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The Role of Telemedicine in Type 1 Diabetes Children during COVID-19 Pandemic Era: A Systematic Review and Meta-analysis

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Abstract

BACKGROUND: The COVID-19 pandemic determined a profound impact on the routine follow-up of type 1 diabetes (T1D) children. Telemedicine represents a critical tool to guarantee regular care for these patients in this form.

AIM: The purpose of this study was to assess the impact of telemedicine programs during the COVID-19 pandemic era on T1D children.

PATIENTS AND METHODS: Studies from PubMed, Cochrane, and Directory of Open Access Journals from December 2021, to February 18, 2022, were conducted to calculate the pooled mean difference using either a random or fixed-effect model in Review Manager version 5.3. Our study has applied to ensure that our procedures, including record collection, extraction of data, quality evaluation, and statistical analysis, adhere to the Preferred Reporting Items for Systematic Examination and Meta-Analysis guidelines.

RESULTS: Three articles relevant to the current study (436 children). Our pooled analysis found that there was an impact of telemedicine in reducing the HbA1c (mean diff: 5.64 [95% confidence interval (CI) 3.71–7.57], $p < 0.00001$). However, the physical activity was not affected by the telemedicine program (mean diff: −37.25 [95% CI −317.53–243.02], $p = 0.79$).

CONCLUSION: Our findings suggest that telemedicine has a role in T1D children controlling HbA1c during the COVID-19 pandemic. Meanwhile, telehealth has emerged as a promising alternate mode of health-care delivery. Its utility during the pandemic warrants further investigation.

Introduction

Type 1 diabetes (T1D) is an autoimmune disease entity that causes absolute insulin deficiency, and the cost of care is estimated at $237 billion/year or 7% in the United States [1]. The global prevalence of T1D is estimated at 9.5/10,000 people, with an annual incidence of 15/100,000 people. On the prevalence of T1D, it was reported that the Americas accounted for the highest number of cases of the disease, with 20 cases for every 100.000 people.

The pathogenesis of this disease includes the destruction of pancreatic beta-cells. This leads to absolute insulin deficiency conditions so that patients require insulin replacement therapy to compensate for the function of these cells as natural insulin producers [3], [4]. The administration of exogenous insulin to replace the role of natural insulin could lead to hypoglycemia, and ketoacidosis can arise in patients. This condition even contributes to 4–10% of deaths in T1D patients [5]. Poor glycemic control (hyperglycemia) due to decreased insulin compliance can also lead to various microvascular and macrovascular complications [6].

Reducing of HbA1c through intensive diabetes management, particularly early in the disease, is associated with a significant reduction in the incidence and progression of microvascular disease (approximately 70%) [7]. Although HbA1c is affected by glycosylation rates that vary from person to person, this marker remains the best in demonstrating the patient's glycemic control over the past few months, reflecting the patient's compliance with treatment [8].

Strict glycemic control of patients plays a key role in inhibiting disease progression and preventing complications in T1D patients. However, the accessibility of patients to health centers has experienced a dramatic decline during the COVID-19 pandemic due to restrictions on the number of patients and limited resources. In addition to the limited availability of resources, the fear of transmission of this

disease is also decreasing access to health centers [9]. The implementation of the prioritization system is also too favorable for emergency conditions and diseases related to upper respiratory tract infections [10]. Patients who require regular control of their chronic disease are hampered by this condition, which cannot be avoided.

Telemedicine innovation is here to break the barrier between patients and health centers. Long before the pandemic, this technology had been applied in several countries, especially for people living far inland [11], [12]. In Indonesia, this technology has not been used en masse. Its use has also only become popular recently and is thought to be concentrated in large cities. In addition, there are no clear standards and protocols related to telemedicine in Indonesia [13].

According to the World Health Organization, telemedicine refers to the remote provision of health-care services by professionals using information and communication technologies. Telemedicine services include teleradiology, tele-electrocardiography, tele-ultrasonography, clinical teleconsultation, and other services [14]. From the point of view of the purpose of making the idea related to telemedicine, this technology is considered to bridge patients and doctors hassle-free. Xu *et al.* [11] reported that diabetes care through telemedicine is safe and is associated with time savings, cost savings, high appointment adherence rates, and high patient satisfaction.

However, telemedicine technology requires operational costs to be charged to health centers and patients. Implementation of this technology requires consideration of efficiency and effectiveness. To date, there have been no meta-analytical studies evaluating the effectiveness of the technology, particularly for monitoring adherence and disease severity in T1D patients. Therefore, a systematic review and meta-analysis of this study will be conducted to establish the impact of telemedicine programs on T1D children during the COVID-19 Pandemic.

Methods

The study has used the Preferred Reporting Items for Systematic Examination and Meta-Analysis (PRISMA) guidelines from PRISMA to ensure that our procedures, including record collection, data extraction, quality evaluation, and statistical analysis, follow the PRISMA guidelines [15].

Search strategy

A number of scientific databases (PubMed, Embase, Cochrane, and Directory of Open Access Journals) were searched for studies evaluating the role of telemedicine in T1D children during the COVID-19 pandemic era. The article searching was conducted from December 2021, to February 18, 2022. This study did not limit to a specific time of publication. Medical Subject Heading terms were used and other addition keywords: ("Telemedicine" "eHealth" or "Telehealth") and ("Diabetes Mellitus Type 1" or "T1DM") and ("Children or Pediatric or Pediatric or Child") and ("COVID-19" or "Pandemic" or "Coronavirus") were used in a systemic search. The documents with larger samples only were included in the search strategy and were included that documents were with the same study details.

Study selection

The articles in this review met the following criteria: (1) evaluating the role of telemedicine in T1D children during the COVID-19 pandemic era; (2) having sufficient data to calculate the standard mean difference (MD) and 95 percent confidence interval (CI); and (3) observational studies (cross-sectional, case–control, and cohort). Furthermore, the following were the exclusion criteria: (1) titles and abstracts that are unrelated; (2) reviews and commentaries; (3) incomplete and/or ungeneralized data; and (4) non-English language articles. The search, selection, and screening processes were recorded and are documented in the PRISMA flow diagram (Figure 1).

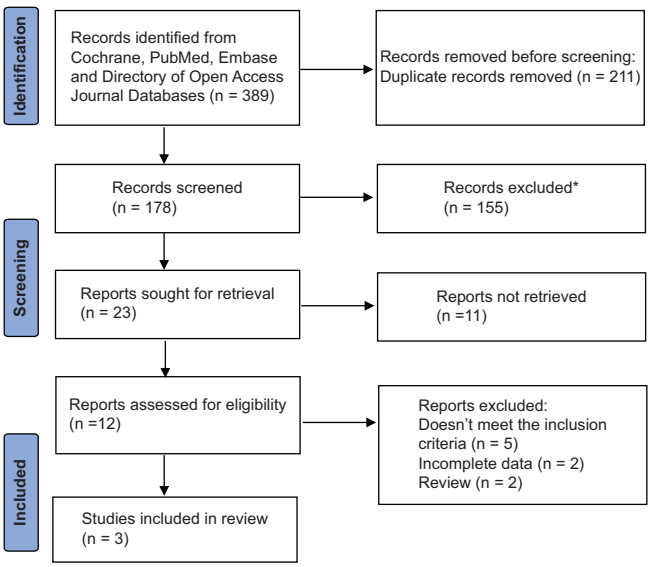

*Figure 1: PRISMA flow diagram of study selection process. *If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools. PRISMA: Preferred Reporting Items for Systematic Examination and Meta-Analysis*

Data extraction

The following data were extracted from each paper: (1) first author name, (2) year of publication, (3) case and control sample size, (4) age of participants, (5) ethnicity, (6) main findings, (7) HbA1c (mmol/mol) in pre-and post-telemedicine program, and (8) physical

activity (minutes/week) in pre-and post-telemedicine program. To avoid human error and provide high-validity data, two independent authors extracted the data (FF and WYD). If a discrepancy was discovered, we had a group discussion.

Outcome measures

The role of telemedicine was the predictor covariate in this current study. HbA1c (mmol/mol) and physical activity (minutes/week) were the outcome measures. Both of this outcome were discovered after the preliminary searches were done.

Assessment of the methodological quality

The quality of each paper was assessed using the New Castle-Ottawa scale (NOS) before being included in the meta-analysis. The NOS score ranged from 0 to 9, with three points for patient selection (4 points), group comparability (2 points), and exposure determination (3 points). Low quality scores (4–6), moderate quality scores (5–6), and high quality scores (7) were assigned to the paper. A NOS was assessed by three independent investigators (FF, QAN, and TM), and if a discrepancy was discovered, a consultation with senior researchers (NR and MF) was conducted.

Statistical analysis

The MD between pre- and post-telemedicine in T1D children during the COVID-19 pandemic era was calculated and summarized with the corresponding 95% CI. The overall effect (Z test) was considered significant if p value was < 0.05. Data were checked for heterogeneity and potential publication bias before determining the significant factors. The I^2 test was used to determine study heterogeneity. If there was heterogeneity (I^2 > 50%), a random effect model was used; otherwise, a fixed effect model was used. The Egger test was used to determine whether there was a reporting or publishing error, (p < 0.05 was considered to have publication bias). After that, a forest plot was used to present the correlation and effect estimates. Review Manager version 5.3 was used to analyze the data (Revman Cochrane, London, UK). Two independent authors (KF, QA) conducted statistical analyses to avoid methodological errors

Results

Eligible studies

This searching strategy identified 389 potential relevant articles. Among them, 366 papers were excluded due to irrelevant titles and abstracts. In total, 12 papers were included for review in the full text. Of those, we excluded eight papers due to review (n = 2), do not meet the inclusion criteria (n = 4), and incomplete data (n = 2). Finally, three papers were included in this study analysis. Figure 1 summarizes the paper selection pathway in this study, and Table 1 outlines the baseline characteristics of papers included in this meta-analysis.

Data synthesis

In data synthesis, this meta-analysis included three papers assessing the role of telemedicine program during the COVID-19 pandemic era in T1D children. The impact of a telemedicine program is determined by decreasing HbA1C levels in children. The pooled analysis found that telemedicine has an impact on reducing HbA1c (mean diff: 5.64 [95% CI 3.71–7.57], p ≤ 0.00001). However, physical activity was not significantly affected by the telemedicine program (mean diff: −37.25 [95% CI −317.53–243.02], p = 0.79) (Figures 2 and 3). The summary of the correlation between telemedicine programs and outcome measures present study is shown in Table 2.

Source of heterogeneity

Heterogeneity among studies

Because this study analysis revealed evidence of heterogeneity in HbA1C and physical activity covariates, the author used a random effect model to assess the correlation between the telemedicine program and HbA1c levels in T1D children. The evidence of heterogeneity among studies of the present meta-analysis is in Table 2.

Table 1: Baseline characteristics of articles included in this study

Author and year	Sample size	Case setting	Age (year) (mean ± SD)	Ethnicity	NOS	Main findings
Odeh *et al*., 2020 [16]	235	T1DM	10.8 ± 3.9	Arabic	6	COVID-19 lockdown causing a lack of insulin and glucose monitoring in Jordanian children with T1DM. Nevertheless, the families were enthusiastic about the usage of telemedicine to provide direction and assistance
Lazzeroni *et al*., 2021 [17]	139	T1DM	13.9 ± 5.27	Caucasian	7	The glycemic control in children and adolescents with T1DM showed an improvement during COVID-19 lockdown due to the extensive use of telemedicine and strict parental supervision
Predieri *et al*., 2020 [18]	62	T1DM	11.1 ± 4.37	Caucasian	8	Children and adolescents with T1DM experienced improved glucose control and no increase in acute complication during a lockdown The use of real-time CGM, continuous parental management, and telemedicine may be effective on T1DM care

NOS: Newcastle-Ottawa scale, T1DM: Type 1 diabetes mellitus, SD: Standard deviation. CGM: Continuous glucose monitor.

Table 2: Summary of glycemic control and physical activity in children with type 1 diabetes mellitus, pre- and post-telemedicine

Parameters	Outcome measure		Mean difference	95% CI	pE	pHet	p
	Pre-telemedicine	Post-telemedicine					
HbA1C (mmol/moL)	65 ± 15	59.7 ± 12.7	5.64	3.71–7.57	0.002	0.45	< 0.00001
Physical activity (min/week)	123 ± 106.5	160 ± 183	−37.25	−317.53–243.02	0.012	0.00001	0.79

Data were presented in mean ± SD. CI: Confidence interval; pE: p Egger, pHet: p Heterogeneity, T1DM: Type 1 diabetes mellitus, HbA1C: Hemoglobin A1C, SD: Standard deviation.

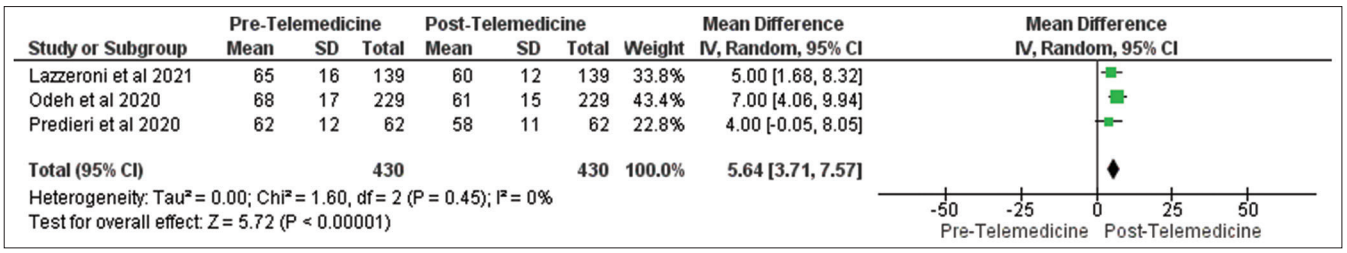

Figure 2. Forest Plot HbA1c outcomes

Potential publication bias

This study used Egger's test to determine the potential publication bias among studies. Overall, there was no publication bias in this study. The summary of publication bias is in Table 2.

Discussion

In this meta-analysis, the author sought to explore the effectiveness of telemedicine in controlling T1D patients during the COVID-19 pandemic lockdown period. Barriers to access to health had become a significant problem during this period, and telemedicine attempted to bridge the need for patients to seek care and health workers as care providers. Three observational studies measuring glycemic control in the form of HbA1c during the COVID-19 lockdown period were included in this meta-analysis. This study found a significant effect of telemedicine on decreasing HbA1c levels. Two of the three studies reported a significant reduction in HbA1c levels after telemedicine [16], [17]. One study reported no significant difference, although the mean HbA1c levels were relatively lower after introducing this system. The difference in HbA1c levels before and after telemedicine was recorded at 5.64% (95% CI, 3.71–7.57), p < 0.001, which indicates a strong association between the administration of telemedicine and the patient's low mean HbA1c levels. In addition, heterogeneity between studies was very low (I2 = 0%); thus, there is a lower risk of bias and can be extrapolated to the population corresponding to the study population.

Lazzeroni *et al*. [17] included 139 T1D patients both pediatric and young adults. They recorded HbA1c levels of 64.44% ± 15.61 post-telemedicine, compared with 60.66% ± 11.54 before telemedicine (p=0.002). 16) Odeh R *et al*. included 229 pediatric patients with a mean age of 10.8 ± 3.9 years. However, measurement of HbA1c could be performed in 97 patients. This study reported HbA1c levels before telemedicine were at 67.2% ± 17.0 mmol/mol, significantly higher than after telemedicine (61.7% ± 15.3).

It should be noted that there was no significant increase in the average daily insulin consumption in this period [17]. Although there was an increase in the average basal insulin use during the lockdown period, the total daily dose of insulin did not change significantly [18]. The increased percentage of basal insulin requirement during this lockdown period was thought to be related to an increase in persistent behavior. However, without an increase in the total daily insulin dose, a prandial insulin dose was decreased due to a reduction in carbohydrate consumption [19]. About 58.3% of T1D patients have difficulty accessing insulin for various reasons. The most popular reason for this insulin shortage is the limited access to hospitals due to the lockdown [16].

The patient's body mass index also did not experience significant changes. The contradictory thing found was that physical activity significantly decreased during the lockdown period. The mean time spent doing

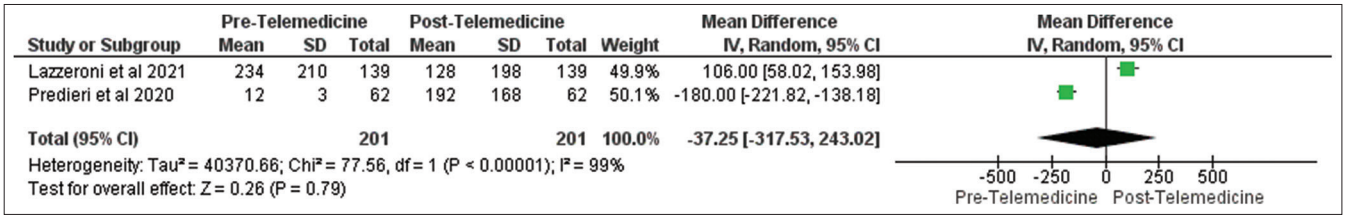

Figure 3.Forest Plot of Physical activity (minutes/week) outcome

moderate physical activity was 3.91 ± 3.56 h/week before the lockdown and was 2.13 ± 3.33 h/week after the lockdown [17]. Predieri *et al.* [18] reported a very extreme decrease in physical activity. The average time spent doing physical activity during the lockdown was 0.24 ± 0.59 hours per week, much lower than the previous period of 3.27 ± 2.82 ($p < 0.0001$). Glycemic control and BMI have been maintained, even though the decrease in physical activity felt due to changes in eating habits during the lockdown [17]. Christoforidis *et al*. [19] found that the breakfast rate for T1D patients dropped from 80.67% to 41.46% ($p = 0.0001$) and the dinner rate dropped from 60.22% to 53.78% ($p = 0.019$).

In patients with T1D, regular physical activity is associated with several positive physical health effects, including improvements in cardiovascular function, lipid profiles, and improvements in psychological well-being [20]. However, physical activity was not directly correlated with improvements in glycemic control due to increased glucose variability during exercise [21]. Tornese *et al*. [22] found that adolescents with T1D who continued their physical activity during the lockdown period showed improved glycemic control compared to five adolescents who stopped their regular physical activity.

Various media have been used in telemedicine, such as Email, voice calls, or video calls. Sixteen patients' monitoring is recommended every 3 months, by asking the patient to make anthropometric notes every month (weight and height), a diet diary, a blood sugar chart, and an insulin dose. Care providers are also recommended to provide some brief material on physical activity and diet to maintain blood sugar variability [16].

Although telemedicine exists as a bridge for patient monitoring, all control over health lies with the patient himself. Care providers who have tried to provide the best service will be powerless when patients continue to ignore the suggestions that have been given. Objective assessment of glycemic control (with HbA1c, for example) also remains challenging due to decreased accessibility of health centers, and measurement of HbA1c cannot be carried out as quickly as measuring blood glucose levels. About 91.1% of T1D patients did not check their HbA1c levels during the lockdown [16]. Most patients (or their families) are worried that they will contract the coronavirus if they go to the hospital. On the one hand, glucose test strips experienced a dramatic drop in stock during the lockdown period [23].

This meta-analysis has succeeded in providing an overview of the impact of the presence of telemedicine amid the COVID-19 pandemic, especially for those who need access to health centers to control chronic diseases. Telemedicine can effectively monitor T1D patients during the COVID-19 pandemic. Despite all the findings obtained in this study, several study weaknesses would like to be highlighted. First, each study applies different telemedicine protocols regarding telemedicine's duration, frequency, and media. Second, all of the included studies were conducted in countries with above-average economic levels. Telemedicine's glycemic control effects may also be due to good local awareness and adequate facilities, which may not be available in middle- or low-income countries. Third, glycemic control is not only influenced by a single factor. In this review, the included studies have not been able to control the factors of dietary habits, nutritional status, and the presence of other comorbidities that can affect holistic glycemic control.

To the best of the author's knowledge, this is the first systematic review and meta-analysis of the telemedicine in T1D children during the COVID-19 pandemic. This meta-analysis review also has limitations. The study about telemedicine in children with T1DM was still limited during the COVID-19 pandemic, so the result of this analytical study cannot represent the actual problem yet. We recommend further studies about the role of telemedicine in children with other chronic illnesses during pandemics COVID-19.

Conclusion

This meta-analysis study suggests that telemedicine may have a role in T1D children controlling HbA1c during the COVID-19 pandemic, even though telehealth has emerged as a promising alternate mode of health-care delivery, its utility during the pandemic warrants further investigation.

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