Trends of childhood diabetes in Southern Thailand: 20-year experience in a tertiary medical center

Somchit Jaruratanasirikul, Sudarat Thammaratchuchai, Hutcha Sriplung
Songkhla, Thailand

Original article

Background: **The incidence and/or prevalence of both childhood diabetes and the percent of type 2 diabetes mellitus (T2DM) cases in children and young adolescents have been increasing worldwide. This study aimed to examine the 20-year trends of childhood diabetes in a single tertiary medical center in Southern Thailand.**

Methods: **The medical records of pediatric diabetic patients, aged 0-15 years, diagnosed at Songklanagarind Hospital from 1995 to 2014 were retrospectively reviewed.**

Results: **During the 20-year period, 156 children were diagnosed with DM: 99 (63.4%) with T1DM, 43 (27.6%) with T2DM, 2 (1.3%) with neonatal diabetes, and 12 (7.7%) with secondary diabetes. The estimated incidence of new patients with diabetes per 100 000 per year doubled from 0.12 in 1995-2000, to 0.24-0.28 in 2001-2004, and further increased to 0.39-0.48 in 2005-2012 and 0.59-0.64 in 2013-2014; and also the proportion of T2DM cases increased from 10%-15% during 1995-2003 to 25%-30% during 2004-2008, and 35%-40% during 2009-2014. At the time of diagnosis, the fasting plasma glucose and glycated hemoglobin levels were significantly greater in T1DM than T2DM patients while the lipid profiles were more abnormal in T2DM than T1DM patients.**

Conclusion: **The estimated incidences of both T1DM and T2DM in pediatric patients have increased markedly over the 20-year period, and also the percentage of T2DM cases, from 10%-15% in 1995 to 35%-40% in 2014.**

World J Pediatr 2017;13(6):566-570

Key words: **childhood diabetes mellitus; type 1 diabetes mellitus; type 2 diabetes mellitus**

Introduction

In recent years, the incidence and/or prevalence of childhood onset diabetes mellitus (DM) per 100 000 per year has been increasing worldwide.[1] The incidence/prevalence varies greatly among countries: from a high of 57 in Finland to more than 20 in the United Kingdom, the United States of America, and Australia to 0.1 in China and Thailand.[1-3] Twenty years ago, about 90% of childhood DM cases were type 1 (T1DM) and only 10% were type 2 (T2DM).[2] In recent years, however, with an increasing incidence of obesity in children and young adolescents, the percent of T2DM cases has also been increasing, to as high as 30%-40% in some studies.[4,5]

In Thailand, the nationwide incidence of T1DM per 100 000 per year increased from 0.12-0.29 in 1984-1985 to 0.20-0.42 in 1991-1995.[6] T2DM is now diagnosed more frequently in children and adolescents with the percentage of all DM cases increasing from 5% in 1986-1995 to 18% in 1996-1999[7,8] and 23.4% in 2001-2013.[9] In Southern Thailand, the incidence of T1DM per 100 000 per year as indicated in the national survey increased from 0.12 in 1984-1985 to 0.42 in 1991-1995.[6]

The Pediatric Diabetes Clinic in Songklanagarind Hospital, the only university hospital in Southern Thailand, has most cases of childhood diabetes in Southern Thailand referred for management and education, thus we are in a good position to assess trends for this disease over time. It was our aim in this current study to evaluate the trends of childhood diabetes during the last 20 years in Southern Thailand, with a secondary outcome to determine the type of diabetes in children and the major clinical manifestations in each type.

Methods

The medical records of pediatric patients, aged 0-15 years, who had been diagnosed with DM at the Pediatric Diabetes Clinic at Songklanagarind Hospital during 1995 and 2014, were retrospectively reviewed. The diagnosis of diabetes was based on an elevated fasting plasma glucose of >126 mg/dL or random measurement of >200 mg/dL in at least 2 samples at different occasions (1995-2014), or glycated

Author Affiliations: Department of Pediatrics (Jaruratanasirikul S, Thammaratchuchai S) and Epidemiology Unit, Faculty of Medicine (Sriplung H), Prince of Songkla University, Hat Yai, Songkhla, Thailand

Corresponding Author: Somchit Jaruratanasirikul, MD, Department of Pediatrics, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla 90110, Thailand (Tel/Fax: 66-074-429618; Email: somchit.j@psu.ac.th)

doi: 10.1007/s12519-017-0049-y

hemoglobin (HbA1c) >6.5% (a new criterion used in our clinic since 2012). The diabetes types were classified based on the 1999 WHO criteria and the 2011 American Diabetes Association criteria.[10] T1DM and T2DM were diagnosed by the different clinical features and serum insulin levels: T1DM in patients with normal weight or overweight who presented with typical symptoms of polyuria and/or nocturia, polydipsia and weight loss or diabetic ketoacidosis (DKA), and with high plasma glucose and a relatively low insulin level <15 μU/mL, and T2DM in obese patients who had high plasma glucose and a high insulin level >15 μU/mL.

Data collected from the medical records included demographic data, clinical symptoms and signs related to diabetes, physical examination and laboratory findings. In patients who presented with DKA, a plasma glucose evaluation was performed at the time of admission. Diabetic patients who were asymptomatic had plasma glucose assays and other laboratory tests done after an overnight fast of at least 8 hours. Weight and height measurements were taken in the standard standing position without shoes and socks to the nearest 0.1 kg and 0.1 cm, respectively. To account for age and sex discrepancies, weight and height in kg and cm were calculated to a standard deviation score based on chronological age using standardized reference data of Thai children.[11] Obesity was defined as weight over the 95th percentile for age and sex. Hypertension was diagnosed when systolic or diastolic blood pressure was over the 95th percentile for age. Metabolic syndrome was defined in an individual who had at least 3 of the clinical characteristics of obesity, hypertension, high density lipoprotein-cholesterol (HDL-C) level of <40 mg/dL, and triglyceride (TG) level of >150 mg/dL.[12]

Data were expressed as number and percentage, or mean±standard deviation. The estimated incidence of diabetes per 100 000 per year was calculated by the number of new cases divided by the total number of children aged 0-15 years in the 14 provinces of Southern Thailand. The Chi-squared test or Fisher exact test was used to compare differences in categorical data. Student's *t* test or Mann-Whitney *U* test or Kruskal-Wallis test were used for analysis of continuous data with normal distribution or nonparametric distribution, respectively. The statistical findings were considered significant at $P<0.05$.

The protocol for this study was approved by the Institutional Review Board and the Ethics Committee of the Faculty of Medicine, Prince of Songkla University.

Results

During 1995 and 2014, 156 children and adolescents diagnosed with diabetes at our institute. Of these, 99 (63.4%) were T1DM, 43 (27.6%) were T2DM, 2 (1.3%) were neonatal DM, and 12 (7.7%) were secondary DM; and the latter comprising 6 cases of hemochromatosis from frequent blood transfusions for major thalassemia disease (1994-1999), 3 of steroid-induced diabetes, 2 of post 99% pancreatectomy, and 1 who developed diabetes after treatment with 3 doses of L-asparaginase for acute lymphoblastic leukemia.

From 1995 to 2014, we found that the estimated incidence of newly diagnosed patients with either T1DM or T2DM increased, and the proportion of those with T2DM also increased (Fig. 1). The estimated incidence of newly diagnosed diabetic patients per 100 000 per year doubled from 0.12 in 1995-2000 to 0.24-0.28 in 2001-2004, and further increased to 0.39-0.48 in 2005-2012 and 0.59-0.64 in 2013-2014. And the proportions of T2DM also increased during the same period, from 10%-15% during 1995-2003 to 25%-30% during 2004-2008 and 35%-40% during 2009-2014.

The clinical features of patients with T1DM and T2DM at the time of diagnosis are shown in Table 1. Dividing the age at presentation of T1DM and T2DM patients to <5 years, 5-<10 years, and 10-15 years

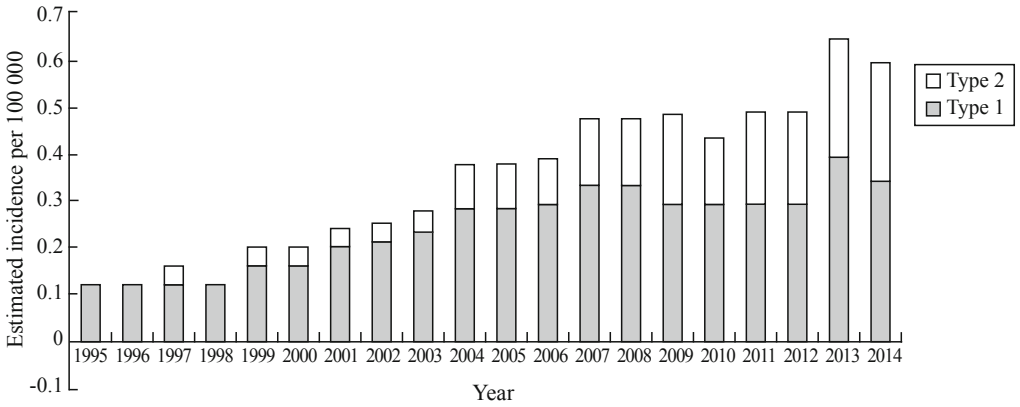

Fig. 1. The estimated incidence of diabetes in children and adolescents aged 0-15 years per 100 000 during 1995-2014.

Table 1. Comparison of clinical features between patients with type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM)

Characteristics	T1DM (*n*=99)	T2DM (*n*=43)	*P* value
Age at onset (y), mean±SD	8.8±3.9	13.0±2.5	<0.01
Male, *n* (%)	41 (41.4)	27 (62.8)	0.02
Obesity in family member, *n* (%)	2 (2.0)	26 (60.5)	<0.01
Diabetes in family member, *n* (%)	3 (3.0)	18 (41.9)	<0.01
Presenting symptoms, *n* (%)	99 (100)	21 (48.8)	<0.01
Weight loss	86 (86.9)	8 (18.6)	<0.01
Polyuria	89 (89.9)	14 (32.6)	<0.01
Diabetic ketoacidosis	72 (72.7)	3 (7.0)	<0.01
Obesity, *n* (%)	7 (7.1)	43 (100)	<0.01
Weight (kg), mean±SD	32.4±14.4	79.9±22.5	<0.01
Weight standard deviation score, mean±SD	0.28±1.39	5.59±2.90	<0.01
Height (cm), mean±SD	131±23	152±14	<0.01
Height standard deviation score, mean±SD	-0.22±1.30	0.94±1.56	<0.01
Systolic blood pressure (mmHg), mean±SD	105±10	125±18	<0.01
Diastolic blood pressure (mmHg), mean±SD	66±7	84±10	<0.01
No. of obese patients, *n* (%)	5 (5.0)	43 (100)	<0.01
No. of patients with hypertension, *n* (%)	0 (0)	14 (32.5)	<0.01
No. of patients with metabolic syndrome, *n* (%)	0 (0)	21 (48.8)	<0.01
Fasting plasma glucose (mg/dL), mean±SD	451±175	260±147	<0.01
Glycated hemoglobin (%), mean±SD	11.9±2.8	10.4±2.8	0.02
Fasting serum insulin (μU/mL), mean±SD	10.3±5.2 (*n*=40)	45.3±23.4 (*n*=32)	<0.001
Cholesterol (mg/dL), mean±SD	192±41	215±71	0.03
Triglyceride (mg/dL), mean±SD	103±81	178±121	<0.01
High density lipoprotein-cholesterol (mg/dL), mean±SD	56±17	40±14	0.15
Low density lipoprotein-cholesterol (mg/dL), mean±SD	120±36	148±51	0.03

SD: standard deviation.

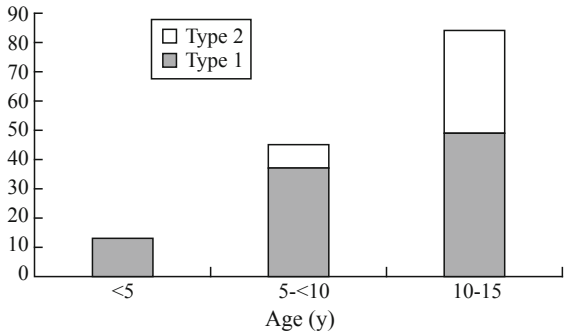

Fig. 2. Number of cases with newly diagnosed diabetes in children and adolescents according to the age at diagnosis.

groups, the numbers of T1DM patients aged 10-15 years and <10 years were about the same whereas the number of T2DM patients aged 10-15 years was about 4 times greater than those aged <10 years, with a statistically significant difference (P<0.001) (Fig. 2).

The main presenting symptoms of the T1DM patients were polyuria, weight loss, and diabetic ketoacidosis. Of the total 43 T2DM cases, 32 (51.2%) were asymptomatic and T2DM was diagnosed after yearly screening identified fasting plasma glucose >126 mg/dL and/or HbA1c >6.5%. The weights and heights of T1DM patients at initial presentation were about the average for age, whereas the weights of T2DM patients were notably above average for age. The number of T2DM patients with obesity, hypertension, and metabolic syndrome were significantly greater than in T1DM patients (P<0.01).

Table 2. Time-interval comparison of the percentages of obesity, hypertension, and metabolic syndrome between T1DM and T2DM patients

Characteristics	T1DM	T2DM	*P* value
1995-2004			
Total patients	34	8	
No. of obese patients, *n* (%)	0 (0)	8 (100)	<0.01
No. of patients with hypertension, *n* (%)	0 (0)	0 (0)	-
No. of patients with metabolic syndrome, *n* (%)	0 (0)	0 (0)	-
2005-2009			
Total patients	32	14	
No. of obese patients, *n* (%)	1 (3.1)	14 (100)	<0.01
No. of patients with hypertension, *n* (%)	0 (0)	4 (28.6)	<0.01
No. of patients with metabolic syndrome, *n* (%)	0 (0)	7 (50.0)	<0.01
2010-2014			
Total patients	33	21	
No. of obese patients, *n* (%)	4 (12.1)	21 (100)	<0.01
No. of patients with hypertension, *n* (%)	0 (0)	10 (47.6)	<0.01
No. of patients with metabolic syndrome, *n* (%)	0 (0)	14 (66.7)	<0.01

T1DM: type 1 diabetes mellitus; T2DM: type 2 diabetes mellitus. "-": no value.

The average plasma/serum levels of glucose, HbA1c, and HDL-C at initial diagnosis were significantly greater in T1DM than in T2DM patients. The average levels of serum insulin, cholesterol, triglyceride, and low-density lipoprotein cholesterol were significantly greater in T2DM than in T1DM patients.

Dividing the study period into three time intervals, 1995-2004, 2005-2009, and 2010-2014, we found that the percentages of obese T1DM patients increased from none in 1995-2004, to 3% in 2005-2009, and to 12.5% in 2010-2014, although the increase were without statistical significance (P=0.35). Also, the percentages of cases with hypertension and metabolic syndrome increased over time in T2DM patients, although again without statistically significant differences (P=0.31 for hypertension and P=0.48 for metabolic syndrome). The percentages of obesity, hypertension and metabolic syndrome in T2DM patients were significantly higher than in T1DM patients in each time interval (Table 2).

Discussion

Our study found that the estimated incidence of newly diagnosed diabetes in children and adolescents had risen significantly over the two decades from 1995 to 2014. Although T1DM remained to be the most common type of diabetes in these age groups, the percentage of T2DM patients had increased from 10%-15% in 1995 to 35%-40% in 2014. Also, the percentages of co-morbidity disorders associated with diabetes such

as hypertension and metabolic syndrome had risen significantly greater in T2DM patients.

The incidence of type 1 diabetes has been increasing worldwide. It has been estimated that 79 000 children worldwide develop T1DM annually, and that more than half of these cases are from Caucasian countries while less than 10% are from Asian countries.[1] Despite the geographic variation in the incidence of T1DM, there are well-documented secular trends over time, which differ among countries and from time period to time period.[1-5] Analysis of national diabetes registries in European countries[13] and Australia[14] revealed increases per year of 3.9% and 2.8%, respectively, in the incidences of T1DM in children younger than 15 years. Studies in Asian countries such as Japan[15] and China,[16] where the incidence of childhood T1DM is relatively low, have found a rapidly rising incidence of T1DM of 10%-14% per year during the last two decades. Such time trends have also been shown in Thailand as studies examining the incidence of T1DM per 100 000 per year showed increases from 0.12-0.29 in 1984-1985 to 0.20-0.42 in 1991-1995.[4,6] T1DM is caused by an interplay of genetic factors (such as human leukocyte antigens or immunological factors) and environmental factors (such as viral infection, etc). However, an increase such as we have noted in the incidence of T1DM over a 20-year interval cannot be explained by genetic changes, but is more likely to be from changes in environmental risk factors which may aggravate autoimmune reactions or accelerate beta-cell destruction.[13]

In our current study, the proportion of T2DM cases in 2012-2014 was 3-4 times higher than in 1995-2000. In Thailand, the T2DM prevalence and also the proportion of T2DM to total diabetes cases in children and adolescents have risen over the last 20 years.[6-9] A study in Taiwan of China also found a striking rise of T2DM pediatric cases, from fewer than 3% of all newly diagnosed diabetes cases in 1985 to 45% of cases in 2000.[17] The main factors recognized so far as related to this increase of T2DM in children are the increasing prevalences of obesity, unhealthy eating habits and increasingly sedentary lifestyles.[18,19] Long duration obesity is associated with and may be the cause of metabolic abnormalities in glucose and lipid metabolisms such as insulin resistance and/or impaired glucose tolerance leading to T2DM by various complex mechanisms.[20,21] In our study, 60% of T2DM patients were obese and 40% had T2DM family members, which might represent a genetic predisposition to diabetes that might be triggered by similar behaviors and/or life styles in the family. Various studies have found various types of evidence supporting genetic and environmental involvement in T2DM development in children and adolescents.[22,23]

T1DM and T2DM pediatric patients have different clinical courses. In our study, all T1DM cases had classic symptoms of polyuria/nocturia and weight loss and 70% of cases presented with DKA. However, only about 50% of T2DM patients had clinical symptoms and the other 50% were "silent diabetes" detected by yearly screening of both fasting plasma glucose and/or HbA1c levels in morbidly obese children and adolescents. Fasting plasma glucose and HbA1c levels were significantly higher in T1DM than T2DM patients, indicating the greater severity of abnormal glucose metabolism in T1DM children for a period of time before presentation. Despite the lower plasma glucose and HbA1c levels, plasma lipid profiles were significantly more abnormal in T2DM than T1DM patients, indicating a long duration of metabolic complications in obese children. It is known that typical symptoms of T2DM take long duration to manifest, and patients may pass from normality through an intermediate stage of prediabetes (impaired fasting glucose, impaired glucose tolerance) and finally develop T2DM. Metabolic syndrome is defined in an individual who has at least three of the risk factors of obesity, hypertension, low HDL-C, high TG, and impaired glucose metabolism.[12,24,25] Patients with metabolic syndrome who also have prediabetic conditions have been found to progress to T2DM at nearly twice the rate of patients who have prediabetes alone. Hence, at-risk patients should be screened, identified and monitored prior to progression to T2DM.[18,23] In our study, obese T2DM patients were diagnosed at an average age of 13 years at which time they were in the middle stage of puberty. It is known that puberty is a time of physiological insulin resistance.[2] Hence, obesity that starts during childhood and continues through adolescence may lead to greater insulin resistance and make the child more prone to developing impaired glucose metabolism and T2DM, particularly in children with a family history of T2DM.

The study had some notable limitations. First, it was a retrospective study from a major tertiary care hospital in which the increased prevalence rates of both T1DM and T2DM in children and adolescents might have been influenced by a selection bias due to the number of referred cases. However, the more than 3-fold increase in the number of diabetes cases over 20 years could not be simply explained by a referral bias, but more than likely indicates an actual increased diabetes incidence in the pediatric population in Southern Thailand. Second, the differentiation between T1DM and T2DM might not have been totally accurate, as the diagnoses were based on the clinical characteristics of obesity and serum insulin levels without the "gold standard" confirmation of immunological studies. However, the

same methodology is common in many studies, in which obese patients with positive insulin antibodies and high serum insulin level have been diagnosed as T2DM and patients with normal weight and negative insulin antibodies diagnosed as T1DM.[4,7-9,23]

In conclusion, we found that the number of both T1DM and T2DM pediatric patients in Southern Thailand has risen sharply in number over the last 20 years, and although T1DM remains the most common type of diabetes in this age group, it is notable and of concern that the percentage of T2DM patients also increased 4-fold from 10% of diabetes cases in 1995 to 40% in 2014. Major at-risk-for-diabetes patients such as obese children and adolescents with a family member affected with T2DM should be screened, identified and monitored for possible progression to T2DM.

Acknowledgements

We would like to extend our appreciation to Mr. David Patterson of the International Affairs Office in the Faculty of Medicine, Prince of Songkla University, for editorial assistance.

Funding: None.
Ethical approval: This study was approved by Ethics Committee of the Faculty of Medicine, Prince of Songkla University.
Competing interest: None.
Contributors: Jaruratanasirikul S performed project proposal, concept and design, data collection, data analysis and drafting of the article. Thammaratchuchai S and Sriplung H contributed to data collection, data analysis and drafting of the article. All authors approved the final version of the manuscript.

References

1 Patterson C, Guariguata L, Dahlquist G, Soltész G, Ogle G, Silink M. Diabetes in the young-a global view and worldwide estimates of number of children with type 1 diabetes. Diabetes Res Clin Pract 2014;103:161-175.
2 Cameron FJ, Wherrett D. Care of diabetes in children and adolescents: controversies, changes, and consensus. Lancet 2015;385:2096-2106.
3 DIAMOND Project Group. Incidence and trends of childhood type 1 diabetes worldwide 1990-1999. Diabet Med 2006;23:857-866.
4 Dileepan K, Feldt MM. Type 2 diabetes mellitus in children and adolescents. Pediatr Rev 2013;34:541-548.
5 Pinhas-Hamiel O, Zeitler P. The global spread of type 2 diabetes mellitus in children and adolescents. J Pediatr 2005;146:693-700.
6 Tuchinda C, Likitmaskul S, Unachak K, Panamonta O, Patarakijavanich N, Chetthakul T. The epidemiology of type 1 diabetes mellitus in Thai children. J Med Assoc Thai 2002;85:648-652.
7 Likitmaskul S, Kiattisathavee P, Chaichanwatanakul K, Punnakanta L, Angsusingha K, Tuchinda C. Increasing prevalence of type 2 diabetes mellitus in Thai children and adolescents with increasing prevalence of obesity. J Pediatr Endocrinol Metab 2003;16:71-77.
8 Likitmaskul S, Wacharasindhu S, Rawdaree P, Ngarmukos C, Deerochanawong C, Suwanwalaikorn S, et al. Thailand diabetes registry project: type of diabetes, glycemic control and prevalence of microvascular complications in children and adolescents with diabetes. J Med Assoc Thai 2006;89 Suppl 1:S10-S16.
9 Trepatchayakorn S, Supornsilchai V, Wacharasindhu S, Aroonparkmongkol S, Sahakitrungruang T. Trends and characteristics of childhood diabetes in a tertiary care center in Thailand. Asian Biomed 2014;8:707-715.
10 American Diabetes Association. 2. Classification and diagnosis of diabetes. Diabetes Care 2015;38 Suppl:S8-S16.
11 Department of Health, Ministry of Public Health. Reference for weight, height and nutritional indices in Thai children aged 1 day to 19 years. Bangkok, Thailand, 2000.
12 D'Adamo E, Santoro N, Caprio S. Metabolic syndrome in pediatrics: old concepts revised, new concepts discussed. Pediatr Clin North Am 2011;58:1241-1255.
13 Rawshani A, Landin-Olsson M, Svensson AM, Nyström L, Arnqvist HJ, Bolinder J, et al. The incidence of diabetes among 0-34 year olds in Sweden: new data and better methods. Diabetologia 2014;57:1375-1381.
14 Catanzariti L, Faulks K, Moon L, Waters AM, Flack J, Craig ME. Australia's national trends in the incidence of type 1 diabetes in 0-14-year-olds, 2000-2006. Diabetes Med 2009;26:596-601.
15 Tajima N, Morimoto A. Epidemiology of childhood diabetes mellitus in Japan. Pediatr Endocrinol Rev 2012;10 Suppl 1:44-50.
16 Zhao Z, Sun C, Wang C, Li P, Wang W, Ye J, et al. Rapidly rising incidence of childhood type 1 diabetes in Chinese population: epidemiology in Shanghai during 1997-2001. Acta Diabetol 2014;51:947-953.
17 Wei JN, Sung FC, Lin CC, Lin RS, Chiang CC, Chuang LM. National surveillance for type 2 diabetes mellitus in Taiwanese children. JAMA 2003;290:1345-1350.
18 Garber AJ. Obesity and type 2 diabetes: which patients are at risk? Diabetes Obes Metab 2012;14:399-408.
19 Jiang X, Ma H, Wang Y, Liu Y. Early life factors and type 2 diabetes mellitus. J Diabetes Res 2013;2013:485082.
20 Iamopas O, Chongviriyaphan N, Suthutvoravut U. Metabolic syndrome in obese Thai children and adolescents. J Med Assoc Thai 2011;94 Suppl 3:S126-S132.
21 Lloud LJ, Langley-Evans SC, McMullen S. Childhood obesity and risk of the adult metabolic syndrome: a systematic review. Int J Obes 2012;36:1-11.
22 Wei JN, Li HY, Wang YC, Chuang LM, Lin MS, Lin CH, et al. Detailed family history of diabetes identified children at risk of type 2 diabetes: a population-based case-control study. Pediatr Diabetes 2010;11:258-264.
23 Badaru A, Pihoker C. Type 2 diabetes in children: clinical characteristics and role of β-cell autoimmunity. Curr Diab Rep 2012;12:75-81.
24 Poyrazoglu S, Bas F, Darendeliler F. Metabolic syndrome in young people. Curr Opin Endocrinol Diabetes Obes 2014;21:56-63.
25 Owen S, Galloway R. Childhood obesity and the metabolic syndrome. Curr Atheroscler Rep 2014;16:436.

Received January 22, 2016
Accepted after revision July 18, 2016