DIABETES MELLITUS: A REVIEW

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Abstract:
Diabetes mellitus is resulted from high level of blood sugar level for extended period of time. There are three main type of diabetes. Type 1- which affect the younger population; Type 2- which affect affects the population above 40; and gestational diabetes-which affect the women during third trimester of their pregnancy. Hereditary, obesity, problem with the beta cell of pancreas are the general cause of the diabetes mellitus. Blurred vision, retinopathy, dry skin, nerve damage, and kidney damage are the complication associated with diabetes mellitus. Sugar concentration in the blood is major factor for diabetes, so understanding the sugar content of fat, carbohydrate and protein is essential. It can be controlled by diet, exercise, medication such as oral hypoglycemic drugs and insulin. Currently there is no known care for diabetes.

Key words: diabetes mellitus introduction, signs and symptoms, complication, causes, diagnosis, management, and new invention in diabetes.

Universal symbol of diabetes is shown in figure 1

Figure 1 Universal symbol of diabetes

Introduction:
Diabetes mellitus is a metabolic disorder which is because of either pancreas not produce insulin or cells not respond to produce insulin. The patient with diabetes mellitus is suffering from high blood glucose level. There are mainly three types of diabetes mellitus.

Type 1: It is also called as Insulin Dependent Diabetes Mellitus (IDDM). It is due to failure of body for insulin production.[1][2] It is often childhood disease so it is also called as Juvenile onset diabetes mellitus.

Type 2: It is also called as Non Insulin Dependent Diabetes Mellitus (NIDDM). In this type cells are unable for insulin usage.[1][2] The other name of this type is adult onset diabetes mellitus.

The THIRD TYPE is Gestational Diabetes Mellitus: This is usually established during pregnancy. It is usually diagnosis during middle or last pregnancy. As the high blood glucose is distributed from placenta to fetus, it must be controlled for proper growth and development of fetus. This type of diabetes is usually resolves after pregnancy by itself. Gestational diabetes increases the risk of mother to develop the type 2 diabetes in her later life. It may develop from few weeks to months or years after pregnancy. With this type risk of unborn baby is much higher than that of mother for developing diabetes mellitus.

The risk factors for the baby include[10];

- Abnormally increased weight before birth,
- Breath problem at birth,
- Obesity.

The risk factor for the mother includes[11]

- Need caesarean section due to overly large baby
- Damages heart, kidney, nerves and eyes.
Other type of the diabetes: This type is result from disease of pancreas, certain surgeries and medication, or due to infection.

Signs and Symptoms:
The signs and symptoms of diabetes mellitus are as follows[17][18]:

- Loss of weight,
- Polyuria (frequent urination),
- Polydipsia (frequent thirst),
- Polyphagia (frequent hunger),
- Blurred vision,
- Itchiness,
- Peripheral neuropathy,
- Recurrent vaginal infection,
- Fatigue,
- Lethargy,
- Stupor (feeling of distress),
- Hyper ventilation,
- Nausea,
- Vomiting,
- Abdominal pain,
- Glycosuria,
- Infection of Bladder,
- Extreme glucose may also leads to coma,
- Constipation,
- Candidias,

Early symptoms increased blood glucose level and loss of glucose in urine, which may leads to increased urine output and dehydration. And this dehydration cause increased thirst. Symptoms are more rapid in type 1 than type 2. The symptoms are similar in both the type but are different in their intensity.

Complications:
The complications are related to the disease of blood vessel which is classified into,

**Micro vascular disease**[13]: A small vessel disease which involves eye, kidney and nerves.

**Macro vascular disease**[13]: A large vessel disease which involves heart and blood vessels.

Diabetes may also lead to atherosclerosis (hardening of arteries) of the large blood vessels, which leads to angina, stroke and pain in lower extremities.

**EYE COMPLICATION**[5][6][7]
The major complication of diabetes on eye is DIABETIC RETINOPATHY. This causes leakage of the protein and blood in retina because of diseased small vessel in the back of the eye. The disease in these blood vessels may also cause the formation of small aneurysms and new but brittle blood vessels. Spontaneous bleeding from these new blood vessel leads to retinal detachment and impair the vision.

Cataract or glaucoma are also most common in diabetic patient.

**KIDNEY DAMAGE**[5][6][7]
This is also called as DIABETIC NEPHROPATHY. The onset of kidney damage is varied from patient to patient. Initially diseased blood vessels of the kidney lead to leakage of the protein in the urine. Later on, the kidney loses their ability to cleanse and filter the blood which leads to accumulation of toxic waste products in the kidney.

**NERVE DAMAGE**[8][9]
The nerve damage from the diabetes is called as DIABETIC NEUROPATHY. It is also caused by micro vascular disease. In this disease most essentially blood flow to the nerves is decreased, and leave the nerve without blood as a result the nerves get damaged. Symptoms of the diabetic nerve damage are numbness, burning and aching of the feet and lower extremities. When the diabetic neuropathy causes the complete loss of sensation to the feet, patient may not be aware of the injury to the feet.

Diabetic neuropathy also causes the erectile dysfunction by affecting the nerve which is important for penile erection. Diabetic neuropathy may also nausea, diarrhea, weight loss and other gastro paresis by affecting the nerve of the stomach and intestine.
Causes:

Causes of the diabetes is depends on the type
Type 1 diabetes is partly inherited and caused by certain infection, with some evidence of Coxsackie B4 virus. The cause of type 1 diabetes is unrelated to the lifestyle. Type 2 diabetes is caused by lifestyle, genetic, and due to certain medical condition. Lack of sleep may also cause type 2 diabetes. Nutrition of a mother during fetal development may also play an important role.

Lifestyle:

This includes obesity, lack of physical activity, poor diet, and stress. Dietary factors may also affect the risk of type 2 diabetes. Consumption of excess sugar or sweetened drink increases the risk of type 2 diabetes. The risk of type 2 diabetes is higher with saturated fats and Trans fatty acid than with poly unsaturated and mono unsaturated fats. Eating lots of white rice may also increase the risk.

Genetics:

Generally most cases involve the many genes and they all are small contributor to increase the probability of producing type 2 diabetes. More than 36 genes are found. For example, TCF7L2 allele increase the risk of developing diabetes by 1.5 times. There are numbers of the cases which arise due to abnormality in single gene. This includes Maturity Onset Diabetes of the Young (MODY), rabson-mendenhall syndrome.

Medical condition:

There are number of the medication which increases the risk of diabetes. This may include glucocorticoids, thiazides, beta blockers, atypical antipsycotics, statins.

Overview of causes are shown in to figure 2

Figure 2: overview of causes of diabetes mellitus

Diagnosis:

The diagnosis of diabetes is done by either Fasting plasma glucose ≥ 7.0 mmol/l (126 mg/dl). Or with Oral Glucose Tolerance Test, two hrs. after the oral dose of glucose ≥ 11.1 mmol/l (200 mg/dl).
Glycated haemoglobin (HbA1c) \( \geq 6.5\% \) is the other method for diagnosis. This test has advantage that fasting is not required and the result is more stable. And the disadvantage is this test more costly than measurement of blood glucose\(^{[18]}\).

The Oral Glucose Tolerance Test (OGTT):
With an OGTT the person should fast overnight then firstly plasma glucose is tested. After this, the person receives 75 gms of glucose and the blood samples are taken after two hours to measure blood glucose level. For the reliable result of the test person should be in good health, should not taking any medicine that affect blood glucose, should be normally acting, and at the morning of the test, the person should not smoke or drink coffee\(^{[12]}\).

Criteria for diagnosis of diabetes mellitus are explain in table 1

<table>
<thead>
<tr>
<th>Criteria for diagnosis of Diabetes Mellitus</th>
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</thead>
<tbody>
<tr>
<td>CONDITION</td>
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<tr>
<td>-----------</td>
</tr>
<tr>
<td>Normal</td>
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<tr>
<td>Impaired Fasting Glycaemia</td>
</tr>
<tr>
<td>Impaired Glucose Tolerance</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
</tr>
</tbody>
</table>

Once the diagnosis is confirmed, the class of diabetes is conformed. In that the followings are generally favor type 1
- Onset at young age
- Acute onset
- Weight loss
- Ketonuria

Factors which affect type 2 are:
- Onset at old age
- Absence of classical symptoms of diabetes
- Obesity

For a complete diagnosis patient's full history and complete examination is required.

Simplified scheme for diagnosis is shown in figure 3
Management:

Management of NIDDM:
Management of type 2 diabetes focus on maintaining blood glucose level in normal range and lowering the risk of cardiovascular disease.
Managing the cardiovascular disease such as hypertension, high cholesterol, microalbuminuria may improve person's life.
The goal of the treatment should be to maintain HbA1C level to 6.5%, but not lower than that.
It is recommended that patient with type 2 diabetes should check their eye on regular basis[21]
The major component of the treatment is Diet (with exercise if possible), Oral hypoglycemic therapy, and insulin treatment.

Education:
The patient should have adequate knowledge about[3][4],
- Nutritional requirement and meal planning,
- Therapy target,
- Types and extent of exercise and physical activity,
- Interaction of food and physical activity insulin and oral hypoglycemic drugs,
- Self monitoring,
- Improvement of life style,
- How to cope with emergency.

Dietary treatment:
Treatment is not effective until adequate attention on proper nutrition is not taken.
It is aimed at:
• Ensuring weight control,
• Allowing good glycaemic control,
• Providing nutritional requirements,
• Correcting any other blood lipid abnormalities.

**Oral Hypoglycemic Drugs (OHD):**

It is considered only when dietary treatment with an exercise is fail.

There are two major groups of OHD: 1) Sulphonylureas (SUs) and 2) biguanides (BGs).

SUs act by stimulating insulin release from beta cells whereas BGs act by decreasing gluconeogenesis and by increasing peripheral utilization of glucose. SUs can cause hypoglycemia so their use is closely monitored in elderly and those with kidney damage. Tolbutamide, a short-acting SU, can be given to the patient with renal impairment with the initial dose of 0.5 g which can be increased to 1.5 g in divided doses, if necessary.

Metformin is the only BGS preparation which is used in obese patients who are not responding to dietary therapy. Initial dose is 500-850 mg with or after food once daily. These doses can be increased to 500-850 mg twice a day. Due to the risk of lactic acidosis, metformin is contraindicated in patients with renal impairment, patients above 70 years of age, patients with heart failure, hepatic failure, and predisposition to lactic acidosis. SUs can be combined with metformin when therapy target is not achieved by either alone drug. Both SUs and BGs are contraindicated during pregnancy and breast feeding.

**Insulin:**

Insulin in type 2 diabetes is indicated in the following situations:

• When the diet and OHD fail to achieve therapy target,
• During pregnancy when diet alone is inadequate,
• When OHD is contraindicated,
• During surgery and infection.

Simplified scheme for treatment of NIDDM is shown in figure 4.
Management of IDDM:
The principles, guidelines and recommendation which apply to NIDDM can also be apply to IDDM. The attention should also be given to the thyroid function. Investigation on long term complication can not be done at initial stage. Height and weight of children should be measured. Growth should be monitored periodically.

Insulin therapy:
Treatment with insulin is main aspect of management.
Close co operation between the patient and his family member and the member of health care team is essential. Insulin therapy aims at minimizing risk of hypoglycemia, achieving good metabolic control by reproducing insulin secretion as much as possible. Insulin preparation of any species can be used.
The types of insulin used are: rapid acting insulin, short acting insulin, intermediate insulin, long acting insulin and premixed insulin.
Two major type of insulin preparations are usually used for injection.
1) Short acting
2) Intermediate acting.

Long acting insulin are generally not needed. Insulin is generally given through subcutaneous route. Intramuscular and Intravenous routes are used in emergencies such as diabetic ketoacidosis.

Insulin regimen:
Intermediate acting insulin injection, once daily, may be effective in some patient.
Mixture of short and long acting insulin preparation, twice daily, is commonly used regimen.
In some cases these mixture is given in morning. In some cases further doses short acting insulin are given before the lunch and at evening meal. Evening dose of intermediate acting insulin is given at bed time. The dose of insulin preparation is based on blood glucose level[6][9].
Self monitoring is required for adjusting insulin regimen. So it should be practiced by IDDM patient.

Home remedies which are used in the treatment of diabetes mellitus are: Jamun, Bitter guard, Fenugreek, Guava, Mango leaves, Cinnamon, Aloe Vera, Water, Sun light, Indian gooseberry, Fig leaves, Apple, Black seed, Olive oil, Grape seed extract, Bitter melon, Avocado.

Newer invention in diabetes:

Artificial pancreas:
The patient of type 1 diabetes must check their blood glucose level every few hours through out day and night, to determine when and how much insulin is require to ba lance the level. A new artificial pancreas is developed, which could make this task automatically. It is for home use and it is combination of an off the shelf glucose sensor and insulin pump, which is connected to computer that programs the information and stipulate the amount of insulin that should be released. If there is any problem, it also conveys an alert[3][8].
Artificial pancreas is shown in figure 5

Gastric stimulator:
It named as DIAMOND. This medical device is an implantable gastric stimulator with electrodes attached to the outer stomach. The original purpose of this device is for treating obesity by enhancing stomach muscle contraction which gives greater feeling of fullness, and to stimulate the release of hormones that affect the hunger. Further research concludes that this device can also control the blood glucose level as well, or better than synthetic insulin or any other medicine. It also improves the diabetes associated condition such as hypertension, cholesterol, and triglycerides[11][20].
Gastric stimulator is shown in figure 6
Laposcopic surgery:
It is effective for type 2 diabetes. The procedure involves removing of Ghrelin producing area of stomach which acts against insulin[^7]. Then a segment of small intestine is transplanted on to the upper part of the small bowel, where a lot of undigested food gets stimulated. Here special L cells respond to this stimuli by secreting a lot of GLP-1 hormone. This hormone acts on beta cell of pancreas and produce more insulin[^9].

Insulin inhaler:
After more than two decade of daily needle injection to treat the diabetes, insulin inhaler is developed. This insulin inhaler eliminates the pain cause by needle injection[^12].
Insulin inhaler is shown in figure 7

Dissolving hypodermic needle:
This is the small array micro needles design to deliver the drug. These fine needles are made by firstly mixing the drug in a sticky material and then thinly coated on a surface. Pointed subjects are used to touch this mixture and draw up fine needle shape. Once it becomes hard fine needles are strong enough to penetrate the skin and not cause the pain[^16].
Dissolving hypodermic needle is shown in figure 8
Implantable insulin:
Scientist develop implantable capsule that continuously produce insulin and release it into blood stream\(^{[12][18]}\). This capsule contains insulin secreting cells which receive the nutrition from the body to produce insulin. Scientist also overcomes the biocompatibility problems which is the obstacle in implantable device. This capsule, made by using microchip technology, would not attack or destroy body's immune system.

Breath test:
This invention comes from the discovery that the amount of carbon monoxide which we breath out is linked with the amount of glucose in our blood. Excess glucose stimulate the production of an enzyme called "heme oxygenase" and catalyze the reaction that release carbon monoxide and other by products\(^{[13][17]}\).

Conclusion:
By concluding the current review it shows that diabetes mellitus is still not curable although so many treatments are available. There are some techniques which can be used to manage the blood glucose level. They are; enhancing the efficiency of the beta cells, increasing the utility of glucose, converting glucose into other form or by injecting the insulin. The Insulin Inhaler, which is discovered to deliver the exact amount of dose and which can be used to reduce the pain of insulin injection. This can make the use of the insulin much easier. For diagnosis and treatment of diabetes mellitus, there are many inventions are available like Insulin Inhaler. In future, the transplant of beta cells can be used to cure the disease.

References

