COVID-19 Outcomes in Diabetic Patients with Continuous Glucose Monitoring: Role of Informatics Tools to Advance Clinical Research

By

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Table of Contents

Figures and Tables

Abstract

The coronavirus disease 2019 (COVID-19) has impacted healthcare systems and economies worldwide. Diabetes mellitus (DM) is another disease with global implications. Continuous glucose monitoring (CGM) systems have become a valuable tool for monitoring glucose levels and trends around the clock. This study sought to demonstrate that COVID-19 and diabetic patients with CGM are linked to better outcomes than those without CGM. The University of California, Davis Health System's (UCDHS) electronic health record (EHR) data and the analytical platform ATLAS were used. The following outcomes were defined: visits to the emergency room (ER), hospital stays, mechanical ventilation (MV), deaths, and glycated hemoglobin (A1c). ATLAS found 8,576 (11.51%) patients confirmed to have a positive COVID-19 result. Of them, 1,514 (17.65%) had a diagnosis of diabetes. 24 (1.59%) of them had a CGM, and 1,490 (98.41%) did not have a CGM. The ATLAS results support that COVID-19 and diabetic patients with CGM had better outcomes than those without CGM.

Introduction

The coronavirus disease 2019 (COVID-19) pandemic has impacted healthcare systems and economies around the globe. It is a severe public health burden. COVID-19 has affected more than 450 million people, and more than 60 million individuals have died worldwide as of March 2022 [1]. Diabetes mellitus (DM) is another primary medical concern on a global scale, and its severity has increased over the past 20 years. Diabetes afflicted 30 million people in 1985 and 463 million people in 2019. By 2045, 700 million individuals worldwide are expected to have diabetes [2]. In 2017, it was thought that the estimated annual economic burden of diabetes in the United States was $327 billion, an upswing of 60% from 2007 [3].

Type 1(T1D) or type 2 diabetes (T2D) is a significant risk factor for COVID-19 [4]. Diabetes has been estimated as the second most prevalent comorbidity in patients with serious COVID-19 caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) [5]. The pathophysiological mechanism is linked to short-term hyperglycemia caused by SARS-CoV-2, which suppresses the immune system, boosts coagulation activity, and directly damages the pancreatic islet cells responsible for insulin production [6]. Most existing research suggests that people with comorbidities, particularly diabetes, have a 2.3 times higher risk of severe COVID-19 infection and are at a 2.5 times higher risk of mortality [4], [6]. This is especially true when there is poor glycemic control. Patients with severe COVID-19 are also more likely to need mechanical ventilation and be sent to intensive care units (ICU) [4], [8].

In prior viral pandemics, an increase in morbidity and mortality rates in patients with T2D has also been observed. During the 2002–2003 SARS-CoV-1 outbreak, T2D was an independent risk factor for acute complications and death. During the Middle East respiratory syndrome

coronavirus (MERS-CoV) epidemic in 2012, people with T2D had a 35% higher chance of dying and a significantly higher odds ratio (7.2–15.7) for acute infection [7].

Personalized glycemic control is vital to effectively managing one's diabetes. This recommendation is especially crucial since it has been demonstrated to be highly connected to the mortality risk associated with COVID-19 [9]. Continuous glucose monitoring (CGM) systems have become a valuable tool for monitoring glucose levels and trends around the clock. The technology of CGM has been available to aid with diabetic self-management for nearly two decades [10]. The patient wears an adhesive sensor on their arm or stomach with a glucose-sensing electrode placed subcutaneously under the skin to measure the amount of glucose in the interstitial fluid (ISF). CGM sensors can be worn for up to 14 days [11].

The CGM devices have many appealing features. The sensors come with factory calibration and accuracy close to most blood glucose monitors [12]. The CGM alarms warn the patient of high, low, or rapid fluctuations in blood glucose levels, allowing for early intervention, thus improving glycemic control and preventing complications. CGM shows the user's current glucose and trends in glucose levels. Fingerstick self-monitoring of blood glucose (SMBG) gives you 2-4 data points. CGMs give you 288 data points in 24 hours, which is a much more thorough and complete glucose profile [11].

Real-time (rtCGM) and intermittently scanned CGM (isCGM), often known as flash glucose monitoring (FGM), are two different types of CGM devices that measure glucose in the interstitial fluid. IsCGM systems (which capture glucose every 15 minutes) only transfer data when the user scans their sensor with a dedicated reader or smartphone app. RtCGM systems capture glucose every five minutes and actively transmit data wirelessly from the sensor to a

dedicated reader, smartphone app, or integrated insulin pump. The captured data is then communicated to the "cloud." These cloud-based platforms that make it easy to share diabetic data have made it possible for clinicians to remotely check their patients' glucose levels and make treatment suggestions, especially during the COVID-19 pandemic shutdown [11], [13], [14].

Since the onset of COVID-19, various studies have been conducted to add value to diabetic care. Still, it is essential to note that most research examining the relationship between diabetes and COVID-19 used traditional point-of-care testing (POCTs) of blood glucose for glucose monitoring [15]. Of the current studies using the CGM device, some authors have evaluated the relationship between measurements of glycemic control, such as time-in-range (TIR), time-above-range (TAR), and time-below-range (TBR) and COVID-19 [16]. In contrast, others have investigated the threshold of glycemic control and its relationship to the outcomes of COVID-19 [9]. A few studies demonstrated the ongoing challenges faced by people with diabetes during the COVID-19 lockdown (LD) and the availability of services to manage diabetes, from education to technology [10], [17]. Finally, various researchers have explored the safety and accuracy of CGM technology use in a hospital during the pandemic. These studies also looked into reducing the number of POCTs, the risk of exposure to staff, and the use of personal protective equipment (PPE) in a hospital setting [18]–[20].

Although the subject of CGM and COVID-19 infection in diabetics has been receiving attention during the pandemic, opportunities exist for further research and clinical data to be extracted and evaluated to supplement the current evidence. This study sought to demonstrate that COVID-19 and diabetic patients with CGM are associated with better outcomes than those

without CGM using the analytical platform ATLAS. ATLAS (version 2.7) is an open-source, web-based software platform that generates reliable evidence from patient-level observational data [21]. ATLAS executed analyses on the data sourced from DataPATH, a de-identified database at the University of California, Davis Health System (UCDHS). The ATLAS data was used to test the hypothesis and provide additional information about the patients with and without CGM. The findings of this study may add value to the available research and emphasize the significance of CGM use in people with diabetes in the presence of COVID-19. Ultimately, this study offers an opportunity to use advanced informatics tools such as ATLAS to conduct research and generate knowledge.

Methods

Study design and Participants

The present study was conceived as a retrospective observational design. Two groups were defined in ATLAS for comparison from the DataPATH database: patients with COVID-19 disease and diabetes with CGM (Group 1 or G1) and patients with COVID-19 disease and diabetes without CGM (Group 2 or G2). The database's observation period must have occurred from 2020-01-01 to the present. Individuals must also be at least 18 years old. Each group was evaluated and described using the following variables: emergency room (ER) visits, inpatient visits, mechanical ventilation (MV), deaths, and glycated hemoglobin (A1c). Additional descriptive statistics were obtained using the following features: The demographic characteristics included ethnicity, gender, and age. The Diabetes Comorbidity Severity Index (DCSI) is a scale that ranks the severity of diabetic complications [22]. The Charlson Comorbidity Index (CCI) assists in predicting the risk of mortality due to comorbid diseases [23]. Finally,

Condition Group Era Long Term is defined as “one covariate per condition era rolled up to groups in the condition_era table overlapping with any part of the long-term window.” [21]

Data Sources and Analytical Platforms

The Observational Health Data Sciences and Informatics (OHDSI) is a multi-stakeholder, multi-disciplinary collaboration aimed at maximizing the value of health data through large-scale analytics and data standardization. The global OHDSI community creates and disseminates a standard data model known as the Observational Medical Outcomes Partnership (OMOP) Common Data Model (CDM) CDM v5.4 [24]. The OHDSI community has made the analytical platform ATLAS [21] so that studies can be done across observational databases that have been standardized to the OMOP CDM.

Figure 1 illustrates how data is converted at UCDHS from EHR databases into OMOP CDM and then consumed by OHDSI’s ATLAS for analyses. Patient data from Epic, an EHR, is stored in hierarchical databases called Chronicles. The data is then extracted into a relational database called Clarity. Clinical data from Clarity is further transformed into specific domains (e.g., procedure, visit, measurement) and standard vocabularies (e.g., CPT, SNOMED, LOINC) in the UCDHS Identified OMOP database. Lastly, the standardized data is extracted as de-identified data, stored in UCDHS DataPATH, and connected to the ATLAS instance [25]. Permission was obtained to access the ATLAS platform at UCDHS for analysis.

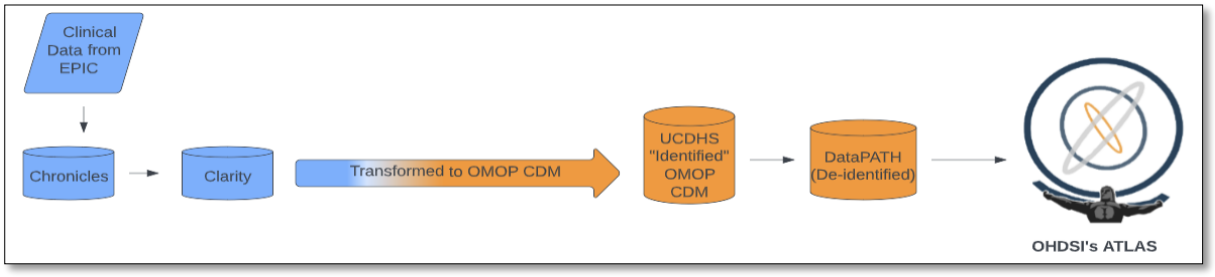

Figure 1: Data conversion from Epic to OMOP CDM for ATAS

ATLAS includes numerous critical features that aid in the search for concepts, creating concept sets, and using these concept sets to form cohorts. Moreover, using the person-level data from these cohorts, the cohort(s) of interest may be characterized to produce descriptive summary statistics. A cohort must be defined to perform analyses within ATLAS. The Book of OHDSI defines a cohort as a group of people who meet one or more inclusion criteria for a given period [21]. The following parts of the paper will discuss how cohorts were generated for this study.

ATLAS' Search Tool

The search function in ATLAS enables users to explore OMOP standardized vocabulary and find the set of concepts to build cohorts. Athena is another tool within OHDSI that affords users the same ability to search for concepts (21). The set of concepts and codes that define a cohort were found using both tools for this study.

ATLAS' Concept Set Tool

Concept sets are another prominent feature of the ATLAS instance. A concept set is an expression that represents a list of concepts that can be reused in various cohort definitions. A concept set comprises of multiple words from the standardized vocabulary and logical indicators that let the user choose whether to include or exclude similar words from the

vocabulary hierarchy. Each concept set has a unique concept ID and a code accompanying that specific concept name. In addition, every concept set belongs to a domain in the CDM table mapped to a medical vocabulary [21]. All the generated concept sets for this study were saved in ATLAS to be used later to build cohort definitions (

Table 1).

Table 1: Concept sets created in ATLAS

ID	Concept Set Name	Concept Set Expression	Included Concepts	Domain	Vocabulary	Standard	Descendants
77	Diabetes Mellitus (DM)	1	127	Condition	SNOMED	Yes	Yes
102	CGM	5	7	Measurement Procedure	SNOMED CPT4	Yes	Yes
109	COVID-19	12	45	Measurement	LOINC	Yes	Yes
113	ER Visit	1	3	Visit	Visit	Yes	Yes
79	Inpatient Visit	1	29	Visit	Visit	Yes	Yes
105	Mechanical Ventilation	11	12	Observation Measurement Procedure	SNOMED LOINC ICD9Proc	Yes	Yes
112	A1c	2	2	Measurement	LOINC	Yes	Yes

ATLAS' Cohort Definition Tool

The cohort definition function in ATLAS uses the previously created concept sets while applying a rule-based approach to build cohorts and identify the groups of patients for the present study. The results from cohort definitions allows researchers to draw conclusions based on HER data. A cohort definition specifies when a person qualifies (or does not qualify) for a cohort throughout the clinical observation period. OHDSI employs three building blocks for a cohort definition: cohort entry event, inclusion criteria, and cohort exit. A cohort entry event occurs at a specific time to qualify an individual for cohort entry. Inclusion criteria search for observations that qualify or disqualify someone from continuing in the cohort by using the cohort entry event as an anchor in time to construct temporal logic. Cohort exit is the point in time when an individual no longer qualifies for a cohort and exits [21].

Table 2 and Table 3 illustrate the cohort definitions and the three building blocks for G1 and G2, respectively. The COVID-19 concept set was imported and used as the initial event establishing entry for both groups. In addition, the measurement concept values (positive, detected, and reactive) that describe a COVID-19 test were added to limit the entry to only patients with positive COVID-19 test results. The cohort entry date must have occurred on or after 2020-01-01. The patients also must be age 18 or older. Lastly, these patients must have a diagnosis of diabetes. Since there were limited observations before the cohort entry date, which would have reduced the number of patients, this data was not included. Inclusion criteria were applied to further constrain the patients from entering the cohort based on initial entry. Previously created concept sets were imported into the inclusion criteria specific to each cohort definition, as depicted in the tables. The patients exited the cohort when the continuous observation concluded.

Table 2: Cohort Definitions constructed for G1

Cohort Definitions	Cohort Entry Event	Inclusion Criteria	Cohort Exit
COVID-19 and Diabetes with CGM (initial)	→ COVID-19 Test → Values as: Positive, Detected, and Reactive → On/after 2020-01-01 → Age ≥ 18 → Diabetes → Continuous observation of at least 0 days before and 0 days after → All events per person	√ CGM	The event will persist until the end of continuous observation.
COVID-19 and Diabetes with CGM: ER Visits		√ CGM √ ER Visits	
COVID-19 and Diabetes with CGM: Inpatient Visits		√ CGM √ Inpatient Visits	
COVID-19 and Diabetes with CGM: MV		√ CGM √ Mechanical Ventilation	
COVID-19 and Diabetes with CGM: Deaths		√ CGM √ Deaths	
COVID-19 and Diabetes with CGM: A1c ≥ 9%		√ CGM √ A1c value	
COVID-19 and Diabetes with CGM: A1c < 8% after 6-12 months later		√ CGM √ A1c value < 8% after 6-12 months	

Table 3: Cohort Definitions constructed for G2

Cohort Definitions	Cohort Entry Event	Inclusion Criteria	Cohort Exit
COVID-19 and Diabetes without CGM (initial)	→ COVID-19 Test → Values as: Positive, Detected, and Reactive → On/after 2020-01-01 → Age ≥ 18 → Diabetes → Continuous observation of at least 0 days before and 0 days after → All events per person	× CGM	The event will persist until the end of continuous observation.
COVID-19 and Diabetes without CGM: ER Visits		× CGM √ ER Visits	
COVID-19 and Diabetes without CGM: Inpatient Visits		× CGM √ Inpatient Visits	
COVID-19 and Diabetes without CGM: MV		× CGM √ Mechanical Ventilation	
COVID-19 and Diabetes without CGM: Deaths		× CGM √ Deaths	
COVID-19 and Diabetes with CGM: A1c ≥ 9%		× CGM √ A1c value ≥ 9%	
COVID-19 and Diabetes with CGM: A1c < 8% after 6-12 months later		× CGM √ A1c value < 8% after 6-12 months	

ATLAS' Cohort Characterization Tool

Lastly, the characterization tool in ATLAS describes the pre- and post-index traits of the patients in the cohort. OHDSI characterizes clinical observations in an individual's history using descriptive statistics, essentially providing an enhanced summary of the group(s) of interest

being studied [21]. The cohort definitions of the two interest groups were imported into the characterization tool for analyses with the following features: DCSI, Charlson Index, Condition Group Era Long Term, ethnicity, gender, and age Figure 2

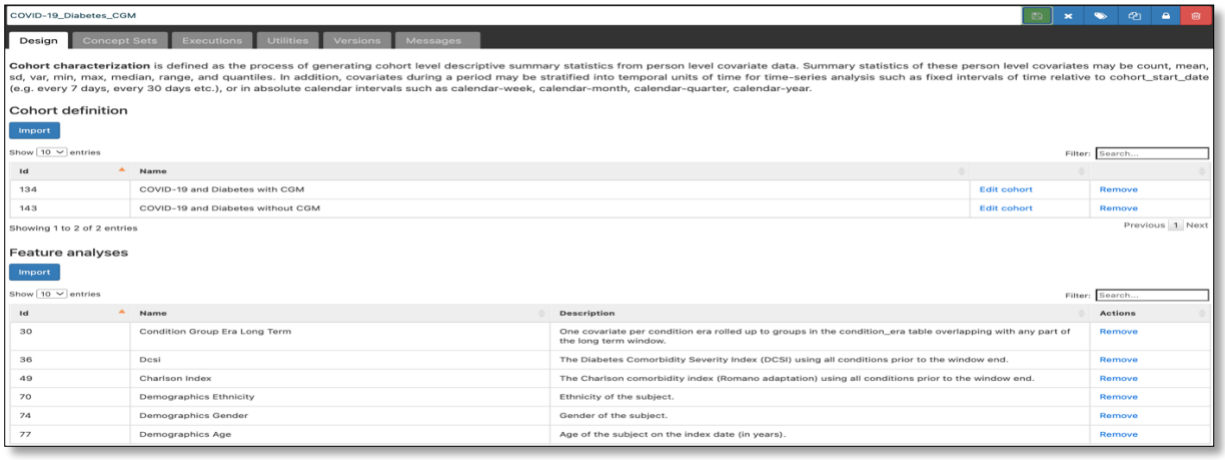

Figure 2: Cohort characterization tool displaying the cohorts of interest

Results

Each cohort definition was executed for G1 and G2; the output is summarized in the table below. ATLAS found 74,517 patients with a COVID-19 test, 33,628 patients with diabetes, and 350 patients with CGM in the DataPATH database. It is also important to note that only one percent of the total diabetic population in DataPATH had a prescription for a CGM. Among the COVID-tested patients, 8,576 (11.51%) patients were confirmed to have a positive COVID-19 result. Of the COVID-19-positive patients, 1,514 (17.65%) of them had a diagnosis of diabetes. Finally, 24 (1.59%) of the COVID-19-positive and DM patients had a CGM, and 1,490 (98.41%) did not have a CGM. The characterization tool also contributed person-level summary statistics of the selected covariates described later in this section.

Execution of Cohort Definitions

The ATLAS-generated results of each cohort definition for G1 are listed in Table 4. Only 24 (1.59%) patients with COVID-19 infection and diabetes had a CGM device. The data showed that roughly one percent (n=6) of the group had an ER visit, and only two had an inpatient record. ATLAS did not find any patients on the ventilator that met the specific cohort definition for that variable. Two deaths were found among this group. Approximately one percent (n=16) of the 1,514-person population met the cohort definition for an A1c $\geq$ of 9%. 5 (31.25%) patients showed an improved A1c of $<$ 8% after six to twelve months.

Table 4 also summarizes the output for G2. ATLAS identified 1,490 (98.41%) patients with COVID-19 infection and diabetes without a CGM device. The findings showed that 308 (20.34%) had ER visits, and 467 (55.75%) had inpatient visits. The data also showed 7 (0.46%) of the patients were on the ventilator. ATLAS reported 107 (7.07%) deaths in the G2 population. Approximately 494 (32.63%) of the 1,514-person population met the cohort definition for an A1c $\geq$ of 9%. 101 (20.45%) patients showed an improved A1c of $<$ 8% after six to twelve months.

Table 4: The output of each cohort definition for GI and G2
Count (N and %) is out of 1,514

Cohort Definitions	**G1**	**G2**
	N (%)	**N (%)**
COVID-19 and DM with CGM	24 (1.59)	1,490 (98.41)
COVID-19 and DM without CGM		
COVID-19 and DM with CGM- ER Visits	6 (0.99)	308 (20.34)

COVID-19 and DM without CGM- ER Visits		
COVID-19 and DM with CGM- Inpatient Visits	2 (0.13)	467 (55.75)
COVID-19 and DM without CGM- Inpatient Visits		
COVID-19 and DM with CGM- MV	0	7 (0.47)
COVID-19 and DM without CGM- MV		
COVID-19 and DM with CGM- Deaths	2 (0.13)	107 (7.07)
COVID-19 and DM without CGM- Deaths		
COVID-19 and DM with CGM- A1c ≥ 9 %	16 (1.06)	494 (32.63)
COVID-19 and DM without CGM- A1c ≥ 9%		
COVID-19 and DM with CGM- A1c < 8% after 6-12 months (N is out of 16)	5 (31.25)	101 (20.45)
COVID-19 and DM without CGM- A1c < 8% after 6-12 months (N is out of 494)		

Execution of Cohort Characterization

Table 5 summarizes the descriptive statistics produced by the characterization tool. G1 had 19 (79.17%) individuals non-Hispanic or Latino and 5 (20.83%) Hispanic or Latino. Moreover, 11 (46.00%) were females, and 13 (54.00%) were males in this group. The mean age of the group was 50.08 (range 18-78). The mean CCI was 5.33, and the mean DSCI was 5.79. In G2, the characterization tool revealed that 1,106 (74.23%) of patients were non-Hispanic or Latino, while 329 (22.08%) were Hispanic or Latino. In addition, the tool characterized 758 (51.00%)

females and 732 (49.00%) males with a mean age of 60.45 (range 18-90). The CCI mean was 5.00, and the DSCI mean was 3.66.

Table 5: Summary statistics of selected covariates: demographics, CCI, and DSCI

Covariate	COVID-19 and Diabetes with CGM (G1)	COVID-19 and Diabetes without CGM (G2)
Not Hispanic or Latino	19 (79.17%)	1,106 (74.23%)
Hispanic or Latino	5 (20.83%)	329 (22.08%)
Female	11 (46.00%)	758 (51.00%)
Male	13 (54.00%)	732 (49.00%)
Mean Age	50.08 (range: 18-78)	60.45 (range: 18-90)
CCI Mean	5.33 (min: 1.00, max: 18:00)	5.00 (min:0, max:21.00)
DSCI Mean	5.79 (min: 0, max: 10.00)	3.66 (min:0, max:13.00)

Table 6 displays the baseline prevalence of the selected conditions using the characterization tool. The findings indicated that the baseline prevalence of diabetes was higher in G1 (95.83%) than in G2 (77.99%) before the cohort entry date. The baseline prevalence of hypertensive disorders was the highest after conditions related to diabetes and pain. The difference (G1- 54.17% and G2- 55.97%) in prevalence between both groups was insignificant. A higher prevalence of diabetes-related complications such as CKD (25.00% vs. 21.28%), neuropathy (29.17% vs. 10.67%), retinopathy (33.33% vs. 7.38%), and PVD (8.33%

vs. 4.63%), was observed in G1. Conditions such as Cerebrovascular disease (8.33% vs. 4.70%) also prevailed in this group prior to the cohort entry. The occurrence of heart disease (36.64% vs. 25.00%) was higher in the G2 population, while the occurrence of CHF in both groups was 12%. Malignant neoplastic diseases (15.10% vs. 8.33%) and obesity (23.76% vs. 12.50%) prevailed in G2. While COPD (7.32% vs. 4.17%) was predominating in G2, PHTN (12.50% vs. 2.62%) was more dominant in G1.

Table 6: Prevalence of selected covariate: Conditions

Covariate	**COVID-19 and Diabetes with CGM (G1)**	**COVID-19 and Diabetes without CGM (G2)**
DM	23 (95.83%)	1,162 (77.99%)
T1D	12 (50.00%)	55 (3.69%)
T2D	16 (66.67%)	1,106 (74.23%)
Hypertensive disorder	54.17%	55.97%
Chronic kidney disease (CKD)	25.00%	21.28%
Neuropathy due to DM	29.17%	10.67%
Retinopathy due to DM	33.33%	7.38%
Obesity	12.50%	23.76%
Congestive heart failure (CHF) **Heart disease**	12.50% 25.00%	12.62% 36.64%
Malignant neoplastic disease	8.33%	15.10%

Cerebrovascular disease	8.33%	4.70%
Chronic obstructive pulmonary disease (COPD) **Pulmonary hypertension (PHTN)**	4.17% 12.50%	7.32%, 2.62%
Peripheral Vascular Disease (PVD) due to DM	8.33%	4.63%
Immunodeficiency disorders	0	3.29%

Discussion

In this observational study, the ATLAS results supported that COVID-19 and diabetic patients with CGM (G1) had better outcomes than those without CGM (G2). Patients with COVID-19 and diabetes using a CGM (G1) were linked to having fewer hospital stays, trips to the ER, mechanical ventilation, and deaths despite having a significantly high baseline prevalence of neuropathy, CKD, retinopathy, CVD, PHTN, and PVD. In addition, the findings showed a lower occurrence of an A1c of $\geq$ 9% in the G1 group (16 (1%) vs. 494 (33%)). A more significant improvement in A1c of < 8% after six to twelve months was seen in this CGM population (5 (31%) vs. 101 (20%)). ATLAS' characterization tool also summarized that in the G2 population, only 1,162 (78%) of the patients had a baseline prevalence of DM prior to cohort entry. During the pandemic, more attention was paid to CGM systems to manage diabetes remotely and lower the risk of COVID-19 transmission [1]. The ability of CGM sensors to provide access to detailed glucose data makes it easier for healthcare professionals (HCPs) to use real-time data

to make informed decisions about patient care. The detailed information lets HCPs figure out how well the treatments work, change the dosages of medications, and have enlightening conversations about how diet, exercise, stress, and illness affect glycemic control. Patients can also use glucose data to learn how their actions affect their blood sugar levels and change their behavior to improve glycemic control [11], [17].

Patients with COVID-19 and diabetes using a CGM (G1) were associated with fewer hospital stays, trips to the ER, mechanical ventilation, and deaths despite having a significantly high baseline prevalence of several diabetic-related complications. One possible explanation is that because G1 patients had these complications, a CGM was prescribed to prevent life-threatening illnesses. Miller noted in a study that candidates for CGM are individuals with comorbidities, poorly managed diabetes, and are at risk for hospitalization for complications related to uncontrolled glucose [26]. However, due to the CGM's ability to measure TIR, TBR, and TAR, the device indirectly benefited the G1 population during the COVID-19 pandemic.

Researchers have found that people with COVID-19 and diabetes who have dysglycemia, when their blood sugar levels are low, high, or fluctuating, are more likely to have complications and adverse outcomes [18]. This study suggests that having access to detailed glucose data from the CGM may have made it possible to treat dysglycemia early, thus reducing the risk of adverse outcomes in the G1 population. The technology of CGM is the best way to measure exposure to high, low, and fluctuations in blood sugar levels. In a cross-sectional study, researchers found that people with more fluctuations in their blood sugar levels had a higher risk of composite (ICU admission, need for mechanical ventilation, or morbidity with critical illness) adverse COVID-19 outcomes and more extended hospital stays. Furthermore, patients who had the

composite adverse outcomes had significantly higher TBR (4.43 ± 11.4% vs. 0.54 ± 0.65%) [P < 0.01] than patients without the composite adverse outcomes. Another retrospective analysis reported that ICU patients with more significant fluctuations in their blood sugar levels were more likely to die [18]. Lastly, Longo et al. [27] found that people with diabetes who used a CGM had stable or even better glucose control during the pandemic, even though their lifestyles had changed and they had limited mobility.

The findings showed fewer patients in the G1 group with an A1c of 9% or more than in the G2 group. Moreover, more patients had an A1c reduction of less than 8% in the G1 group than in the G2 group after 6-12 months. A1c has been used a lot as a measure of glycemic management because it is very good at predicting complications from diabetes. Fingerstick SMBG only measures the blood glucose level at the testing time. Also, SMBG needs to give a complete picture of how glucose levels change or how they are managed [26]. We only found evidence of improved A1c in patients with diabetes and CGM before the COVID-19 pandemic. One such example was seen in a study by Wright et al. [28] that included 1,034 participants with T2D receiving non-insulin treatments and basal insulin therapy with a prescription for flash CGM. The proportion of patients with an A1c of 12.0% at baseline dropped by more than half (a reduction of 3.7%). There was also a significant rise in the number of people who achieved A1c levels of less than 8 or 7%. In another study, Gilbert et al. [29] found similar results with 248 diabetic patients with CGM whose A1c went from 8.2% at baseline to 7.1%, which is a significant change. This study of diabetes with CGM in people with SARS-CoV-2 showed similar results for A1c levels, which is in line with what other studies have found prior to the pandemic.

The characterization summary from ATLAS also showed that in the G2 population, 1,162 (78%) of the patients had a prevalence of diabetes. The question is, what happened to 328 (22%) of the individuals? One reason could be that some cohort participants were not observed in the database before entering the cohort. Another reason could be that some may have acquired diabetes after contracting COVID-19 infections. The most recent cohort study found that veterans with COVID-19 were around 40% more likely than veterans in the control groups to develop diabetes up to a year later. Also, almost three times as many people got diabetes if the COVID-19 infection was severe enough to require hospitalization or the ICU [30]. A new study says that SARS-CoV-2 may also directly hurt the pancreas, worsening hyperglycemia and causing people who did not have diabetes before to get it [2].

There were several limitations to this study. A major limitation was the observational design. It is also important to note the unevenness of the sample sizes of the groups and the small sample size for the CGM group. Another limitation of this study was the use of a single database from one hospital. Another point to be noted is that much like clinical databases at other hospitals, UCDHS does not successfully capture deaths outside of the hospital after discharge to home or residential homes.

Because of the limited accessibility, we did not use programming languages in the data-gathering process. In the future, ATLAS and using a programming language in combination would significantly benefit the study. While ATLAS provides the original programming, it can be customized and run-on database servers to extract additional information on the individuals within the cohort of interest. For example, we could further investigate using programming language to determine if 22% of the people were diagnosed with DM after getting COVID-19 or

if some were out of the database before the entry date. Lastly, another limitation is that we did not have the glucose metrics from the CGM. This information would serve as a major strength.

Conclusion

Diabetes and COVID-19 are two diseases that have global implications. Personalized glycemic control is essential for diabetes management. CGM's ability to measure TIR, TAR, and TBR is critical for preventing short-term and long-term complications of diabetes. Despite several study limitations, ATLAS results support that COVID-19 and diabetic patients with CGM had better outcomes than those without CGM. Though a high prevalence of diabetes-associated complications (kidney damage, heart and blood vessel disease, blindness, nerve damage, and abnormalities of the lower limbs) in G1 were seen, COVID-19-related outcomes such as inpatient visits, ER visits, MV, and deaths were seen less. Reductions in the A1c values were noted in this population as well. The results of this study emphasize the significance of CGM use in people with diabetes in the presence of COVID-19. The preliminary findings obtained from OHDSI's ATLAS create an opportunity to explore the research question further using a larger sample size, multiple hospitals for the data source, and data gathering using advanced informatics tools combined with a programming language.

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