Original Paper

US Trends in Glycemic Control, Treatment, and Comorbidity Burden in Patients With Diabetes

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This study explored trends over time in diabetes prevalence, glycemic control, and antidiabetic therapy choices among adults (18–64 years) and older adults (≥65 years). Factors that predict diabetes outcomes were explored. The study was cross-sectional, with data from the 1999 to 2004 National Health and Nutrition Examination Survey. The study group consisted of 1211 persons with self-reported diabetes. Other information obtained from the study included self-reported medication for diabetes, hypertension, stroke, heart failure, and health status. The survey also provided examination or laboratory tests of obesity, nephropathy, and glycosylated hemoglobin level. Descriptive and logistic regression analyses were used in the study. The study showed that the proportion of diabetics with good glycemic control increased during the period from 1999 to 2004. However, nearly half of the adults and one third of older adults with diabetes did not reach glycemic control in 2003–2004. Overall, 59% of adults and 46% of older adults were obese. There was a high prevalence of hypertension, heart failure, stroke, and nephropathy among patients with diabetes, especially in older adults. The results indicate a high percentage of poor glycemic control among persons with diabetes. There were also a substantial number of comorbid conditions associated with diabetes. J Clin Hypertens (Greenwich). *2010;12:826–832.* ©*2010 Wiley Periodicals, Inc.*

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Manuscript received December 8, 2009; revised May 21, 2010; accepted May 25, 2010

doi: 10.1111/j.1751-7176.2010.00365.x

Diabetes is a chronic disorder that is expected to become one of the greatest health care burdens for the US population in coming decades. Previous analysis of National Health and Nutrition Examination Survey (NHANES) data show that the prevalence of diagnosed diabetes increased substantially from 5.1% in 1988–1994 to 6.5% in 1999–2002.[1] According to the Centers for Disease Control and Prevention's (CDC's) estimates, in 2007, 23.5 million Americans (10.7%) 20 years and older had diabetes, including 12.2 million persons (23.1%) 60 years and older.[2] The prevalence of diagnosed diabetes is disproportionately increasing among older adults[3] and obese persons.[4] Diabetes is often accompanied by serious comorbidities, such as cardiovascular disease, stroke, hypertension, and renal failure.[5,6] Complications of diabetes include vision degeneration, peripheral neuropathy, and infection.[7,8]

According to the American Diabetes Association (ADA), the total medical cost of diabetes in 2007 was $116 billion, including $27 billion for care

directly related to diabetes, $58 billion for diabetes-related complications, and $31 billion for excess general medical costs.[9] Moreover, diabetes and its associated complications have a substantial impact on life expectancy and quality of life. For example, men diagnosed with diabetes at age 40 will lose 11.6 life-years and 18.6 quality-adjusted life-years (QALYs); women will lose 14.3 life-years and 22.0 QALYs.[10] Diabetic persons who have comorbidities may have less QALYs than those without. Therefore, diabetes is a big burden for the society, and patients with diabetes can seriously affect their life expectancy and quality.

An important intermediate diabetes care outcome is glycemic control, measured by glycosylated hemoglobin (HbA_{1c}) level. The UK Prospective Diabetes Study (UKPDS) demonstrated that each percentage-point reduction in HbA_{1c} is associated with a 35% reduction in the risk of developing complications in persons with type 2 diabetes.[11] Despite many efforts aimed at managing diabetes, a high rate of poor glycemic control in the US population has been documented. In adults 20 years and older with diagnosed diabetes in the 1999–2000 NHANES, 63.0% did not achieve the control target HbA_{1c} <7.0%.[12] Older adults with middle-age–onset diabetes have worse glycemic control than diabetic adults (HbA_{1c} >7.0%, 59.9% vs 55.3%, respectively).[13] Although the age-adjusted overall proportion of diabetics with adequate glycemic control had increased from 35.8% in 1999–2000 to 57.1% in 2003–2004,[14] diabetes outcomes remain suboptimal.

According to the ADA and the European Association for the Study of Diabetes (EASD), oral antidiabetic drugs (OADs) should be used in combination with lifestyle changes, such as diet modification and exercise, starting at the time of diagnosis.[15] Additional therapy agents, such as insulin, should be used to achieve and maintain glycemic control targets. A recent investigation demonstrated that the proportion of diabetics using antidiabetic therapies (ie, OADs, insulin, or both) was approximately 80% in the 1999–2004 period,[14] suggesting that the remaining 20% may rely on lifestyle changes alone to manage their condition. There is insufficient current evidence about trends in antidiabetic treatment and resulting glycemic control, especially in older adults. It also remains unclear how increasing comorbidity impacts antidiabetic therapies and glycemic control.

Our study extended prior work by examining trends over time in diabetes prevalence, glycemic control, and antidiabetic therapy choices among adults (18–64 years of age) and older adults (65 years and older). We further explored factors that predict glycemic control in patients with diabetes.

METHODS

We used the 1999–2000, 2001–2002, and 2003–2004 NHANES datasets to explore trends in diabetes prevalence and in the utilization of antidiabetic medications in US adults and older adults. The NHANES surveys use a multistage cluster sample design to provide nationally representative estimates on the health and nutritional status of the US civilian, noninstitutionalized population.

The study cohort was comprised of individuals with self-reported diabetes. The identification of persons with diabetes was based on a positive response to the question, "Other than during pregnancy, have you ever been told by a doctor or health professional that you have diabetes or sugar diabetes?" Based on affirmative responses to the question, a total of 1545 individuals were identified as having diabetes. The HbA_{1c} value was obtained from NHANES laboratory tests. Targets for glycemic control were defined as HbA_{1c} <7.0% and <6.5%, as proposed by the ADA[16] and the EASD,[17] respectively. We aggregated HbA_{1c} measures to 4 levels: <7, 7≤ HbA1c<8, 8≤HbA1c<9, and ≥9.

Current use of insulin and OADs were identified based on respondent self-report obtained from 2 questions: "Are you now taking insulin?" and "Are you now taking diabetic pills to lower your blood sugar?" Patients with diabetes who were identified as being "on diet alone" did not take insulin or diabetic pills.[18]

Covariates included comorbidities, specifically hypertension, stroke, heart failure, obesity, and nephropathy. The identification of diabetes with hypertension, stroke, or heart failure was based on individuals who responded "yes" to the following questions: "Have you ever been told by a doctor or other health professional that you had hypertension, also called high blood pressure?", "Has a doctor or other health professional ever told you that you had a stroke?", or "Has a doctor or other health professional ever told you that you had a heart attack (also called myocardial infarction)?" Obesity was defined as a body mass index (BMI) ≥30 kg/m^2. Nephropathy was defined as the presence of microalbuminuria (albumin/creatinine 30–299 μg/mg), macroalbuminuria (albumin/creatinine ≥300 μg/mg), and/or a positive response to the question "Has a doctor or other health professional ever told you that you had weak or failing kidneys?"

Table 1. Characteristics of Patients With Diabetes Overall and by Age

	Patients With Diabetes (N=1211), No. (%)	Adults (18–64 Y) (n=622), No. (%)	Older Adults (≥65 Y) (n=589), No. (%)	*P* Value
Sex				
Men	603 (49.6)	310 (52.5)	293 (44.5)	.0116
Ethnicity				
Non-Hispanic whites	475 (64.7)	192 (58.2)	283 (75.7)	<.0001
Non-Hispanic blacks	277 (14.8)	164 (16.9)	113 (11.2)	
Other	459 (20.5)	266 (24.9)	193 (13.2)	
Mean age (standard error),y	58.4 (0.5)	50.1 (0.4)	72.6 (0.3)	
Hypertension				
Yes	779 (61.6)	356 (53.8)	423 (75.0)	<.0001
Heart Failure				
Yes	145 (11.3)	46 (6.8)	99 (18.8)	<.0001
Stroke				
Yes	96 (7.1)	29 (4.1)	67 (12.1)	<.0001
Nephropathy				
Yes	438 (31.6)	199 (28.5)	239 (36.7)	<.008
Obesity				
Yes	589 (54.1)	353 (59.1)	236 (46.1)	<.0013
Health insurance				
Yes	1063 (88.9)	488 (82.7)	575 (99.5)	<.0001
Year survey				
1999–2000	363 (27.2)	184 (27.0)	179 (27.4)	.0748
2001–2002	392 (33.0)	229 (35.6)	163 (28.7)	
2003–2004	456 (39.8)	209 (37.4)	247 (43.9)	

The status of health insurance for individuals with diabetes was assessed by the question, "Are you covered by health insurance or some other kind of health care plan?" Demographic factors included age, sex, race, and dummy time serials (1999–2000, 2001–2002, and 2003–2004). Persons were categorized into age subgroups based on per 10-year increment.

We excluded 334 patients missing information on any of the variables. A total of 1211 participants were included in the study. Individuals with diabetes were classified into 2 groups: adults in the age group of 18 to 64 years and older adults in the age group of 65 years and older. Baseline characteristics of patients between two age groups were compared. Chi-square analysis was used to compare categoric variables between the two groups, and a *t* test was applicable to assess the difference of continuous variables between the two groups. Descriptive analysis assessed trends in diabetes prevalence, treatment patterns, glycemic control, and HbA_{1c} levels over time. Descriptive analyses also evaluated the trends in HbA_{1c} by age, sex, treatment patterns, and comorbidity strata. Logistic regression analysis was used to assess factors affecting glycemic control (HbA_{1c} <7.0%) among individuals with diabetes, adjusting for potential confounders including baseline demographics, geographic factors, and comorbidities.

All statistical analyses were conducted using SAS for Windows software 9.1.3 (SAS Institute, Cary, NC). All analyses were run with sampling weights provided by the NHANES surveys, allowing population-based effect estimates.

RESULTS

Table I describes characteristics of individuals with diabetes overall and by age. The majority of diabetics in this analysis were non-Hispanic whites (64.7%) and approximately half were men (49.6%). The mean age was 58 years. The proportion of each comorbidity (including hypertension, heart failure, stroke, nephropathy, and obesity) among older adults were 75%, 18.8%, 12.1%, 36.7%, and 46.1%, respectively. Each proportion in older adults was higher than that in adults. The proportion of diabetics covered by insurance was 99.5% in older adults and 82.7% in adults. The 334 patients excluded from the study had similar distribution on sex, hypertension, heart failure, obesity, and health insurance status as those in the study. However, these patients were older, and the proportion of non-Hispanic blacks was higher. The proportion of

Table II. Prevalence of Diabetes, Glycemic Control, Diet, and Pharmacologic Treatment Among US Patients With Diabetes Over Time

Time Interval		1999–2000 No. (%)	2001–2002 No. (%)	2003–2004 No. (%)	*P* Value
Persons with diabetes among adults (95% CI)		3.9 (3.1–4.6)	4.9 (3.9–5.8)	5.2 (4.2–6.2)	.0826
Adults with diabetes	No.	184	229	209	
	HbA_{1c} <7.0%	55 (34)	99 (46.1)	90 (50.2)	.2441
	HbA_{1c} <6.5%	38 (24)	76 (35.6)	67 (34.6)	.4710
	Mean HbA_{1c} (SE)	8.2% (0.3)	7.7% (0.2)	7.5% (0.2)	.2016
	Diet alone	33 (25.0)	43 (19.3)	34 (19.9)	.6146
	OADs only	112 (50.6)	141 (61.2)	119 (54.9)	.1464
	Insulin only	22 (12.7)	26 (12.5)	28 (14.4)	.9029
	OADs and insulin	17 (11.7)	19 (7.0)	28 (10.8)	.4574
Persons with diabetes among older adults (95% CI)		15.3 (13.0–17.6)	15.2 (13.6–16.7)	19.0 (15.6–22.5)	.1354
Older adults with diabetes	No.	179	163	247	
	HbA_{1c} <7.0% (SE)	71 (37.5)	94 (55.6)	146 (67.3)	<.0001
	HbA_{1c} <6.5 (SE)	48 (28.0)	63 (34.4)	96 (49.3)	.0039
	Mean HbA_{1c} (SE)	7.5 (0.2)	7.1 (0.1)	6.8 (0.1)	.0007
	Diet alone	15 (11.5)	26 (17.6)	37 (18.1)	.3916
	OADs only	111 (54.9)	93 (52.6)	159 (62.8)	.2946
	Insulin only	34 (24.1)	27 (17.8)	29 (11.6)	.0701
	OADs and insulin	19 (9.5)	17 (12.0)	22 (7.5)	.4587

Abbreviations: CI, confidence interval; HbA_{1c}, glycosylated hemoglobin; SE, standard error; OADs, oral antidiabetic drugs.

persons with stroke or nephropathy was higher in patients excluded from the study compared to those included in the study.

Table II describes the prevalence of diabetes over time and glycemic control by age. Overall, the prevalence of diabetes among adults increased over time. The prevalence of diabetes among older adults was highest during 2003–2004. The proportion of adults with diabetes who achieved target HbA_{1c} levels $\leq$7% (per ADA criteria) increased over time. Based on the EASD criteria (HbA_{1c} $\leq$6.5%), the percentage of adults with glycemic control was highest during 2001–2002; however, a majority of adults did not achieve glycemic control. Regardless of the criteria from the ADA or EASD, the percentage of older adults with glycemic control increased over time. Mean HbA_{1c} levels among individuals with diabetes decreased over time.

Table II also indicates the diet and pharmacologic treatment patterns in the United States for persons with diabetes. Over time, a greater proportion of older adults with diabetes relied on diet alone as a treatment option, and the prevalence of insulin use decreased. No notable trends were observed in the prevalence of OADs or OADs/insulin combination use.

Persons with diabetes were placed into HbA_{1c} subgroups to characterize major demographics as shown in Table III. The average age was approximately 50 years among adults with diabetes and 73 years in the older adults with diabetes. The proportion of insulin users was highest in the HbA_{1c} subgroup 8% to 8.9% for adults, while the proportion of insulin users was higher as HbA_{1c} increased among the older adults. The proportion of OAD users was statistically highest in the 7% to 8% HbA_{1c} group for adults. The proportion of OAD users was also highest in the 7% to 8% HbA_{1c} group for older adults, but the result was not statistically significant. The medium number of comorbidities was similar across subgroups regardless of age.

Multivariate logistic regression analysis revealed that non-Hispanic whites had better glycemic control than non-Hispanic blacks or other race (Table IV). Individuals with diabetes who took insulin or OADs or both had lower glycemic control than those without antidiabetic medication. Individuals with nephropathy had less glycemic control than those without. Glycemic control was better in the later time intervals of 2001–2002 and 2003–2004 than in 1999–2000. Persons with diabetes in 2001–2002 were 95% more likely to have glycemic control than those in 1999–2000, and diabetic patients in 2003–2004 were 149% more likely to have glycemic control than those in 1999–2000.

Table III. Characteristics of Adults and Older Adults With Diabetes by HbA_{1c} Level

HbA_{1c}, %	No.	Age (SE)	*P* Value	Men, No. (%)	*P* Value	Insulin, No. (%)	*P* Value	OADs, No. (%)	*P* Value	Median No. of Comorbidities (Range)
Adults										
<7	244	50 (0.58)	.1662	116 (51.5)	.6434	30 (11.6)	.0004	150 (59.4)	.0283	2 (0–4)
$7 \leq HbA_{1c} < 8$	132	50.7 (1.11)		67 (53.5)		33 (24.2)		104 (77.7)		1 (0–4)
$8 \leq HbA_{1c} < 9$	96	51.3 (1.05)		50 (47.6)		30 (41.0)		72 (69.7)		2 (0–5)
≥9	150	47.9 (1.13)		77 (57.0)		47 (32.6)		110 (66.7)		1 (0–4)
Older adults										
<7	311	73.2 (0.36)	.0324	150 (42.3)	.5430	45 (15.3)	.0001	217 (65.0)	.6971	2 (0–4)
$7 \leq HbA_{1c} < 8$	150	72.3 (0.51)		76 (50.2)		51 (36.4)		114 (72.1)		2 (0–4)
$8 \leq HbA_{1c} < 9$	60	72.1 (0.81)		31 (44.7)		25 (37.0)		40 (71.3)		2 (0–4)
≥9	68	70.5 (0.91)		36 (42.2)		27 (52.1)		50 (61.6)		2 (0–4)

Abbreviations: HbA_{1c}, glycosylated hemoglobin; SE, standard error; OADs, oral antidiabetic drugs.

Table IV. Logistic Regression Analysis of Glycemic Control (HbA_{1c} <7%) Among Patients With Diabetes (N=1211)

Variable	Odds Ratio	95% CI	*P* Value
Age (each 10-y increase)	1.222	1.082–1.379	.0012
Race			
Non-Hispanic white	1.000	–	–
Non-Hispanic black	0.573	0.390–0.841	.0045
Other race	0.524	0.364–0.755	.0005
Men	0.943	0.669–1.329	.7375
Antidiabetic therapy			
Diet only	1.000	–	–
Insulin only	0.077	0.036–0.164	<.0001
OADs only	0.207	0.119–0.358	<.0001
Insulin and OADs	0.085	0.040–0.182	<.0001
Hypertension	1.246	0.861–1.803	.2430
Heart failure	0.701	0.470–1.047	.0825
Stroke	1.378	0.685–2.771	.3683
Nephropathy	0.575	0.397–0.831	.0033
Health insurance	1.269	0.633–2.547	.5019
Obesity	1.246	0.788–1.971	.3462
Year survey			
1999–2000	1.000	–	–
2001–2002	1.951	1.237–3.077	.0041
2003–2004	2.492	1.563–3.974	<.0001

Abbreviations: CI, confidence interval; HbA_{1c}, glycosylated hemoglobin; OADs, oral antidiabetic drugs.

DISCUSSION

Our study examined diabetes prevalence, glycemic control, and antidiabetic treatment pattern during a 6-year period. Our data showed a 33% increase (from 3.9% to 5.2%) in the prevalence of diabetes among adults and a 24% increase (from 15.3% to 19.0%) in older adults during the period of 1999–2004. The CDC report also indicated the increasing prevalence of diabetes over time. The proportion of diabetics with good glycemic control (HbA_{1c} <7%) increased approximately 46% in adults and 79% in older adults over this period. Nevertheless, nearly half of adults and one third of older adults with diabetes still did not achieve the control target HbA_{1c} <7.0% in 2003–2004, suggesting that there is room to improve diabetes outcomes. Two studies also used NHANES 1999–2004 to evaluate the trend of glycemic control over time among persons with diabetes, and findings from our study are consistent with results from the two studies.[14,19] In predicting glycemic control, older adults and non-Hispanic whites were more likely to achieve the HbA_{1c}<7% target. The latter is consistent with a meta-analysis comparing HbA_{1c} levels between African Americans and non-Hispanic whites, suggesting that the racial differences in glycemic control may contribute to disparities in diabetes morbidity and mortality.[20]

Depending on the severity of diabetes, OADs alone or in combination with insulin are recommended for treatment in addition to lifestyle changes starting at the time of diagnosis.[15] Results from the Diabetes Control and Complications Trial (DCCT) and the UKPDS have shown that intensive therapies to lower HbA_{1c} levels may reduce the risk of development or progression of diabetes complications.[21,22] However, we found a significant proportion of persons with diabetes who did not take any antidiabetic agents and, instead, relied on diet alone to manage diabetes. The proportion with diet therapy alone was especially high among adults, which may partially explain poorer glycemic control in this population compared with older adults. On the

other hand, insulin use (alone or in combination with OADs) decreased over time, from 34% in 1999–2000 to 19% in 2003–2004 in older adults, but not in adults. Since insulin therapy in general targets individuals with more complicated diabetes, this trend in insulin use also reflects poor glycemic control among the adult population.

Obesity is a major risk factor for many chronic diseases, including diabetes. The prevalence of obesity among individuals 20 years and older increased from 19.4% in 1997 to 26.4% in 2006.[23] Our data showed a large burden of obesity among individuals with diabetes—59% of adults and 46% of older adults. In addition, hypertension, heart failure, stroke, and nephropathy were highly prevalent in our sample, especially in the older adults group. For instance, more than 62% of patients with diabetes (54% of adults and 75% of older adults) had hypertension while 32% reported nephropathy. Obesity (particularly visceral obesity) along with hypertension is an essential component of the metabolic syndrome, a group of related factors that increase the risk of cardiovascular disease.[24] Individuals with diabetes who have higher HbA_{1c} are also at increased risk of fatal myocardial infarction or stroke (odds ratio, 1.37 per 1% increase in HbA_{1c}; P=.007).[25] Moreover, since diabetes is a disease with high risk for comorbidities, use of treatments that are safe within these disease states is essential.

Limitations

In interpreting the results presented here, several notes of caution are important. First, survival bias may affect our estimates of glycemic control in favor of older adults because individuals with the poorest glycemic control may die at a younger age, leaving survivors who are better controlled in the population. Moreover, some older adults may have been diagnosed early and have better responsiveness to treatment.[26] These factors lead to a higher percentage of older adults with good glycemic control compared with adults. Second, we did not have information to distinguish between individuals with type I and type II diabetes. Thus, we were unable to determine treatment pattern and glycemic control by the types of diabetes. Third, we did not have information on the severity of diabetes. Persons who took insulin or OADs or both may have more serious diabetes than persons with diet only. The severity of diabetes may be one reason why persons with insulin or OADs or both had less glycemic control than persons with diet only. Fourth, evidence has shown that individuals with diabetes are likely underdiagnosed, especially in older adults.[1,26] Our prevalence figures may have been low because of reliance on self-reported diabetes status. Similarly, comorbidities also were obtained from survey data, which may have contained errors in data collection, editing, and imputation. We did not find a significant relationship between glycemic control and hypertension, heart failure, stroke, or obesity, whereas nephropathy appeared to reduce the likelihood of having good glycemic control by 2%. The effect of comorbidities on glycemic control merit further investigation.

CONCLUSIONS

Despite these limitations, our study documented an increasing trend in diabetes prevalence and a high percentage of poor glycemic control, even with increasing improvements in glycemic control as years progressed. Low proportion of glycemic control among adults compared with older adults indicates that it is necessary to focus on how to effectively treat younger persons with diabetes. Our findings highlight the increase in substantial comorbidity burden and the challenge of managing these concomitant conditions. Effective use of diabetes treatments that address appropriate use in diabetics with multiple comorbidities within a system of care coordination are needed to improve outcomes.

Disclosure: The authors state that there are no conflicts of interest.

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