Some important comparative parameters between Patients with Chronic Renal Failure and Patients with Diabetic Nephropathy in Erbil

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ABSTRACT

Background and Objectives: Patients with chronic renal failure and diabetic nephropathy reveals biochemical changes .This study aim to investigate the differences of some important biochemical changes in these two groups of patients in comparison with normal controls.

Methods: (80) patients were selected with different Renal disease complications. A control group of (30) healthy,18 males and 12 females were included in this study. Patients were divided into two groups the first group with chronic renal failure, include (40) patients,(25) male and (15) female ; the second group with diabetic –nephropathy , include (40) patients,(25) male, and (15) female. Determination of the biochemical compound level as creatinine ,urea ,uric acid ,total protein (T.P) , albumin ,total cholesterol (TC), triglyceride (TG), low density lipo-protein (LDH-c) ,high density lipoprotein (HDL-c) , and LDL-c/HDL-c ratio.

Results: Patients with chronic renal failure showed increasing levels of (creatinine, urea, -uric acid) in their serum, and lower levels of (total protein, albumin). Mild increase in levels of (TC, LDL-c), while great increased level of triglyceride were recorded, also a great decline in the level of HDL-c was found, which indicate a high risk factor and moderate increase in (LDL-c/HDL-c) ratio .Patients with diabetic nephropathy showed slight increase in the levels of (creatinine, urea, uric acid), however still lower than that in chronic renal failure group. Also they showed decreased levels of (total protein, albumin) ,but still lower than in chronic renal failure and Increased level of (TC,TG, LDL-C, LDL-c/HDL-c) which were greater than the increase in chronic renal failure .Also decrease in the level of HDL-c, but still less than that in chronic renal failure.

Conclusions: Patients with chronic renal failure or with diabetic nephropathy showed significant increase in the levels of creatinine, urea, and uric acid; and decreased levels of albumin and total protein. Both group of patients showed variation in their cholesterol, LDL-c, triglyceride, and LDL/HDL-c ratio.

Key words: Chronic renal failure, Diabetic nephropathy, lipid profile, Total protein.

INTRODUCTION:

Chronic renal insufficiency is defined as patients with serum creatinine of greater than 1.5 mg/dl in female and greater than 2 mg/dl in males. The majority of patients with chronic renal insufficiency are diabetic, The prevalence of chronic renal failure disease is increasing worldwide as a consequence of a rise in the prevalence of disorders that damage the kidney , such as diabetes[1]. Impaired renal function and proteinuria are both of importance in the development of dyslipidemia [2]. Dyslipidemia associated with chronic renal disease is characterized by a low plasma concentration of high density cholesterol (HDL-C), a high concentration of triglycerides (TG) .HDL particles remove excess cholesterol and TG from peripheral vessels ,it

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also inhibit the oxidation of low-density lipoprotein (LDL)[3]. Diabetic nephropathy is the leading cause of renal failure .It is defined by proteinuria >500 mg in 24 hours in the setting of diabetes, but this is preceded by lower degrees of proteinuria,or microalbuminuria. Microalbuminuria is defined as albumin excretion of 30-299 mg/hours[2]. Without intervention, diabetic patients with microalbuminuria typically progress to proteinuria and overt diabetic nephropathy. This progression occurs in both type 1 and type 2 diabetes[3]. An increased concentration of plasma lipids is a risk factor for nephropathy in type 1 (insulin-dependent) diabetes[4]. Caramori and associates(2004) found that diabetic nephropathy develops in at most, 40% of patients with diabetes, even when high glucose levels are maintained for long periods of time [29]. An adverse lipid profile can be secondary to glomerular disease, but recent follow-up studies suggest that it may cause nephropathy, as normoalbuminuric type 1 diabetic patients who developed diabetic nephropathy have been found to have higher initial triglyceride (TG) or LDL- cholesterol concentrations than who did not [4].This hypothesis is also supported by (Kasiske, 1988) showing that manipulations in lipid concentrations can alter glomerular disease [5]. Plasma lipids have been recognized as predictors of diabetic nephropathy in longitudinal follow-up studies in type 1 diabetic patients, the plasma concentration of total cholesterol and low-density lipoprotein were related to the stages of diabetic nephropathy [6]. Chronic renal failure results in profound lipid disorders ,which stem largely from dysregulation of high-density lipoprotein (HDL) and triglyceride –rich lipoprotein metabolism[7].Impaired maturation of HDL in chronic renal failure is primarily due to down regulation of lecithin-cholesteryl acyltransferase and to lesser extent, increased plasma cholestryl ester transfer protein[8].Triglyceride enrichment of HDL in chronic renal failure is primarily due to hepatic lipase deficiency and elevated cholestryl ester transfer protein activity [7]. Chronic renal failure –induced hypertriglyceridemia ,abnormal composition ,and impaired clearance of triglyceride-rich lipoprotein and their remnants are primarily due to down regulation of lipoprotein lipase, hepatic-lipase, and the very-low-density lipoprotein receptor[8]. Liang and his colleagues (1999) found that impaired HDL metabolism contributes to the disturbances of triglyceride-rich lipoprotein metabolism .These abnormalities are compounded by down regulation of apolipoproteins apoA -1,apoA-11,and apo C-11 in chronic renal failure[9]. Together, these abnormalities may contribute to the risk of arteriosclerotic cardiovascular disease and may adversely affect progression of renal disease.

Aim of the study: This study was taken to investigate a comparative study of some important biochemical changes between chronic renal patients and diabetic nephropathy patients.

PATIENTS AND METHODS:

All patients were informed & signed a consent before the study. (80) patients , aged between 35-65 years included in this study & were divided into two groups ,the first group represents patients with chronic renal failure (C.R.F) ,(40) cases (25) male, (15) female .the Second group were nephritic diabetic patients (D.N) ,(40) cases (25) male,(15) female. The patients were attending Rizgari and Hawler Teaching Hospital in the period from 1st of April 2008 to the 31 May 2009.Thirty apparently healthy people were included as control group (18) male, (12) female, with comparable age to the study group 35-65 years . Blood samples were taken after 12 hours fasting. Each sample was transferred with plastic centrifuge tube. Sera were separated by centrifugation at 1000 rpm for 10 minutes, the sera were stored at -4C. and analyzed for creatinine, urea, uric acid, total protein, albumin, TC,TG, LDL-C, HDL-C, LDL-C/HDL-C.

Serum creatinine measurement:
Serum creatinine was measured by using creatinine kit (Syrbio dagnostic reagent for laboratories Paris-France) using colorimetric method with deproteinisation

Blood urea measurement :
Blood urea was measured by urea kit (bioMerie using ux-SA, France) using an enzymatic method.

Uric acid measurement :
Uric acid was measured by uric acid kit (BIOLABO SA,France) using an enzymatic method.

Total Protein measurement :
Total protein was measured by total protein kit (BIOLABO SA,France)using Biuret method.

Total Albumin measurement :
Albumin was measured by total albumin kit (bioMerie using ux-SA, France) .

Serum cholesterol (TC) measurement:
Serum cholesterol was measured by cholesterol kit (CHOD PAP) (BIOLABO SA,France) using an enzymatic method.

Serum triglyceride (TG) measurement:
Serum triglyceride was measured by triglyceride kit (CHOD PAP) (BIOLABO SA,France) using an enzymatic method.

Serum High density lipoprotein (HDL-C) measurement:
Serum high density Lipoprotein was measured by HDL kit (CHOD PAP) (BIOLABO SA,France) using an enzymatic method.

Serum Low density Lipoprotein (LDL-C) measurement : Serum low density lipoprotein cholesterol LDL-C was calculated indirectly by using Fried ward Equation [10].

LDL-C = Total cholesterol-HDL-c + (Trigyceride/5)

Statistical evaluation: All data are expressed as mean±SD. Differences between means of patients and control were evaluated statistically using students t-test. A value of $P< 0.05$ was considered statistically significant.

RESULT:

(80) patients were selected with different kidney complication , from this number first group (40) patients complain from chronic renal failure .

Table (1) show biochemical changes in chronic renal failure .

Creatinine (6.7±2.8)mg/dl, Urea (175±51) mg/dl , and uric acid (9.6 ±2.9) mg/dl was significantly increased, while TC (198±22) mg/dl and LDL-c (125±21) mg/dl slightly increased . Lower level of total protein (4.9±0.3)g/dl,albumin (2.3±0.2) g/dl were noticed with great increase in triglyceride level (234±36) mg/dl and significant reduction in HDL-c level (33±5) mg/dl.

The ratio of LDL-c/HDL-c moderately increased (3.78).

Second group including (40) patients complain from diabetic nephropathy . Table (2) show slight increase in creatinine (3.2±1.7) mg/dl ,urea (93±33)mg/dl, and uric acid (8.5±2.1)mg/dl also it show decrease in level of total protein(5.95±0.3) g/dl and albumin (2.9±0.15) g/dl while there was significant increase in the level of TC (256±30)mg/dl and LDL-c (176±35) mg/dl, reduction in the level of HDL-c (35±5.1)mg/dl was noticed. The ratio of LDL-c/HDL-c significantly increased (5.0).

Table 1: Biochemical changes in chronic renal failure patients.

Variables	Male Control mean No= 18	Male patient mean No=25	t. test	Female control mean No=12	Female patient mean No=15	t.test
Creatinine (mg/dl)	0.8 ± 0.25	6.7 ± 2.8	P<0.001	0.65±0.26	6.4± 3.1	P<0.001
Urea (mg/dl)	25.9 ± 10	175 ± 51	P<0.001	27± 11	163 ± 43	P<0.001
Uric acid (mg/dl)	5.8 ± 2.5	9.6 ± 2.9	P< 0.001	5.1±1.55	8.4 ± 2.6	P<0.001
T. protein (g/dl)	6.9 ± 0.7	4.9 ± 0.3	P< 0.001	6.8± 0.75	5.2 ±0.2	P<0.001
Albumin (g/dl)	3.9 ± 0.4	2.3 ± 0.2	P< 0.001	3.7± 0.3	2.2± 0.1	P<0.001
T.cholestrol (mg/dl)	78.6 ± 23	198 ± 22	P< 0.05	176±20	217 ±33	P<0.05
Triglyceride (mg/dl)	115 ± 31	234 ± 36	P< 0.001	107±28	197±2	P<0.001
HDL-C (mg/dl)	47 ± 15	33 ± 5	P< 0.001	48±6	32.5 ±4	P<0.001
LDL-C (mg/dl)	116 ± 23	125 ± 21	P< 0.05	123±19	155±20	P<0.05
LDL/HDL	2.46	3.78	P< 0.01	2.56	4.84	P<0.01

Table 2: Biochemical changes in Diabetic Nep ropathy

Variables	Male Control mean No= 18	Male patient mean No=25	t.test	Female control mean No=12	Female patient mean No= 15	t.test
Creatinine (mg/dl)	0.8 ± 0.25	3.2 ± 1.7	P< 0.001	0.65±0.26	3.55±1.9	P<0.001
Urea (mg/dl)	25.9 ± 10	93± 33	P< 0.001	27± 11	82± 29	P<0.001
Uric acid (mg/dl)	5.8 ± 2.5	8.5 ± 2.1	P< 0.01	5.1±1.55	8.0± 1.9	P<0.01
T. protein (g/dl)	6.9 ± 0.7	5. 95 ±0.3	P< 0.01	6.8± 0.75	6.32± 0.4	P<0.01
Albumin (g/dl)	3.9 ± 0.4	2.9 ± 0.15	P< 0.01	3.7± 0.3	2.61±0.2	P<0.01
T.cholestrol (mg/dl)	78.6 ± 23	256 ± 30	P< 0.001	176±20	254 ± 31	P<0.001
Triglyceride (mg/dl)	115 ± 31	260± 42	P< 0.001	107±28	229±38	P<0.001
HDL-c (mg/dl)	47 ± 15	35 ± 5.9	P< 0.001	48±6	34± 5.6	P< 0.001
LDL-c (mg/dl)	116 ± 23	176 ± 35	P< 0.001	123±19	190 ± 30	P<0.001
LDL/HDL	2.46	5.0	P< 0.001	2.56	5.58	P<0.001

DISCUSSION:

Creatinine level increased in chronic renal failure (6.7± 2.8) mg/dl (Table-1), this stage characterized by high blood urea concentration and disorders happened in secretion, absorption of kidney tubules. .Creatinine level increasing is an important test for kidney function [7]. In diabetic nephropathy there was increasing in creatinine level with mean (3.2±1.7)mg/dl (Table-2), but the increase is less when compared with chronic renal failure, because in renal failure there is more progressive and irreversible destruction of nephron mass [12.] Mostly the complication of diabetes appear after (10-15) years because of improper Controlling of sugar in serum which lead to increased glomerular basement membrane thichness,microaneurysm formation [11]. Blood urea level was very high in the serum of the patients with chronic renal failure, it reach mean level of (175 ± 51) mg/dl with significant difference (P<0.001) when compared with control, this result is comparable with other studies [10,11,12]. Patients with diabetic nephropathy showed increased level of blood urea but much less than the level in patients of chronic renal failure which might be due to less destruction of nephron mass [12]. The level in patients with

diabetic nephropathy was (93±33) mg/dl with high significant difference (P<0.001). Uric acid level was high in chronic renal failure patients it reach (9.6± 2.9) mg/dl with significant difference (P<0.001) (Table -1). This increase in uric acid is related to impairment of the secretion ,infilteration and absorption of the kidney which cause increased level of uric acid [13]. In diabetic nephropathy there was an increase in uric acid level but was less than in chronic renal failure, also because profound loss of renal function[13], The mean value of uric acid reached (8.5± 2.1) mg/dl with significant difference (P<0.01) . Total protein level in the serum of chronic renal failure patients decreased and reached (4.9 ± 0.3) g/dl with significant difference (P<0.001) (Table-1) because the kidney is unable to retain the formed elements that like red cells,white cells, and proteins at the level of the glomerulus., protein will leave the blood through the kidney with urine [14]. In diabetic nephropathy there was a decrease in total protein but it is less than that in chronic renal failure with mean value (5.95± 0.3) g/dl and significant difference (P<0.001) , this result comparable with other studies [15,16]. There was significant decrease (P< 0.001) in albumin level in chronic renal failure because of infiltration of some low molecular weight protein including albumin and secreted out side through urine, the level of albumin reach as in table 1(2.3±0.2) mg/dl, and this was comparable with other study[15]. In patients with diabetic nephropathy (D.N) the decrease in albumin level was less (2.9± 0.15) but still significant (P<0.01). In chronic renal failure, total cholesterol level in the serum of patients complaining from chronic renal failure approximately near the level of control or slightly more with mean value (198± 22) mg/dl and mild significant difference(P<0.05) when compared with the control (Table-1) .The result of this study comparable with results of other studies[17,23,25,]. Sultan (1986) found marked reduced in total cholesterol in chronic renal failure patients[18]. However in this study and other studies [17,23,25] found that total cholesterol not elevated markedly when compared with the control group. In patients with diabetic nephropathy there was high increase in total cholesterol reaching mean value (256± 30) mg/dl with significant difference (P< 0.001). This result agree with the result of (Szolkiewicz,2000) and coworkers [19]. LDL -C level is very important for the diagnosis of atherosclerosis because cholesterol is the main component of LDL-C [20]. In this study the patients showed mild increase in level of LDL-C (125 ± 21) mg/dl (P<0.05), which agree with the results of other studies [20,21,22]. In diabetic nephropathy there was high increase level of LDL-C; this increase the incidence of atheroscleros[22], it reach mean value (176± 35) mg/dl (P<0.001). Plasma triglyceride concentration is frequently elevated in patients and experimental animals with chronic renal failure [22]. Hypertriglyceridemia is a common feature of chronic renal failure [22]; potential causes include increased synthesis and/or diminished clearance from the circulation[26]. In this study triglyceride level increased reached mean value of (234 ± 36) mg/dl (P<0.001). This increase of triglyceride in chronic renal failure patients caused by high blood urea in those patients which indirectly cause decrease in the function of enzyme Lipoprotein lipase which contribute in the degradation of triglyceride to fatty acid , this result agree with results of other studies [22,23,24]. In diabetic nephropathy patients there was high increase in triglyceride level in serum in comparing with the control, it reach (260 ± 42) mg/dl (P<0.001). HDL-C level decreased in the serum of chronic renal failure patients, it reached (33 ± 5) mg/dl, with highly significant difference (P<0.001).This significant decrease related to many causes including loosing of large amount of protein through urine including (apo-CTT, apo-AII, apo-AI) which constitute 90% of HDL-C as well effect of (apo-AI) on Lecithin Acyl Transferase enzyme and (apo-CII) effect on the secretion of lipoprotein lipase enzyme [25].

In diabetic nephropathy mild decrease in HDL-C was noticed (Table-2) and this decrease was less than in chronic renal failure and it reach (35 ± 5.9) mg/dl (P<0.001), and this agree with other studies[26, 27,30]. The ratio of LDLc/HDLc;-This ratio is important in cardiovascular diseases .In this study patients showed ratio of (3.78) with significant difference (P<0.01), and this result agree with Vaziri and Liang (1996) study[28]. In diabetic nephropathy patients there was high increase in LDL-C/HDL-C ratio (5.0) which was highly significant (P<0.001) & agree with other studies[27,28,31].

CONCLUSION :

In conclusion, patients with chronic renal failure showed 1.significant increase in the levels of (creatinine- urea-uric acid) and triglyceride. 2.mild increase in the level of (cholesterol - LDLc), 3.decrease in the level of (albumin-total protein), 4.low level of HDLc with 5. significant increase in LDLc/HDLc ratio .Patients with diabetic nephropathy showed a.high increase in the level of (Cholestrol-LDLc-TG- and LDL/ HDLc), b. increase in (reatinine-urea-uric acid) and c.decrease in the level of (Albumin and total protein), d.decrease in the level of HDLc but less than that in patients with chronic renal failure.

REFERENCES:

1. Dirks JH, de Zeeuw D, Agarwal SK. Prevention f chronic kidney and vascular Disease: Toward global health equity- The Bellagi Declaration.Kidney Int. 2005; 68: SI-S6.
2. Ozsoy RC, Kastelein JJ, Arisz L, Koopman MG. Atorvastatin and the dyslipidemia Of early renal failure .Atherosclerosis 2003; 166:187-194.
3. Snideman AD, Scantlebury T, Cianflone K . Hypertriglyceridemic hyperapob: the unappreciated atherogenic dyslipoproteinemia in type 2 diabetes mellitus .An intern Med 2001; 135:447-459.
4. Coonrod BA, Ellis D, Bicker DJ.Predictors of microalbuminuria in individuals with IDDM. Diabetes care 1993; 16:1376-1383.
5. Kasiske BL, Donnell MP ,Cleary MP,Kean WF.Treatment of hyperlipidemia reduces glomerular injury in obese zucker rats .Kidney Int, 1988;333:667-672.
6. Watts GF, Powrie JK, Brien SF, Shaw KM.Apolipoprotein B independently predicts progression of very –low level albuminuria in insulin-dependent diabetes mellitus. Metabolism 1996; 45:1101-1107.
7. Majumdar A and Wheeler DC.Lipid abnormalities in renal disease .J R Soc Med 2000;178-182.
8. McLeod R, Reeve CE, and Frohlich J .Plasma lipoprotein and lecithin: cholesterol acyltransferase distribution in patients with dialysis.Kidney Int. 1984; 25:683-688.
9. Liang K, Oveisi F, and Vaziri ND. Down regulation of hepatic high-density lipoprotein receptor,SR-BI in nephritic syndrome.Kidney Int. 1999; 56:621-626.
10. Alemzadeh R, Wyatt DT. Diabetes mellitus in chidren. Nelson Textbook of pediatrics. 18th ed. Philadelphia:Saunder. 2008; 2404-2431.
11. Keyiro, S.Shiro, J and Bozh, A,J.Dyslipidemia and the progression of renal disease in chronic renal failure patients. Kidney Int. 1996; 49:488
12. Miguel, H. S. and Lapuz, M.D.,J.Diabetic Nephropathy : Diagnosis,prevention,and Treatment. Medical clinics of North America. 1997;81(3),
13. Majumdar A and wheeler DC.Lipid abnormalities in renal disease.JR soc.Med 2000;93:178-182...
14. Almadtae, .M.Assesment of function kidney from chronic renal failure, thesis MSc Baghdad University ,College of Medicine 1988;75-92 .
15. Rutkowski B, Szolkiewicz M, Korczynsk J. The role of lipogenesis in the development of uremic hyperlipidemia. Am J Kidney Dis.2003; :41:84-88.
16. Al Hadithe ,A.H ., Biochemical study of Bronchogenic carcinoma .thesis M.Sc ,Baghdad University ,College of Pharmacy .1992.(94-104).
17. Mcleod R, Reeve CE, and Frohlich J. Plasma lipoproteins and lecithin :Cholestrol acyltransferase distribution in patients on dialysiss. Kidney Int 1995; 25:683-688.
18. Sultan ,T.R., Serum lipid profile in chronic renal failure . Thesis, M.SC, Baghdad University , College of Medicine .1986.
19. Shoji T, Nishizawa Y , Nishitani H. Impaired metabolism of high density lipoprotein in uremic patients.Kidney Int. 1999; 41: 1653-1661.
20. SZolkiewicz M, Nieweglowski T, Korczynska J. Upregulation of fatty acid synthase gene expression in experimental chronic renal failure. Metabolism. 2000;51:1605-1610.
21. Vaziri N.Dyslipidemia of chronic renal failure:the nature,mechanisms,and Potential consequences .Am J Renal physiol 2005;290:F262-F272.
22. Attman PO, Samuelsson O, and Alaupovic P.Lipoprotein metabolism and renal failure.Am J Kidney Dis1999; 21:573-592.
23. Shoji,T., Nishizawa, Y.,Kawagishi, T., and Tamaka ,M., J. Atherosclerosis 2001 ; 13 (2):229.
24. Craven P A, Studer R K, Negrete H. Protein in diabetic nephropathy. J Diabetes complications 1995;9: 241-245.

25. Genest J Jr, Marcil M, and Yu L.High lipoproteins in health and in disease.J Investig Med 1999; 47:31-42.
26. Hakim RM and Lazarus JM. Biochemical parameters in chronic renal failure. Am J Kidney Dis 1998; 11(3): 238-247.
27. Ali J, Junita K, Vivian A. Diabetic nephropathy. Medical Clinics of North America 2004; volume 88.
28. Gall MA, Hougaard P,Borch-Johnsen K. Risk factors for development of incipient and overt diabetic nephropathy in patients with non insulin dependent diabetes mellitus .BMJ 1997;314:783-788.
29. Vaziri ND and Liang K. Down regulation of LDL and HDL in experimental nephrosis.Kidney Int . 1996;50: 887-893.
30. Caramori ML, Kim Y, Huang C. Cellular basis of diabetic nephropathy . Diabetes 2004;51:506-513.
31. Michael J.Fowler,MD . Complication of Diabetes.clinical diabetes.2008;26;77-82.