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Research Article

SERUM LEPTIN LEVELS IN KASHMIRI TYPE 2 DIABETIC PATIENTS WITH DIABETIC NEPHROPATHY

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ABSTRACT

Background: Diabetic nephropathy [DN] is characterized by hypertension, progressive albuminuria, glomerulosclerosis, and decline in glomerular filtration rate (GFR) leading to end state renal disease.

Aims and objectives: The objective was to study the effect of leptin levels in Type 2 DN patients and healthy subject.

Material and Methods: The case control study included 150 type 2 diabetic patients and 50 apparently healthy subjects as control group. The diabetic patients were classified into three groups, Group I comprised of 54patients with normoalbuminuria, Group II included 78patients with microalbuminuria and Group III included 18 patients with macroalbuminuria. Patients and controls were matched for sex, age and body mass**.** The following laboratory investigations were done in patients and controls: fasting serum leptin, HbA1c, serum triglyceride, cholesterol, HDL cholesterol, LDL cholesterol, serum creatinine, creatinine clearance and 24 hours urinary albumin.

Results: Fasting serum leptin was significantly higher in the microalbuminuric (17.3±3.6µg/L) and the macroalbuminuric (20.4±4.8µg/L) groups compared to control (11.7±3.8 µg/L) group (<0.05, P<0.01) respectively. No significant statistical difference was observed between the normoalbuminuric group (13.3±3.3µg/L) and the control group. There was significant positive and negative correlation between serum leptin and serum triglyceride (r=0.3, P<0.05) and creatinine clearance (r=-0.34, P<0.05) respectively. No significant correlation was seen between serum leptin and BMI, HbA1c%, serum creatinine, cholesterol, HDL cholesterol and LDL cholesterol.

Conclusion: Serum leptin levels are elevated in type 2 diabetic patients with microalbuminuria and macroalbuminuria, suggesting that renal leptin degradation is diminished in the early stages of renal disease and this impairment increases with the advancement of the disease.

INTRODUCTION

One adult in ten will have diabetes by 2030: figures signify that the number of people living with diabetes is estimated to rise from 366 million in 2011 to 552 million by 2030, if no urgent action is taken. This equates to roughly three new cases every ten seconds or almost ten million per year, between 2010 and 2030, there will be a 69% increase in number of adults with diabetes in developing countries and a 20% increase in developed countries [1] DN is the single most common cause of end- stage renal disease in the western world and is associated with greatly increased cardiovascular morbidity and mortality. With the rising prevalence of T2DM it has come to pose a heavy burden on healthcare systems worldwide. [2]Leptin, a 167-amino-acid product of the human leptin gene, was originally discovered through positional cloning of *ob/ob* mice. [3] Leptin is secreted mainly by white adipose tissue, and levels are positively correlated with the amount of body fat [4] leptin has a significant diurnal variation with higher levels in the evening and early morning hours Circulating leptin levels reflect primarily the amount of energy stored in fat and secondarily acute changes in caloric intake [5-6]. Numerous studies have demonstrated markedly elevated serum leptin levels in patients with chronic renal failure [CRF] and it has been speculated that hyperleptinemia may contribute to the uremic anorexia and malnutrition [7]. Circulating leptin, which is partly cleared by the kidney, has been reported to increase in CRF and thus may play a role in weight loss in such patients [8]. Aninitial sign of impending nephropathy is Microalbuminuria[MAU], which is defined as the urinary

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excretion of albumin at the rate of 30-299mg/24hr[9-11]. This excretion of small amount of albumin in the urine has been documented to predict renal failure and cardiovascular morbidity as well as mortality in diabetics[12-13].Studies conducted have demonstrated that the prevalence of MAU varies among races, even within the same community [14] Diabetes is also associated with dyslipidemia and worsening of glycaemic control deteriorates lipid and lipoprotein abnormalities and particularly of diabetes mellitus (DM) [15]. Dyslipidemia associated with metabolic syndrome and insulin resistance syndrome increases the risk of coronary artery disease(CAD).

The serum leptin levels of Kashmiri population with DN has not been calculated and to the best of my knowledge the present study is the first of its kind. Moreover, the correlation of serum leptin levels in Diabetics with lipid profile and body mass index (BMI) has not been investigated till date. So, our aim was to investigate the serum leptin levels in T2DMpatients with DN in Kashmir and investigate the relationship with various biochemical and demographic parameters.

MATERIALS AND METHODS

Study design and study population

This study was designed as a case control study conducted over a period of 6 months at the Government Medical College Srinagar Kashmir India. A total of 150 confirmed diabetic patients with normal or abnormal lipid profile and controlled/uncontrolled hypertension, and 50 healthy controls attending OPD of Government medical college, Srinagar Jammu and Kashmir India were enrolled. Individuals with hematuria and/or polyuria, history of urinary tract infection within last one year or at present were excluded.

Confidentiality: All information gathered in this study was stored in a personal computer, kept confidential and accessed only by authorized personnel.

Sample collection, laboratory methods and analysis

Overnight fasting venous blood samples were collected from the patients in using standardized protocol and equipment. They were separated into two samples: the first sample containing whole blood for the measurement of HbA1c and the other plasma specimen was used for fasting blood glucose (FBG) and lipid profile levels (Abbott C4000, USA).

- Estimation of FBG was done using glucose oxidase‑peroxidase method [16]
- Determination of HbA1c in blood [17]
- Lipid profile: Plasma levels of total cholesterol (TC), TG and HDL‑cholesterol. [18] LDL ‑ cholesterol was measured according to Friedewald formula. [19]
- Immunoturbidimetric methods was used to determine microalbumin levels in the urine sample.
- Serum Leptin levels were determined using sandwich enzyme-linked immunosorbent assay kit (Linco Research)
- Urine albumin and creatinine was estimated in fresh urine

After written informed consent by all study participants, baseline data regarding medical history and smoking behavior were collected. Physical examination consisted of measurement of weight, height and blood pressure. Weight and height were measured barefooted in light clothing and BMI were calculated as body weight(kg) divided by the square of height (m). A BMI less than 25 was taken as normal, BMI between 25kg/m as overweight and greater than 30kg/m as obesity. Blood pressure was measured twice on the right arm in sitting position after 15 minutes of rest using astandard mercury sphygmomanometer mean of the two readings, five minutes apart, was taken as the overall result.Subjects were classified according to the urinaryalbumin to creatinine ratio (ACR):<30 mg/g, 30-299 mg/g, >300mg/g as normoalbuminuric, MAU and macroalbuminuric, respectively. Normoalbuminuric and microalbuminuric subjects as a whole were further divided into three groups according to their BMIs:<23, 23-24.and>25, asnon-obese, overweight and obese, respectively.

Ethical justification

Informed and written consent [in language they best understood] was taken before collecting data and blood sample. Only those individuals, who volunteered to participate in the study, were selected and the data was kept confidential. The study did not impose any financial burden on the study subjects and the institute, therefore the study was ethically justified.

Data management and statistical analysis

During data collection completed questionnaires were checked regularly to rectify any discrepancy, logical errors or missing information. All statistical analyses were performed with Statistical Package for Social Services (SPSS vs 21 for Mac. IBM Inc. Chicago). Descriptive data were expressed by mean±standard deviation (95% CI) or frequency (95% CI). Comparisons between two groups were performed using independent t-tests. Qualitative data are presented as percent and were compared by Chi square test. Pearson's correlation coefficient (r) was performed to assess the degree of association between different variables A value of $p<0.05$ was considered statistically significant.

RESULTS

Among 150 type 2 diabetic patients analyzed, the prevalence of MAU and overt proteinuria was 52% and 12%, respectively (Table 1). Prevalence of MAU in female was marginally higher than in males (54 females and 42 males out of total of 96 microalbuminuric subjects($p>0.05$). The results showed that the serum leptin levels in the Type 2 diabetes was significantly higher $p < 0.05$(Table-3). High values of mean systolic blood pressure (SBP), diastolic blood pressure (DBP) and duration of diabetes was found in microalbuminuric than in normoalbuminuric subjects (Table-2).Low values of HDL were observed in microalbuminuric than in normoalbuminuric subjects. Similarly, though insignificant, higher value of triglyceride (TG) and total cholesterol (TC) was found in microalbuminuric than innormoalbuminuric subjects ($p>0.05$) (Table-2).

Table 1 Prevalence of various grades of albuminuria in type 2 Diabetes mellitus (n=150)

	n	%
Normoalbuminuric	54	36
Microalbuminuria	78	52
Macroalbuminuria	18	12

Table 2 Demographic Characteristics in controls normoalbuminuric and microalbuminuric

	Control group	Group I (normo-albuminuria)	Group II (Micro-albuminuria)	GroupIII (Macro-albuminuria)
Age (years)	50.05±1.3	52.05±1.5	55.5±1.66	56±1.7
Duration (years)		5.2+1.4	11.5+4.2a	13.2+4.1
BMI (kg/m2)	25.5+4.42	28.32±0.56	28.78±0.54	26.09+2.52
Urinary albumin (mg/24hrs)	11.3+2.3	13.32+3.21	185+14.3	2034+67
SBP (mmHg)		126±2.2	131±5.76	
DBP		85±1.32	87±1.53	

Table 3 Biochemical Characteristics in Control Group, Group I, Group II and Group III

	Control	Group I(normo-albuminuria)	Group II(Micro-albuminuria	GroupIII(Macro-albuminuria
Leptin(µg/L)	11.7+3.8	13.3+3.3	17.3+3.6*	20.4+4.8*
HbA1c %	4.4+0.12	7.77+3.25*	7.89+3.23*	10.07+3.87*
Triglyceride	87.4+37.01	111.6+38.58	138.56+33.76*	149.93+98.67*
Cholesterol	140.4+29.7	137.4+32.48	156+65	169.36+48.12
HDLC(mg/dl)	42.7+9.29	36.2+14.86	34.56+11.03	42.5+17.72
LDLC (mg/dl)	80.6+32.6	79.78+26.35	93.41+55.86	97.7+45.43
Creatinine (mg/dl)	0.73+0.13	0.88+0.33	0.89+0.27	1.71+1.19
Creatinine clearance mg/min)	109.4+4.42 90 – 130	103.1+21.79 63 –130	80.62+11.4* 64 –105	60.17+21.41* 32.8 -97

Table 4 Correlation between serum leptin and other variables.

	r	P value	Significance
BMI	0.16	>0.05	Not significant
HbA1c	0.001	>0.05	Not significant
Creatinine	0.01	>0.05	Not significant
Creatinine Clearance	-0.34	<0.05	Significant
Triglyceride	0.3	<0.05	Significant
Cholesterol	0.05	>0.05	Not significant
HDL c	0.09	>0.05	Not significant
LDLc	-0.12	>0.05	Not significant

DISCUSSION

Chronic kidney disease (CKD) is common and the estimated prevalence is about 9–13% in the general adult population. [20] DM is the leading cause of CKD in the U.S., accounting for approximately 44% and 38% of incident and prevalent cases of end-stage renal disease (ESRD), respectively.[21] Leptin influences intake, energy expenditure and body weight. This protein produced by adipocytes, exerts its effects on brain, endocrine pancreas and other organs by activating transmembrane receptors and is cleared from plasma mainly by the kidney [22]. Increasing albumin level in urine is considered as key characteristics of DN [23].The present study showed that mean serum leptin level in the three diabetic groups was higher than the control group, however the difference was significant only in patients with MAU and macroalbuminuria (P<0.05, 0.01 respectively) and was not significant in the normoalbuminuric group. On comparing the microalbuminuric and the macroalbuminuric groups with the normoalbuminuric group the mean serum leptin showed no significant difference although the serum leptin levels were higher in the micro and macro-albuminuric groups compared to normoalbuminuric groups. Also on comparing the microalbuminuric group with the macroalbuminuric group the mean serum leptin showed no significant difference. Serum triglyceride is significantly higher in diabetics with microalbuminuria and macroalbuminuria compared to control group (P<0.01 and 0.05 respectively). No significant difference in serum triglyceride between the normoalbuminuric group and the control group. Hypertriglyceridemia is common in diabetes and is due to overproduction of VLDL in the liver and to a disposal defect in the periphery, the latter being the consequence of a deficiency of lipoprotein lipase, an insulin dependent enzyme[24]. In our study we found a significant positive correlation between leptin and triglyceride.

In our study, there was no correlation between leptin level and HbA1c, which indicate that leptin is not affected by the degree of glycemic control There was a significant positive correlation of BMI in Type 2 DN compared with control p <0.05 (Table-2) but there wasn't any significant correlation between BMI and leptin level in Type 2 DN as shown in(Table-3). This correlation may be explained by the presence of additional factor which would increase the impaired degradation by the affected kidney. Furthermore, there were no significant correlation between serum creatinine levels with serum leptin levels in Type 2 DN[24], but creatinine and urea levels increase in Type2 diabetes; this may be dueto renalimpairment inType 2 DN[25]. We conclude that serum leptin levels are elevated in type 2 DN suggesting that renal leptin degradation is impaired in the early stages of renal disease and this impairment increases with the progression of renal disease.

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Conflicts of interest

There are no conflicts of interest.

References

1. Kaur H, Bhaskar N, Ishaq S, Najeeb Q. (2012):Stem Cells: Source for diabetes cell therapy. *Journal.Of. Diabetology.* 3:3.
2. Foggensteiner L, Mulroy S, Firth J.(2001): Management of diabetic nephropathy. *J. R. Soc. Med*. 94(5): 210–217.
3. Zhang Y, Proenca R, Maffei M, Barone M, Leopold L, Friedman JM. (1994): Positional cloning of the mouseobese gene and its human homologue. *Nature*.372 (6505):425–32.
4. Considine RV, Sinha MK, Heiman ML, Kriauciunas A, Stephens TW, Nyce MR, *et al*. (1996): Serum immunoreactive-leptin concentrations in normal-weight and obese humans. *N. Engl. J. Med*.334 (5):292–295.
5. Licinio J, Mantzoros C, Negrao AB, Cizza G, Wong ML, Bongiorno PB, *et al*. (1997): Human leptin levelsare pulsatile and inversely related to pituitary-adrenal function. *Nat. Med*.3(5):575–579.

6. Sinha MK, Ohannesian JP, Heiman ML, Kriauciunas A, Stephens TW, Magosin S, *et al*. (1996): Nocturnal rise of leptin in lean, obese, and non-insulin-dependent diabetes mellitus subjects. *J Clin Invest* 97 (5):1344–1347.
7. Stenvinkel P (1999): Leptin and its clinical implication in chronic renal failure. *Miner Electrolyte Metab*,25:298-302.
8. Odamki M, Furuya R, Yoneyama T *et al*. (1999): Association of serum leptin con-centration with weight loss in chronic hemodialysis patients. *Am. J. Kidney. Dis*. 33(2):361-8.
9. Burtis CA, Ashwood ER, Bruns DE, editors.(2006):Teitz Textbook of Clinical Chemistry and Molecular Diagnosis (4th ed.). Elsevier Limited, New Delhi
10. American Diabetes Association Diabetes Care 2004 Jan; 27(suppl1): s79-s83. https://doi.org/10.2337/diacare.27.2007.S79
11. De Boer IH, Sibley SD, Kestenbaum B *et al*.(2007): Central obesity, incident microalbuminuria and change in creatinine clearance in the epidemiology of diabetes interventions and complications study. *J. Amer. Soc.Nephrol.*18: 235-243
12. Naidoo DO.(2002): The link between microalbuminuria, endothelia dysfunction and cardiovascular disease in diabetes. Cardiovasc*.J .South Africa*. 13: 194-9.
13. Romundstad S, Holman J, Hallman H, Kvenild K, Ellekjaer H.(2003): Microalbuminuria and all-cause mortality in treated hypertensive individuals: Does sex matter? The nord- trondelag health study (HUNT), Norway. Circulation. 108: 2783-2789.
14. Dreyer G, Hull S, Aitken Z, Chesser A, Yaqoob MM.(2009): The effect of ethnicity on the prevalence of diabetes and associated chronic kidney disease. QJM. 102:261–9.
15. Ishaq S, Shabir I, Bhat AA, Shafi I, Mushtaq S, Shah PA, Baba A, Majid S. Glycated haemoglobin(2017): A marker of circulating lipids in patients with type 2 diabetes. *J.Diabetol*. 8:18-21.
16. Trinder P. Enzymatic determination of glucose. (1969):*Ann.Clin.Biochem*. 6:24‑27.
17. Abraham EC, Huff TA, Cope ND, Wilson JB Jr., Bransome ED Jr., Huisman TH.(1978): Determination of the glycosylated hemoglobins (HB AI) with a new microcolumn procedure. Suitability of the technique for assessing the clinical management of diabetes mellitus. *Diabetes*. 27:931‑937.
18. Assmann G, Schriewer H, Schmitz G, HägeleEO.(1983): Quantification of high‑density‑lipoprotein cholesterol by precipitation with phosphotungstic acid/MgCl2. *Clin. Chem*.29:2026‑30.
19. Friedewald WT, Levy RI, Fredrickson DS. (1972): Estimation of the concentration of low‑density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin.Chem*. 18:499‑502.
20. Shiba N, Shimokawa H. (2011): Chronic kidney disease and heart failure-Bidirectional close link and common therapeutic goal. *Journal. of Cardiology*. 57, 8—17.
21. Rhee CM, Leung AM, Kovesdy CP, Lynch KE, Brent GA, Kalantar-Zadeh K. (2014): Updates on the Management of Diabetes in Dialysis Patients. Seminars in dialysis. 27(2):135-145. doi:10.1111/sdi.12198.
22. Coelho M, Oliveira T, Fernandes R. Biochemistry of adipose tissue: an endocrine organ. *Archives of Medical Science :* AMS. 2013;9(2):191-200. doi:10.5114/aoms.2013.33181.
23. Glassock RJ. (2010): Is the Presence of Microalbuminuria a Relevant Marker of Kidney Disease? Current. Hypertension. Reports.12(5):364-368. doi:10.1007/s11906-010-0133-3.
24. Paglialunga S, Julien P, Tahiri Y, *et al*. (2009): Lipoprotein lipase deficiency is associated with elevated acylation stimulating protein plasma levels. *Journal.Of. Lipid. Research.* 50(6):1109-1119. doi:10.1194/jlr.M800430-JLR200.
25. Dabla Pk. (2010): Renal function in diabetic nephropathy. *World. Journal. of Diabetes*. 1(2): 48–56. http://doi.org/10.4239/wjd.v1.i2.48

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