Introduction

Diabetes mellitus describes a complex metabolic disorder characterized by chronic hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Inadequate insulin secretion and/or diminished tissue responses to insulin in the complex pathways of hormone action result in deficient insulin action on target tissues, which leads to abnormalities of carbohydrate, fat, and protein metabolism. Impaired insulin secretion and/or action may coexist in the same patient ***(Craig et al., 2014).***

It is the most common endocrine-metabolic disorder of childhood and adolescence (90% of cases) and accounts for only 5-10% of all cases of diabetes, with important consequences for physical and emotional development ***(Wyatt, 2008).***

Complication include acute and chronic complication, chronic complications including micro-vascular disease; diabetic retinopathy ***(Ciulla et al., 2003),*** diabetic neuropathy ***(Gross et al., 2005)*** and diabetic cardiomyopathy ***(Bell, 2003)*** while macro-vascular diseases are coronary artery disease, ischemic stroke, peripheral vascular disease and diabetic myonecrosis ***(Reyes-Balaguer et al., 2005)***, patients with type 1 diabetes are also more likely to have other autoimmune disorders, such as autoimmune thyroiditis, Addison's disease, and celiac disease ***(Ize-Ludlow and Sperling, 2005).***

Diabetes complications are common and cost almost triple the annual cost of managing diabetes ***(Bate and Jerums, 2003).*** A recent population-based study conducted in Sweden reported that compared with the non-diabetic population, the direct medical cost for children with T1DM aged 0–14yrs was 7.7 times higher. These costs included healthcare expenditure in primary healthcare, outpatient and inpatient care, and prescribed drugs. The additional cost per person with diabetes in children was 3930 Euros ***(Pihoker et al., 2014).***

Specialized care is, therefore, mandatory for patients with diabetes mellitus. Assessing the quality of diabetes care is of outmost value in guiding resources and redirecting therapy ***(Schiel et al., 2004).***

Aim of the Work

1) To assess quality of diabetic care in children and adolescents with type 1 Diabetes Mellitus in diabetes clinic of children's hospital, Ain Shams University.

2) To assess the patient’s opinion about diabetic care received during the past 12 months prior to the study as well as to determine patients’ satisfaction about the care.

3) To suggest recommendation for improving the quality of such care.

Chapter (I): Type 1 Diabetes Mellitus

Type 1 diabetes is one of the most common endocrine and metabolic conditions in childhood and the number of children developing this form of diabetes every year is increasing rapidly, especially among the youngest children. In a growing number of countries, type 2 diabetes is now also being diagnosed in children ***(IDF, 2013).*** Type 1 diabetes or juvenile onset diabetes is a chronic autoimmune disease characterized by selective destruction of beta-cells in the pancreatic islet- cells, accompanied by antibody formation against beta-cells components ***(Alemzadeh et al., 2004).*** Activated T-helper cells provoke beta cells to produce several autoantibodies which act to destroy insulin producing beta-cells of pancreas ***(Haller et al., 2005).***

Type 1 diabetes is most commonly diagnosed in children and adolescents, usually presents with symptomatic hyperglycemia, and imparts the immediate need for exogenous insulin replacement. It seems that two peaks of type 1 diabetes presentation occur in childhood, one between 5 and 7 years of age and the other at puberty ***(Haller et al., 2005).*** Over the past 30 years, the ability to predict the development of type 1 diabetes has improved dramatically with the combined use of genetic, autoantibody, and metabolic markers ***(Haller et al., 2005).***

Epidemiology:

Epidemiological studies over the last few decades have shown an increase in the rate of incidence of T1DM in many countries, with disproportionately greater increase in the youngest age group, under the age of 5 years ***(Patterson et al., 2009; Harjutsalo et al., 2008).***

- **Incidence and prevalence:**

<u>According to the international diabetes federation **(IDF 2013)**</u>:

- **382 million** people have diabetes in 2013; by 2035 this will have risen to **592 million**.
- **79,000** children develop type 1 diabetes every year.
- **80%** of people with diabetes live in low and middle income countries.
- Diabetes caused **5.1 million deaths** in 2013, every 6 seconds, a person dies from diabetes.
- **175 million** people (46%) with diabetes are **undiagnosed.**

The estimated prevalence of type 1 diabetes mellitus in children and adolescents is 0.38/1000 in Egypt ***(Salem et al., 2010).*** Differences in disease prevalence and changes in incidence rates suggest that a combination of multiple genetic and environmental factors contribute to type 1 diabetes mellitus risk ***(Haller et al., 2005).***

According to the map below, the incidence of type 1 DM in Egyptian children under **15 years** in 2013 was **5.0-**

8.5 per 100,000 children per year. The incidence of type 1 diabetes among children is increasing in many countries, at least in those under the age of 15 years. There are strong indications of geographic differences in trends but the overall annual increase is estimated to be around **3%.** Evidence shows that incidence is increasing more steeply in some central and eastern European countries where the disease is less common. Also, several European studies have suggested that, in relative terms, increases are greatest among younger children. There is also evidence that similar trends exist in many other parts of the world, but in sub-Saharan Africa incidence data are limited or non-existent ***(IDF 2013).***

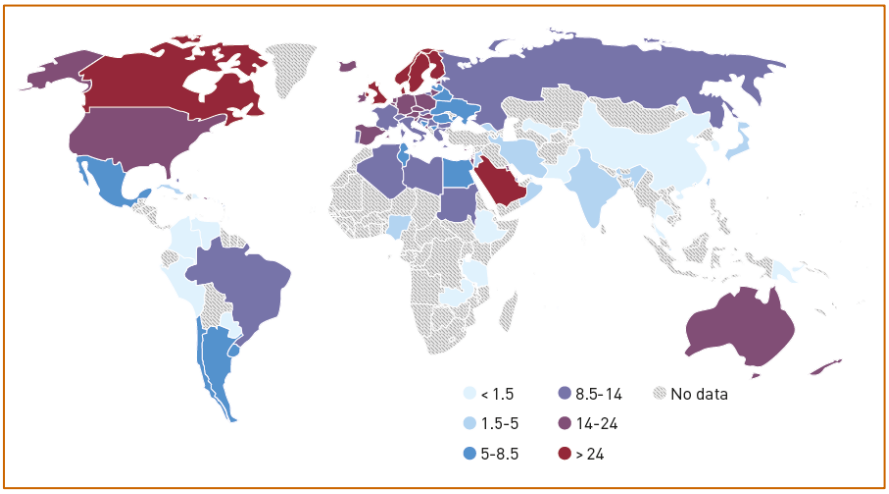
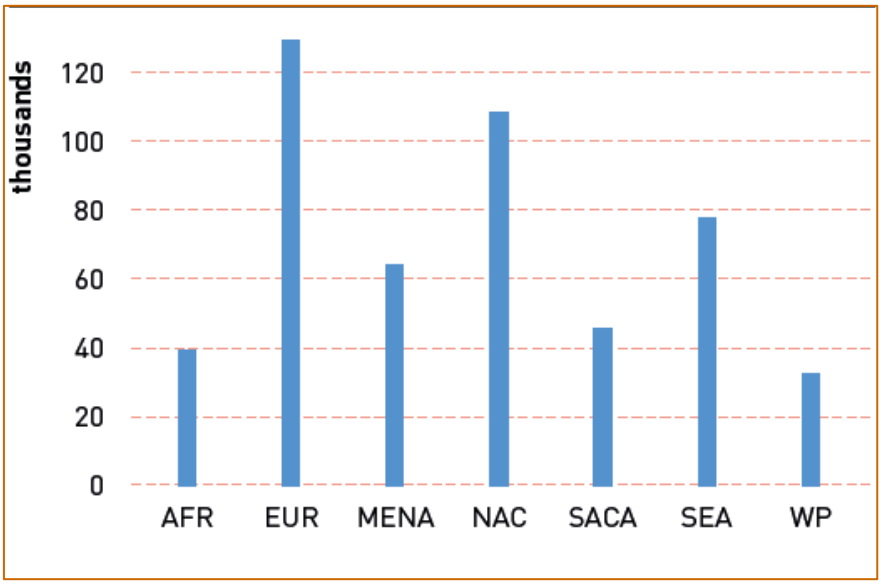


Fig. (1): New cases of type 1 diabetes (0-14 years) per 100,000 children per year, 2013



WP, Western pacific-**SACA,** South and central America-**AFR,** Africa-**NAC,** North America and Caribbean-**MEMA,** Middle east and north Africa-**SEA**, South East Asia-**EUR,** Europe

Fig. (2): Estimated number of children (0-14 years) with type 1 diabetes by IDF region, 2013

Some **79,000** children under 15 years are estimated to develop **type 1diabetes** annually worldwide. Of the estimated to 497,000 children living with type 1 diabetes, **26%** come from the European Region, where the most reliable and up-to-date estimates of incidence are available, and **22%** in the North America and Caribbean Region ***(IDF 2013).***

The rising incidence and decreasing age at diagnosis of type 1 diabetes is accounted for by the impact of environment on children with lower-risk HLA class 11 genes, who previously would not have type 1diabetes in childhood ***(Fourlanos et al., 2008).***

Because clinical type 1 diabetes mellitus typically does not present until approximately 80% to 90% of the beta cells have been destroyed, there is a marked gap between the onset of autoimmunity and the onset of diabetes ***(Haller et al., 2005).***

Risk factors:

a) Age:

Diabetes is one of the most common diseases in school-aged children. According to the 2011 National Diabetes Fact Sheet, about 215,000 young people in the US under age 20 had diabetes in 2010. This represents 0.26 percent of all people in this age group ***(National Diabetes Fact Sheet, 2011).*** On average, in children under age 15, T1DM incidence increases as a child gets older. In other words, a person 10-14 years old has a higher risk of developingT1DM, someone 5-9 years old has a middle risk, and someone 0-4 years old has a lower risk. Someone 10-14 has about twice the risk of developing type 1 diabetes as someone under 5. This trend generally does not vary by gender ***(Diamond Project group, 2006).*** There is also a relatively high incidence in people in their late 30s and early 40s, in whom the disease tends to present less aggressively (with early hyperglycemia without ketoacidosis and gradual onset of ketosis). This slower-onset adult form of type 1 diabetes is referred to as latent autoimmune diabetes of the adult (LADA) ***(National Diabetes Fact Sheet, 2011).***

b) Season:

The incidence of type 1 diabetes varies with seasonal changes and geography. Incidence rates are higher in autumn and winter and are lower in the summer ***(Haller et al., 2005).***

Patterns in seasonality for both the month of birth and the month of diagnosis of T1DM have been reported. While the seasonality of T1DM diagnosis seems intuitively obvious given the well-documented environmental role in T1DM's pathogenesis, it is also hypothesized that the seasonal environment at birth may have an influence on diabetes incidence later in life. Among **9,737** youth with T1DM in the SEARCH study, the percentage of observed to expect births differed across the months with a deficient of November-February births and an excess in April-July births. This birth month effect was not observed in youth recruited from the centers in role in this observation. Reports on the seasonality of T1DM in adults have been mixed, but a recent report from Sweden on more than 5800 patients 15-34 years of age found the higher incidence during January-March and the lower during May-July with no difference by gender ***(Ostman et al., 2008).***

c) Race:

Type 1 diabetes is more common among non-Hispanic whites, followed by African Americans and Hispanic Americans, it is comparatively uncommon among Asians ***(Lal et al., 2011).***

d) Countries:

Internationally, rates of type 1 diabetes are increasing. In Europe, the Middle East, and Australia, rates of type 1 diabetes are increasing by 2-5% per year ***(Imkampe and Gulliford, 2011)***.

Etiology and pathogenesis of type I diabetes:

Twin studies have revealed that 70-75% of the risk of type 1 diabetes is related to genetic effects and 25-30% to environmental factors. The estimated proportion of HLA of the genetic risk varies. Candidates for environmental components includes for instance viral infections, early introduction of cow's milk in infancy, short duration of breast feeding, or nitrites and nitrosamines in the diet, however, convincing evidence for some major environmental factor to be the initiator of the disease process has so far not been presented risk, Individuals in the United States have first degree relative with type 1 diabetes have a 1 in 20 risk for developing type 1 diabetes, whereas the general population has a 1 in 300 lifetime risk ***(Pociot and Mc Dermoot, 2002).***

A) Gene:

Monozygotic twins have a concordance rate of 30% to 50%, whereas dizygotic twins have a concordance rate of 6% to 10%. Eighty-five percent of cases of type 1 diabetes occur in individuals with no family history of the disease. Differences in risk also depend on which parent has diabetes. Children of mothers who have type 1 diabetes have only a 2% risk of developing type 1 diabetes, whereas children of fathers who have type 1 diabetes have a 7 % risk (Table 1) ***(Hamalaninen and Knip, 2002).***

Table (1): Genetic susceptibility to type 1diabetes:

General population: 0.3%
Relatives: 2-50%
Twins: Monozygotic: 30-50%
Dizygotic: 6-10%
Siblings: 5%
Offspring: Of affected father: 7%
Of affected mother: 2%
Parents: 3%

(Hamalainen and Knip, 2002)

B) Environmental:

1) Viral infection:

Although viral disease has long been proposed as a potential trigger of beta cell destruction, insufficient exposure to early infections might increase the risk of T1DM as the maturation of immune regulation after birth is driven by exposure to microbes. The evidence linking specific infections with T1DM remains inconclusive ***(Goldberg and Krause, 2009).***

2) Dietary factor:

There is increasing evidence that vitamin D3 might contribute to pathogenesis and prevention of T1DM. Active vitamin D3 prevents T1DM in animal models, modifies T-cell differentiation, modulates dendritic cell action and modulates cytokine secretion, shifting the balance to regulatory T-cells. Maternal intake of vitamin D in food during pregnancy was significantly associated with a decreased risk of islet autoimmunity appearance in offspring ***(Rewers et al., 2008).***

C) Triggering of autoimmunity:

About 80-90% of newly diagnosed patients with T1DM have Islet cell antibodies (ICA) which are the classical antibodies present in their serum ***(Makinen et al., 2008).***

Some T1DM patients (30-40%) have spontaneous anti-insulin antibodies (AIA) at initial diagnosis. In children less than 5 years, almost 100% have AIA at diagnosis that probably was present before clinical manifestation of diabetes. These higher levels usually reflect more aggressive disease ***(Hickey et al., 2007).***

Complications of type I DM:

Diabetes is associated with development of micro- and macro-vascular complication that lead to high morbidity, mortality and associated costs. Over 200,000 people die each year due to diabetes related complication. In fact, micro-vascular complication in type 1 diabetes may not develop signs until 10 years after diagnosis of diabetes ***(Zimmermans, 2005).***

Diabetes complications are common and cost almost triple the annual cost of managing diabetes ***(Bate and Jerums, 2003).***

Table (2): Complication of type 1 diabetes:

Acute:
▪ Ketosis.
▪ Ketoacidosis.
▪ Hypoglycemic episodes.
▪ Infections.
Chronic:
Micro-vascular disease:
▪ Retinopathy, cataract.
▪ Nephropathy.
▪ Neuropathy.
▪ Polyneuropathy, mono-neuropathy, autonomic dysfunction.
▪ Foot ulcers(vascular disease is also a cause)
▪ Impotence.
Macro-vascular disease:
▪ Coronary heart disease.
▪ Cerebrovascular disease.
▪ Peripheral vascular disease.
▪ Skin (infection, mycosis, lipodystrophy).
▪ Psychosocial, depression.

(Salma, 2003)

A- Acute complication:

1. Diabetic coma:

Diabetic coma is a medical emergency in which a person with diabetes is comatose (unconscious) because of one of the acute complications of diabetes either severs diabetic hypoglycemia, DKA, hyperosmolar non Ketotic coma ***(Khardori, 2012).***

2. Diabetic ketoacidosis:

DKA is an acute and dangerous complication that is always a medical emergency. Diabetic ketoacidosis (DKA) is the leading cause of morbidity and mortality in children with type 1 diabetes mellitus (T1DM). Mortality is predominantly related to the occurrence of cerebral edema:

Low insulin level cause the liver to turn fatty acid to ketone for fuel (i.e ketosis), ketone bodies are intermediate substrates in that metabolic sequence. This is normal when periodic, but can become a serious problem if sustained.

Elevated levels of ketone bodies in the blood decrease the blood pH, leading to DKA. On presentation in the hospital the patient in DKA is typically dehydrating, and breathing rapidly and deeply. Abdominal pain is common and may be severe. The level of consciousness typically normal until late in the process and lethargy may progress to coma. Ketoacidosis can easily become severe enough to cause hypoglycemia, shock and death. Prompt, proper treatment usually results in full recovery, though death can result from inadequate or delayed treatment or from complications (e.g, brain edema) ***(Glaser, 2006).***

DKA is always a medical emergency and requires medical attention. Ketoacidosis is much more common in type 1 diabetes than type 2. Every year worldwide, approximately 79,100 children under 15 years of age develop type 1 diabetes. Up to 80% of these young people

already have DKA when they are diagnosed with diabetes. There is a significant variation in the frequency of DKA between and in some cases within different countries around the world ***(IDF 2013).***

Frequency of DKA:

- **At disease onset:**

DKA at diagnosis is more common in younger children (<5 years of age), and in children whose families do not have ready **(Quinn et al., 2006).**

- **In children with established diabetes (recurrent DKA)** ***(Rewers et al., 2002; Hanas et al., 2009):***

The risk is increased in:

- Children with poor metabolic control or previous episodes of DKA.
- Peripubertal and adolescent girls.
- Children with psychiatric disorders, include those with eating disorders.
- Children with difficult or unstable family circumstances.
- Children who omit insulin.
- Children with limited access to medical services.
- Insulin pump therapy (as only rapid- or short- acting insulin is used in pumps, interruption of insulin delivery for any reason rapidly leads to insulin deficiency).