Childhood diabetes identified in mass urine screening program in Taiwan, 1993–1999

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Abstract

Objective: To describe the gender differences in cases and characteristics of diabetes mellitus (DM) that can be identified from a mass urine screen program for school children in Taiwan. *Method:* Screening for the childhood asymptomatic proteinuria and glucosuria began in 1992 for school children. Students were instructed to collect mid-stream samples of the first morning urine for glucosuria and proteinuria tests using urine strip devices. Students with positive results for glucose and/or protein and/or occult blood in the first examination received a second urine test. The third screening test was performed for urine and fasting blood sample for 11-item examinations if the second test was positive. The 1997 criteria of American Diabetes Association were used for defining DM. *Results:* Approximately 2 615 000–2 932 000 students received the preliminary screening each semester. The overall average rates of newly identified diabetes from 1993 to 1999 were 8.3 per 100 000 among boys, and 12.0 per 100 000 among girls. The average rate of new cases increased significantly from sixth grade for boys and fourth grade for girls, with peak rates of 14.7 per 100 000 in eighth grade for boys and 19.0 per 100 000 in sixth grade for girls. Similar prevalence trends by sex and grade were observed, higher in girls than in boys. *Conclusions:* This mass screening data suggest that childhood diabetes of all types in Taiwan is elevated in the age of puberty and higher in girls than in boys.
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1. Introduction

Epidemiological studies have shown a large geographical and racial variation in prevalence of diabetes mellitus (DM) for childhood type 1 diabetes [1–5], and there is a recent disturbing

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trend of increasing prevalence of type 2 diabetes in children [6–12]. Diabetes is the seventh leading cause of death in the US [13] and the fifth in Taiwan [14]. The world population based age-adjusted mortality rate from diabetes for Taiwan in 2001 ($21.7/10^5$) is 1.6 times higher than that in the US and 5.1 times higher than that in Japan in 1994 [15]. The age-adjusted mortality rate for diabetes was 3.7 per 100 000 in 1960 [16], which increased to 21.7 per 100 000 in 2001 [14], a 5.9-fold increase over four decades.

Although, screening for the childhood asymptomatic proteinuria and hematuria was considered not cost-effective for children with benign or transient urinary abnormalities [17]. The Put Prevention Into Practice Campaign also considers screening for childhood glucosuria to be of questionable value [18]. In Taiwan, mass urine screening for asymptomatic glucosuria and proteinuria has been conducted in school children since 1992, aimed at identifying children with glucosuria and proteinuria. Thus, the present report seeks to estimate the sex differences in cases of childhood diabetes can be newly identified and ever been identified in this screening program from 1993 to 1999, according to the 1997 American Diabetes Association recommendations based on fasting plasma glucose (FPG) levels [19]. Selected characteristics such as obesity rate, blood pressure and total cholesterol level were also compared by diabetes status.

2. Materials and methods

With the support of Taiwan Provincial Department of Health and approval by the Provincial Education Board, the Chinese Foundation of Health (CFH) initiated urine screening for all school children from grades 1 to 9 since 1992, and grades 10 to 12 since 1993. The numbers of students screened each semester were 2 615 207 in 1992 and approximately 2 932 000 since 1993.

With cooperation from County and City Bureaus of Health in all 21 counties and cities in Taiwan Province and with the assistance of public health nurses at 326 local health stations, urine sample bottles were delivered to school students by teachers and collected as scheduled. Students were demonstrated sampling techniques, and teachers, school nurses and parents received instructions explaining details of the sampling procedure.

The screening process included strategic steps as shown schematically in Fig. 1. The children collected and delivered to school their mid-stream urine samples at the first morning urination. A refrigerated automobile was stationed for collecting urine samples with student identifications. The student was instructed to collect the mid-stream sample of the first morning urine after 8-h fasting. The sample was brought to school where a refrigerator-car was stationed and transferred within few hours to a laboratory for the measurement of glucose, pH, protein and occult blood using Hemscomistrix IV urine strip (Ames Division, Miles Lab, Inc., Elkhart, USA). Students with positive results for glucose and/or protein and/or occult blood in the first examination received a second urine test within 2 weeks using Hemscomistrix IV urine strip and microscopical examination of precipitation. A third urine test was performed and a fasting blood sample was drawn for the student if the second test was also positive, and body height, body weight and blood pressure were measured as well. All samples for the third examinations were transferred to the central laboratory at the CFH headquarter for 11-item examinations, including total protein, albumin, A/G ratio, BUN, creatinine, ALSO, complement 3, total cholesterol, HbsAg, IgA and blood glucose by automatic analyzer (Technican RA 2000 serum Autoanalyzer, Bayer Diagnostic, Germany).

For quality control, medical technologists performed five quality control procedures for the calibration of urine analyzer Bayer CTK-200, life calibration, and KOVA TROL I, II, III. CFH participated in the College of American Pathologists quality assurance program and won a Good Performance award.

Students' parents received a report for results of all screening examinations and a Health Care Guide prepared by CFH. They were advised to seek follow-up care with their physicians. Based on the level of FPG, this report stratified students in the data analysis into three categories according to 1997 ADA recommendations: students with dia-
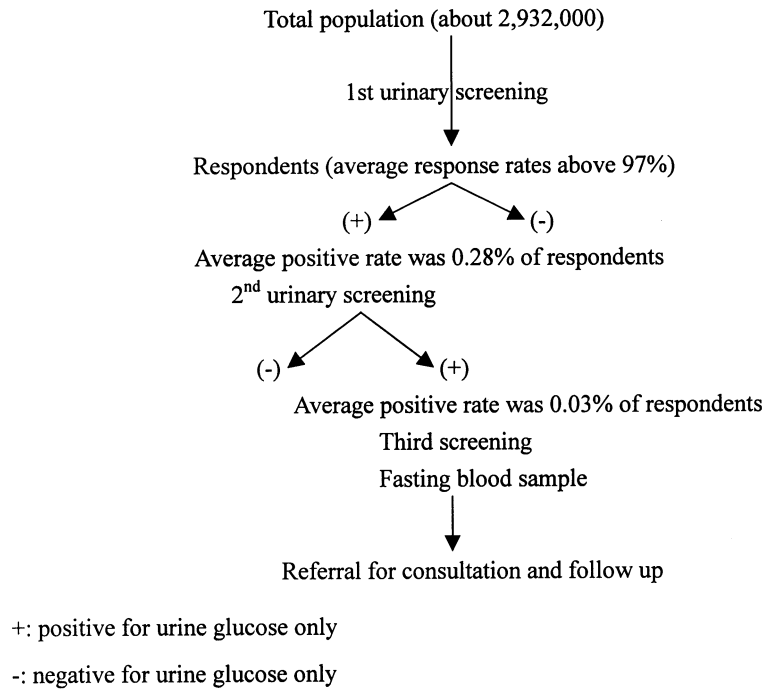
Total population (about 2,932,000)

1st urinary screening

Respondents (average response rates above 97%)

(+) ↖ ↗ (-)

Average positive rate was 0.28% of respondents

2nd urinary screening

(-) ↙ ↘ (+)

Average positive rate was 0.03% of respondents

Third screening

Fasting blood sample

↓

Referral for consultation and follow up

+: positive for urine glucose only

-: negative for urine glucose only

Fig. 1. The scheme of diabetes identification in urine screening program for school children in Taiwan, 1993–1999.

betes (FPG $\geq$ 126 mg/dl), impaired fasting glycemia (IFG: 110 mg/dl $\leq$ FPG $<$ 126 mg/dl), and normal fasting glycemia (NFG: FPG $<$ 110 mg/dl).

Since urine strip screening provided no information about sensitivity and specificity, students with newly identified FPG $\geq$ 126 mg/dl in their screening history and no history of DM in questionnaire were defined as 'new case' instead of incidence cases. The average rates estimated for ever identified cases instead of prevalence from 1993 to 1999 were compared by sex and grade.

Data analysis also compared children with diabetes, IFG and NFG for their differences in BMI, obese, blood pressure and cholesterol level. For defining obesity, we used the sex- and age-specific 95th percentile BMI as the cut-offs based on children anthropometrics in Taiwan [20]. A P-value below 0.05 was considered significant. The statistical analyses were performed using SPSS statistical Package (SPSS base 10.0, SPSS Inc. Chicago).

3. Results

Table 1 shows the distribution of average rate of newly identified DM by grade and gender from 1993 to 1999. There were 876 boys and 1190 girls newly classified as diabetes. The average rates of new diabetes cases for the first graders were 3.0 per 100 000 for boys and 3.4 per 100 000 for girls. The rate of new cases significantly increased for boys at sixth grade and for girls at fourth grade, with peak rates at 14.7 per 100 000 for the eighth grade boys and at 19.0 per 100 000 for the sixth grade girls. Fig. 2 shows the annual average rates of all identified diabetes cases with the highest rate in the eighth grade for both boys and girls, higher in girls than in boys (Fig. 2).

Table 2 compares the demographic and clinical characteristics of among children ever identified as diabetes cases and children with IFG and NFG in the third screening from 1993 to 1999. Students with diabetes, in both girls and boys, were more likely to have elevated blood pressure and total

Table 1
Average rate (per 100 000) of newly identified diabetes by grade and gender in school children in Taiwan from 1993 to 1999

| Grade	Boys			Girls		
	Cumulated cases	Average population	Rate	Cumulated cases	Average population	Rate
1	29	139 380	3.0	30	127 063	3.4
2	29	139 000	3.0	41	127 071	4.6
3	30	136 653	3.1	52	125 439	5.9
4	39	137 645	4.1	94	126 879	10.6
5	43	132 227	4.7	114	122 937	13.3
6	85	132 967	9.1	165	123 968	19.0
7	126	135 816	13.3	143	127 743	16.0
8	142	137 807	14.7	172	129 871	18.9
9	123	146 010	12.0	156	138 217	16.1
10	95	100 659	13.5	79	93 120	12.1
11	74	92 165	11.5	82	87 633	13.4
12	61	86 091	10.1	62	86 504	10.2
Total	876	1 516 420	8.3	1190	1 416 435	12.0
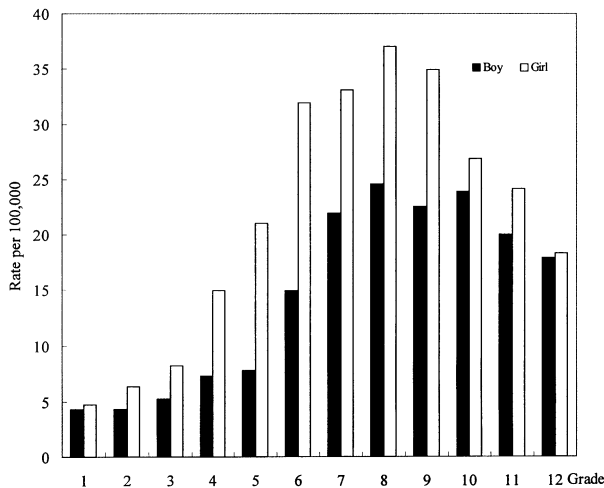
Fig. 2. The rate of prevalent cases of DM by gender and grade based on FPG in the glucosuria screening program for school children in Taiwan, 1993–1999.

cholesterol. Obesity was very prevalent in students with DM, 37.9% for boys and 39.5% for girls.

4. Discussion

Type 1 DM is the most common chronic metabolic disease in children and adolescents. However, more epidemiological studies have re-vealed an increasing emergence of type 2 diabetes in early childhood. Although our present study was not able to differentiate the type 1 and type 2 DM for screened students in this mass survey data, we found a clear evidence of diabetes in the early ages in Taiwan. The rate of new DM estimated by glycemia screening for school children in Taiwan was approximately 10 per 100 000. Epidemiological studies in Taiwan show that the incidence of type 1 DM is approximately 1.5 per 100 000 for the population less than 30 years old [21]. In addition, the sex ratio is generally considered equal in children diagnosed under the age of 15 years for type 1 DM [22]. However, there is a distinguished sex difference in incidence among children with type 2 diabetes. The female-to-male ratio of type 2 diabetes were 6:1 for First Nations children in Canada [23], 5:1 for Pima Indian [6], 3:1 for Mexican Americans [7] and 1.2:1 for Japanese children [24]. In this study, we found that both rates of new and prevalent cases were higher for girls than for boys. Compared with NFG and IFG, children with diabetes were the most obese, and had highest blood pressure. Obesity is very common in children with type 2 diabetes [25–29]. Therefore, we suspect that the diabetic individuals screened in the present study are largely type 2 diabetes.

Table 2
Comparisons of selected demographic and biochemical characteristics among schoolchildren with diabetes, IFG and NFG in Taiwan, 1993–1999

Variable	Boy			Girl		
	DM	IFG	NFG	DM	IFG	NFG
N	988	1833	51 328	1356	2386	83 936
Age	13.0±2.8	12.4±2.6	12.4±2.8*	12.5±2.6	11.7±2.4	11.8±2.8*
FPG (mg/dl)	224±106	117±9	85±12*	229±99	116±9	84±12*
BMI (kg/m^2)	23.9±6.6	20.2±5.3	19.3±3.8*	23.3±6.4	19.4±4.3	18.8±3.5*
Obesity rate (%)	37.9	12.7	7.4*	39.5	10.2	6.9*
Systolic BP	118±19	114±16	111±15*	113±17	108±14	106±13*
Diastolic BP	74±11	70±12	69±11*	73±13	68±11	67±10*
Total cholesterol (mg/dl)	191±48	175±43	161±42*	199±48	178±40	166±34*

All numbers are in Mean±standard deviation except specified. DM, diabetes mellitus; IFG, impaired fasting glycemia; NFG, normal fasting glycemia; FPG, fasting plasma glucose; BMI (body mass index) (kg/m^2) = weight/height^2; BP, blood pressure.
  * $P \leq 0.001$.

The rates of new and prevalent cases reached peak levels between sixth and eighth graders (12–14 years old), corresponding with the time of peak adolescent growth and development. These data were in consistent with previous studies of children with type 2 DM [30–32]. Puberty has long been recognized as a state of relative insulin resistance, with normally a 2–3-fold increase in peak insulin response to oral or intravenous glucose. In those with type 1 diabetes, substantial increase in insulin dose is required in puberty [33].

In this study, since no information in screening sensitivity and specificity is available, the rates of newly identified and prevalent cases can not represent the true incidence and prevalence. This screening program had an average recapture rate of 46.5%, ranged from 41.0 to 52.2%. This screening campaign may underestimate the prevalence. Our screening protocol has urged students screened with glucosuria to have a follow-up referral care. Some students with diabetes may have received medical care or put on a diet, and therefore not detected for the glucosuria screening program in the following semesters. The other reason of underestimation may result from the sensitivity in this screening test.

This study is the largest screening program and comprised the widest age-range of children. The results suggest that screening effort for youth diabetes targeting children at puberty, particularly obese children, is more likely to be efficient.

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