RESEARCH ARTICLE ISSN: 2349-2678

Contents lists available at www.ijpba.in

International Journal of Pharmaceutical and Biological Science Archive

Volume 5 Issue 2; March-April; 2017; Page No.24-29

TO ESTIMATE AND COMPARE THE SERUM LEVELS OF PANCREATIC HORMONES, ADIPOCYTOKINES, AND LIPID PROFILE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS WITH AND WITHOUT OBESITY

Dr. Wrishikesh M. Barabde

Assistant Professor Dept. of General Medicine Dr. Panjabrao Deshmukh Memorial Medical College, Amravati

ABSTRACT

BACKGROUND: Diabetes complications are the main burden of type 2 diabetes mellitus (T2DM), a metabolic disease. Therefore, it is crucial to address the underlying biology of diabetes rather than just treating the symptom complex, which can be done by doing early screenings and managing those who are at risk. Early and vigorous intervention options that combine maximum glucose lowering efficacy with potential cell-preserving characteristics may offer a chance to slow or stop the progression of the illness for patients who have just been diagnosed with T2DM. Insulin resistance and visceral obesity, which are frequently linked to diabetes, may also be connected to changes in adipose tissue mass and metabolism. Higher pancreatic hormone levels and abnormal levels of adipocyte-derived iii hormones have been linked to insulin resistance, a frequent problem in T2DM and obesity.

AIM: To calculate and compare the serum levels of adipocytokines (leptin and adiponectin), pancreatic hormones (insulin and C-peptide), and lipid profile in individuals with type 2 diabetes mellitus who are obese and those who are not.

MATERIAL AND METHOD: The present study was carried out in the Department of Medicine. Informed consent, both in English as well as vernacular language, was taken from all the participants included in the study.

RESULTS: The levels of serum insulin, C-peptide, leptin, and adiponectin in obese people may help determine their risk of developing insulin resistance, and later, diabetes and cardiovascular disease. This would allow for the implementation of suitable preventive measures to safeguard the high-risk subjects from developing diabetes and its complications.

CONCLUSION: The levels of insulin, C-peptide, leptin, and adiponectin in obese people may help determine how likely they are to develop insulin resistance, which could lead to diabetes and cardiovascular disease (CVD). This would make it possible to put appropriate preventative measures into place in such high-risk people to safeguard them from DM and its consequences.

KEYWORDS: Diabetes mellitus, Obesity, Adipocytokines, Insulin resistance and Lipid profile.

INTRODUCTION:

Coronary heart disease (CHD), cerebral vasculature, and peripheral arterial vasculature are examples of atherosclerotic vascular illnesses. Coronary artery disease (CAD) continues to be the leading cause of mortality and disability despite significant global efforts for its prevention and treatment.[1] Recent demographic and health studies have shown an increase in CAD among people from all socioeconomic groups. In low- and middle-income nations like India, the rate of CAD-related death and disability has risen alarmingly. The fact that the majority of CAD patients in India are in their prime earning years adds to the gravity of the situation. This might have disastrous long-term effects on the socioeconomic situation. As seen by the rapidly rising prevalence of obesity, insulin resistance, diabetes mellitus, atherogenic dyslipidemia, and high blood pressure, conventional cardiovascular risk is related to changes in lifestyle and changed metabolic activity.[2]

Diabetes, often known as diabetes mellitus (DM) or just diabetes, is a set of common metabolic illnesses that share the phenotype of hyperglycemia, either because the body does not make enough insulin or because the cells do not react to the insulin that is produced.[3] For the foreseeable future, DM will be a major source of

Corresponding author: Wrishikesh M. Barabde |

morbidity and mortality due to its rising occurrence around the world.[4,5] Between 1985 and 2000, there were an estimated 177 million cases of diabetes globally, a sharp increase from the estimated 30 million cases in 1985.[6]

Adipose tissue mass in excess is the condition of obesity. Although it's commonly assumed that being overweight equates to having more body weight, this isn't always the case. Lean but extremely muscular people might be numerically overweight without having more adiposity. Therefore, examining how obesity is related to illness or mortality helps characterise obesity more accurately. Body Mass Index (BMI), which is equal to weight/height, is the most commonly used technique to assess obesity even though it is not a direct indicator of adiposity. Anthropometry (measures of skin fold thickness), densitometry (under-water weighing), CT or MRI, and electrical impedance are additional methods for calculating obesity. Although there are numerous contributing factors to diabetes, obesity is a key risk factor for the disease, and up to 80% of people with T2DM are obese.[7,8] Changes in lipids and lipoproteins as well as an increased risk of coronary heart disease are linked to variations in body fat distribution. Diabetes patients may have a variety of dyslipidemias. High serum triglycerides, low HDL-C, and a qualitative change in low density lipoprotein (LDL) particles are the most notable characteristics of the insulin resistance syndrome in obese patients with type 2 diabetes mellitus.24 Activity of adiponectin is associated with leptinand with steroid and thyroid hormones, glucocorticoids, and nitric oxide. Endothelial cells' expression of extracellular matrix sticky proteins is suppressed, as are cytokines that promote atherosclerosis.

Additionally, there is a gender difference in serum leptin levels, with women having higher levels than men. Despite the fact that leptin levels rise in obesity, those with type 2 diabetes who are obese show lower leptin levels, which may be related to altered fat distribution.[9] On the other hand, information gathered from several investigations has shown that leptin levels in diabetes individuals have grown or remained the same.[10,11] In order to fill in the gaps in our understanding of the intricate interactions between leptin, adiponectin, insulin, and C-peptide in obese and non-obese diabetes, more research is needed.

MATERIAL AND METHODS

The Department of Medicine conducted the current study. The study's subject pool consisted of 380 individuals, regardless of gender, between the ages of 30-70. 190 type 2 diabetes mellitus patients who were presenting to the OPD and/or being treated in the hospital's wards, as well as 190 healthy individuals in the same age group who were present with the patients and volunteers, served as the study's controls.

SELECTION OF PATIENTS

According to the American Diabetes Association's diagnostic standards for diabetes mellitus, patients were given a diabetes diagnosis.[12]

One hundred ninety patients diagnosed as diabetic by the Department of Medicine were divided into 2 groups in the following manner:

Group I:95 patients having diabetes mellitus (T2DM) with obesity.

Group II: 95 patients having diabetes mellitus (T2DM) without obesity.

One hundred ninetyage and sex matched subjects without diabetes selected to serve as controls were also divided into 2 groups as under:

Group III: 95 subjects having only obesity and no diabetes.

Group IV:95 subjects having no obesity and no diabetes.

A thorough history of the patient's current and prior illnesses was taken, and the clinical examination was conducted in accordance with the proforma attached.

INCLUSION CRITERIA

Patients suffering from Type 2 diabetes mellitus and under treatment, Patients of T2DM having documented obesity, Patients of T2DM having no obesity, Subjects having no diabetes but having documented obesity, Subjects having no diabetes and no obesity, Age 30-70 years of either sex.

EXCLUSION CRITERIA

Patients taking antioxidant medications, corticosteroids, insulin, during pregnancy, for hyperthyroidism or hypothyroidism, for Cushing syndrome, or for any other endocrinopathy besides diabetes mellitus. Patients with type 1 diabetes mellitus, rheumatoid arthritis, coronary artery disease, and those taking antioxidant medications.

Parameters for biochemical analysis

- Fasting plasma insulin levels were measured by Chemiluminescence immunoassay (CLIA).[13]
- Fasting serum C-peptide levels were measured by Chemiluminescence immunoassay (CLIA).[14]
- Serum adiponectin was measured by competitive enzyme immunoassay (ELISA).[15]
- Serum Leptin levels were estimated using Sandwich Enzyme Immunoassay (ELISA) technique.[16]

- Serum total cholesterol (TC) was determined by Cholesterol Oxidase-Peroxidase in Aminoantipyrine (CHOD-PAP) method.[17]
- Serum triglycerides (TG) were measured by Glycerol Phosphate Oxidase (GPO)-Trinder method.[18]
- Serum high density lipoprotein-cholesterol (HDL-C) levels were determined using Precipitation method.[19]
- Low Density Lipoprotein-Cholesterol (LDL-C) was calculated using Friedwald formula, based on assumption that very low-density lipoprotein (VLDL) is present in serum at a concentration equal to 1/5th of triglyceride concentration.[20]
- C-reactive protein (CRP) test in serum was done using diagnostic reagent kit for in vitro detection of CRP by Qualitative and Semi-quantitative rapid Latex Slide Tests.[21]

Statistical analyses

Software SPSS version 20.0 was used to conduct statistical analysis. For many aspects of the subjects, descriptive statistics were computed. The statistical differences between continuous variables were compared using the Student t-test and one-way ANOVA (Analysis of Variance).

RESULT:-

For the study, 180 clinically diagnosed type 2 diabetes mellitus (DM) patients between the ages of 30-70 years, of either sex, with obesity (95 patients) and without obesity (95 patients), attending the OPD and wards of the Department of Medicine, were chosen. equal amounts A total of 190 non-diabetic subjects—95 with and 95 without obesity were chosen to act as controls. These 380 study participants were split up into four (4) groups.

Table 1: Showing variations in serum Total cholesterol, TG, HDL-C, LDL-C,VLDL-C, Leptin, Adiponectin, FPG, Insulin, C-peptide levels amongst different groups under this study.

Parameters	Diabetic Obese Group I	Diabetic Non-Obese Group II	Non-Diabetic Obese Group III	Non-Diabetic Non-Obese Group IV
Total cholesterol (mg/dl)	173.2±40.1	185.5±58.4	160.33±42.07	167.44±48.22
TG (mg/dl)	187.14±108.3	203.6±116.6	163.71±87.44	164.07±68.45
HDL-C (mg/dl)	42.89±13.35	44.57±11.52	42.31±10.46	43.22±14.64
LDL-C (mg/dl)	96.82±27.61	104.8±49.7	85.69±36.33	90.88±37.60
VLDL-C (mg/dl)	41.21±33.33	43.16±25.50	36.05±18.59	34.26±17.14
Leptin (ng/ml)	35.46±36.92	18.15±19.21	32.10±30.84	15.58±14.93
Adiponectin (µg/ml)	11.75±7.81	17.85±9.06	14.94±5.79	14.86±6.77
FPG (mg/dl)	149.44±58.17	170.5±72.9	88.63±11.64	89.55±13.66
Insulin (µIU/ml)	15.86±10.07	10.8±7.79	15.91±11.70	9.94±6.08
C-PEPTIDE (ng/ml)	4.61±2.70	3.36±2.24	3.81±2.67	2.52±0.68

Table 1 showed that the greatest mean FPG levels were found in non-obese diabetic participants, followed by obese diabetics, non-obese non-diabetics, and obese non-diabetics. Obese diabetics were shown to have the highest plasma insulin levels, followed by obese non-diabetics. Comparatively, the plasma insulin levels of non-obese participants with and without diabetes were lower. Obese persons had elevated mean blood C-peptide levels in both diabetes and non-diabetic individuals. In contrast, non-obese diabetic individuals and non-obese non-diabetics both had serum C-peptide levels.

Obese participants with diabetes and those without diabetes both showed elevated serum leptin levels. The mean serum leptin levels of both diabetic and non-diabetic, non-obese patients were lower than those of their obese counterparts. Both non-obese diabetics and non-obese non-diabetics have high levels of adiponectin. Comparatively, both obese diabetics and obese non-diabetics had reduced adiponectin concentrations. Obese diabetic patients had mean serum total cholesterol levels compared to non-diabetic controls. Subjects who were not obese or diabetic had mean serum total cholesterol levels that were greater than those who were. Serum total cholesterol levels in the study groups varied in a statistically significant way. Diabetes patients who were obese had mean triglyceride levels that were lower than those of diabetics who weren't obese.

In comparison to diabetic non-obesity patients, obese diabetes patients exhibited somewhat lower HDL-C levels. In comparison to obese diabetics and non-diabetics, non-obese patients both had high levels of HDL-C. Both diabetes and non-diabetic non-obesity patients were found to have higher LDL-C values than their obese counterparts. Patients with diabetes who were not obese had somewhat greater serum VLDL-C levels than diabetics who were. In contrast to non-obese participants who had serum VLDL-C levels, obese non-diabetics showed greater VLDL-C levels.

DISCUSSION

The greatest public health problems of the twenty-first century are diabetes mellitus (DM) and obesity. Particularly in those who are genetically susceptible to the condition, obesity is regarded to be the main contributor to type II diabetes. Over the past 50 years, rates of DM have significantly increased alongside obesity rates.

In a study that examined Asian Indians' insulin secretion, **Snehlata et al. (1999)** found that non-obese subjects had insulin levels that were lower than those of obese subjects, indicating that obese patients may be hyperinsulinemic.[22] Jones et al. also found that plasma insulin and C-peptide concentrations are higher in obese than non-obese subjects.[23] Although obese diabetic individuals had greater insulin levels than non-obese diabetic patients, the difference in C-peptide levels was insignificant. This could be because the liver extracted too much insulin. Leptin is a multipurpose adipocytokine that controls how much food is consumed, how much energy is stored, and how carbohydrates and fats are metabolised. In a study by **Wannamethee et al. 2007**[24], plasma leptin levels were noticeably elevated in obese patients. Several studies have suggested that serum leptin levels are higher in diabetics than in non-diabetics.[25,26]

This is in accordance with study done by **Barma et al2011[27]and Mukhyaprana et al.2004[28]** The most characteristic lipid abnormality in diabetics was hypertriglyceridemia which was similar to the findings of **Dixit et al.2014[29] and Zargar et al.1995[30]Sinharoy et al2008** also reported elevated triglycerides in lean type 2 diabetics compared to normal weight and obese type 2 diabetics.[31] Likewise, there were no appreciable differences in total cholesterol, HDL cholesterol, LDL cholesterol, or VLDL cholesterol between obese and non-obesity type 2 diabetes. Most diabetic patients are found to have a varying combination of excess or underuse of triglycerides. LPL activity is significantly decreased in cases of severe insulin insufficiency. According to the current study, diabetic obese people had greater levels of serum total cholesterol, LDL cholesterol, HDL cholesterol, VLDL cholesterol, and triglycerides than non-diabetic obese subjects did. This is consistent with what Kim and the study's other authors discovered.[32] **Zargar et al1995** showed that all lipid fractions (except HDL-C) are abnormally elevated in obese diabetics when compared with obese non-diabetics.[30] However, LPL activity is still moderately active in mild to severe type 2 diabetics, which increases endogenous triglyceride synthesis, especially when obesity and an appropriate insulin level are present.[30] Studies conducted by **Jaleel et al.2006[33], Kolahi et al.2012[34] and Weyer et al.2001[35]** have shown high leptin levels and low adiponectin levels in overweight and obese subjects. According to the level of adiposity, serum leptin levels are significantly higher in obese individuals, indicating that hyperleptinemia may contribute to the pathogenesis of complications associated with obesity. 36 It was discovered that obese people had much greater serum C-peptide levels than non-obese people, indicating insulin resistance. These findings were similar to those obtained in study done by **Abdullah et al 2012 and Abdullah BB et al.2010[37,38]** Few studies done by **Buyukvese et al 2004[39] and Zimmet et al 1998[40]** found reduced levels of leptin in type 2 diabetics which has been related to insulin deficiency and difference in distribution of fat tissue throughout the body.

Novel adipocytokines-related treatment strategy may offer exciting new opportunities in a spectrum of metabolic diseases with several unmet clinical needs.

CONCLUSION:

In conclusion, measuring the levels of insulin, C-peptide, leptin, and adiponectin in obese people may help determine their risk of developing insulin resistance, which could lead to diabetes and cardiovascular disease (CVD). This would make it possible to put appropriate preventative measures into place in such high-risk people to safeguard them from DM and its consequences. This opens up a brand-new area for the research and development of cutting-edge medications to treat obesity and insulin resistance.

REFERENCES:

1. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PLoS Med 2006; 3(11):e442.
2. Gupta S, Gudapati R, Gaurav K, Bhise M. Emerging risk factors for cardiovascular

diseases: Indian context. Indian J Endocrinol Metab 2013; 17(5):806-14.
3. Gardner DG, Shoback D. Greenspan's Basic and Clinical Endocrinology. 9 th Edition. New York: McGraw-Hill Medical, 2011:p.724-750.
4. Arner P. Insulin resistance in Type 2 diabetes: role of fatty acids. Diabetes Metab Res Rev 2002; 18(2): 5-9.
5. Antuna-Puente B, Feve B, Fellahi S, Bastard J. Adipokines. The missing link between insulin resistance and obesity. Diabetes Metab 2008; 34: 2- 11.
6. Diabetes Action Now: An initiative of the World Health Organization and International Diabetes Federation 2004. Available at: http://whqlibdoc.who.int/publications/2004/924159151X.pdf?ua=1. Accessed on May 21, 2014.
7. Libby P, Ridker PM. Novel inflammatory markers of coronary risk: theory versus practice. Circulation 1999; 100: 1148-50.
8. Farooqi IS, O'Rahilly S. Genetics of obesity. Philos Trans R Soc Lond B Biol Sci 2006; 361(1471): 1095-1105.
9. Flier JS. Obesity wars: Molecular progress confronts an expanding epidemic. Cell 2004; 116(2): 337-50
10. Farooqi S, O'Rahilly S. Leptin: a pivotal regulator of human energy homeostasis. Am J Clin Nutr 2009; 89(3): 980S-984S.
11. Mohammadzadeh G, Zarghami N. Serum leptin level is reduced in nonobese subjects with type 2 diabetes. Int J Endocrinol Metab 2013; 11(1): 3-10.
12. Al-Daghri N, Al-Rubean K, Bartlett WA, Al-Attas O, Jones AF, Kumar S. Serum leptin is elevated in Saudi Arabian patients with metabolic syndrome and coronary artery disease. Diabet Med 2003; 20(10): 832-7.
13. American Diabetes Association. Diagnosis and Classification of diabetes mellitus. Diabetes Care 2012; 35(1): 64-71.
14. Kricka LJ. Optical techniques. In: Teitz Textbook of Clinical Chemistry and Molecular Diagnostics. Burtis CA, Ashwood ER, Bruns DE, editors. 4 th edition. New Delhi: Saunders, 2008: 85.
15. Risch L, Hoefle G, Saely C, Berchthold S, Weber M, Gouya G et al. Evaluation of two fully automated novel enzyme-linked immunosorbent assays for the determination of human adiponectin in serum. Clin Chim Acta 2006; 373(1-2): 121-6.
16. Considine RV, Sinha MK, Heiman ML, Kriauciunas A, Stephens TW, Nyce MR et al. Serum Immunoreactive-leptin concentrations in normal weight and obese humans. N Engl J Med 1996; 334(5): 292-5.
17. Roeschlau P, Bernt E, Gruber WA. Dynamic extended stability CHODPAP method (with LCF). J Clin Chem Clin Biochem 1974; 12: 226-8.
18. Trinder P. Dynamic extended stability with lipid clearing agent GPOTrinder End Point method for triglycerides. Ann Clin Biochem 1969; 6: 24-7.
19. Nauk M, Wiebe D, Warnick G. Measurement of high density-lipoprotein cholesterol. In: Handbook of Lipoprotein testing. Rifai N, Warnick R, Dominiczak MH, editors. 2nd edition. Washington DC: AACC Press, 2000: 221-44.
20. Freidewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma without use of preparative ultracentrifuge. Clin Chem 1972; 18(6): 499-502.
21. Hyde RM and Garb S. In vitro detection of C - reactive protein (CRP) in human serum. Amer J Clin Path 1965; 44: 436.
22. Snehalatha C, Satyavani K, Sivasankari S, Vijay V, Ramachandran A. Insulin secretion and action in different stages of glucose tolerance in Asian Indians. Diabet Med 1999; 16(5):408-14.
23. Jones CN, Abbasi F, Carantoni M, Polonsky KS, Reaven GM. Role of insulin resistance and obesity in regulation of plasma insulin concentration. Am J Physiol Endocrinol Metab 2000; 278(3):E501-8.
24. Wannamethee SG, Tchernova J, Whincup P, Lowe GDO, Kelly A, Rumley A, et al. Plasma leptin: Associations with metabolic, inflammatory and homeostatic risk factor for cardiovascular disease. Atherosclerosis 2007; 191(2):418-26.
25. Das P, Bhattacharjee D, Bandyopadhyay SK, Bhattacharya G, Singh R. Association of obesity and leptin with insulin resistance in type 2 diabetes mellitus in Indian population. Indian J PhysiolPharmacol 2013; 57(1):45-50.
26. Uslu S, Kebapci N, Kara M, Bal C. Relationship between adipocytokines and cardiovascular risk factors in patients with type 2 diabetes mellitus. Exp Ther Med 2012; 4(1):113-120.
27. Barma PD, Ranabir S, Prasad L, Singh TP. Clinical and biochemical profile of lean type 2 diabetes mellitus. Indian J Endocrinol Metab 2011; 15(Suppl 1): 40-3.
28. Mukhyaprana MP, Vidyasagar S, Shashikaran U. Clinical profile of type 2 diabetes mellitus and

body mass index-is there any correlation. Calicut Med J 2004; 2(4):3.
29. Dixit AK, Dey R, Suresh A, Chaudhuri S, Panda AK, Mitra A, et al. The prevalence of dyslipidemia in patients with diabetes mellitus of Ayurveda Hospital. J Diabetes MetabDisord 2014; 13:58.
30. Zargar AH, Wandroo FA, Wadhwa MB, Laway BA, Masoodi SR, Shah NA. Serum lipid profile in non-insulin-dependent diabetes mellitus associated with obesity. Int J Diab Dev Countries 1995;15:9-13.
31. Sinharoy K, Mandal L, Chakrabarti S, Paul UK, Bandyopadhyay R, Basu AK. A study on clinical and biochemical profile of low body weight type 2 diabetes mellitus. J India Med Assoc 2008; 106(11):747-50.
32. Kim C, Park J, Park J, Kang E, Ahn C, Cha B, et al. Comparison of body fat composition and serum adiponectin levels in diabetic obesity and nondiabetic obesity. Obesity 2006; 14(7):1164-71.
33. Jaleel F, Jaleel A, Rahman MA, Alam E. Comparison of adiponectin, leptin and blood lipid levels in normal and obese post-menopausal women. J Pak Med Assoc 2006; 56(9):391-4.
34. Kolahi S, Mahdi F. Adiponectin in relation to lipid profile indexes and body composition in middle- aged obese males. J Basic Appl Sci Res 2012; 2(2):2045-8.
35. Weyer C, Funahashi T, Tanaka S, Hotta K, Matsuzawa Y, Pratley RE, et al. Hypoadiponectinemia in obesity and type 2 diabetes: close association with insulin resistance and hyperinsulinemia. J Clin Endocrinol Metab 2001; 86(5):1930-5.
36. Leibel RL. The role of leptin in the control of body weight. Nutr Rev 2002; 60(10):15-9
37. Abdullah A, Hasan H, Raigangar V, Bani-Issa W. C-peptide versus insulin: Relationships with risk biomarkers of cardiovascular disease in metabolic syndrome in young Arab females. Int J Endocrinol 2012; 2012: 420792.
38. Abdullah BB, Patil BS, Thaseen A. Significance of C-peptide in type 2 diabetics- A study in North Karnataka population of India. Al Ameen J Med Sci 2010; 3(1):65-70.
39. Buyukbese MA, Cetinkaya A, Kocabas R, Guven A, Tarakcioglu M. Leptin levels in obese women with and without type 2 diabetes mellitus. Mediators Inflamm 2004; 13(5-6):321-5.
40. Zimmet PZ, Collins VR, de Courten MP, Hodge AM, Collier GR, Dowse GK, et al. Is there a relationship between leptin and insulin sensitivity independent of obesity? A population-based study in the Indian Ocean Nation of Mauritius. Mauritius NCD Study Group. Int J ObesRelatMetabDisord 1998; 22(2):171-7