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# Obesity at the Onset of Diabetes in an Ethnically Diverse Population of Children: What Does It Mean for Epidemiologists and Clinicians?

Rebecca B. Lipton, PhD, MPH, RN*‡; Melinda Drum, PhD‡; Deborah Burnet, MD, MSc*; Barry Rich, MD*; Andrew Cooper, BA*; Elizabeth Baumann, MD*; and William Hagopian, MD, PhD§

**ABSTRACT.** *Objective.* **It is often difficult to determine the pathophysiology of childhood diabetes at onset, particularly in overweight children, because obesity has been associated with both type 1 and type 2 diabetes. We compared children at the diagnosis of diabetes in a multiethnic population-based registry to understand the epidemiology of the disease during a time of rapidly changing diagnostic and treatment norms.**

*Methods.* **Incident diabetes was ascertained in Chicagoans who were aged 0 to 17 years from 1985 to 2001. We classified as type 2 those with polycystic ovary syndrome, acanthosis, or a physician's note indicating type 2 or those who reported subsequent use of oral agents ($n$ = 203); 73% of them were also obese. Patients with obesity at onset but no other indicator of possible type 2 ($n$ = 197) were classified as having obesity-related/undetermined type. The remaining 842 cases were classified as type 1. Logistic regression analyses were conducted.**

*Results.* **Fully 32% of cases were classified as non–type 1, including 37% of non-Hispanic blacks, 30% of Latinos, and 14% of non-Hispanic whites. The proportion of obesity-undetermined and type 2 increased over the 17 years. Comparing the 3 patient groups, type 2 cases were more often female, non-Hispanic black, and older and had a first-degree diabetic relative, whereas Latino boys were overrepresented among the obese/undetermined.**

*Conclusion.* **Obesity is prevalent in youths with newly diagnosed diabetes, particularly during recent years. The growth in non–type 1 diabetes in children since 1985 likely reflects both a true increase and greater physician awareness of the possibility that type 2 diabetes may occur in children.** *Pediatrics* **2005;115:e553–e560. URL: www.pediatrics.org/cgi/doi/10.1542/peds.2004-1448;** ***epidemiology, type 1 diabetes, type 2 diabetes, children and adolescents, ethnic minorities, obesity, diagnosis, incidence.***

ABBREVIATIONS. OR, odds ratio; CI, confidence interval.

From the Departments of *Pediatrics and ‡Health Studies, University of Chicago, Chicago, Illinois; and §Pacific Northwest Research Institute, University of Washington, Seattle, Washington.

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Address correspondence to Rebecca B. Lipton, PhD, MPH, RN, Department of Pediatrics, University of Chicago Pritzker School of Medicine, 5841 S Maryland Ave, M/C 1027, Chicago, IL 60637. E-mail: lipton@uchicago.edu



Over the past decade, major changes have taken place in the diagnostic norms for childhood diabetes. Concurrently, the prevalence of childhood overweight, a hypothesized risk factor for type 1 and especially for type 2 diabetes, has increased dramatically across the developed world. Investigators in the United States and elsewhere have observed a marked increase in the diagnosis of type 2 diabetes in youth during the past few years, disproportionately affecting minority young people (Native Americans, Latinos and non-Hispanic blacks).[1,2] However, many children who develop type 2 diabetes are severely ill at onset and indistinguishable on clinical grounds from those with classic type 1 diabetes.[3] Our group used available criteria to tentatively distinguish patients with youth-onset type 2 diabetes in a population-based registry; clinical studies conducted on average 8 years after diagnosis showed that a substantial fraction of those who were classified with type 2 displayed features of type 1 diabetes, ie, absent $\beta$-cell function, autoantibodies, and/or type 1 diabetes–related HLA-DQ alleles.[4] In addition, reports from Europe[5–7] have linked early childhood obesity with type 1 diabetes, suggesting that youth-onset diabetes may often result from an interplay of autoimmunity and type 2 risk factors. Specifically, overnutrition may play a role in stimulating or prolonging autoimmune insulitis.[5,8] The body of knowledge on these relationships in non–European-origin children is extremely limited, despite the fact that these ethnic groups carry an increased risk for type 2 diabetes. It is essential to understand the role of obesity at the onset of diabetes in young people for both clinical and research purposes.

The Chicago Childhood Diabetes Registry includes patients of African and Latino descent, as well as non-Hispanic whites. First, we sought to detect any clear differences at diagnosis between those who were classified as having type 1 and type 2 diabetes, excluding those who were obese alone. Second, we evaluated those who were obese at the time of diagnosis, without other indications of type 2 diabetes, to determine which of the other 2 diagnostic groups they most closely resembled. Because diagnostic norms for childhood diabetes have changed greatly since the first incident cases were ascertained in 1985, an important question is whether there are discernible temporal differences in the frequency of type 1,

type 2, and obesity-related/undetermined type diabetes.

## METHODS

This report presents sociodemographic characteristics and clinical information from medical records at the time of diagnosis, as well as self-reported traits from interviews, in non-Hispanic black and Latino diabetic children who were aged 0 to 17 at disease onset and whose diabetes was diagnosed between 1985 and 2001; non-Hispanic white children were included from 1992.

The Chicago Childhood Diabetes Registry is a city-wide registry of patients who have diabetes and were 0 to 17 years of age at initial diagnosis; the primary source of ascertainment is hospital records, augmented by outpatient sources as described previously in detail.[9,10] Briefly, eligible cases are identified by review of medical records at 37 of the 40 area hospitals that have a pediatrics ward and at least 200 total inpatient beds; patients are included if they were diagnosed from January 1, 1985, and were a resident of Chicago at the time of diagnosis. When diagnosed before January 1, 1992, only children who were classified as non-Hispanic black or Latino and were discharged on insulin treatment were registered. However, it should be noted that before the mid-1990s, virtually every patient who developed diabetes before the age of 18 was discharged from the hospital on insulin. More recently, all young Chicago residents with a diagnosis of diabetes were included, irrespective of ethnic group or initial treatment, although the number of children who were not initially treated with insulin continues to be extremely small. Ethnicity is defined as being listed as non-Hispanic white, non-Hispanic black, or Latino on the medical record and/or having a surname classified as Hispanic by the US Census Bureau.[11] Those with a Hispanic surname but classified as non-Hispanic white or non-Hispanic black on the medical record are considered to be Latino. The data set also includes 14 subjects classified as "other" ethnicity (primarily Asian); these subjects were omitted, although analyses including this subgroup yielded nearly identical results to those reported here.

Camp lists from the Northern Illinois Affiliate of the American Diabetes Association, a survey of unaffiliated neighborhood clinics, medical chart review at 16 clinics maintained by the Chicago Department of Health, and the payment database of the Illinois Department of Public Aid were used as secondary sources of cases. Overall completeness of ascertainment was estimated to be 85% for the years 1985–1999 using the capture-mark-recapture method.[12]

Medical records from the initial diabetes hospitalization were available for 1242 (77.7%) of the cases; these patients form the study group for this report. Those with onset records were not different from the remainder of patients for most relevant variables (gender, ethnicity, family history), although fewer patients classified as having type 1 diabetes had available onset records (76% vs 81% of non–type 1 patients; $P = .021$). Those with onset records were somewhat younger at diagnosis (mean ± SD: 10.7 ± 4.5 vs 11.6 ± 4.3 years of age; $P = .002$), and they were diagnosed, on average, 1 year earlier ($P < .001$).

A subset of patients ($n = 262$) was contacted and interviewed on average 5.7 years after diagnosis. There was no formal randomization procedure to select those who were interviewed, but these patients did not differ from the remaining patients on relevant variables. Fewer patients with obesity but no other indication of possible type 2 diabetes were interviewed, and those who were interviewed were on average 1 year younger at the time of their diagnosis (9.6 ± 4.6 [SD] years) compared with those who were not interviewed (11.0 ± 4.4 years; $P < .001$). In addition, fewer non-Hispanic whites and those with onset of disease after 1999 have been interviewed because they were more recently ascertained. Human Subjects Research committees at the University of Chicago and the other participating institutions city-wide approved the study protocol. Written informed consent was obtained from participants before the telephone interview.

Exposure and outcome measures were abstracted from medical records and derived from patient/family interviews. We distinguished a group of 203 probable type 2 patients from the body of registered cases on the basis of documentation in the medical record of 1 or more of the following: a physician note of "possible type 2," "unusual," or "atypical" diabetes ($n = 166$); a diagnosis of acanthosis nigricans ($n = 40$) or polycystic ovary syndrome ($n = 4$); or initial treatment with oral antidiabetic agents. In addition, those who responded positively to 1 or more specific questions during the interview were considered likely to have type 2. These questions elicited information on cessation of insulin use after the "honeymoon" period (for >2 weeks and at >6 months after initial diagnosis; $n = 24$), as well as on current treatment with any oral antidiabetic agent ($n = 18$). Patients were classified as having obesity-related/undetermined type diabetes when they had a clinical note on the medical record indicating obesity ($n = 133$) or a body mass index (BMI) ≥95th percentile for their gender and age in months ($n = 122$), using current Centers for Disease Control and Prevention growth charts,[13] but no other indicator of possible type 2 diabetes. For brevity, we refer to this classification as "obese/undetermined" type. One child who was aged 8 months and 21 patients whose height was not recorded on the chart exceeded the 95th percentile for age- and gender-specific weight; 11 of these patients had no other indicators of type 2 diabetes. Those who did not meet 1 or more of the criteria above were considered to have type 1 diabetes (Fig 1).

Sources of medical care were classified as tertiary care institutions when they had a specialized pediatric endocrinology clinic and were directly associated with 1 of the local medical schools (Children's Memorial Hospital, Christ Hospital, Cook County Hospital, Evanston Hospital, Loyola University Medical Center, Michael Reese Hospital, Rush-Presbyterian-St. Luke's Medical Center, University of Chicago Children's Hospital-LaRabida, or University of Illinois Hospital). All other hospitals and clinics were considered to be community facilities. The purpose of examining this variable was to discern whether there were differences in physicians' diagnostic practices by where they practiced. Furthermore, an earlier analysis by our group[14] showed significantly lower risk for being rehospitalized after the initial diagnosis for young patients whose diabetes was diagnosed at tertiary care institutions, compared with those whose diabetes was diagnosed in community settings. Rehospitalization after initial diagnosis is generally considered to indicate inadequate routine diabetes management.

### Data Collection and Statistical Methods

Incidence data were abstracted from medical records by research assistants onto paper forms or, more recently, handheld electronic devices (Palm IIIx). Trained interviewers conducted telephone interviews using a standardized protocol. Univariate associations between diabetes categories and patient characteristics were tested using $\chi^2$ and $t$ tests using an unadjusted $\alpha$ of .05 as the significance level; then multiple logistic regression analysis was conducted. Separate multivariable logistic models were fit for type 1 versus type 2, type 1 versus obese, and type 2 versus obese, because we expected different predictors in each model. Variables with $P < .20$ in univariate models were entered as potential covariates in multivariable models, with variable selection based on the likelihood ratio criterion. Gender was included in all models, and all models were adjusted for year of onset and tertiary versus community hospital diagnosis. $\chi^2$ tests for trend were used to identify secular changes in classification patterns. Patients

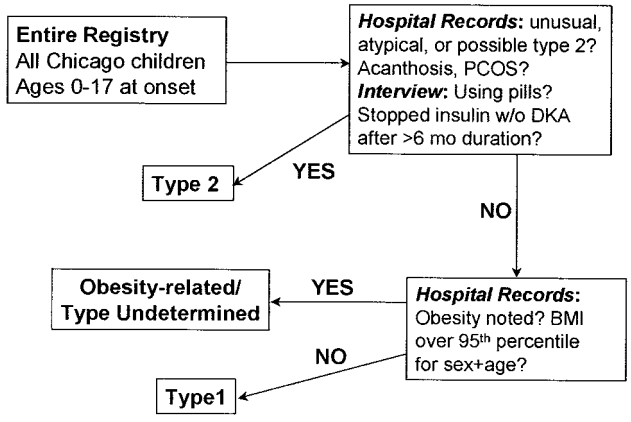


**Fig 1.** Criteria for classifying youths as having type 1, obese/undetermined type, or type 2 diabetes.

**TABLE 1.** Type 1, Type 2, and Obese/Undetermined Type Diabetes in Chicago Youth 0 to 17 Years Old, According to Ethnicity

| | Type 1 | Non–Type 1 Diabetes | | Total |
|---|---|---|---|---|
| | | Obese/ Undetermined | Type 2 | |
| Non-Hispanic black, *n* (%) | 458 (62.6) | 119 (16.3) | 155 (21.2) | 732 |
| Latino, *n* (%) | 250 (70.4) | 65 (18.3) | 40 (11.3) | 355 |
| Non-Hispanic white, *n* (%) | 134 (86.5) | 13 (8.4) | 8 (5.2) | 155 |
| Total, % obese* | 842 (0) | 197 (100) | 203 (73.4) | 1242 (27.9) |

* Obesity is defined as body mass index ≥95th age- and gender-specific percentile or diagnosis on medical record.

whose information regarding onset signs and symptoms was unavailable in the medical records were omitted from the analysis.

## RESULTS

Overall, the majority of cases, 68%, were classified as having type 1 diabetes (Table 1). Of those who were classified as non–type 1, the patients who were obese without other type 2 characteristics made up 16% of non-Hispanic black, 18% of Latino, and 8% of non-Hispanic white cases, whereas 21% of non-Hispanic black, 11% of Latino, and 5% of non-Hispanic white cases were type 2 ($P < .001$). Of the 203 patients who were classified as having type 2 diabetes, 149 (73%) were also obese.

For comparability, time trends were evaluated for non-Hispanic blacks and Latinos only, ie, those with the full 17 years of data, 1985–2001 (Fig 2). The distribution of categories changed over time (Fig 2A), with fewer children receiving a diagnosis of type 1 and more with type 2 diabetes in recent years ($P < .001$). The proportion of obese/undetermined patients also increased over time ($P = .022$) but at a slower rate than type 2. The proportion of all children who had diabetes and were obese at the time of diagnosis, including those identified as type 2 (Fig 2B), increased dramatically over the study years ($P < .001$). Finally, the absolute number of cases increased over time, from an average of 52 cases per year in the first 5 years of the study, 1985–1989, to an average of 64 per year in 1995–1999, again considering only non-Hispanic blacks and Latinos (Fig 2A).

### Comparing Type 1 and Type 2 Diabetes: Univariate Associations

There were more non-Hispanic blacks and girls in the type 2 group (Table 2), and their diabetes was diagnosed, on average, more recently than those with type 1. The average age at diagnosis was ~4 years younger (9.7; SD: 4.6) for type 1 patients, compared with those with type 2, whose average age was 13.6 years (SD: 2.9) at diagnosis.

The medical records of approximately one fourth of the type 1 patients and more than half of those with type 2 diabetes indicated a first-degree relative with diabetes. The type 2 patients were more likely to have asthma (15.3% vs 10.5% in type 1 patients), hypertension (8.4% vs 1.4%), hyperlipidemia (3.0% vs 0.8%), or a learning disability (5.4% vs 2.5%), listed as a comorbidity on the medical record, but no more likely to have a psychiatric diagnosis or sickle cell trait. More of those with type 2 diabetes used Medicaid or had no health insurance at all, but they were no less likely to have received a diagnosis at a tertiary care hospital (Table 2).

The severity of onset was greater among the type 1 patients, although substantial morbidity was found in the type 2 patients as well, on the basis of their signs and symptoms as recorded in the hospital charts (Table 2). Forty percent of type 2 and 62.4% of type 1 patients had a diagnosis of diabetic ketoacidosis; the mean initial pH values were correspondingly higher and the mean glucose values were lower among the type 2 patients than among those with type 1. The type 1 patients were more likely to have had weight loss and polyuria and marginally more likely to have had polydipsia documented on the onset record but no more likely than the type 2 patients to have had polyphagia.

### Comparing Obese/Undetermined Type Diabetes With Type 1 and Type 2: Univariate Associations

We found that the obese/undetermined patients were intermediate between the type 1 and type 2 patients in many of their demographic features and onset signs and symptoms (Table 3). Fully one third of the obese/undetermined group were of Latino ethnicity (Fig 3, Table 3). The prevalence of a first-degree relative with diabetes was statistically similar for the obesity-related and the type 2 groups (47% and 55%, respectively). The obese/undetermined group resembled those with type 1 diabetes with respect to their mean initial pH values, whereas their mean initial glucose values were not statistically different from the type 2 patients. On the medical records, documented weight loss, polyuria, polydipsia, and polyphagia were not statistically different when comparing the obese/undetermined cases with the other 2 groups. In general, severe onset signs and symptoms were present in the majority of patients, irrespective of category. Significantly fewer obese/undetermined type children received a diagnosis at a tertiary care hospital, compared with both the type 1 ($P = .017$) and type 2 ($P = .024$) patient groups (Table 3). This suggests differences in diagnostic practices between community-based physicians and those who are affiliated with academic centers.

### Multivariate Models I: Comparing Type 1 and Type 2

Multiple logistic regression models were constructed, with the type 1 patients serving as the ref-

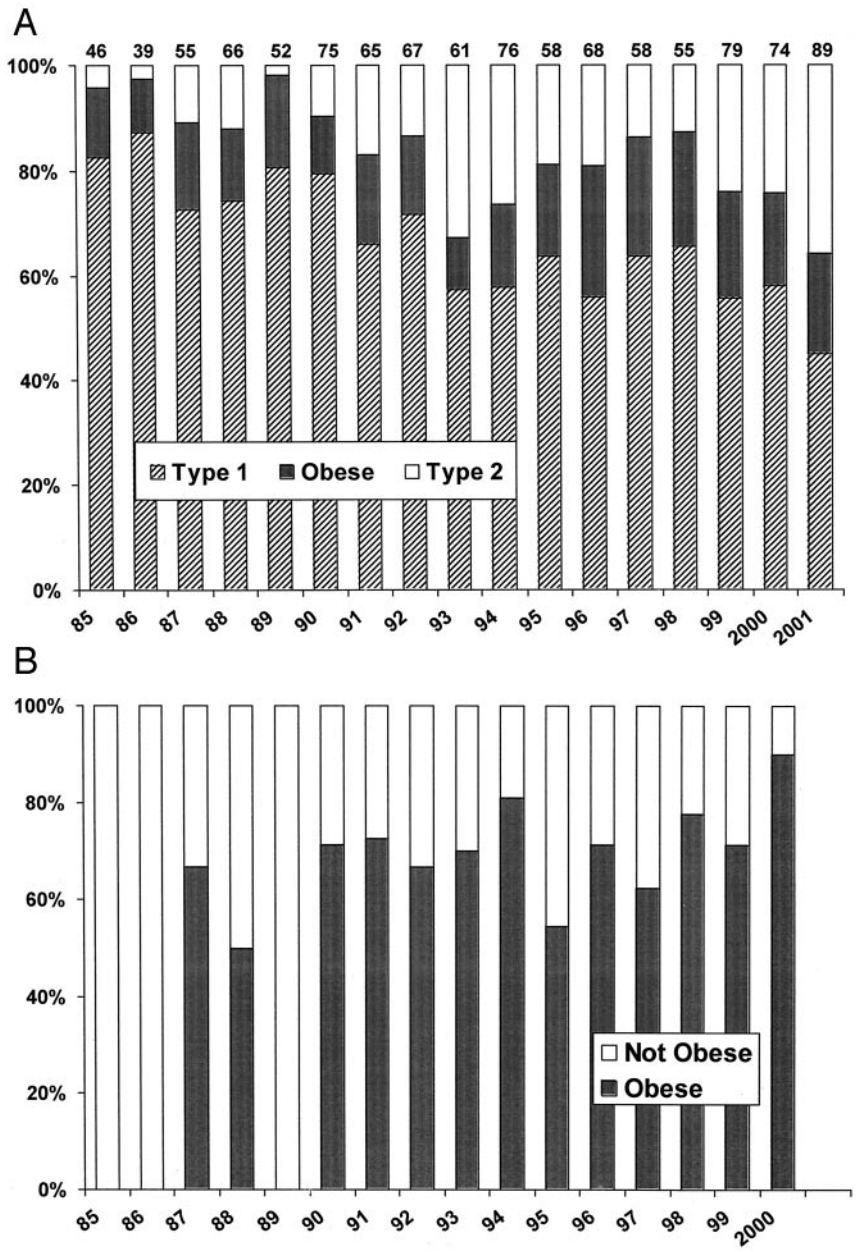


**Fig 2.** A, Distribution of type 1, obese/undetermined type, and type 2 diabetes by year, non-Hispanic black and Latino children aged 0 to 17. B, Proportion of type 2 diabetes patients with coexisting obesity (defined as having a chart notation of obesity or exceeding the age- and gender-specific 95th percentile for body mass index) by year, non-Hispanic black and Latino children aged 0 to 17.

erence category and the obese/undetermined group excluded. Significant demographic predictors of type 2 phenotype were female gender (65% increased odds), age at onset (28% increased odds per year), and having a first-degree relative with diabetes noted on the medical records (odds ratio [OR]: 2.6; Table 4). Both non-Hispanic whites and Latinos were less likely to be in the type 2 group than were non-Hispanic blacks (OR: 0.17 and 0.47, respectively). When clinical findings and symptoms were added to the model, the demographic variables were retained, although female gender was only marginally significant ($P = .077$). In addition, the presence of hypertension was associated with type 2 diabetes. The presence of diabetic ketoacidosis, 2 or more of 3 classic symptoms (weight loss, polyuria, and polydipsia), and a higher initial glucose value were associated with having type 1 diabetes (Table 4). Both models were adjusted for the year of diagnosis and the type of hospital where the patient was first seen (community or tertiary care facility). The odds of type 2 increased significantly from one year to the next, by 15% (95% confidence interval [CI]: 11% to 20%) in the demographics-only model and by 7% per year (95% CI: 1% to 13%) in the full model. Patients who received a diagnosis in a tertiary care facility were more likely to have type 2 than type 1 (OR: 1.7; 95% CI: 1.1 to 2.7 in the demographics-only model; OR: 2.0; 95% CI: 1.1 to 3.5 in the full model). The Hosmer-Lemeshow test demonstrated acceptable goodness of fit for the models.

### Multivariate Models II: Comparing Type 1 and Type 2 With Obese/Undetermined Type Diabetes

We constructed separate mutivariate models comparing the type 1 and type 2 patients with the obese/undetermined group as the reference category, again controlling for the year of diagnosis and the type of

**TABLE 2.** Demographic and Clinical Features of Types 1 and 2 Diabetes in Youth 0 to 17 Years Old

| | Type 1 | Type 2 | *P* Value |
|---|---|---|---|
| *N* (male/female) | 842 (423/419) | 203 (82/121) | .012 |
| Age at diagnosis, y, mean (SD) | 9.7 (4.6) | 13.6 (2.9) | <.001 |
| Ethnicity, *n* (%) | | | |
| Non-Hispanic black | 458 (54.4) | 155 (76.4) | <.001 |
| Latino | 250 (29.7) | 40 (19.7) | |
| Non-Hispanic white | 134 (15.9) | 8 (3.9) | |
| Year of onset, mean (SD) | 1993.6 (4.8) | 1995.7 (4.3) | <.001 |
| Parent and/or sibling with diabetes, % | 25.1 | 55.0 | <.001 |
| Chronic conditions recorded on the medical record, % | | | |
| Asthma | 10.5 | 15.3 | .052 |
| Hypertension | 1.4 | 8.4 | <.001 |
| Hyperlipidemia | 0.8 | 3.0 | .014 |
| Sickle cell trait | 2.3 | 1.0 | .247 |
| Learning disability | 2.5 | 5.4 | .030 |
| Any psychiatric diagnosis | 3.7 | 4.9 | .412 |
| Medicaid or no health insurance | 47.7 | 56.7 | .031 |
| Diagnosed at tertiary care hospital | 72.1 | 74.0 | .597 |
| Onset of signs and symptoms* | | | |
| Diabetic ketoacidosis, % | 62.4 | 40.1 | <.001 |
| Weight loss, % | 71.9 | 56.0 | <.001 |
| Polyuria, % | 92.9 | 88.3 | .046 |
| Polydipsia, % | 91.1 | 86.5 | .070 |
| Polyphagia, % | 28.2 | 30.7 | .542 |
| Glucose, mmol/L, mean (SD) | 32.5 (16.1) | 26.7 (17.8) | <.001 |
| Arterial pH, mean (SD) | 7.27 (0.12) | 7.31 (0.11) | <.001 |

* Obese/undetermined type was excluded ($n = 197$).

**TABLE 3.** Obese/Undetermined Type Diabetes Compared with Type 1 and 2 Diabetes in Youth

| | Type 1 | Obese | Type 2 | *P* Value | |
|---|---|---|---|---|---|
| | | | | Obese vs Type 1 | Obese vs Type 2 |
| *N* (male/female) | 842 (423/419) | 197 (90/107) | 203 (82/121) | .250 | .285 |
| Age at diagnosis, y, mean (SD) | 9.7 (4.6) | 12.5 (3.5) | 13.6 (2.9) | <.001 | .002 |
| Ethnicity, *n* (%) | | | | | |
| Non-Hispanic black | 458 (54.4) | 119 (60.4) | 155 (76.4) | .003 | .003 |
| Latino | 250 (26.7) | 65 (33.0) | 40 (19.7) | | |
| Non-Hispanic white | 134 (15.9) | 13 (6.6) | 8 (3.9) | | |
| Year of onset, mean (SD) | 1993.6 (4.8) | 1994.6 (4.7) | 1995.7 (4.3) | .009 | .014 |
| Parent and/or sibling with diabetes, % | 25.1 | 47.0 | 55.0 | <.001 | .121 |
| Chronic conditions recorded on the medical record, % | | | | | |
| Asthma | 10.5 | 13.7 | 15.3 | .190 | .657 |
| Hypertension | 1.4 | 7.1 | 8.4 | <.001 | .635 |
| Hyperlipidemia | 0.8 | 1.0 | 3.0 | .802 | .166 |
| Sickle cell trait | 2.3 | 2.0 | 1.0 | .846 | .390 |
| Learning disability | 2.5 | 1.5 | 5.4 | .414 | .034 |
| Any psychiatric diagnosis | 3.7 | 8.1 | 4.9 | .007 | .195 |
| Medicaid or no health insurance, % | 47.7 | 54.4 | 56.7 | .114 | .675 |
| Diagnosed at tertiary care hospital, % | 72.1 | 63.4 | 74.0 | .017 | .024 |
| Onset of signs and symptoms* | | | | | |
| Diabetic ketoacidosis, % | 62.4 | 52.9 | 40.1 | .031 | .025 |
| Weight loss, % | 71.9 | 65.0 | 56.0 | .103 | .117 |
| Polyuria, % | 92.9 | 91.7 | 88.3 | .570 | .303 |
| Polydipsia, % | 91.1 | 89.8 | 86.5 | .604 | .342 |
| Polyphagia, % | 28.2 | 28.4 | 30.7 | .957 | .665 |
| Glucose, mmol/L, mean (SD) | 32.5 (16.1) | 29.2 (16.6) | 26.7 (17.8) | .021 | .181 |
| Arterial pH, mean (SD) | 7.27 (0.12) | 7.27 (0.12) | 7.31 (0.11) | .99 | .003 |

* Obese/undetermined type excluded ($n = 197$).

health care facility where the patient first received a diagnosis. These models also fit the data reasonably well when tested.

Comparing the type 1 patients with the obese/undetermined group, younger age at onset and non-Hispanic white ethnicity were significantly predictive of type 1 (Table 5), whereas having a first-degree relative with diabetes and the presence of hypertension were more likely in the obese/undetermined group. The odds for type 1 compared with obese/undetermined type decreased significantly from one year to the next, by 8% (95% CI: 4% to 11%); there was no difference in having received a diagnosis in a tertiary care versus community hospital (OR: 1.1; 95% CI: 0.8 to 1.6).

When compared with the obese/undetermined

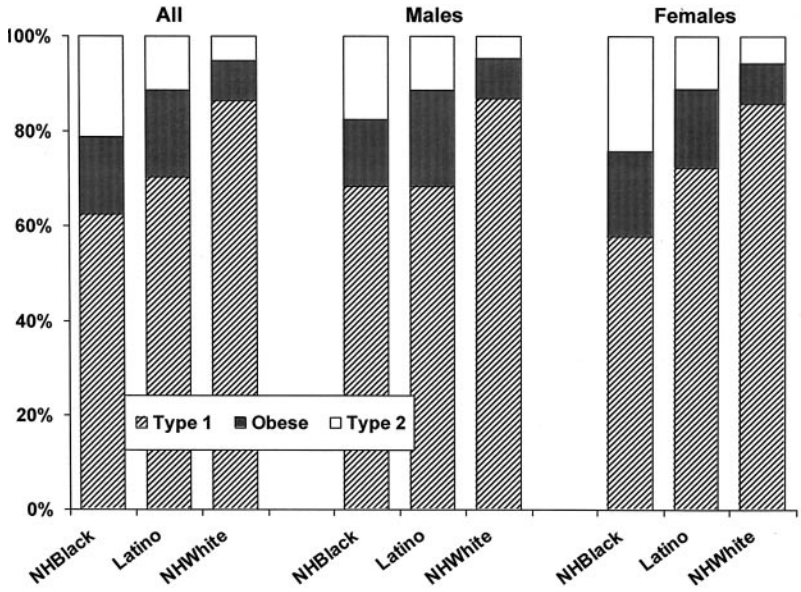


**Fig 3.** Type 1, obesity-related, and type 2 diabetes in youth by ethnicity (excludes 14 patients of "other" ethnic groups, all of whom were classified as type 1) and gender.

**TABLE 4.** Multivariate Predictors of Type 2 Versus Type 1 Diabetes in Youths

| Variable | Contrast | OR | 95% CI |
|---|---|---|---|
| Demographic variables only ($N$ = 961)* | | | |
| Female gender | vs male gender | 1.65 | 1.13 to 2.42 |
| Age at onset | Per year | 1.28 | 1.21 to 1.35 |
| Latino ethnicity | vs non-Hispanic black | 0.47 | 0.29 to 0.74 |
| Non-Hispanic white ethnicity | vs non-Hispanic black | 0.17 | 0.08 to 0.40 |
| Parent and/or sibling with diabetes | vs neither | 2.82 | 1.93 to 4.12 |
| Demographic variables plus signs and symptoms ($N$ = 660)* | | | |
| Female gender | vs male gender | 1.57 | 0.96 to 2.55 |
| Age at onset | Per year | 1.28 | 1.20 to 1.38 |
| Latino ethnicity | vs non-Hispanic black | 0.38 | 0.21 to 0.70 |
| Non-Hispanic white ethnicity | vs non-Hispanic black | 0.15 | 0.05 to 0.41 |
| Parent and/or sibling with diabetes | vs neither | 2.61 | 1.60 to 4.28 |
| Hypertension | Present vs absent | 6.46 | 2.04 to 20.5 |
| Diabetic ketoacidosis | Present vs absent | 0.55 | 0.33 to 0.92 |
| Weight loss, polyuria, polydipsia | At least 2 vs none or 1 | 0.39 | 0.17 to 0.90 |
| Initial glucose value | Per 10 mmol/L | 0.71 | 0.58 to 0.87 |

* Obese group was excluded. The data were adjusted for year of diagnosis and type of hospital (community versus tertiary care facility). Additional candidate variables were asthma, hyperlipidemia, learning disability, and arterial pH.

patients, the type 2 patients were older at onset, less likely to be of Latino ethnicity, and less likely to have had diabetic ketoacidosis (Table 5). The odds for type 2 compared with obese/undetermined type did not change significantly over time (annual change: 3%; 95% CI: −3% to 9%). The type 2 patients were significantly more likely to have received a diagnosis in a tertiary care versus community hospital (OR: 1.9; 95% CI: 1.1 to 3.3).

## DISCUSSION

We present data on a large group of patients ascertained from the entire community so that they represent those who were seen at tertiary care facilities and those who were treated by community-based primary care physicians. These young people received diagnoses over a 17-year period of marked change both in the prevalence of overweight among children[1,2] and in clinical diagnostic and treatment norms. Specifically, there was an increase in the recognition that type 2 diabetes can occur among young people: physicians were much more likely to have considered a diagnosis of type 2 diabetes in children after the mid-1990s, when the first reports of this phenomenon appeared in the literature.[1,15,16] This report includes the largest number of minority children in any US study and the largest number of African-origin children in the world. It also covers a longer period of time than most population-based studies. The value of this study is, first, that it includes enough cases to allow subgroup analysis and also that the clinical features associated with type 2 and obese/undetermined type diabetes in previous small clinical series' were examined in a large, unselected cohort representing children of diverse ethnic backgrounds. Other US studies of type 2 diabetes in youths are clinic series rather than population-based and therefore subject to even more bias from selective referrals, time trends in diagnostic practice, etc.

The population at risk, Chicagoans aged 0 to 17 years, has remained relatively constant over the

**TABLE 5.** Multivariate Predictors of Type 1 and 2 Versus Obese/Undetermined Type Diabetes in Youths

| Variable | Contrast | OR | 95% CI |
|---|---|---|---|
| Type 1 vs obesity-related diabetes ($N$ = 954)* | | | |
| Female gender | vs male gender | 0.78 | 0.55 to 1.11 |
| Age at onset | Per year | 0.86 | 0.82 to 0.90 |
| Latino ethnicity | vs non-Hispanic black | 0.96 | 0.65 to 1.42 |
| Non-Hispanic white ethnicity | vs non-Hispanic black | 2.53 | 1.27 to 5.03 |
| Parent and/or sibling with diabetes | vs neither | 0.46 | 0.32 to 0.66 |
| Hypertension | Present vs absent | 0.21 | 0.08 to 0.54 |
| Type 2 vs obesity-related diabetes ($N$ = 300)† | | | |
| Female gender | vs male gender | 1.38 | 0.85 to 2.25 |
| Age at onset | Per year | 1.09 | 1.01 to 1.18 |
| Latino ethnicity | vs non-Hispanic black | 0.51 | 0.29 to 0.90 |
| Non-Hispanic white ethnicity | vs non-Hispanic black | 0.41 | 0.13 to 1.28 |
| Diabetic ketoacidosis | Present vs absent | 0.57 | 0.35 to 0.91 |

* Type 2 group was excluded. The data were adjusted for year of diagnosis and community versus tertiary care facility. Additional candidate variables were gender, asthma, any psychiatric diagnosis, initial glucose value, diabetic ketoacidosis, and weight loss.
† Type 1 was group excluded. The data were adjusted for year of diagnosis, community versus tertiary care facility. Additional candidate variables were gender, first-degree relative with diabetes, hyperlipidemia, learning disability, any psychiatric diagnosis, weight loss, initial glucose value, and arterial PH.

study years.[17] Nonetheless, the absolute number of non-Hispanic black and Latino children who have received a diagnosis of diabetes has increased over time (Fig 2A), as has the proportion of children who are overweight or obese at the onset of the disease.[10] In Chicago, the increase in the proportion of youths who have received a diagnosis of type 2 diabetes directly mirrors a decline in the proportion of those with type 1 (Fig 2A). The proportion in the obese/undetermined category increased as well over time but more gradually. This suggests that not all of the change is attributable to heightened awareness of type 2 diabetes in youths: at least some young people may have a distinct phenotype combining features of both autoimmunity and insulin resistance. Our findings concur with those of the Allegheny County Registry, documenting a rise in obesity at diagnosis among insulin-treated young people over a 20-year period that includes most of the years of this report[18] and suggesting a heterogeneous etiology.[19]

Our study includes patient groups whose diabetes etiology is uncertain, such as patients who were assigned as type 2 because of clinician doubts (eg, "atypical," "unusual") but with 1 or more factors usually associated with type 1 (age <18 at diagnosis, abrupt onset of severe symptoms). Obesity is not known to protect from autoimmunity, and type 1 diabetes incidence is slowly rising across the world.[20,21] Therefore, the decline in type 1 diagnosis observed in Chicago may be an artifact of clinicians' assigning uncertain status to any patient with signs of insulin resistance. Although our study does not include every possible clinical correlate of diabetes etiologic type (eg, ultimate insulin dose required in U/kg per day, probable type of diabetes in family members with diabetes), it is likely that these alone would not provide sufficient information to significantly improve the classification. We therefore have initiated clinical studies to characterize more definitively the groups of young patients in Chicago using highly sensitive assays for multiple type 1 diabetes autoantibodies, genetic markers, and measures of endogenous insulin production.

We used the data available from medical records in a population-based epidemiologic study, supplemented by self-reported information, to categorize the diabetic phenotype of these young people. There were more similarities than differences between those with typical type 1, obese/undetermined type, and early-onset type 2 diabetes, confirming the many clinical reports that it is not easy to distinguish the diabetic phenotype in children at the time of diagnosis.[15,16,19,20] The obese/undetermined group was more likely to be treated in a community facility or by a community practitioner than either those with type 1 or type 2 diabetes, highlighting variations in diagnostic norms between community- and academically based practitioners.

There are several limitations to the current study. First, patients who were not hospitalized or those who were not treated with insulin (before 1992) would have been missed; although virtually all pediatric patients in that era were discharged from the hospital on insulin, those who were not would have been children with less severe onset of symptoms. The registry study did not include non-Hispanic white and children of other ethnic backgrounds until 1992. Ascertainment for the most recent years, since 2000, is incomplete. Another difficulty is that limited and inconsistent data were available, a result of using medical records from 37 different institutions. For this reason, we considered it important to control for both year of diagnosis and the type of hospital setting in which the diagnosis was made. Because the assignment to diagnostic category was based in part on subsequent treatment as reported by patients, those who were not interviewed are less likely to be included in the type 2 group. Additional biases are possible, because the analysis was restricted to those with onset records, who were somewhat younger at diagnosis and, on average, received a diagnosis 1 year earlier in time, thus rendering them less likely to

have had type 2 diabetes. It is reassuring to note that temporal trends in diagnosis that were similar to these were observed among patients who attended the 3 university-based diabetes centers in Florida.[22] Finally, although this is the largest study of its kind in the United States, diabetes in youths is a relatively infrequent outcome, so the actual numbers of cases is small. Thus, the possibility of type II error remains, particularly for the subgroup analyses.

The role of obesity in the etiology of childhood diabetes is still unclear. For epidemiologists, this indicates the need to collect as much onset data as possible, in a consistent manner, to phenotype cases correctly. Furthermore, clinicians must recognize that a substantial fraction of young patients may have features of both type 1 and type 2 diabetes at onset and that the optimal treatment for these individuals will change over time. We have initiated clinical studies to characterize more definitively the range of youth-onset diabetes in Chicago, measuring autoantibodies, genetic markers, and endogenous insulin production; we anticipate that the current report will stimulate descriptive epidemiologic and clinical studies of childhood diabetes elsewhere. Diabetes in youth creates a substantial social burden on both the family and the community, which is likely worsened in underserved populations. Increased understanding of the etiology and epidemiology of diabetes in youth can lead to improved quality of care.

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# Obesity at the Onset of Diabetes in an Ethnically Diverse Population of Children: What Does It Mean for Epidemiologists and Clinicians?

Rebecca B. Lipton, Melinda Drum, Deborah Burnet, Barry Rich, Andrew Cooper, Elizabeth Baumann and William Hagopian

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