 2Kidney function test andprolactin levels in CKD patients and control group

Parameters	Control	CKD patients	T-Test analysis
	Mean ± SD	Mean ± SD	
Prolactin(ng/dl)	21±2.2	57±3.21	S
Insulin(μIU/mL)	12.89±1.08	19.31±.2.25	S
Insulin resistance	2.96±0.55	6.56±1.37	S
Glucose (mmol/L)	5.09±0.11	7.19±0.11	NS

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 4, 2021, Pages. 9064 - 9069
Received 05 March 2021; Accepted 01 April 2021.

Blood urea(mg/dl)	15.3±2.1	76±3.11	S
Creatinine (mg/dl)	0.91±0.11	2.1±0.12	S
Uric acid(mg/dl)	3.3±0.42	8.1±1.2	S
Total protein (mg/dl)	6.5±0.51	5.4±1.3	S
Albumin (mg/dl)	4.7±0.22	3.8±1.1	S

Results are reported as mean ± SD.S: Significant (P>0.05), NS: Not Significant.

Results revealed high levels of all parameters in CKD patients in comparison with the control group except total protein, which was slightly higher than that in CKD patients. Results were analysed statistically by t-test andrecorded a significant difference in all parameters between CKD patients and the control group, however, no significant difference was observed in glucose levels among groups.

Prolactin levels in CKD patients were higher than that in the control group, which was in line with that recorded by [21] and [22].This confirms that CKD patients have increased levels of prolactin hormone (hyperprolactinemia) as declared by [23]. Moreover, high prolactin levels contribute in arteriosclerosis, which in turn, leads to insulin resistance and may contribute to vascular derangements.[24]. This was obvious in the current study as the insulin resistance recorded high levels in CKD patients in comparison to the control group.

In particular, diets with high fat arerelated with insulin resistance, asfatty acid composition play an important role in insulin resistance development by effecting on membrane lipids composition [25].Furthermore, blood urea in the current study recorded high levels in CKD patients in comparison to the control group, which could be attributed to the degradation of muscles leading to increaseblood urea levels [26] and the later causes kidney damage [22].Moreover, kidney function test was also determined between males and females as shown in Table 3.

Table 3 Kidney function test for males and females

Parameters	Control		CKD patients	
	Male	Female	Male	Female
Prolactin (ng/dl)	19±1.2	23±2.4	47±3.22	68±1.21
Insulin(µIU/mL)	12.19±1.1	13.29±1.1	19.01±2.25	19.61±1.5
Insulin resistance	2.79±0.31	3.07±0.31	5.99±1.12	6.39±0.51
Glucose (mmol/L)	5.16±0.11	5.21±0.11	7.09±0.10	7.34±0.10
Blood urea (mg/dl)	15.8±2.1	14.3±3.1	81±3.11	72±3.11
Creatinine (mg/dl)	0.91±0.11	0.91±0.11	2.1±0.12	2.1±0.12
Uric acid (mg/dl)	3.5±0.12	3.1±0.42	8.71±1.2	7.61±2.2
Total protein (mg/dl)	6.6±0.51	6.3±0.51	6.0±1.1	5.0±2.2

Results are reported as Mean ± SD

Results have shown that prolactin hormone recorded high levels in CKD patient for both males and females (47±3.22 and 68±1.21ng/dl) respectively in comparison to that recorded for the control group (19±1.2 and 23±2.4 ng/dl) respectively. Insulin also recorded high levels in CKD patients for both males and females (19.01±2.25 and 19.61±1.5µIU/mL) respectively in comparison to that for the control group (12.19±1.1and13.29±1.1µIU/mL).Insulin resistance achieved high levels(5.99±1.12 and 6.39±0.51) in CKD patients than that recorded in the control group(2.79±0.31and 3.07±0.31) for males and females respectively. Glucose recorded high levels (7.09±0.10 and 7.34±0.10mmol/L) in CKD patients for both males and females

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 4, 2021, Pages. 9064 - 9069
Received 05 March 2021; Accepted 01 April 2021.

respectively in comparison to the control group (5.16±0.11 and 5.21±0.11 mmol/L) respectively. Blood urea achieved high levels in CKD patients (81±3.11and72±3.11 mg/dl) for males and females respectively in comparison to that recorded for the control group (15.8±2.1and14.3±3.1mg/dl) respectively. Creatinine levels in CKD patients were slightly higher (2.1±0.12 and 2.1±0.12 mg/dl) in both males and females respectively in comparison to that in the control group (0.91±0.11and0.91±0.11 mg/dl) respectively. Uric acid recorded high levels in CKD patients for both males and females (8.71±1.2and7.61±2.2 mg/dl) respectively in comparison to that in the control group (3.5±0.12 and 3.1±0.42 mg/dl) respectively. Total protein in CKD patients was almost as same (6.0±1.1and 5.0±2.2 mg/dl) as that for the control group (6.6±0.51and 6.3±0.51 mg/dl) in both males and females respectively. In CKD patients, data exhibited high levels of prolactin hormone(hyperprolactinemia) in females rather than that recorded in males, however, prolactin levels were higher than that recorded in the control group. Hyperprolactinemia is a normal phenomenon in males and females with CKD due to changes in biological activities, which leads to increase the production of prolactin hormone [22].Insulin resistance was nearly the same for both males and females. The current study reveals that insulin resistance is realtedwith kidney dysfunction due to increased levels of parameters that has been determined for kidney function test in CKD patients, which indicates the fact that CKD patients have high insulin resistance in comparison to healthy individuals, as declared by [27]. Particularly, insulin resistance is exist in early stages of CKD and becomes widespread in CKD progression [28]. Increasing levels of blood urea were recorded in males in comparison to females, however, the recording levels were extremely higher than that for the control group for both males and females, which was in line with that recorded by [22]. In addition, uric acid recorded nearly the same levels in both males and females. Finally, total protein recorded same levels in both males and females.

Conclusion

The current study has shown that CKD is related with high serum levels of prolactin hormone.High prolactin levels (Hyperprolactinemia) leads to insulin resistance. A significant difference was observed in CKD patients for all parameters that reflects kidney function test in comparison to the control group.

References

1. Redmon, J.H., Elledge, M.F., Womack, D.S., Wickremashinghe, R., Wanigasuriya, K.P. and Peiris-John, R.J. (2014) ′Additional perspectives on chronic kidney disease of unknown etiology CKDu in Sri Lanka - lessons learned from the WHO CKDu population prevalence study′, *BMC Nephrology*, 15(1), pp. 125.
2. Freeman, M.E., Kanyicska, B., Lerant, A. and Nagy, G. (2000) ′Prolactin: structure, function, and regulation of secretion′, *Physiol Rev*., 80(4), pp.1523-631.
3. KDIGO Kidney International (2009) ′KDIGO Clinical Practice Guideline for the Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease-Mineral and Bone Disorder CKD-MBD′, *Official Journal Of TheInternational Society OfNephrology*, 76 (Suppl 113).
4. Eknoyan, G., Norbert, L., Rashad, B., Kai-uwe, E., Adeera, L., Nathan, L., Francesco, L., Alison, M., Raymond, V., Rowan, W. and Haiyan, W.(2004) ′The burden of kidney disease: Improving global outcomes′, *Kidney International*, 66, pp. 1310-1314.
5. Martínez-Castelao, A., José, L., Julián, S., Jesús, C., Javier, E., Enric, E., Lorenzo, F., Javier, G., Silvia, G., Julio, H., José, L., Pilar, M., Rosario, M., Francisco, M., Manuel, M., Pedro, D., Ana, D., Marta, S., Carmen, S. and Salvador, T. (2014) ′Consensus document for the detection and management of chronic kidney disease′, *Nefrologi*a, 34(2), pp. 243-62.
6. Foley, R. and Allan, J. (2007) ′End-Stage Renal Disease in the United States: An Update from the United States Renal Data System′, *J Am Soc Nephrol*., 18, pp. 2644-2648.

7. Cefalu, W. (2001) ′Insulin resistance: cellular and clinical concepts′, *Exp Biol.*,226, pp.13-26.

8. Govers, E., Slof, E., Verkoelen, H., Ten Hoor-Aukema, N. and KDOO (2015) ′Guideline for the Management of Insulin Resistance′,*Int J Endocrinol MetabDisord*., 1(3), pp. 1-10.
9. Reaven, G. (2004) ′The metabolic syndrome or the insulin resistance syndrome? Different names, different concepts, and different goals′,*Endocrinol Metab Clin North Am*., 33(2), pp. 283-303.
10. WHO Obesity and overweight, Fact sheet N°311.Updated January 2015.
11. Ndisang, J., Alfredo, V. and Sharad, R. (2017) ′Insulin Resistance, Type 1 and Type 2 Diabetes, and Related Complications 2017′, *Journal of Diabetes Research***,** 2017.
12. Jaffe, M. (2009) ′The method of analysis, which is based on Pikrinsäure in the normal manner and is based on a new reaction to creatinine′, *bchm*, 10(5), pp. 391-400.
13. Kingsley, G. (1942) ′The direct biuret method for the determinations of serum proteins as applied to photoelectric and visual colorimetry′,*J Clin. Lab*., 27, pp. 840-847.
14. Doumas, B., Waston, W. and Bigg, H. (1971) ′Albumin standards and the measurement of serum albumin with BCG′, *Clin Chim Acta*, 31, pp. 87-96.
15. Varley, H. (1967) ′Practical clinical biochemistry′ 4th ed. The White Friars Press Ltd.UK.
16. Burtis, C. and Ashwood, E. (1999) ′Tietz textbook of clinical chemistry′. 3rd ed .W. B. Saunders Company, USA.
17. Tinder, P. (1969) ′Determination of glucose in blood using glucose oxidase with an alternative oxygen acceptor′, *Ann. Clin. Biochem.*, 6, pp. 24-27.
18. Wu, K., Zheng, I., Niwa, H., Takebayashi, T., Takahashi, K. and Zhang, M. (2017) ′Chronic endometritis modifies decidualization in human endometrial stromal cells′, *Reproductive biology and endocrinology*′,15(16), pp. 1-10.
19. Gerbitz, V. (1980) ′Pancreatic B-cell peptides: Kinetics and Concentration of proinsulin insulin and C-peptides in plasma and urine problems in the clinical and literature literature′, *J. Clin. Chem. Biochem*, 18, pp.313-326.
20. Maheria, P., Parchwani, D., Upadhyay, A. and Sharma, M. (2011) ′Analysis of resistance in various components of metabolic syndrome′,*Nat. J. of Med. Res*., 1(2), pp. 37-41.
21. Peces, R., Casado, S., Frutos, M., Horcajada, C., López-Novoa, J. and Hernando, L. (1979) ′Prolactin in chronic renal failure, haemodialysis and transplant patients′, *Proc Eur Dial Transplant Assoc*., 16, pp.700-2.
22. Al-Zuhairi, W.and Alzahraa, I. (2019) ′Evaluation Of Serum Prolactin Level In Chronic Kidney Disease In Iraq′, *Biochem. Cell. Arch*, 19(1), pp. 489-493.
23. Anil, K. (2017) ′Estimation of levels of serum prolactin in chronickidney disease′, *International Journal of Medical and Health Research*, 12(3), pp. 8-10.
24. Raaz, D., Wallaschofski, H., Stumpf, C., Yilmaz, A., Cicha, I. and Klinghammer, L. (2006) ′Increased prolactin in acute coronarysyndromes as putative co – Activator of ADP – Stimulated P – Selectin expression′, *Horm Metab Res*., 38(11), pp. 767-772.
25. Sampath, H. and Ntambi, J. (2004) ′Polyunsaturated fatty acid regulation of gene expression′, *Nutr Rev*, 62, pp. 333–9.
26. Khaled, M., Faiz, A. and Abdelgader, A. (2015) ′Effect ofhaemodialysis on some metabolic products of CKD patients inLibya′, *WJPPS*, 4, pp. 45-54.
27. Vladu, M., Diana, C., Ion, C., Mircea-Cstalin, F., Anca, A., Simona, T., Maria, M. and Maria, F. (2017) ′Insulin Resistance and Chronic Kidney Disease in Patients with Type 1 Diabetes Mellitus′, *Journal of Nutrition and Metabolism*, 2017, pp. 1-5.
28. Sarah, J., Christopher, J., Jesse,Y., Perry, W., Xiaoming, Z., James, James, P., Bruce, M., Raymond, R., Jing, C., Leon, F., Patricia, K., Richard, L.,

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 4, 2021, Pages. 9064 - 9069
Received 05 March 2021; Accepted 01 April 2021.

29. Daniel, J., Lee, H., Amanda, H.and Harold, I. (2019) ′Insulin resistance and chronic kidney disease progression, cardiovascular events, and death: findings from the chronic renal insufficiency cohort study′, *BMC Nephrology*, 20(60), pp. 1-1