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# The Factors Affecting Glycemic Control in Japanese Adolescents with Type 2 Diabetes Mellitus

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**Abstract**

The factors affecting glycemic control were examined using $HbA_{1C}$ as an index in a total of 22 patients with type 2 diabetes mellitus whose ages at onset were less than 18 years old. As a result, the presence or absence of the following cases were considered possible factors for significant exacerbation of glycemic control: diabetic microangiopathy; school phobia or nonworking situation; drug therapy; use of more than two kinds of oral hypoglycemic agents (OHAs) or insulin for the drug therapy cases.

No improvement in glycemic control could be achieved even by increasing the number of OHAs for co-administration or by insulin use unless dietary/exercise therapy, a basic therapeutic option, was adequately performed.

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**Key words**: type 2 diabetes, $HbA_{1C}$, drug therapy

## Introduction

Until recently, diabetes in pre-pubertal children and adolescents meant type 1 diabetes mellitus, and type 2 diabetes mellitus was rare. However, with the increasing prevalence of obesity, pre-pubertal and adolescent type 2 diabetes mellitus have been reported not only in Japan but also in many other countries[1–9], and the incidence of the disease is also increasing year by year. In races or districts with a high incidence of adult type 2 diabetes mellitus, the incidence of the disease is rapidly increasing also in children and adolescents. However, there has been no reports on the factors affecting glycemic control in adolescents with type 2 diabetes mellitus. And in regard to therapeutic methods affecting glycemic control, there has been only one report about the effect of metformin[10].

With the aim of achieving better quality of life (QOL) in adolescents with type 2 diabetes mellitus, we examined the factors affecting glycemic control using $HbA_{1C}$ as an index.

## Materials and Methods

A total of 22 study subjects (including 12 males and 10 females) were recruited from among patients with type 2 diabetes mellitus whose ages at onset were less than 18 years old, and who visited our department for medical examination in the period from January to December 2002. Their ages, ages at onset and morbidity periods were 12～25 years (17.8 ±3.4 years), 8～17 years (13.4±2.6 years) and 3 months～12 years (4.6±2.9 years), respectively. The mean value of their $HbA_{1C}$ of the last 6 months was

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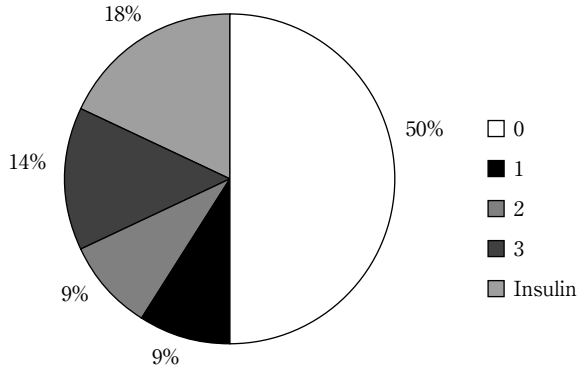


Fig. 1 Distribution of the usage rate of oral hypoglycemic agents (OHAs) by number of co-administered and that of insulin use

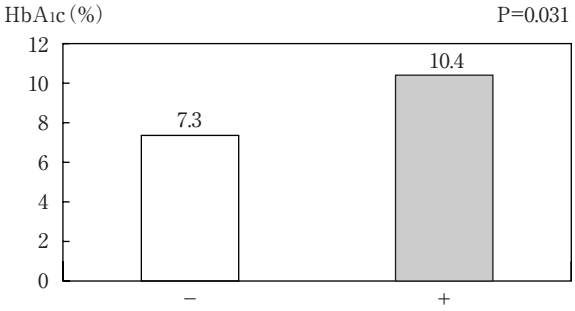


Fig. 2 Difference in $HbA_{1C}$ value by the presence (+) or absence (−) of diabetic microangiopathy

used as an index of diabetic control.

For the statistical analysis of the present study, Student's t-test and Duncan's multiple range test (a significance criterion with $P<0.05$) were used for comparisons between two subgroups and among more than three subgroups, respectively.

## Results

### 1. Patient's Background

In 77% (ca. 3/4) of the patients, obesity was observed at onset. In 68% (ca. 2/3) of the patients, the family history of diabetes mellitus (relative within the second degree) was observed. The onset was induced by soft-drink ketoacidosis in 14% of the patients. The fasting IRI and ΣIRI values of O-GTT of three patient groups were in the order, obese diabetic group > non-obese diabetic group > non-obese healthy group. Insulin resistance was observed even in non-obese adolescents with type 2 diabetes mellitus[11].

Diabetic microangiopathy was observed in 14% of the patients. For complications other than diabetes, hyperlipidemia, fatty liver, hypertension, hyperuricemia and acanthosis nigricans were observed in 73% (ca. 3/4), 36% (ca. 1/3), 18% (ca. 1/4), 36% (ca. 1/3) and 14% of the patients, respectively.

Eighteen percent of the patients belonged to athletic clubs. Eighteen percent of the patients were school phobia or nonworking.

Fifty percent of the patients had been receiving drug therapy. Therapeutic details: The therapeutic protocol with which the patients of the present study were treated was pursuant to the one which has been used in our department[11]. Out of all patients, 50% received no drug therapy, while of the remaining 9%, another 9%, 14%, and 18% received one, two, three kinds of oral hypoglycemic agents (OHAs), and insulin, respectively. The OHAs included α-glycosidase inhibitor (voglibose) (3 patients), biguanide (metformin) (6 patients), thiazolidinedione (pioglitazone) (1 patient), and sulfonylurea (glibenclamide) (5 patients) (**Fig. 1**).

Their mean $HbA_{1C}$ of the last 6 months was 7.7 ± 2.7%.

### 2. Factors affecting $HbA_{1C}$ value

Regardless of the presence or absence of obesity, family history, soft-drink ketoacidosis and the membership in athletic club, there were no differences in $HbA_{1C}$ value.

The mean $HbA_{1C}$ value of patients with diabetic microangiopathy was 10.4 ± 1.1%, while that of patients without the microangiopathy was 7.3 ± 2.7%, the group with diabetic microangiopathy showing a significantly higher mean $HbA_{1C}$ value ($P=0.031$) (**Fig. 2**).

The mean $HbA_{1C}$ value of patients with school phobia or nonworking situation was 9.8 ± 2.9%, while that of patients without it was 7.3 ± 2.5%, the group with school phobia or nonworking situation showing a significantly higher $HbA_{1C}$ value ($P=0.045$) (**Fig. 3**).

The mean $HbA_{1C}$ value of patients receiving drug therapy was 9.4 ± 2.4%, while that of patients without drug therapy was 6.0 ± 1.8%, the group

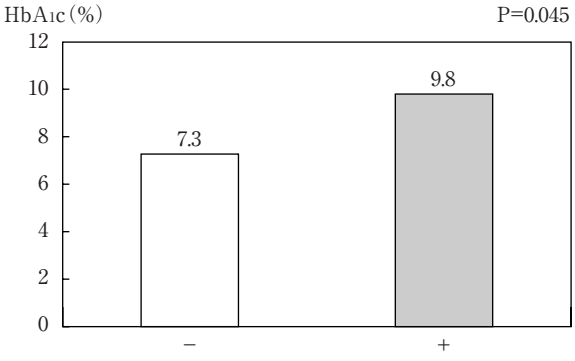


Fig. 3 Difference in $HbA_{1C}$ value by the presence (+) or absence (−) of school phobia or nonworking situation

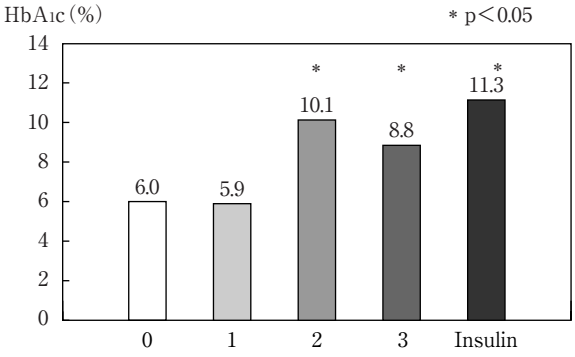


Fig. 5 Differences in $HbA_{1C}$ value by the number of co-administered OHAs and insulin use

receiving drug therapy showing a significantly higher $HbA_{1C}$ value ($P<0.001$) (**Fig. 4**). In addition, the mean $HbA_{1C}$ values of the patients receiving one, two, three kinds of OHAs, and insulin were $5.9 \pm 1.1\%$, $10.1 \pm 0.3\%$, $8.8 \pm 1.6\%$, and $11.3 \pm 1.9\%$, respectively, the group using more than two kinds of OHAs or insulin resulting in a significantly worse glycemic control ($P<0.05$) (**Fig. 5**).

## Discussion

The prevalence of type 2 diabetes mellitus is increasing not only in adults but also in pre-pubertal children and adolescents[1−9]. However, there has been no reports on the factors affecting glycemic control in adolescents with type 2 diabetes mellitus. And in regard to therapeutic methods affecting glycemic control, there has been only one report about the effect of metformin[10].

In the present study, we examined factors affecting glycemic control in adolescents with type 2

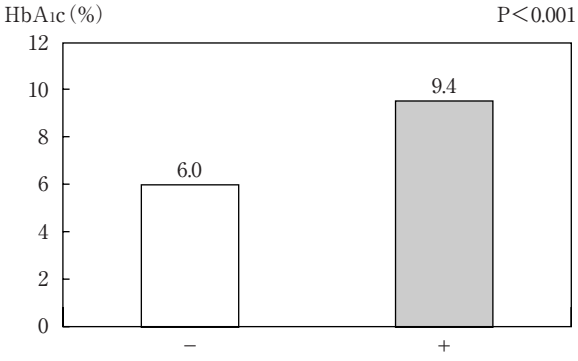


Fig. 4 Difference in $HbA_{1C}$ value by the use (+) or non-use (−) of antidiabetic agents

diabetes mellitus using $HbA_{1C}$ value as an index. As a result, the following were considered possible factors relevant to the exacerbation of diabetic control in adolescents with type 2 diabetes mellitus: the presence of diabetic microangiopathy; the presence of school phobia or nonworking situation; the presence of drug therapy, and for the drug therapy cases, the use of more than two kinds of OHAs or insulin.

In other words, inadequate glycemic control may lead to diabetic microangiopathy, school phobia or nonworking, and that no improvement in glycemic control can occur even by increasing the number of oral drugs or by insulin use unless dietary/exercise therapy, a basic therapeutic option, is adequately performed.

Most adolescent patients with type 2 diabetes are asymptomatic, and this delays the diagnosis and/or therapy and causes the early onset of diabetic complications [3,8,12]. As observed in our present study, the therapy for adolescents with type 2 diabetes appears very difficult even with early diagnosis and early therapy.

Guidance on the prevention and/or improvement of obesity, the establishment of therapeutic method and the organization of an elaborate follow-up system for the prevention of diabetic complications are required[13−15].

## References

1. Dabelea D, Hanson RL, Bennett PH, Roumain J, Knowler WC, Pettitt DJ: Increasing prevalence of type II diabetes in American Indian children.

Diabetologia 1998; 41: 904–910.
2. Dean HJ, Young TK, Flett B, Wood-Steinman P: Screening for type-2 diabetes in aboriginal children in northern Canada. Lancet 1998; 352: 1523–1524.
3. Dean HJ: NIDDM-Y in First Nation children in Canada. Clin Pediatr 1998; 37: 89–96.
4. Harris SB, Perkins BA, Whalen-Brough E: Non-insulin-dependent diabetes mellitus among First Nations children. New entity among First Nations people of northwestern Ontario. Can Fam Physician 1996; 42: 869–876.
5. Pinhas-Hamiel O, Dalan LM, Daniels SR, Standiford D, Khoury PR, Zeitler P: Increased incidence of non-insulin dependent diabetes mellitus among adolescents. J Pediatr 1996; 128: 608–615.
6. Kadiki OA, Reddy MRS, Marzouk AA: Incidence of insulin-dependent diabetes (IDDM) and non-insulin-dependent diabetes (NIDDM) (0-34 years at onset) in Benghazi, Libya. Diabetes Res Clin Pract 1996; 32: 165–173.
7. Kitagawa T, Owada M, Urakami T, Yamauchi K: Increased incidence of non-insulin dependent diabetes mellitus among Japanese school-children correlates with an increased intake of animal protein and fat. Clin Pediatr 1998; 37: 111–116.
8. Neufeld ND, Chen Y-DI, Raffel LJ, Vadheim CM, Landon C: Early presentation of type 2 diabetes in Mexican-American youth. Diabetes Care 1998; 21: 80–86.
9. Pihoker C, Scott CR, Lensing SY, Cradock MM, Smith J: Non-insulin dependent diabetes mellitus in African-American youths of Arkansas. Clin Pediatr 1998; 37: 97–102.
10. Jones KL, Araslanian S, Peterokova VA, Park J-S, Tomlinson MJ: Effect of metformin in pediatric patients with type 2 diabetes. Diabetes Care 2002; 25: 84–89.
11. Ohki Y, Kishi M, Orimo H, Ohkawa T: Insulin resistance in Japanese adolescents with type 2 diabetes mellitus. J Nippon Med Sch 2003 ; 71 : 87–90.
12. Yokoyama H, Okudaira M, Otani T, Watanabe C, Takaike H, Miura J, Yamada H, Mutou K, Satou A, Uchigata Y, Iwamoto Y: High incidence of diabetic nephropathy in early-onset Japanese NIDDM patients; risk analysis. Diabetes Care 1998; 21: 1080–1085.
13. Fagot-Compagna A, Pettit DJ, Engelgau MM, Burrows NR, Geiss LS, Valdez R, Beckles GLA, Saddine J, Gregg EW, Williamson DF, Narayan KMV: Type 2 diabetes among north American children and adolescents; An epidemiologic review and a public health perspective. J Pediatr 2000; 136: 664–672.
14. American Diabetes Association: Type 2 diabetes in children and adolescents. Diabetes Care 2000; 23: 381–389.
15. Rosenbloom AL, Young RS, Joe JR, Winter WE: Emerging epidemic of type 2 diabetes in youth. Diabetes Care 1999; 22: 345–354.

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