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Study of Leptin and Adiponectin in Type 2 Diabetes Mellitus

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ABSTRACT

Introduction: *The diabetes mellitus is a metabolic disorder and forthcoming epidemic all over the globe that is caused due to insulin resistance. In this background the adipokine-leptin could be potential and beneficial alternative treatment modality. Leptin promotes weight loss, regulation of appetite & can reverse diabetes by improving glucose tolerance by its action on hypothalamus.*

Objectives: *Present study will be conducted to evaluate the role of leptin in obesity associated maturity onset diabetes. Other biochemical markers such as TRIGLYCERIDES, Total CHOLESTEROL, HDL, LDL, Adiponectin, tumor necrosis factor and insulin would also be studied as they are associated with obesity of patient and insulin resistance. This study has been approved by ethical committee of the institution.*

Methods: *Study was performed as a randomized controlled trial and with parallel design. Physical examination and preliminary lab investigations patients of obesity induced DM will be selected. Serum glucose, cholesterol, triglycerides, HDL, LDL and HbA1c will be performed on semi auto analyzer according to the methodology & instructions given on literature accompanying commercially available kits of ERBA™.*

Results: *Study was done on 200 patients with type 2 diabetic patients to analyze the role of Leptin hormone in obesity induced type 2 DM. In the present study type-II diabetes patients were had significantly higher fasting blood glucose (P<0.001), glycosylated hemoglobin [HbA1c] (P <0.001), cholesterol (P=0.015) and high-density lipoprotein (P = 0.009), Low-density lipoprotein (<0.001) and non-significantly triglycerides (0.066) were observed. Further type-II diabetes patients were had significantly higher insulin (P<0.001), TNF- α (P <0.001), Leptin (P<0.001) and high adiponectin (P=0.001) were observed.*

Conclusion: *Although Type 2 diabetes can be treated with oral hypoglycemic drugs for long time but ultimately they require insulin to control their diabetes which has its side effects & available in injectable form only which is very cumbersome for the patient. Therefore it is necessary to look for other alternative therapy which has lesser side effects. Leptin together with other molecules that are secreted from adipose tissue does affect the insulin sensitivity & is accepted to play a major role in pathogenesis of obesity related diabetes.*

Keywords: *Diabetes, Obesity, Glucose, Leptin.*

INTRODUCTION

Diabetes is a metabolic disorder that causes hyperglycemia and giving rise to various vascular complications (Prajapat *et al*., 2017). Diabetes is a forthcoming epidemic all over the globe that caused due to ineffective secretion of insulin or insulin resistance (Awasthi *et al*., 2016). Diabetes Mellitus is classified on the basis of the pathogenic process that leads to hyperglycemia. The two mainly classified categories of DM include type 1 and type 2 DM (WHO, 1985).

Obesity and dyslipidemia take upper hand in the initiation, progression and complications of type 2 diabetes (Snehalatha *et al*., 2003; Kumar *et al*., 2017). Presently there are more than 62,000,000 people suffering from T2DM in India. Obesity and dyslipidemia are shown to play important role in its complications resulting in morbidity and mortality of T2DM (Kumar *et al*., 2017).

Obesity and type 2 diabetes are closely associated with low plasma levels of cytokine adiponectin in different ethnic groups of the society and indicate that the degree of hypoadiponectinemia is often more closely related to the degree of insulin resistance and hyperinsulinemia than to the degree of adiposity and glucose intolerance. (Weyer *et al*.,2001)

Patients with Type 2 diabetes are associated with more than a two-fold excess mortality from cardiovascular disease, microvascular complic-ations affecting the eyes, kidneys and nerves. If left untreated, these complications will lead to blindness, kidney failure, foot ulcers and finally leading to amputations of limbs. (Hanson *et al*., 2000).

Drugs have been targeting different defects of metabolism in diabetes patients, leaving the clinician with much better tools to tailor a more optimal treatment strategy towards diabetic patients. It is extremely important for medical professionals to have a proper knowledge and constantly updated scientific training in diabetes research, which will ultimately leads to the implementation of better and more cost-effective treatment and care programs for patients with diabetes (Thomas *et al*., 2016).

Type 2 diabetes can be treated with oral hypoglycemic drugs for long time but ultimately they require insulin to control their diabetes which has its side effects (Brunetti and Julie, 2012; Noureddine *et al*., 2014).

Therefore it is necessary to look for other alternative therapy which has lesser side effects. Leptin together with other molecules that are secreted from adipose tissue does affect the insulin sensitivity & is accepted to play a major role in pathogenesis of obesity related diabetes (Mohamed *et al*., 1998, Prins, 2002).

Adipocyte derived proteins with anti diabetic action include leptin, adiponectin, Omentin & Visfatin (Masur *et al*., 2008).In this background the adipokine-leptin could be potential and beneficial alternative treatment modality. Leptin promotes weight loss, regulation of appetite & can reverse diabetes by improving glucose tolerance by its action on hypothalamus (Paz-Filho *et al*., 2012). About 80% of type 2 DM patients are overweight and in fact obesity is a primary risk factor for type 2 diabetes. Thus a study is urgently required to explore the role of Leptin in the etiology of obesity induced DM (Al-Goblan *et al*., 2014).

MATERIALS AND METHODS

Study was performed in Department of Biochemistry, in Goldfield Medical College, Faridabad, Haryana and the project was approved by Geetanjali medical College, Geetanjali University, Udaipur [Rajasthan] INDIA, as a randomized controlled trial and with parallel design. According to ADA [2006], the whole study comprised of 400 patients including 200 cases and 200 patients serving as control with type 2 diabetic of age group range from 30 to 80 years were selected.

Participants will be adults having obesity with Type 2 diabetes mellitus. Blood samples would be drawn to determine biochemical markers after taking consent from the patient.

On the basis of history, physical examination and preliminary lab investigations patients of obesity induced DM will be selected. Serum glucose (Myers et al., 2006) cholesterol (Kannel et al., 1979), triglycerides, HDL (Castelli et al., 1977), LDL (Nauck et al., 2002) and and HbA1c (Jeppsson et al., 2002) will be performed on semi auto analyzer according to the methodology & instructions given on literature accompanying commercially available kits of ERBA company.

Hormone Leptin along Adiponectin and tumor necrosis factor estimation will be done with help of ELIZA assay kit commercially available kits are based on the principle of ELIZA. Insulin will be done by chemiluminense essay (Khoo *et al.*, 2011).

All the markers mentioned above would be done from serum by collecting venous blood sample in the vacutainers. Blood sample would be withdrawn from anticubital vein. Subjects would be asked to have fasting of 8 to 12 hours. Results of biochemical markers would be analyzed to establish their role as predictor of obesity induced DM.

While analyzing the individual biochemical markers, we would consider the following value`s as their cut off upper limit.

- Cholesterol - 210 mg/dl.
- Triglycerides - 208 mg/dl.
- HDL - 35 mg/dl
- LDL - 80 mg/dl
- Leptin
- Adiponectin
- Tumor necrosis factor-α
- Insulin.

RESULTS

Blood samples of patients were drawn to determine biochemical markers after taking consent from the patients.

On the basis of history, physical examination and preliminary lab investigations patients of obesity induced DM will be selected. Cholesterol, triglycerides, HDL, LDL was performed auto analyzer according to the methodology and instructions given on literature accompanying commercially available kits of ERBA^{TM}.

Table 1 explains the ratio of male and female patients and table 2 and 3 explain about past and present medical history of patients that were selected for study.

Table 1: Ratio of male and female patients selected for study

GENDER	Diabetic patients (%)	Control group (%)	TOTAL (%)
MALE	99 (49.5%)	93 (46.5%)	192 (48%)
FEMALE	101 (50.0%)	107 (53.5%)	208 (52%)
TOTAL	200 (100%)	200 (100%)	400 (100%)

Table 2: Past/ Present History of Disease of Male and Female of Control Group

DISEASES	Control group		χ 2-value	P Value	Significance
	MALE (%) N = 93	FEMALE (%) N = 107			
ANEMIA	25 (26.88%)	61 (57.01%)	17.22	<0.001	Significant
HYPERTENSION	59 (63.44%)	78 (72.9%)	1.647	0.199	Non- Significant
HYPOTENSION	52 (55.91%)	47 (43.93%)	2.401	0.121	Non- Significant

Table 3: Past/ Present History of Disease of Study Subjects

DISEASES	Diabetic patients (%) N = 200	Control group (%) N= 200	Total (%) N= 400	χ 2-value	P Value	Significance
ANEMIA	101 (50.5%)	86 (43.0%)	187 (46.75%)	1.968	0.161	Non- Significant
HYPERTENSION	132 (66.0%)	137 (68.5%)	269 (67.25%)	5.926	0.015	Significant
HYPOTENSION	100 (50.0%)	99 (49.5%)	199 (49.75%)	0.090	0.765	Non- Significant

Table 4: Biochemical parameters of subjects with diabetes and the control group

BIOCHEMICAL MARKERS	Diabetic patients Mean ± SD N = 200	Control group Mean ± SD N= 200	t-value	P-value	Significance
Fasting Blood Glucose [mg/dl]	178.78 ± 11.34	94.83 ± 1.49	103.80	<0.001	Significant
HbA1C [mmol/mol]	8.82 ± 0.41	5.8 ± 0.06	103.07	<0.001	Significant
Cholesterol [mg/dl]	184.04 ± 38.78	175.68 ± 70.16	2.44	0.015	Significant
Triglycerides [mg/dl]	179.98 ± 78.17	166.28 ± 70.16	1.84	0.066	Non-significant
High-density lipoprotein cholesterol [mg/dl]	39 ± 8.40	36.9 ±7.49	2.64	0.009	Significant
Low-density lipoprotein cholesterol [mg/dl]	110 ± 34.8	92.37 ± 11.35	6.81	<0.001	Significant
Insulin [IU]	11.81 ± 8.48	6.29 ± 3.42	8.54	<0.001	Significant
TNF- α [ng/ml]	8. 79 ± 8.38	2.61 ± 2.52	9.99	<0.001	Significant
Adiponectin [IU/ml]	9.37 ± 5.13	12.52 ± 4.6	-6.47	<0.001	Significant
Leptin [ng/ml]	34.97 ± 16.38	41.51 ± 22.07	-3.36	<0.001	Significant

DISCUSSION

The mean ± SD values of fasting blood glucose (FBG) was 178.78 ± 11.34 with observed significant P-value was <0.001. The mean ± SD values of HbA1C was 8.82 ± 0.41 with observed significant P-value was <0.001. The mean ± SD values of triglycerides was 179.98 ± 78.17 with non-significant P-value was <0.001, mean ± SD value of HDL was 39 ± 8.40 and LDL was 110 ± 34.8 with significant p-value (<0.001). The mean ± SD values of insulin was 11.81 ± 8.48 with significant P-value was <0.001. The mean ± SD values of insulin were 8. 79 ± 8.38 with significant P-value was <0.001.

The mean ± SD values of adiponectin 9.37 ± 5.13 with significant P-value was <0.001. The mean ± SD values of leptin 34.97 ± 16.38 with significant P-value was <0.001 (Table 4).

The observed t – value of adiponectin was -6.47 (Table 4), that indicate a low level of adiponectin is an independent risk factor for developing, metabolic syndrome and diabetes mellitus (Nedvídková *et al*., 2005).

Renju *et al* (2012) reported that the fasting insulin, serum adiponectin levels and its correlation in patients with type 2 diabetics. Serum insulin and adiponectin levels were significantly decreased in patients compared to control subjects. In our study there is no significant correlation between adiponectin levels and insulin resistance in diabetic cases. (Fruhbeck *et al*., 2001).

Biochemical parameters of subjects with diabetes and control of the study are shown in table - 4. The type-II diabetes patients were had significantly higher fasting blood glucose (*P*<0.001), glycosylated hemoglobin [HbA1c] (P

<0.001), cholesterol (P=0.015) and high-density lipoprotein (P = 0.009), Low-density lipoprotein (<0.001) and non-significantly triglycerides (0.066) were observed.

Further type-II diabetes patients were had significantly higher insulin (*P*<0.001), TNF- α (P <0.001), adiponectin (P=0.001) and Leptin (*P*<0.001) were observed [Table 4].

Leptin plays an important role in energy homeostasis of an indiviual. Administration of leptin through gene therapy directly to specific targets located in the hypothalamus will definitely help in regulating glucose homeostasis via mobilization of these descending hypothalamic neural relays to peripheral organs. Leptin directly to hypothalamic targets, with the aid of recombinant adeno-associated virus (rAAV) vector encoding leptin gene, evoked stable glycemic in the blood lasting for the duration of the experiments in all type 1 and 2 diabetes animal models (Lundberg *et al*., 2001). It is obvious that leptin definitely improves glucose tolerance by enhancing insulin sensitivity.

CONCLUSION

The diabetes is a metabolic disorder and forthcoming epidemic all over the globe that caused due to ineffective secretion of insulin. In the present study type-II diabetes patients were had significantly higher fasting blood glucose (*P*<0.001), glycosylated hemoglobin [HbA1c] (P <0.001), cholesterol (P=0.015) and high-density lipoprotein (P = 0.009), Low-density lipoprotein (<0.001) and non-significantly triglycerides (0.066) were observed. Further type-II diabetes patients were had significantly higher insulin (*P*<0.001), TNF- α (P <0.001), Leptin (*P*<0.001) and high adiponectin (P=0.001) were observed. The observed t – value of adiponectin was -6.47 (Table 4), that indicate a low level of adiponectin is an independent risk factor for developing, metabolic syndrome and diabetes mellitus. Type 2 diabetes can be treated with oral hypoglycemic drugs but also require insulin to control diabetes which has its side effects on patient. Therefore it is necessary to look for other alternative therapy which has lesser side effects.

Leptin definitely improves glucose tolerance by enhancing insulin sensitivity. Leptin together with other molecules that are secreted from adipose tissue does affect the insulin sensitivity and is accepted to play a major role in pathogenesis of obesity related diabetes.

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