Alexandria University
High Institute of Public Health
Department of Epidemiology

CARDIOVASCULAR DISEASE RISK FACTORS AMONG DIABETIC ADOLESCENTS IN ALEXANDRIA

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by

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Declaration

I declare that no part of the work referred to in this thesis has been submitted in support of an application for another degree or qualification of this or any other University or other Institution of learning.

Amany Ahmed Loutfy Ali Salama

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CONCLUSION

From the present study it can be concluded that:

- The proportion of type 1 DM among diabetic adolescents was 98% and only 2% had type 2 DM.
- Despite the majority of diabetic adolescents taking diabetic medication regularly, measuring blood sugar, and visiting diabetic clinic, they did not have good glycemic control.
- The most prevalent CVDs risk factor among diabetic adolescents was abnormal HbA1c and it was more prevalent among females than males with statistical significant difference.
- The majority of diabetic adolescents had positive family history of diabetes and almost half of them had family history of CVDs. About one quarter of the diabetic adolescents had abnormal blood pressure. Overweight and obesity were more prevalent among females than males with statistical significant difference.
- About one fifth of diabetic adolescents had 2 risk factors of CVDs. The most common combination was elevated HbA1c and positive family history of DM.
- Almost one third of diabetic adolescents had 3 risk factors of CVDs. The most prevalent combination was elevated HbA1c and positive family history of DM and CVDs.
- Logistic regression analysis of CVDs risk factors revealed that socioeconomic level and sex were significantly and independently associated with the prevalence of two and more CVDs risk factors among diabetic adolescents.
- Almost half of the diabetic adolescents had fair level of knowledge regarding CVDs and the physician was the main source of knowledge.
- Logistic regression analysis showed that age, residence, socioeconomic level, and source of knowledge were significantly and independently associated with adolescents' knowledge regarding CVDs among diabetic adolescents.
- The majority of diabetic adolescents had moderate levels of perception of susceptibility, severity, benefit, and barrier about CVDs.
- The perception of severity and barrier with the diabetic adolescents' level of knowledge about CVDs among diabetic adolescents was highly statistically significant.
- Almost half of the diabetic adolescents had moderate dietary habit (moderate consumption of salt and fat, high consumption of fruits and vegetables and eating fish twice or one per week) and physically inactive.
- About two thirds of diabetic adolescents had fair level of self-care behavior.
- Multivariate analysis showed that three independent factors were found to be significant affecting the adolescents' self-care behavior; sex, socioeconomic score and total score of knowledge about CVDs.
- The mean score of knowledge, perception, and self-care behavior about CVDs were significantly improved after implementation of the intervention program.

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LIST OF ABBREVIATIONS

ACE:	Angiotensin Converting Enzyme
AER:	Albumin Excretion Rate
BMI:	Body Mass Index
BP:	Blood Pressure
CHD:	Coronary Heart Disease
CI	Confidence Interval
CFRD:	Cystic Fibrosis Related Diabetes
CVDs:	Cardiovascular Diseases
DBP	Diastolic Blood Pressure
DKA:	Diabetic ketoacidosis
DM:	Diabetes Mellitus
DSME:	Diabetes Self-management Education
DSMS:	Diabetes Self-management Support
EDIC:	Epidemiology of Diabetes Intervention and Complications
ETS:	Environmental Tobacco Smoke
FET:	Fisher Exact Test
FPG:	Fasting Plasma Glucose
GAD65:	Glutamic Acid Decarboxylase
GFR:	Glomerular Filtration Rate
HbA1c:	Hemoglobin A1C
HBM:	Health Belief Model
HDL:	High-Density Lipoprotein
ID:	Identification
IGT:	Impaired Glucose Tolerance
IFG:	Impaired Fasting Glycemia
JNC7:	Seven Report of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of high Blood Pressure
LDL:	Low-Density Lipoprotein
MODY:	Maturity Onset Diabetes of the Young
NHBPEP:	National High Blood Pressure Education Program
OGTT:	Glucose Tolerance Test
PVD:	Peripheral Vascular Disease
QOL:	Quality of Life
SBP:	Systolic Blood Pressure
SMBG:	Self-Monitoring of Blood Glucose
TC:	Total Cholesterol
TDEI:	Total Daily Energy Intake
TG:	Triglyceride
UNICEF:	United Nations Children’s Fund
WC:	Waist Circumference
WHO:	World Health Organization

AIM OF THE STUDY

General objective:

To study selected cardiovascular disease risk factors among diabetic adolescents in Alexandria.

Specific objectives:

1) To determine the prevalence of cardiovascular risk factors among diabetic adolescents in Alexandria.
2) To assess knowledge and perceptions of diabetic adolescents concerning cardiovascular disease risk factors.
3) To construct and implement an educational program for diabetic adolescents concerning cardiovascular disease risk factors.
4) To evaluate the impact of the educational program on their self care behavior.

INTRODUCTION

Diabetes is a complex, chronic illness requiring continuous medical care with multifactorial risk-reduction strategies beyond glycemic control. Ongoing patient self-management education and support are critical to preventing acute complications and reducing the risk of long-term complications. (1)

Diabetes is a disease defined by abnormalities of fasting or postprandial glucose and is frequently associated with disorders of the eyes, kidneys nerves, and circulatory system. The circulator disorders include coronary heart disease (CHD), stroke, peripheral arterial disease, cardiomyopathy, and congestive heart failure. Diabetes generally results in early death from cardiovascular diseases (CVDs).(2)

Both type 1 and type 2 diabetes can occur in children and adolescents, although type 1 is in most countries still more common and in fact is still often referred to as childhood or juvenile-onset diabetes. Type 1 and type 2 diabetes present somewhat different disease patterns and require different management; people with type 1 diabetes require daily insulin, which is literally a life-saving treatment. Depending on clinical parameters and treatment success, individuals with type 2 diabetes may require insulin. Whether type 1 or type 2, all forms of diabetes pose potentially grave dangers to health.(3)

The rapidly rising incidence of both type 1 and type 2 diabetes in young people is a clear evidence that the rules' of diabetes epidemiology are being broken. It is preceded by a dangerous period, including diabetic ketoacidosis (DKA), from which children continue to die, as a result of ignorance and lack of education.(4)

Diabetes in childhood and adolescence presents very different challenges from diabetes in adults. Diabetes has an impact on every aspect of an adolescent's life and experience. It imposes a burden to the adolescent, his or her parents, siblings and the rest of the family, the school and local community.(5)

Many children and adolescents are facing a greater burden associated with early appearance of diabetes and an increased risk of complications with longer duration of disease. Early detection, improved access to and delivery of care and better self-management are key strategies for reducing much of the burden of diabetes.(6) Diabetes is a major cost in health care budgets in both developed and developing countries and the costs are rising exponentially in tandem with the rising incidence worldwide.(7)

The prevalence of type 2 diabetes and associated co-morbidities are rising worldwide. The epidemiological evidence suggests that without effective prevention and control programs the prevalence will continue to increase globally. Most of the risk factors associated with type 2 diabetes are preventable.(8)

Cardiovascular diseases, which include CHD, cerebrovascular disease, and peripheral vascular disease (PVD), are the leading cause of mortality in populations, particularly among diabetics. Individuals with diabetes have at least a two-fold to four-fold increased risk of having cardiovascular events and a double risk of death compared with age-matched subjects without diabetes.(9)

A: Adolescence:

World Health Organization (WHO) identifies adolescence as the period in human growth and development that occurs after childhood and before adulthood, from ages 10 to 19 years. It represents one of the critical transitions in the life span and is characterized by a tremendous pace in growth and change that is second only to that of infancy. Biological processes drive many aspects of this growth and development, with the onset of puberty marking the passage from childhood to adolescence. [10]

Adolescence begins around age 10, 11, or 12 and concludes somewhere between 18 and 21 years of age. It is important to remember that age alone does not signify the beginning and end of adolescence, but rather achieving key developmental milestones indicates when a particular stage of development has begun or concluded. While a variety of changes are taking place during adolescence, these changes can, for the most part, be classified within three major categories; *physical*, *cognitive*, and *socio emotional*.[11] The phases of adolescent according to United Nations Children's Fund (UNICEF) are early adolescence (10–14 years) and late adolescence (15–19 years). [12]

Adolescents aged 10-19 years accounted 1.2 billion (20 % of world total population) and in Middle East and North Africa, they constituted 82 million in the year 2010. In Egypt, they constituted 20% of total population in the year 2010 and are expected to be 14% in the year 2050. [13] Mortality rates are low in adolescents compared with other age groups. [14]

B: Diabetes Mellitus:

Diabetes mellitus (DM) is a group of metabolic diseases characterized by chronic hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The abnormalities in carbohydrate, fat, and protein metabolism that are found in diabetes are due to deficient action of insulin on target tissues. If ketones are present in blood or urine, treatment is urgent, because ketoacidosis can evolve rapidly.[15]

Magnitude of diabetes mellitus among adolescents:

It is estimated that by 2025, 380 million people will have developed diabetes, amongst them an increasing number of children and adolescents who will face lifelong treatment and risk for acute and chronic complications. [7] The incidence of type 1 diabetes is increasing in children and youth by about 3% (range about 2–5%) annually. [4]

In USA, about 208,000 Americans under age 20 are estimated to have diagnosed diabetes, (approximately 0.25% of that population). [16] The SEARCH for Diabetes in Youth (SEARCH) study estimated that there were 166. 018 to 179. 388 youth with type 1 diabetes in the United States in 2010. [17] The incidence of type 1 diabetes shows a large worldwide variation (from 0.6 per 100 000 in Korea and Mexico to 35.3 per 100 000 in Finland. [18]

In 2015, the number of children (0-14 years) with type 1 diabetic and number of newly diagnosed children each year is 542.000 and 86.000 worldwide, in Africa (46,400

and 7.600), in Middle East and north Africa (60.700 and 10.200) respectively. In Egypt, the number of children with type 1 DM (0-14) per 1.000s is 5.8. [19]

Before the 1990s, type 2 diabetes was rarely diagnosed in youth, but its rates are now parallel to the increasing rates of pediatric obesity. Although rates of type 2 diabetes in youth have increased in recent decades. [4, 17] Type 2 diabetes has been estimated at between 2–50 / 1000 in various populations. [18]

Type 2 diabetes continues to be less common than type 1 diabetes. The SEARCH study estimated that there were between 20.203 and 22.820 youth with type 2 diabetes in the United States in 2010. By 2050, the prevalence of type 2 diabetes in youth is estimated to be 30.111 to 84.131 constituting 10% to 15% of all diabetes mellitus in youth in the United States. [17]

The causes of diabetes mellitus among adolescents:

The main causes are genetic and environmental. Insufficient insulin secretion can occur in association with destruction of pancreatic islet β-cells or due to dysfunction within the pancreatic β-cells themselves. Besides the decrease in insulin supply, decreased insulin sensitivity can contribute to relative insufficient insulin action. In either case, the principal mechanism for development of diabetes is decreased functional pancreatic β-cell mass that results in failure to provide adequate insulin action on the organs. The associated metabolic disorders can be improved by various therapeutic means to ameliorate insufficient insulin action.[20]

- The cause of type 1 diabetes is an absolute deficiency of insulin secretion. Individuals at increased risk of developing this type of diabetes can often be identified by serological evidence of an autoimmune pathologic process occurring in the pancreatic islets and by genetic markers.
- The cause of type 2 diabetes is a combination of resistance to insulin action and an inadequate compensatory insulin secretory response. [21]

Pathogenesis of type 1 diabetes:

- Individuals have an absolute deficiency of insulin secretion and are prone to ketoacidosis.
- Most cases are primarily due to T-cell mediated pancreatic islet β-cell destruction, which occurs at a variable rate, and becomes clinically symptomatic when approximately 90% of pancreatic beta cells are destroyed.
- Serological markers of an autoimmune pathologic process, including islet cell, GAD, IA-2, IA- 2β, or insulin autoantibodies, are present in 85-90% of individuals when fasting hyperglycemia is detected.
- Susceptibility to autoimmune type 1 diabetes is determined by multiple genes; in a recent meta-analysis more than 40 distinct genomic locations provided evidence for association with type 1 diabetes. [15]
- The environmental triggers (chemical and/or viral) which initiate pancreatic beta cell destruction remain largely unknown, but the process usually begins months to years

before the manifestation of clinical symptoms. [22] Enterovirus infection has been associated with development of diabetes associated autoantibodies in some populations [23] and enteroviruses have been detected in the islets of individuals with diabetes. [24, 25]

- When the clinical presentation is typical of type 1diabetes (often associated with DKA) but antibodies are absent, then the diabetes is classified as Type 1B (idiopathic).[15]

Classification of diabetes mellitus:

There are type 1, type 2 and monogenic diabetes. The differentiation between them has important implications for both therapeutic decisions and educational approaches. [26]

- Measurement of diabetes associated autoantibody markers, e.g. ICA, GAD, IA2, IAA and/or HbA1c may be helpful in some situations.
- Measurement of fasting insulin or C-peptide may be useful in the diagnosis of type 2 diabetes in children. Fasting insulin and C-peptide levels are usually normal or elevated, although not as elevated as might be expected for the degree of hyperglycemia. [15]

The possibility of other types of diabetes should be considered in the child who has:

1. An autosomal dominant family history of diabetes.
2. Associated conditions such as deafness, optic atrophy or syndromic features.
3. Marked insulin resistance or require little or no insulin outside the partial remission phase.
4. A history of exposure to drugs known to be toxic to beta cells or cause insulin resistance. [27]

Type 1 diabetes (β_-cell destruction, usually leading to absolute insulin deficiency):

Immune-mediated diabetes. This form of diabetes, which accounts for only 5–10% of those with diabetes, previously encompassed by the terms insulin dependent diabetes, type I diabetes, or juvenile- onset diabetes, results from a cellular-mediated autoimmune destruction of the β-cells of the pancreas. Markers of the immune destruction of the β-cell include islet cell auto antibodies, auto antibodies to insulin, autoantibodies to glutamic acid decarboxylase (GAD65), and autoantibodies to the tyrosine phosphatases IA-2 and IA-2_In this form of diabetes, the rate of β_cell destruction is quite variable, being rapid in some individuals (mainly infants and children) and slow in others (mainly adults). Some patients, particularly children and adolescents, may present with ketoacidosis as the first manifestation of the disease. At latter stage of the disease, there is little or no insulin secretion, as manifested by low or undetectable levels of plasma C-peptide. [21]

Idiopathic diabetes. Some forms of type 1 diabetes have no known etiologies. Some of these patients have permanent insulinopenia and are prone to ketoacidosis, but have no evidence of autoimmunity. Although only a minority of patients with type 1 diabetes fall into this category, of those who do, most are of African or Asian ancestry. 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 β-cell autoimmunity. [21, 28]

Type 2 diabetes (ranging from predominantly insulin resistance with relative insulin deficiency to predominantly an insulin secretary defect with insulin resistance):

This form of diabetes, which accounts for 90–95% of those with diabetes, previously referred to as non-insulin dependent diabetes, type II diabetes, or adult-onset diabetes, encompasses individuals who have insulin resistance and usually have relative (rather than absolute) insulin deficiency. At least initially, and often throughout their lifetime, these individuals do not need insulin treatment to survive. There are probably many different causes of this form of diabetes. Although the specific etiologies are not known, autoimmune destruction of β-cells does not occur, most patients with this form of diabetes are obese, and obesity itself causes some degree of insulin resistance. [21]

Monogenic diabetes:

Monogenic β-cell diabetes (1–2% of all diabetes cases) amongst the vast majority who have type 1 or 2 diabetes. [29] Genetic defects of β-cell function or insulin action, formerly termed 'Maturity onset diabetes of the young' (MODY) was originally described as a disorder with the following characteristics: onset before 25 years of age, autosomal dominant inheritance, nonketotic diabetes mellitus. [30] Since the classification of diabetes was revised in 1998 to reflect etiology, the term MODY is now obsolete and that the correct monogenic names of the different forms of young-onset diabetes should be used when possible.[29]

Cystic fibrosis related diabetes:

Cystic Fibrosis related diabetes (CFRD) is primarily due to insulin deficiency, but insulin resistance during acute illness, secondary to infections and medications (bronchodilators and glucocorticoids), may also contribute to impaired glucose tolerance and diabetes. CFRD tends to occur late in the disease, typically in adolescence and early adulthood. Cirrhosis, if present, may contribute to insulin resistance. The onset of CFRD is a poor prognostic sign, and is associated with increased morbidity and mortality. Poorly controlled diabetes will interfere with immune responses to infection and promote catabolism. [15]

Drug induced diabetes: [15]

In neurosurgery, large doses of dexamethasone are frequently used to prevent cerebral oedema (eg dexamethasone 24 mg per day). The additional stress of the surgery may add to the drug-induced insulin resistance, and cause a relative insulin deficiency, sufficient to cause a transient form of diabetes.

In oncology, protocols which employ L-asparaginase, high dose glucocorticoids, cyclosporin or tacrolimus (FK506) may be associated with diabetes. L-asparaginase usually causes a reversible form of diabetes.Tacrolimus and cyclosporin may cause a permanent form of diabetes possibly due to islet cell destruction. Often the diabetes is

cyclical and associated with the chemotherapy cycles, especially if associated with large doses of glucocorticoids.

Following transplantation, diabetes most frequently occurs with the use of high dose steroids and tacrolimus; the risk is increased in patients with pre-existing obesity. Diabetes can also be induced by the use of atypical antipsychotics including olanzapine.

Impaired glucose tolerance and impaired fasting glycemia:

Impaired glucose tolerance (IGT) and impaired fasting glycemia (IFG) are intermediate stages in the natural history of disordered carbohydrate metabolism between normal glucose homeostasis and diabetes.[31] Patients with IFG and/or IGT are now referred to as having "pre-diabetes" indicating the relatively high risk for development of diabetes in these patients.[28, 31]

Risk factors of type 1 diabetes:

Based on comparative studies to determine the effect of genetic and environmental factors on the onset of diabetes, 88% of phenotypic variances are ascribable to genetic factors, and the rest to unshared environmental factors. Environmental risk factors are thought to be 'initiators' or 'accelerators' of β-cell autoimmunity.[32]

The environmental trigger may cause an uncontrollable autoimmune response that attacks insulin- producing β cells. Some epidemiological studies suggest that breast feeding reduces the risk for developing the disease later in life, presumably by protecting against infections, enhancing the infant's immune system and delaying exposure to foreign food antigens. Cow's milk protein has been proven conclusively. Epidemiological studies have shown that supplementing infant diets with gluten- containing foods before 3 months of age is associated with an increased risk of developing the disease. Giving children 2000IU of vitamin D per day during their first year of life is associated with a reduced risk for type 1 diabetes. [33] Heavy weight during infancy has been implicated as risk factors for type 1 diabetes. [4]

Risk factors of type 2 diabetes:

The primary risk factors for type 2 diabetes are increased weight and lack of physical activity. Over the past decade, there have been profound changes in the quality, quantity and source of food consumed in many developing countries. Processed food, for instance, typically offers greater caloric content but lower nutritional value, at a lower cost. An increasingly sedentary lifestyle and limited physical and sporting activities in school also play a part in the development of overweight and obesity. Overweight and obesity is acting as a driver to the development of type 2 diabetes in youth, particularly after onset of adolescence. [5] By the age of 15 more than 25% of obese adolescents have early signs of diabetes. [34]

- Antenatal risk factors associated with the development of childhood obesity, type 2 diabetes and cardiovascular disease include prenatal factors such as placental