IJP (2014), Vol. 1, Issue 10 **(Research Article)**

IJP International Journal of Pharmacognosy

Received on 19 July 2014; received in revised form, 13 September 2014; accepted, 29 September 2014; published 01 October 2014

CHANGE IN SERUM-FREE FATTY ACID (FFA) LEVEL ASSOCIATED WITH DM TYPE-II IN OBESE PERSON

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Keywords:

ELISA,
DM Type-II
Insulin resistance, Blood sugar

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ABSTRACT: Introduction: Obesity is associated with DM Type-II. The major basis for the association between these two is the ability of obesity to engender insulin resistance. Insulin resistance is a fundamental aspect of etiology of DM Type-II. Different factors increase insulin resistance, but FFA is the most common factor to increase insulin resistance. **Aims and Objectives:** Most of the obese person (80%) is DM Type-II, but all obese are not diabetic, why? To study the FFA level in obese without DM Type-II verses obese with DM Type-II subjects. **Materials and Methods:** Subjects were taken from OPD & IPD, Department of Medicine, SRMS, IMS Bareilly (U.P.) India, of both sexes, coming from reasonable distances around Bareilly city. They were from the lower and middle class of rural area having moderate physical activities, with vegetarian as well as non-vegetarian dietary habits and were obese as per new Asian BMI guidelines and have symptoms of diabetes. Subjects were not on any drug treatment before taken blood sample. Serum FFA level estimated by ELISA method and blood sugar was estimated by GOD-POD method. **Results and Conclusion:** FFA level in obese without DM Type-II verses obese with DM Type-II were either normal or below normal, so we concluded that FFA level was not so much related with insulin resistance in our study group.

INTRODUCTION: Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. Several distinct types of DM exist and are caused by a complex interaction of genetic and environmental factors. Depending on the etiology of the DM, factors contributing to hyperglycemia include reduced insulin secretion, decreased glucose utilization, and increased glucose production.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.IJP.1(10).668-71

Article can be accessed online on: www.ijpjournal.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.IJP.1(10).668-71

Diabetes mellitus is the third largest killer disease at present around the globe; its number is at present around 17 crores 70 lacs out of which nearly 5 crores 70 lacs alone are in India, an alarming number in our country. It means that 5% of deaths are due to this disease, the main reason for which is that the developing world is changing from being thin to fat, not a good sign.

Among patients, 25% retinopathy, 9% neuropathy, and 8% nephropathy were diagnosed. DM Type II was formerly known as NIDDM (Non-Insulin Dependent Diabetes Mellitus). Most of the patients (95%) belong to this type [1]. The disease is due to the decreased biological response to insulin, otherwise called insulin resistance. This disease is seen commonly in individuals of above 40 years

age. These patients are less prone to develop ketosis. About 80% of patients are obese; these patients have high plasma insulin levels. The hallmarks are abdominal obesity, increased insulin resistance and decreased glucose tolerance. For DM Type II to develop both peripheral insulin resistance and insulin secretory defect should exist.

All overweight individuals have insulin resistance but only those with an inability to increase β-cells as associated with older age, obesity, family history of diabetes, previous history of diabetes, previous history of gestational diabetes, physical inactivity and ethnicity, develop DM type II. 4 major metabolic abnormalities characterize Type 2 diabetes mellitus: obesity, impaired insulin action, insulin secretory dysfunction, and increased endogenous glucose output (EGO) [2, 3].

Diabetes mellitus (DM) and obesity have a complex relationship, with type 2 diabetes strongly associated with obesity [4]. Obesity stands out as a risk factor for Type 2 DM, but we see some lean adult Type 2 diabetics subjects probably having latent autoimmune disease. Thus obesity may be a precursor for Type 2 DM, followed by insulin resistance [5]. Role of higher FFA level in the development of DM Type II in obese persons has not been reported so far in our knowledge. Though the FFA level in the blood has been reported to increase in case of obesity, the extent of increase may not be the same in all the obese person. Furthermore, all obese persons do not develop DM Type 2. In this study, we planned to examine the association of level of serum FFA, with the development of DM Type 2 in an obese person.

MATERIALS AND METHODS: The present study was conducted in the Department of Biochemistry, Shri Ram Murti Smarak Institute of Medical Sciences (SRMS, IMS) Bareilly, Uttar Pradesh, India.

Materials: 25 Adult normal persons, 25 Adult obese persons without DM Type II and 40 Adult, obese persons with DM Type II, were selected for the study. BMI was measured for each subject and proposed biochemical parameters were estimated in their blood samples. The subjects chosen were not on any drug treatment during days of blood collection.

Age of the subjects was between 25-65 years. Fasting blood glucose was estimated by Glucose oxidase and peroxidase (GOD-POD) method) [6]. Estimation of serum FFA was done by human FFA ELISA kit (Biomedical assay) [7].

RESULTS: Serum FFA level was estimated in the normal and obese persons with varying BMI. **Table 1** shows the prevalence of cases with serum FFA level below 500 µmol/l in the normal and obese group. There is a clear demonstration of very high frequency (91%) of cases with lower serum FFA level in the obese group as compared to the normal group with only 12% cases having lower serum FFA level The difference in the mean serum FFA level in the normal and obese group has been presented in **Table 2**. It shows serum free fatty acid level in normal healthy cases varied from 165 µmol/l to 4040 µmol/l with mean 1510.44 µmol/l and in obese cases varied from 0 µmol/l to 975 µmol/l with mean 217.83 µmol/l. There is a large difference in mean serum FFA level between normal and obese group (1510.44 *vs.* 217.83). The difference is statistically highly significant (p-value 0.001).

TABLE 1: PERCENTAGE PREVALENCE OF FREE FATTY ACID (FFA) LEVEL BELOW CUT OFF VALUE (500µmol/l) IN THE STUDY GROUPS

Groups	No. of cases taken	No. of cases below cut off the value	Percentages of cases below cut off the value
Normal	25	3	12%
Obese	65	59	91%
Obese without DM Type-II	25	20	80%
Obese with DM TYPE-II	40	39	98%

TABLE 2: STATISTICAL ANALYSIS OF THE SERUM FFA LEVEL IN CONTROL AND OBESE GROUP

Groups	No. of cases	Serum FFA(µmol/l)			P- value
		Range	Mean	SD	
Control	25	165 - 4040	1510.44	1143.90	0.0001
Obese	65	0 - 975	217.83	238.19	

TABLE 3: STATISTICAL ANALYSIS OF THE SERUM FFA LEVEL IN DIABETIC OBESE AND NON- DIABETIC OBESE GROUP

Groups	No. of cases	Serum FFA(µmol/l)			P-value
		Range	Mean	SD	
Obese without DM Type-2	25	15 - 975	277.72	319.60	0.10
Obese with DM Type-2	40	0 - 645	180.40	162.81	

NS- Not significant

The mean serum FFA level in diabetic and non-diabetic obese group was statistically analyzed and is given in **Table 3**. **Table 3** shows serum free fatty acid in obese without DM Type 2 varied from 15 µmol/l to 975 µmol/l with mean 277.72 µmol/l and in obese with DM Type 2 varied from 0µmol/l to 645 µmol/l with mean 180.40 µmol/l. There is an only a small difference (277.72 *vs.* 180.40) in the mean serum FFA level between the diabetic and non-diabetic obese group. The difference is not statistically significant (p-value 0.10). These results show that in our obese group the obesity is associated with lowering of serum FFA level. Thus it can be concluded that obesity is associated with a high prevalence of cases with lowered serum FFA and a large decrease in serum FFA in our study of obese cases.

Prevalence of cases with lower serum FFA level in diabetic and non-diabetic obese groups has been shown in **Table 3**. There is an only a small difference in the cases with lower serum FFA level between the diabetic and non-diabetic obese group. It can be inferred that the prevalence of cases lower serum FFA level is associated with obesity but not with DM Type 2 caused by obesity. This suggests that the decrease in the level of serum FFA is associated with obesity but not with DM Type 2 developed due to obesity.

DISCUSSION: Main source of serum FFA is the hydrolysis of fat stored in the adipose tissue by hormone-sensitive lipase [6, 3]. This enzyme is activated by hyperglycemic hormones glucagon, epinephrine, cortisone, thyroid hormones, and ACTH and inhibited by insulin [1]. Therefore serum FFA level increase during fasting and starvation. Its level has been reported to be higher in the case of DM type-I in a major way and DM Type-II in a minor way due to a corresponding increase in hyperglycemic hormones mainly glucagon. In obesity also the serum FFA level is expected to be higher due to increased fat mass and leptin action. Serum FFA level has also been reported to decrease the insulin response in muscle tissue, contributing thus to the development of DM-II, similar studies done by Pankow *et al*., Von Greevenbroek *et al*. [8, 9]

In our studies, a large decrease in the fasting serum FFA level has been found in the obese group in comparison to the normal BMI group, **Table 1**. This implies that the mobility of FFA from adipose tissue to blood is low in our obese group. Similar observation is showing down-regulation of the rate of mobilization of FFA from adipose tissue in obese person by Arner *et al*. and MacQuaid *et al*. [10, 14] This can be only explained by the low level of hormone-sensitive lipase in the adipose tissue of persons in our obese group, which is determined genetically.

This result provides a very new and interesting molecular mechanism for the development of obesity in our obese group. Even if the synthesis of fat and its deposition is normal, the low level of fat mobilization will result in a saving of fat and development of obesity. Thus the individuals with low level of HSL will be prone to obesity. The obese group studied by others may not be having the reduced level of hormone-sensitive lipase and therefore will not show the decrease in serum FFA level. As already discussed a variety of factors other than hormone-sensitive lipase may play a role in the development of obesity in the study group of other workers.

In our study no significant difference in serum FFA level between obese without diabetes and obese with diabetes was observed. Increase in serum FFA level in obese persons is expected on development of DM-II due to increased insulin resistance Alen Dresner *et al*., Boden *et al*., Pankow *et al*., Chai *et al*., & Salgin B *et al*. [12, 13, 14, 15, 16] and increased level of hypoglycemic hormones which activate the hormone-sensitive lipase. The contradictory result in our study can be explained by the fact that our obese group has a limited level of hormone-sensitive lipase, which is already fully activated in

obese persons, this also suggested by Arner P *et al*. [10] Increase in the level of activating hormones on the development of DM-II will not cause any further change in serum FFA level as expected on the development of DM II in our obese group.

CONCLUSION: Finally, we observed that the lowering of serum free fatty acid is associated with obesity but not responsible for the development of diabetes type 2 due to obesity.

ACKNOWLEDGEMENT: Nil

CONFLICT OF INTEREST: Nil

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How to cite this article:
Gupta M, Ziledar and Yadav N: Change in serum-free fatty acid (FFA) level associated with DM Type-II in obese person. Int J Pharmacognosy 2014; 1(10): 668-71. doi link: http://dx.doi.org/10.13040/IJPSR.0975-8232.IJP.1(10).668-71.