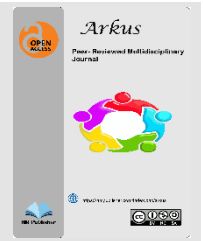




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An Overview of Diabetes Mellitus Type I

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ABSTRACT

Diabetes mellitus (DM) is a complex metabolic disorder characterized by the condition of persistent hyperglycemia due to abnormalities in insulin secretion, insulin action, or both. DM type 1 is more often found in children but with increasing obesity rates, the number of children with type 2 diabetes is increasing. In children who have been diagnosed, determining the type of DM becomes important because of its large clinical implications especially for the choice of therapy. The determination of the type of DM is based on the clinical characteristics of the patient, but differentiating the various types is not always easy and is still a challenge in itself. DM management aims to achieve controlled glucose levels and prevent complications, both acute or chronic complications. Complications related to metabolic control and duration of suffering from DM, so early detection of DM especially in high-risk children should be sought as part of the prevention of DM and its various complications.

1. Introduction

Control of Non-Communicable Diseases (NCD) is one of the Sustainable Development Goals (SDGs) agenda. The incidence of NCD such as diabetes mellitus (DM) has increased every year. DM does not only attack adults but also children. DM in children, primarily type 1 DM, the incidence is increasing. Along with the increasing incidence of obesity in children, type 2 diabetes is also increasing along with early cardiometabolic complications. Other types of DM are caused by genetic disorders, such as maturity-onset diabetes of the young (MODY) or monogenic diabetes. From September 2009 to September 2016, there were 1200 new cases of DM.^{1,2} Diagnosis is often delayed, especially the emergency of Diabetic Ketoacidosis (DKA), which is often

misdiagnosed. Awareness of health workers is essential to catch these cases, which is an iceberg phenomenon. In children who have been diagnosed, determining the type of DM becomes essential because of the significant clinical implications, especially for the choice of therapy. Determining the type of DM is based on the patient's clinical characteristics, but distinguishing the various types is not always easy. More than 90% of diabetes cases in children and adolescents are type 1 DM. DM management aims to achieve controlled glucose levels and prevent acute (hypoglycemia, DKA) and chronic (microvascular and macrovascular) complications. Complications and comorbidities are related to metabolic control and duration of suffering from DM,



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so that early detection of DM, especially in high-risk children, should be sought as part of preventing DM and its various complications. In some cases, such as type 2 diabetes mellitus or monogenic diabetes, children generally do not show typical symptoms or are even asymptomatic, so that they can only be detected when complications have occurred.

Definition

Diabetes mellitus (DM) is a complex metabolic disorder characterized by persistent hyperglycemia due to abnormalities in insulin secretion, insulin action, or both. Glucose homeostasis depends on insulin secretion by pancreatic beta cells and insulin action on tissues.

Epidemiology

The prevalence of DM in children is increasing in various parts of the world. Of the various types of DM, type 1 diabetes is the most common type, with 90% of all DM in children, followed by type 2 diabetes by 10% and monogenic diabetes by 1-4%. Research in America in 2001-2009 found an increase in the prevalence of DM in children by 21.1% in type 1 DM and 30.5% in type 2 DM. Type 1 DM was primarily found in Caucasian ethnicity, while the highest type 2 DM was found in Indian ethnic -America (49.4%), followed by Asia (22.7%).³

Pathophysiology

Under normal physiological conditions, insulin is secreted by pancreatic cells in response to an increase in blood glucose. In the fasting state, glucagon is secreted by pancreatic cells to prevent hypoglycemia by activating gluconeogenesis in the liver. In DM, there is an imbalance in this homeostasis. Type 1 diabetes is characterized by chronic pancreatic-cell destruction characterized by absolute insulin deficiency. Damage to pancreatic cells can occur due to autoimmune processes or other unknown causes (idiopathic). Nearly 45 per

cent of sufferers do not have a family history of the disease. This type of diabetes is most common in children, which is 90% of all cases of DM in children. Anyone can get type 1 diabetes.

In contrast to type 1 diabetes, in type 2 diabetes, the failure of pancreatic cells to produce insulin is not mediated by an autoimmune process but occurs due to a combination of insulin resistance and relative insulin deficiency. When a child is diagnosed, it is estimated that there has been a decrease in pancreatic cell function up to 80%.⁴ The pathogenesis of type 2 DM is a complex process with a multifactorial aetiology, including genetic factors, obesity, low-fibre and high-fat diet habits with excess calories, lack of physical activity, and sedentary lifestyle. As many as 25-45% of children with obesity have type 2 diabetes, and conversely, more than 85% of children with type 2 diabetes are children with more nutritional status or obesity. In obese children, there is a condition of hyperinsulinemia due to decreased insulin sensitivity up to 40%.⁵ Adipose tissue that develops in obesity conditions synthesizes and secretes metabolites and signalling proteins such as leptin, resistin, and tumour necrosis alpha (TNF- α). These factors are known to decrease insulin sensitivity in various clinical trials. Another study found that TNF- and free triglycerides lead to inflammation and β -cell damage leading to impaired glucose tolerance.

Decreased tissue response to insulin and inadequate insulin secretion will cause carbohydrate, fat, and protein metabolism disturbances. Puberty is also known to have a significant role in the development of type 2 diabetes in children. During puberty, there is increased resistance to insulin action resulting in hyperinsulinemia. Basal and stimulated insulin responses decrease by about 30% in adolescents in middle and late puberty.

The increase in growth hormone during puberty is thought to play a role in insulin resistance, so that type 2 diabetes generally appears at the same time as



the middle age of puberty. For type 1 DM, puberty will also increase insulin doses due to this physiological insulin resistance. Another type of diabetes that commonly appears in adolescence is monogenic diabetes or MODY.

Monogenic diabetes is a familial form of DM in the form of a group of disorders caused by mutations in genes that are important for the development or function of pancreatic cells. Currently, monogenic diabetes is generally categorized based on its genetic subgroup, namely abnormalities on chromosome 12 (HNF1A, MODY3), chromosome 7 (GCK, MODY2), chromosome 20 (HNF4B, MODY1), chromosome 13 (IPF1, MODY4), chromosome 17 (HNF1B, MODY5), chromosome 2 (NEUROD1, MODY6), chromosome 2 (KLF11, MODY7), chromosome 9 (CEL, MODY8), chromosome 7 (PAX4, MODY9). In the various diagnostic groups for monogenic diabetes, variations in the degree of hyperglycemia, insulin requirements, and risk of complications were found.⁶⁻⁸

Clinical manifestations

In type 1 DM, the clinical symptoms that appear can vary. Non-emergency manifestations include enuresis, candidiasis vaginalis in girls, weight loss, irritability, and recurrent skin infections. Emergency conditions that can occur are severe dehydration, shock, and ketoacidosis. Typical symptoms of type 1 diabetes include polyuria, polydipsia, and weight loss within 2-4 weeks. Failure to detect type 1 DM can result in complications, especially diabetic ketoacidosis. There is type 2 DM, most of the children have more nutritional status or obesity. Most patients present with glucosuria without ketonuria, with or without polyuria and polydipsia, with little or no weight loss. Age is usually more than ten years and is in middle or late puberty. In asymptomatic children, type 2 diabetes is often diagnosed through routine laboratory tests, especially urinalysis. A family history, acanthosis nigricans, dyslipidemia, hypertension, and polycystic ovary syndrome are

common conditions in children with type 2 diabetes. Most children with monogenic diabetes are diagnosed initially as type 1 diabetes or less often as type 2 diabetes. In children whose parents and grandparents also suffer from DM, especially in patients with DM characteristics that are not typical for type 1 or type 2. The presence of a stable and non-progressive hyperglycemia condition can be a symptom of MODY2, a type of monogenic diabetes that occurs most often.

Diagnosis and differential diagnosis

The diagnosis of DM was made based on the presence or absence of clinical symptoms of DM and the results of measurements of plasma glucose levels. The classic clinical symptoms of DM are polyuria, polydipsia, nocturia and unexplained weight loss. In the absence of clinical symptoms of DM, the examination should be repeated at a different time. The diagnosis of DM can be made if one of the following criteria is found, namely clinical symptoms of polydipsia, polyphagia, polyuria, nocturia, decreased body weight and blood glucose levels (GDS) 200 mg/dl, or fasting blood sugar 126 mg/dL; or GDS 200 mg/dl after 2 hours of glucose tolerance test. Most patients with type 1 diabetes have a history of an acute clinical course. Polyuria, polydipsia, and polyphagia are accompanied by rapid weight loss 2-6 weeks before the diagnosis, sometimes with visual disturbances. If these clinical symptoms are accompanied by hyperglycemia, the diagnosis of DM cannot be doubted. Type 1 and type 2 diabetes should be distinguished by their insulin or c-peptide levels based on the pathogenesis. In type 1 diabetes, insulin and c-peptide levels will be low or very low. Whereas in type 2 DM, insulin/c-peptide levels will be normal or increased. In addition, in type 1 diabetes, auto-antibodies will be detected against pancreatic beta cells, whereas in type 2 diabetes, they will not. These two things are theoretically differentiating between type 1 and type 2 DM. Patients with type 1 diabetes



who are obese may have higher residual c-peptide levels.⁹

2. Conclusion

Diabetes mellitus is a condition of persistent hyperglycemia caused by defects in insulin secretion, insulin action, or both. Most people with diabetes mellitus in children are type 1 diabetes, although the prevalence of type 2 diabetes in children also increases with increasing cases of obesity at an early age. Determining the type of DM after the diagnosis is made is very important because it affects therapy and monitoring complications and co-morbidities. The ability of health workers to detect risk factors and clinical manifestations is very necessary to avoid errors or delays in diagnosis.

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