INTRODUCTION

Diabetes mellitus is a group of metabolic diseases characterized by chronic hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Metabolic abnormalities in carbohydrates, lipids, and proteins result from the importance of insulin as an anabolic hormone ***(Kharroubi and Darwish , 2015).***

Self monitoring blood glucose (SMBG) includes an assessment of the capillary glucose concentration (self-measurement) as well as the interpretation of and responding to the readings (self-regulation) ***(Hortensius et al., 2012).***

The aim of self-monitoring is to collect detailed information about blood glucose levels over time at multiple points. It helps maintain constant glucose levels and prevent hypoglycemia, and allows the following to be scheduled accordingly: The treatment regime/insulin doses, dietary intake and Physical activity ***(Kirk and Stegner 2010)***

Self-monitoring of blood glucose by persons with diabetes is an integral part of intensive glycemic treatment and is widely believed to improve the control of blood glucose levels and health outcomes ***(American Association of Diabetes Educators 2002).***

Children and adolescents with T1DM showed that after adjustment for multiple confounders, increased daily frequency of SMBG was significantly associated with lower glycated hemoglobin (HbA1C) along with added benefits of fewer acute complications***(Ziegler et al., 2011)***

The number and regularity of SMBG should be individualized depending on availability of the equipment, type of insulin regimen, and ability of the patient to identify hypoglycemia, Fasting, pre prandial targets, and postprandial targets for SMBG have been outlined in several guidelines ***(ISPAD, 2009a).***

Quantitative research shows several barriers to SMBG. These include a longer duration of the disease, pain, low self-efficacy, low self-esteem, increased anxiety and depression, alcohol abuse, smoking, complex treatment regimes, decreased social supports, poor communication between patients and health care providers, lack of education, and lack of health insurance ***(WHO, 2003; Vincze et al., 2004; Davidson 2005; Mollema et al., 2000; Fisher et al., 2011).***

AIM OF THE WORK

The aim of the study is to measure patients' compliance to self monitoring of blood glucose, identify factors and barriers that affect self monitoring of blood glucose(SMBG), and to correlate performance of SMBG to HbA1c.

Chapter 1
TYPE 1 DIABETES MELLITUS

Definition of diabetes:

Diabetes is a group of metabolic diseases characterized by hyperglycemia resulting from defect in insulin secretion, insulin action, or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of different organs, especially the eyes, kidney, nerves, heart, and blood vessels ***(ISPAD, 2014a).***

The classical symptoms of diabetes are polyuria, polydepsia, and polyphagia ***(Cooke and Plotnick, 2008).*** The major forms of diabetes are divided into those caused by deficiency of insulin secretion due to pancreatic Beta-cell damage (type 1 DM), and those that are consequence of insulin resistance occurring at the level of skeletal muscles, liver, and adipose tissue with various degrees of beta-cell impairment (type 2 DM) ***(Alemzadeh and Ali, 2011).***

Global burden:

Diabetes in all its forms imposes unacceptably high human, social and economic costs on countries at all income levels ***(Figure 1)*** 387 million people have diabetes; by 2035 this will rise to 592 million. The number of people with type 2 diabetes is increasing in every country ***(IDF Diabetes Atlas, 2014)***.

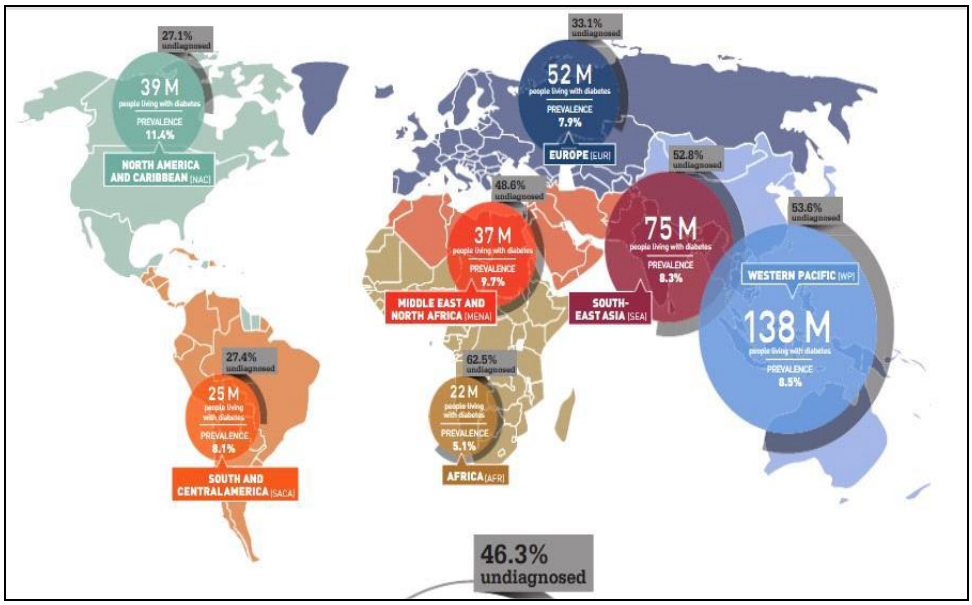

Figure (1): Global diabetes prevalence ***(IDF Diabetes Atlas, 2014).***

Classification:

WHO classified DM into clinical types (normoglycemia, impaired glucose tolerance (IGT)/ impaired fasting glucose (IFG), diabetes) and etiological types ***(World Health Organization, 1999).***

The vast majorities of cases with diabetes fall into two etiopathogenetic categories; type 1 and type 2 diabetes mellitus ***(ISPAD, 2014a)***. In most of western countries, type 1 diabetes accounts for over 90% of childhood and adolescent diabetes, although less than half of individuals with type 1 diabetes are diagnosed before the age of 15 years. Type 2 diabetes is becoming more common and accounts for a significant proportion of youth onset of diabetes in certain risk populations ***(Thunander et al., 2008).***

The comparison between both types is presented in Table (1).

Table (1): Clinical characteristics of type 1 diabetes, type 2 diabetes and Monogenic diabetes in children and adolescents

Characteristics	Type 1	Type 2	Monogenic
Genetics	Polygenic	Polygenic	Monogenic
Clinical presentation	6 months to young Adulthood	Usually pubertal (or later)	Often post pubertal except Glucokinase and neonatal diabetes
Association Autoimmunity Ketosis Obesity Acanthosis nigricans	Yes Common Population Frequency No	No Uncommon Increased Frequency Yes	No Common in neonatal diabetes, Rare in other form Population Frequency No
Frequency (% of all diabetes in young people)	Usually 90%+	Most countries <10%	?1-3%
Parent with diabetes 2	2-4%	80%	90%

(Craig et al., 2009)

Classification of Type 1 diabetes:

Type 1a (The autoimmune form):

This form of diabetes, which accounts for only 5-10% of those with diabetes, previously known insulin dependent diabetes, type 1 diabetes, or juvenile-onset diabetes, results from a cellular-mediated autoimmune destruction of pancreatic Beta-cells representing about 90% of type 1 cases in Europe. The presence of other autoimmune disorders is highly raised ***(ADA, 2015a).***

Type 1b (the idiopathic form):

The cause of insulin deficiency is not related to autoimmunity and it remains undefined. These cases are categorized as type 1b or idiopathic type 1DM and are relatively more common in African and Asian population. This category is heterogeneous, may be caused by different mechanisms in different population, and remain poorly understood at this time ***(Umpierrez et al., 2006).*** Individuals with this form of diabetes suffer from episodic ketoacidosis and exhibit varying degrees of insulin deficiency between episodes. This form of diabetes is strongly inherited, lacks immunological evidence for beta-cell autoimmunity, and is not HLA associated ***(ADA, 2015a).***

Type 1c:

It is the fulminant type 1 diabetes mellitus (FT1DM), it was first reported by ***Imagawa et al. (2000)*** and it is a unique subtype of diabetes. It is characterized by a short clinical history, before the first acute metabolic decompensating with impairment of beta and alpha cells of pancreatic islet and no autoimmune etiology ***(Arai et al., 2012).***

Clinical presentation of new onset diabetes:

The presentation of new onset T1DM is distributed among three typical patterns: classic new onset diabetes, silent and diabetic ketoacidosis. Children who have classic new onset

diabetes typically present with polydipsia, polyuria, polyphagia, enuresis in a previously toilet trained child and pyogenic skin infections and monilial vaginitis in teenage girls ***(International Society of Pediatrics and Adult Diabetes [ISPAD], 2014a).***

Diabetic ketoacidosis (DKA) is the usual emergency presentation of type 1 diabetes. An explosive onset of symptoms in a young lean patient with ketoacidosis always has been considered diagnostic of type 1 DM ***(Lamb, 2011).***

Partial remission or honey moon phase in type 1 diabetes:

The definition of the partial remission phase has been uncertain but a recent definition is when the patient requires less than 0.5 units of insulin per Kg of body weight per day and has a HbA1c <7% ***(Couper and Donaghue, 2009).***

Chronic phase of lifelong dependence on insulin:

The progression from the partial remission phase into the chronic phase of lifelong dependence on insulin is usually a gradual decrease in residual Beta-cell function but clinically may be accelerated by a current illness ***(Couper and Donaghue, 2009).***

Diagnosis of T1DM:

Diagnostic criteria of T1DM are shown in Table 2.

Table (2): Criteria for diagnosis of diabetes ***(International Society of Pediatric and Adolescent Diabetes [ISPAD], 2014a)***

Classic symptoms of diabetes or hyperglycemic crisis, with plasma glucose concentration ≥ 11.1 mmol/L (200 mg/dL)
OR
Fasting plasma glucose ≥ 7.0 mmol/L (≥ 126 mg/dL). Fasting is defined as no caloric intake for at least 8 h*
OR
Two hour postload glucose ≥ 11.1 mmol/L (≥ 200 mg/dL) during an OGTT*.
The test should be performed using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water or 1.75 g/kg of body weight to a maximum of 75 g.
OR
HbA1c > 6.5% †
The test should be performed in a laboratory using a method that is National Glycohemoglobin Standardization Program (NGSP) certified and standardized to the Diabetes Control and Complications Trial (DCCT) assay.

HbA1c, hemoglobin A1c; OGTT, oral glucose tolerance test

*****In the absence of unequivocal hyperglycemia, the diagnosis of diabetes based on these criteria should be confirmed by repeat testing.

†A value of less than 6.5% does not exclude diabetes diagnosed using glucose tests. The role of HbA1c alone in diagnosing type 1 diabetes in children is unclear.

Complications can be acute or chronic:

Acute complications include the following:

a) Diabetic ketoacidosis (DKA):

Diabetic ketoacidosis (DKA) is a serious acute complication that may lead to cerebral edema, diabetic coma, and if not treated, death. Although DKA may occur in anyone with diabetes, it is far more common in patients with T1DM compared to those with T2DM ***(Kitabchi, 2012).***

The combination of low serum insulin and high counter regulatory hormone concentrations results in an accelerated catabolic state with increased glucose production by the liver and kidney (via glycogenolysis and gluconeogensis), impaired peripheral glucose utilization resulting in hyperglycemia and hyperosmolality, and increase lipolysis and ketogenesis, causing ketonemia and metabolic acidosis ***(ISPAD, 2009).***

b) Hypoglycemia:

Most children with T1DM can accept mild hypoglycemia each week, moderate hypoglycemia a few times each year and sever hypoglycemia every few years. These episodes are usually not predictable, although exercise, delayed meals or snacks, and wide swings in glucose levels increase the risk ***(ADA, 2015b).***

The child may show pallor, sweating, hunger tremors, and tachycardia, all due to the surge in catecholamines as the body attempts to counter the excessive insulin effect. Behavioral changes such as tearfulness, irritability, aggression, and naughtiness are more prevalent in children. As glucose levels decline further, cerebral glucopenia occurs with drowsiness, personality changes, mental confusion, and impaired judgment (moderate hypoglycemia), progression to inability to seek help and seizures or coma (severe hypoglycemia) ***(Alemzadeh and Ali, 2011).***

c) Hyperglycemic Hyperosmolar state (HHS):

HHS was previously termed hyperosmolar hyperglycemia non ketotic coma (HHNC). However, the terminology was changed because coma is found in fewer than 20% of patients with HHS ***(Nugent, 2005).***

Chronic complications are further subdivided into macrovascular and microvascular:

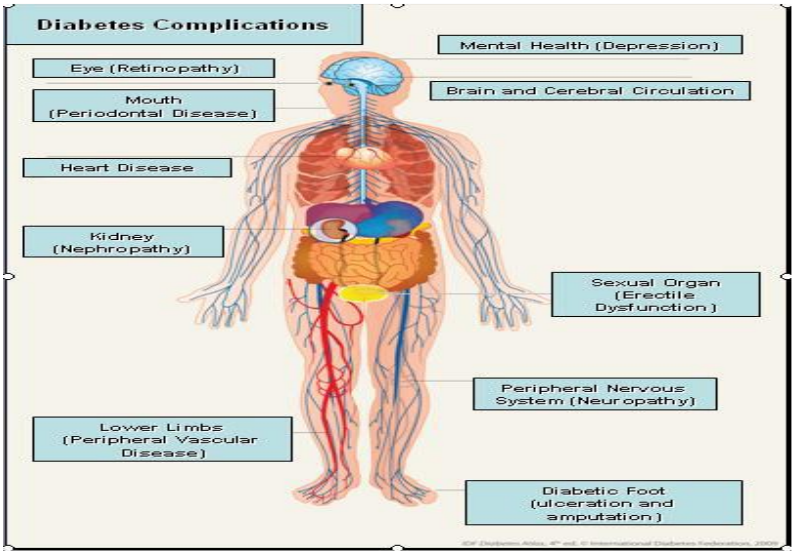

Figure (2): Chronic Diabetic complications ***(Bode, 2004).***

a) Macrovascular complications:

The central pathological mechanism in macrovascular disease is the process of atherosclerosis, which leads to narrowing of arterial walls throughout the body. Atherosclerosis is thought to result from chronic inflammation and injury to the arterial wall in the peripheral or coronary vascular system ***(Fowler, 2008).*** Macrovascular disease is the leading cause of death in patient with diabetes, causing 65-75% of deaths in this group, compared with approximately 35% of deaths in people without diabetes. Diabetes increases the risk of myocardial infarction (MI) 2-fold in men and 4-fold in women ***(Gerstein et al., 2010).***

b) Microvascular complications:

I. Diabetic nephropathy.

II. Diabetic retinopathy.

III. Diabetic neuropathy.

(Fowler, 2008)

Risk factors for the development of micro-vascular complications:

- Young age at the onset of the diabetes.
- Long duration of diabetes.
- Poor glycemic control**.**
- Family history of diabetic complications.
- Higher body mass index (BMI).
- Smoking.
- Abnormal lipid metabolism, weight and BMI.
- Hypertension.
- Sedentary life style.

(Donaghue et al., 2009)

Management of type 1 diabetes:

1- Education:

According to ***ISPAD Clinical Practice Consensus Guidelines (2014b)***, education is the key to successful management of diabetes. There is evidence that educational interventions in

childhood and adolescent diabetes have a beneficial effect on glycemic control and on psychosocial outcomes.

2- Diet:

One of the first steps in managing type 1 DM is diet control. According to ADA policy, dietary treatment is based upon nutritional assessment and treatment goals. Dietary recommendations should take into account the patient's eating habits and lifestyle. For example, patients who participate in Ramadan may be at higher risk of acute diabetic complications. Although these patients do not eat during the annual observance, they should be encouraged to actively monitor their glucose, alter the dosage and timing of their medication, and seek dietary counseling and patient education to counteract these complications ***(Ahmedani et al., 2012).***

3- Activity:

Exercise might greatly benefit many patients with diabetes by improving their metabolic profile, dyslipidemia, aiding in their weight loss and maintaining their blood pressure. Exercise improves glycemic control by reducing HbA1c values and is dispensable component in the medical treatment of patients with T1DM as it improves glycemic control and decreases cardiovascular risk factors among them ***(Salem et al., 2010).***

Regular exercise (>20 min/day) in people with type 1 diabetes has been shown to:

- Reduce total cholesterol, low density lipoprotein (LDL)-cholesterol and Triglycerides.
- Increase high density lipoprotein (HDL)-cholesterol.
- In addition to marked improvement in life expectancy.

(Haider et al., 2006)

4- Medications:

Insulin therapy is recommended for most individuals with type 1 diabetes.

- Treat with multiple-dose insulin injections (3-4 injections/day of basal and prandial insulin) or continuous subcutaneous insulin infusion.
- Match prandial insulin dose to carbohydrate intake, premeal blood glucose, and anticipated activity.
- Use insulin analogs to reduce risk of hypoglycemia.
- Consider using sensor-augmented low glucose suspend threshold pump in patients with frequent nocturnal hypoglycemia and/or hypoglycemia unawareness

(ADA, 2015b)