How to Cite:

**Evaluation of PPAR-γ With Lipid Profiles and Blood Glucose in Obese Persons with DM Type 2 and Obese Persons Without DM Type 2**

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*Abstract*---PPAR-γ is expressed at high levels in adipose tissue and is a central regulator of adipocyte gene expression and differentiation. PPAR-γ is induced during adipocyte differentiation, and retroviral expression of PPAR-γ stimulates adipose differentiation of cultured fibroblasts. Several studies demonstrate that PPAR-γ is both necessary and sufficient to promote differentiation of fat cells both in vivo and in vitro. The present study has been conducted at the Department of Biochemistry, Shri Ram Murti Smarak Institute of Medical Sciences (SRMS IMS), Bareilly U.P. India. Among 30 Adult normal persons, 30 Adult obese persons without DM type 2 and 30 Adult obese persons with DM type 2 were selected for the study. BMI was measured for each subject and proposed biochemical parameters were estimated in their blood samples. The Subject chosen were not on any drug treatment during days of blood collection. Age of the subject was between 25-65 years. For the present study 30 normal (control) and 60 obese cases were taken. Out of 60 obese cases, 30 were found to be without DM Type-2 and 30 cases with DM Type-2. The level of PPAR-γ in obese with DM-2 varies from 0.01mg/dl to 35.6mg/dl with mean 8.04mg/dl and control group varied from 0.2mg/dl-8mg/dl with mean 2.45mg/dl. The difference in the level of PPAR-γ between obese with DM-2 and control group is significant (p value 0.008). The level of PPAR-γ in obese without DM-2 varied from 0.1ng/ml to 36ng/ml with mean 8.03ng/ml and control group varied from 0.2ng/ml-8.1 ng/ml with mean 2.45ng/ml. The difference in the level of PPAR-γ between obese without DM-2 and control group is significant (p value 0.01) Considering the wide range of actions on glucose, lipid metabolism and cell proliferation/apoptosis, PPARs and
their modulators are suggested for the treatment of metabolic disorders such as hyperglycaemia, dyslipidemia and atherosclerosis. The prevention and treatment of both lipid and glucose profile disorders should consider the potency and affinity of selective PPARs and their potential influences.

**Keywords**—PPAR-γ, lipid profiles, blood glucose, DM type 2.

**Introduction**

The incidence of obesity (defined as having a body mass index (BMI) of greater than 30 kg per m$^2$) is increasing dramatically in virtually all societies of the world, and with it come important pathological consequences such as type 2 diabetes mellitus and cardiovascular disease. The global incidence of type 2 diabetes is projected to double to 350 million cases by the year 2030. Although progression to type 2 diabetes occurs more frequently in obese humans compared with lean individuals, this association is highly dependent on genetic background. Inbred mouse strains vary widely in their metabolic response to high-fat diets and to the impact of obesity on insulin sensitivity and development of diabetes.

Likewise, despite an increased risk, many obese human subjects do not progress to the diabetic state, which suggests that genetic and/or environmental factors also play a part. Nonetheless, it is generally accepted that two features are particularly critical for obesity to elicit type 2 diabetes. First, impaired responsiveness of skeletal muscle to insulin is a primary condition in obesity and a precondition for the onset of type 2 diabetes. The association between obesity and skeletal muscle insulin resistance is probably a causal relationship, as studies in humans and animals indicate that weight loss and gain correlate with increasing and decreasing insulin sensitivity, respectively. In insulin-resistant individuals that are not diabetic, glycaemic control can be maintained by compensatory increases in insulin secretion by pancreatic β-cells. Thus, a second defect required for progression from insulin resistance to type 2 diabetes is the failure of β-cells to secrete the required levels of insulin that maintain normal fasting blood glucose levels.

PPAR-γ is expressed at high levels in adipose tissue and is a central regulator of adipocyte gene expression and differentiation. PPAR-γ is induced during adipocyte differentiation, and retroviral expression of PPAR-γ stimulates adipocyte differentiation of cultured fibroblasts. Several studies demonstrate that PPAR-γ is both necessary and sufficient to promote differentiation of fat cells both in vivo and in vitro. In contrast, PPAR-γ antagonists inhibit adipocyte differentiation. Consistent with these findings, humans with dominant-negative mutations in PPAR-γ manifest partial lipodystrophy and severe peripheral and hepatic insulin resistance because of increased triglyceride and fatty acid deposition into skeletal muscle and liver.

Clearly, there would be great benefits if research could achieve effective prevention and therapies for obesity and associated type 2 diabetes. Hampering these efforts are many complexities in studying metabolic disease, including a
strong social influence on the incidence of obesity. This is reflected in the Indian
by the striking inverse correlation between obesity and income. Furthermore, it is
difficult to determine the molecular mechanisms that underlie metabolic disease
from studies on human subjects.

Materials and Methods

The present study has been conducted at the Department of Biochemistry, Shri
Ram Murti Smarak Institute of Medical Sciences (SRMS IMS), Bareilly U.P. India.
Among 30 Adult normal persons, 30 Adult obese persons without DM type 2 and
30 Adult obese persons with DM type 2 were selected for the study. BMI was
measured for each subject and proposed biochemical parameters were estimated
in their blood samples. The Subject chosen were not on any drug treatment
during days of blood collection. Age of the subject was between 25-65 years.
Subjects were taken from out-patient Department and Indoor-patient Department
of Medicine, SRMS IMS Bareilly U.P. India. Subjects were of both sexes coming
from reasonable distance around Bareilly city, U.P. India. They were from lower
and middle class of rural area having moderate physical activities, with vegetarian
as well as non-vegetarian dietary habits.

The Height (meters), weight (kg) and BMI were recorded. Obese subjects had a
BMI equal or greater than 25 and normal subject had a BMI less than 25. The
waist (waist circumference was measured with a soft tape a standing subject mid
way between the lower rib and iliac crest) (hip circumference was measured over
the widest part and gluteal region) and therefore waist to hip ratio measured. The
detailed history of all the subjects were taken, and it was insured that the patient
were not any drug treatment and were on overnight fasting for statistical
significance and comparison, all these cases were divided into four different
groups.

Group-1: Control Group
Serum PPAR-γ level along with lipid profile and fasting Blood glucose was done in
30 normal healthy individuals of both sexes. Each individual of this group was
examined clinically and was included in the study after finding them a normal
individual.

Group-2: Obese Group: Serum PPAR-γ level along with lipid profile and fasting
Blood glucose was estimated in 60 cases of obese persons.

Group-3: Obese without DM type-2
Out of 60 cases of obese, 30 were obese without DM type-2 selected as the basis
of fasting Blood glucose level.

Group-4: Obese with DM type-2
Out of 60 cases of obese, 30 were obese with DM type-2, selected on the basis of
fasting Blood glucose level.
**Inclusion Criteria**

1. All the patients were without any drugs treatment during blood sample collection.
2. Had some symptoms of Diabetes Mellitus.
3. Obese on the basis of BMI i.e. more than 25

**Exclusion Criteria**

2. Cases suffering from chronic diseases.

Following estimation were done in Department of Biochemistry, SRMS IMS Bareilly U.P. India.

1. Fasting Blood Glucose level in serum.
2. Serum PPAR-γ

Local Research Ethic Committee approval was taken for the study before it commenced. Written consent was taken from the subject included in the study.

**Sample processing**

Before collecting venous blood sample using standard venipuncture into vial subjects were asked to have a fasting period of 12 hrs. for the standardization blood was drawn in sitting position from anticubital vein. These samples were collected in three different vial are for measuring factor included in the study i.e. PPAR-γ. Blood was allowed to clot and was immediately centrifuged at 5000rpm for 10 minutes. Serum was collected and stored immediately at -20c until assay performed.

**Method of serum PPAR-γ level estimation**

The qualitative estimation of PPAR-γ in human serum was done by ELISA method using ELISA kit from E lab science Biotechnology co.ltd.

**Result**

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Phenotypic characters of the studied groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age Range</td>
<td>Group 1 (30-57)</td>
</tr>
<tr>
<td>(year) Mean±SD</td>
<td>44.8± 8.1</td>
</tr>
<tr>
<td>Fasting bl. glucose Range(mg/dl)</td>
<td>60 - 90</td>
</tr>
<tr>
<td>Mean±SD</td>
<td>64.8± 5.35</td>
</tr>
<tr>
<td>Post prandial glucose.</td>
<td>100-130</td>
</tr>
</tbody>
</table>

p= 0.75

<0.001
<table>
<thead>
<tr>
<th>Range (mg/dl) Mean±SD</th>
<th>105.34±10.38</th>
<th>112.36±10.97</th>
<th>124.4±12.5</th>
<th>166.6±12.3</th>
<th>&lt;0.001</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting Insulin. Range (µu/ml)</td>
<td>5.9 -10</td>
<td>7 -15</td>
<td>8.2 -15.5</td>
<td>12 -15.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean±SD</td>
<td>7.98±1.1</td>
<td>8.4±1.6</td>
<td>9.8 ± 1.14</td>
<td>14.57±0.99</td>
<td></td>
</tr>
</tbody>
</table>

BMI: Body Mass Index HOMA-IR homeostasis model assessment of insulin resistance.

### Table 2
The distribution of cases taken

<table>
<thead>
<tr>
<th>Group</th>
<th>BMI (Kg/m²)</th>
<th>No. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>&lt;25</td>
<td>30</td>
</tr>
<tr>
<td>Group 2</td>
<td>&gt;25</td>
<td>60</td>
</tr>
<tr>
<td>Group 3</td>
<td>&gt;25</td>
<td>30</td>
</tr>
<tr>
<td>Group 4</td>
<td>&gt;25</td>
<td>30</td>
</tr>
</tbody>
</table>

For the present study 30 normal (control) and 60 obese cases were taken. Out of 60 obese cases, 30 were found to be without DM Type-2 and 30 cases with DM Type-2. This is shown in Table-2

### Table 3
Lipid profile of the studied groups

<table>
<thead>
<tr>
<th>Lipid profile</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol</td>
<td>211.01±18.1</td>
<td>231.12±17.5</td>
<td>241.01±18.2</td>
<td>281.01±19.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>149.7±12.1</td>
<td>150.1±11.3</td>
<td>268.9±12.4</td>
<td>279.2±13.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HDL</td>
<td>42.9±3.1</td>
<td>43.1±4.2</td>
<td>40.6±4.1</td>
<td>37.9±3.9</td>
<td>&lt;0.048</td>
</tr>
<tr>
<td>LDL</td>
<td>126.2±8.9</td>
<td>127.2±8.9</td>
<td>117.6±9.2</td>
<td>128.3±9.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VLDL</td>
<td>158.3±9.3</td>
<td>159.1±11.4</td>
<td>147.8±12.1</td>
<td>159.6±13.2</td>
<td>&lt;0.037</td>
</tr>
</tbody>
</table>

### Table 4
Statistical analysis of level of PPAR-γ in obese cases with DM-2 and control group. (Non obese non Diabetic)

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of cases</th>
<th>PPAR-γ (ng/ml)</th>
<th>P-value</th>
<th>Remark</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Range</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Obese with DM Type 2</td>
<td>30</td>
<td>0.1-35.6</td>
<td>8.04</td>
<td>10.94</td>
</tr>
<tr>
<td>Control group- Non obese Non Diabetic</td>
<td>30</td>
<td>0.2-8.1</td>
<td>2.45</td>
<td>1.99</td>
</tr>
</tbody>
</table>

Table 4 shows level of PPAR-γ in obese with DM-2 varies from 0.01mg/dl to 35.6mg/dl with mean 8.04mg/dl and control group varied from 0.2mg/dl-8mg/dl with mean 2.45mg/dl. The difference in the level of PPAR-γ between obese with DM-2 and control group is significant (p value 0.008)
### Table 5
Statistical analysis of level of PPAR-γ in obese cases without DM-2 and control group. (Non obese non Diabetic)

<table>
<thead>
<tr>
<th>Groups</th>
<th>No. of cases</th>
<th>PPAR-γ (ng/ml)</th>
<th>P-value</th>
<th>Remark</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Range</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Obese without DM-2</td>
<td>30</td>
<td>0.1-36</td>
<td>8.03</td>
<td>11.16</td>
</tr>
<tr>
<td>Control group</td>
<td>30</td>
<td>0.2-8.1</td>
<td>2.45</td>
<td>1.99</td>
</tr>
</tbody>
</table>

Table 5 shows the level of PPAR-γ in obese without DM-2 varied from 0.1ng/ml to 36ng/ml with mean 8.03ng/ml and control group varied from 0.2ng/ml-8.1 ng/ml with mean 2.45ng/ml. The difference in the level of PPAR-γ between obese without DM-2 and control group is significant (p value 0.01)

### Discussion

Obesity and diabetes mellitus, significant risk factors for the development of CAD, are becoming a global epidemic, which is related to environmental, behavioral, and genetic factors. Although changes in lifestyle are effective in preventing both diabetes and obesity in high-risk adults with impaired glucose tolerance, achieving modifications in lifestyle have proven to be difficult. Current recommendations suggest that in addition to nonpharmacological methods, drug therapy should be considered for patients with a BMI ≥30 kg/m² or a BMI of 27 to 30 kg/m² with ≥1 obesity-related disorders. Currently available antiobesity medications either decrease food intake or reduce intestinal fat absorption. However, short-term clinical trials evaluating antiobesity medications demonstrated only modest weight loss compared with placebo, and there are no long-term clinical trials to examine mortality and cardiovascular morbidity.

The adipose tissue plays a crucial role in the regulation of food intake, because it secretes a number of endocrine and paracrine mediators, including leptin, adiponectin, resistin, and TNF-α, which have been shown to influence appetite. Understanding the complex signaling system that underlies appetite control will likely offer new approaches for treatment strategies. The ability of PPAR-δ agonists to induce adaptive thermogenesis and protect against both diet-induced and genetically predisposed obesity in animal models suggest that PPAR-δ might be an exiting new target in the treatment of obesity. Of particular interest are the dual PPARs, a single ligand activating both γ and α and the pan PPARs, activating α, γ, and δ.

All 3 of the PPAR isotypes attenuate inflammatory responses, which is important, because inflammation is intimately connected to appetite, insulin resistance, obesity, and atherosclerosis. These antiinflammatory actions result in improvement of atherosclerosis in some animal models, although the effect on atherosclerosis is also related to the PPAR ability to regulate foam cell formation. Future studies are required to elucidate these interactions and the role of PPAR ligands as potential candidates for treatment of obesity, type 2 diabetes, and atherosclerosis.

PPARγ function might be modulated by inflammatory signalling is through its interactions with co-activators and corepressors. Numerous such activities have been found in association with PPARγ and other nuclear receptors.
effect of PPARγ on energy storage (as triglyceride) compared with energy use (through oxidative pathways) depends in part on the balance among coregulators, which favour distinct pathways. Co-activators of PPARγ include steroid receptor co-activator-2 (SRC-2) and C-terminal-binding protein (CBP), which promote adipogenesis and energy storage. The nuclear hormone corepressor-receptor-interacting protein-140 (RIP140), however, negatively regulates oxidative pathways in adipocytes at least in part through interaction with PPARγ. Conversely, PPARγ activity can be enhanced by the PPARγ co-activator-1α (PGC-1α), initially identified through its interaction with PPARγ in brown fat.

**Conclusion**

Considering the wide range of actions on glucose, lipid metabolism and cell proliferation/apoptosis, PPARs and their modulators are suggested for the treatment of metabolic disorders such as hyperglycaemia, dyslipidemia and atherosclerosis. The prevention and treatment of both lipid and glucose profile disorders should consider the potency and affinity of selective PPARs and their potential cancerogenic influences. Therefore, natural compounds and their close derivatives are being targeted as future drugs against metabolic diseases. Even though early preclinical data are very promising, it is necessary to evaluate the clinical properties of new PPAR agonists and their influence on patient health.

**References**

8. Boitier E, Gautier JC, Roberts R: Advances in understanding the regulation of apoptosis and mitosis by peroxisome proliferator activated receptors in pre-


