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Cost-effectiveness of telemedicine care for patients with uncontrolled type 2 diabetes mellitus during the COVID-19 pandemic in Saudi Arabia

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Abstract

Background and aim: Telemedicine could be used to provide diabetes care with positive clinical outcomes. Consequently, this study evaluated the cost-effectiveness of telemedicine for patients with uncontrolled type 2 diabetes mellitus (i.e. HbA1c >9).

Patients and methods: This was a retrospective chart review of patients with uncontrolled type 2 diabetes attending an outpatient integrated care clinic. The study consisted of two arms, namely a telemedicine care model and a traditional care model with 100 patients in each. The clinical effectiveness (i.e. reduction in HbA1c) and the total cost in both arms were determined, and the incremental cost-effectiveness ratio was calculated. This study adopted propensity score matching.

Results: The patients in the telemedicine care model had a mean reduction in their HbA1c level of 1.82 (95% CI = 1.56–2.09, $p < 0.001$), while those in the traditional care model had a mean reduction of 1.54 (95% CI = 1.23–1.85, $p < 0.001$). Consequently, the incremental effect was 0.28 (95% CI = −0.194 to 0.546). The mean total costs were SAR 4819.76 (US$1285.27) and SAR 4150.69 (US$1106.85) for patients in the telemedicine and traditional care models, respectively. Consequently, the incremental cost was SAR 669.07 (US$178.42) [95% CI = SAR 593.7 (US$158.32)–SAR 1013.64 (US$270.30)]. The ICER was estimated to be SAR 2372.52 (US$632.67) per 1% reduction in the level of HbA1c. Moreover, the telemedicine care model resulted in a higher cost and better outcome (i.e. reduction in the HbA1c level) with an 81.80% confidence level.

Conclusion: Telemedicine care is cost-effective in managing type 2 patients with poorly controlled diabetes. Consequently, we believe that telemedicine care can be further expanded and incorporated into routine diabetes care.

Keywords: cost-effectiveness, COVID-19, glycemic control, Saudi Arabia, telemedicine, type 2 diabetes

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Introduction

Diabetes mellitus (DM) is one of the most prevalent diseases worldwide. In 2019, the global prevalence of DM was estimated to be 9.3%, with 463 million individuals being diagnosed around the world, and it is expected to reach 700 million by 2045.[1] In Saudi Arabia, the prevalence has significantly increased in the last two decades,[2] with 18.3% of adults in 2019 estimated to have diabetes.[3] Globally, the major driving factors for the increasing prevalence of type 2 DM include sedentary lifestyle, overweight and obesity, unhealthy diets (e.g. frequent consumption of sugar-sweetened beverages), smoking, and psychological stress.[4,5] Similarly, in Saudi Arabia, these risk factors are highly prevalent and contribute to the epidemic of DM.[6–8] For example, in a recent nationwide cross-sectional study in 2020, the prevalence of obesity was estimated to be 24.7%.[9]

Patients with DM, especially those with poor glycemic control, are at a higher risk of morbidity and mortality when infected with COVID-19. Many studies have reported that DM patients who are infected with COVID-19 have a higher risk of complications, hospitalizations, intensive care unit (ICU) admissions, morbidity, and mortality.[10–18] For example, a study from the United States reported that the mortality rate of COVID-19 among patients with diabetes was 28.8% compared with 6.2% for patients without diabetes.[16] Another study from Saudi Arabia reported a higher mortality rate among hospitalized patients with diabetes (20.5%) compared with patients without diabetes (12.3%).[19] These complications are thought to be due to uncontrolled glycated hemoglobin (HbA1c), which increases the risk of infection, impaired immune system, and other pre-existing comorbidities, such as cardiac and renal diseases.[20–24] This emphasizes the need for stringent control of such risk factors to prevent the occurrence of complications.

During the COVID-19 pandemic, especially during lockdowns, the in-person care appointments at outpatient clinics were canceled or largely reduced, causing interruptions in routine diabetes care.[25] Consequently, virtual clinics and telemedicine interventions have been increasingly utilized to provide appropriate care to patients, including those with diabetes. This, in turn, helped to protect patients from COVID-19 infections and, at the same time, helped in providing medical care.[25–27] A recent study from Saudi Arabia reported the experience and satisfaction with the rapid implementation of diabetes telemedicine clinics during the outbreak of the COVID-19 pandemic. The majority of patients (97%) reported that telemedicine was essential for maintaining good glycemic control during the pandemic. Encouragingly, 86% of patients supported the use of virtual clinics in the future.[25] Other studies during[28,29] and before the pandemic reported high levels of patient satisfaction with telemedicine interventions.[30–32]

Before the pandemic, many studies indicated the clinical effectiveness of telemedicine in diabetes care, including significant and clinically relevant reductions in HbA1c.[31–38] Moreover, during the COVID-19 pandemic, two studies from Japan[39] and Saudi Arabia[40] reported similar positive clinical outcomes in terms of glycemic control. In addition, it has been shown that increasing patient contact through frequent phone calls improves patient therapy adherence, motivation, and metabolic control.[41] However, only limited literature is currently available on the cost-effectiveness of telemedicine for diabetes care.[32,42,43] It is currently believed that telehealth could decrease costs on the health system, particularly when telehealth services prevent health system-funded travel, leading to reductions in secondary care, and when telehealth mitigates the need for costly specialist interventions by providing quality care in an efficient manner, including telemonitoring.[44] In addition, it has been reported that telemedicine has the potential to provide significant cost savings by increasing patients' working ability, independent living ability, quality of life, and reducing travel costs.[45]

Consequently, the current study evaluates the cost-effectiveness of a telemedicine diabetes care clinic for high-risk patients with uncontrolled diabetes during the COVID-19 pandemic. Given the lack of data in the literature on the cost-effectiveness of telemedicine care, we believe that the findings of this study will provide useful information to health policymakers and can provide further guidance on the clinical and economic implications of expanding telemedicine care services.

Methods

Study design and setting

This was a retrospective chart review of adult patients aged 18 years and above with uncontrolled type 2 DM attending an outpatient diabetes clinic affiliated with a tertiary care hospital. The patients were recruited from an integrated care clinic at the chronic illness clinics of the Family and Community Medicine Department at Prince Sultan Military Medical City (PSMMC), Riyadh, Saudi Arabia. At PSMMC, high-risk patients with uncontrolled type 2 diabetes (i.e. HbA1c > 9) are referred to this integrated care clinic from other chronic illness clinics. At the integrated care clinic, the patients receive comprehensive diabetes care (i.e. intensive diabetes management with multicomponent interventions and frequent follow-ups and clinical visits) from a multidisciplinary clinical team, including a senior family physician, clinical pharmacist, diabetes educator, and other healthcare professionals whenever needed. Once their diabetes is controlled, patients are referred back to the chronic illness clinics for standard care. The description of this specialized integrated care clinic has been published elsewhere.[46,47] Due to the partial and complete lockdown in Saudi Arabia from March to June 2020, appointments for in-person care at the outpatient clinics were largely reduced, including the cancelation of many in-person care appointments. Consequently, the integrated care clinic was shifted to a virtual clinic to continue providing diabetes care to patients during the lockdown period. Patients in the virtual clinic arm were followed up remotely with the same clinical team, similar to the in-person integrated care clinic before the pandemic. The detailed description and setup of this clinic have been published elsewhere.[40] In brief, the virtual clinic was run based on a workflow that has been thoroughly discussed and agreed upon among our clinical team and the clinic's administration to ensure smooth operation. Moreover, to ensure consistency and quality of care, a clinical guideline on type 2 diabetes management during the COVID-19 pandemic was developed and distributed among all members of the clinical team. Telemedicine service was an interactive, real-time telemedicine intervention using a synchronous communication method (i.e. telephone calls/consultations). Based on the clinical protocol, for these high-risk patients with uncontrolled diabetes, the frequency of the virtual appointments was typically every 1–2 weeks during the first 3 months for reviewing the agreed plan and insulin titration and was conducted by the case manager of the virtual clinic. In addition, WhatsApp® was used to provide written instructions when needed or for further confirmation (e.g. new dosage instructions, dose modifications, added or stopped medications), educational materials, audio–visual aids, and so on. SMS text messages were also used in the clinic. Telemedicine care included several services, such as reviewing patients' therapeutic plans, therapeutic interventions (e.g. dose adjustment), patient counseling about their medications, and patient education about the risk of COVID-19 to patients with diabetes and the importance of preventive measures (e.g. wearing masks, social distancing).

Study population, model of care, and inclusion and exclusion criteria

This study consisted of two arms. The first arm (telemedicine care model) included patients who were attending the virtual integrated care clinic during the pandemic, in which partial and complete lockdown was imposed between March and June 2020. The second arm (traditional care model) included patients who received in-person care, which requires physical attendance at the integrated care clinic between August and November 2020. The average time horizon was approximately 4 months for both models of care. As previously mentioned, the patients in the virtual integrated clinic were managed mainly through telemedicine with few in-person care visits when medically necessary and were followed up remotely to receive similar care as the in-person integrated care clinic and with the same clinical team. In addition, in the telemedicine care model, prescription medicines and medical supplies [e.g. glucometer, swabs, and lancets to perform self-monitoring of blood glucose (SMBG)] were shipped to the patients' homes.

In both arms of this study, the inclusion criteria included the following: adult patients with type 2 DM with an HbA1c value >9 (i.e. uncontrolled diabetes) before the study period for each model and with a valid HbA1c value after the follow-up period. Consequently, all patients aged <18 years and those with HbA1c values <9 at baseline or patients with no HbA1c values after receiving telemedicine care or traditional care were excluded. Based on these inclusion and exclusion criteria, in the traditional care model, we included all the first 100 patients who met the criteria. Based on the inclusion and exclusion criteria, 100 patients who matched the traditional care patients whenever possible in terms of socioeconomic and clinical characteristics, such as age, sex, and comorbidities, were included in the telemedicine care model. Hence, a matching ratio of 1:1 was used to include the patients managed through telemedicine and traditional care models (i.e. 100 patients in each arm). The minimum sample size of 100 patients in each arm was estimated based on an effect size (d) of 0.4 for the difference between the two group means (i.e. the mean difference in the HbA1c reduction), level of significance $(\alpha)=0.05$, $\beta=0.2$, and power of 0.8 using the Gpower® software version 3.1.

Data collection

Patients who were managed using traditional and telemedicine care models were identified through electronic medical records. Patients were followed for at least 3 months or more from the baseline to assess the impact of either health delivery model (i.e. telemedicine *versus* traditional) on the HbA1c level. Patients' age, sex, disease duration, follow-up period, comorbidities, baseline and follow-up HbA1c levels, laboratory tests (e.g. complete blood count, serum creatinine, liver function tests, HbA1c), medications, medical supplies (e.g. glucometer, swabs, lancets, lancing pens, strips), shipping, and the frequency of physical and virtual clinic visits were collected. Consequently, the costs, namely the costs of medications, laboratory tests, medical supplies, shipping, phone calls, and clinic visits (in-person and virtual visits), were collected. The costs of visits to the clinic and laboratory tests were retrieved from the cost center of the Ministry of Health, Saudi Arabia. The costs of medications, medical supplies, phone calls, and shipping of medicines and medical supplies were retrieved from the relevant departments of our institution.

Statistical analysis

To compare the baseline characteristics of the patients managed through the telemedicine care model with those managed through the traditional care model, chi-square test, Fisher's exact test, and Student's *t*-test were conducted as appropriate. The mean reduction in the HbA1c levels before and after the follow-up period was presented together with the standard deviation for both the telemedicine and traditional care models, with the paired Student's *t*-test being used for the intragroup differences. Similarly, the mean total costs for the patients managed through the care models were presented together with their standard deviations. The ICER was calculated based on the mean difference in the total cost and effect (i.e. reduction in HbA1c level). Non-parametric bootstrapping with 10,000 replications was conducted to generate the 95% confidence intervals (95% CI) for the mean total costs and reduction in the HbA1c level for the models. Propensity score matching (PSM) bin bootstrapping with 10,000 replications based on age, sex, number of comorbidities, HbA1c levels, and follow-up period was performed to generate the cost-effectiveness quadrants. All statistical analyses were conducted using SAS® version 9.4 (SAS Institute Inc., Cary, NC, USA).

Ethics statement

The study received ethical approval from the Institutional Review Board (IRB), Scientific Research Center, Prince Sultan Military Medical City, Riyadh, Saudi Arabia (IRB approval number 1521). All information was obtained from patient records after obtaining written consent from the patients. The study was conducted according to the World Medical Association Declaration of Helsinki.

Results

Patients' characteristics at the baseline

This study included a total of 200 patients (i.e. 100 patients per care model). More than half (58%) were between the ages of 50 and 70 years, and the patients in the traditional care group were relatively older than those in the telemedicine care group ($p = 0.047$). Approximately 52% were female, with no statistically significant difference between patients in both models in terms of sex ($p = 0.322$). The majority of the patients (72.5%) had two to four chronic health conditions, with no statistically significant difference among those in both models in terms of the number of chronic conditions ($p = 0.197$). However, the percentage of patients with hypertension in the traditional care model was relatively higher in comparison to their counterparts in the telemedicine care model (84% *versus* 72%, $p = 0.041$). The mean duration of illness was 14 years, with no significant difference between the two groups ($p = 0.254$). Moreover, patients in both models had a baseline HbA1c level over 10, with no statistically significant difference among both models ($p = 0.201$). The baseline characteristics of the patients are reported in Table 1.

The cost-effectiveness of the telemedicine care

As shown in Table 2 and Figure 1, patients in the telemedicine care model had a mean reduction in their HbA1c level of 1.82 (95% CI = 1.56–2.09, $p < 0.001$; from 10.31 ± 1.26 pre-telemedicine intervention to 8.49 ± 1.39, $p < 0.001$), while those in the traditional care model had a mean reduction of 1.54 (95% CI = 1.23–1.85, $p < 0.001$; from the baseline 10.53 ± 1.18 to 8.99 ± 1.53, $p < 0.001$). Moreover, the mean difference in the HbA1c level between the telemedicine and traditional care models (i.e. the incremental effect) was 0.28 (95% CI = −0.194 to 0.546).

Table 1. Baseline characteristics of the patients.

Characteristic	Total $N = 200$	Telemedicine care $n = 100$	Traditional care $n = 100$	*p*
Age (years)				
<40	10 (5%)	7 (7%)	3 (3%)	0.047
40–50	40 (20%)	27 (27%)	13 (13%)	
50–60	67 (33.50%)	31 (31%)	36 (36%)	
60–70	49 (24.50%)	20 (20%)	29 (29%)	
70–80	28 (14%)	14 (14%)	14 (14%)	
>80	6 (3%)	1 (1%)	5 (5%)	
Sex				
Male	97 (48.50%)	52 (52%)	45 (45%)	0.322
Female	103 (51.50%)	48 (48%)	55 (55%)	
Comorbidities				
Congestive heart failure	3 (1.5%)	0 (0%)	3 (3%)	0.081
Chronic kidney disease	20 (10%)	6 (6%)	14 (14%)	0.059
Stroke	3 (1.5%)	2 (2%)	1 (1%)	0.561
Cardiovascular disease	31 (15.5%)	16 (16%)	15 (15%)	0.845
Dyslipidemia	187 (93.50%)	94 (94%)	93 (93%)	0.774
Depression	3 (1.5%)	0 (0%)	3 (3%)	0.246
Hypertension	156 (78%)	72 (72%)	84 (84%)	0.041
Hypothyroidism	34 (17%)	17 (17%)	17 (17%)	1.00
No. of comorbidities				
<2	37 (18.5%)	23 (23%)	14 (14%)	0.197
2–4	145 (72.5%)	70 (70%)	75 (75%)	
4–6	18 (9%)	7 (7%)	11 (11%)	
Disease duration, mean ± SD	13.99 ± 7.92	13.35 ± 11.87	14.63 ± 12.97	0.254
HbA1c mean ± SD	10.42 ± 1.23	10.31 ± 1.26	10.53 ± 1.18	0.201

HbA1c, glycated hemoglobin; SD, standard deviation.

The mean total costs were SAR 4819.76 (US$1285.27) and SAR 4150.69 (US$1106.85) for patients in the telemedicine and traditional care models, respectively. The mean difference in the total cost between models was SAR 669.07 (US$178.42; 95% CI = SAR 593.7 (US$158.32)–SAR 1013.64 (US$270.30)) (Table 2).

Consequently, the ICER was estimated to be SAR 2372.52 (US$632.67) per 1% reduction in

Table 2. Changes in the HbA1c after > 3 months of follow-up and the costs of treatment for the telemedicine and traditional care models.

Variable	Telemedicine care model Mean ± SD	Traditional care model Mean ± SD	Mean difference (95% CI)
Difference in the HbA1c	1.82 ± 1.35	1.54 ± 1.56	0.28 (−0.1935 to 0.546)
Cost of treatment (SAR)	4819.76 ± 712.30	4150.69 ± 910.43	669.07 (593.37–1013.64)

CI, confidence interval; HbA1c, glycated hemoglobin; SAR, Saudi Riyals (1 SAR = US$3.75, US dollars (USD) as of 16 May 2021); SD, standard deviation.

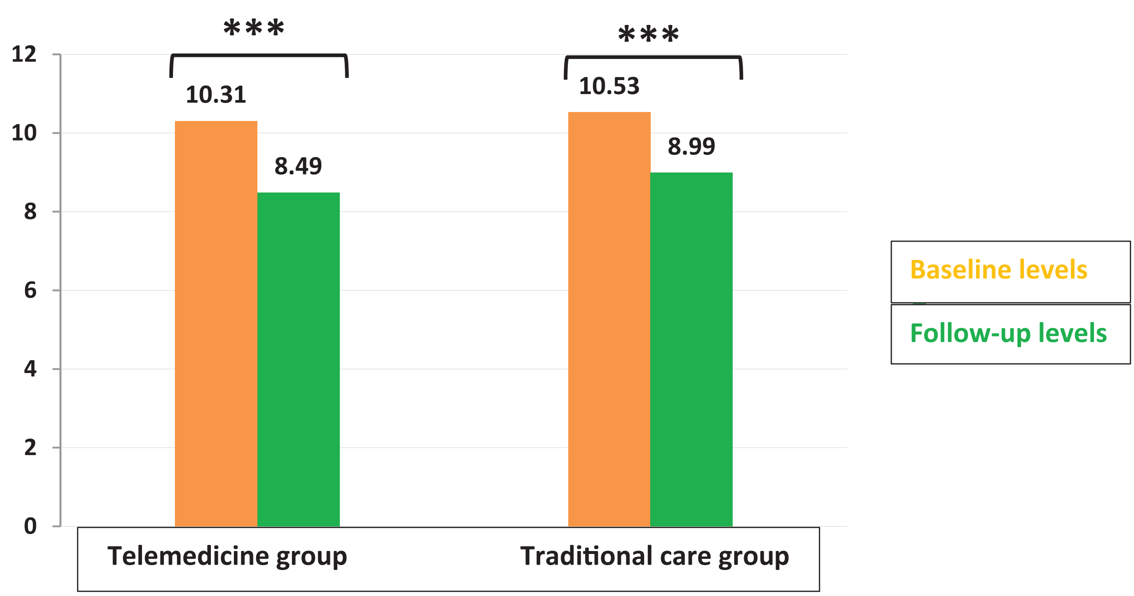

Figure 1. HbA1c levels at the baseline and at the end of the follow-up period of ⩾ 3 months (*** indicates statistical significance at $p < 0.001$).

HbA1c level. As shown in Figure 2, the telemedicine care model was shown to result in a higher cost and better outcome (i.e. greater reduction in the HbA1c level) with an 81.80% confidence level and a higher cost and worse outcome with an 18.20% confidence level.

The breakdown of the cost for each care model in terms of the percentage of cost for each segment within the care model is illustrated in Figures 3 and 4. It included costs for medications, laboratory tests, labor costs for in-person and virtual visits, and miscellaneous items (i.e. medical supplies, shipping, and phone calls). As previously mentioned, medical supplies included glucometers, swabs, lancets, lancing pens, and strips. The miscellaneous items in the telemedicine model were relatively higher than those in the traditional care model (5.89% *versus* 0.89%, respectively).

Discussion

The current study provides new insights into the clinical and economic impact of implementing a telemedicine service to a high-risk group of patients with uncontrolled diabetes during the COVID-19 pandemic. The findings indicate that both models of care were clinically effective and improved patient outcomes in terms of HbA1c level reduction. Furthermore, the effect of HbA1c level was more favorable for those who were managed through the telemedicine care model (1.82 for the telemedicine care model *versus* 1.54 for the traditional care model). This could be explained by the frequent remote follow-ups and telecommunications that were provided for the patients who were managed through the telemedicine care model during the pandemic. In fact, as the integrated clinic is established to specifically manage high-risk patients with type 2 DM (i.e.

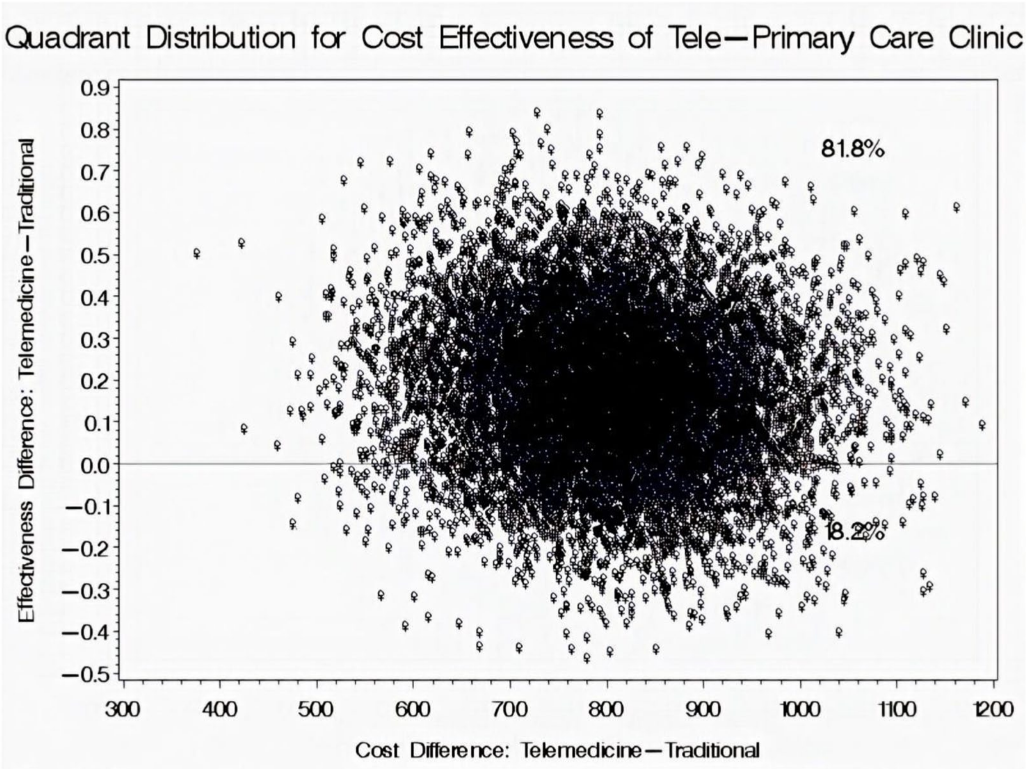

Figure 2. Probabilistic sensitivity analysis of the cost-effectiveness of the telemedicine care model versus the traditional care model in the management of diabetes.

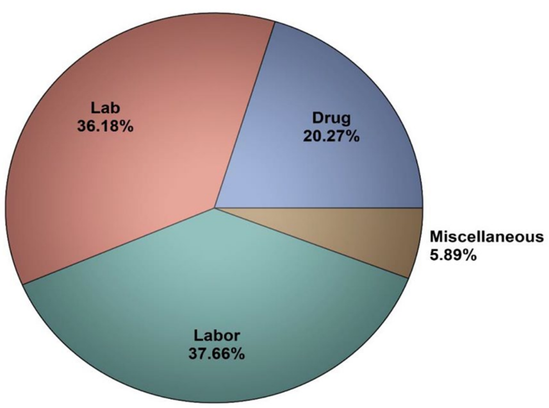

Figure 3. Cost breakdown for the telemedicine care model.

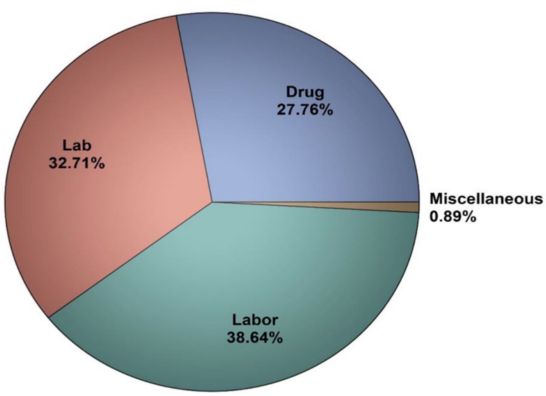

Figure 4. Cost breakdown for the traditional care model.

uncontrolled diabetes), the virtual appointments were scheduled every 1–2 weeks in the first 3 months of patient enrollment in this specialized clinic. However, the traditional care model during the pandemic had less frequent in-person visits in the clinic due to preventive and precautionary measures (i.e. typically one in-person care consultation per month). This is in line with the findings in the literature that revealed that proper and more frequent telecommunication between patients and healthcare providers results in better adherence to medications and interventions and overall better diabetes care.[41] Moreover, telemedicine (i.e. teleconsultations) encompassing frequent and intense patient–healthcare provider communication interactions resulted in significant clinically relevant reductions in HbA1c (−1.20%, 95% CI = −2.30 to −0.10; $p < 0.001$).[35] Therefore, the implementation of telemedicine has the benefit of increasing patient–healthcare provider contact without the risk of infection and exposure during the COVID-19 pandemic. Several studies have reported the clinical effectiveness of telemedicine interventions on HbA1c levels. For example, according to a systematic review and meta-analysis by Zhai and colleagues,[33] a statistically significant reduction in the HbA1c level in the telemedicine group compared with that of the control group was reported (pooled mean difference = −0.37, 95% CI = −0.49 to −0.25, $p < 0.001$). Moreover, a recent meta-analysis by Correia and colleagues,[36] which focused on telemedicine interventions implemented in low- and middle-income countries, indicated that telemedicine interventions were effective for diabetes management and resulted in significant reductions in HbA1c levels (standardized mean differences = −0.38, 95% CI = −0.52 to −0.23). In a study from Japan, Onishi and colleagues[39] reported that among patients with diabetes having HbA1c ⩾ 7% before the pandemic outbreak, providing diabetes care through telemedicine during the state of emergency resulted in an improvement to HbA1c < 7% after the emergency period in Japan. In addition to the clinical benefit, the patients on telecare also reported feeling more secure and more care, and the telecare helped the patients and their families take more active roles in their diabetes self-care management.[30,48]

The study determined that the telemedicine care model was more expensive and more effective in reducing HbA1c compared with the traditional care model (i.e. cost-effective). Telemedicine costs US$1285.26 per person to reduce HbA1c by 1.82%, with an ICER of US$632.67 per percentage point of HbA1c improvement. Similarly, Schechter and colleagues reported a moderate cost of telemedicine intervention of US$176.61 per person to reduce HbA1c by 0.36%. The ICER was US$490.58 per incremental percentage point of HbA1c improvement.[49] The additional costs are related to the costs of telephone calls, medical supplies (e.g. glucometer, swabs, lancets to perform SMBG), and shipping costs of medicines and medical supplies. As previously mentioned, there is limited literature on the cost-effectiveness of telemedicine interventions. Consequently, we hope that the findings of the current study shed light on the potential role of telemedicine as part of diabetes care during and beyond the pandemic outbreak.

Overall, the telemedicine model of care was found to be cost-effective for diabetes management, including patients with poorly controlled diabetes. Consequently, despite the higher cost of telemedicine care, the better outcomes could help reduce the burden of diabetes on the healthcare system in the long term. In particular, it may contribute to saving costs for the care of diabetes-related complications. Of great importance, it helped to ensure continuity of care for this vulnerable high-risk group of patients with diabetes during the COVID-19 pandemic. It facilitated sufficient access to diabetes care, especially during the lockdown and for patients who were hesitant to visit the clinics due to the fear of exposure to COVID-19. In addition to these clinical and economic implications, telemedicine has additional benefits. For example, it reduces the exposure of healthcare professionals to infections from patients. Similarly, it protects patients from contracting infections. In addition, it could save patients' time and cost of travel to receive medical care.[50,51] It could also help patients in other aspects of their life, such as work and productivity (i.e. to avoid missing work hours). Other advantages include flexibility in rescheduling and cancelation of virtual visits.[50] Consequently, we believe telemedicine services could be further expanded and incorporated into daily routine diabetes care. Therefore, more efforts are needed to promote telemedicine care. These could include the development and dissemination of guidelines for best practices to provide guidance for healthcare professionals on telemedicine care for patients with diabetes. In addition, more training for healthcare professionals could enhance the adoption of telemedicine and shed light on its benefits. This could be provided as part of continuing professional development (CPD) programs.

Strengths and limitations

To the best of our knowledge and based on the literature search, we believe this is probably one of the very few studies in the recent literature that assesses the cost-effectiveness of telemedicine in diabetes care. Furthermore, we used an objective measure (i.e. HbA1c) to assess the clinical outcomes of both models of care. In addition, from the perspective of health service providers, we included all the relevant direct costs, including costs of medications, medical supplies, laboratory investigations, clinical and virtual visits, telecommunication costs (i.e. telephone calls), shipment, and delivery. However, the study period was relatively short and could not assess the long-term impact of the model of care. In addition, due to the feasibility, resources, and the challenges during the COVID-19 pandemic, it was conducted at one institution and included 200 patients. However, we have implemented advanced statistical methods [i.e. PSM and probabilistic sensitivity analysis (PSA)] to enhance the robustness of the results/analysis, control confounders, and address uncertainty.[52–54] However, future studies could be conducted in more centers (i.e. multicenter studies) with a larger sample size to further explore this topic. However, given the current gap in the literature on the potential economic impact and value of telemedicine for patients with diabetes, we believe our findings add new insights on this topic and provide further guidance to health policymakers and healthcare professionals on the cost-effectiveness of telemedicine.

Conclusion

Our findings indicated that telemedicine care was cost-effective in the management of type 2 patients with poorly controlled diabetes during the COVID-19 pandemic. Moreover, it provided sufficient access to diabetes care during the lockdown and offered a suitable alternative to in-person care consultations in clinics. Consequently, we believe that telemedicine care can be further expanded and incorporated into routine diabetes care. This could enhance access to diabetes care and successfully replace many avoidable in-person care visits at outpatient clinics.

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Author contributions

MFA, AMT, AAA, and YA contributed to the conceptualization and design of the study; MFA, AMT, and TJA contributed to the data curation; YA and AAA contributed to the formal analysis; MFA, AMT, AMB, and MA contributed to conduct of the study and the investigation process; TJA, AMB, and MA contributed to the resources for the study; MFA, AAA, and YA contributed to the writing of the original draft. All authors contributed to the writing (review and editing).

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Conflict of interest statement

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