INTERNATIONAL JOURNAL OF SCIENCE AND NATURE

www.scienceandnature.org

STATUS OF SERUM FREE FATTY ACID (FFA) LEVEL IN OBESE PERSON AND ITS ASSOCIATION WITH DM TYPE-II

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ABSTRACT
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. Insulin resistance is increased by different factors but FFA is the most common factor to increase insulin resistance**.** The hallmarks are abdominal obesity, increased insulin resistance and decreased glucose tolerance. Most of the obese people (80%) are DM Type-II but all obese are not diabetic, why? Aim of this study was to studied the FFA level in obese without DM Type-II verses obese with DM Type-II subjects. 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 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 guide lines 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. 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 this study group.

KEY WORDS: Free fatty acid, obesity, diabetes mellitus, insulin.

INTRODUCTION

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 crore 70 lacs alone are in India, an alarming number in our country. It means that 5% deaths are due to this disease, the main reason of 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 [1]. Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia[2], several distinct types of DM exist and are caused by a complex interaction of genetic and environmental factors[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 have seen 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]. Depending on the etiology of the DM, factors contributing to hyperglycemia include reduced insulin secretion, decreased glucose utilization, and increased glucose production[1,2]. 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[1,3]. About 80% patients are obese; these patients have high plasma insulin levels. 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. Type 2 diabetes mellitus is characterized by 4 major metabolic abnormalities: obesity, impaired insulin action, insulin secretory dysfunction, and increased endogenous glucose output (EGO) [2, 3]. 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 blood has been reported to increase in case of obesity, but the extent of increase may not be same in the entire obese person. Furthermore, all obese persons will not develop DM Type 2. In view of the aforementioned controversial literature, it was decided to evaluate the association of level of serum FFA, with development of DM Type 2 in obese person.

MATERIALS & METHODS

The present study was conducted in the Department of Biochemistry, Shri Ram Murti Smarak Institute of Medical Sciences (SRMS, IMS) Bareilly, U.P. India. 25 Adult normal persons, 25 Adult obese persons without DM Type II and 40 Adult obese persons with DM Type II were selected for this study. BMI was measured for each subject and proposed biochemical parameters were estimated in their blood samples. Inclusion criteria of the study the subjects chosen were not on any drug treatment during days of blood collection. Exclusion criteria of study the subjects who were on drugs or treatment of DM. Age

of the subjects were between 25 – 65 years. Blood sample 5ml were collected by all subjects. 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]. A *p* value < 0.05 was considered significant. Statistical analysis was performed using GraphPad Prism version 5.00 for Windows (GraphPad software, San Diego California USA, www.graphpad.com).

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 500µmol/l in normal and obese group. There is a clear demonstration of very high frequency (91%) of cases with lower serum FFA level in obese group as compared to normal group with only 12% cases having lower serum FFA level.

TABLE 1: Percentage prevalence of free fatty acid (FFA) level below cut off value (500 µmol/l) in the study groups

Groups	No. of cases taken	No. of cases below cut off value	Percentages of cases below cut off 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%

The difference in the mean serum FFA level in 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 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	

The mean serum FFA level in diabetic and nondiabetic 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 15µmol/l to 975 µmol/l with mean 277.72 µmol/l and in obese with DM Type 2 varied from 0 µmol/l to 645µmol/l with mean 180.40 µmol/l. There is only small difference (277.72 vs. 180.40) in the mean serum FFA level between diabetic and non diabetic obese group. The difference is not statistically significant (p value 0.10).

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

Results showed that in obese group the obesity was associated with lowering of serum FFA level. There was only small difference in the cases with lower serum FFA level between 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.

DISCUSSION

Main source of serum FFA is the hydrolysis of fat stored in the adipose tissue by hormone sensitive lipase[6]. 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. It's level has been reported to be higher in case of DM type –I in major way and DM Type-II in minor way due to 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 large decrease in the fasting serum FFA level has been found in obese group in comparison to 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 showing down regulation of rate of mobilization of FFA from adipose tissue in obese person by Arner *et al* & MacQuaid *et al* [10,14]. This can be only explained by 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 into saving of fat and development of obesity. Thus the individuals with low level of HSL will be prone to obesity.

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 variety of factors other than hormone sensitive lipase may play role in the development of obesity in the study group of other workers. In our study there were not found any 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*)[12-16] and increased level of hypoglycemic hormones which activate the hormone sensitive lipase. Contradictory result in our study can be explained by the fact that our obese group have 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 development of DM-II will not cause any further change in serum FFA level as expected on development of DM II in our obese group.

CONCLUSION

In this study we were 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. Thus it can be concluded that the obesity is associated with high prevalence of cases with lowered serum FFA and large decrease in serum FFA in obese cases. 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.

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Abbreviations used: FFA- free fatty acid, DM- diabetes Mellitus, BMI- body mass index, ELISA- enzyme linked immuno sorbent assay.