CHAPTER II
REVIEW OF LITERATURE

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CHAPTER II
REVIEW OF LITERATURE

2.1. Introduction

The history of diabetes has its beginning in antiquity. Writings attributed to the earliest civilizations (Asia minor, China, Egypt and India) refer to a condition with boils and infections, excessive thirst, loss of weight, and the passing of large quantities of honey-sweet urine, which often drew ants and flies.

The earliest known record of diabetes is found on 3rd dynasty Egyptian papyrus. Ebers papyrus by physician Hesy-Ra (1552 BC) mentions polyuria as a symptom. The first known clinical description of diabetes appears to have been made by Aulus Cornelius Celsus (30BC-50AD).

The term diabetes was first coined by Areteaus of Cappadocia(81-133AD). It was derived from the Greek word diabainein, which is a combination of the prefix dia - ‘across, apart’, and the verb bainein, ‘to walk, stand’. The word diabainein meant ‘to stride, walk, or stand with legs asunder’. Hence its derivative diabetes meant ‘one that straddles,’ or specifically ‘a compass, siphon’. The sense siphon gave rise to the use of the diabetes as the name for a disease involving the discharge of excessive amount of urine.

Areteaus described diabetes in the following words; “Diabetes is a dreadful affection, not very frequent among men, being a melting down of the flesh
and links into urine. The patients never stop making water and the flow is incessant, like the opening of aqueducts. Life is shocked and pleasant and painful, thirst unquenchable, drinking excessive, and disproportionate to the large quantity of urine.”

Diabetes is first recorded in English, in the form diabetes, in a medical text written around 1425. In 1675, Thomas Willis added the word mellitus, which in Latin means ‘honey’, a reference to the sweet taste of urine. This sweet taste had been noticed in urine by ancient Greeks, Chinese, Egyptians, Indians and Persians.

Diabetes mellitus appears to have been a death sentence in ancient times. Hippocrates makes no mention of it, which indicates that he felt the disease was incurable. Areteaus did attempt to treat it but could not give a good prognosis.

Sushruta (6th century BC) identified diabetes and named it Medhumeha. He was the first physician to relate it with obesity and sedentary lifestyle. He recommended exercise as a best way to ‘cure it’. The ancient test for diabetes in India was to observe whether ants were attracted to a person’s urine, and from the process, the ailment got the name ‘sweet urine disease’ (Medhumeha). The Chinese, Japanese, and Korean words for diabetes are based on the same ideographs which mean ‘sugar urine disease’.

In medieval Persia, Avicenna (980-1037) providing a detailed account on diabetes mellitus in his Canon of Medicine pointed out its symptoms such as
“abnormal appetite and the collapse of sexual functions”. He too documented the sweet taste of diabetic urine. He recognized a primary and a secondary diabetes. He dealt with diabetic gangrene, and treated diabetes using a mixture of lupine, trigonella, and zedoary seed, which was found to effect considerable reduction in the excretion of sugar, a treatment which is still prescribed in modern times. Avicenna noted diabetes insipidus very precisely for the first time, though it was later Johann Peter Frank (1745-1821) who first differentiated between diabetes mellitus and diabetes insipidus.

In 1766 Mathew Dobson proved that the sweet taste of diabetic urine was due to its sugar content. He made the crucial observation of the excess of sugar in blood. Accounts of the diets of the middle class in northern European countries during the 15th, 16th and 17th centuries carry description of meals consisting of many courses of roast meat, dripping with fat, rich and sugary pastries, and plenty of butter and cream, but little coarse red or green leafy vegetables.

However, it was not until 1869 that the islets of cells were discovered in pancreatic tissue by Paul Langerhans (1849-1888) and were later given his name. He was never to know the significance of his discovery as he died in 1888, one year before the key observation of Von Mering (1849-1908) and Oscar Minkowski (1858-1931) that removal of the pancreas led to the development of diabetes in dogs.
In 1910, Sir Edward Albert Sharpey-Schafer suggested that people with diabetes were deficient in a single chemical substance that was normally produced by the pancreas – he proposed calling this substance insulin, from the Latin insular, meaning island, in reference to the insulin-producing Islets of Langerhans in the pancreas.

The endocrine role of pancreas in metabolism, and indeed the existence of insulin, was not further investigated into until 1921, when Sir Fredrick Grant Banting and Charles Herbert Best repeated the experiment of Von Mering and Minkowski, and further demonstrated that they could reverse induced diabetes in dogs by giving them an extract from the pancreatic islets of Langerhans of healthy dogs. Banting and Best and their partners succeeded in purifying the hormone insulin from bovine pancreases at the University of Toronto. This led to the availability of an effective treatment-insulin fit for injections-and the first patient was treated with it in 1922. For this, Banting and the laboratory director Macleod were awarded the Nobel Prize in physiology and medicine. In 1923, Banting was further honoured by celebrating World Diabetes Day on his birthday, November 14.

The distinction between what is now known as type 1 diabetes and type 2 diabetes was first clearly made by Sir Harold Percival (Harry) Himsworth in his treatise, published in January 1936.
2.2. Anatomy

The pancreas (pan=all; kreas=flesh) is a gland that is partly exocrine and partly endocrine. The exocrine part secretes the digestive pancreatic juice and the endocrine part secretes hormones. Pancreas lies behind the peritoneum between the greater curvature of the stomach and the duodenum. It is an elongated structure approximately 15cms long, weighing approximately 85 to 100 grams. The head of the pancreas lies near the duodenum and its body and tail extends towards the spleen.

The endocrine function of the pancreas is derived from the cells scattered throughout the substance of the gland. They take part in glucose homeostasis and are also involved in the control of upper gastrointestinal motility and function. The pancreas is salmon pink in color with a firm lobulated smooth surface. The main portion is divided into 4 parts, head, neck, body and a tail. There are only very minor functional or anatomical differences between each part. With age, the amount of exocrine tissue tends to decline, as does the amount of fatty connective tissue within the substance of the gland, and this leads to a progressive thinning atrophy.

The endocrine pancreas consists of pancreatic islets of Langerhans, composed of spherical or ellipsoid clusters of cells, embedded in the exocrine tissue. The human pancreas may contain more than a million islets, usually
most numerous in the tail. An islet is a mass of polyhedral cells, each in close proximity to fenestrated capillaries and rich autonomic innervations. The most numerous cells, types alpha (20%) and beta (75%) secrete glucagon and insulin respectively. Alpha cells tend to be concentrated at the periphery of islets, and beta cells more centrally. The delta cells secrete somatostatin and gastrin. The autonomic neurotransmitters acetylcholine and noradrenalin hinder islet cell secretion. Noradrenalin inhibits glucose induced insulin release.

2.3. Biochemistry

Carbohydrates are widely distributed in plants and animals. They have important structural and metabolic roles. Glucose is the most important carbohydrate. The dietary carbohydrate is absorbed into the blood stream as glucose, and other sugars are converted to glucose in the liver. Glucose is the major metabolic fuel of mammals and a universal fuel of the foetus. It is the precursor for the synthesis of all the other carbohydrates in the body.

2.3.1. Insulin

Although the presence of the hormone in the islets which have a strong anti-diabetic action was suspected for a long time, it was Frederick Banting and Charles Herbert Best of Canada, who for the first time produced evidence of insulin in 1922 and was awarded the Nobel Prize in 1923. Insulin is a polypeptide hormone. It has profound influence on the metabolism of
carbohydrates, fat and protein. It is considered as anabolic hormone as it promotes the synthesis of glycogen, triglycerides and proteins. This hormone has been implicated in the development of diabetes mellitus. Insulin was the first hormone to be isolated, purified and synthesized, to be produced by recombinant DNA technology.

Human insulin (molecular weight 5734) contains 51 amino acids arranged in 2 polypeptide chains. The chain A has 21 amino acids while B has 30 amino acids. Both are held together in 2 interchain disulphide bridges. There is an interchain disulphide link in chain A between the amino acids 6 and 11. The gene for the protein synthesis is located on chromosome 11. The synthesis of insulin involves 2 precursors namely preproinsulin with 108 amino acids (molecular weight 11,500) and proinsulin with 86 amino acids (mw 9000). They are sequentially degraded to form the active hormone, insulin and a connecting C-peptide. Insulin and C-peptide are produced in equimolar concentrations. C-peptide has no biological activity; however its estimation in the plasma serves as a useful index for the endogenous production of insulin in the beta cells. Insulin combines with zinc to form complexes. In this form, insulin is stored in the granules of the cytosole, which is released in response to various stimuli by exocytosis.

2.3.2. Control of Insulin Secretion

There are 3 kinds of control. (1) Substrate control, (2) Hormonal control and (3) Neural control. The substrate control is the most important variety of
control. The 2 substrates which effect insulin regulation are glucose and amino acids. After a carbohydrate meal, blood glucose level rises. This stimulates beta cells, insulin secretion is increased and blood sugar level comes back to normal. When the blood glucose level is less than 70mg%, beta cells stop insulin secretion. As the level of glucose rises, insulin begins to be secreted in larger quantities. When the glucose level exceeds 300mg%, increase in insulin production stops.

In addition to the stimulation of insulin secretion by excess of blood glucose, some of the amino acids too do a similar work. The most potent among these are arginine and lysine. This effect differs from glucose stimulated insulin secretion in the following way. Amino acids administered in the absence of a rise in blood glucose cause only a small increase in insulin secretion. When administered simultaneous with elevated blood glucose concentration, the glucose induced secretion of insulin maybe as much as doubled in the presence of excess amino acids. Thus the amino acids strongly potentiate the glucose stimulus for insulin secretion.

A mixture of several important gastrointestinal hormones-gastrin, secretin, cholecystokinin, and gastric inhibitory peptide cause a moderate increase in insulin secretion. They can cause an anticipatory increase in the blood insulin in preparation for the glucose and amino acids to be absorbed from the meal. They almost double the rate of insulin secretion as the blood glucose level rises.
Parasympathetic and beta adrenergic stimulation accelerates insulin secretion while alpha adrenergic stimulation inhibits it. Diabetes is particularly common in giants or acromegalic people with growth hormone secreting tumors, and in people whose adrenal gland secretes excess glucocorticoids.

2.3.3. Action of Insulin Secretion

About 40-50 units of insulin is secreted daily by the human pancreas. The normal insulin concentration permits rapid metabolic changes in accordance with the alteration in the circulating levels of insulin. A protease enzyme insulinase, mainly found in liver and kidney, degrades insulin.

On carbohydrate metabolism

1. Transport and uptake of glucose to peripheral utilization of glucose.
2. Peripheral utilization of glucose.
3. Storage of glucose.
4. Inhibition of glycogenolysis.
5. Inhibition of gluconeogenesis.

On protein metabolism

1. Transport of amino acids into the cell.
2. Accelerates protein synthesis.
3. Prevents catabolism of proteins.
4. Prevents conversion of proteins into glucose.

On fat metabolism

1. Synthesis of fatty acids and triglycerides.
2. Transport of fatty acids into adipose tissue


2.4. Physiology

In a normal person, the blood glucose concentration is controlled, usually between 80 and 90 mg/100ml of blood in the fasting person each morning before breakfast. This concentration increases to 120 to 140mg/100ml during the first hour or so after a meal, but the feedback system for control of blood glucose returns the glucose concentration rapidly back to control level, usually within 2 hrs after the last absorption of carbohydrate. Conversely in starvation, the gluconeogenesis function of the liver provides the glucose that is required to maintain the fasting blood glucose level.

The liver functions as an important blood glucose buffer system. That is, when the blood glucose rises to a high concentration after a meal and the rate of insulin secretion also increases, as much as two third of the glucose absorbed from the gut is almost immediately stored in the liver in the form of glycogen. Then during the succeeding hours, when both the glucose concentration and the rate of insulin secretion fall, the liver releases the glucose back into blood. In this way the liver decreases the fluctuation in blood glucose concentration to about one third of what they would otherwise be. In fact, in patients with severe liver disease, it becomes almost impossible to maintain a narrow range in the variation of blood glucose concentration.
Both insulin and glucagons function as important feedback control systems for maintaining a normal blood glucose concentration. When the glucose concentration rises too high, insulin is secreted, the insulin, in turn, causes the blood glucose concentration to decrease towards normal. Conversely, a decrease in blood glucose stimulates glucagon secretion. The glucagon then functions in opposite directions to increase the glucose towards normal. Under most normal conditions, the insulin feedback mechanism is much more important than the glucagon mechanism, but in the event of starvation or excessive utilization of glucose during exercise and in other stressful situations, the glucagon mechanism also becomes valuable.

2.5. Classification

Table 1
Clinical Classification of Diabetes Mellitus by WHO

1. Diabetes mellitus(DM)
   a. Insulin dependent diabetes mellitus (IDDM type 1)
   b. Non insulin dependent diabetes mellitus (NIDDM type 2)
   c. Malnutrition dependent diabetes mellitus (MRDM)
   d. Other types. (Secondary to pancreatitis, hormonal, drug induced, genetic and other abnormalities)

2. Impaired glucose intolerance (IGT)

3. Gestational diabetes mellitus (GDM)
Table 2
Etiological Classification of Diabetes Mellitus
(As per American Diabetes Association 2007)

<table>
<thead>
<tr>
<th>Classification</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. TYPE 1 DIABETES MELLITUS (10%)</td>
<td></td>
</tr>
<tr>
<td>a. TYPE 1A DM: Immune mediated</td>
<td></td>
</tr>
<tr>
<td>b. TYPE 1B DM: Idiopathic</td>
<td></td>
</tr>
<tr>
<td>2. TYPE 2 DIABETES MELLITUS (80%)</td>
<td></td>
</tr>
<tr>
<td>3. OTHER SPECIFIC TYPES OF DIABETES (10%)</td>
<td></td>
</tr>
<tr>
<td>a. Genetic defect of beta-cell function due to mutations in various enzymes</td>
<td></td>
</tr>
<tr>
<td>b. Genetic defect in insulin action</td>
<td></td>
</tr>
<tr>
<td>c. Diseases of exocrine pancreas</td>
<td></td>
</tr>
<tr>
<td>d. Endocrinopathies</td>
<td></td>
</tr>
<tr>
<td>e. Drug or chemical induced</td>
<td></td>
</tr>
<tr>
<td>f. Infections</td>
<td></td>
</tr>
<tr>
<td>g. Uncommon forms of immune mediated diabetes mellitus</td>
<td></td>
</tr>
<tr>
<td>h. Other genetic syndromes</td>
<td></td>
</tr>
<tr>
<td>4. GESTATIONAL DIABETES MELLITUS</td>
<td></td>
</tr>
</tbody>
</table>
2.6. Epidemiology

Table 3
Top 5 Countries for Estimated Number of Adults with Diabetes
-in millions (Wild et al. 2009)

<table>
<thead>
<tr>
<th>Country</th>
<th>2000</th>
<th>2030</th>
</tr>
</thead>
<tbody>
<tr>
<td>India</td>
<td>31.7</td>
<td>79.4</td>
</tr>
<tr>
<td>China</td>
<td>20.8</td>
<td>42.3</td>
</tr>
<tr>
<td>United states</td>
<td>17.7</td>
<td>30.3</td>
</tr>
<tr>
<td>Indonesia</td>
<td>8.4</td>
<td>21.3</td>
</tr>
<tr>
<td>Japan</td>
<td>6.8</td>
<td>8.9</td>
</tr>
</tbody>
</table>

Table 4
Age of Onset of Type 2 Diabetes in %

<table>
<thead>
<tr>
<th>Age</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Below 30 years</td>
<td>4</td>
</tr>
<tr>
<td>31-40</td>
<td>25</td>
</tr>
<tr>
<td>41-50</td>
<td>37</td>
</tr>
<tr>
<td>51-60</td>
<td>20</td>
</tr>
<tr>
<td>61-70</td>
<td>9</td>
</tr>
<tr>
<td>Above 70</td>
<td>5</td>
</tr>
</tbody>
</table>
Table 5
Ethnic Variation of Type 2 Diabetes
-Prevalence in Individuals Aged 30-64 yrs in % (WHO)

<table>
<thead>
<tr>
<th>Ethnic group</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pima Indians</td>
<td>50</td>
</tr>
<tr>
<td>Nauruan (south pacific)</td>
<td>40</td>
</tr>
<tr>
<td>Native Australians</td>
<td>25</td>
</tr>
<tr>
<td>South Asians</td>
<td>20</td>
</tr>
<tr>
<td>West Africans</td>
<td>12</td>
</tr>
</tbody>
</table>

Table 6
Break Up of Types of Diabetes Mellitus Seen in a Tertiary Care Hospital in Trivandrum 2005-2007 in %

<table>
<thead>
<tr>
<th>Type of Diabetes</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type2 DM</td>
<td>96.0</td>
</tr>
<tr>
<td>Type1 DM</td>
<td>0.8</td>
</tr>
<tr>
<td>Gestational DM</td>
<td>1.2</td>
</tr>
<tr>
<td>DM secondary to drugs, pancreatic diseases &amp; viral infections</td>
<td>2.0</td>
</tr>
</tbody>
</table>
Review of Literature

Table 7
The Current Cost of Diabetes in UK

- 10-30% reduction in life expectancy
- Most common cause of blindness in the age group 20-65 years
- 1000 patients per annum reach end stage renal failure
- Lower limb amputation raised 20 fold
- Use of hospital beds increased six folds
- 5-7% of total National Health Service Budget.

Figure 3
World Wide Estimated Number of Adults with Diabetes by Age group and Year (WHO)
2.7. Aetiopathogenesis

There are many factors behind the fast increase in the number of diabetics in the world. The three main factors that determine the presence of the disease are lifestyle, diet and genetic predisposition. The rapid modernization and industrialization allows the individual more time for leisure. The net outcome is a decrease in physical and an increase in food, which, in turn, lead to obesity and overweight. This state puts the body and all the organs thereof to much strain in their functions, of which the need to produce adequate insulin becomes the most cardinal issue.
Type 2 diabetes mellitus is characterized by impaired insulin secretion, insulin resistance, excessive hepatic glucose production, and abnormal fat metabolism. Insulin resistance, the decreased ability of insulin to act effectively on target tissues especially muscle, liver and fat, is a prominent feature, results from a combination of genetic susceptibility and obesity.

Increased hepatic glucose output predominantly accounts for increased fasting plasma glucose levels, whereas decreased peripheral glucose usage results in postprandial hyperglycemia. Insulin secretion initially increases in response to insulin resistance to maintain normal glucose tolerance. Initially, the insulin secretory defect is mild and selectively involves glucose-stimulated insulin secretion. Eventually, the insulin secretory defect progresses to a state of grossly inadequate insulin secretion. The reason for the decline in insulin secretory capacity is unclear. The assumption is that a second genetic defect superimposed upon insulin resistance, leads to beta cell failure. The metabolic environment of diabetes may negatively impact islet function.

Elevation of free fatty acid level and dietary fat may also worsen islet function. Beta cell mass is decreased in individuals with long standing type 2 diabetes. The lipid storage in the liver may lead to non-alcoholic fatty liver disease which may call for an abnormal liver function test. Increased hepatic glucose production occurs early though likely after the onset of insulin secretory abnormalities and insulin resistance in skeletal muscles.
2.7.1. Insulin Resistance Syndrome

Table 8
Features of the Insulin Resistance Syndrome

<table>
<thead>
<tr>
<th>Hyperinsulinemia</th>
<th>Microalbuminuria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 2 diabetes or impaired glucose tolerance</td>
<td>Increased fibrinogen</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Increased plasminogen activator inhibitor 1+</td>
</tr>
<tr>
<td>Low HDL cholesterol</td>
<td>Elevated plasma uric acid</td>
</tr>
<tr>
<td>Elevated triglycerides</td>
<td>Increased sympathetic neural activity</td>
</tr>
<tr>
<td>Central(visceral obesity)</td>
<td></td>
</tr>
</tbody>
</table>

A condition which comprises a spectrum of disorders including insulin resistance, hypertension, dyslipidemia, central or visceral obesity, and accelerated cardiovascular disease with hyperglycemia. Acanthosis nigricans and signs of hyperandrogenism are also common physical features. Polycystic ovary syndrome (affects premenopausal women) is a common disorder which substantially increases the risk for type 2 diabetes, independent of the effects of obesity. Environmental factors such as high fat diet and low levels of physical activity may exacerbate insulin resistance. Whether or not tissue insulin resistance is a fundamental metabolic defect which links these abnormalities together, is not yet known. There is considerable evidence to show that insulin resistance is associated with an increased risk of cardiovascular disease.
2.7.2. Pre-disposing Factors

- Heredity
- Obesity
- Genetics and environmental factors
- Dietary habits
- Physical Inactivity
- Stress
- Migration
- Urbanization

The family history of the patient gives useful information in determining the type of diabetes as well as the risk of complications, since there is a genetic susceptibility to the development of these complications. History of diabetes with the age of onset and presence of complications in grandparents, parents, siblings, uncles, aunts and their children should be recorded. A history of the lifestyle of the patients in terms of occupation, exercise, alcohol, smoking, tobacco chewing and the dietary habits is necessary in planning and presenting dietary advice and for suggesting lifestyle modifications. There is a stronger inheritance pattern for type2 diabetes. Those with first-degree relatives with type2 have a much higher risk of developing type2, increasing with the number of those relatives.
**Table 9**  
**Major Risk Factors of Type 2 Diabetes Mellitus**  
*(ADA recommendations 2007)*

- Family history of type 2 diabetes mellitus  
- Obesity  
- Habitual physical inactivity  
- Race and ethnicity (blacks, Asians, pacific islanders)  
- Previous identification of impaired fasting glucose or impaired glucose tolerance.  
- History of gestational diabetes mellitus or delivery of baby heavier than 4kg.  
- Hypertension  
- Dyslipidemia (HDL level <35mg/dl or Triglycerides >250mg/dl.)  
- Polycystic ovary disease  
- Acanthosis nigricans.  
- History of vascular disease.
Type 2 diabetes usually comes to light in the middle years of life and thereafter begins to rise in frequency. The prognosis is worse in younger diabetics who tend to develop complications earlier than older diabetics. The overall male female ratio is almost equal. The genetic nature of diabetes is undisputed. Generally transmission does not follow simple Mendelian rules and this polygenic pattern presumably reflects the inheritance of a critical mass of minor diabetogenic minor polymorphism which interferes with insulin action and/or insulin secretion. Insulin sensitivity appears to be largely genetically determined, at least in some populations. Genes leading to insulin resistance could encode regulators of energy balance, metabolic enzymes, or the proteins that signal insulin action, and presumably include thirty genes favoring fat deposition. Mutations affecting the insulin receptor and glucose transporters do not appear to cause common type 2 diabetes, although mutations of insulin receptors can lead to severe insulin resistance. Diabetogenic genes leading to inadequate production of insulin could decrease insulin secretion in response to glucose, or impair β cell viability. Environmental factors play a critical role, because obesity and type 2 Diabetes are spreading too rapidly to be explicable by changes in the genome. They are also important in practice because they can be modified to treat and prevent the disease. They mostly induce insulin resistance. Hyperglycemia can impair insulin sensitivity and impaired insulin secretion results in gluco-toxicity.
The obesity accompanying type 2 diabetes mellitus particularly in a central or visceral location is thought to be part of the pathogenic process. The increased adiposites mass leads to increased levels of circulating free fatty acids and other fat cell products. The increased production of free fatty acids and some adipokines may cause insulin resistance in liver and promote glucose production by the liver and impair β cell function. The production by adiposities of adiponectin is reduced in obesity. This may contribute to hepatic insulin resistance. Adiposite products and adipokines also produce an inflammatory state and may explain why markers of inflammation such as IL-6 and C-reactive proteins are often elevated in type 2 diabetes mellitus. Maternal diabetes associated with intra uterine growth retardation and low birth weight, when associated with rapid growth catch up later on, appears to increase the risk of subsequent diabetes in the child.

**Figure 5**

**Elevations of circulating glucose initiate a vicious circle**
2.7.3. Lifestyle

A number of lifestyle factors are known to be important to the development of type 2 diabetes. Epidemiological studies provide evidence that type 2 diabetes is associated with overeating, especially when combined with obesity and under activity. Studies have shown that middle aged people with diabetes eat significantly more and are fatter and less active than their non diabetic siblings. Although the majority of middle aged diabetic people are obese, only a minority of obese people develop diabetes. Obesity probably acts as a diabetogenic factor only in those who are genetically predisposed both to insulin resistance and to \( \beta \) cell failure. The risk of developing type 2 diabetes increases tenfold in people with a body mass index more than 30 \( \text{kg/m}^2 \). In addition to the effect of total calorie content on obesity, the constituents of the diet and the style of eating are important factors. Sweet foods rich in refined carbohydrate consumed frequently may increase the demand for insulin secretion, while high fat foods may increase free fatty acids and exacerbate insulin resistance.

Those who had high levels of physical activity, a healthy diet, did not smoke, and consumed alcohol in moderation had an 82% lower rate of diabetes. When a normal weight was included, the rate was 89% lower. A healthy diet is defined as one high in fiber, with a high poly unsaturated to saturated fat ratio, and a lower mean glycemic index. Decreasing consumption of saturated fats and Trans fatty acids by replacing them with unsaturated fats may
decrease the risk. The increased rate of childhood obesity is believed to have led to the increase to the type 2 diabetes in children and adolescence. Environmental toxins may be a contributory factor to the increase in the rate of type 2 diabetes. A positive correlation has been found between the concentration in the urine of bisphenol A, a constituent of a certain kind of plastics and in the incidence of diabetes.

**Table 10**

**Risk of Developing Type 2 Diabetes for Siblings of Probands with Type 2 Diabetes**

<table>
<thead>
<tr>
<th>Age at onset of type 2 diabetes in Proband</th>
<th>Age corrected risk of type 2 diabetes in siblings (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>25-44</td>
<td>53</td>
</tr>
<tr>
<td>45-54</td>
<td>37</td>
</tr>
<tr>
<td>55-64</td>
<td>38</td>
</tr>
<tr>
<td>65-80</td>
<td>31</td>
</tr>
</tbody>
</table>

Subclinical Cushing syndrome (cortisole excess) may be associated with diabetes. The percentage of subclinical Cushing syndrome in the diabetic population is about 9%. Diabetic patients with pituitary microadenoma can improve insulin sensitivity by the removal of these microadenomas. Hypogonadism is often associated with cortisole excess. Testosterone deficiency is also associated with type 2 diabetes.
2.7.4. Common Causes

- Age: The disease may occur at any age. Increased age is a factor which gives more possibilities than in younger age.

- Poor diet: improper nutrition, low protein and fiber intake and high intake of refined products.

- Obesity and fat distribution: being overweight means increased insulin resistance; body fat is more than 30%, BMI 25+, waist girth 35 inches in women and 40 inches in men.

- Sedentary lifestyle: people with sedentary lifestyle are more prone to Diabetes when compared to those who exercise at least thrice a week.

- Stress: either physical injury or emotional disturbance can be rightly balanced as initial cause of the disease.

- Infection: some of the streptococci are supposed to be responsible for infection in pancreas.

- Gender: Diabetes is commonly seen in males and predominantly in women with multiple pregnancy or suffering from Polycystic Ovarian Syndrome.

- Hypertension: it has been reported in many studies that there is direct relation between high systolic blood pressure and Diabetes.

- Serum lipids and lipoproteins: high triglyceride and cholesterol level in the blood is related to high blood sugar.
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- Diseases of Pancreas or conditions that damage the pancreas, such as pancreatitis and cystic fibrosis.
- Excess amounts of certain hormones resulting from medical conditions, such as cortisol in Cushing’s syndrome, that work against the action of insulin.
- Medications that reduce insulin action such as glucocorticoids that destroy beta cells.
- Infections such as congenital rubella and cytomegalovirus.

2.7.5. Gestational Diabetes

During normal pregnancy, insulin sensitivity is reduced through the action of placental hormones and this affects glucose tolerance. The insulin secreting cells of the pancreatic islets may be unable to meet this increased demand in women genetically predisposed to develop diabetes. The term Gestational diabetes refers to hyperglycemia occurring for the first time during pregnancy. Repeated pregnancy may increase the likelihood of developing irreversible diabetes, particularly in obese women. 80% of women with gestational diabetes ultimately develop permanent diabetes.

2.7.6. Risk Factors for Gestational Diabetes

- Older women
- Women with a history of impaired glucose tolerance
- Women with a family history of diabetes in a first degree relative
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- Women who have had glycosuria during pregnancy in the past
- Women who are overweight or obese
- Women with a pregnancy complicated by polyhydramnios

2.8. Clinical Features

Table 11
Symptoms of Hyperglycemia

- Thirst, dry mouth
- Polyuria
- Nocturia
- Tiredness, fatigue
- Recent change in weight
- Blurring of vision
- Pruritis vulvae, balanitis (genital candidiasis)
- Nausea, headache,
- Hyperphagia; predilection for sweet foods
- Mood change, irritability, difficulty in concentrating, apathy

The classical symptoms are polyuria (frequent urination), polydypsia (increased thirst) and polyphagia (increased hunger). A considerable number of Patients with type 2 diabetes are asymptomatic or have nonspecific complaints such as chronic fatigue and malaise. Uncontrolled diabetes is associated with an increased susceptibility to infection.
2.8.1. Symptomatology of Hyperglycemia

Early mild symptoms such as moderate blood sugar which are likely to lead to serious complications in due course.

- Headache
- Sweating
- Impaired vision
- Dizziness
- Fast heartbeat
- Hunger
- Irritability
- Weakness
- Skin boils
- Foot tingling and numbness, hand numbness
- Sexual problems, erectile failure, premature menopause, amenorrhea
- Poor healing- any type of infections, injury
- Weight loss or weight gain

More extreme symptoms when blood sugar gets higher

- Excessive thirst and urination
- Dehydration and excessive hunger
- Weight loss
- Severe blurred vision
• Muscle cramps and aches
• Fatigue and muscular weakness
• Persistent fungal infection

2.9. Diagnosis

Diabetics with classic symptoms can be diagnosed clinically. Since many cases may be asymptomatic, diabetes should be suspected even in the absence of symptoms. The clinical symptoms and the biochemical alterations do not go hand in hand in many cases. Diabetes, being generally a biochemical disease with several different but interrelated biochemical and molecular abnormalities, should always be diagnosed and managed with biochemical monitoring along with clinical examinations.

Diagnosis of diabetes is important from two different perpectives. Firstly, it helps define thresholds for various interventional strategies to control symptoms and ameliorate development of long term complications. Secondly, it helps in epidemiological studies to estimate its prevalence and incidence along with risk factors with a view to formulate preventive and treatment strategies.

In non-pregnant symptomatic individuals (polydypsia, polyuria, polyphagia, unexplained weight loss, drowsiness or coma) casual plasma glucose level above 200mg/dl or fasting plasma glucose level above 126mg/dl or two hours post 75gms glucose level above 200 mg/dl is considered diagnostic of
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diabetes mellitus. These individuals need not be subjected to oral glucose tolerance test (OGTT).

Fasting plasma glucose level (FPG) less than 110 mg/dl is considered normal. However FPG level of 111 – 125mg/dl is referred to as impaired fasting glucose (IFG). In asymptomatic individuals, individuals with IFG and those with casual plasma glucose values between 110-200 mg/dl, and OGTT is strongly recommended for diagnosis.

The patient who is scheduled for OGTT is instructed to eat a high carbohydrate diet for at least 3 days prior to the test and come after an overnight fast of the test (for at least 8 hours). A fasting blood sugar sample is first drawn. Then 75gm of glucose dissolved in 300ml water is given. Blood and urine specimen are collected at half-hourly intervals for at least 2 hours.

Table 12
Diagnosis of Diabetes Mellitus (WHO)

<table>
<thead>
<tr>
<th>Glucose concentrations, mg/dl (mmol/l)</th>
<th>(venous plasma)</th>
<th>(capillary blood)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting*</td>
<td>&gt;126mg/dl (&gt;7.0)</td>
<td>&gt;110 (&gt;6.1)</td>
</tr>
<tr>
<td>2 hours post glucose</td>
<td>&gt;200mg/dl (&gt;11.1)</td>
<td>&gt;200 (&gt;11.1)</td>
</tr>
<tr>
<td>Casual**</td>
<td>&gt;200 (&gt;11.1)</td>
<td></td>
</tr>
</tbody>
</table>

* Fasting is defined as no calory intake for at least 8 hours.
**casual is defined as any time of day without regard to time since last meal.
2.9.1. Clinical Presentation Requiring Thorough Investigation

1. Non healing ulcers
2. Recurrent respiratory or urinary tract infection
3. Rapid change in the refraction of the eyes and premature cataract
4. Unexplained rapid weight loss
5. Increased tendency for fungal infection
6. Unexplained peripheral neuropathy
7. Premature onset of ischemic heart diseases, stroke or vascular occlusions
9. Retinopathy
10. Impotence in male.

2.9.2. Fasting Plasma Glucose Test

The plasma glucose test (FPG) is the most preferred test for diagnosing diabetes because of its convenience and low cost. The FPG test is most reliable when done in the morning. People with a fasting glucose level of 110-125mg/dl may have a kind of pre-diabetes called impaired fasting glucose (IFG). Having IFG means a person has an increased risk of developing type 2 Diabetes but hasn’t developed it yet. A level of 126mg/dl or above should be confirmed by repeating the test on another day.
Table 13
Fasting Plasma Glucose Test (FPG)

<table>
<thead>
<tr>
<th>Plasma glucose result (mg/dl)</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>99 or below</td>
<td>Normal</td>
</tr>
<tr>
<td>110-125</td>
<td>Pre-Diabetes (Impaired Fasting Glucose)</td>
</tr>
<tr>
<td>126 or above</td>
<td>Diabetes</td>
</tr>
</tbody>
</table>

2.10. Prognosis

A long held a prevalent misconception is that type 2 diabetes is mild. The fact is that patients who have relatively unexciting or asymptomatic hyperglycemia can develop complications enough to wreck their lives. Life expectancy is shortened by up to a quarter in patients with type 2 diabetes, manifesting in their forties, with vascular disease (myocardial infarction and stroke) becoming the main cause of premature death. Renal failure from diabetic nephropathy is as common as their survival from vascular complications. Type 2 diabetes is therefore an important threat to the patient’s health and survival and must be taken seriously even if the blood glucose concentrations are not dramatically raised. Patient education, understanding, and participation is vital since the complications of diabetes are far less common and less severe in people who have well managed blood...
sugar levels. Wider health hazards may accelerate the deleterious effects of diabetes. These include smoking, elevated cholesterol levels, obesity, high blood pressure and lack of exercise. Glucose tolerance progressively declines with age and lead to higher rate of prevalence and post challenge hyperglycemia in the older segment of the population.

2.10.1. Glycosylated Haemoglobin (HbA1C)

Table 14

Relation between Glycated Haemoglobin and Mean Blood Sugar

<table>
<thead>
<tr>
<th>HbA1c (%)</th>
<th>Mean blood sugar(mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>135</td>
</tr>
<tr>
<td>7</td>
<td>170</td>
</tr>
<tr>
<td>8</td>
<td>205</td>
</tr>
<tr>
<td>9</td>
<td>240</td>
</tr>
<tr>
<td>10</td>
<td>275</td>
</tr>
<tr>
<td>11</td>
<td>310</td>
</tr>
<tr>
<td>12</td>
<td>345</td>
</tr>
</tbody>
</table>

The red blood cells that circulate in the body live for about 3 months before they die off. When sugar sticks to these cells it is easy to find out how much sugar is around for the preceding three months. Once the hemoglobin is glycosylated, it remains in circulation. Of all the glycated forms of
haemoglobin HbA1c is the most stable. More than 80% of the glycated form is HbA1. Hence its measurement is taken to be the ideal parameter to identify a long term diabetic. A diabetic is considered to be well controlled if the HbA1C is below 6.5%. As the life of an RBC is about 120 days, HbA1C is an index of the average sugar levels over the previous 3 months.

2.11. Complications

Diabetes mellitus is associated with several complications throughout the course of the disease. Short-term control of diabetes can be achieved in almost all cases by the use of dietary regimen, exercise and drugs. In many diabetics the disease may be first detected when the patient has already developed a complication.

2.11.1. Acute Complications (Short-term Complications)

1. Metabolic derangements
   a. Diabetic ketoacidosis & coma.
   b. Hypoglycemia.
   c. Hyperosmolar nonketotic coma.
   d. Lactic acidosis.

2. Infections
   a. Acute infections such as skin infections, respiratory tract infections, urinary tract infections, genital infections.
b. Boils, carbuncles, cellulitis, superficial and deep abscesses, gangrene, foot infections.

3. Acute consequences of long term complications
   a. Ischemic heart disease – acute
   b. Renal failure.
   c. Peripheral vascular occlusion.
   d. Loss of vision.

4. Obstetric complication
   a. Intra uterine fetal death.
   b. Hydramnios
   c. Higher frequency of preeclamptic toxemia.
   d. Large baby (more than 4 kg) giving rise to complications during delivery and perinatally.
   e. Infections of the genital tract.
   f. Worsening of the diabetic state during pregnancy and postpartum.

2.11.2. Long-term Complications

1. Cardiovascular
   a. Earlier onset of atheroma.
   b. Ischemic heart disease.
   c. Cerebral vascular accidents.
   d. High incidence of hypertension (about 30% have hypertension).
2. Neurological
   a. Peripheral neuropathy.
   b. Autonomic neuropathy.
   c. Mononeuritis multiplex including cranial nerve palsies, urinary retention and incontinence and diabetic autonomic diarrhea.

3. Peripheral occlusive vascular diseases

4. Renal
   a. Recurrent urinary infections.
   b. Chronic pyelonephritis.
   c. Diabetic glomerulosclerosis.
   d. End stage renal failure.

4. Ocular
   a. Cataract.
   b. Retinopathy.
   c. Glaucoma.
   d. Refractive changes.

5. Respiratory
   Pulmonary tuberculosis and other infections.

6. Alimentary
   a. Xerostomia.
   b. Stomatitis.
   c. Gingivitis.
d. Dental sepsis.

e. Loosening of teeth.

f. Halitosis.

g. Hepatomegaly.

h. Gastric dilatation.

i. Nocturnal diarrhea.

j. Paralytic ilius.

7. Bone and joints

   a. Osteoporosis.

   b. Osteoarthritis.

   c. Neuropathic joints (Charcot’s joint).

8. Skin

   a. Chronic fungal infections of skin.

   b. Moniliasis of the mucus membrane of the genitalia and mouth.

   c. Pruritis vulvae.

   d. Necrobiosis lipoidica diabeticorum.

   e. Trophic ulcers of feet.

   f. Scleroderma.

9. Drug induced complications

   a. Hypoglycemia

   b. Drug allergy.
Table 15
Major Complications Seen In Long Standing Diabetics at the Time of First Examination in a Tertiary Care Hospital at Trivandrum

<table>
<thead>
<tr>
<th>Complication</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nephropathy</td>
<td>70</td>
</tr>
<tr>
<td>Hypertension</td>
<td>50</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>12</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>21</td>
</tr>
<tr>
<td>Retinopathy</td>
<td>20</td>
</tr>
<tr>
<td>Carotid artery disease</td>
<td>18</td>
</tr>
<tr>
<td>Elevated low density lipid</td>
<td>12</td>
</tr>
<tr>
<td>Hypertriglyceridemia</td>
<td>18</td>
</tr>
</tbody>
</table>

Even though the major long term complications produce clinical deterioration in the patient, sometimes they may be ignored and the patient may not seek medical attention.
2.11.3. Factors accounts for Frequency and Time of Onset of Complications

- Glucose level.
- Genetic factors.
- Smoking.
- Obesity.
- Hypertension.
- Hyperlipidemia.

2.12. Management

Diabetes mellitus and its complications produce a wide range of symptoms and signs. Those secondary to acute hyperglycemia may occur at any stage of the disease, whereas those related to chronic complications begin to appear during the second decade of hyperglycemia. Individuals with previously undetected type2 diabetes might have developed chronic complications by the time of diagnosis.

The goals of therapy for diabetes are

1. Eliminate the symptoms related to hyperglycemia
2. Reduce or eliminate the long term micro vascular and macro vascular complications.
3. Allow the patient to achieve a lifestyle as normal as possible.
The ideal management for diabetes would allow the patient to lead a completely normal life, help to remain not only symptom free but in good health, to achieve a normal metabolic state and to escape the long term complications. This is achievable to varied extent. The importance of lifestyle changes such as taking regular exercise, following a healthy diet habit should not be under-estimated in gaining glycemic control but many people, particularly the middle-aged and the elderly, consider it difficult to subject themselves to a strict regimen. Patients should also be encouraged to minimize alcohol consumption and to give up smoking altogether.

2.12.1. Factors Associated With Increased Mortality and Morbidity in People with Diabetes

- Duration of diabetes
- Early age at onset of the disease
- High Glycated haemoglobin
- Raised blood pressure.
- Proteinuria
- Microalbuminurea
- Dyslipidemia.
- Obesity
<table>
<thead>
<tr>
<th>Index</th>
<th>Goal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycemic control</td>
<td></td>
</tr>
<tr>
<td>• HbA1c</td>
<td>Less than 7%</td>
</tr>
<tr>
<td>• Pre Prandial capillary plasma glucose</td>
<td>90-130 mg/dl</td>
</tr>
<tr>
<td>• Peak post Prandial capillary plasma glucose</td>
<td>Less than 180 mg/dl</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>130/80 mm Hg</td>
</tr>
<tr>
<td>Lipids</td>
<td></td>
</tr>
<tr>
<td>• Low density lipoprotein</td>
<td>Less than 100 mg/dl</td>
</tr>
<tr>
<td>• High density lipoprotein</td>
<td>More than 40 mg/dl</td>
</tr>
<tr>
<td>• Triglycerides</td>
<td>Less than 150 mg/dl</td>
</tr>
</tbody>
</table>

Table 16
Treatment Goals for Adults with Diabetes
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Figure 6

Essential Elements in Comprehensive Care Of Type 2 Diabetes

MANAGEMENT OF TYPE 2 DIABETES

GLYCEMIC CONTROL

- Diet / lifestyle
- Exercise
- medication

TREAT ASSOCIATED CONDITIONS

- Dyslipidemia
- Hypertension
- Obesity
- Coronary heart disease

SCREEN FOR / MANAGE COMPLICATIONS OF DIABETES

- Retinopathy
- Cardiovascular diseases
- Nephropathy
- Neuropathy
- Other complications
2.13. Lifestyle Changes

2.13.1. Diet

2.13.1.1 Medical Nutrition Therapy (MNT)

A term used by the American Diabetes Association to describe the optimal coordination of caloric intake with other aspects of diabetes therapy (medicine, exercise & weight loss). The ADA has issued recommendations for three types of MNT. Primary prevention measures of MNT are directed at preventing or delaying the onset of Type 2 diabetes in high risk individuals (Obese or with pre diabetes) by promoting weight reduction.

Secondary prevention measures of MNT are directed at preventing or delaying diabetes related complications in diabetic individuals by improving glycemic control.

Tertiary prevention measures are directed at managing diabetes related complications such as cardiovascular disease and nephropathy. As for the general population, a diet that includes fruits, vegetables, fiber rich foods and low fat milk is advised.

2.13.1.2. Goals of Medical Nutrition Therapy

1. To achieve and maintain normal blood glucose level.

2. To achieve and maintain optimal lipid profile.

3. To achieve and maintain normal blood pressure.
4. To adjust the nutrient intake to restore and maintain ideal body weight to avoid dyslipidemia, cardiovascular disease, hypertension and nephropathy. During childhood and pregnancy adjustments for growth also should be provided.

5. For elderly patients, provision for proper nutrition and psychosocial needs.

In type 2 diabetic patients the first step would consist of dietary control along with exercise. They should be given a trial of dietary therapy for 4-8 weeks. About 50 percent of the patients favourably respond to dietary therapy. Proper patient education helps to improve adherence and co-operation to treatment on the part of the patient.

The following factors have to be considered while prescribing a diet for a diabetic:

1. The weight of the individual in comparison with his ideal body weight (BMI).

2. His occupation and activities demanding his caloric requirements.

3. The presence of any complication.

The total caloric intake is the most important step while prescribing a diet. Obesity is an important factor in terms of target cell resistance to insulin action. The body mass index (BMI) will help to determine the total caloric requirement.

\[ \text{BMI} = \frac{\text{Weight (kg)}}{\text{height (m)}^2} \]
It is desirable to keep the BMI between 22 and 25.

Ideal body weight = height in cm – 100

2.13.2. Exercise

In Type 2 Diabetes, regular exercise along with dietary regulation forms an important component of the therapy. A careful assessment of the expected benefits and associated risks of exercise in individual patients should be made while incorporating an exercise programmed in the treatment. Appropriate monitoring should also be done to avoid complications.

2.13.2.1. Endocrine/Physiological Responses during Exercise

1. Suppression of insulin release—directly as well as through epinephrine.

2. Sympathetic system activation—which inhibits insulin release (by alpha-receptor stimulation) and stimulates glycolysis.

3. Non insulin dependent glucose uptake in the periphery.

2.13.2.2 Benefits of Exercise

• It lowers blood glucose concentration.

• It improves insulin sensitivity.

• Decreases Triglycerides, increases HDL cholesterol and increases LDL cholesterol.

• It lowers blood pressure in mild to moderate hypertension.

• It causes weight reduction by metabolizing adipose tissue.
• It helps in cardiovascular conditioning.
• It improves the sense of wellbeing and the quality of life.

2.13.2.3. Risks of Unsupervised Exercise in Uncontrolled Diabetics

• Hypoglycemia

• Hyperglycemia after very strenuous exercise, particularly in poorly controlled diabetes.

• Precipitation or exacerbation of cardiovascular disease and acute cardiac events like arrhythmias, cardiac failure and sudden death.

• Worsening of long-term diabetic complications - particularly proliferative retinopathy, nephropathy, peripheral neuropathy and autonomic neuropathy.

2.13.3. Stress

Stress is defined as an organism’s total response to environmental demands or pressures. When stress was first studied in the 1950s, the term was used to denote both the causes and the experienced effects of these factors. However, in recent times, the word stress has come to denote the stimulus that provokes a stress response. Stress in humans results from interactions between persons and their environment that are perceived as straining or exceeding their adaptive capacities, thereby threatening their well being. The element of perception indicates that human stress responses vary according to the difference in personality as well as in the physical strength or general health.
Risk factors for the stress-related ailments are a mix of personal, interpersonal and social variables. This factor includes lack or loss of control over one’s physical environment and lack or loss of social support networks.

The high stress levels have been found to be the leading factor in the development of diabetes. Hypertension, faulty diet and lack of physical exercise are responsible for the increasing incidence of diabetes in young adults.

- Stress can be physical or mental.
- It can complicate diabetes directly by distorting the mechanism that maintains balanced blood glucose level.
- Learning to relax and making lifestyle changes can help to reduce mental stress.

Stress results when something causes body to behave as if it were under attack. Sources of stress can be physical like an injury or illness. Or they can be mental, like problems in marriage, job, health or finances. When stress occurs the body prepares to take action. This preparation is called fight or-flight response. In the fight-or-flight response, levels of many hormones shoot up. Their net effect is to take a lot of stored energy – glucose and fat-available to cells. These cells are then activated to help the body get away from danger. In people who have diabetes, the fight-or-flight response does
not work efficiently. Insulin is not always able to carry the extra energy to the cells, so glucose gets accumulated in the blood.

Many sources of stress are long term threats. For example, it can take many months to recover from a surgery. Stress hormones that are designed to deal with short term danger stay turned on for a long time. As a result long term stress can cause long term high blood glucose levels. Many of the long term sources of stress are mental. Mind sometimes misbehaves and reacts to a harmless event as if it were a real threat. Mental stress can be of a short duration too. The stress developed when getting stuck in a traffic jam belongs to this category. It can also be long term: one as the stress coming from a demand of the boss to take care of an ageing parent. With mental stress, the body pumps out hormones not to avail. Neither fighting nor fleeing is of any help when the “enemy” is one’s own mind.

In people with stress can alter blood glucose level in two ways:

- People under stress may not take good care of themselves. They may drink more or exercise less, they may forget, or may not have time to check their glucose levels or plan good meals.

- Stress hormones may also alter blood glucose level directly.

Scientists have studied the effect of stress on glucose levels of animals and human beings. Diabetics under physical or mental stress have been found to have elevated glucose levels. Glucose levels of most people go up with
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mental stress, while in some others glucose levels go down. In people with type 2 diabetes, mental stress often raises blood glucose levels. Physical stress, such as illnesses or injury, cause higher blood glucose levels in people with either type of diabetes.

It is easy to find out whether mental stress affects glucose control. Before checking glucose levels, write down a number rating mental stress level on a scale of 1-10. Then write down glucose level next to it. After a week or two, look for a pattern. Drawing a graph may help to see a trend more reliable.

2.14. Homoeopathic Approach

Homoeopathy is a method of curing the sufferings of a person by the administration of the drugs which have been experimentally proved to possess power of producing similar sufferings in a healthy human being. It is a specialized system of drug therapy. Homoeopathy implies a particular way of applying drugs to diseases according to a specific principle, known as ‘Similia Similibus Curentur’ (let likes be treated by likes).

Homoeopathy is a therapeutic method which assumes that a deviation from the fundamental mean within reversible limit can be restored to normal by means of stimuli, usually applied in the form of drugs, only sub physiological doses of which are necessary because of hypersensitivity in disease and whose action is always directed towards the normal by virtue of altered
receptivity of tissue to stimuli in disease. It is a method of pure factual observation.

The scope of homoeopathy comprises two sets of phenomena, clinical disease phenomena and clinical drug action phenomena, and the therapeutic law (*Similia Similibus Curentur*) discovered by Hahnemann which supplies the coping stone to the arch of Homoeopathy. This law fulfils the requisite characters of a scientific law for the following considerations:

- This law expresses only the relation between two series of phenomena i.e., the disease and the drug phenomena.

- This law is evidently justified by strict adherence to scientific procedure of observation, generalization, and formation of hypothesis (i.e., provisional supposition) by induction, deduction and experimental verification.

- This law based on no hypotheses – because hypotheses are framed or overthrown by accumulation of hitherto unobserved new facts and by the overall progress in knowledge.

- There is no question about the essential cause or ‘*modus operandi*’ of the law. There is no involvement of metaphysical diathesis.

- This law, like laws in other scientific subjects, affords us the means provision. E.g:- the science of astronomy, basing its calculations upon
the laws of gravitation can predict the exact time and date of solar and lunar eclipses.

Homoeopathy is a medical discipline, whose basic characteristic is that it is a non-invasive form of therapeutics. It is a low-cost, safe therapeutic system employing exclusively non toxic remedies. It may be effectively used to treat both acute and chronic disorders. All the same, its greatest utility lies in its amazing potential in curing or controlling many chronic illnesses that are difficult or impossible to manage with other therapeutic methods.

The disciplines of homoeopathy essentially entail a holistic approach towards the sick person and treat the patient’s disturbances on the emotional, mental and physical levels in an integrated manner. The basic aim of this medical system is to restore the lost equilibrium of the sick individual at all these three levels, by stimulating and strengthening his intrinsic defense and curative mechanisms (the so called vital forces).

The numerous peculiarities, variables or modalities of the patient in response to food, weather, noise, crowds, motion etc are all carefully studied and evaluated before deciding upon the therapy. Then such a remedy is decided upon that it is not only congruent to the totality of the symptom, but also unique to the individual, his or her lifestyle, the pattern of constitution and diathesis.
2.14.1. History

The roots of homoeopathy lie embedded in the findings, teachings and writings of Dr. Samuel Hahnemann (1755-1843). Samuel Hahnemann was a German physician who earned his Doctor of Medicine degree in 1779. It was a time when great advances were being made in science especially in the fields of chemistry, physics, physiology and anatomy. The clinical practice of medicine, however, was still rife with superstition lacked of scientific rigor. The potions and accessories employed in treatment, such as purgatives, plasters, herbal preparations and emetics had no rational basis, which, more often did more harm than good. Hahnemann recognized this and wrote critically of the prevailing practices in several papers on topics such as arsenic poisoning, hygiene, dietetics and psychiatric treatment.

While translating William Cullen's 'A treatise of the materia medica’ into German, Hahnemann was struck by a passage that dealt with cinchona bark, which was used to treat malaria. Cullen described its mechanism of action as a function of its stomach-strengthening properties. Hahnemann did not accept this view. He consumed ‘four good drams of Peruvian bark, twice a day for several days’ in an effort to find out the properties of the quinine-containing bark. Hahnemann reported that he began to develop symptoms identical to those of malaria. He concluded from this experience that effective drugs must produce symptoms in healthy people that are similar to those of the diseases they are expected to cure or subdue. Today this principles is known
as the ‘Law of Similars’ and is the basis for the use of the term homeopathy (‘similar suffering’).

Hahnemann and his colleagues began testing various substances to determine the types of symptoms they produced. The results suggested to Hahnemann what the drugs would be useful to treat. Hahnemann reasoned that doses of these substances that produced overt symptoms would be inappropriate for treatment of diseases with the same symptoms. Thus he advocated reduction of the dose to infinitesimal levels by multiple serial dilutions of ten to hundred folds. Soluble compounds or liquids were diluted in alcohol; insoluble materials were serially diluted by grinding with lactose. He compiled the results (his findings) into a treatise called the ‘Organon of rational therapeutics’, which was first published in 1810. The sixth edition, published in 1921, is still used today as basic text. Hahnemann presented the essence of the curative system as a complete therapeutic method of healing, based on clinically demonstrable laws and principles.

2.14.2. Principles

Every science embodies certain fundamental principles which guide the whole system. Homoeopathy as a science of medical treatment has a philosophy of its own and its therapeutics is based on certain fundamental principles. These are:

1. Law of Similia

2. Law of Simplex
3. Law of Minimum

4. Doctrine of Drug Proving

5. Theory of Chronic Disease

6. Theory of Vital Force


2.14.2.1. Law of Similia

Homeopathy is a therapeutic method based on the concept of symptom-similarity. The principle was in vague even before Hahnemann. Paracelsus, Hippocrates, and some ancient Ayurvedic texts carry occasional mentions of this phenomenon. But it was Hahnemann who first recognized the universality of this fact and lifted it into the status of a scientific law and made it the basis of a new comprehending system of medicine.

According to this system, the choice of the medicine is fundamentally based on the principle that the medicine must have the capability of producing in healthy people most similar symptoms of the disease sought to be cured. In aphorism 26 of ‘Organon of Medicine’, Hahnemann states this law: “A weaker dynamic affection is permanently extinguished in the living organism by a stronger one, if the latter (whilst differing in kind) is very similar to the former in its manifestations.”
2.14.2.2. Law of Simplex – The Single Remedy

Hahnemann in the aphorisms 272-274 of ‘Organon of Medicine’ states that only one single, simple medicinal substance is to be administered at a time in a given case. This is due to the following reasons:

1. The homoeopathic remedies were proved singly, and the Materia Medica was built up on the observed effects of drugs given singly, both in planned proving and in accidental proving.

2. Only one remedy can be the most similar at any given time to the condition of any given patient.

3. Moreover, if more than one remedy is used the doctor will never know which of the ingredients the curative element was, thereby shutting the door for future guidance.

4. If more than one drug is administered in one prescription, the possibility of synergistic action cannot be ruled out, but it cannot be argued that the effect will be the sum total of the effects of the separate drugs. The ingredient drugs may even result in interactions that may have adverse effects in the body. A mixture of more than one remedy in a single dose would constitute a new remedy, which would require to be proved as such for a proper estimate of its probable effects.

2.14.2.3. Law of Minimum Dose

The suitableness of a medicine for any given case does not depend on its accurate homoeopathic selection alone but on the proper size of the dose as
well. Under this principle medicine are to be given to the patients in minute
doses. A minute dose means that quantity of a medicine is such as to produce
the least possible excitation of the vital force and yet sufficient to effect the
necessary change in it. The quantity is minimum, yet adequate to create a
gentle remedial effect. This concept of minimum dose led to the discovery of
a practical process called potentisation. Administration of the minimum dose
has the following advantages:

1. To avoid unwanted aggravation

2. The smallness of the dose does not allow the drug to do any organic
damage nor does it lead to any risk of drug addiction or side effects.

3. The concept of minimum dose can be verified by Arndt-Schultz law
that small doses stimulate, medium doses paralyze and large doses kill.
In other words, the action of small and very large doses of the same
substance on living matter is contradictory.

4. The Law of Least Action, formulated by Maupertius, the French
mathematician, states: “The quantity of action necessary to effect any
change in nature is the least possible; the decisive amount is always a
minimum, an infinitesimal”.

Health is a matter of perfect equilibrium, perfect balance, trifling
circumstances may disturb it, and so may it be balanced by the least possible
in medication.
2.14.2.4. Doctrine of Drug Proving

In Homoeopathy only those medicines are prescribed whose medicinal properties have been tested and established through ‘drug proving’. Drug proving is a systematic investigation of the pathogenic (disease-producing) power of the medicine on healthy human beings of different ages, both sexes and of various constitutions. These recordings of drug proving give the only reliable knowledge of medicines, which is very vital in treating a patient homeopathically. Different medicines must be tested thoroughly in order to obtain full details of their curative properties. The efficacy of the drug must be proved on human beings because:

1. Animals do not give subjective or mental symptoms.
2. Effects of the same drug on animals and on human beings may differ.
3. We can’t ascertain the modalities and finer symptoms in animal proving.

The efficacy of the drug must be proved on healthy human beings because:

1. The symptoms of the drug and the disease may be mixed together.
2. Moreover, the action of a drug on a sick person is different from that on a normal person.

2.14.2.5. Theory of Chronic Disease

During the early days of his homeopathic practice Hahnemann observed that in spite of best homoeopathic treatment the recurrence of symptoms at intervals could be noticed in some cases. This fact ed him to investigate
thoroughly a large number of chronic cases and after 12 years of intensive research he arrived at the conclusion that chronic diseases are caused by chronic miasms. The miasms are Psora, Syphilis and Sycosis. Psora is the real fundamental cause and producer of innumerable forms of disease. It is the mother of all diseases and at least 7/8th of all the chronic maladies spring from it while the remaining eighth springs from Syphilis and Sycosis. Cure is possible only by means of proper anti-miasmatic treatment.

2.14.2.6. Theory of Vital Force

The concept of a vital force or vital energy in the body is as old as the beginning of civilization. The Bible teaches that God breathed into man and made him a living being. In fact, the earliest idea of a life-giving principle, a vital force, dates at least 3000 years before the beginning of the Christian era. According to the traditional Egyptian belief, the living body contains ‘a divine spark’ called “Chu”, which was developed in the soul, “Ba”. After death “Chu” was freed from “Ba” (the soul) and as it was immortal, it was converted into a demon or spirit. The remarkable thing in the Egyptian belief is that the vital spirit was recognized separate from the soul, and that its unique function was to give life to the body.

The Hindu philosophy was even more advanced in its conceptualization. The Bhagavat Gita considers Soul to be the chief life force and does not speak of the existence of a separate vital force. In chapter XVII the slogans state “the
material body is governed by senses above which are the mind, which in turn, is ruled by the intellect. Above all is the everlasting soul.”

The teachings of Vedanta are nearly congruent to Hahnemann’s concept of the vital force. Whenever Brahman wished to transform himself and take the form of jiva, he reflected; “by whose sojourn shall I depart.” He then created the Prana (vital force) and from Prana came out, ether, air, fire, water, earth, the senses and sense organs and the material body. It is most likely that Hahnemann was well aware of these eastern philosophies through the Hebrew and Arabic classics.

The vital principle is termed the Chief Prana, because it functions prior to all other life actions and senses. It is only by the action of the Chief Prana that the paternal seed is thrown into the maternal soil and there the seed fertilizes, develops, acquires an image and becomes a full grown Jiva. Ultimately, on the completion of the Jiva’s present cycle, the Chief Prana leaves the body together with the self and enters another cycle of existence.

The autocracy and superiority of the vital force is explained in an exquisite allegory in the Chandogya Upanishad and also in Prasana Upanishad. To put it briefly, the Chief Prana is called the supreme energy. From whatever limb the Prana leaves, it withers. At death, the functions of the mind get merged in Prana.

The ancient Chinese concept of ‘Qi’, the vital energy is clearly explained in the classic of Lao Tsu, the Tao Te Jim. The energetic concept of Yin and
Yang used in traditional Chinese medicine is based on Qi, giving rise to the five elements and the twelve stems. The present day practice of acupuncture is based on this concept.

The Jewish concept is based on the Legend of the origin of man in the Genesis. The soul and the vital force are understood to be identical in Judaism. God gave life to man by breathing into him. This is the Judeo-Christian concept.

The most celebrated intellectual of ancient Greek philosophy, Aristotle, considered the Soul as the vital principle. Galen, the father of antipathy system of medical treatment also considered that Vital Force to be the life giving principle, which was derived from “anima-mundi”, the World-Soul.

In Europe, until the sixteenth century, issues concerning the science of medicine were generally decided by reference to authority and the greatest sources of authority were Pare, Brissot, Linacre and Bacon. The most prominent of the scientist of the Middle Ages was Theophrastus Bombast Von Hohenheim, popularly known as Paracelsus, who combined research and speculations (theorizing) together. He held almost the same concepts of the Vital Force as the ancient Greeks. He stated that “Archaeus” present in all living bodies was an active, living agent and this was the life-giver to man. “Archaeus” was from God and was entirely spiritual in nature. It was Von Helmot of the Paracelsus school, who first postulated that, due to the action of various external influences, this Archaeus (the Vital Spirit) produced
certain kinds of diseases in living organisms. This idea was a further development beyond the hypotheses of Hippocrates and the “vis medicatrix naturae” of Paracelsus.

Sylvius, the founder of the chemical school of philosophy brought the idea of a dynamic material principle and called it the “Vital Spirit”. Gaul expatiated on the idea of a separate and independent vital principle, possessed of nature and its receptivity. Stahl postulated that the Soul was the Vital Force. Borden introduced the idea of a Vital Force and he maintained that life was the harmonious working of the individual lives of all the organs and ancillary tissues of the organism. Barthez conceived the presence of the Vital Force in every part of the body, but thought that it was unable to work separately. He maintained that the diseases were affections of this Vital Force. Reil (1800), a contemporary of Barthez, hypothesized that this Vital Force was inherent in matter and inseparable from it. The doctrine of the Vital Force of Hahnemann maintained that disease was a morbid affection of this force. This force gave animation to the body and mind, and this animation was weakened during illness.

Vital Force as defined by Hahnemann is the spirit-like dynamic power of life. It is this Life Force which maintains life in living beings. A person is capable of self-protection because of this Vital Force. Unceasingly, we are exposed to millennia of disease forces, but we do not constantly fall ill because the Vital Force is continually affording protection against these morbific forces.
It is the Life Force which is deranged first by disease forces. The Life Force strives to overcome the disease forces continually. Either due to the long continued exposure or due to the greater strength of the disease forces, the Vital Force may get deranged. Then it starts producing abnormal signs and symptoms, which indicate its disharmony due to overpowering effect of the disease. The normal functions of the body are changed. The body starts behaving abnormally. Sensations of various kinds are felt. The power of self-protection is diminished and the body is subjected to many sufferings. The normal co-ordination between the mind and the body is altered, causing organic dysfunction. The Vital Force then starts mobilizing help by producing discomforting signs and symptoms. The Vital Force is itself a dynamic power; hence it can be only affected by other dynamic forces. The dysfunction of the Vital Force can be set right only by the dynamic power of medicines.

2.14.2.7. Doctrine of Dynamisation

Homoeopathic Dynamisation is a process by which the medicinal properties which are latent in natural substances while in their crude state, become awakened and developed into activity to an incredible degree.

According to Dr. Stuart Close, “Homoeopathic potentisation is a mathematic-mechanical process for the reduction, according to scale, of crude, inert or poisonous medicinal substances to a state of physical solubility, physiological
assimilability and therapeutic activity and harmless, for use as homeopathic healing remedies.”

Drugs are potentised by two methods:

1. Trituration – in case of insoluble substances.

The objectives of potentisation in Homoeopathy are:

1. Homeopathy believes that the vital force is dynamic in nature and that is affected by disease, and can that it be cured only by the dynamic power of serviceable medicine, not by its material quantity.
2. Substances which are medicinally inert in their crude natural state are thus rendered active and effective for healing the sick.
3. The medicinal qualities of other drugs which are more or less active in their natural state are enhanced and their sphere of action is broadened by this process.
4. The action of potentised medicines is deeper, longer and more widespread.

**2.15. Prevention of Diabetes Mellitus**

India stands as the worst diabetes affected nation in the world and on the ascending curve of the diabetic epidemic. No country is immune and no country is fully equipped to repel this common enemy.
Type 2 diabetes mellitus is preceded by a period of impaired glucose tolerance (IGT) and a number of lifestyle modifications and pharmacological agents prevent or delay the onset of diabetes. The Diabetes Prevention Programme (DPP) demonstrated that intensive changes in lifestyle (diet and exercise for 30mts a day, 5times per week) in individuals with IGT prevented or delayed the development of type2 diabetes by 58% compared to placebo. This effect was seen in individuals regardless of age, sex, or ethnic group. The lifestyle intervention group lost 5-7% of their body weight during the 3years of study.

To prevent diabetes and its complications, people should,

- Achieve and maintain healthy body weight.
- Be physically active- at least 30 minutes of regular, moderate-intensity activity on most days.
- Eat a healthy diet of between 3 and 5 servings of vegetables a day and reduce sugar and saturated fat intake.
- Avoid tobacco use- smoking increase the risk of cardio vascular diseases.

2.15.1. Primary Prevention

Two strategies for primary prevention have been suggested,

1. Population strategy
2. High- risk strategy
Population strategy:- The development of prevention is pressing need for primordial prevention, that is, prevention of the emergence of risk factors in countries in which they have not yet appeared. The preventive measures comprise maintenance of normal body weight through adoption of healthy nutritional habits and physical exercise. The nutritional habits include an adequate protein intake, a high intake of dietary fiber and avoidance of sweet foods. Elimination of other less well defined factors such as protein deficiency and food toxins may be considered in some populations. These measures should be fully integrated into other community based programmes for the prevention of non-communicable diseases (coronary heart disease).

High risk strategy:-- since diabetes appears to be linked with sedentary lifestyle, over nutrition and obesity, correction of these may reduce the risk of diabetes and its complications. Subjects at risk should avoid diabetogenic drugs like oral contraceptives. It is wise to reduce factors that promote atherosclerosis, smoking, high blood pressure, elevated cholesterol and high triglyceride levels. These programmes may most effectively be directed at target population groups.

2.15.2. Secondary Prevention

When diabetes is detected, it must be adequately treated. Good control of blood glucose protects against the development of complications. Routine checking of blood sugar, of urine for proteins and ketones, of blood pressure,
visual acuity and weight should be done periodically. The feet should be examined for any defective blood circulation, loss of sensation and the health of the skin. Primary health care is of great importance to diabetic patients since most care is obtained at this level.

There should be an estimation of glycated hemoglobin at half yearly intervals. This test provides a long term index of glucose control. This test is based on the following rationale; glucose in the blood is complexed to a certain fraction of hemoglobin to an extent proportional to the blood glucose concentration.

A crucial element in secondary prevention is self care. The diabetic should take a major responsibility for his own care with medical guidance-adherence to diet and drug regimens, examination of his own urine and where possible monitoring of blood glucose level, maintenance of optimum weight, attending periodic checkups, recognition of symptoms associated with glycosuria and hypoglycemia.

The patient should carry an identification card showing his name, address, telephone number and details of treatment he is receiving. In short, he must have a working knowledge of diabetes. All these mean education of patients and their families to optimize the effectiveness of primary healthcare services.
2.15.3. Tertiary Prevention

Diabetes is the major cause of blindness, kidney failure, coronary thrombosis and gangrene of lower extremities. The main objective at the tertiary level is to organize diabetic clinics and units capable of providing diagnostic and management skills of a high order. The tertiary level should also be involved in basic, clinical and epidemiological research.

With proper nutrition in pregnancy, prevention of low birth weight and proper physical activity, we can prevent diabetes epidemic.

2.15.4. Screening

Screening is a search for unrecognized disease or defect by means of rapidly applied tests, examinations or other procedures in apparently healthy individual. the annual health examinations were meant for the early detection of hidden disease. Today screening is considered a preventive care function and it is a logical extension of health care. Screening is carried out in diseases that earlier diagnosis and subsequent treatment favorably alters the natural history of the disease in significant proportion of those who are identified as positive.

Widespread use of fasting plasma glucose as a screening test for type 2 DM is recommended because:

1. A large no: of individual who meet the current criteria for the diabetes mellitus are asymptomatic and unaware that they have the disorder.
Review of Literature

2. Epidemiologist studies suggest that type 2 DM may be present up to a decade for diagnosis.

3. As many as 50% of individuals with type 2 DM have one or more diabetic-specific complication at the time of their diagnosis.

4. The treatment of type 2 DM may favorably alter the natural history of diabetes mellitus.

5. Untreated or uncontrolled diabetes can cause serious complications like, coma, blindness, kidney disease, kidney failure, amputations, heart disease or stroke.

2.16. Summary

The investigator has made an extensive search of the literature related to lifestyle changes and Type 2 Diabetes Mellitus. She has found that so far no studies have been conducted to explore the role of lifestyle changes in the development and management of Type 2 Diabetes Mellitus in Kerala at Homoeopathic level. The literature study considerably helped the investigator throughout her research work.