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The effect of the Covid-19 shutdown on glycemic testing and control

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ABSTRACT

Background: The coronavirus disease 2019 (COVID-19) pandemic caused a halt to in-person ambulatory care. We evaluated how the reduction in access to care affected HbA1c testing and patient HbA1c levels.

Methods: HbA1c data from 11 institutions were extracted to compare testing volume and the percentage of abnormal results between a pre-pandemic period (January-June 2019, period 1) and a portion of the COVID-19 pandemic period (Jan-June 2020, period 2). HbA1c results greater than 6.4% were categorized as abnormal.

Results: HbA1c testing volumes decreased in March, April and May by 23, 61 and 40% relative to the corresponding months in 2019. The percentage of abnormal results increased in April, May and June (25, 23, 9%). On average, we found that the frequency of abnormal results increased by 0.31% for every 1% decrease in testing volume (p < 0.0005).

Conclusion: HbA1c testing volume for outpatients decreased by up to 70% during the early months of the pandemic. The decrease in testing was associated with an increase in abnormal HbA1c results.

1. Introduction

The year 2020 brought with it the coronavirus disease 2019 (COVID-19) pandemic that resulted in a global shutdown [1]. In March 2020, after the World Health Organization (WHO) declared the pandemic, many outpatient clinics were closed to in-person visits in an attempt to slow the spread of disease. This resulted in many institutions scrambling to get telehealth platforms in place to provide continuity of care to their patients with chronic diseases. In Northern America (U.S. and Canada), diabetes mellitus is amongst the most prevalent chronic diseases [2,3]. Primary care teams screen and make the initial diagnosis of diabetes mellitus. Standard of care for people with diabetes mellitus includes follow up visits every 3–6 months depending on the patient’s medication regimen and the previous glycemic control [4]. In both scenarios, measurement of HbA1c typically occurs at the time of these in person visits and is essential for monitoring glycemic control.

With the shift to telehealth, many diabetes centers had to adjust their chronic care flow. In Padua, Italy, there was a 47.7% decrease in outpatient visits during shutdown [5]. With this reduction, they saw that older patients with more comorbidities were less likely to be...
seen. Worryingly, the use of medications to reduce complications from diabetes mellitus was decreased.

2. Methods

HbA1c data from 11 institutions was extracted to compare testing volume and the percentage of abnormal results between a pre-pandemic period (January-June 2019, period 1) and a portion of the COVID-19 pandemic period (Jan-June 2020, period 2). We determined the median and the interquartile range (IQR) of the monthly volume of HbA1c testing. We also determined the median and IQR of the percentage of abnormal HbA1c results. HbA1c results greater than 6.4% were categorized as abnormal. Point-of-care results and laboratory-based results were aggregated.

We determined the impact of the pandemic by comparing the testing volumes and the percentage of abnormal results for each month in period 1 and period 2. We calculated the percent change in testing volume, ΔV and the change in abnormal results, ΔA for each month at each location (change was calculated relative to the corresponding month in 2019). We also calculated the median percentage change in volume, ΔVm and median percentage change in the number of abnormal results, ΔAm over all locations. We calculated these statistics (ΔVm and ΔAm) for three cohorts: all patients, inpatients and outpatients.

Data from all sites were aggregated and five-point summaries were calculated (minimum, 25th percentile, median, 75th percentile, maximum) for each statistic by month for each patient cohort. The monthly change was visualized by creating box plots of the percent change in volume and abnormal results by month. We also tested for a relationship between ΔV and ΔA using hierarchical regression with location as a random effect and plotted the relationship between ΔV and ΔA for each site (the slope and intercept were both modeled as random effects).

We also compared the change in testing volume for HbA1c with the change in total testing (exclusive of Covid-19 testing) at ARUP and at the University of Utah hospital laboratory. ARUP is a national reference laboratory that performs testing for hospitals across 50 states. Testing volume for ARUP was selected as an indicator of testing nationally. The study was limited to adults aged 18 to 70. We determined the sex and age distribution of outpatients who received HbA1c testing.

3. Results

Table 1

Demographics of Tested Outpatients at University of Utah Hospital Laboratory. The cell entries represent the percentage in each category. For example, in January 2019, 45% of those were tested were male and 13% of all patients (male and female) were between 19 and 30 (inclusive).

| Year | Month | Male | Age Range | 19-30 | 31-40 | 41-50 | 51-60 | 61-70 |
|------|-------|------|-----------|-------|-------|-------|-------|-------|
| 2019 | Jan   | 45   | 13        | 18    | 18    | 19    | 18    | 18    |
|      | Feb   | 44   | 14        | 19    | 18    | 19    | 18    | 17    |
|      | Mar   | 44   | 14        | 18    | 18    | 19    | 18    | 18    |
|      | Apr   | 43   | 15        | 19    | 18    | 17    | 18    | 17    |
|      | May   | 44   | 14        | 18    | 19    | 18    | 18    | 17    |
|      | Jun   | 45   | 13        | 19    | 19    | 19    | 17    |       |
|      | Average | 44  | 14       | 19    | 18    | 18    | 18    |       |
| 2020 | Jan   | 43   | 15        | 19    | 19    | 19    | 19    | 16    |
|      | Feb   | 43   | 16        | 20    | 18    | 18    | 15    |       |
|      | Mar   | 44   | 16        | 20    | 17    | 18    | 17    |       |
|      | Apr   | 40   | 20        | 21    | 14    | 16    | 17    |       |
|      | May   | 43   | 14        | 17    | 16    | 17    | 20    |       |
|      | Jun   | 44   | 12        | 19    | 16    | 18    | 19    |       |
|      | Average | 43  | 16       | 19    | 17    | 18    | 17    |       |

Table 2

Characteristics of participating institutions.

| Institution                              | Baseline HbA1c Testing (2019 average) |
|------------------------------------------|---------------------------------------|
|                                          | Monthly Volume | Percent Abnormal |
| University of Saskatchewan               | 12,202         | 31               |
| University of Utah                       | 5623           | 15               |
| University of CA, San Francisco          | 3237           | 30               |
| Los Angeles County, USC Medical Center   | 3320           | 41               |
| McMaster University                      | 262            | 41               |
| University of Iowa                       | 2852           | 36               |
| Kaiser Permanente, Washington            | 11,588         | 34               |
| Geisinger                                | 15,372         | 50               |
| Washington University, Saint Louis       | 3037           | 33               |
| University of Texas Southwestern Medical Branch | 4968         | 57               |
| University of Pennsylvania               | 10,270         | 43               |

geographically across the US (N = 9) and Canada (N = 2), the median monthly volume of HbA1c testing in period 1 was 4968 (IQR: 3137 – 10929) for all patients, 826 for inpatients (IQR: 366-1181), and 3057 (IQR: 2256 – 9768) for outpatients. The median percentage of abnormal HbA1c results was 38% (IQR: 32 – 44) for all patients, 41% (IQR: 36 – 46) for inpatients, and 35% (IQR: 29 – 44) for outpatients.

Impact of Shutdown on Overall Testing at ARUP and the University of Utah. The relative testing volume at ARUP and at the University of Utah increased slightly in January and February but decreased in March through May (Fig. 1). Similar results were seen for 25-OH vitamin D, basic metabolic profile, and complete metabolic profile (Supplementary Figs. 1 and 2).

Demographics of Tested Outpatients at the University of Utah: Forty-two percent of the tested population was male. Ages were evenly distributed and demonstrated little variation by year (Table 1).

Impact of Shutdown on HbA1c Testing Volume and Abnormal Results. Across all participating institutions, the volume of HbA1c testing for all patients increased by about 16% in 2020 relative to 2019 over the months of January and February (Fig. 2, Supplemental Table 1). Testing volumes decreased in March, April and May by 23, 61 and 40% relative to the corresponding months in 2019 but increased by 2% in June. There was little change in the frequency of abnormal results over the first three months of 2020 (ΔAn = 2, −1 and −4%); however, the frequency of abnormal tests increased by about 19% in April and May, and returned to baseline in June (ΔAn = 2%).

The volume of HbA1c testing for inpatients increased by about 7% in

Fig. 1. Change in Relative Testing Volume by Month. The figure shows the ratio of total testing (2020/2019) for ARUP and the University of Utah hospital laboratory. Covid testing was excluded.
January and February, decreased by approximately 17% during March and April, and recovered to 2019 levels in May and June (Δ\(V_m\) = -5 and 7%) (Fig. 2). The percentage of abnormal results showed little change in 2020 relative to 2019. The percent change of abnormal results ranged from a decrease of 2% to an increase of 5%.

The volume of HbA1c testing for outpatients increased by 14 and 23% in January and February, decreased 28, 70 and 50% March to May, and recovered to 2019 levels in June. The percentage of abnormal results was similar to 2019 in January to March of 2020 (Δ\(A_m\) = -1, 5, and 2) but increased in April, May and June (Δ\(A_m\) = 25, 24, 9%).

We tested for a relationship between the percent change in testing volume (Δ\(V\)) and the percent change in abnormal HbA1c results (Δ\(A\)) among outpatients Ten of 11 locations showed a negative relationship between testing volume and abnormal HbA1c result frequency (Fig. 3). The relationship varied by site. For example, at one site there was a 0.85% decrease in abnormal results for every one percent increase in testing volume. At another site, there was a 0.09% increase in abnormal results for every one percent increase in testing volume. On average, we found that the Δ\(A\) decreased by 0.31% for every 1% increase in Δ\(V\) (p < 0.0005). That is, decreases in testing volume were associated with an increase in the frequency of abnormal results.

4. Discussion

The COVID-19 pandemic brought with it the harsh reality that outpatient care for people with diabetes mellitus was not equipped for remote monitoring. The data show that testing for the quintessential ‘standard of care’ measurement for glycemic control (HbA1c) was decreased up to 70% during the height of shutdown (April 2020) suggesting that many patients went without formal assessment of glycemic control for at least 3–4 months. This could have been prevented.

The current recommendation is to monitor the HbA1c every 3 months in patients with diabetes mellitus (depending on prior glycemic control), annual screening in adults with prediabetes and screening at least every 3 years in adults over the age of 65 years and adults who are overweight/obese with at least one risk factor [6]. This is a large group and encompasses a significant portion of people receiving primary care and endocrinology outpatient clinics. The recommendation of monitoring HbA1c quarterly is based on prior data showing that decreased testing is associated with a 1.5% increase in HbA1c (i.e., worse glycemic control), whereas frequent monitoring was associated with a 3.8% decrease in HbA1c (i.e. improved glycemic control) [7]. Given the prolonged trajectory of the pandemic, continued lack of testing may result in worsening of glycemic control which can eventually result in worsened health outcomes in those with diabetes mellitus [8], and in a

![Fig. 2. Change in the Relative Testing Volume and Relative Percentage of Abnormal HbA1c Results by Month. Relative change was measured as 2020 results relative to 2019. HbA1c results greater than 6.4% were categorized as abnormal. Each month represents results from 11 sites. The white line in the box indicates the median and the length of the box indicates the interquartile range. Dots indicate outliers. Numerical values corresponding to the figure are detailed in supplemental Table 1.](image-url)
increased and then a delayed increase in HbA1c testing volume was seen after hypertension (56.6%) and obesity (41.7%). It is likely that the lack of diabetes mellitus was the third most common comorbidity (33.8%) seen in the care of diabetes mellitus but across all outpatient specialties due to increased inpatient management of people with diabetes mellitus.

The most important strength of this study is the broad sampling across the United States and Canada. In addition, the relationship between the testing volume and the frequency of abnormal results was consistent in 91% of centers (10/11). The data reflect sampling from people who accessed care and are therefore at risk to selection and/or convenience bias. The parameters measured were volume of HbA1c testing and therefore further conclusions beyond those mentioned are unable to be drawn. Underlying characteristics of the individuals who were tested and why they did get tested are unknown. In particular, we were unable to distinguish between tests performed for screening, diagnosis and monitoring.

The COVID-19 pandemic brought with it a major disruption to outpatient care. This highlighted a significant deficit in glycemic monitoring by traditional measures (HbA1c). It also brought to light the benefits of telehealth. As we look ahead, outpatient diabetes care teams should shift gears and focus on education and implementation of the available technologies to perform effective, complete virtual care. Telehealth can fill the gap in traditional care models and prevent disruption to standard of care whenever the next pandemic strikes.

This study has several limitations. The study only covered a single test. A survey of a broader range of tests could have provided more insight into the impact of Covid-19; however, for clarity and for logistical reasons, we decided to limit the study to HbA1c. We selected HbA1c because it is an important test that affects a large population and has a widely accepted reference limit for abnormal results. We found that the decrease in HbA1c testing during the early phase of the pandemic was consistent with the pattern of total testing performed at a national reference laboratory and with the pattern of testing at a university hospital laboratory. Thus, the decrease in laboratory testing was widespread and was not isolated to HbA1c.

We did not collect data on subpopulations such as type I or type II diabetes, pediatric patients, or explore the underlying reason for the HbA1c test (e.g., diagnosis, annual exam, follow-up). While these data would provide additional insight, our objective was to identify broad patterns across multiple institutions. Collecting such data could be possible in a single institution but would have been challenging to collect across multiple institutions. We did not include the pediatric population which could account for a large portion of tests. It is possible that results differ for the pediatric population. Despite this, we believe our results show the impact of reduced access to testing on an important population.

The objective of the study was to identify broad patterns in testing volume and in abnormal results. Consequently, we did not perform a longitudinal analysis by patient to look for detailed patterns in testing. We assumed that testing would be approximately uniformly distributed over time and, for that reason, it was sufficient to compare aggregate results beginning in Jan 2019.

For more information, please refer to the diagram and the detailed description within the text.
Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cca.2021.04.018.

References

[1] Y.-C. Liu, R.-L. Kuo, S.-R. Shih, COVID-19: The first documented coronavirus pandemic in history, Biomed. J. 43 (4) (2020) 328–333.
[2] CDC, Chronic Diseases in America, 2020. https://www.cdc.gov/chronicdisease/resources/infographic/chronic-diseases.htm. (Accessed November 20 2020).
[3] Canadian Chronic Disease Indicators, Quick Stats, 2017. https://www.canada.ca/en/public-health/services/reports-publications/health-promotion-chronic-disease-prevention-canada-research-policy-practice/vol-37-no-8-2017/at-a-glance-2017-canadian-chronic-disease-indicators.html. (Accessed November 20th 2020).
[4] 6. Glycemic Targets: &em;gt;Standards of Medical Care in Diabetes—2020&lt;/em&gt;, Diabetes Care 43(Supplement 1) (2020) S66.
[5] B.M. Bonora, M.L. Morieri, A. Avogaro, G.P. Fadini, The Toll of Lockdown Against COVID-19 on Diabetes Outpatient Care: Analysis From an Outbreak Area in Northeast Italy, Diabetes Care (2020) dc201872.
[6] Standards of Medical Care in Diabetes—2020, Abridged for Primary Care Providers, Clinical Diabetes 38(1) (2020) 10–38.
[7] O.J. Driskell, D. Holland, J.L. Waldron, C. Ford, J.J. Scargill, A. Heald, M. Tran, F. W. Hanna, P.W. Jones, R.J. Pemberton, A.A. Fryer, Reduced testing frequency for glycated hemoglobin, HbA1c, is associated with deteriorating diabetes control, Diabetes Care 37 (10) (2014) 2731–2737.
[8] D.M. Nathan, The Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Study at 30 Years: Overview, Diabetes Care 37 (1) (2014) 9–16.
[9] Long-term effects of lifestyle intervention or metformin on diabetes development and microvascular complications over 15-year follow-up: the Diabetes Prevention Program Outcomes Study, The Lancet Diabetes & Endocrinology 3(11) (2015) 866–875.
[10] S.Y. Patel, A. Mehrotra, H.A. Huskamp, L. Uscher-Pines, I. Ganguli, M.L. Barnett, Trends in Outpatient Care Delivery and Telemedicine During the COVID-19 Pandemic in the US, JAMA Intern. Med. (2020).
[11] H. Sperling, G. Ruiz-Mercado, E.M. Schechter-Perkins, Impact of the 2020 COVID-19 Pandemic on Ambulatory Hepatitis C Testing, J. Prim. Care Community Health 11 (2020), 215012720969554.
[12] J.S. Riley, V.L. Lukas, L.F. de Pina, Z. Al Adas, J.B. Stoeker, B.M. Jackson, B. M. Braslow, D.N. Holena, COVID-19 Pandemic Significantly Decreases Acute Surgical Complaints, Am. Surg. (2020), 313G820949560.
[13] N. Braithe, W.U. Rehman, M. Alom, V. Skovira, N. Breiteh, I. Rehman, A. Yarkoni, H. Kahnsou, A. Rehman, Decrease in acute coronary syndrome presentations during the COVID-19 pandemic in upstate New York, Am. Heart J. 226 (2020) 147–151.
[14] K. Malik-Tabasum, M. Crooks, A. Robertson, C. To, L. Maling, G. Selmon, Management of hip fractures during the COVID-19 pandemic at a high-volume hip fracture unit in the United Kingdom, J. Orthop. 20 (2020) 332–337.
[15] S.J. Ferrando, L. Klepacz, S. Lynch, S. Shahar, R. Dornbush, A. Smiley, I. Miller, M. Tavakkoli, J. Regan, A. Bartell, Psychiatric emergencies during the height of the COVID-19 pandemic in the suburban New York City area, J Psychiatry. Res. (2020).
[16] Telemedicine: A Guide to Assessing Telecommunications in Health Care., 1996. https://www.ncbi.nlm.nih.gov/books/NBK45445/. (Accessed Nov 30th 2020).
[17] D. Su, J. Zhou, M.S. Kelley, T.L. Michaud, M. Shieh, J. Kim, F. Wilson, J. P. Stimpson, J.A. Pagán, Does telemedicine improve treatment outcomes for diabetes? A meta-analysis of results from 55 randomized controlled trials, Diabetes Res. Clin. Pract. 116 (2016) 136–148.
[18] H. Tchero, P. Kargambega, C. Briatte, S. Brunet-Houdard, G.R. Retali, E. Rusch, Clinical Effectiveness of Telemedicine in Diabetes Mellitus: A Meta-Analysis of 42 Randomized Controlled Trials, Telemed. J. E Health 25 (7) (2019) 569–583.
[19] D.A. Greenwood, S.A. Blois, H.M. Young, T.S. Nesbitt, C.C. Quinn, Overcoming Clinical Inertia: A Randomized Clinical Trial of a Telehealth Remote Monitoring Intervention Using Paired Glucose Testing in Adults With Type 2 Diabetes, J. Med. Internet Res. 17 (7) (2015), e178.
[20] F.A. Wilson, S. Rampa, K.E. Trout, J.P. Stimpson, Reimbursements for telehealth services are likely to be lower than non-telehealth services in the United States, J. Telemed. Telecare 23 (4) (2017) 497–500.
[21] S. Andrikopoulos, G. Johnson, The Australian response to the COVID-19 pandemic and diabetes – Lessons learned, Diabetes Res. Clin. Practice 165 (2020), 108246.
[22] N. Verougstraete, B. Lapauw, S. Van Aken, J. Delanghe, C. Stove, V. Store, Volumetric absorptive microsampling at home as an alternative tool for the monitoring of HbA1c in diabetes patients, Clin. Chem. Lab. Med. 55 (3) (2017) 462–469.
[23] P. RamsRumbe, How diabetes management is adapting amid the COVID-19 pandemic, Lancet Diabetes Endocrinol. 8 (7) (2020) 571.