DOI : 10.35124/bca.2019.19.2.4503

Biochem. Cell. Arch. Vol. 19, No. 2, pp. 4503-4508, 2019 | www.connectjournals.com/bca | *ISSN 0972-5075*

ADIPOCYTOKINES AS A RISK FACTOR FOR CORONARY ARTERY DISEASE AND ITS RELATIONSHIPS WITH OBESITY

Maytham H. Tarrad*, Mufeed J. Ewadh and Alaa Hussain Haider

College of Medicine, University of Babylon, Hilla, Iraq.
*e-mail: maithamh.traad@gmail.com

(Received 26 March 2019, Revised 14 June 2019, Accepted 25 July 2019)

ABSTRACT : Obesity is a major health problem consistently increasing many severe complications such as metabolic syndrome the risk for cardiovascular diseases, respiratory disorders and diabetic. Adipose tissue is an endocrine organ that manufacture actively biological structures defined as "adipocytokine". Aims of the study are investigate the association of a set of adipocytokines, including adiponectin, leptin and plasminogen activator inhibitor-1 (PAI-1) with CAD events in obsess patient. This study was included (88) males, There were 22 obese males and 22 normal weightmales with CAD. (44 subjects) who were an apparently healthy control group their ages between (45-65 years) in Babylon province /Iraq were enrolled in this study The present study, observed, a significantly decrease in adiponectin, in both CAD groups (obese and normal weight)when compared with control)groups and lower in obese when compared with control, while significant increase in leptinand plasminogen activator inhibitor-1 (PAI-1) in both CAD groups (obese and normal weight) when compared with control groups and more elevation in obese groups.

Key words : Adipocytokines, coronary artery disease, obesity.

INTRODUCTION

Coronary heart disease occurs when the coronary arteries which carry oxygen to the heart muscle become narrowed and blocked because of the accumulate cholesterol within the artery wall. If the build-up is only mild symptoms may include a feeling of pressure or tightness in the chest at times of increased activity or stress and/or shortness of breath or fatigue with physical exertion. When the blood supply to the heart muscle is severely reduced, chest pain or arrhythmia may occur (Bhopal ***et al***, 2019). Coronary atherosclerosis is often irregularly distributed in different vessels but typically occurs at points of turbulence (e.g., vessel bifurcations). As the atheromatous plaque grows, the arterial lumen progressively narrows, resulting in ischemia. The degree of stenosis required to cause ischemia varies with oxygen demand (Todua and Gachechiladze, 2018). Occasionally, an atheromatous plaque ruptures.theReasons are unclear but probably relate to plaque morphology, plaque calcium content, and plaque softening due to an inflammatory process. Rupture exposes collagen and other thrombogenic material, which activate platelets and the coagulation cascade, resulting in an acute thrombus, which interrupts coronary blood flow and causes some grade of myocardial ischemia. The consequences of acute ischemia, collectively referred to as (ACS), depend on the location and degree of obstruction and range from unstable angina, non-ST elevation myocardial infarction (NSTEMI), to ST-elevation myocardial infarction (STEMI), which can result in transmural infarction, and including malignant ventricular arrhythmias, conduction defects, heart failure and sudden death (Herr, 2018).

Almost risk factors for acute coronary syndromes are rise blood pressure, rise blood cholesterol,smoking, Physical inactivity, Unhealthy diet, Obesity, Diabetes (type 2), Older age and Family history of chest pain, heart disease (Arnett ***et al***, 2019).

Aims of study

To sought investigate a set of the association of adipocytokines : leptin, total adiponectin and plasminogen activator inhibitor-1 in serum of patients diagnosed with coronary artery disease relationship with obesity.

MATERIALS AND METHODS

Ethical issues

- Approval by the scientific committee of the Clinical Biochemistry Department, College of Medicine, University of Babylon, Iraq.
- Approval by Babylon Health Directorate, Ministry

of Health and Information Center for Research and Development of Babylon Province.

- The objectives and methodology were explained to all subjects and verbal consent was taken from the patient if conscious or fromhis or her escort if unconscious to contribute in the current study.

Date and duration

The samples of participants were collected from first of September 2018 till December 2018. The part that deals with the practical aspect of the study were accomplished at the laboratory of the department of biochemistry, College of Medicine, University of Babylon.

Design : The study is case control study

Patients and control

A total of 44 patients with coronary artery disease were enrolled in this study. There were 22 obese males and 22 non-obese males with coronary artery disease. 44 subjects (22 obese males, 22 non-obese males), who were an apparently healthy control group.

Inclusion criteria

All patients with diagnosed acute coronary artery disease.diagnosed bya physician in the cardiac care unit (CCU).

Exclusion Criteria

- Patient with heart failure
- Insulin drug dependency.
- women.
- Patients with chronic coronary artery disease.
- smoker

Determination of adipocytokines

Determination of totaladiponectin level, leptin level and PAI-1 level in the patient and control group were done by use Elabscience ELISA kits.

In the current study, the level of adiponectin was significantly lower in coronary artery disease (CAD) patients groups compared with the Control group. The result exhibit that the levels of adiponectin was significantly decreased in groups (obese, non obese) and (p-value 0.001, 0.032) respectively.when compared with control group. In addition, there was a significant lower in obese patients when compared with control group.

In the current study, the level of leptin was significantly higher in coronary artery disease (CAD) patients groups compared with the Control. In the current study, the results revealed that levels of leptin was significantly elevated in groups (obese, non obese) and (p-value 0.001,0.001) respectively when compared with control group. In addition, there was a significant increased in obese patientsgroup when compared with control group.

In the current study, the level of plasminogen activator inhibitor-1(PAI-1) was significantly higher in coronary artery disease (CAD) patients groups compared with the Control group. In the current study, the results revealed that levels of PAI-1 was significantly elevated in groups (obese,non-obese) and (p-value 0.001,0.001) respectively when compared with control group. In addition, there was a significant increase in obese patients group when compared with control group.

DISCUSSION

Obesity is a major health problemmay be risk for many complications such as metabolic syndrome, CAD, type two diabetic, and cancer. adipose tissue is an endocrine organ that produces biologically active molecules defined “adipocytokines,” protein hormones with various functions involved in the organization of energy metabolism as well as in appetite, insulin sensitivity, inflammation, atherosclerosis, and cell reproduction. Probably in obesity fat accumulation lead to dysregulation of adipokine production that strongly lead to the onset of obesity-related diseases, so the level of adiponectin was reduced in (CAD) obese and non-obese. The result exhibit that the levels of adiponectin was significantly decreased in groups (obese,non-obese) and (p-value 0.001, 0.032), respectively when compared with control group. In addition, there was a significant lower in obese patients when compared with control group association with obesity. In our study is in agreement with (Nigro et al, 2014).who showed the role and associations of adiponectin with obesity in related diseases complications such as metabolic syndrome, cardiovascular diseases, respiratory disorders, diabetic and (Kishida ***et al***, 2014). The adiponectin level is inversely related to body weight especially visceral fat accumulation. The mechanism of this paradoxical relation remains obscure. Decrease adiponectin concentrations are associated with a variety of diseases, including dysmetabolism: type-2diabetes, insulin resistance, hypertension, dyslipidemia, metabolic syndrome and CAD.

Most patients with CAD participated in the current study is a hypertensive, type 2 diabetes, overweight, dyslipidemia and age range 45-65 years. This is consistent with many studies that indicate a correlation between it. which is in agreement with Mittal ***et al*** (2013), who showedIn the present study the protective association of adiponectin was independent of several other recognized cardiovascular risk factors including BMI, smoking,

dyslipidemia and the greatest increase in risk for CAD in the present study was seen low adiponectin. This suggests that the pathophysiological role of adiponectin is related more to the stability of atherosclerotic plaque, although a role for adiponectin in the development of atherosclerotic plaque is also likely. These data suggest that low plasma concentrations of adiponectin are a risk factor for CAD and an independent variable for CAD. Consequently, it is conceivable that low plasma concentrations of adiponectin may facilitate rupture of the atherosclerotic plaques, lead to CAD.

In our study, the level of leptin was significantly higher in coronary artery disease (CAD) patients groups compared with the Control. The results revealed that levels of leptin was significantly elevated in groups (obese,non-obese) and (p-value 0.001,0.001) respectively when compared with control group. In addition, there was a significant increase in obese patients when compared with control groupin (Table 3). We have found weight gain leading to leptin height and the likelihood of increased adipose tissue in obese patients and heart disease leads to systemic inflammatory condition that produces higher serum concentrations of adipokines, such as leptin as proinflammatory and adiponectin as anti-inflammatory.in our study is an agreement with Montazerifar ***et al*** (2016) evaluate the leptin levels in obesity and some risk factors of CAD and elevated BMI showed higher serum leptin levels in obese patients compared to non-obese patients. Leptin a 16-kDa and 167 amino acid protein secreted by white adipocytes, has been shown to have a role in the regulation of food intake, energy expenditure and whole-body energy balance in humans (Chen ***et al***, 2003). Leptin serum levels correlate with fat stores and react according to changes in energy balance (Ren, 2004). The expression and secretion of leptin is highly correlated with body fat mass and adipocyte size. Cortisol and insulin are potent stimulators of leptin expression, and beta-adrenergic agonists, cAMP and thiazolidinediones attenuate expression. Leptin is secreted by different sites to white adipose tissue, such as placental trophoblasts and amnion cells in the uteri of pregnant women (Zurowski ***et al***, 2001). The amount of body fat is the main determinant of the circulating levels of this hormone. Many studies have shown an association between the concentration of leptin and cardiovascular risk, such as acute MI (Sahu, 2003), stroke (Soderberg ***et al***, 1999). CAD (Söderberg ***et al***, 1999). Chronic heart failure (Wallace ***et al***, 2001) and left cardiac hypertrophy (Schulze ***et al***, 2003). It has been recently suggested that obesity is related to subclinical inflammation, as reflected by increased CRP levels (Azuma ***et al***, 2003), (Rajala ***et al,*** 2003), (Martin, ***et al***, 2012) showed that leptin levels with inflammatory activity might play an important role in the development of inflammatory mechanisms and promote the progression of atherosclerotic disease (Martin ***et al***, 2012; Zhang ***et al***, 2003). Leptin stimulates T lymphocytes towards a Th1 (proinflammatory) adaptive immune response while promoting monocyte recruitment, macrophage foam cell formation and secretion of proinflammatory cytokines (Martin ***et al***, 2008). This functional profile, along with structural relation to proinflammatory cytokines, and signaling through the IL-6 glycoprotein-130 cytokine receptor, frame leptin as an "adipocytokine." The discovery of the leptin receptor in human atherosclerotic lesions (Parhami ***et al***, 2001; Kang ***et al***, 2000) and epidemiologic data associating leptin levels with measures of CVD and CVD risk [(Martin ***et al***, 2008), (Reilly ***et al***, 2004), (Qasim ***et al***, 2008), (Beltowski, 2006) support a role for leptin in human atherogenesis. The mean differences of PAI-1 in study groups (control, obese and non-obese patients with CAD) are 9.53,12.27 and 11.03 respectively in the Table 4. In our study, the level of plasminogen activator inhibitor-1 (PAI-1) was significantly higher in (CAD) patients groups compared with Control group. The results revealed that levels of PAI-1was significantly elevated in groups (obese, non-obese) and (p-value 0.001,0.001) respectively when compared with control group. In addition, there was a significant increase in obese patients when compared with control group. The probability of this increase in the concentration of PAI-1 has to do with obesity and factors injurious to the endothelium, such as hypertension, DM and lipid abnormality which is considered a risk factor for heart diseasewhich is in agreement with (Somodi. S, et al, 2018) The increased level of (PAI-1) in an obese patient with metabolic syndrome and in patients with type 2 diabetes is well established and Iacoviello ***et al*** (2013), who indicate the significantly increased of PAI-1 in cardiovascular disease. The principal proteolytic enzyme of fibrinolysis is Plasmin. The inactive precursor of plasmin is Plasminogen. Tissue-type plasminogen activator and urokinase-type plasminogen activator catalyze converting of plasminogen to plasmin. plasminogen activation is inhibited by PAI-1 (Chapin and Hajjar, 2015). Plasminogen activator inhibitor acts as the principal inhibitor of fibrinolysis by antagonizing intrinsic plasminogen activation (Hendrix ***et al***, 2017). A mechanism to increase in PAI-1 concentration may be by factors injurious to the endothelium, such as hypertension, DM, smoking and lipid abnormality, increase the risk of MI. In addition, a serial increase in PAI-1 level provides additional information on the subsequent

Table 1 : Coronary heart disease; clinical manifestation and Pathophysiology (Ralston ***et al***, 2018).

Clinical problem	Pathophysiology
Stable angina	Ischaemia due to fixed atheromatous stenosis of one or more coronary arteries.
Unstable angina	Ischaemia caused by dynamic obstruction of a coronary artery due to plaque rupture or erosion with superimposed thrombosis.
Myocardial infarction	Myocardial necrosis caused by acute occlusion of a coronary artery due to plaque rupture or erosion with superimposed thrombosis.
Heart failure	Myocardial dysfunction due to infarction or ischmia
Arrhythmia	Altered conduction due to ischaemia or infarction.
Sudden death	Ventricular arrhythmia, a systole or massive Myocardial infarction.

Table 2 : The mean ± SD of Adiponectin(ADP) in CAD patients compared to the control group.

Variable	Study Groups	No.	Mean±SD	P-value <0.05
Adiponectin (ng/ml)	Control	44	68.10 ± 7.21	0.001
	Obese patient	22	59.52 ± 8.86	
	Control	44	68.10 ± 7.21	0.032
	Non obese patient	22	63.22 ± 6.82	

*P value ≤ 0.05 was significant.

Table 3 : The mean ± SD of leptin(lep) in CAD patients compared to the control group.

Variable	Study Groups	No.	Mean±SD	P-value
Leptin (ng/ml)	Control	44	3.80 ± 0.67	0.001
	Obese patient	22	5.43 ± 0.27	
	Control	44	3.80 ± 0.67	0.001
	Non obese patient	22	4.82 ± 0.84	

*P value ≤ 0.05 was significant.

Table 4 : The mean ± SD of plasminogen activator inhibitor-1(PAI-1) in CAD patients compared to the control group.

Variable	Study Groups	No.	Mean±SD	P-value
Plasminogen activator inhibitor-1 PAI-1ng/mL	Control	44	9.53 ± 1.75	0.001
	Obese patient	22	12.27 ± 0.74	
	Control	44	9.53 ± 1.75	0.001
	Non obese patient	22	11.03 ± 0.62	

*P value ≤ 0.05 was significant.

risk of cardiovascular disease (Barnard ***et al***, 2016). The relation between PAI-1 and MI risk. It remains uncertain is causal versus how much is as a marker of vascular disease, since there is enhanced PAI-1 expression in diseased vessels (Schneiderman ***et al***, 1992). Plasminogen activator inhibitor may increase MI risk in several ways. As the major inhibitor of the endogenous fibrinolytic system, raised PAI-1 level in the blood lead to decrease in the capacity of the fibrinolytic system to prevent fibrin deposition in vessel walls and thrombus formation (Feinbloom ***et al***, 2005). Microvascular thrombosis and lead to progress of atherosclerotic lesions (Dohgu ***et al***, 2011). PAI-1 play role in the impairment of normal vascular remodeling through effects on cellular migration.Circulating PAI-1 influence smooth muscle cell proliferation as well as cell migration (Ghosh ***et al***, 2012). PAI-1, are demonstrable and persist stably for up to two years in stored serum samples, suggesting that a single measurement of these markers may be sufficient for utilization in clinical and epidemiological studies (Linkov ***et al***, 2009).

CONCLUSION

There was significant reduction in serum level of adiponectin patients as compared with those normal subjects and observed, a significantly decrease in adiponectin, in both CAD groups (obese and normal weight) when compared with (control) groups and lower in obese when compared with control, while significant increase in leptin and plasminogen activator inhibitor-1 (PAI-1) in both CAD groups (obese and normal weight) when compared with (control) groups and more elevation in obese groups when compared with normal subjects.

ACKNOWLEDGMENTS

The authors would like to thank the staff of the Department of Biochemistry at the Faculty of Medicine, University of Babylon, Iraq, for their efforts and facilities to accomplish the task of this study. The authors also would like to thank the staff of the Cardiac Unit Unit at MarjanTeaching Hospital, Hilla, Iraq, for their assistance in collecting samples.

REFERENCES

Arnett D K, Blumenthal R S, Albert M A, Michos E D, Buroker A B, Miedema M D, Goldberger Z D, Muñoz D, Hahn E J, Smith S C and Himmelfarb C D (2019) ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease. ***Journal of the American College of Cardiology*** 26029.

Azuma K, Katsukawa F, Oguchi S, Murata M, Yamazaki H, Shimada A and Saruta T (2003)Correlation between serum resistin level

and adiposity in obese individuals. ***Obesity Research*** **11**(8), 997-1001.

Barnard S A, Pieters M and De Lange Z (2016) The contribution of different adipose tissue depots to plasma plasminogen activator inhibitor-1 (PAI-1) levels. ***Blood Reviews*** **30**(6), 421-429.

Beltowski J (2006) Leptin and atherosclerosis. ***Atherosclerosis*** **189**(1), 47-60.

Bhopal R S (2019) ***Epidemic of Cardiovascular Disease and Diabetes: Explaining the Phenomenon in South Asians Worldwide***. Oxford University Press.

Chapin J C and Hajjar K A (2015) Fibrinolysis and the control of blood coagulation. ***Blood Reviews*** **29**(1), 17-24.

Chen H, Montagnani M, Funahashi T, Shimomura I and Quon M J (2003) Adiponectin stimulates production of nitric oxide in vascular endothelial cells. ***Journal of Biological Chemistry*** **278**(45), 45021-45026.

Dohgu S, Takata F, Matsumoto J, Oda M, Harada E, Watanabe T, Nishioku T, Shuto H, Yamauchi A and Kataoka Y (2011) Autocrine and paracrine up-regulation of blood–brain barrier function by plasminogen activator inhibitor-1. ***Microvascular Research*** **81**(1), 103-107.

Feinbloom D and Bauer K A (2005) Assessment of hemostatic risk factors in predicting arterial thrombotic events. ***Arteriosclerosis, Thrombosis, and Vascular Biology*** **25**(10), 2043-2053.

Ghosh A K and Vaughan D E (2012) PAI 1 in tissue fibrosis. ***Journal of Cellular Physiology*** **227**(2), 493-507.

Hendrix P, Foreman P M, Harrigan M R, Fisher III W S, Vyas N A, Lipsky R H, Lin M, Walters B C, Tubbs R S, Shoja M M and Pittet J F (2017) Association of Plasminogen Activator Inhibitor 1 (SERPINE1) Polymorphisms and Aneurysmal Subarachnoid Hemorrhage. ***World Neurosurgery*** **105**, 672-677.

Herr K D (2018) Scientific and Educational Abstracts Presented at The 30th Anniversary ASER 2018 Annual Scientific Meeting and Postgraduate Course in Emergency and Trauma Radiology September 26-29, McLean, Virginia. ***Emergency Radiology*** **25**, 565-611.

Iacoviello L, Agnoli C, De Curtis A, Di Castelnuovo A, Giurdanella M C, Krogh V, Mattiello A, Matullo G, Sacerdote C, Tumino R and Vineis P (2013) Type 1 plasminogen activator inhibitor as a common risk factor for cancer and ischaemic vascular disease: the EPICOR study. ***BMJ Open*** **3**(11), e003725.

Kang S M, Kwon H M, Hong B K, Kim D, Kim I J, Choi E Y, Jang Y, Kim H S, Kim M S and Kwon H C (2000) Expression of leptin receptor (Ob-R) in human atherosclerotic lesions: potential role in intimal neovascularization. ***Yonsei Medical Journal*** **41**(1), 68-75.

Kishida K, Funahashi T and Shimomura I (2014) Adiponectin as a routine clinical biomarker. ***Best practice & research Clinical endocrinology & metabolism*** **28**(1), 119-130.

Linkov F, Gu Y, Arslan A A, Liu M, Shore R E, Velikokhatnaya L, Koenig K L, Toniolo P, Marrangoni A, Yurkovetsky Z and Zeleniuch-Jacquotte A (2009) Reliability of tumor markers, chemokines, and metastasis-related molecules in serum. ***European Cytokine Network*** **20**(1), 21.

Martin S S, Qasim A and Reilly M P (2008) Leptin resistance: a possible interface of inflammation and metabolism in obesity-related cardiovascular disease. ***Journal of the American College of Cardiology*** **52**(15), 1201-1210..

Martin S S, Qasim A N, Rader D J and Reilly M P (2012) C Reactive Protein Modifies the Association of Plasma Leptin With Coronary Calcium in Asymptomatic Overweight Individuals. ***Obesity*** **20**(4), 856-861.

Mittal A, Gupta M D, Meennahalli Palleda G, Vyas A and Tyagi S (2013) Relationship of plasma adiponectin levels with acute coronary syndromes and coronary lesion severity in north Indian population. ***ISRN Cardiology***.

Montazerifar F, Bolouri A, Paghalea R S, Mahani M K and Karajibani M (2016) Obesity, serum resistin and leptin levels linked to coronary artery disease. ***Arquivosbrasileiros de Cardiologia*** **107**(4), 348-353.

Nigro E, Scudiero O, Monaco M L, Palmieri A, Mazzarella G, Costagliola C, Bianco A and Daniele A (2014) New insight into adiponectin role in obesity and obesity-related diseases. ***BioMed Research International***.

Parhami F, Tintut Y, Ballard A, Fogelman A M and Demer L L (2001) Leptin enhances the calcification of vascular cells: artery wall as a target of leptin. ***Circulation Research*** **88**(9), 954-960.

Qasim A, Mehta N N, Tadesse M G, Wolfe M L, Rhodes T, Girman C and Reilly M P (2008) Adipokines, insulin resistance, and coronary artery calcification. ***Journal of the American College of Cardiology*** **52**(3), 231-236.

Rajala M W and Scherer P E (2003) Minireview: the adipocyte—at the crossroads of energy homeostasis, inflammation, and atherosclerosis. ***Endocrinology*** **144**(9), 3765-3773.

Ralston S H, Penman I D, Strachan M W and Hobson R (2018) ***Davidson's Principles and Practice of Medicine E-Book***. Elsevier Health Sciences.

Reilly M P, Iqbal N, Schutta M, Wolfe M L, Scally M, Localio A R, Rader D J and Kimmel S E (2004) Plasma leptin levels are associated with coronary atherosclerosis in type 2 diabetes. ***The Journal of Clinical Endocrinology & Metabolism*** **89**(8), 3872-3878.

Ren J (2004) Leptin and hyperleptinemia-from friend to foe for cardiovascular function. ***The Journal of Endocrinology*** **181**(1), 1-10.

Sahu A (2003) Leptin signaling in the hypothalamus: emphasis on energy homeostasis and leptin resistance. ***Frontiers in Neuroendocrinology*** **24**(4), 225-253.

Schneiderman J, Sawdey M S, Keeton M R, Bordin G M, Bernstein E F, Dilley R B and Loskutoff D J (1992) Increased type 1 plasminogen activator inhibitor gene expression in atherosclerotic human arteries. ***Proceedings of the National Academy of Sciences*** **89**(15), 6998-7002.

Schulze P C, Kratzsch J, Linke A, Schoene N, Adams V, Gielen S, Erbs S, Moebius Winkler S and Schuler G (2003) Elevated serum levels of leptin and soluble leptin receptor in patients with advanced chronic heart failure. ***European Journal of Heart Failure*** **5**(1), 33-40.

Söderberg S, Ahren B, Jansson J H, Johnson O, Hallmans G, Asplund K and Olsson T (1999) Leptin is associated with increased risk of myocardial infarction. ***Journal of Internal Medicine*** **246**(4), 409-418.

Soderberg S, Ahrèn B, Stegmayr B, Johnson O, Wiklund P G, Weinehall L, Hallmans G and Olsson T (1999) Leptin is a risk marker for first-ever hemorrhagic stroke in a population-based cohort.

***Stroke* 30**(2), 328-337.

Somodi S, Seres I, Lõrincz H, Harangi M, Fülöp P and Paragh G (2018) Plasminogen Activator Inhibitor-1 Level Correlates with Lipoprotein Subfractions in Obese Nondiabetic Subjects. ***International Journal of Endocrinology***.

Todua F and Gachechiladze D (2018) ***Noninvasive Radiologic Diagnosis of Extracranial Vascular Pathologies***. Springer.

Wallace A M, McMahon A D, Packard C J, Kelly A, Shepherd J, Gaw A and Sattar N (2001) Plasma leptin and the risk of cardiovascular disease in the west of Scotland coronary prevention study (WOSCOPS). ***Circulation* 104**(25), 3052-3056.

Zhang J L, Qin Y W, Zheng X, Qiu J L and Zou D J (2003) Serum resistin level in essential hypertension patients with different glucose tolerance. ***Diabetic Medicine* 20**(10), 828-831.

Zurowski D, Koprowska B and Thor P J (2001) The role of leptin in metabolic regulation. ***Folia medica Cracoviensia* 42**(1-2), 83-93.