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Original Article

Audit of childhood diabetes control in Indonesia

Jose RL Batubara, MD
on behalf of the Diabcare-Indonesia 2001 Study Group

ABSTRACT

Objectives To determine the status of diabetes control in children and adolescents in Indonesia.

Methods We collected data from seven pediatric diabetes centers in Indonesia from January to September 2001. Data were obtained either by patient interview during the enrollment visit or by reviewing medical records of the most recent clinical examination and treatment information. Blood samples were also collected for the assessment of HbA_{1c}.

Results Most patients recruited had type 1 diabetes (n=64, 93%) and the focus of this report was on this group. The mean of centrally measured HbA_{1c} in the 60 type 1 patients was 10.5 (SD 2.7%) with 90% having values exceeding 7.5%, indicating inadequate glycemic control. The mean HbA_{1c} was higher in patients older than 10 years but not necessarily in children with longer diabetes duration or older age of diabetes onset. The frequency of severe hypoglycemic or diabetic ketoacidosis was 75 and 20 per 100 patient-years, respectively. Severe hypoglycemia was higher in children younger than five years than those older. Chronic complications including microalbuminuria, neuropathy and retinopathy, were reported in older children but not necessarily in children with longer duration of diabetes or earlier age of diabetes onset. Glycemic control tended to be better for patients on thrice rather than twice daily insulin injections. However, only 12% were on three or four times daily insulin injection regimen compared to 88% who were on twice daily insulin injections.

Conclusions The present audit shows that 90% of the type 1 and all of the type 2 patients did not achieve adequate glycemic control (HbA_{1c} >7.5%). The frequency of severe hypoglycemia was higher in the younger children and glycemic control was worse in the older children **[Paediatr Indones 2002;42:280-286].**

Keywords: *diabetes, HbA_{1c}, children, adolescents, hypoglycemia*

The number of patients with diabetes mellitus (DM) is growing worldwide including in Asia, affecting people of all ages. Children and adolescents with DM form a distinct group that is mainly managed by pediatricians. Although the majority of patients in this group suffer from type 1 autoimmune-induced diabetes mellitus (T1DM), type 2 diabetes mellitus (T2DM) has also emerged in this population in the last decade.[1,2] In this age group, the risks of hypoglycemia and ketoacidosis are more immediate than the risks of micro and macro-vascular complications. Furthermore, the pubertal years during adolescence also present a challenge to glycemic control.

Surveillance of diabetes is a necessary first step toward its prevention and control. Some countries in Asia still have incomplete or lack diabetes data. In Indonesia, available data show that the prevalence of diabetes in the urban areas of Jakarta increased from 1.7% in 1982 to 5.7% in 1995;[3] unfortunately little information on the status of pediatric diabetes is avail-

From Diabcare-Indonesia 2001 Study Group

Reprint requests to: Jose RL Batubara. Department of Child Health, Medical School, University of Indonesia/Cipto Mangunkusumo Hospital, Jakarta, Indonesia. Tel. 62-21-3907740; Fax. 62-21-3907743; e-mail: joserlb@pacific.net.id

able. A cross-sectional survey is required to provide information on diabetes control to facilitate health care policy making in this area. For this reason, the delegates of the International Diabetes Federation (IDF) Leadership Needs Assessment Workshop on Childhood and Adolescent Diabetes held in Kuala Lumpur, August 2000 voted unanimously for an audit and benchmarking project. The objective of the present cross-sectional non-population based audit was to establish the baseline data on control and management of diabetes in children and adolescents in the Western Pacific Region (WPR). The audit involved pediatric diabetes centers from Australia, China, Indonesia, Japan, Korea, Malaysia, Philippines, Singapore, Taiwan and Thailand. This paper reports the status of metabolic control and management of patients from seven centers in three main geographical regions of Indonesia ¾ four centers in Java (Jakarta, Bandung, Semarang, and Surabaya), two centers in Sumatra (Medan and Palembang) and one in Sulawesi (Makassar).

Methods

Patients who were managed at the participating centers for at least 12 months were recruited between 1 January and February 2002 during their visits to the clinics. The study was performed in accordance with the revised Declaration of Helsinki Guidelines for Biomedical Research involving human subjects[4] and was approved by the Human Ethics Review Board in each clinic. All patients and/or their parents/guardians gave informed consent.

Data were entered into standardized case record forms (CRF) designed for the present study. Data were obtained either by patient interview during the enrollment visit or by reviewing medical records. Apart from basic data, information was also obtained on various aspects of current diabetes management including treatment, glucose self-monitoring, and complications.

Basic patient data included date of birth, sex, time since the patient visited the center for diabetes management, onset of diabetes, type of diabetes, weight, height, and blood pressure. The definition of types of diabetes was carried out at individual center, based on individual doctor's clinical judgment. Information on complications included frequency of hypoglycemia and diabetic ketoacidosis (DKA), as well as existence of retinopathy, cataract, neuropathy, microalbuminuria, end-stage renal failure or advanced eye disease. DKA was defined as heavy glucosuria (>55 mmol/L) and ketouria, hyperglycemia (blood glucose concentration >11 mmol/l), acidosis (pH<7.3 and/or [bicarbonate] <15 mmol/l), and dehydration (³5% body weight). Information on current diabetes treatment included insulin regimen and type of oral anti-diabetic drugs.

Analytical methods of HbA_{1c}

During the enrollment visit, finger capillary blood specimen was collected using the Bio-Rad HbA_{1c} sample preparation kit. All specimens were stored at 4°C and mailed by batches to Eijkman Institute for Molecular Biology, Jakarta for analysis. HbA_{1c} analysis was performed by automatic high-pressure liquid chromatography (Bio-Rad VARIANTÔ, Bio-Rad Laboratories, Hercules, CA). The method of analysis completed the National Glycohemoglobin Standardization Program and was traceable to the DCCT reference method. The comparison was performed with the University of Minnesota Standard Reference Laboratory #6. The normal range for this assay was 4.6% to 6.5%.

Definition for child overweight and obesity

The adult cut off points of 25 kg/m^2 for overweight and 30 kg/m^2 for obesity are related to health risks. In the present study, these adult cut offs were linked to body mass centiles for children to provide child cut off points.[5] Overweight and obesity was defined by the age and sex specified cut offs provided by Cole *et al*.[6] Those with BMI below these categories will be referred to as "normal".

Statistical analysis

All data processing and statistical analysis were performed at Novo Nordisk Asia Pacific Center in Singapore by entering into a database (Microsoft® Excel) by electronic scanning. All data were then tabulated and descriptive analyses performed (SAS version 6.12, SAS Institute Inc., Cary, USA).

TABLE 1. PATIENTS' CHARACTERISTICS

Characteristics	Type 1	Type 2
Number	64 (93%)	5 (7%)
Age (yrs), mean (SD)	10.6 (4.2)	13.0 (1.2)
Gender ratio (Male:Female)	45:55	75:25
Duration of diabetes (yrs), mean (SD)	3.1 (2.9)	1.0 (0.8)
Age at onset (yrs), mean (SD)	7.5 (3.9)	11.8 (1.5)
Blood pressure (mmHg), mean (SD)		
Systolic	109 (14)	100 (8)
Diastolic	72 (11)	68 (10)
BMI (kg/m^2), mean (SD)	16.4 (2.8)	25.5 (6.3)

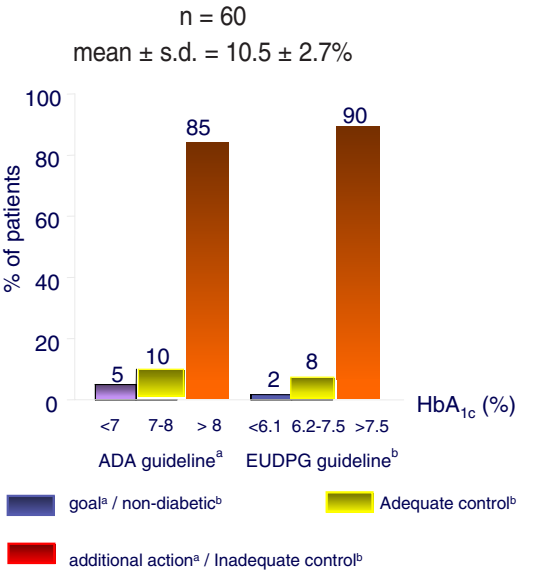

Figure 1. HbA1c profile according to the ADA and EUDPG

Results

Demographics

The number of patients recruited from the seven centers was 76, out of which 7 (9%) were excluded from statistical analysis due to missing critical data. The majority (n=64 or 93%) of the 69 patients recruited were diagnosed as type 1 diabetes while four patients as type 2 and one patient could not be classified. The mean age of type 1 patients was 10.6 (SD 4.2) years. The age of diabetes onset ranged from 1 to 17 years with a mean of 7.5 (SD 4.2) years. Most (92%) of the type 1 patients were of normal body weight **(Table 1)**

HbA_{1c}

Centrally measured HbA_{1c} was available in 60 (94%) of the type 1 patients; the mean of HbA_{1c} level was 10.5 (SD 2.7)%. **Figure 1** shows the HbA_{1c} profiles categorized according to the American Diabetes Association (ADA)[7] and European Diabetes Policy Group (EUDPG)[8] recommended targets for glycemic control. According to ADA guidelines, 85% of the patients (HbA_{1c}>8%) would be recommended for additional action,[7] while according to EUDPG guidelines, 90% of the patients (HbA_{1c}>7.5%) would be classified as having inadequate control.[8] The means HbA_{1c} of those aged <5, 5-10, 10-15 and >15 years were 9.7 (SD 2.6)%, 9.6 (SD 2.0)%, 11.2 (SD 3.2)%,

TABLE 2. ACUTE COMPLICATIONS IN 64 TYPE 1 DM PATIENTS

Number of episodes	Severe hypoglycemic[1]	Diabetic ketoacidosis[2]
None	58 (91%)	52 (81%)
Once	2 (3%)	11 (17%)
Twice	-	1 (2%)
Thrice or more	3 (5%)	-
Unknown	1 (2%)	-

[1]Hypoglycemia resulting in coma, convulsion, or requiring the assistance of another person for treatment. [2]Heavy glucosuria (>55mmol/L) and ketouria, hyperglycaemia (BG>11 mmol/L), acidosis (pH<7.3 and/or bicarbonate <15 mmol/L) and dehydration (≥5% BW).

and 10.8 (SD 2.3)%, respectively. The mean HbA_{1c} of those with duration of diabetes <3, 3-6, 6-9 and >9 years were 10.3 (SD 2.6)%, 10.2 (SD 2.6)%, 12.1 (SD 2.7)%, 9.1 (SD 2.9)%, respectively. The mean HbA_{1c} of those with age of diabetes onset <5, 5-10, 10-15 and >15 years were 9.5 (SD 2.2)%, 10.3 (SD 2.6)%, 11.8 (SD 3.2)%, 10.2 (SD 1.0)%, respectively.

Local measurement of HbA_{1c} was performed in 63% of the patients within 12 months before the clinic visit. Of those patients who had local glycated hemoglobin assessments (n=39), most had only one (41%) or two (26%) local glycated hemoglobin assessments in the last year.

Acute diabetic complications

Table 2 shows the frequency of severe hypoglycemic episode and DKA. Five (8%) type 1 patients experienced at least one episode of severe hypoglycemia in the previous three months. The frequency of severe hypoglycemia in this cohort was more than 0.75 event/patient/year or 75 per 100 patient per years.

Table 3 shows the frequency and proportion of patients who experienced severe hypoglycemia by age group and HbA_{1c} but one patient did not have this data. The frequency of hypoglycemia and proportion who experienced hypoglycemia were higher in children aged less than five, and also in those with HbA_{1c} <8% compared to older children and those with HbA_{1c} >8%, respectively.

Twelve (19%) type 1 patients experienced at least one episode of DKA in the previous 12 months. The frequency of DKA in this cohort was 20 per 100 patient-years. **Table 3** shows the frequency and proportion of patients who experienced DKA by duration of diabetes and HbA_{1c}. The frequency of DKA and proportion who experienced DKA were higher in children with diabetes for less than three years and also in those with HbA_{1c} <8% compared to those with longer duration of diabetes and those with HbA_{1c} >8% respectively (Table 3).

Chronic diabetic complications

There were six (9%) cases of neuropathy, two (3%) cases of retinopathy and three (5%) cases of microalbuminuria in the 64 type 1 patients. There was no report of end-stage renal disease, cataract or advanced eye disease. Ten patients (16%) had at least one chronic diabetic complication. **Table 3** compares the characteristics of patients who had at least one chronic complication and patients who did not. The patients who had at least one chronic complication appeared to be older ($p<0.01$), have longer duration of diabetes, and be on a higher daily insulin dosage ($p<0.05$) than those who did not. The difference in duration of diabetes between the groups, however, was not statistically significance (Table 3).

Diabetes treatment and glucose self-monitoring

Of the 64 type 1 patients, 48 (75%) were on insulin therapy only, one (2%) was on insulin and sulphonylurea. Treatment information was not available in 15 (23%) patients. Of the 49 patients on insulin therapy, 43 (88%) were on twice daily injection regimen, five (10%) were on three times daily injection regimen, and one (2%) was on four times daily injection regimen, respectively. The mean daily insulin dose was 1.0 (SD 0.3) U/kg·day (n=46). The duration of diabetes was similar between patients on twice and thrice daily insulin injection regimens, but the mean HbA_{1c} of patients on thrice daily injection appeared to be lower i.e., 8.4 (SD 1.4) % than that of those on twice daily injection i.e., 10.3 (SD 2.4) %. However,

TABLE 3. RELATIONSHIP BETWEEN COMPLICATIONS AND CHARACTERISTICS OF TYPE 1 DM PATIENTS

	Yes (n=5)	No (n=58)	P value between columns
Hypoglycemia complication			
Age (years), mean (SD)	8.3 ± 5.2	10.8 ± 4.1	ns
Sex M:F ratio	20:80	48:52	ns
BMI (kg/m^2), mean (SD)	16.9 ± 3.3	16.4 ± 2.8	ns
Duration of disease (yrs), men (SD)	5.0 ± 5.7	2.9 ± 2.6	ns
Age of onset (yrs), mean (SD)	3.0 ± 1.7	7.9 ± 3.8	<0.01
HbA_{1c} (%), mean (SD)	9.1 ± 2.1	10.7 ± 2.7	ns
Insulin dose (U/kg/day)	0.98 ± 0.18	0.95 ± 0.26	ns
Ketoacidosis complication			
Age (years), mean (SD)	10.1 ± 5.1	10.8 ± 4.0	ns
Sex M:F ratio	33:67	48:52	ns
BMI (kg/m^2), mean (SD)	16.5 ± 3.3	16.3 ± 2.7	ns
Duration of disease (yrs), mean (SD)	2.4 ± 3.7	3.2 ± 2.7	ns
Age of onset (yrs), mean (SD)	7.6 ± 4.9	7.5 ± 3.7	ns
HbA_{1c} (%), mean (SD)	9.9 ± 2.8	10.6 ± 2.7	ns
Insulin dose (U/kg/day), mean (SD)	0.95 ± 0.31	0.97 ± 0.24	ns
Chronic complications			
Age (years), mean (SD)	13.5 ± 3.0	10.0 ± 4.1	<0.01
Sex M:F ratio	50:50	44:56	ns
BMI (kg/m^2), mean (SD)	18.5 ± 4.3	16.2 ± 2.4	ns
Duration of disease (yrs), mean (SD)	5.1 ± 4.3	2.7 ± 2.5	ns
Age of onset (yrs), mean (SD)	8.4 ± 4.4	7.2 ± 3.8	ns
HbA_{1c} (%), mean (SD)	9.9 ± 2.3	10.3 ± 2.7	ns
Insulin dose (U/kg/day), mean (SD)	1.11 ± 0.24	0.90 ± 0.20	<0.05

Comparison between columns for ratio by Chi-square test and all others by non-parametric Kruskal-Wallis test; ns = not significant

the difference was not statistically significant.

Of the 64 type 1 patients, 38 (59%) practiced blood glucose self-monitoring and five (8%) practiced urine glucose self-monitoring. The average numbers of blood and urine glucose self-monitoring per month were 32 times and 13 times, respectively. The average number of blood glucose self-monitoring per month were 68, 41, 22 and 20 in the age groups <5, 5-10, 10-15 and >15 years, respectively.

Type 2

The mean of centrally measured HbA_{1c} for the type 2 patients was 8.7 ± 0.4% (n=4) and all had HbA_{1c} exceeding 8%. One of the patients was treated with insulin (once daily injection 0.2 U/kg), one with metformin and two were not treated with oral diabetic medicine or insulin. None of the four type 2 patients experienced any severe hypoglycemic episodes in the last three months or any DKA episodes during the previous 12 months. The only chronic complication reported was microalbuminuria in an obese child whom diagnosed diabetes of less than three years.

Discussion

Review of 69 young diabetic patients from 7 pediatric centers in Indonesia, found 64 were type 1 patients. Therefore, this study essentially gave a snapshot of the glycemic control and management of these type 1 patients.

The overall mean of HbA_{1c} for type 1 patients was 10.5 (SD 2.7)%, which is much higher than the 8.3% (DCCT adjusted) of the Hvidore study.[9,10] Only 15% of these young patients achieved glycemic control of HbA_{1c} value <8% compared to the 34% from the Hvidore study. According to European guidelines, 90% of these patients did not achieve adequate control of HbA_{1c} £7.5%. Due to the increased risk of hypoglycemia with low HbA_{1c} levels, it has been debated if blood glucose control for children should be as low as that recommended for adults, for example <6.5%. This issue may appear less relevant for this population with less than 4% achieving HbA_{1c} <6.5%. Urgent measures would have to be taken to improve glycemic control of these patients in general.

It was estimated that the frequency of severe

hypoglycemia in the type 1 patients was more than 0.75 event/patient/year. However, it has to be noted that this was a crude cross-sectional retrospective study in which the data obtained from patients' memory and not the usual method of longitudinal record. It is speculated that such a retrospective method has resulted in an overestimation because a patient is likely to indicate positively rather than negatively when uncertain. Therefore, any comparison to other data must be done with caution. The number of severe hypoglycemic events is equivalent to 75 per 100 patient-years. This is much higher than the 22 events and 26.7 events per 100 patient-years in the Hvidore study[10] and adolescents in the intensive treatment of the DCCT[11]. Therefore the high incidence of severe hypoglycemia in these patients may be due to factors other than glycemic control.

The increased frequency of severe hypoglycemic episodes observed in children less than 5 years of age also indicates that tight control in this group should be undertaken with caution, because hypoglycemia may impair normal brain development. Nonetheless, this must also be weighed against the risk of future complications. Furthermore, it has also been shown that lower HbA_{1c} was significantly associated with better adolescent-rated quality of life[12].

The pubertal years during adolescence are consistently identified as a period of deteriorating glycemic control[13] and heightened family conflict over diabetes management.[14] In the present study, glycemic control tended to be worse in older children (>10 years old) but not necessarily in children with longer duration of diabetes or later diabetes onset. This may partly be explained by pubertal insulin resistance which occurs in both normal children[15] and children with diabetes.[16] The combined effects of puberty and diabetes on insulin action may help explain why control of glucose is more difficult to achieve in adolescent patient. In addition, the frequency of blood glucose self-monitoring tended to be lower in those aged 10 and above. Conflicts may exist between the tasks of managing diabetes and the normative development tasks facing the young adolescent – defining an identity, establishing a new role in the family and gaining peer acceptance. The difficulty in resolving this conflict may also explain the worse glycemic control in this group of patients in the present and other studies.

It has been reported that risk factors for microalbuminuria and retinopathy were high blood pressure, cholesterol, HbA_{1c}, pubertal staging, older age, and longer diabetes duration.[17]17.

Of those 49 patients who had information on insulin regimen, more than 88% were on twice a day injection regimen while 12% were on three or four injections per day. Glycemic control was better in those on three daily injection regimen compared to those on twice daily injection regimen. The difference in HbA_{1c} between the two groups was not statistically significant. This is probably because there were too few patients in the three daily injections group. However, since the present study was a cross-sectional audit and not a randomized design, the interpretation of the effect of the frequency of injection on glycemic control is difficult. Nevertheless, the value of an intensive insulin regimen in glycemic control is clear.[1]

In conclusion, the present audit showed that 90% of the type 1 and all of the type 2 patients in the present cohort did not achieve adequate control of HbA_{1c} £7.5%. Furthermore, the frequency of severe hypoglycemic events was higher in the younger children while glycemic control was worse in older children. Further studies are necessary to determine if a more intensive insulin regimen may improve glycemic control and lower the incidence of hypoglycemic events.

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Appendix

Diabcare-Indonesia 2001 Study Group Members

- Dr. Jose RL. Batubara, Ciptomangunkusumo National General Hospital - Jakarta
- Dr. Diet S. Rustama, Hasan Sadikin Hospital – Bandung
- Dr. Bambang Tridjaja, Ciptomangunkusumo National General Hospital - Jakarta
- Dr. Aman B. Pulungan, Ciptomangunkusumo National General Hospital - Jakarta

- Dr. R.M. Ryadi Fadil, Hasan Sadikin Hospital – Bandung
- Dr. Dedy Subardja, Hasan Sadikin Hospital – Bandung
- Dr. Rudy Susanto, Karyadi Hospital – Semarang
- Dr. Connie Untario, Sutomo Hospital – Surabaya
- Dr. Satriono, Wahidin Sudirohusodo Hospital – Makassar
- Dr. Hakimi, Adam Malik Hospital – Medan
- Dr. Charles Darwin Siregar, Adam Malik Hospital – Medan
- Dr. Aditiawati, M. Hoesin Hospital – Palembang
- Dr. Yeo Jing Ping and Joseph Lai (Novo Nordisk Asia Pacific)
- Dwi Nofiarny and Maria Mila Erastuti (Dexa Medica Group)

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