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Case report

The Value of Telemedicine for the Follow-up of Patients with New Onset Type 1 Diabetes Mellitus During COVID-19 Pandemic in Turkey: A Report of Eight Cases

Evin F et al. COVID 19 and Telemedicine in Type 1 Diabetes

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What this study adds?
Good glycemic control can be achieved by preventing the effects of the pandemic with the telemedicine in type 1 diabetes.

What is already known on this topic?
The use of telemedicine systems reduce glycemic variability parameters; coefficient of variation (CV) and standard deviation (SD) values.
Using telemedicine, the time in range may be achieved at recommended levels in children with T1D.

ABSTRACT
Background: The current COVID-19 pandemic has forced health care teams to look for alternative approaches to manage a great number of children with diabetes not only in rural but also in urban locations. Our aim in this COVID-19 pandemic was to provide information about the follow-up of new onset type 1 diabetes (T1D) patients and to discuss the integration of telemedicine into routine clinical care in the long term.
Methods: The changes in Coefficient of variation (CV), standard deviation (SD); percentage of time in range (TIR), time below range (TBR) and time above range (TAR) were evaluated in 8 patients with new-onset T1D diagnosed in Pediatric Diabetes division of Ege University, during COVID-19 pandemic over a period of two-months follow-up using telemedicine system.
Results: Median follow-up time was 51 (24-66) days. Two of the patients were using low glucose suspend system and 6 were on multiple ~~dose~~ daily injection therapy (MDI). Target TIR values were achieved in 7 patients in the last televisit and according to last consensus suggestions' TBR <70 mg/dl (3.9 mmol/l) (level 1 hypoglycemia) of <4% and a TBR <54 mg/dl (3.0 mmol/l) (level 2 hypoglycemia) of <1% were achieved in all patients. Seven patients achieved a CV of < 36 % in their last televisit.
Conclusions: Telemedicine as an alternative follow-up tool during unusual circumstances such pandemics, even in countries where it is not routinely used, could be beneficial to achieve optimum glycemic control in patients with new-onset T1D.
Keywords: Type 1 diabetes, telemedicine, COVID-19, technology, sensor augmented pump

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INTRODUCTION
Telemedicine can be defined as, "the remote delivery of healthcare services". It allows patients and physicians to communicate in real-time (1,2). The current COVID-19 pandemic has forced health care teams to look for alternative approaches to manage a great number of children with diabetes not only in rural but also in urban locations. Patients with new-onset type 1 diabetes

(T1D) represent one of the most challenging health conditions in the quarantine period.

Data on the use of telehealth in patients with diabetes is encouraging (3). Telemedicine has been associated with improved cost-effectiveness and patient satisfaction (4). A study run with school children showed the benefits of telemedicine communication between the school nurse and the diabetes team in addition to the regular care. Telemedicine group had lower HbA1c, improvement in Quality of Life, and fewer hospitalizations/ emergency department visits (5). In studies conducted before pandemic, telemedicine is more successful in adolescents with a mean difference in HbA1c than those with longer duration of diabetes and with higher baseline HbA1c values (6).

The immediate cost of implementing telemedicine can be high to afford (7). Today, less costly smartphones and other devices make this technology accessible and cost-effective. Our aim in this COVID-19 pandemic was to provide information about the follow-up of new onset T1D patients and to discuss the integration of telemedicine into routine clinical care in the long term.

CASES

When the first COVID-19 patient was diagnosed in Turkey on March 11, 2020; four new onset T1D were in the hospital and they are included in the study. Additionally, during two months period, 9 patients were diagnosed under the shade of COVID-19 pandemic and four of these were included in the study. Five patients were excluded; because one of them did not continue with telemedicine and 4 patients were still hospitalized when the manuscript was written. Totally 8 patients were included in this case series and characteristics of the patients are given in Table 1. Median follow-up time was 51 (24-66) days. Patients with continuous glucose monitoring (CGM)/flash glucose monitoring system (FGMS) were asked to share their glucose profile by using CareLink Personal software version 3.0 (Medtronic, Minneapolis, MN) or FreeStyle LibreLink from homeland. Patients who did not use CGM/FGMS shared their daily self-monitor of blood glucose (SMBG) measurements by either smartphones/ email and the doses were adjusted by the same diabetes team. When we evaluated the cases one by one; two of the patients admitted with ketoacidosis and were changed to sensor augmented pump (SAP) with predictive low glucose suspend (PLGS) (Minimed 640G®) after 5 days of multiple ~~dose~~ daily insulin (MDI) therapy because of the anxiety and fear of the family about hypoglycemia (case 2 and 3). MDI insulin treatment protocol included a fixed basal insulin administration subcutaneously once daily (insulin aspart or detemir) and rapid acting insulin administration (either insulin aspart/glulisin or lispro insulin) before meals with a dosing based on carbohydrate counting and blood sugar concentrations. Insulin doses of the patients are given in Table 2. In case 3, with ongoing education with telehealth we achieved excellent glycemic metrics with a time in range (TIR) 96.3%, time below range (TBR) 0.5 % and time above range (TAR) 3.2% on the 2nd week. Cases 1 and 4 were admitted with severe diabetic ketoacidosis and were started on MDI therapy and used FGMS Abbott FreeStyle Libre. Insulin doses were adjusted based on the outputs through televisits by the pediatric diabetologist. In case 4, after one month unfortunately she neglected daily glucose sharing. At her last televisit TIR decreased to 61 %, TAR increased to 36% with TBR 3%. We think that despite using FGMS, the deterioration of metrics may be due to early cessation of televisits.

Case 5 was a 2.3-year-old girl diagnosed with hyperglycemia and mild ketosis. As a result of her young age, and unpredictable eating habits and activity, using a SAP-PLGS was recommended but the family declined due to financial burden since SAP-PLGS is not covered by insurance in Turkey. Therefore MDI treatment was initiated. Since the parents declined learning carbohydrate counting, she was discharged with an exchange meal plan after 7 days of hospitalization. The parents also declined using any type of CGM due to financial issues and lack of insurance coverage. For the first 30 days, parents were encouraged to share SMBG measurements every day and family's education continued and insulin doses was adjusted together with the diabetes team. She had the worst glycemic control in our cases in 2nd week with a TIR of 48.7 % but with ongoing education via telemedicine her TIR increased to 81.7% without any documented level 1 hypoglycemia. Case 6 and 8 were diagnosed as severe diabetic ketoasidosis (DKA) and after one day of pediatric intensive unit hospitalization MDI treatment started ~~and~~ with SMBG. Case 7 was admitted to the hospital with ketosis and she was again treated with MDI therapy and SMBG.

In all the patients the follow up visits were scheduled every day for first 14 days and ~~than~~ then every week virtually for the first two months and when needed. Glycemic variability index of first 14 days after discharge and the last televisit are given in Table 3.

DISCUSSION

In the late fall of 2019, Wuhan city, in China, announced an outbreak of an infection, which was later designated coronavirus disease (SARS-2 CoV2 or COVID-19) by World Health Organization (WHO) (8,9). The coronavirus disease was declared pandemic by WHO on March 11, 2020; the date on which the first positive case was detected in Turkey.

COVID-19 has required dramatic changes to our delivery of health care, some of which improved access and outcomes for our patients with diabetes. The Stay at Home order in Turkey during COVID-19 pandemic for children <20 years have forced a majority of the diabetes teams to adapt a diabetes care remotely through telehealth. Moreover, parents of many children with T1D postponed their appointments due to fear and anxiety of contracting COVID-19 infection in healthcare settings.

Digital platforms are places where diabetes teams and patients can meet in a virtual meeting room and share downloadable data from glucometers, CGMs and insulin pumps. Furthermore, with telehealth; SMBG data and insulin doses of MDI patients can be evaluated. Telehealth can be by teleconferencing, telephone, text messaging, and/or e-mail. This system can provide a good alternative to the physical, and perhaps risky, routine outpatient meeting, where a patient could be accidently infected by COVID-19 during either transport to or at the visit in hospital (10).

There are still a lot of areas in Turkey and even in US with no internet access. Healthcare through telemedicine depends on the availability of wireless network systems, smart phones and regular phones on both ends, ie. both the healthcare providers and the patients and families should have access to internet and phones. Since our case group had a middle-high socioeconomic status, their

access to health services using telemedicine was sufficient. In order to follow up metabolic control of our patients through telehealth we used e mail and whatsapp and received SMBG, or PDF results of CGMS or SAP and calculated glucose metrics.

The number of daily blood glucose measurements was in the desired range with 7.1 ± 1.1 times/day. According to consensus report a TIR > 70% is recommended target for T1D [7]. But this target should be personalized and targets should be set according to age of children. In Garg et al case report, TIR was 30% in a -one year old- patient with T1DM diagnosed during COVID-19 pandemic (11). Target TIR values were achieved in 7 (87.5%) patients in the last televisit and according to last consensus suggestions' TBR <70 mg/dl (3.9 mmol/l) (level 1 hypoglycemia) of <4% and a TBR <54 mg/dl (3.0 mmol/l) (level 2 hypoglycemia) of <1% were achieved in all patients (7).

GV is a metric that provides an integrated picture of postprandial hyperglycemia and hypoglycemic episodes. GV has been hypothesized to be an independent risk factor for vascular disease independent of HbA1c (12,13,14). Increased GV is consistently associated with mortality and is a consistent predictor of hypoglycemia, both in prospective studies and randomized clinical trials (15,16). For CV; 36 % threshold has been adopted as the primary metric to separate stable from unstable diabetes. Peters et al. determined CV value as 18% and 20.3% in 2 adult patients with T1DM diagnosed during COVID-19 pandemic (17). In our study, seven patients achieved a CV of < 36 % in their last televisit.

According to SEARCH for Diabetes in Youth study of 1396 youth aged < 20 years with newly diagnosed T1D, 28 % had DKA at presentation (18) and in our study it was 75 %. 2 of the patients admitted to the primary care physician and were misdiagnosed as upper respiratory tract infection and abdominal pain which may be due to lack of information of the physicians about pediatric diabetes, or their anxiety concerning COVID-19. All patients were negative for COVID-19 and hospital stay of 4 patients (case 5-8), whose diagnosis and treatment were after COVID-19, were shortened (19.2 ± 8.0 versus 8.2 ± 2.6) and some of their training continued at home via telemedicine but this difference seems to not effect glucose metrics.

We recently reported managing diabetes remotely especially in new onset patients with T1D during this pandemic. With telehealth, optimum glycemic targets can be achieved in pediatric patients with new onset T1D. However, the fact that patients cannot be physically examined and the level of HbA1c cannot be measured are the most important limitations of this system. If this new way of follow-up with telehealth continue after the pandemic is over, it could provide significant improvements for patients because it does not only protect patients from the troublesome of visiting the hospital, but also can provide the benefits of daily follow-up.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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Table 1: Patient characteristics
SDS: standard deviation score, Anti-GAD: glutamic acid decarboxylase antibody, HbA1c: glycated hemoglobin a1c

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8
Age	6.4	9	10.7	13.7	2.3	7.4	12.6	8
Gender	M	M	M	F	F	M	M	F
Weight SDS	-0.38	0.47	2.42	0.63	-0.74	-1.13	0.73	-1.71
Height SDS	0.97	2.29	2.28	0.40	-0.66	2.0	1.25	
BMI SDS	-1.52	-1.9	1.94	0.43	-0.55	-5.16	0.27	
Diagnosis during COVID-19 pandemic	-	-	-	-	+	+	+	+
Clinical presentation	Severe DKA	Diabetic ketosis	Severe DKA	Severe DKA	Mild DKA	Severe DKA	Diabetic ketosis	Severe DKA
Co-morbidity	-	-	-	Hashimato thyroiditis	-	-	Asthma Depression	-
Anti-GAD (iU/mL)	>120	> 120	14.06	>120	>120	3.81	49.1	0.7
Anti-insulin autoantibody (U/mL)	2.12	3.6	-	3.06	10.44	2.75	2.56	2.37
Hospitalization (days)	25	27	10	15	7	6	8	12
Follow-up (days)	62	66	51	65	51	51	24	27
Insulin delivery method	MDI	CSII	CSII	MDI	MDI	MDI	MDI	MDI
HbA1c at diagnosis (%)	12.4	9,9	11.6	11.6	9.5	13.9	13.6	13.7
C-peptide (nmol/l)	0.180	0.52	0.23	0.3	0.1	0.1	0.46	0.52

Table 2: Total daily insulin doses (IU/kg) of patients at first 2 weeks and last 2 weeks

	Insulin doses (IU/kg)		
	2nd week	1st month	Last control
Case 1	0.44	0.50	0.60
Case 2	0.36	0.44	0.57
Case 3	0.38	0.37	0.41
Case 4	0.75	0.78	0.71
Case 5	0.91	1.08	1.07
Case 6	1.00	0.70	0.82
Case 7	1.43	1.32	1.23
Case 8	1.23	1.15	1.19

Table-3: Glycemic variability and glucose metrics of patients at first 2 weeks and last 2 weeks

	TIR (%)			TAR >180 mg/dl (%)			TBR <70 mg/dl (%)			SD			CV (%)			Mean glucose (mg/dl)		
	2nd week	1st month	Last control	2nd week	1st month	Last control	2nd week	1st month	Last control	2nd week	1st month	Last control	2nd week	1st month	Last control	2nd week	1st month	Last control
Case 1	69	75	85	29	24	12	2	1	3	66.1	57.1	42.8	41.6	38.9	34.5	159.1	147	124
Case 2	79.2	86.7	79.6	19.5	6.7	12.6	1.2	6.6	0.7	43	35.1	36.9	30.1	25.6	25.3	143.1	137.4	146.2
Case 3	96.3	96.4	96	3.2	2.7	3.7	0.5	0.9	0.3	25	24.8	24.2	19.9	19.9	18.9	125.3	125	128
Case 4	82	81	61	9	14	36	9	5	3	40.3	42.6	51.1	33.5	31.6	31.1	135	135	159
Case 5	48.7	61.2	81.7	51.3	36.6	18.3	0	2.2	0	95.5	64.9	38.8	47	39.7	27.3	202.8	163.4	140.3
Case 6	64.7	82.1	89.6	27.7	15	8.8	7.6	2.9	1.7	62.6	44.2	45.8	42.5	33.7	32.6	147.3	131.1	140.4
Case 7	86.3	-	89.6	13.7	-	9.4	0	-	1	33.1	-	30.9	24.2	-	22.6	136.9	-	136.7
Case 8	69.6	-	69.8	29.4	-	29.2	1	-	1	56.3	-	59.2	36.6	-	42.1	153.6	-	140.3

TIR: time in range, TAR: time above range, TBR: time below range, SD: standard deviation, CV: coefficient of variation