Title: Quantifying worsened glycemic control during the COVID-19 pandemic

Running Title: Glycemic control in COVID-19

Authors: Ledford CJW[1], Roberts C[2], Whisenant E[2], Walters C[2], Akamiro K[2], Butler J[2], Ali A[2], Seehusen DA[2]

1- Department of Family Medicine, Uniformed Services University of the Health Sciences, Bethesda, MD

2- Department of Family Medicine, Augusta University, Augusta, GA

Corresponding Author:

Dean A. Seehusen, MD, MPH

Professor and Interim Chair

Department of Family Medicine

Medical College of Georgia

Augusta University

Augusta, Georgia 30912-3500

Office Telephone: (706) 721-3159

Email: dseehusen@augusta.edu

Abstract word count: 235

Text word count: 1488

References: 17

Funding: none

Conflicts of Interest: Dr. Seehusen is the Deputy Editor of JABFM

Aims: We hypothesized that glycemic control in outpatients, measured by HbA1c, was worse during the early months of the COVID-19 pandemic than the prior year. We sought to quantify how much worse mean glycemic control was in 2020 compared to 2019. We also sought to determine if social determinants of health were associated with these differences.

Materials and Methods: Data were extracted from the electronic medical records of two cohorts of patients seen in the family medicine clinic of a Southeastern academic health center. A total of 300 patients with baseline HbA1c results, as well as HbA1c results in May 2019 or May 2020, were evaluated.

Results: The groups had similar mean baseline HbA1c (7.65, SD = 1.50 for 2019; 7.61, SD = 1.71 for 2020; p = 0.85). Mean May HbA1c decreased from baseline in 2019 (7.19, SD = 1.45) but rose in 2020 (7.63, SD = 1.73), a statistically significant difference ($p < 0.01$). Controlling for age, gender, race, and insurance status, HbA1c in May 2020 ($mean_{adj}$= 7.73) was significantly higher than in May 2019 ($mean_{adj}$= 7.16). No demographic variables were associated with HbA1c levels.

Conclusions: During the early months of the COVID-19 pandemic, glycemic control in our patient population was significantly worse than during the same period in 2019 (mean HbA1c difference = 0.57). Contrary to our expectations, we did not find associations between patient demographic variables and glycemic control, including race.

Introduction

While the COVID-19 pandemic presents the immediate health risk of viral infection, the pandemic along with the local and national governmental response to it potentially increase short- and long-term health risks for patients living with chronic disease. Reports of COVID-19 in the US began in late January 2020.[1] As a pandemic response strategy, in Georgia, the governor declared a state of emergency March 14, 2020, which was followed by a shelter-in-place order issued March 23, 2020, continuing through April 2020.[2] Pandemic response strategies may limit 1) patients' ability to adhere to nutritional or physical activity guidelines and 2) patients' access to healthcare.[3] Stay at home and social distancing policies may also contribute to social isolation, which can negatively impact mental health. These effects of pandemic response strategies can inhibit patients' disease self-management.[4] For patients living with type 2 diabetes or pre-diabetes, it is not clear how significantly pandemic response strategies impact glycemic control.

The social determinants of health framework suggests that the social responses to the pandemic, such as shelter in place orders, closure of businesses, and loss of some public services may have had a disproportionate effect on racial and ethnic minority groups.[5] Minority groups have less financial capacity to enact healthy nutritional decisions in the midst of the financial hardships that have emerged following pandemic response strategies.[6] Pandemic response strategies, which encouraged the public to stay at home and close to home, likely amplified the effect of "place" on patients' ability to manage chronic conditions. Predominately Black American communities have less access to healthy foods and higher access to fast food[7,8], each of which makes chronic disease management more difficult. Similarly, African American women neighborhood safety concerns and lack of sidewalks as barriers to physically activity close to home.[9]

The purpose of this study was to investigate the impact of local pandemic response strategies on glycemic control. Our hypothesis was that glycemic control in our patient population was significantly worse in the early months of the pandemic as compared to the same months in 2019. A secondary hypothesis was that race, payment model, and median household income would be associated with differences in mean HbA1c.

Materials and Methods

After receiving an exemption from the Augusta University Institutional Review Board, all adult (aged 18 years and older) outpatient HbA1c results of 5.5 or higher from May 2019 and May 2020 were identified in our electronic medical record (EMR) - Cerner. The range of 5.5 or higher was applied to include patients at the upper ends of normoglycemia, prediabetes, and diabetes. We anticipated that the glycemic control of all of these populations may have been negatively impacted by the pandemic. Data extraction included the May HbA1c plus an appropriate comparison HbA1c for a baseline. The May HbA1c was used to measure glycemic control during the first 3 months of the U.S. pandemic response. The baseline timeframe was defined as the preceding October through February and reflected a recent measure of glycemic control prior to the influence of U.S. and local pandemic response strategies.

All patients were enrolled in the outpatient family medicine clinic of an academic health center within the Diabetes Belt in the Southeastern United States. Patients in this clinic receive care from faculty and resident family physicians as well as nurse practitioners.[10] A total of 335 records were retrieved that had an outpatient laboratory HbA1c result in May and a baseline outpatient laboratory HbA1c result in the preceding October to February. The May glycemic value represents a patient's glycemic control during the implementation of the strictest pandemic response strategies (from March through May) in Georgia. We chose to compare HbA1c change in 2020 to 2019 instead of a simple pre-, post-pandemic analysis as a control for any seasonal variation of HbA1c levels that might exist in this patient population.

Patient records were excluded for: other diagnosis (type 1 diabetes) (n=1), race other than black or white (n=16), or nonspecific HbA1c value in chart (listed as greater than 15) (n=1). All cases with baseline HbA1c outliers (greater than 2 standard deviations) were also removed (n=17). Thus, 300 patients are included in analysis.

Results

Table 1 shows demographic characteristics of the 2019 and 2020 group. The group demographic variables were not statistically different. The groups had similar mean baseline HbA1c (7.65, SD = 1.50 for 2019; 7.61, SD = 1.71 for 2020; $p = 0.85$).

Mean May HbA1c decreased from baseline in 2019 (7.19, SD = 1.45) but rose in 2020 (7.63, SD = 1.73), a statistically significant difference ($p < 0.01$). In univariate analysis, age, gender, race, insurance status, were not statistically associated with mean May HbA1c results. Medication regimen was significantly associated with May HbA1c levels (no anti-diabetic medications: mean = 6.17, SD = 0.65; non-insulin medications only: mean 7.18, SD = 1.44; regimen included insulin: mean = 8.63, SD = 1.60 [$p < 0.001$]).

For hypothesis testing, a full factorial model of covariance (ANCOVA), including the fixed factors of year (2019 or 2020) and race (Black American or White American) and covariates baseline HbA1c, patient age, and estimated household income, was tested onto the dependent variable May HbA1c. In the model, the baseline HbA1c had a significant association with the dependent variable, $F\,(1, 295) = 347.7$, $p < .001$. Controlling for covariates, year was significantly associated with HbA1c, $F\,(1, 295) = 18.85$, $p < .001$. Patient HbA1c in May 2020 ($mean_{adj}$= 7.73) was significantly higher than patient HbA1c in May 2019 ($mean_{adj}$= 7.16). No main effect was detected for race. No interaction effect for year by race was detected.

Discussion

It has been previously reported that COVID-19 infection can lead to dramatic worsening of existing or new onset diabetes, perhaps by alteration of glucose metabolism.[11] Glycemic control during the pandemic has already been shown to be worse in patients with type 1 diabetes.[12] Theoretical concerns about glycemic control among outpatients with type 2 diabetes has been expressed in the medical literature.[13] Additionally, some potential mitigation strategies have been suggested.[14]

Our findings suggest that the COVID-19 pandemic indeed worsened glucose control in the short term among our patient population. Comparing adjusted mean HbA1c between the two years, the COVID-19 pandemic, and the socio-political response to it, resulted in a mean HbA1c 0.57 higher in May 2020 than May 2019. During Spring 2020, as compared to Spring 2019, patients were more likely to experience financial and social stress, to struggle with changes in the food supply that reduced healthy nutritional choices, to encounter obstacles to established exercise patterns, to have limited access to healthcare, and to experience heightened barriers to medication adherence.

This elevated HbA1c may put patients at a greater risk for long-term diabetes complications since higher HbA1c levels are associated with higher risk for cardiovascular and other complications.[15,16] Recent evidence also suggests that significant swings in HbA1c may also be associated with long term cardiac outcomes.[17]

Contrary to our secondary hypothesis, we did not find associations between patient socio-demographic variables and glycemic control, including race. In fact, while both white and black patients had worse glycemic control in 2020 compared to 2019, white patients had a greater rise in year-over-year HbA1c than black patients did, although this was not statistically significant. The reasons for this are unclear, but one intriguing possibility is that black patients with diabetes may have developed strong resiliency and were therefore more capable of dealing with the shifting landscape of the pandemic.[18]

Findings are limited by study design. The study compares two separate cohorts, rather than a single patient population. In this clinic, we did not have access to a large number of patients that had HbA1c data available in both years. However, the two cohorts belong the same general patient population, were followed in the same clinic, mostly by the same primary care clinicians. That, combined with the fact that their mean baseline HbA1c were so similar, indicates that direct comparison of these two cohorts is reasonable.

As a single institution study, findings here are interpreted in accordance with the pandemic response strategies of this local area. The severity of the COVID-19 pandemic, and the aggressiveness of the local response to it, are local effects. The impact on population glycemic control may be sensitive to these factors, limiting generalizability of these findings. Data retrieved from an EMR, such as race, is subject to error. Lastly, the mean household income was estimated based on the patients' zip code. In some cases, this method may have over- or underestimated an individual patient's income.

Future research should look at other patient populations to determine if our findings are representative or unique. Patients living in regions that experienced more significant, and longer, impacts from the COVID-19 pandemic may observe greater changes in glycemic control. Additional research could also evaluate how local COVID-19 infection rates and governmental responses influenced glycemic control. Qualitative inquiry should also evaluate individual patient factors and strategies that mitigated the influence of pandemic response strategies on glycemic control.

Disclaimer: "Views expressed within this publication represent those of the authors and do not reflect the official position of the Uniformed Services University of the Health Sciences, or the U.S. Government, the Department of Defense at large."

References

1. Hartmann-Boyce J, Morris E, Goyder C, et al. Diabetes and COVID-19: Risks, Management, and Learnings From Other National Disasters. *Diabetes Care*. 2020;43(8):1695-1703. doi:10.2337/dc20-1192
2. Nedelman M. New report on first US case of novel coronavirus details mild symptoms followed by pneumonia. Available at: https://www.cnn.com/2020/01/31/health/washington-coronavirus-study-nejm/index.html. Accessed: 30 July 2020.
3. ACLU Georgia. Timeline of Georgia Government Actions Regarding COVID-19. Available at: https://www.acluga.org/en/timeline-georgia-government-actions-regarding-covid-19. Accessed 24 July 2020.
4. Usher K, Bhullar N, Jackson D. Life in the pandemic: Social isolation and mental health. J Clin Nurs. 2020 Aug;29(15-16):2756-2757.
5. Turner-Musa J, Ajayi O, Kemp L. Examining Social Determinants of Health, Stigma, and COVID-19 Disparities. Healthcare (Basel). 2020;8(2):168. Published 2020 Jun 12. doi:10.3390/healthcare8020168
6. Tai DBG, Shah A, Doubeni CA, Sia IG, Wieland ML. The Disproportionate Impact of COVID-19 on Racial and Ethnic Minorities in the United States. Clin Infect Dis. 2020 Jun 20:ciaa815. doi: 10.1093/cid/ciaa815. Epub ahead of print.
7. Baker EA, Schootman M, Barnidge E, Kelly C. The role of race and poverty in access to foods that enable individuals to adhere to dietary guidelines. Prev Chronic Dis. 2006 Jul;3(3):A76. Epub 2006 Jun 15. PMID: 16776877; PMCID: PMC1636719.

8. James, P., Arcaya, M.C., Parker, D.M., Tucker-Seeley, R.D. and Subramanian, S.V., 2014. Do minority and poor neighborhoods have higher access to fast-food restaurants in the United States?. *Health & place*, *29*, pp.10-17.
9. Joseph RP, Ainsworth BE, Keller C, Dodgson JE. Barriers to Physical Activity Among African American Women: An Integrative Review of the Literature. *Women Health*. 2015;55(6):679-699. doi:10.1080/03630242.2015.1039184
10. Barker LE, Kirtland KA, Gregg EW, Geiss LS, Thompson TJ. Geographic Distribution of Diagnosed Diabetes in the U.S.: A Diabetes Belt. *American Journal of Preventive Medicine.* 2011;40(4):434-439.
11. Rubino F, Amiel SA, Zimmet P, et al. New-Onset Diabetes in Covid-19 [published online ahead of print, 2020 Jun 12]. N Engl J Med. 2020;NEJMc2018688. doi:10.1056/NEJMc2018688
12. Verma A, Rajput R, Verma S, Balania VKB, Jangra B. Impact of lockdown in COVID 19 on glycemic control in patients with type 1 Diabetes Mellitus [published online ahead of print, 2020 Jul 13]. Diabetes Metab Syndr. 2020;14(5):1213-1216. doi:10.1016/j.dsx.2020.07.016
13. Koliaki C, Tentolouris A, Eleftheriadou I, Melidonis A, Dimitriadis G, Tentolouris N. Clinical Management of Diabetes Mellitus in the Era of COVID-19: Practical Issues, Peculiarities and Concerns. *J Clin Med*. 2020;9(7):E2288. Published 2020 Jul 18. doi:10.3390/jcm9072288
14. Gujral UP, Johnson L, Nielsen J, et al. Preparedness cycle to address transitions in diabetes care during the COVID-19 pandemic and future outbreaks. *BMJ Open Diabetes Res Care*. 2020;8(1):e001520. doi:10.1136/bmjdrc-2020-001520

15. Wan EYF, Yu EYT, Chen JY, Wong ICK, Chan EWY, Lam CLK. Associations between usual glycated haemoglobin A1c and Cardiovascular Disease in Patients with Type 2 Diabetes Mellitus: A 10-year Diabetes cohort study [published online ahead of print, 2020 Aug 3]. Diabetes Obes Metab. 2020;10.1111/dom.14157. doi:10.1111/dom.14157
16. Kelly TN, Bazzano LA, Fonseca VA, Thethi TK, Reynolds K, He J. Systematic review: glucose control and cardiovascular disease in type 2 diabetes. Ann Intern Med. 2009;151(6):394-403. doi:10.7326/0003-4819-151-6-200909150-00137
17. Segar MW, Patel KV, Vaduganathan M, et al. Association of Long-term Change and Variability in Glycemia With Risk of Incident Heart Failure Among Patients With Type 2 Diabetes: A Secondary Analysis of the ACCORD Trial. Diabetes Care. 2020;43(8):1920-1928. doi:10.2337/dc19-2541
18. Kim JH, Islam SJ, Topel ML, Ko YA, Mujahid MS, Vaccarino V, Liu C, Sims M, Mubasher M, Searles CD, Dunbar SB, Pemu P, Taylor HA, Quyyumi AA, Baltrus P, Lewis TT. Individual Psychosocial Resilience, Neighborhood Context, and Cardiovascular Health in Black Adults: A Multilevel Investigation From the Morehouse-Emory Cardiovascular Center for Health Equity Study. Circ Cardiovasc Qual Outcomes. 2020 Oct 7:CIRCOUTCOMES120006638. doi: 10.1161/CIRCOUTCOMES.120.006638. Epub ahead of print.

Table 1. Demographic variables and HbA1c results for May 2019 and May 2020 patients.

	2019 (n=156)	2020 (n=144)	p-value
Age (mean, SD)	61.0 (11.7)	60.4 (13.4)	NS
Women (%)	111 (71.2)	89 (61.8)	NS
White (%)	53 (34.0)	45 (31.1)	NS
Insurance Status (%)			NS
Medicaid	85 (54.5)	68 (47.2)	
Medicare	14 (9.0)	22 (15.3)	
Insurance	52 (33.3)	47 (32.6)	
Self Pay	5 (3.2)	7 (4.9)	
Antidiabetic Medication (%)			NS
None	25 (16.0)	32 (22.2)	
Only non-insulin medications	87 (55.8)	66 (45.8)	
Insulin	44 (28.2)	46 (31.9)	
Median Household Income (mean, SD)	$38,529 (15,732)	$40,399 (13,707)	NS
Baseline HbA1c (mean, SD)	7.65 (1.50)	7.61(1.71)	NS
May HbA1c (mean, SD)	7.19 (1.45)	7.63 (1.73)	< 0.01