The need for co-ordinated studies for obesity-related problems like diabetes mellitus in Libyan population

Obesity is one of the major risk factors of type 2 diabetes and is associated with many metabolic derangements that impair insulin sensitivity (1, 2). These abnormalities include excess lipolysis causing increased concentrations of non-esterified fatty acids and triglycerides in blood and skeletal muscle. Muscle glucose uptake is suppressed.

Figure 1 gives the possible biochemical mechanisms involved in the evolution of insulin resistance and insulin-resistant states including diabetes.

Obesity is reported to affect insulin action by changing the secretion of adipocytokines, specifically of leptin and adiponectin (3) and leads to proinflammatory conditions (4). Features of insulin resistance, including hypertriglyceridaemia and increased abdominal or visceral fat, are seen even in non-obese populations (5). There is a positive association between body mass index and glucose intolerance in most of the studies reported in the literature. Although the WHO body mass index figure should be retained as an international classification, individual countries could make decisions about the definition of increased risk for their populations (5).

Insulin resistance is associated with visceral and subcutaneous fat content (6). Glucose disposal rate and plasma adiponectin concentration are inversely related to fat-cell size (6).

Fatty acid influx to the liver is an important pathogenetic factor for fatty liver and is also a determinant of excess triglyceride-rich lipoproteins. Dyslipidaemia in type 2 diabetes is more severe in the presence of fatty liver (7).

Ectopic fat accumulation in the liver and skeletal muscle is an important determinant of insulin resistance and can also predispose to development of type 2 diabetes (8). The twin cycle hypothesis put forth in a review by Taylor (9) explains the cycle of reactions linking muscle insulin resistance, ectopic fat deposition in the liver and islets, hepatic insulin resistance and β-cell dysfunction, eventually resulting in the onset of type 2 diabetes (Fig. 2).

Cycle A. Development of fatty liver, which leads to an increase in plasma glucose levels and basal levels of insulin in the plasma. *Cycle B.* Sequences of changes in tissue when exposed to higher concentration of triacylglycerol that results in decreased response to insulin following glucose ingestion. Postprandial response to glucose becomes blunted. These vicious cycles have an adverse inhibitory effect on islet cell, resulting in the precipitation of clinical diabetes.

Such pathogenetic mechanisms are cited as possible mechanisms of insulin resistance and islet cell response affected by maladaptation to modernisation and affluence.

Certain populations produce higher amounts of adenosine triphosphate despite being more insulin resistant and have higher intramuscular triglyceride concentrations than do Western populations (10). It is suggested that intramuscular triglycerides may vary from population to population as seen in Asian Indians having higher levels of triglycerides compared to Western counterparts with and without diabetes, suggesting a possible difference in the association of insulin resistance and diabetes in this population (8). Moreover, plasma triglycerides and non-muscle triglycerides are strongly associated with insulin sensitivity (11).

A pathophysiological link has been shown between obstructive sleep apnoea and excess visceral fat, independent of overall body fat (12). Obstructive sleep apnoea might be directly related to insulin resistance in both obese and non-obese people (12). Physical inactivity and sleep deprivation might also be contributing factors for many of the inflammatory, oxidative, endothelial and coagulation abnormalities that are associated with phenotype hypotheses, which seem to apply to Asian populations.

Offspring of women who are obese or have diabetes are at an increased risk of diabetes and other cardiometabolic complications (13–15). In view of the increase in childhood obesity and increasing number of women with young-onset diabetes in most countries, including Libya, this link will further exacerbate the situation by creating a vicious cycle of diabetes begetting diabetes.

The mechanism underlying such transgenerational inheritance of disease risk is under intense investigation; it is thought to involve epigenetic silencing of target genes via methylation or histone modification during development, resulting in a mismatch between the metabolic phenotype that was programmed during development and the nutritionally rich adult environment (Fig. 3) (12). Again, this mismatch might be most pronounced in countries that are undergoing the most rapid economic development. Improved understanding of the effect of maternal imprinting phenotype hypotheses may also apply to Libyan populations.
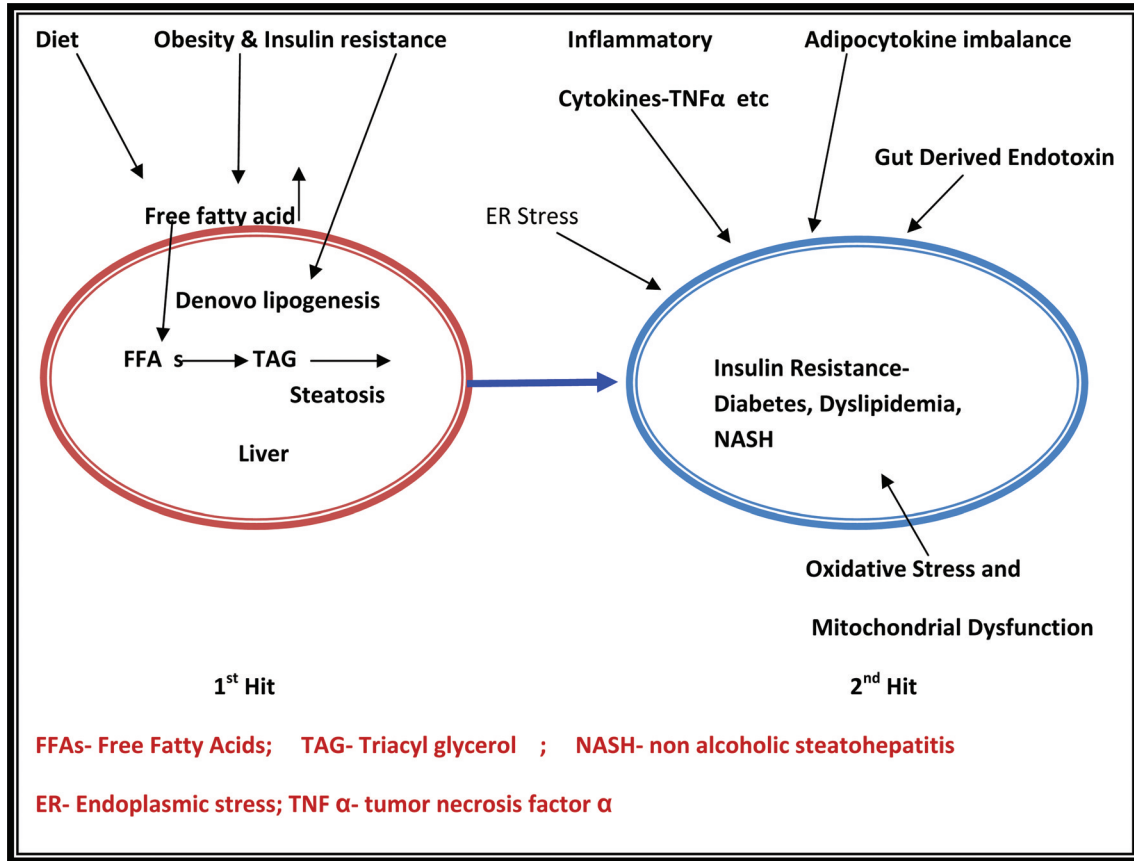
Fig. 1. Diagrammatic representation of development of insulin resistance and diabetes.
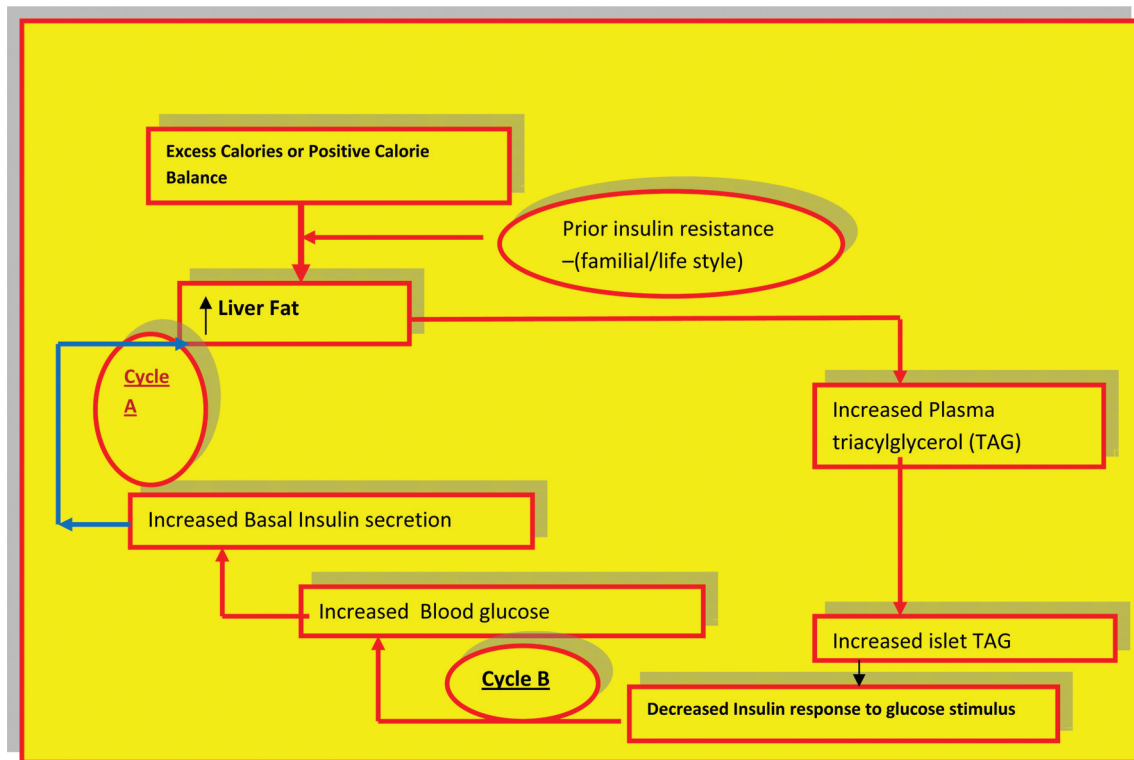

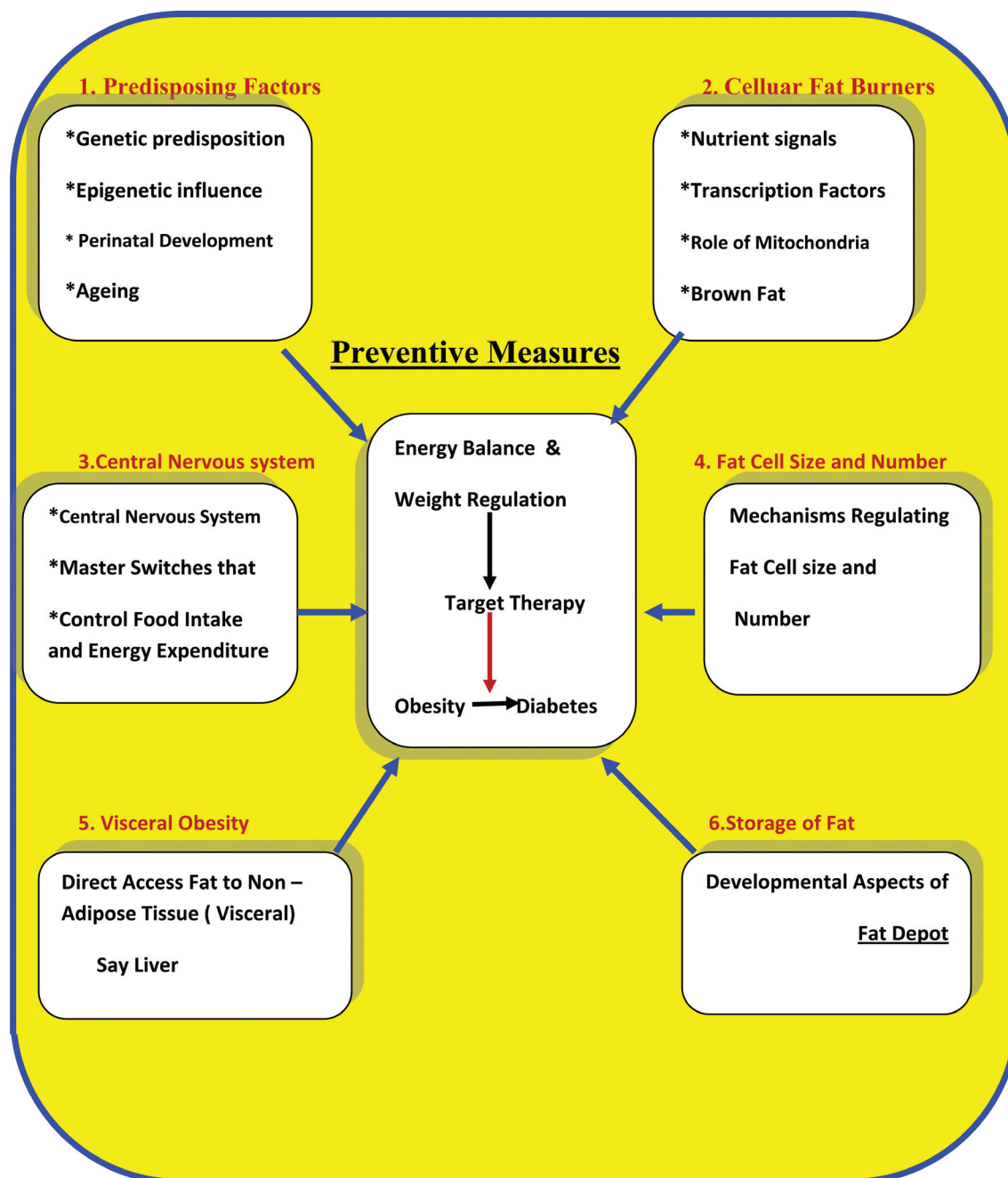Fig. 2. Pathogenesis of diabetes mellitus-twin cycle model.

1. Predisposing Factors
- *Genetic predisposition
- *Epigenetic influence
- * Perinatal Development
- *Ageing

2. Celluar Fat Burners
- *Nutrient signals
- *Transcription Factors
- *Role of Mitochondria
- *Brown Fat

Preventive Measures

Energy Balance & Weight Regulation → **Target Therapy** → **Obesity → Diabetes**

3.Central Nervous system
- *Central Nervous System
- *Master Switches that
- *Control Food Intake and Energy Expenditure

4. Fat Cell Size and Number
Mechanisms Regulating Fat Cell size and Number

5. Visceral Obesity
Direct Access Fat to Non – Adipose Tissue (Visceral) Say Liver

6.Storage of Fat
Developmental Aspects of Fat Depot

Fig. 3. Possible influence of genetic, metabolomics, environmental factors on the development progression of obesity to clinical diabetes mellitus.

An understanding of the various factors involved in obesity pandemic leading to diabetes is illustrated in Fig. 3.

The little scientific data available regarding diabetes in Libya (16–21) warn of the possibility of a diabetic pandemic that warrants an institution of a National Diabetic Control Policy.

A co-ordinated study related to obesity and obesity-related diseases needs to be planned and undertaken. Such a study could focus on: (1) predisposing factors including perinatal development, ageing, genetic and epigenetic influences; (2) certain cellular burners explained by the role of nutrient signals, their influences on transcription factors involved in lipogenesis, mitochondrial generation of reactive oxygen species (ROS) including the role of brown adipose tissue; (3) the role of central nervous system (CNS) regulating food intake and energy expenditure; (4) a greater understanding of the role of adipose tissue, its developmental aspects, adipocyte size and number, secretion of adipocytokines like adiponectin,

leptin and other proinflammatory markers like tumor necrosis factor α (TNF α), metabolic dynamics of fat storage and release including insulin resistance (22–24) and the pathological effect of visceral adiposity (abdominal obesity) (4).

These studies, in combination with environmental and metabolic aspects of obesity, will help to devise ways and means to regulate energy balance and weight regulation. The results of such studies will help to formulate therapeutic measures to fight obesity and obesity-related problems. This will help translate the findings of such studies to prevent the progression of obesity towards the precipitation of clinical diabetes in Libya, a society with high levels of consanguineous marriage.

Conclusion

A national road map, designed with such factors as those explained in Fig. 3, will help give direction and devise research methods to study obesity and obesity-related disorders in Libya. As obesity threatens the health of a community, particularly children and young adults, its sociological aspect mandates planning to prevent such precipitation of non-communicable diseases like diabetes, hypertension and cardiovascular diseases.

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