Excess All-Cause and Cause-Specific Mortality Among People with Diabetes During the COVID-19 Pandemic in Minnesota: Population-Based Study

INTRODUCTION

Diabetes and its comorbidities are risk factors for severe, including fatal, COVID-19 disease.[1] Diabetes also requires regular monitoring, pharmacologic treatment, and access to medical care, all of which may have been disrupted during the COVID-19 pandemic. While preliminary data suggested that diabetes-specific mortality in the general population increased in the USA in association with the COVID-19 pandemic,[2] population-level data on the rates, circumstances, and causes of death during the pandemic among people with diabetes are scarce.

METHODS

Minnesota death certificates from 2018 to 2019 and 2020 were examined to identify those with diabetes as the primary or contributing (among all causes listed) cause of death. Deaths were then classified based on the primary cause of death; however, deaths listing COVID-19 among the top five contributing causes were classified as COVID-19 deaths. Deaths per 100,000 people with diabetes were calculated using population statistics for Minnesota[3] and compared between time periods using incidence rate ratios with 95% confidence intervals. Sensitivity analyses examined all-cause and diabetic ketoacidosis (DKA)/hyperglycemic hyperosmolar state (HHS) deaths for 2018, 2019, and 2020 separately. Demographics and death characteristics were compared using two-sided Fisher's exact and chi-squared tests adjusted using the Benjamini-Hochberg correction.[4] This study was exempt from Institutional Board Review because data was publicly available, all subjects are deceased, and no identifiable information was included.

RESULTS

COVID-19 resulted in 246 deaths per 100,000 Minnesotans with diabetes in 2020 (Table 1). All-cause mortality increased from 1,484 to 1,922 per 100,000 (IRR 1.30 [95% CI 1.26–1.33]), increasing most between 2019 and 2020. The proportion of deaths with diabetes as the primary cause that were caused by DKA/HHS decreased in 2020 (2018: 5.09%; 2019: 5.43%; 2020: 4.85%). Non-COVID mortality increased from 1,484 to 1,675 per 100,000 (IRR 1.13 [95% CI 1.10–1.16]). Deaths with diabetes as the primary cause increased slightly (IRR 1.08 [95% CI 1.01–1.15]); this was not significant after adjustment for multiple comparisons (corrected P-value 0.07). However, deaths from cardiovscular disease (IRR 1.08 [95% CI, 1.02–1.15]), cancer (IRR 1.27 [95% CI, 1.17–1.37]), and non-COVID-19 infectious diseases (IRR 1.47 [95% CI, 1.18–1.84]) increased by statistically significant amounts.

Deceased people with diabetes in 2020 were more likely to belong to a racial or ethnic minority group (Table 2). There was no difference in other demographics or the proportions of deaths that occurred in rural vs. urban areas and at home vs. other locations.

DISCUSSION

We did not find a significant increase in deaths with diabetes as the primary cause among Minnesotans with diabetes. However, all-cause mortality among people with diabetes increased 30% in 2020 compared to prior years, an excess of 438 deaths per 100,000 people with diabetes. This increase represents a reversal in diabetes-related mortality gains that were described previously through 2015.[5] COVID-19 contributed to 246 deaths per 100,000 people, with the remainder due to other causes, particularly cardiovascular disease, cancer, and other infections. These deaths may stem from deferral of care for both chronic and acute health concerns,[6] resulting in potentially preventable deaths. Importantly, these deaths may also reflect

Table 1 Causes of Death in Minnesota with Diabetes as a Primary or Contributing Cause

	2018-2019 (N = 12101)		2020 (N = 7953)		Incidence rate ratio (IRR)		
	Deaths No.	Per 100,000	Deaths No.	Per 100,000	IRR	95% CI	P-value*
All-cause mortality	12101	1483.72[†]	7953	1921.89	1.30	1.26–1.33	<0.001*
COVID-19	0	0.00	1020	246.49	—	—	—
Non-COVID mortality	12101	1483.72	6933	1675.40	1.13	1.10–1.16	<0.001*
Cause-specific mortality (as primary cause of death)							
Cardiovascular diseases	3096	379.61	1699	410.57	1.08	1.02–1.15	0.03 *
Diabetes	2679	328.48	1462	353.30	1.08	1.01–1.15	0.07
All others	2294	281.27	1367	330.34	1.17	1.10–1.26	< 0.001 *
Malignant neoplasms (cancer)	1598	195.93	1028	248.42	1.27	1.17–1.37	< 0.001 *
Cerebrovascular diseases	581	71.24	340	82.16	1.15	1.01–1.32	0.09
Chronic lower respiratory diseases	515	63.14	273	65.97	1.04	0.90–1.21	0.84
Alzheimer's disease	464	56.89	245	59.21	1.04	0.89–1.21	0.87
Infectious diseases	181	22.19	135	32.62	1.47	1.18–1.84	0.003 *
Parkinson's disease	115	14.10	73	17.64	1.25	0.93–1.68	0.32
Kidney disease	113	13.86	57	13.77	0.99	0.72–1.37	1.00
Alcoholic liver disease	82	10.05	50	12.08	1.20	0.85–1.71	0.58
Pneumonia/other acute lower respiratory infections	105	12.87	49	11.84	0.92	0.66–1.29	0.88
Accidental poisoning or exposure to noxious substances	69	8.46	43	10.39	1.23	0.84–1.80	0.58
Cirrhosis/other chronic liver disease	58	7.11	38	9.18	1.29	0.86–1.94	0.50
Other unintentional injury	55	6.74	28	6.77	1.00	0.64–1.58	1.00
Influenza	42	5.15	16	3.87	0.75	0.42–1.34	0.62
Malnutrition	9	1.10	12	2.90	2.63	1.11–6.24	0.09
Motor vehicle accident	26	3.19	11	2.66	0.83	0.41–1.69	0.88
Suicide	17	2.08	7	1.69	0.81	0.34–1.96	0.88

P-values (not confidence intervals) were adjusted for multiple comparisons; statistical significance after adjustment is indicated by an asterisk. [†]In a sensitivity analysis, we examined all-cause mortality in 2018 and 2019 separately. There were 5901 deaths in 2018 (1450.99 per 100,000) and 6205 deaths in 2019 (1516.27 per 100,000); IRR 1.045 (95% CI, 1.008–1.083) for 2019 vs. 2018. Comparing 2020 to 2019, we get IRR 1.268 (95% CI, 1.226–1.310)

worsening long-term complications of diabetes (e.g., cardiovascular disease) and complications of poor glycemic control (e.g., infection). Reasons for deferral of care are multifactorial, including reduced routine visit availability secondary to COVID-19-related visits, as well as patients deferring non-urgent care to decrease COVID-19 exposure. Importantly, Hispanic, American Indian, Asian/ Pacific Islander, and Black Minnesotans experienced a disproportionate increase in deaths in 2020, underscoring the impact of the pandemic on minority communities. Finally, the full impact of the pandemic on long-term control of diabetes and its complications are likely to manifest over the years to come, calling for continued

surveillance for increased morbidity and mortality in this high-risk population.

While this is the first population-based study examining the impact of COVID-19 on mortality among people with diabetes, it is limited to one state and may not generalize to other populations. There is risk for misclassification of causes of death and underascertainment of diabetes when using causes of death to identify people with diabetes. Deaths due to COVID-19 are likely undercounted due to undiagnosed disease, complications of prior COVID-19 that were not coded as such, or attribution to other causes even if COVID-19 was present. Nevertheless, our findings underscore the need for uninterrupted comprehensive care

Table 2 Characteristics of Deceased Individuals with Diabetes in 2020 Compared to 2018–2019

	2018–2019 (N = 12101)	2020 (N = 7953)	P-value
Sex			.26
Female	5399 (44.6%)	3483 (43.8%)	
Male	6702 (55.4%)	4470 (56.2%)	
Age group			.16
0–4 years	0 (0.0%)	0 (0.0%)	
5–14 years	0 (0.0%)	2 (0.0%)	
15–24 years	11 (0.1%)	8 (0.1%)	
25–34 years	63 (0.5%)	37 (0.5%)	
35–44 years	140 (1.2%)	97 (1.2%)	
45–64 years	1800 (14.9%)	1227 (15.4%)	
65–84 years	6229 (51.5%)	4172 (52.5%)	
≥85 years	3858 (31.9%)	2410 (30.3%)	
Race and ethnicity			<0.001*
Hispanic	181 (1.5%)	165 (2.1%)	
Non-Hispanic American Indian	230 (1.9%)	179 (2.3%)	
Non-Hispanic Asian/Pacific Islander	314 (2.6%)	225 (2.8%)	
Non-Hispanic Black	547 (4.5%)	419 (5.3%)	
Non-Hispanic White	10791 (89.2%)	6937 (87.2%)	
Other	20 (0.2%)	19 (0.2%)	
Unknown	18 (0.1%)	9 (0.1%)	
Marital status			0.03*
Never married	1399 (11.6%)	940 (11.8%)	
Married	4543 (37.5%)	3016 (37.9%)	
Separated or divorced	2050 (16.9%)	1438 (18.1%)	
Widowed	4084 (33.7%)	2539 (31.9%)	
Unknown	25 (0.2%)	20 (0.2%)	
County of residency			0.81
Non-rural county	8599 (71.1%)	5664 (71.2%)	
Rural county	3502 (28.9%)	2289 (28.8%)	
Place of death			0.61
Decedent's home	3858 (31.9%)	2546 (32.0%)	
Hospice facility	292 (2.4%)	170 (2.1%)	
Hospital—outpatient	542 (4.5%)	368 (4.6%)	
Hospital—inpatient	2790 (23.1%)	1886 (23.7%)	
Nursing home/long-term care facility	4128 (34.1%)	2678 (33.7%)	
Other	491 (4.1%)	305 (3.8%)	

P-values were adjusted for multiple comparisons; statistical significance after adjustment is indicated by an asterisk

for people with diabetes, particularly those from racial/ethnic minority populations.

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Declarations:

Conflict of Interest: In the last 36 months, Dr. McCoy has received unrelated support from NIDDK, PCORI, and AARP®. She also serves as a consultant to Emmi® (Wolters Kluwer) on the development of patient education materials related to prediabetes and diabetes. In the past 36 months, Dr. Jeffery has received unrelated funding from the US Food and Drug Administration; the National Heart, Lung, and Blood Institute; the National Institute on Drug Abuse; the National Center for Advancing Translational Sciences; the Agency for Healthcare Research and Quality; and the American Cancer Society. Her spouse holds shares in Goodness Growth Holdings. Dr. Clements serves as a consultant to Vail Scientific for an area unrelated to this work (sepsis). Dr. Campbell is an author for UpToDate and a consultant to Byrn Pharma for an area of unrelated to this work (anaphylaxis).

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