病院・医院・クリニック
先生侍史

平成21年3月吉日

「若年発症2型糖尿病の合併症発症率の全国専門施設における調査」
3年目の調査のお願い

拝啓

新春の候、先生におかれましては益々ご清栄のこととお慶び申し上げます。

３年前の年末から、先生には「若年発症２型との合併症発症率の全国専門施設における調査」にご協力いただいております。まことにありがとうございます。

３回目の調査としまして、**本年末に一番近い月日の**状況（2008年末ないし２００９年年初）をお知らせいただきたく、**調査用紙（イエロー色）（御礼の図書券も）**をＥＸＰＡＣＫ５００**にて、**郵送いたしております。

本調査には、たいへんお世話になっておりますところ、今後とも、よろしくお願い申し上げます。

末筆になりましたが、先生にはよい新年をお迎えでありますことを慶び、先生のご健康と、益々のご発展をお祈り申し上げます。

敬具

若年発症２型糖尿病調査研究委員会
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（厚生労働省循環器等生活習慣病対策総合研究事業から助成を受けております）

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20歳未満発症の２型糖尿病患者調査登録用紙 3年目

貴施設でのカルテ番号＿＿＿＿＿＿＿＿該当者 姓＿＿＿＿名＿＿＿＿
記載年月日：2009/平成21年＿＿月

記載した先生：医療機関名＿＿＿＿病(医)院（＿＿＿科）＿＿＿＿＿先生

以下、2008年12月にもっとも近い時期をお聞きします。数値の記入、もしくはあてはまるものに○をして下さい。

1. 年月： 200 /平成＿＿年＿＿月

2. 家族歴に追加があればご記入お願いします。

糖尿病が：なし／あり（２型は：父、母、祖母、祖父、姉妹、兄弟　←○で印を）、
１型は＿＿＿＿に）

3. 体重＿＿.＿＿kg　身長＿＿.＿＿cm　腹囲＿＿.＿＿cm　血圧＿＿/＿＿mmHg

4. 血糖:空腹時/随時＿＿＿mg/dl（記入時IRIがあれば空腹時/随時＿＿.＿＿μU/ml）

5. HbA1c ＿＿.＿＿ %

6. 治療：食事運動のみ／ SU／ﾋﾞｸﾞｱﾅｲﾄﾞ／α-GI／ﾁｱｿﾞﾘｼﾞﾝ／ｸﾞﾘﾆﾄﾞ／インスリン
<薬物治療は使用しているものに丸をしてください。重複可>

7. ｺﾚｽﾃﾛｰﾙ＿＿＿＿mg/dl 中性脂肪 ＿＿＿＿mg/dl

8. アキレス腱反射：なし／あり／不明

9. 眼底所見：なし／単純性／前増殖性／増殖性

10. 光凝固療法（１眼でも）：なし／あり（初回実施日西暦＿＿＿＿年/平成＿＿年）

少なくとも１眼が光覚弁以下：なし／あり（決定日西暦＿＿＿＿年/平成＿＿年）

11. Cr＿＿.＿＿mg/dl ｱﾙﾌﾞﾐﾝ/ｸﾚｱﾁﾆﾝ比(ACR)(尿)＿＿＿＿mg/gCr

人工透析：　なし／あり（初回透析日西暦＿＿＿＿年/平成＿＿年）

腎移植：　なし／あり（移植日西暦＿＿＿＿年/平成＿＿年）

12. 心筋梗塞:なし／あり（初回西暦＿＿＿＿年/平成＿＿年）
脳梗塞:なし／あり（初回西暦＿＿＿＿年/平成＿＿年）
壊疽:なし／あり（初回西暦＿＿＿＿年/平成＿＿年）
指趾切断:なし／あり（初回西暦＿＿＿＿年/平成＿＿年、部位＿＿＿＿）

13. 最終学歴：中学卒 ／ 高校卒 ／ 専門学校卒 ／ 短大卒 ／ 大学卒 ／ 大学院卒

14. 就労状況：あり/なし（学生／主婦／その他）

15. 喫煙歴：あり/なし（おおよそ　　歳から）

西暦と平成＿年はどちらかをお書き下さい。

III. 研究に使用した刊行物

1. Ogawa Y, Uchigata Y, Iwamoto Y. Proprtion od diabetes type in early-onset diabetes in Japan Diabetes Care 30(5), e30, 2007

2. 浦上達彦　若年2型糖尿病の疫学的動向　日本臨床 66(Supple 4):21－25、2008

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全容は、平成19年度報告書参照

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OBSERVATIONS

Proportion of Diabetes Type in Early-Onset Diabetes in Japan

Since 1990, we have reported hospital-based studies concerning Japanese patients with early-onset diabetes in our Diabetes Center, Tokyo Women's Medical University, Japan (1). Our goal is to confirm the proportion of type 1 versus type 2 diabetes in early-onset diabetes in Japan in our center with that of the Asian group in The SEARCH for Diabetes in Youth, a recent population-based study concerning the prevalence of diabetes in youth (2).

Our study consists of 4,063 Japanese patients who were initially diagnosed as having diabetes under the age of 30 years and who registered in our Diabetes Center between 1960 and 2004. Of the 4,063 patients, 1,746 (43.0%) had type 1 and 2,317 (57.0%) had type 2 diabetes based on the diagnostic criteria of the Japan Diabetes Society (3), which is identical to that of the World Health Organization. Other specific types of diabetes were excluded from the study. We divided the subjects into three groups according to age at onset of diabetes, namely, 525 patients with diabetes diagnosed from 0 to 9 years, 1,382 from 10 to 19 years, and 2,156 from 20 to 29 years, to investigate the proportion of type 1 versus type 2 diabetes in each group. The proportion of type 1 versus type 2 diabetes in the three groups was 95.0 versus 5.0%, 50.9 versus 49.1%, and 25.2 versus 74.8%, respectively.

Approximately 10% of diabetic patients who resided in the Tokyo metropolitan area were registered in our Diabetes Center (4); therefore, although our study was hospital based, we believe it reflects a general trend of a proportion of diabetes type in early-onset diabetes in Japan. The SEARCH for Diabetes in Youth showed that the proportion of type 1 versus type 2 diabetes in Asian/Pacific Islander patients from 0 to 9 and 10 to 19 years of age at onset is 86.6 versus 6.7% and 58.5 versus 40.1%, respectively (2). Not only The SEARCH for Diabetes in Youth but also our study suggests that type 2 diabetes accounts for ~5–7% of Asian children with diabetes and that the proportion of type 2 diabetes is nearly half of all Asian adolescents with diabetes.

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我が国における糖尿病の疫学—諸外国との比較—

若年2型糖尿病の疫学的動向

Change in the incidence of juvenile-onset type 2 diabetes

浦上達彦

Key words：小児・思春期，2型糖尿病，肥満，生活習慣

はじめに

21世紀になり2型糖尿病の患者数は明らかに増加している．全糖尿病患者の90-95%は2型糖尿病であるが，全世界の2型糖尿病患者数は現在2-3億人と推定される[1]．2型糖尿病患者の大半は成人であるが，近年になり全世界的に成人だけでなく小児・思春期においても2型糖尿病の発症頻度が増加していると報告されている[2-4]．

表1に米国，カナダおよび我が国における小児・思春期2型糖尿病の有病率および発症率[2-8]を示すが，米国の報告では，近年オハイオ州で発症した小児・思春期糖尿病の約1/3は2型糖尿病であり，カリフォルニア州在住小児・思春期ヒスパニック糖尿病患者の約1/3が2型糖尿病に罹患しているという[4]．ここで注目されるのは，2型糖尿病の発症頻度には成人でも小児でも人種差を認めることであり，ピマインディアン，ヒスパニック，アフリカ系米国人およびアジア民族に2型糖尿病の発症頻度が高い．そして日本人では，肥満児の増加と食習慣の欧米化(動物性タンパク，脂肪摂取の増加)および室内娯楽の増加，運動の減少を主とする生活習慣の破綻により，小児・思春期の2型糖尿病発症頻度が増加していると考えられる[5,7]．

1. 我が国における小児2型糖尿病の頻度の推移

我が国では欧米諸国に先駆けて，学校検尿・

表1　各国における小児・思春期2型糖尿病の頻度

年次	地域	人種	年齢(歳)	頻度
1992-96	アリゾナ	ピマインディアン	10-14 15-19	22.3/1,000* 50.9/1,000*
1996-97	マニトバ	先住者(女児)	10-19	36.0/1,000*
1988-94	NHANES III, 米国	白人，黒人	12-19	4.1/1,000*
1994	シンシナティ，オハイオ，米国	白人，黒人	10-19	7.2/100,000**
1998-2000	日本全国調査	日本人	18>	3.3/100,000**
1982-2001	横浜	日本人	7-15	3.2/100,000**
1974-2005	東京	日本人	7-15	2.6/100,000**

*有病率，**発症率

Tatsuhiko Urakami: Department of Pediatrics, Surugadai Nihon University Hospital　駿河台日本大学病院 小児科

0047-1852/08/¥40/頁/JCLS

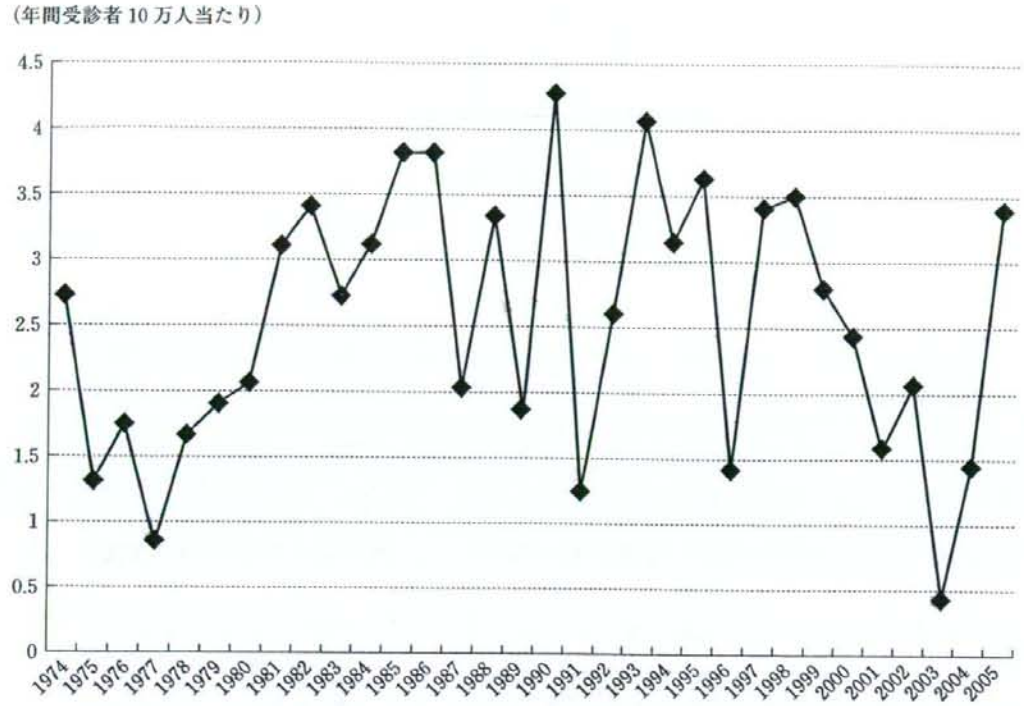

図1 1974-2005年における東京都学校検尿・糖尿病検診による受診者10万人当たり年間小児2型糖尿病発見頻度の推移

尿糖検査による小児糖尿病検診を実施しており，その結果として小児2型糖尿病の頻度がある程度判明している[7]．1974年に最初の試みとして東京都において小・中学校の学童を対象に学校検尿・糖尿病検診が行われたが，その後1992年からは全国規模で学校検尿の必須項目として尿糖検査が実施されるようになり，多数の小児2型糖尿病がほぼ無症状のうちに初期段階で発見されるようになった[5]．

a. 東京都における小児2型糖尿病発見頻度の推移

東京都における1974-2005年の学校検尿・糖尿病検診の成績では，32年間に9,268,730人の小学生，中学生に対して検診を行い，合計243人が2型糖尿病と診断された．この期間の受診者10万人当たりの2型糖尿病発見頻度は2.62人/年に相当する．これを小学生，中学生に分類すると，小学生では6,375,132人の受診者に対して48人が2型糖尿病と診断され，その発見頻度は受診者10万人当たり0.75人/年であった．一方，中学生では2,893,598人の受診者に対して195人が2型糖尿病と診断され，その発見頻度は受診者10万人当たり6.73人/年であり，中学生の発見頻度は小学生に比べて明らかに高いことが判明した．

次に1974-2005年における発見頻度の推移を図1に示す．初年度(1974年)は糖尿病と診断されていない症例の蓄積がある可能性があるが，1980年以前とそれ以降で発見率を比較すると，1980年以降で2型糖尿病の発見率は明らかに増加している[5](5年ごとの発見頻度の比較；年間受診者10万人当たり1974-80年：1.73，1981-85年：3.23，1986-90年：3.05，1991-95年：2.90，1996-2000年：2.70，2001-05年：2.50)．そして5年ごとの発見頻度の比較から，1981-85年をピークとして，2001年以降は発見頻度は減少傾向にあり，少なくとも1991年以降は増加傾向を示していない[6,7]．しかし，2005年に

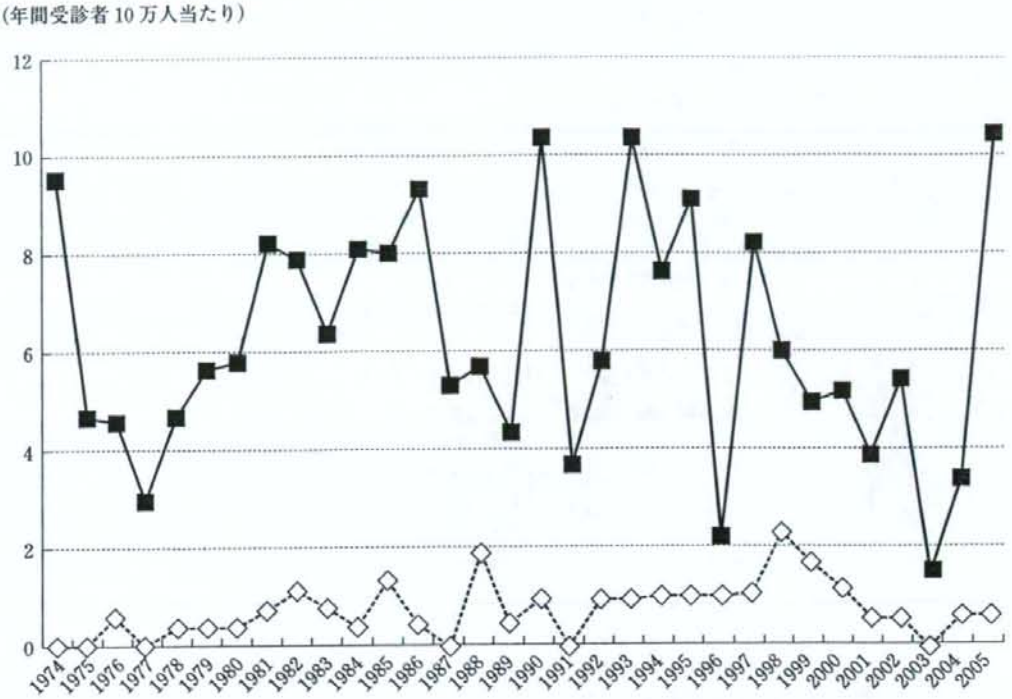

図2 1974-2005年における東京都学校検尿・糖尿病検診による小学生(◇), 中学生(■)別の受診者10万人当たり年間小児2型糖尿病発見頻度の推移

は再び発見頻度が受診者10万人当たり3.0人を超過しており，今後の発見頻度の動向について注意深く追跡する必要がある．

このような発見頻度の推移を小学生，中学生別に分類し示したのが**図2**である．小学生に比べて中学生では明らかに発見頻度が高く，1980年以降はしばしば受診者10万人当たり8-10人を超過している．1998年以降，中学生の発見頻度はやや低下傾向を示したが，2005年では再び10人を超過して，この結果が全体の発見頻度の増加に影響しているのは明白である．

b. 全国主要都市の小児2型糖尿病発見頻度の推移

我が国の主要都市(東京都，横浜市[8,9]，福岡市[10]，新潟市[11])における学校検尿・糖尿病検診で発見された2型糖尿病発見頻度とその推移を**表2**に示す．各都市の発見頻度は，受診者10万人当たり年間2.62-3.57人であり，いずれの都市も小学生に比べて中学生で発見頻度が4-5倍高かった(受診者10万人当たり年間0.75-1.62人：小学生 対 5.05-6.73人：中学生)．また各都市の2型糖尿病発見率の推移に関しては，横浜市では1982-86年に比べてそれ以降で明らかに発見頻度が増加しており[9]，新潟市においても特に中学生において1989-93年に比べてそれ以降で発見頻度が2倍になっている[11]．しかし近年(2000年以降)では横浜市，新潟市ともに増加傾向は認められておらず，若干ではあるが減少傾向にある[9,11]．

2. いかなる要因が小児2型糖尿病発症に影響するか

表3に東京都の学校検尿・糖尿病検診で発見された小児2型糖尿病の特徴を示す．発見された2型糖尿病の80%以上は肥満を伴い，その中でも肥満度40%以上の肥満児が約半数を占めている[7]．このほかの特徴としては，家族的要素(2型糖尿病の家族歴)が強いこと，小学生

表2 主要都市における学校検尿・糖尿病検診による小児2型糖尿病発見頻度

実施地方自治体	2型糖尿病発見頻度 (年間受診者10万人当たり)
東京都(1974-2005)[5-7]	全体2.62(小学生0.75, 中学生6.73) 推移：1974-80: 1.73, 1981-85: 3.23, 1986-90: 3.05, 1991-95: 2.90, 1996-2000: 2.70, 2001-05: 2.50
横浜市(1982-2001)[8,9]	全体3.20(小学1.50, 中学生6.65) 推移：1982-86: 1.89, 1987-91: 3.19, 1992-96: 4.97, 1997-2001: 4.56
福岡市(1989-98)[10]	全体2.77(小学生1.62, 中学生5.05)
新潟市(1982-2003)[11]	全体3.57 推移(小学生) 1982-88: 0, 1989-93: 1.7, 1994-98: 1.3, 1999-2003: 2.8 推移(中学生) 1982-88: 0, 1989-93: 6.0, 1994-98: 14.6, 1999-2003: 13.4

表3 東京都における学校検尿・糖尿病検診で発見された小児2型糖尿病の特徴

(1) 男女比は1：1.2で有意差は認めない.

(2) 全体の比率は小学生が16.7%, 中学生が83.3%. また発見頻度は, 受診者10万人当たり小学生が0.75人/年, 中学生が6.73人/年で, 中学生で頻度が高い.

(3) 83.7%の症例が肥満度20%以上の肥満児であり, 肥満度40%以上の高度肥満児が48.7%を占める. そして肥満傾向は男児に強く, 肥満度40%以上の高度肥満の比率は男児では65.1%, 女児では36.5%である.

(4) 2型糖尿病の家族歴は, 第1度近親者の39.2%, 第1度および第2度近親者の56.5%に認められ, 家族集積性が高い.

に比べて中学生で発症頻度が明らかに高い(思春期の内分泌学的要因や中学生になってからの生活習慣の変化)ことが発症に関与していることがうかがわれるが[7], いずれにしても本症の発症に肥満が関与していることは明らかである.

文部科学省学校保健統計調査報告書によると, 小学校・中学校における肥満傾向児の頻度が1970-80年以降飛躍的に増加しており, 2000年では小学校高学年～中学生の約10%が肥満傾向を有している[12]. このような肥満傾向児の増加が, 小児2型糖尿病頻度の増加に関与していることは明らかである. しかし, 2000年以降は各年齢ともに肥満傾向児の頻度は頭打ちか, わずかではあるが減少傾向を示している[12].

2000年以降, 小児肥満そしてメタボリック症候群に関する一般社会の関心が増大してきたように思われる. そしてメタボリック症候群の一項目として, 小児においても2型糖尿病が注目されるようになった. これらの関心に伴い, 大人も子どもも以前に比べて動物性脂肪に富んだ食品, ファーストフードや清涼飲料水の摂取が減少し, スポーツクラブへの参加や運動量が多くなった感がある. 逆に最近やせ志向が増えたことも問題視されるが[12], このような生活習慣の改善に伴う肥満傾向の減少が, 小児2型糖尿病頻度の増加に歯止めをかけたことが推測される. 今後このような考えが社会に拡大し, 小児肥満と2型糖尿病の発症が抑制されるものと期待される.

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Time-course changes in clinical features of early-onset Japanese type 1 and type 2 diabetes: TWMU hospital-based study

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ABSTRACT

Using a database of patients with type 1 ($n = 1675$) and type 2 ($n = 2259$) diabetes diagnosed before the age of 30 years at the Diabetes Center, Tokyo Women's Medical University (TWMU), in which such Japanese patients have been registered at the time of first visit since the 1960s, we performed a hospital-based study over the last 40 years to clarify time-course changes in clinical features of type 1 and type 2 diabetes diagnosed before the age of 30 years. Type 2 diabetes had a male dominancy, while there has been a female dominancy in patients with type 1 diabetes as in previous reports of Japanese childhood-onset type 1 diabetes. Such dominances had been continued over the last 40 years. The number of patients with type 2 diabetes and with a past history of obesity increased with time. The age at which type 2 diabetes was diagnosed was suggested to have been getting lower with time, whereas that of type 1 diabetes has been higher with time. There was no marked difference in family history of diabetes in the first-degree relatives of patients with type 2 diabetes, regardless of the presence or absence of a past history of obesity. More female patients with type 2 diabetes diagnosed before the age of 15 years had mothers with type 2 diabetes compared to corresponding male patients.

1. Introduction

Patients with early-onset diabetes in their teens or 20s have been reported in young Pima Indians, Hispanics, blacks, and whites [1–3]. We initially reported the presence of Japanese patients with type 2 diabetes diagnosed before the age of 30 years (defined as early-onset diabetes) in an epidemiological survey performed by the Diabetes Center of Tokyo Women's Medical University (TWMU) School of Medicine in 1990 [4].

At that time, type 1 diabetes was assumed to be juvenile diabetes in Japan. Although urine glucose screening in school had been detected as type 2 diabetes in children since 1974 in metropolitan area [5] (nationwide screening since 1992), the importance of juvenile or early-onset type 2 diabetes was not sufficiently recognized in Japan. For example, when 135 patients who developed proliferative retinopathy before the age of 35 years were taken from patients with early-onset type 2 diabetes diagnosed before the age of 30 years using a database of first-visit patients between 1970 and 1990 at the Diabetes Center [6], patients with type 2 diabetes diagnosed by the age of 18 years accounted for about 40% of the 135 patients. Another example is our study which investigated the impact

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of the school urine screening test system toward prevention of complications of early-onset type 2 diabetes in 283 patients with type 2 diabetes diagnosed before the age of 18 years using a database of first-visit patients between 1980 and 1998 [7]. The presence or absence and severity of complications at the time of the first visit were closely related to the presence or absence of intermittence or discontinuation of therapy before visiting the Diabetes Center [7].

In 2006, the SEARCH study showed that the proportion of type 2 diabetes is nearly half of Asian adolescents with diabetes who were residence in North America [8]. We reported that the ratio of type 1/type 2 diabetes in teenager in our center was similar to that of the SEARCH Asian group [9]. It means that the ratio of type 1/type 2 diabetes in youth in our center may be a representative of Japanese adolescents with diabetes.

Using the 1960–2003 database of first-visit patients with early-onset type 1 and type 2 diabetes at the Diabetes Center, we performed a hospital-based study to investigate time-course changes in the clinical features in patients with type 1 and type 2 diabetes over the last 40 years, especially the relationship between a past history of obesity and a family history of diabetes in type 2 diabetes. We speculated that patients with earlier-onset type 2 diabetes would have a higher frequency of family history of diabetes than that of past history of obesity. There has been no similar population-based study in Japan.

2. Methods

2.1. Study population

We performed a hospital-based observational longitudinal study. Patients could visit our outpatient clinic at the Diabetes Center, Tokyo Women's Medical University, without any referrals, and the charge to the patients for treatment was the same as in other hospitals. A large population of diabetic patients ($n = 26,731$) who resided in the metropolitan area (about 5400 km^2) attended the outpatient clinic between 1960 and 2003, which corresponds to approximately 10% of diabetic patients attending medical clinics in the metropolitan area. Among them, 3934 (14.7%) had early-onset diabetes (diagnosed before the age of 30 years), which consisted 1675 patients with type 1 diabetes and 2259 patients with type 2 diabetes.

The diagnosis of diabetes and classification of diabetes type (type 1 and type 2) was made according to the World Health Organization criteria [10], ADA criteria [11], and reports of the committee of Japan Diabetes Society on the classification and diagnostic criteria of diabetes mellitus [12]. For the patients who visited us before 1999, we re-checked the medical records. The classification of diabetes type using such criteria was done by at least two attending doctors who were board certified members of the Japan Diabetes Society. Briefly, type 1 diabetes was defined as the patient being prone to ketosis with acute onset and requiring insulin therapy within 1 year of diagnosis. The three issues were the fundamental ones to classify type 1 diabetes. Type 2 diabetes was diagnosed if the patient was found not to be ketosis prone, did not require insulin therapy for more than 1 year after the diagnosis, and/or exhibited preserved insulin secretion even when treated with insulin. Type 2 diabetes was diagnosed from symptoms (28%), other complaints (27%), or a screening test (45%). After serum C-peptide levels and anti-glutamic acid decarboxylase (GAD) antibody representative for anti-islet autoantibodies became available, such titers became additional criteria (C-PEPTIDE RIA; Shionogi, Tokyo, Japan, the limit of detection, 0.1 ng/ml) and RIA kits (GAD RIA kit; Hoechst, Tokyo, Japan, cut-off; 5 U/ml, before March 1997 and Cosmic Corp., Tokyo, Japan, cut-off; 1.5 U/ml, after April 1997).

2.2. Methods

Patient profiles regarding the diagnosis of diabetes and medical treatment of diabetes, the past history of obesity (body mass index, BMI, of 25 or more), and data on the history of diabetes in first-degree relatives were complied from information obtained through interviews. Although there are various reports according to the definition of obesity in children and adolescence, BMI was used in this study.

The patients included in the study were divided into three groups according to following events. Major health care and infrastructure changes occurred from the mid-1970s; free medical care for diabetic patients under the age of 18 years and urine screening tests for school children started in 1974, and summer camps for children with diabetes were introduced all over Japan during the same period. A measurement of HbA1 started in 1978 and that of HbA1c started in 1983 at our Diabetes Center, TWNU. Children could not legally inject themselves with insulin before 1981. A nation-wide blood laboratory company started HbA1c measurement in 1983. The Japan Diabetes Society established a national registry of authorized diabetologists to encourage internists and paediatricians to become diabetes specialists in 1985. The measurement of blood glucose by patients with insulin therapy was included in the application of the health insurance in 1986. Taken together described above and without a big difference in each group, the subjects were divided into three groups with age at diagnosis in 1960–1978, 1979–1988, and 1989–2003, respectively.

3. Results

3.1. Ratio of patients with type 1 and type 2 diabetes

Fig. 1 shows the numbers of males and females grouped by age of onset in the 1675 patients with type 1 diabetes and the 2259 patients with type 2 diabetes diagnosed before the age of 30 years. There was female dominancy in all diagnosis age groups for type 1 diabetes, but more patients with type 2 diabetes were male in the group with an age at diagnosis of 15 years or older.

Table 1 shows the number of the three groups by gender and by age at diagnosis (under 10 years, teens, and 20s). The male/female ratio of the total was 609:1066 for type 1 diabetes (Table 2). Regarding the male ratio as 1, the female ratio was 1.75, showing that the incidence of type 1 diabetes was higher in females, as reported in studies of the sex ratio of Japanese

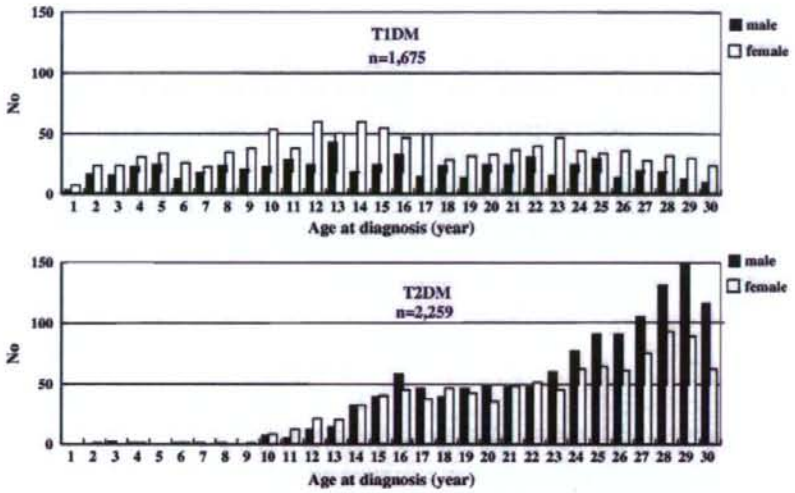

Fig. 1 – Numbers of patients with type 1 and type 2 diabetes diagnosed in three chronological periods before the age of 30 years and visited Diabetes Center, TWMU from 1960 to 2003.

type 1 diabetes patients [13,14]. The male/female ratio of the total was 1267:992 for type 2 diabetes, showing that males were dominant (Table 2). The ratio of type 1/type 2 diabetes patients was 1:1.35, showing that type 2 diabetes was dominant in the total number of patients.

As shown in Table 2, the ratios of type 1/type 2 diabetes patients in the three groups were 1:1.72, 1:1.24, and 1:1.22, respectively. The male/female ratios for type 1 diabetes were 1:1.74, 1:1.59, and 1:1.92, respectively, and those for type 2 diabetes were 1:0.80, 1:0.78, and 1:0.76, respectively. The total number of type 2 diabetes patients and the male/female ratio was not significantly different among the three groups. The ratio of type 1/type 2 diabetes patients with time showed that the increase rate in patients with type 2 diabetes with time was lower than that of patients with type 1 diabetes with time. The number of patients with early-onset type 2 diabetes (diagnosed before the age of 30 years), did not increase at the Diabetes Center compared to the number of patients with type 1 diabetes.

3.2. *Diabetes type ratio by age at diagnosis in the three groups*

Fig. 2 shows the ratios of patients with type 1 diabetes to patients with type 2 diabetes by age at diagnosis in the three groups. In 1960–1978, 99.14% of diabetic patients under 10 years of age had type 1 diabetes. Type 2 diabetes increased after the age of 10 years. This state intersected with the number of patients with type 2 diabetes at the age of 14–15 years, and type 2 diabetes patients became dominant thereafter. In 1979–1988, the numbers of type 1 and type 2 diabetes patients intersected at the age of 14–15 years, but

Table 1 – Numbers of patients with type 1 and type 2 diabetes diagnosed in three chronological periods

	Age at diagnosis	1960–1978	1979–1988	1989–2003	Total
Males with type 1 diabetes	0–9	72	68	34	174
	10–19	57	106	79	242
	20–29	19	64	110	193
Females with type 1 diabetes	0–9	125	105	57	287
	10–19	92	178	175	445
	20–29	41	95	198	334
Males with type 2 diabetes	0–9	4	4	5	13
	10–19	84	149	115	339
	20–29	299	286	330	915
Females with type 2 diabetes	0–9	2	5	5	12
	10–19	107	120	103	330
	20–29	201	211	238	650
Total		1103	1382	1449	3934

Table 2 – Ratios of patients with type 1 and type 2 diabetes diagnosed in three chronological periods, irrespective of sex and type of diabetes

	1960–1978	1979–1988	1989–2003	Total
Type 1 diabetes	406	606	653	1673
Ratio of male and females with type 1 diabetes	148:258 1:74	238:378 1:59	223:430 1:92	609:1066 1:75
Type 2 diabetes	697	766	796	2259
Ratio of male and females with type 2 diabetes	387:310 1:0.8	430:336 1:0.78	450:346 1:0.76	1267:992 1:0.78
Ratio of type 1/type 2	1:1.72	1:1.24	1:1.22	1:1:35

type 1 diabetes kept being dominant in the high teens compared with the 1979–1988 group, while type 2 subsequently became dominant at the age of 20 years and older. In 1989–2003, the numbers of type 1 and type 2 diabetes patients were similar, in an age range from 15 to 22 years. The period of the intersection was longer than those of other two groups.

3.3. *Ratios of patients with age at diagnosis to the total numbers of type 1 and type 2 diabetes patients*

Fig. 3 shows the ratios of patients with diabetes by the age at diagnosis among the total number of diabetic patients in each group. Fig. 3A and B shows type 1 and type 2 diabetes, respectively. The proportion of patients with early childhood-onset type 1 diabetes was relatively higher in the 1960–1978 group. In contrast, to that of type 1 patients diagnosed in the 20s was relatively higher in the 1989–2003 group. The proportion of patients with type 2 diabetes increased after the age of 10 years in all the three groups, and the increase of type 2 patients diagnosed in the teens, was relatively high in 1979–1988 and 1989–2003, compared to 1960–1978.

We picked up the proportions of type 2 diabetes patients for diagnosis with the age of 0–9 and 10–19 years and compared them (Fig. 4). The proportion with the age at diagnosis in the teens increased in 1979–1988, then slightly decreased in 1989–2003, but the proportion with the age at diagnosis of 0–9 years slowly increased from 1960–1978 to 1989–2003 (0.86, 1.15, and 1.26%, respectively), although there was no statistical significance.

3.4. *Past history of obesity in type 2 diabetes patients*

Fig. 5 shows the past history of obesity (BMI of 25 or more) in patients with type 2 diabetes diagnosed before the age of 30 years in the diagnosis age groups and in the three groups. Obesity was determined by BMI regardless of the age at diagnosis. Fewer patients had a past history of obesity in patients diagnosed at lower ages, but the ratio of patients with a past history of obesity increased with an increase in the age at diagnosis and in the course of time. None of patient with type 1 diabetes had a past history with BMI of 25 or more.

Only a small percentage of patients with type 2 diabetes was lean in the past (maximum BMI in the past <20) in all the three groups and onset age groups. It was clarified that there were patients with type 2 diabetes, who had been lean before developing diabetes, but they accounted for a small percentage in both the past and recent times (data not shown).

3.5. *Family medical history of type 2 diabetes patients in the three groups*

The familial medical history of the first-degree relatives was investigated in patients with type 2 diabetes divided by past history of diabetes. More than 30% of type 2 patients had no first-degree relatives with diabetes at the first visit of our center, regardless of the past history of obesity. The father and mother of the patients had type 2 diabetes in about 20% and less than 20% of the patients, respectively.

The familial history was investigated in patients with a past history of obesity (BMI of 25 or more) in the three groups. The father had diabetes in 20, 26, and 25% of the patients in the 1960–

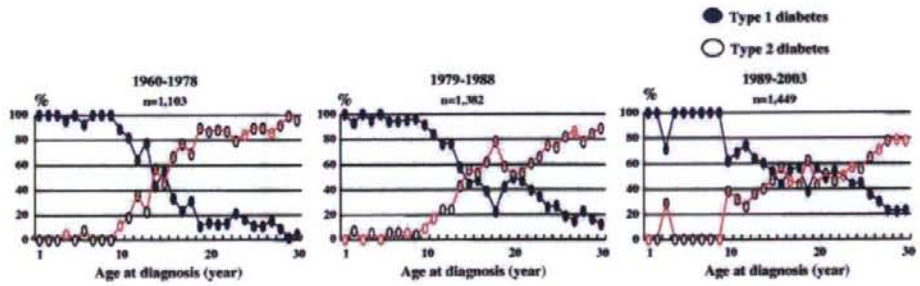

Fig. 2 – The ratios of patients with type 1 diabetes to patients with type 2 diabetes by the age at diagnosis in the three groups.

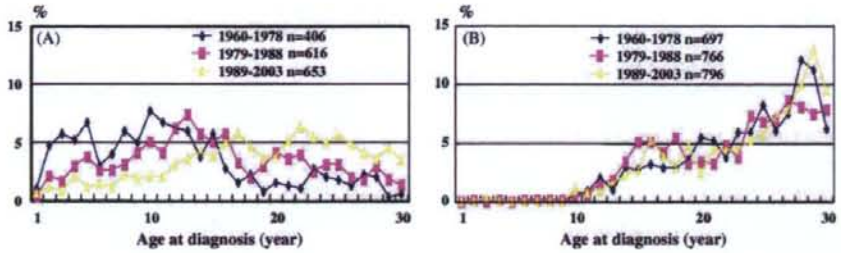

Fig. 3 – The ratios of patients with diabetes by the age at diagnosis among the total number of diabetic patients in three calendar year groups. (A and B) The ratio of patients with type 1 diabetes and type 2 diabetes in each group, respectively.

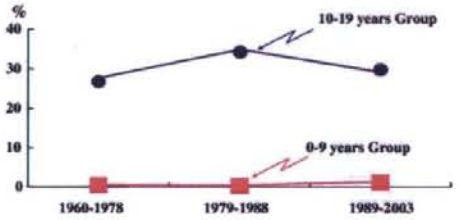

Fig. 4 – The proportions of type 2 diabetes patients with the age at diagnosis of 0–9 and 10–19 years in three calendar year group.

1978, 1979–1988, and 1989–2003 groups, respectively, and the mother had diabetes in 22, 15, and 17%, respectively, showing no significant changes with time. Similarly, the familial history was investigated in patients without a past history of obesity, and the father had diabetes in 11, 21, and 22% of the patients, respectively, and the mother had diabetes in 16, 21, and 20%, respectively, showing that the incidence of diabetes in the first-degree relatives slightly increased with time.

3.6. *Familial medical history of patients with type 2 diabetes developing before the age of 15 years*

Assuming that the incidence of diabetes in the parents was higher in patients with early childhood-onset type 2 diabetes, the presence of diabetic first-degree relatives was re-investigated in patients with type 2 diabetes developing before the age of 15 years in the three groups. The ratio of male patients with a diabetic father changed from 16 to 20% in the course of time, and the ratio of male patients with a diabetic mother changed from 25 to 16%. The ratio of female patients with a diabetic father changed from 15 to 26% in the course of time, and the ratio of female patients with a diabetic mother changed from 23 to 26%. Although there were some tendencies, there were no statistical significance.

3.7. *Therapy at initial examination at the Diabetes Center, TWMU*

Only insulin therapy is available for type 1 diabetes; however, the medical treatment for type 2 diabetes includes not only oral hypoglycemic drugs, but also insulin preparations. To investigate therapies given to type 2 diabetes patients over the last 40 years, the content of therapy at the time of initial examination was investigated in the groups with and without past history of obesity and in the three groups. The ratio of these patients who underwent diet/exercise therapy alone was low, and a high ratio of these patients underwent drug therapy because there were fewer first-visit patients with no past history of obesity than patients with past history of obesity at the Diabetes Center, TWMU in all the three groups. However, quite a number of patients with a past history of obesity also underwent drug therapy at the time of their first visit, suggesting that the patients were not obese at the time of the first visit, and that they needed drug therapy to maintain control of blood glucose.

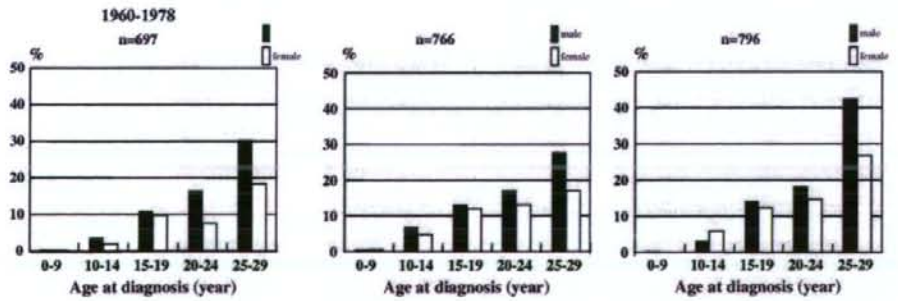

Fig. 5 – Past history of obesity (BMI of 25 or more) in patients with type 2 diabetes in the age at diagnosis group.

4. Discussion

In this study, diabetes with an age diagnosed before 30 years was defined as early-onset diabetes, and changes in the numbers, ratios, and male/female ratio of patients with type 1 and type 2 diabetes, and the presence or absence of a past history of obesity in type 2 diabetes patients were investigated over the last 40 years using the database of patients at the Diabetes Center, TWMU, registered since the 1960s.

There is a school urine glucose screening for children from 6 to 12 years of age, which in the metropolitan area started from 1974 and became a nationwide obligation to perform it from 1992. There was no regulation in the metropolitan area that urine glucose positive students should visit our Diabetes Center, who can visit any clinic or hospital. Therefore, there was no bias in consulting us for patients with type 2 diabetes who were diagnosed by the school urine glucose screening.

Although the increase in patients with early-onset type 2 diabetes has been discussed in the mass media as obese teenagers and the diabetic adult population have increased, no rapid increase was noted in comparison with the number of patients with type 1 diabetes at the Diabetes Center, TWMU. However, to clarify the presence of a rapid increase in the diabetic youth population, it is necessary to perform a population-based study that investigates changes in the number of diabetic patients in a specified region. Recently, Urakami et al. reported annual incidences of type 2 diabetes in children as detected by urine glucose screening in the Tokyo metropolitan area from 1974 to 2002 [5]. This increase of the annual incidences during the period, which was fluctuant, was shown to be slow, but not rapid, though, they also mentioned that the incidence of type 2 diabetes in junior high school students (13–15 years old) was larger than that in primary school students (6–12 years old) ($p < 0.0001$) and the incidence of 6–12-year group was gradually increased with time [5]. In spite of no increase of the percentage of the patients with type 2 diabetes in 10–19-year group in this study, it should be noted that the percentage of patients with type 2 diabetes at the onset age of 0–9 years slowly increased (**Fig. 4**), which is younger than that in the Urakami's study [5]. This finding suggests that the onset age of early-onset type 2 diabetes may become younger toward infancy in the future.

The absence of an increase in the number of patients with type 2 diabetes from 1979–1988 to 1989–2003 at the Diabetes Center, TWMU, suggested that type 2 diabetes patients dispersed with an increase in the number of hospitals and clinics which were not specialized in diabetes in the metropolitan area. The patients with type 1 diabetes may have similarly dispersed. However, the degree of dispersion of patients with type 1 diabetes may have been smaller than that of patients with type 2 diabetes, since the treatment of type 1 diabetes requires more specialized knowledge and insulin therapy and many patients with type 1 diabetes are transferred to the larger medical institutions specializing in diabetes. Another possibility is similar to Urakami's report who speculated that the lifestyle changes may contribute to the decrease in the incidence of type 2 diabetes in 2001–2004 in Tokyo metropolitan area [15].

The percentage of patients with type 1 diabetes developing in their 20s increased with time, as shown in **Table 1** and **Fig. 3**. Since treatment of type 1 diabetes developing the disease in their 20s is less difficult than that of early childhood-onset type 1 diabetes, patients may have dispersed with an increase in the number of hospitals and clinics. No matter how dispersed the patients with type 1 diabetes developing in their 20s have become, the increase in patients with type 1 diabetes developing in their 20s at the Diabetes Center, TWMU, suggests that the population of patients with type 1 diabetes developing in their 20s has increased. As onset peaks were at the age of about 3–5 years and at the late teens in Japanese patients with type 1 diabetes [16], it is suggested that the peak onset at the late teens may slowly be shifting to an older age than the late teens.

The male/female ratio in patients with early-onset type 2 diabetes did not markedly change with time, and there were more male patients than female patients in all of the chronological periods. The dominance of male patients is similar to the feature of adult type 2 diabetes, and this is obviously different from the sex ratio of Japanese patients with type 1 diabetes [13,14]. The higher incidence of type 2 diabetes in males might be due to a greater likelihood of obesity in males than in females, as seen in **Fig. 5**.

Fig. 5 also shows that the percentage of type 2 diabetes patients with a past history of obesity increased as the onset age shifted to a higher age. The correlation of a past history of obesity with type 2 diabetes was low in patients with a low onset age, and the ratio of patients with a past history of obesity increased with an increase in the onset age.

From **Fig. 5**, the patients with a past history of obesity were expected to have a less frequent family history of diabetes compared with those without a past history of obesity, but this was not necessarily the case. About 70% of patients with early-onset type 2 diabetes had a family history regardless of past history of obesity. Moreover, it is difficult to determine whether inheritance from the father or mother is stronger based on this database. However, the incidence of diabetes in the mothers was higher in females than in males in patients with type 2 diabetes developing before the age of 15 years. It is well known that mitochondrial diabetes is transmitted by maternal inheritance. Although not all of the patients were investigated with regard to the presence of an abnormality in the mitochondrial gene in this study, it is possible that type 2 diabetes-associated genes including the mitochondrial gene were transmitted by maternal inheritance. In this connection, there was no abnormality in the mitochondrial gene in patients with type 1 diabetes diagnosed before the age of 30 years [17].

Regarding time-course changes in the clinical features of type 1 and type 2 diabetes developing before the age of 30 years at a medical institution specializing in diabetes in the past 40 years, type 2 diabetes patients with a past history of obesity have increased with time. Concurrent with a shift toward infancy in the age diagnoses as type 2 diabetes, a shift in the age diagnosed as type 1 diabetes toward a higher age was also suggested.

Patients with early-onset type 1 diabetes from the Diabetes Center, TWMU, constituted a relatively large proportion (TWMU group) of the Japanese cohort among Diabetes Epidemiology Research International (DERI) cohort [18]. We reported that the mortality and incidence of ESRD in the

TWMU group among DERI cohort were markedly lower than those in the remaining group among Japanese DERI cohort [19] and the incidence of complications in early-onset Japanese type 1 diabetes has decreased yearly [20]. However, a comparison of the cumulative incidence of diabetic nephropathy in Japanese patients with type 2 diabetes occurring at the same age was shown to be higher than those with type 1 diabetes [20]. More attention is necessary to do with early-onset type 2 diabetes.

Conflict of interest

None.

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Exposure to Rosiglitazone and Fluoxetine in the First Trimester of Pregnancy

Rosiglitazone is a thiazolidinedione oral hypoglycemic drug that seems to be a promising alternative not only as an oral hypoglycemic agent but also for women with polycystic ovary syndrome. However, information regarding exposure to rosiglitazone in pregnancy is limited to two previous case reports. In the first case, a 35-year-old woman was exposed until the 8th week of pregnancy to 4 mg/day rosiglitazone and to glicazide, acarbose, atorvastatin, spironolactone, hydrochlorothiazide, carbamazepine, thiridazine, amitryptiline, chlordiazepoxide, and pipenzolate bromide (1). The second case was a woman exposed to 4 mg/day rosiglitazone between gestational weeks 13 and 17 (2). The two cases delivered normal babies at gestational weeks 36 and 37, respectively.

We are reporting the case of a 29-year-old Korean primiparous woman with a 6-month history of type 2 diabetes. She had been taking 400 mg metformin and 2.5 mg glibenclamide every 12 h. Because of the difficulties in controlling her hyperglycemic levels, 500 mg metformin every 12 h was added to her combined treatment. Five months later, her physician decided to switch her treatment to 4 mg rosiglitazone maleate every 12 h. In addition, she received 20 mg fluoxetine hydrochloride every 12 h for a body weight reduction plan. She had control of her diabetes and took both medications until the 5th week of gestation, when she had symptoms of pregnancy.

She was seen at The Korean Motherisk Program at 8 weeks of pregnancy, where she reported negative exposure to other medications, alcohol, illicit drugs, cigarette smoking, or radiation. She was not taking folic acid. Her BMI was 31.2 kg/m^2 (weight 85 kg and height 165 cm). Her fasting plasma glucose and HbA_{1c} levels were 138 mg/dl and 6.8% (normal range 4.5–6.0), respectively. A single embryo of 20 mm crown-lump length and normal heart rate was identified by ultrasound. Her treatment with rosiglitazone was switched to insulin, and fluoxetine administration was discontinued.

She was followed up periodically by clinical, laboratory, and ultrasound examinations. There were no ultrasonographic evidences of fetal malformations at the different follow-up examinations. The course of her pregnancy was considered to be normal. Previous to delivery, her total weight gain was 15 kg and her BMI was estimated to be 36.7 kg/m^2. At 40 weeks of gestational age, she vaginally delivered a 3.7-kg male baby. A detailed neonatal examination did not detect any clinical evidence of external, cardiac, pulmonary, or gastrointestinal congenital malformations. His cephalic circumference was 34.5 cm (within normal range), and his neurological development was found to be normal by a detailed physical and neurological examination. The baby was periodically followed up by a pediatrician. At the age of 18 months, the child was weighing 13.5 kg, was a healthy baby, and had a neurological development similar to that expected for his age-group.

Preclinical studies on rosiglitazone (GlaxoSmithKline, Mississauga, ON, Canada) found no increase in congenital malformations in rats and rabbits treated with 19 and 73 times the human dose, respectively. The two previous case reports, in addition to the present one, suggest that this drug is also not teratogenic in humans. On the other hand, fluoxetine is a serotonin reuptake inhibitor antidepressant drug with sufficient reproductive and developmental studies in humans to prove a lack of an increased risk of teratogenicity.

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Recent Trend Toward Decrease in the Incidence of Childhood Type 2 Diabetes in Tokyo

We previously reported that the annual incidences of children with type 2 diabetes as detected by urine glucose screening at school in Tokyo during 1981–1995 were significantly higher than the incidence in 1974–1980 (1). We evaluated recent changes in the annual incidence of childhood type 2 diabetes in Tokyo. The results were analyzed using Fisher's exact probability test.

From 1974 to 2004, a total of 9,242,259 school students were tested for glucosuria to detect diabetes. A total of 236 children were diagnosed as having type 2 diabetes through this screening program. Overall, 83.9% of children with diabetes were obese. The overall incidence was 2.55 per 100,000 per year. Junior high school children had a significantly higher incidence than primary

school children (0.75 vs. 6.27 per 100,000; $P < 0.0001$). The annual incidences over the 5-year periods from 1974 to 2004 were 1.73, 3.23, 3.05, 2.90, 2.70, and 1.41 per 100,000, respectively. The incidence in 1974–1980 was significantly lower than those in 1981–1985, 1986–1990, and 1991–1995 ($P = 0.0038$, 0.0091, and 0.0226, respectively) and tended to be lower than that in 1996–2000 ($P = 0.0672$). The incidence in 2001–2004 was also significantly lower than those in 1981–1985, 1986–1990, and 1991–1995 ($P = 0.0056$, 0.0120, and 0.0194, respectively) and tended to be lower than that in 1996–2000, as well ($P = 0.0557$). The annual incidences of junior high school children from 1974 to 2004 were 5.25, 7.70, 6.95, 7.16, 5.28, and 3.66 per 100,000, respectively. The incidence of junior high school children in 2001–2004 was significantly lower than that in 1981–1985 ($P = 0.0315$) and tended to be lower than that in 1991–1995 ($P = 0.0622$). For the same periods, there was no significant change in the incidence of primary school children. Therefore, the overall trend toward decrease in the incidence of childhood type 2 diabetes in 2000–2004 was most strongly associated with the decrease in that among junior high school children.

After the 1970s, the tendency toward childhood obesity rapidly increased in the 8- to 14-year age-group in Japan, contributing to the increase in childhood type 2 diabetes (2). However, this trend has recently seemed to be weakened. The Ministry of Education, Culture, Sports, Science and Technology of Japan reported a recent trend toward a decrease in the prevalence of obesity among junior high school children (3). Recently, significant concern regarding childhood obesity and associated metabolic disorders has spread in the Japanese population, especially among children and adolescents residing in cities (3). They are likely to ingest fewer sugar-sweetened beverages and snacks as well as fat-rich foods than in the past. In addition, they tend to limit sedentary activities and participate in various sports (3). These lifestyle changes may contribute to the decrease in the incidence of type 2 diabetes in 2001–2004 in the Tokyo metropolitan area.

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Association Between High-Sensitive Measurement of C-Reactive Protein and Metabolic Syndrome as Defined by International Diabetes Federation, National Cholesterol Education Program, and World Health Organization Criteria in a Population-Based Cohort of 55-Year-Old Finnish Individuals

Recently, the International Diabetes Federation (IDF) consensus group published a new definition of metabolic syndrome for identifying individuals at high risk for cardiovascular disease (CVD) (1). The high-sensitive measurement of C-reactive protein (hs-CRP), a marker of chronic low-grade inflammation, can also be used in the risk assessment of CVD (2). We investigated whether the new IDF (1), National Cholesterol Education Program (NCEP) (3), and World Health Organization (WHO) (without microalbuminuria) (4) definitions differ at the epidemiological level regarding the strength of their association with elevated hs-CRP (>3 mg/l) (2) among a population of 992 subjects (438 men) born in 1945 and living in the City of Oulu, Finland.

The prevalence of metabolic syndrome was 31, 17, and 19% according to the IDF, NCEP, and WHO criteria, respectively, in women. Among men, the corresponding prevalences were 19, 15, and 24%, respectively. Among women, IDF-, NCEP-, and WHO-defined metabolic syndrome were significantly associated with the increased risk (adjusted risk ratio 1.77 [95% CI 1.40–2.23], 2.00 [1.59–2.53], and 2.07 [1.65–2.60], respectively) of having elevated hs-CRP in analysis after adjustment for smoking, alcohol consumption, physical activity, and educational status. Among men, the corresponding risk ratios were 1.10 (0.76–1.58), 1.87 (1.38–2.54), and 2.23 (1.69–2.94).

In sex-specific receiver-operating characteristic curve analysis, in women, the largest area under curve (AUC) was that of BMI (0.7547), being statistically significantly superior to all other components of metabolic syndrome ($P < 0.05$) regarding their association with elevated hs-CRP. The AUC of homeostasis model assessment of insulin resistance (HOMA-IR) (0.6749) was, per se, the second best but did not differ statistically significantly from triglycerides (0.6333), HDL cholesterol (0.6269), or fasting glucose (0.6136). In men, the AUC of BMI (0.6305) was the highest value but did not differ significantly from HOMA-IR (0.6284), fasting glucose (0.6089), triglycerides (0.5902), or HDL cholesterol (0.5825). As in women, the AUC of waist circumference, waist-to-hip ratio, and blood pressure were significantly inferior to that of BMI in men ($P < 0.05$).

In this middle-aged general population, BMI associated most closely with hs-CRP. In addition, HOMA-IR, fasting glucose, and lipid parameters were moderately associated with hs-CRP in both sexes, albeit being inferior to BMI in female subjects. Interestingly, the other measurements of obesity were significantly inferior to BMI.

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REVIEW ARTICLE

Urine Glucose Screening Program at Schools in Japan to Detect Children with Diabetes and Its Outcome-Incidence and Clinical Characteristics of Childhood Type 2 Diabetes in Japan

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ABSTRACT: A large number of children with type 2 diabetes have been detected by a urine glucose screening program conducted at schools in Japan since 1975. The incidence of type 2 diabetes in children has increased over the last three decades, and the incidence is estimated to be approximately 3.0/100,000/y during 1975–2000. The incidence of type 2 diabetes in junior high school children is three to six times higher than that in primary school children. More than 80% of children with type 2 diabetes are obese, and boys are more likely to be obese than girls. It is speculated that the increase in the incidence of childhood type 2 diabetes over the years may be a consequence of the increase in the frequency of obesity in school children. However, this trend of increasing incidence of childhood obesity has recently become weaker, and perhaps as a consequence, the incidence of type 2 diabetes has also decreased after the year 2000 in some cities of Japan. Improved attention to physical activity and eating habits among young people may be responsible at least in part to the decrease in the incidence of type 2 diabetes noted in recent years in big cities of Japan. (***Pediatr Res* 61: 141–145, 2007**)

In the 21st century, type 2 diabetes is increasing in prevalence all over the world, and approximately 150–160 million people worldwide are currently estimated to suffer from the disease. The World Health Organization (WHO) estimated that as many as 200–300 million people worldwide would be suffering from type 2 diabetes by the end of the year 2005 (1). The majority of patients with type 2 diabetes are adults. However, various reports have indicated that the incidence of childhood type 2 diabetes has increased and continues to be on the rise (2,3). Accumulated evidence has demonstrated that the number of children with type 2 diabetes has elevated in recent years and continues increasing in young people in the United States. Currently, approximately one-third of children and adolescents in Ohio and Arkansas, and one-third of Hispanics in California have type 2 diabetes (4). It is noteworthy that some ethnic groups such as Hispanics, African-Americans, and Asians, including Japanese, have been reported to be at a high risk of developing type 2 diabetes in youth as well as during adulthood (2,3).

Several Japanese studies have indicated a high incidence of childhood type 2 diabetes detected by urine glucose screening program conducted at schools in Japan (5–7). Since 1973, a program involving screening of primary and junior high school children for hematuria and proteinuria using a morning urine specimen has been conducted by the Ministry of Education, Science and Culture for an early detection of chronic renal disease (8). Since 1974, the collected urine has also been tested for glucose to detect children with diabetes, and a number of school children were identified as having diabetes with minimal or no symptoms at the early stage of the disease. While the vast majority of children detected by the screening program are eventually diagnosed as having type 2 diabetes, a small number of children have also been diagnosed as having type 1 diabetes by the screening program. They showed neither symptoms of severe hyperglycemia nor those of ketosis at the time of diagnosis. This novel subtype of diabetes has been described as a slowly progressive form of type 1 diabetes (9).

The incidence of type 1 diabetes in Japanese children has been reported to be among the lowest in the world (10) and it has been estimated to be lower than that of childhood type 2 diabetes. On the other hand, the prognosis of juvenile-onset type 2 diabetes is considerably poorer in Japan possibly due to inadequate management. Yokoyama *et al.* (11) reported a higher incidence of severe diabetic complications in cases with type 2 rather than type 1 diabetes among children with early-onset diabetes. Therefore, it is important to detect children with type 2 diabetes and treat them appropriately during the early stage of the disease to prevent the occurrence and progression of the complications.

This article reviews the urine glucose screening program conducted at schools in Japan to detect children with diabetes and its outcome, *i.e.* the incidence and clinical characteristics of childhood type 2 diabetes in Japan.

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Abbreviations: IGT, impaired glucose tolerance; **OGTT,** oral glucose tolerance test