Original article

Clinical and laboratory features of children with insulin dependent diabetes mellitus of more than two years

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ABSTRACT The incidence rate of IDDM in our clinic during the period from 1989 to 1998 was 0.028%. There were twenty-four IDDM patients with duration of illness of more than 2 years, with a male to female ratio of 1: 1.5. Most of these patients had no diabetic family history and had good nutritional status. The insulin dosage used by these patients ranged between 0.67 - 0.72 IU/kg/day with a mean of 1.06 IU/kg/day. The average frequency of blood glucose home monitoring was less than ideal. Twenty-two out of the 24 patients were fully controlled metabolically; however, these patients still have polyuria, polydipsia, and polyphagia.**[Paediatr Indones 2001;41:256-259]**

Keywords: Insulin dependent diabetes mellitus (IDDM), blood glucose home monitoring, insulin, metabolic control

INSULIN DEPENDENT DIABETES MELLITUS (IDDM), THE MOST commonly found diabetes mellitus type in children,[1] is caused by progressive destruction of pancreatic b-cells leading to inadequate insulin production.[2] The classical clinical symptoms of diabetes, i.e., polyuria, polydipsia, and polyphagia, occur after more than 80% pancreatic b-cells are destructed. This damage continues along the clinical course of IDDM. In pediatric population, the clinical course of IDDM is divided into 4 phases: initial, recovery, honeymoon period, and intensification phase, occurring in the first 2 years after the diagnosis.[3,4] In children with IDDM, optimal insulin requirements in reducing blood glucose levels in the first 2 years should be carefully determined. Some amount of insulin is still synthesized by residual pancreatic b-cells, especially in honeymoon period, the pancreatic b-cells become more active in producing insulin. If the dosage of insulin given is not reduced, hypoglycemia will often take place.[5]

Unlike in 'new' patients, the entire pancreatic b cells in IDDM patients suffering more than 2 years are completely damaged, resulting in the incapability in producing insulin. In this situation IDDM patients depend entirely on extraneous insulin to maintain normal plasma blood glucose levels.[3,6] Clinical and laboratory features at the time of diagnosis have been widely studied, in Indonesia and abroad. However, report on clinical and laboratory features, insulin requirements and metabolic control of IDDM patients with duration illness of more than 2 years is unavailable in Indonesia. There are only a few overseas reports about these 'stable' patients. We reviewed clinical and laboratory features of IDDM children who suffered for more than 2 years.

Methods

This study was conducted at the Pediatric Endocrinology Clinic, Child Health Department, Medical School, University of Indonesia, Jakarta, from April to June 1999. The study population was all IDDM patients treated during the period. Only patients

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diagnosed with IDDM at the age of more than 2 years were contacted, with parental consent to participate. We excluded patients without clear address, or those who refused to participate in the study, or patients who had died.

On presentation their previous day fluid intake and 24 hours urine volume were noted. History taking was done including the history of polyuria, polydipsia, polyphagia, age at diagnosis, age at study, insulin dosage in use, and frequency of blood glucose home monitoring. Complete physical examination was done with reference to bodyweight and height and pubertal status. We measured HbA_1c, fasting blood glucose, fructosamine, cholesterol, C-peptide levels and metabolic control status at the time of study.

Results

There were 41 patients diagnosed to have IDDM during the study period; the number of outpatient visits during that period were 145.719, giving the incidence rate of IDDM of 0.028%. Out of those 41 patients, only 24 met the study criteria, 10 boys and 14 girls. Seventeen patients were just diagnosed less than 2 years before, 5 patients with unknown address and 2 patients had passed away. The mean age of these IDDM patients was 13.6 (SD 2.96) years. **Table 1** shows their age and sex distribution.

TABLE 1. DISTRIBUTION OF AGE BY SEX IN IDDM PATIENTS

Age (years)	Sex		Total
	Boys	Girls	
≤ 12	4	4	8
> 12	6	10	16
Total	10	14	24

Most patients (17/24) had no family history of DM. Two patients had siblings with DM, 2 other had their grandmother with DM and 3 patients had grandfather with DM. Most patients (19/24) were malnourished while the other 5 were well-nourished. Fifteen of the 24 patients had reached puberty, 7 were in prepubertal status, while 2 were classified as delayed puberty.

The mean insulin dosage needed in these IDDM patients was 1.06 (SD 0.25) IU/kg bodyweight/day. Half the patients in this study performed blood glucose home monitoring only once a week (**Table** 2).

TABLE 2. DISTRIBUTION OF BLOOD GLUCOSE HOME MONITORING IN IDDM PATIENTS BY SEX

Blood glucose home monitoring	Sex		Total
	Boys	Girls	
3 x / week	4	5	9
1 x / week	5	7	12
1 x / month	1	2	3
Total	10	14	24

In this group of patients, only 2 patients showed good metabolic control and 22 were not adequately controlled (**Table 3**)

In this study 87.5% of the patients still had polyuria, 29.2% had polydipsia and 12.5% had polyphagia.

TABLE 3. DISTRIBUTION OF METABOLIC CONTROL IN IDDM PATIENTS BY SEX

Metabolic Control	Sex		Total
	Boys	Girls	
Controlled	1	0	1
Initially controlled	0	1	1
Uncontrolled in the last 6-8 weeks	0	0	0
Uncontrolled in the last 8-12 weeks	4	7	11
Uncontrolled	5	6	11
Total	10	14	24

Laboratory features in the present study used median distribution because the blood glucose levels, cholesterol level, HbA_1c, fructosamine and C-peptide were not in normal distributions. Median value of fasting blood glucose was 152.5 mg/dl (range 44-452 mg/dl), cholesterol 186 mg/dl (range 115-253 mg/dl), HbA_1c 10.6% (range 7.0-17.0%), fructosamine 481.5 mmol/l (range 269-503 mmol/l) and C-peptide < 0.5 ng/ml (range < 0.5 - 0.6 ng/ml).

In the present study HbA_1c level was not associated with the nutritional status of these patients (p > 0,05). The following **Table 4** indicates the relationship between HbA_1c levels with IDDM patient's nutritional states.

TABLE 4. RELATIONSHIP BETWEEN HbA_1C LEVELS AND NUTRITIONAL STATUS OF IDDM PATIENTS

HbA_1c levels (%)	Nutritional states		Total
	Good	Poor	
≤ 10	10	1	11
> 10	9	4	13
Total 19	5	25	
$X^2 = 0.638$	df = 1		p > 0.05

Discussion

We found that the hospital incidence rate of IDDM at our clinic was 0.028%. The highest incidence rate of IDDM is found Finland with 30 new cases in 100,000 children per year.[3] In Asian countries such as China the reported incidence rate of IDDM is 0.51 in 100,000 children per year[8] and in India that incidence is only 0.9 per 100,000 children per year.[9]

Our series show that the sex distribution indicated slight female predominance, i.e., 14/24 vs. 10/24. Study in Belgium reported that IDDM patients with duration of disease of more than 2 years were more prevalent in girls, with a mean age of 12.7 (SD 2.29) years.[10] At the time of diagnosis, the most frequent age was 9 years or older (58%). Sutan Assin et al. reported that the most frequent age group at diagnosis was 12 years,[11] whereas Komulainen et al in Finland reported that age group was between 5-15 years.[12]

In this study most of the patients had no family history of diabetes. This is consistent with study of Mc Laren et al. which shows that 80% of children with IDDM do not have family history of diabetes.[13] Similar findings were reported by Nazir et al in Cipto Mangunkusumo Hospital in 1986 that among 22 patients under 19 years, 76% had no family history of DM.[14]

Dorchy et al in Belgium reported that patients affected with more than 2 years IDDM, mostly had good nutritional status with a mean body mass index of 20.5 (SD 3.7) kg/m2.[10] The insulin used by these IDDM patients was anabolic in nature. Insulin increases glycogenesis and decreases protein catabolism, causing weight gain. Poor nutritional status was seen in 5 patients. This might be due to inadequate insulin dosage or there were conditions causing decreased tissue sensitivity to insulin such as puberty, infection et cetera.

Puberty in girls is usually accompanied by weight gain due to increased body mass index (BMI). BMI is inversely proportional to tissue sensitivity to insulin. Therefore, when BMI increases, sensitivity to insulin decreases. Puberty is always accompanied by growth hormone increase, but this hormone will enhance resistance to insulin. In addition, pubertal status will result in an increase of adrenal androgen hormone that enhances resistance to insulin. Accordingly, insulin dosage in pubertal status will usually be higher

than in prepubertal status.[15] Infection also causes increased insulin requirement. If the insulin dosage is not increased, infected IDDM patients will be hyperglycemic. Puberty is heavily influenced by insulin. This insulin will affect hormonal maturational system, so that when insulin dosage declines pubertal disturbance will occur. The delayed puberty in those two patients were very likely due to the insulin dosage inadequacy.

The mean insulin dosage needed in IDDM patients in this present study was 1.06 (SD 0.25) IU/kg bodyweight/day. This result was similar with that of by Dorchy et al reporting insulin dose requirements in IDDM patients with duration illness of more than 2 years was 1.0 (SD 0.3) IU /kg bodyweight/day.[10]

The classical clinical features of IDDM patients, polyuria, polydipsia and polyphagia, will manifest only after the blood glucose levels have been highly elevated. Insulin deficiency will result in increased glycogenolysis and gluconeogenesis processes. Blood glucose levels will increase and cause increase extracellular osmolality. When this osmolality exceeds renal threshold (> 180 mg/dl), glucose will be excreted through urine. Glucose will absorb water and other electrolytes so that patient complains of frequent urination or polyuria. This symptom will be accompanied by frequent thirst and drinking more (polydipsia). Insulin deficiency will also result in decreased amino acid uptake and protein synthesis, reducing muscular nitrogen supply. Moreover glucose cannot be utilized by the tissues, this will make the patient hungry. Symptom of polyphagia would accompany this condition. Increased glycogenesis happen in IDDM patients adequately treated with insulin. As the result the blood glucose level will decline and glucose would not be excreted through urine. So the three signs of polyuria, polydipsia and polyphagia would not be found in metabolically controlled diabetic patients.

The ideal blood glucose level self-examination is 4 times a day, namely 3 times prior to insulin injection and once at midnight.[3] It was revealed in this group of patients with a poor blood glucose home monitoring, only 2 (8.2%) patients showed good metabolic control, resulting in 87.5% of the patients still had polyuria, 29.2% had polydipsia and 12.5% had polyphagia. It is impossible to expect IDDM patients to be symptom free, and to have a good metabolic control without a proper blood glucose monitoring.

Generally the group showed a low frequency of blood glucose home monitoring, resulting mostly in metabolically uncontrolled patients (91.8%) showing still the classical clinical features of polyuria, polydipsia and polyphagia.

For clinical and academic interests, the classical clinical symptoms of IDDM have to be monitored at each patient visit to the Pediatric Endocrinology Clinic of Child Health Department, Cipto Mangunkusumo Hospital. Metabolic control of patients with IDDM more than 2 years, would be more accurate, if interpretation was based on results of fasting blood glucose, HbA_1c, and fructosamine levels. The Pediatric Endocrinology Clinic needs to determine a minimally effective frequency of blood glucose home monitoring by IDDM patients with duration illness more than 2 years.

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