

# Predictors of Diabetic Retinopathy in a Community Health Center Population

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## Abstract

**Objective.** To determine the predictors of diabetic retinopathy (DR) in a Federally Qualified Health Center population of patients.

**Research design and methods.** We retrospectively evaluated 526 patients who were screened for DR in the first year of a newly implemented telemedicine program (July 2009 to June 2010). Through this program, a total of 139 patients were diagnosed with DR, whereas 387 patients were not and then served as the comparator group. Multivariate logistic regression was used to determine the predictors of DR in this cohort of patients.

**Results.** After multivariate analysis, four positive predictors of

DR were found: insulin use (adjusted odds ratio [AOR] 1.94 [1.17–3.22]), years with diabetes (AOR 1.22 [1.16–1.28]), A1C (AOR 1.15 [1.02–1.29]), and kidney disease (AOR 5.11 [2.33–11.20]). No variables were found to decrease the odds of DR.

**Conclusion.** Among patients with diabetes, use of insulin therapy, longer duration of diabetes, presence of kidney disease, and higher A1C values increase the odds of DR. These preliminary data may suggest patients who are at higher risk of DR to further prioritize screening for DR with a newly implemented telemedicine program.

Diabetic retinopathy (DR) is the leading cause of blindness among adults aged 20–74 years in the United States and is the most common microvascular complication of diabetes.<sup>1,2</sup> Nearly all patients with type 1 diabetes and > 60% of patients with type 2 diabetes will develop retinopathy within the first two decades of the disease.<sup>2</sup> In 2000, it was estimated that 4.1 million people with diabetes who were ≥ 40 years of age had DR, and ~0.9 million had vision-threatening diabetic retinopathy (VTDR).<sup>3</sup>

The incidence of DR is expected to increase as the epidemiology of diabetes continues to grow.<sup>3,4</sup> Forecasts predict that the number of people with DR will grow from 5.5 million in 2005 to 16.0 million in 2050,<sup>3</sup> and the incidence of VTDR is expected to grow from 1.2 million in 2005 to 3.4 million in 2050.<sup>3</sup>

The projected increase in DR and VTDR is partially based on estimations of disproportionate growth among black and Hispanic populations, along with additional overall changes in the age and racial/ethnic composition of the U.S. population.<sup>3</sup> Studies have shown that the prevalence and severity of DR and VTDR are significantly greater in blacks (36.7%) and Hispanics (37.4%) than in whites (24.8%).<sup>5,6</sup> Although this higher prevalence of DR and VTDR can be explained in blacks after controlling for differences in glycemic control, duration of diabetes, and blood pressure, the higher prevalence of DR among Hispanics is not clearly understood.<sup>5</sup>

Additional research suggests there are common mechanisms that contribute to DR regardless of race/ethnicity.<sup>7</sup> Contributing biological factors include hyperglycemia, hyper-

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tension, duration of diabetes, greater waist-to-hip ratio, and greater BMI. Public health factors include personal health practices (exercise, self-care), psychosocial factors (social support, internal locus of control), and health care access and utilization factors (access to care, type of care provided, belief in the abilities of the health care system to provide help).<sup>7</sup>

Significant independent predictors of DR have also been identified in specific patient populations. One study that compared the prevalence of DR in a multi-ethnic U.S. population of whites, blacks, Hispanics, and Chinese identified four significant independent predictors of any retinopathy, including longer duration of diabetes, higher serum glucose, use of diabetic oral medication or insulin, and greater waist-to-hip ratio.<sup>5</sup> A similar study identified longer duration of diabetes and use of oral hypoglycemic medication or insulin as significant independent predictors of DR in a multi-racial underserved population.<sup>8</sup> In both studies, race was not an independent predictor for development of DR.<sup>5,8</sup>

Identifying risk factors for DR in patients with diabetes may help to identify a subgroup of patients with higher priority for DR screening and improve early screening rates for those at highest risk. We therefore investigated a cohort of patients who were screened for DR in our telemedicine program to identify predictors of DR in a large Federally Qualified Health Center (FQHC) patient population.

### Research Design and Methods

We performed a retrospective observational cohort analysis using electronic health record (EHR) data to evaluate the independent predictors of DR in an underserved community health center population at Community Health Center, Inc. (CHCI), a statewide network of FQHCs in Connecticut. A previous study from this center<sup>9</sup> demonstrated that telemedicine using digital retinal imaging technology in the primary care office is a strategy that can be used to screen underserved and at-risk patients for DR, increase compliance with screening, and streamline specialist referrals.

However, the patient characteristics associated with the presence of DR in this population of already at-risk patients have not been identified.

CHCI provides comprehensive primary care services to > 100,000 of Connecticut's most underserved patients in 12 towns. More than 60% of CHCI patients are racial/ethnic minorities; > 90% have incomes of < 200% of the federal poverty level; 60% are on Medicaid or state insurance; and 22% are uninsured.

Baseline data on patients with poorly controlled type 2 diabetes show that CHCI's Hispanic patients are the most likely to have poor control of their diabetes, defined as an A1C of > 9% per the Health Resources Services Administration's (HRSA) Uniform Data System (UDS) reporting criteria for all health center grantees. Fifty-three percent of patients with poor control of their diabetes by HRSA UDS standards are Hispanics, whereas 27% are white.

In early 2009, an internal review within CHCI found that, of patients with type 2 diabetes reviewed during a 3-year period, only 600 (18%) had active referrals for annual retinal examinations with an optometrist or ophthalmologist. Only 10–12% of CHCI patients with type 2 diabetes were up to date with recommended DR screenings before implementation of a statewide telemedicine program.

Through a partnership with the Yale Eye Center/Department of Ophthalmology, CHCI launched a telemedicine-based DR program within its primary care centers in July 2009 to improve screening, detection, and referral rates as primary goals. Retinal images and patient data were uploaded into the EyePACS Picture Archiving System (EyePACS, LLC, San Jose, Calif.) for specialist retrieval, review, and consultation. Retinal images were then interpreted by Yale ophthalmologists, who were also certified as EyePACS reviewers through the EyePACS Retinopathy Grading System. Reports indicating retinopathy level and referral recommendations were transmitted back

to primary care providers through the EyePACS site. All consecutive patients screened in the first year of the program were included in this study. A detailed description of the program has been previously published.<sup>9</sup>

We performed a retrospective observational cohort analysis to evaluate the independent predictors of DR using EHR data from multiple CHCI sites in an at-risk population. All adult patients with an International Classification of Diseases, 9<sup>th</sup> Revision, code for diabetes (250.xx) on their problem list in the EHR were eligible for referral to the tele-ophthalmology program. Patients who were not actively engaged in ophthalmology/optometry care or who had a retinal eye exam > 1 year ago were offered an appointment for the telemedicine program.

Approval for this study was obtained from the CHCI institutional review board.

DR was defined as the presence of any of the following on evaluation by the ophthalmologist: mild, moderate, or severe nonproliferative DR or proliferative DR. Control subjects were defined as those with the absence of DR on evaluation by the ophthalmologist.

Continuous variables are presented as a mean with a standard deviation and were compared between groups with a Student's *t*-test. Dichotomous variables are presented as percentages and were compared using a  $\chi^2$  test.

To determine the independent variables that were associated with the presence of DR, univariate analysis was first conducted on the following covariates: age, sex, race/ethnicity (Caucasian, Hispanic, other), insured status, insulin use, A1C, systolic blood pressure, diastolic blood pressure, achievement of blood pressure goal for diabetic patients (defined as < 130/80 mmHg per the American Diabetes Association), years with diabetes, presence of hypertension, presence of heart disease, presence of kidney disease, presence of high cholesterol, BMI, and smoking history (never, former, current).

**Table 1. Patient Characteristics and Demographics**

Patient Characteristics	With DR (n = 139)	Without DR (n = 387)	P value
Age (years, mean ± SD)	54.4±10.5	52.6±12.0	0.112
Male (n [%])	82 (59.0)	196 (50.6)	0.091
Ethnicity (n [%])			0.182
Caucasian	43 (30.9)	137 (35.4)	
Hispanic	71 (51.1)	163 (42.1)	
Other	25 (18.0)	87 (22.5)	
Insured (n [%])	101 (72.7)	299 (77.3)	0.276
Insulin use (n [%])	84 (60.4)	106 (27.4)	< 0.001
A1C (% , mean ± SD)	8.7±1.9	7.9±2.1	< 0.001
Systolic blood pressure (mmHg, mean ± SD)	132.5±17.1	129.4±17.0	0.061
Diastolic blood pressure (mmHg, mean ± SD)	79.8±9.7	79.4±9.8	0.697
Blood pressure at goal (n [%])	60 (43.2)	178 (46.0)	0.565
Diabetes duration (years, mean ± SD)	11.0±6.7	4.3±4.0	< 0.001
Hypertension (n [%])	110 (79.1)	262 (67.7)	0.011
Heart disease (n [%])	17 (12.2)	31 (8.7)	0.138
Kidney disease (n [%])	27 (19.4)	16 (4.1)	< 0.001
High cholesterol (n [%])	98 (70.5)	259 (66.9)	0.438
BMI (kg/m <sup>2</sup> , mean ± SD)	32.9 (8.0)	34.4 (7.8)	0.055
Smoking history (n [%])			0.725
Current	37 (26.6)	104 (26.9)	
Former	35 (25.2)	85 (22.0)	
Never	67 (48.2)	198 (51.2)	

SD, standard deviation

The status of all covariates was determined as of the day of the telemedicine visit (age, sex, race/ethnicity, insurance, presence of insulin prescription in current medication list and patient confirmation of use, presence of comorbidities, and smoking history). Blood pressure was measured at the time of the telemedicine visit. The most recent A1C value, if < 3 months old, was used. If the most recent A1C value was > 3 months old, it was repeated at the telemedicine visit. The most recent BMI was used.

Covariates with a P value ≤ 0.2 were entered into the multivariate

logistic regression model. In the multivariate model, variables were selected in a stepwise, backward elimination, and a P value of < 0.05 was considered significant. Adjusted odds ratios (AORs) with 95% confidence intervals (CIs) were calculated for independent predictors of DR. Statistical analyses were conducted with SPSS version 15 for Windows (SPSS, Inc., Chicago, Ill.).

**Results**

Approximately 3,500 adult patients with diabetes were identified, of whom < 500 were actively engaged with an ophthalmologist/optometrist

or had had a retinal exam < 1 year ago. Of the remaining patients, 610 were screened with the telemedicine program using two mobile retinal cameras deployed across the state in the first year of the program. Of the 610 patients screened between July 2009 and June 2010, 526 had a complete set of data and were included in the analysis. A total of 139 patients were determined to have DR, whereas 387 patients did not have DR as determined by the telemedicine screening. The latter patients served as the comparator group. Of the 139 patients determined to have DR, the majority had DR that was classified as mild (48.2%) or moderate (26.6%). Few patients had DR classified as severe (14.3%) or proliferative (10.8%).

The demographic characteristics of the study population can be found in Table 1. Patients with DR had a significantly mean A1C value and longer duration of diabetes; a greater number of patients with DR used insulin therapy, and a greater number of patients with DR were diagnosed with hypertension and kidney disease, compared to patients without DR (P < 0.05 for all comparisons). Although these baseline characteristics were different between the two groups, they were accounted for in the multivariable logistic regression analysis so that their impact was minimized.

Of the covariates evaluated, those with a significant P value on univariate analysis and therefore incorporated in the multivariate analysis included age, sex, insulin use, A1C, systolic blood pressure, years with diabetes, presence of hypertension, presence of heart disease, presence of kidney disease, and BMI. On multivariate analysis, the covariates found to be independent positive predictors of the presence of DR were the use of insulin therapy, A1C, duration of diabetes, and presence of kidney disease (Table 2). Of these, the presence of kidney disease was associated with the highest increase in the odds of DR (AOR 5.11 [2.33–11.20]). No variables were found to be negative predictors of DR.

**Table 2. Independent Predictors of DR Identified Through Multivariate Logistic Regression**

Independent variables	AOR (95% CI)	P value
Insulin use	1.94 (1.17–3.22)	0.01
A1C	1.15 (1.02–1.29)	0.02
Diabetes duration	1.22 (1.16–1.28)	< 0.001
Presence of kidney disease	5.11 (2.33–11.20)	< 0.001

### Discussion and Conclusion

This study provides important information suggesting patient characteristics that may identify those at higher risk for DR among patients already known to be at risk for complications of diabetes. In a largely minority and underserved health center population in Connecticut, patients who were referred to the telemedicine program and who had longer duration of diabetes, higher A1C values, kidney disease, or who used insulin for their diabetes were more likely to have DR.

The strongest predictor was the presence of kidney disease, which increased the odds of DR fivefold. Although insulin use was identified as a predictor of DR, it is more plausible that insulin use is serving as a marker of patients with more progressive diabetes rather than itself increasing the odds of DR. Similarly, kidney disease may be a marker for patients with a longer duration of diabetes suffering from microvascular complications rather than kidney disease itself increasing the odds of DR.

Previous studies have shown that longer duration of diabetes, use of any medications for diabetes, higher serum glucose levels, and greater waist-to-hip ratios are independent predictors of DR,<sup>5</sup> and this study suggests two additional predictors: A1C and the presence of kidney disease. A study conducted by Harris et al.<sup>6</sup> found that the risk of DR increased with higher A1C levels. However, this statistically significant correlation disappeared in multivariate analysis. In addition, research based on data analyzed from a multi-ethnic U.S. population found that self-reported kidney disease was not a significantly associated risk factor of DR.<sup>5</sup> In our study, A1C remained

a significant predictor even after multivariate analysis.

Race/ethnicity, age, BMI, tobacco use, sex, blood pressure or blood pressure control, being insured, and the presence of heart disease or hyperlipidemia were not independent predictors of DR in our population. Several other multi-racial studies have also found that these factors or characteristics, with the exception of heart disease or hyperlipidemia, are not significantly associated with DR.<sup>5,6,8</sup>

As the incidence of DR increases with exponential growth in the number of patients with diabetes,<sup>2,3</sup> it will be important for clinicians who care for patients with diabetes to be aware of the risk to their patients. In addition, practices serving racial/ethnic minorities, who have disproportionately higher prevalence and increased severity of DR<sup>5,6</sup> and may have limited resources, will need direction on how best to allocate these resources to screen those at highest risk.

The primary limitation of this study is generalizability, because the evaluation only consisted of the variables for which we had data. For example, we did not have data on waist-to-hip ratios or same-day glucose values, which have been shown to predict DR. Therefore, we were unable to adjust for these variables.

To preserve power and increase confidence in results, we limited the number of independent variables considered based on the number of patients with the outcome of interest.<sup>10</sup> As a result, additional exploratory variables, such as the number of risk factors present, were not considered in the model.

Additionally, very few patients diagnosed with DR were classified as having severe or proliferative DR.

Therefore, the model is most applicable to less-severe cases of DR. In the future, a larger sample size would allow a broader representation of DR severity.

There is the potential for selection bias because this cohort of patients only includes those who utilized telemedicine for their retinal screening, rather than all CHCI patients with diabetes. It is possible that patients who utilized telemedicine were those who were more likely to be uninsured and not engaged with ophthalmology or optometry. However, 24% of patients in the study population were uninsured, and the remainder were insured through Medicaid (63%) or private insurers.<sup>9</sup> The possibility remains, however, that primary care providers referred uninsured or publicly insured patients more frequently for telemedicine based on access challenges.

DR is the most common and preventable cause of vision loss in adults in the United States. It is the most common microvascular complication of diabetes,<sup>2,5</sup> and the prevalence of both diabetes and VTDR are expected to increase exponentially in the next 30 years.<sup>3</sup> Disparities in DR also exist; blacks and Hispanics have a significantly increased risk of retinopathy, and these two groups represent a disproportionate share of morbidity as measured by visual impairment and blindness.<sup>11,12</sup>

However, decreasing vision-related morbidity caused by DR is possible.<sup>12</sup> Vision loss from DR can be avoided by early detection through annual ocular screenings,<sup>4</sup> and earlier recognition of diabetes, better glycemic control, and early detection and treatment of DR can slow or prevent the development of blindness. Among minorities and other populations with limited access to specialty medical care, DR screening rates are generally in the range of 10–20%,<sup>1,13–15</sup> and diabetes-related vision loss is disproportionately higher, which makes the need for efficient and cost-effective screening programs imperative for practices serving these populations. However, prioritizing those patients who



would derive the most benefit is a challenge.

Notably, our study did not demonstrate that race/ethnicity was an independent predictor of DR in this population. Other studies have shown that DR prevalence and severity are significantly greater in blacks and Hispanics,<sup>5,6</sup> although, after controlling for certain risk factors and characteristics, the difference between whites and blacks disappears and that between whites and Hispanics remains. Our study may have been underpowered to detect the impact of race/ethnicity on DR because of the overall size of the cohort studied. In the future, a larger cohort would be needed to increase the power to detect whether race/ethnicity truly has an impact of DR.

In addition, certain patient characteristics, including greater BMI and the presence of hypertension, have previously been shown to increase the likelihood of DR independent of demographics.<sup>7</sup> However, these findings were not demonstrated in our population to be independent predictors after adjustment for other covariates, although they were significant in the univariate analysis.

This may be in part because of blood pressure control rates in the cohort; close to half of patients with and without DR (43 and 46%, respectively) were considered to have a blood pressure level at the goal of < 130/80 mmHg. Additionally, the duration and severity of hypertension may influence the risk of DR, although our model did not adjust for duration and specific levels of severity of hypertension. Finally, the limited number of retinal cameras did not allow for unscheduled retinal screening for patients because availability was based on the camera rotation among the sites.

Ideally, this type of study should be conducted for the entire CHCI patient population with diabetes. The findings are most relevant to health center settings, which may face a need to prioritize and streamline specialty referrals as the health center population doubles to nearly 40 million Americans in the next few years, coupled with an equally robust growth in the number of Americans

with diabetes. The relationship between kidney disease and DR for a predominantly Hispanic health center population is one that should be further delineated and explored.

This study demonstrated preliminary predictors of DR in a community health center population. Although this analysis focused on patients enrolled in a telemedicine program at CHCI, these findings may guide prioritization of patients in a telemedicine screening program, particularly for resource-challenged practice settings, starting with those patients with the highest number of risk factors present. In addition, these findings suggest an additional measure for prioritization, which is the targeted screening of diabetic patients with kidney disease, which was the strongest predictor of DR in the study population.

As health care settings providing care for underserved patients seek to improve DR screening rates in the growing number of patients with diabetes, it is paramount to provide evidence-based strategies for prioritizing services in resource-challenged settings. CHCI recently began a major transformation in quality improvement centered on improving the detection and management of chronic kidney disease in patients with diabetes.<sup>16</sup> These study findings will be crucial in developing a dashboard for comprehensive care for patients with diabetes and chronic kidney disease and will bring new light to the importance of DR screening in this segment of the population.

CHCI has already enveloped DR screening for patients with diabetes and chronic kidney disease into its model of patient-centered care, including formal incorporation into provider performance appraisals, weekly data reports on huddles and planned care, quality improvement methodology and planning, and clinical expectations for performance. This approach to screening for DR will be highly applicable for similar health care settings. For broader policy implications, a broader representation of CHCI patients would be ideal, so that results could be applied across sites and settings.

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