Obesity and type 2 diabetes are important causes of morbidity and mortality in youth and middle-aged people all over the world. Often both these conditions co-exist in the same subjects. The metabolic dysregulation and complications of obesity and type 2 diabetes are similar in many respects such as insulin resistance, dyslipidemia, atherosclerosis, hypertension, cardiovascular and cerebrovascular diseases [Klein & Romijn, 2009; Schelbert, 2009]. The most important aspect of metabolic dysregulation in type 2 diabetes is reduced glucose utilisation, excess mobilization of fatty acids from adipose tissue, excessive storage of triacylglycerol and other lipid moieties in non-adipose tissues, impaired oxidation of fatty acids, dyslipidemia, insulin resistance etc. which are particularly conspicuous in skeletal muscle, liver, heart, adipose tissue and pancreatic β cells [Goossens, 2008; Laclaustra et al., 2007; Van Harpen & Schrauwen-Hinderling, 2008].
Recently many studies have indicated several forms of mitochondrial dysfunctions in skeletal muscle, white adipose tissue, liver and beta cells in diabetes and obesity both in clinical subjects and experimental models [Abdul-Ghani & DeFronzo, 2008; Bonnard et al., 2008; Hojlund et al., 2008]. In type 2 diabetes patients and animal models down regulation of genes coding for subunits of respiratory complexes, altered mitochondrial structure, decreased number of mitochondria, diminished mitochondrial DNA (mtDNA) content and decreased mitochondrial respiration have been reported [Choo et al., 2006; Dahlman et al., 2006; Laye et al., 2009; Patti & Corvera, 2010]. Further, several studies have shown the functional status of mitochondria in adipose tissue and skeletal muscles of obese subjects and animal models [Heilbronn et al., 2007; Hojlund et al., 2008; Kraunsøe et al., 2010]. Several forms of mitochondrial dysfunction such as reduction of mitochondrial size and mtDNA content and lower mitochondrial respiration rates have been observed in obesity [Choo et al., 2006; Kaaman et al., 2007; Kraunsøe et al., 2010]. However, it is still not clearly established to what extent obesity impacts the functional status of mitochondria in type 2 diabetes and this is especially important since very often both obesity and type 2 diabetes co-exist in the same subject [Klein & Romijin, 2009; Schelbert, 2009].

There is a possibility that abnormal turnover and accumulation of metabolites in type 2 diabetes can directly affect mitochondrial enzyme systems or oxidative phosphorylation machinery. However, the bioenergetic failure of mitochondria in obese type 2 diabetes or obese non-diabetic
subjects is observed even in isolated mitochondria under in vitro conditions where the organelles are removed from the internal milieu of type 2 diabetes or obesity [Mogensen et al., 2007; Ritov et al., 2005]. This implies that intrinsic changes in mitochondrial structure and functions take place in type 2 diabetes and obesity presumably by modulating the expression of specific genes regulating mitochondrial biogenesis, structure and dynamics, but the molecular details of these alterations are not known. It is a well known fact that non-obese type 2 diabetes constitutes a significant proportion of type 2 diabetes population in some countries like India as well as certain developing countries of Asia and Africa [Kumar et al., 2008; Mohan et al., 1997]. So far most of the studies regarding mitochondrial impairment in type 2 diabetes have included only obese diabetic subjects and it is uncertain to what extent the observations are valid for non-obese type 2 diabetes subjects [Choo et al., 2006; Dahlman et al., 2006; Laye et al., 2009]. The association between mitochondrial dysfunction and type 2 diabetes has not been so far studied in non-obese individuals.

Thus many lacunae and short-comings are present in our understanding of mitochondrial dysfunction in type 2 diabetes and obesity and the present work has been undertaken to address a few of these issues. Firstly, the status of mitochondrial oxidative phosphorylation in isolated preparations in vitro has been assessed in obese non-diabetic, non-obese type 2 diabetes and obese type 2 diabetes patients in the present study. Secondly, an attempt has been made to understand whether the functional incompetence of mitochondria in obesity and obese type 2 diabetes results from decreased
copy number of proteins related to oxidative phosphorylation (OXPHOS) system in an individual mitochondrion and if similar changes also exist in non-obese type 2 diabetes. Further, the changes in mitochondrial biogenesis related transcription factors and co-activators have also been examined in this context. All mitochondria related investigations have been made in the subcutaneous adipose tissue in this study, since the latter along with skeletal muscle is most profoundly affected by the metabolic derangements of type 2 diabetes and obesity.

Adipose tissue apart from its role in lipid metabolism, also secretes several bioactive peptides collectively known as adipokines with paracrine, autocrine and endocrine functions regulating food intake and energy metabolism [Guerre-Millo, 2004; Ronti et al., 2006]. Mitochondrial dysfunction in adipose tissue could result in the alteration of synthesis and secretion of adipokines which might be causally related to the development of diabetic complications [Koh et al., 2007; Patti & Corvera, 2010]. For this purpose, the levels of adiponectin and leptin in sera of control, obese non-diabetic, non-obese type 2 diabetes and obese type 2 diabetes subjects have been examined and correlated to the tissue adipose mitochondrial status in each group.

Altered metabolism of reactive oxygen species (ROS) is one of the important consequences of mitochondrial dysfunction in any tissue. Mitochondria derived ROS can damage mitochondrial proteins, phospholipids and DNA by free radical reactions. They can also alter mitochondrial biogenesis.
programme or can modulate the redox signalling within the cells [Halliwell & Gutteridge, 1999; Piantadosi & Suliman, 2006]. In light of this fact, it has been thought interesting to assess the status in ROS metabolism in mitochondria of adipose tissue of control as well as type 2 diabetes subjects with or without obesity.