Original Research

Assessing the impact of mobile-based interventions provided by pharmacists on glycemic control and diabetes related distress in adolescent patients with type 1 diabetes mellitus in Pakistan

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Abstract

Background: Diabetes is a chronic disease characterized by impaired insulin secretion, insulin resistance or both. Challenges in glycemic control for T1DM adolescents include hypoglycemic episodes and keeping the HbA1c within target range. The aim of this study was to evaluate the impact of using mobile based applications to improve glycemic control, in terms of lowering HbA1c and reducing the number of hypoglycemic or hyperglycemic episodes in adolescents with T1DM in Pakistan, South Asia. We hypothesized that Type 1 diabetic adolescents who used mobile based applications, with counseling provided by pharmacists, to track their glucose would have a beneficial impact on their glycaemic control indicated by lower haemoglobin A1C (HbA1c) values and decreased number of hospital admissions linked to hypoglycemic or hyperglycemic conditions. The Diabetes Distress Scale (DDS) was to assess the emotional well-being of all participants. Methods: A total of 112 patients with T1DM in a tertiary-care hospital specific to diabetes were selected as the study population. This study was conducted from January 1, 2023 to June 1, 2023. Of the 112 patients, 56 were randomly assigned to the mobile app using MTG and 56 were assigned to the routine management RTG group. IBM SPSS 25.0 software was used for descriptive statistics, t tests, chi-square tests, and correlation analyses. Haemoglobin A1c (HbA1c) and number of admissions to the hospital for hypoglycemic or hyperglycemic episodes was the effectiveness parameter decided upon. Results: When compared to the RGT group, participants in the MTG group was associated with significant decreases in HbA1c values (P < 0.03), lower number of severe hypoglycaemic (3±1.9 vs. 9±1.4, p 0.02), and ketoacidotic episodes (5±2.0 vs. 16±1.4, p = 0.05). The MTG also had significantly improved diabetes distress levels in comparison to the RTG. Conclusion: Our study showed a significant association between utilizing mobile based applications and glycaemic control and emotional well-being in adolescents with T1DM. Conclusion: Compared with the routine management that is the current model of treatment, the MTG group for adolescents with T1DM had improved glycemic control and enhanced emotional well-being.

Keywords: diabetes mellitus; type 1 diabetes mellitus; smartphone; applications

INTRODUCTION

Diabetes is a chronic disease characterized by impaired insulin secretion, insulin resistance or both. The prevalence in South Asia of diabetes is higher in comparison to worldwide statistics and Pakistan has 7.1%. Of the different types of diabetes, Type 1 diabetes mellitus (T1DM) is usually accompanied with a host of devastating complications. The incidence of T1DM is increased by 3% per year worldwide and usually affects children and adolescents.

In 2022, over 1.2 million children and adolescents have type 1 diabetes.⁵ This represents a significant proportion of the adolescent cohort worldwide which is approximately 1.2 billion of the world's human population and 90% of them found in

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a low- or middle-income country. These areas are also where most cases of diabetes and thus represents a significant proportion of the youth affected by diabetes.⁶

Achieving target ranges of glycaemic control in diabetes requires persistent management of lifestyle aspects such as diet, exercise, medication and glucose monitoring (Figure 1). The cornerstone in reducing the risk and severity of diabetic complications and the impact these have on patients' lives, remains by adequate glycaemic control which requires appropriate glucose monitoring.⁷



Figure 1. Diabetes management strategies



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With the rapid development of technology, health management regimens based on mobile tools have received more attention than ever before. Keeping track of glucose levels is made easier by mobile apps, most of which are free. Pakistan's mobile connection indicate that 82.2 percent of the total population in January 2022 were utilizing mobile connections. Globally application use is a significant part of the mobile usage experience and Pakistan ranks twelfth on the list of the largest mobile markets by downloads, with 2.604 billion reported app downloads in 2021, among the fastest-growing markets in terms of downloads and hours spent on apps per user, depicting a year-over-year (YoY) growth of 25 percent and 34 percent, respectively. Pakistan also ranks sixth on the list of the largest mobile markets in terms of the hours spent on apps, with 133.98 billion hours spent in 2021, up from 104.4 billion in 2020 and 73.98 billion in 2019.8 These figures highlight the region's substantial mobile usage, the growing importance of mobile applications and suggests that using apps could be acceptable to a significant proportion of the participants involved in our study.

These advances in technology can support the main purpose of diabetes management which is to increase self-management and compensate for traditional treatment regimens that focus on medications alone. The aim of this study was to evaluate the effectiveness of a mobile-based intervention for patients with type 1 diabetes mellitus (T1DM) and compare it with the usual management mode. We hypothesized that by effectively utilizing this unique technology resource, our adolescent study participants would have improved monitoring of their condition, have enhanced compliance, increase self-efficacy and experience empowerment in actively managing their health.

Pharmacists possess in-depth knowledge of diabetes management, including self-monitoring of blood glucose and lifestyle modifications. This can ensure they play a vital role in providing information to the patients on the usage of mobile based applications to guide patients on how to accurately track their glucose levels and interpret the data generated by the app. This would guide and help the patient make informed decisions on their glucose control, promote adherence to treatment plans, and even help recognize early warning signs of hypoglycemia or hyperglycemia.

We used the Diabetes Distress Scale questionnaire, administered by the pharmacist, to identify the areas of distress experienced by the T1DM adolescents. Tracking distress levels over time can assist in monitoring the impact of interventions and identifying those who might benefit from additional support which helps improve the quality of life of affected individuals.⁹

MATERIALS AND METHODS

Study participants

The study included patients of both genders with T1DM registered in the clinical database for enrolment and followup. This study was conducted using the source population of patients who registered from January 1, 2022 to January 1, 2023. A total of 200 potential patients were identified from the registry and contacted. Patients who were not interested in participating in the study and those who had no smartphone were excluded.

Inclusion criteria were unmarried male and female adolescents diagnosed with Type 1 diabetes > 12 months (to exclude reactions to diagnosis); age 10-19 years (according to the adolescence period defined by WHO), individuals with personal smartphones and were aware of how to download and use basic apps. Patients with cognitive and language impairments were excluded.

Sociodemographic data were collected by trained pharmacists working in the center's pharmacy patient counselling room using a pretested semi-structured questionnaire. All study participants were approached during their respective appointment schedule for follow-up.

SH and DKA were defined to obtain the correct information. SH definition required the loss of consciousness and not just an event that required the assistance of someone. This more extreme definition was used because of the concern after our initial data collection that a 'requiring assistance' definition was leading to variable interpretation and reporting by participants and parents. For DKA events, we required overnight hospitalization to ensure correct diagnosis. For both SH and DKA, we only reported the frequency of participants with one or more events in the prior 12 months believing that this is more reliable than self-reported number of events.

In the study, the Diabetes Distress Scale (DDS), a validated questionnaire, was used to evaluate the level of emotional distress experienced by T1DM adolescents. The instrument is frequently used to assess the emotional difficulties and psychological health of young people with Type 1 diabetes. It's 17 items, using a 6 point Likert scale ranging from 1 (not a problem) to 6 (a very serious problem) explores various aspects of diabetes related distress. The total score ranges from 17 to 102, with higher scores indicating higher levels of diabetesrelated distress and lower scores indicating better psychological well-being and adaptation to diabetes management. A mean item score 2.0 – 2.9 should be considered 'moderate distress,' and a mean item score > 3.0 should be considered 'high distress'.9 A proficient translator translated the questionnaire into Urdu, the national language of Pakistan, using the backtranslation technique. By utilizing the back-translation method; the questionnaire was translated method to Urdu, the national language of Pakistan, by a qualified translator. It was then translated back to the English language by a qualified and independent translator who had been blinded to the original questionnaire. To reach a consensus the two source language versions were compared. Cronbach's Alpha that measures internal consistency was 0.85 with a reliability coefficient of 0.82, indicating the Urdu versions were consistent and reliable.

Sample size

Based on the literature, the geometric standard deviation (SD) of change in HbA1c at the last observation period was assumed



to be 0.7%.¹⁰ We estimated that at least 48 patients were required in each treatment group to confer a power of 80% to detect a significant difference of 0.4% change from baseline in the two groups at the end of the intervention. We thus planned to recruit 50 patients per group (100 in total) with consideration for potential discontinuation or dropout of enrolled patients during the study period. We were practically able to recruit 133 adolescent patients in the study. By the time the study started, 21 patients withdrew for reasons unconnected to the study such as time restraints, absence from appointments, engagement for marriage, guardian divorce and interest loss due to lack of financial incentive. A total of 112 individuals participated and provided all the data. See Figure 2 for a chart outlining the flow of participants through each phase of the study.

Statistical analysis

All of the statistical analyses utilized IBM SPSS version 25.0. Descriptive statistics were used to analyse the demographics of study participants. Categorical variables were tabulated as numbers (percentages) and continuous variables as means (standard deviations, SD). Categorical outcome measures were

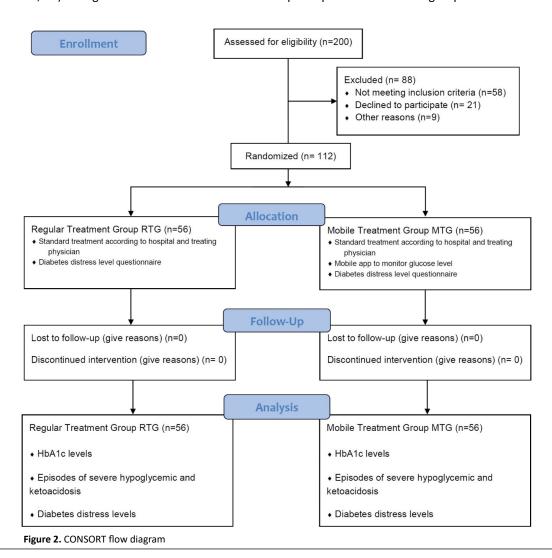
analysed using the chi-square test, and continuous measures were analysed using the t-test or a nonparametric equivalent (e.g., Wilcoxon rank test). Correlation analysis was used to explore the associations between HbA1c and hypoglycemic or hyperglycemic episodes. Statistical significance was set by using a two-tailed P value of <0.05.

Study design

We used computer-generated randomization sequences with participants being allocated to two groups; RTG (Routine treatment group) and MTG (Mobile treatment group). Blinding of the researchers responsible for analysis of results was ensured to prevent bias.

The RTG participants would be treated with the standard hospital and treating physician protocol without any involvement of mobile app use. Participants in the RTG met with the pharmacist to have their demographic data collected only.

The MTG participants would be using the mobile app to record their glucose values. At the initial meeting with the pharmacist, participants in the MTG group had their demographic data



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collected. They were then presented with the option to download any one of the five pre-selected glucose tracking apps available for download with Urdu language enabled. ¹¹ After the app had been downloaded, the pharmacist who had been trained earlier on using all five of the apps proceeded to provide the participant with detailed information about the app use using demonstration and answering queries by the study participant.

The status of diabetes included clinic-recorded HbA1c in the last 3 months and the presence of diabetes complications assessed according to the treating physician criteria. We collected SH and DKA information both directly from the study participant and from data extraction from the medical record. Discrepancies between the two sources could be connected to under reporting in the medical records and over reporting by the study participants and their families, particularly for SH episodes which are generally not connected to hospitalization. For DKA, hospitalization at a facility was counted as an occurrence during the study period.

The Diabetes Distress Scale questionnaire was administered to all study participants by the pharmacist during the counselling session at the start and end of the study.

Ethical approval and consent to participate

The study was conducted in a single clinical center and is in agreement with the ethical guidelines of the Declaration of Helsinki, Good Clinical Practice guidelines, and all applicable regulatory requirements. All enrolled patients and their guardians provided written consent to participate after they were informed of the purpose of the study, the potential risks and benefits related to the study as well as their information that would be recorded.

AIMS AND OBJECTIVES

In this study we aimed to evaluate the usage of mobile based application based on the counselling provided by pharmacists, on glycemic control in our study participants. Specifically, we assessed the HbA1c values and frequency of hypoglycemic or hyperglycemic episodes in this population. We hypothesized that using these applications to track their glucose levels, adolescents with T1DM would have better glycemic control and overall fewer hospital admissions related to hypoglycemic or hyperglycemic conditions.

The primary outcome was glucose control measured by HbA1c at start and end of the study duration. Secondary outcomes included a change in number of hypoglycemic episodes (SH) and hyperglycemic (DKA) episodes as well as fasting blood glucose and change in the DDS scale score between the two groups at the start and end of the study duration.

RESULTS AND DISCUSSION

Patient demographics

The study population consisted mainly of males, with a

proportion of 58.0% (65/112). The mean age of the patients was 15.2 (SD 2.95) years. In the RTG, the proportion of male patients was 59% (33/56), with a mean age of 14.7 (SD 1.11) years. In the MTG, the proportion of male patients was 57.1% (32/56), with a mean age of 16.5 (SD 1.88) years. Differences in baseline information were not statistically significant between the two groups (P < 0.05.). Details are provided in Table 1

Glycemic control

Group RTG compared to Group MTG exhibited higher HbA1c (9.2 vs. 7.5). The difference in HbA1c values between the two groups was 1.8%, and this was statistically significant.

Severe hypoglycaemic and ketoacidotic episodes

The number of severe hypoglycaemic (SH) and ketoacidotic or hyperglycemic (DKA) episodes in 12 months at the end of the study were statistically significant between the groups.

RTG had a higher number of severe hypoglycaemic (9 \pm 2.0 vs. 5 \pm 1.4, p 0.05), and ketoacidotic episodes (6 \pm 1.8 vs. 3 \pm 2.1, p = 0.02) in 12 months when compared to MTG.

Details are provided in Table 2

Emotional well-being

In Group MTG, the average DDS scores were lowered by 32% from baseline. Participants reported fewer concerns and worries associated with diabetes management, as evidenced by the decreased scores in various domains of the DDS, such as treatment-related distress, emotional burden, and physician-related distress. The average DDS scores in the RTG group had minimal changes observed from baseline to the follow-up period.

Correlation analysis

The correlation analysis demonstrated a statistically significant linear association between lower HbA1c levels and a lower number of severe hypoglycemic and ketoacidotic episodes in the 12 months at the end of the study. The study participants with lower HbA1c levels were predominantly from the MTG group and experienced fewer severe hypoglycaemic and ketoacidotic episodes in 12 months at the end of the study. The difference was statistically significant between the groups. This is expected because HbA1c levels indicate a better glycemic control which bodes well for lowering the chances of hypoglycaemic and ketoacidotic episodes. The linear association between HbA1c and number of hypoglycaemic and ketoacidotic episodes (r = 0.43) is shown in Figure 3.

DISCUSSION

The unprecedented surge of medical apps has created numerous opportunities to improve chronic disease management leading to the Agency for Healthcare Research and Quality commissioning a technical report documenting using technology to manage diabetes. ^{12,13} Health related apps have gained popularity since 2020, with studies the suggest their potential use in enhancing diabetes care and with



Table 1. Population characteristics and differences between the patients in RTG (n=56) and those in MTG (n=56) among study participants with type 1 diabetes. Table also includes chi-square test of the differences in between both groups for education, annual household income, duration of diabetes in years, age in years at diagnosis, HbA1c values and number of severe hypoglycaemic and number of ketoacidotic episodes in the past 12 months prior to the start of the study

Variable	N or mean (N or % ±SD) Total N = 112	RTG (N or % ±SD) (N=56)	MTG (N or % ±SD) (N=56)	P values (RTG vs MTG)
Age	14.9 ± 2.03	14.7 ± 1.11	15.2 ± 2.95	0.99
Education Achieved				
No formal education	30±2.2	17±1.8	13±1.3	0.10
One to eleven grade	20±4.3	12±1.6	8±2.7	0.93
High school graduate	45±4.2	23±1.2	22±2.9	0.87
Vocational Training	17±1.6	8±3.6	9±1.2	0.19
Household annual income (\$)				
\$5,000 or less	56 ±4.9	28 ±5.6	33 ±4.2	0.44
\$5,001 – \$10,000	32 ±11.6	13 ±3.6	15±1.0	0.38
\$10,001-\$20,000	19±0.1	12±1.7	6±1.1	0.78
Not aware of income	5±1.4	3±1.8	2±1.6	0.99
Duration of diabetes (years)	3.3±1.8	3.4±1.9	3.5±1.3	0.81
Age at diagnosis (years)	10.1±1.9	11.8±1.2	12.3±1.4	0.67
Start of study HbA1c values (%)	7.8 ± 2.1	8.2 ± 1.1	7.5 ± 1.2	0.25
Number of ketoacidotic episodes (previous 12 months)	19±4.1	10±1.9	9±1.4	0.69
Number of severe hypoglycemic episodes (previous 12 months)	21±2.9	9±2.0	12±1.4	0.38

 $RTG-Regular\ treatment\ group,\ MTG-Mobile\ treatment\ group,\ HbA1c-glycosylated\ hemoglobin.$

Table 2. HbA1c and number of severe hypoglycaemic and number of ketoacidotic episodes at end of study (12 months) differences between the patients in RTG (n=56) and those in MTG (n=56) among study participants with type 1 diabetes. Table includes chi-square test of the differences in between both groups for HbA1c values and number of number of severe hypoglycaemic and number of ketoacidotic episodes

Variable	N or mean (N or % ±SD) Total N = 112	RTG (N or % ±SD) (N=56)	MTG (N or % ±SD) (N=56)	P values (RTG vs MTG)	
End of study HbA1c values (%)	8.1 ± 1.3	7.2 ± 1.3	9.0 ± 1.4	0.03*	
Number of ketoacidotic episodes (during 12 months of study)	9±1.9	6±1.8	3±2.1	0.02*	
Number of severe hypoglycemic episodes (during 12 months of study)	14±1.9	9±2.0	5±1.4	0.05*	

RTG – Regular treatment group, MTG – Mobile treatment group, HbA1c – glycosylated hemoglobin.

Correlation analysis between HbA1c values and number of number of hypoglycemic/ketoacidotic episodes

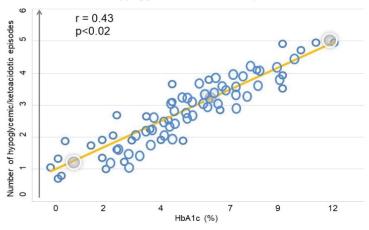


Figure 3. The linear association between glycosylated haemoglobin A1c (HbA1c %) and number of hypoglycaemic and ketoacidotic episodes.



evidence showing the minority of diabetic patients who are using apps have more frequent glucose monitoring and lower HbA1c levels. 14,15

The study by Al et al. emphasized the increased dependency on mobile phones for social activities among Pakistani adolescents which suggests the age groups would be open to using applications for health issues such as diabetes. However, evidence is relatively scare for app usage in T1DM adolescents which is the reason for our focus and with the premise that this age group would be more adept to use apps for disease management. 12,18-20

Adolescents with T1DM require regular support from their healthcare providers to manage the complex and challenging transition to adulthood, facing glucose level control issues due to fluctuating hormones through puberty, the pursuit of independence and tumultuous interpersonal networks with peers. Chronic hyperglycemia is associated with long-term damage, dysfunction, and failure of different organs and organ systems and glycemic control, particularly HbA1c being an important index, remains the cornerstone of diabetes management.21 Our study showed that the HbA1c levels dropped in the MTG by 1.8%. These findings are corroborated in the studies conducted by Gunawardena et al. that using smartphone apps in diabetes self-management was associated with significant drop in HbA1c levels and improved glycemic control.²² Studies have suggested that although HbA1c is lowered, the clinical impact may be low, such as found in the study by Martos-Cabrera et al. but this is usually the case in underpowered studies with very small study samples, a heterogenous patient population (T1DM, T2DM, gestational diabetes) which can lead to lack of sensitivity to detect changes.23,24

Diabetes related distress is highly prevalent in this age group and region, as is evident in the study by Jabeen et al. with one of the daily challenges with diabetes being glucose control. 9,25-28 Although studies have suggested that psychological and psychoeducational interventions may not help universally adolescents with T1DM owing to the unique challenges that characterize this phase, there is evidence that providing selfefficacy to this age group has a significant impact on glycemic control.^{24,29,30} In Group MTG, the average DDS scores were lowered by 32% from baseline. Participants reported fewer concerns and worries associated with diabetes management. as evidenced by the decreased scores in various domains of the DDS, such as treatment-related distress, emotional burden, and physician-related distress. The lack of significant alterations in the diabetes distress levels in Group RTG suggest that routine management does not adequately address the emotional challenges faced by adolescents with Type 1 diabetes. These findings highlight the positive impact of the intervention provided to Group MTG and highlights the effectiveness of incorporating mobile-based applications and pharmacist counseling in relieving diabetes-related distress and improving emotional well-being in T1DM adolescents. The drop in diabetes distress scores in Group MTG could indicate improved coping mechanisms and self-efficacy which can lead to better adaptation to the challenges of diabetes management. This paves the way for improved overall psychological health in this particular population.

The effectiveness of any diabetic treatment plan relies on successful self-management with emotional and psychosocial factors playing a large role in implementation, this is even more important as T1DM adolescents gain a greater desire for independent self-care skills.³¹ By establishing a strong patient-pharmacist relationship, pharmacists can provide comprehensive counseling approach to maximize the benefits of mobile-based applications and help empower patients to take a more active role in managing their own condition effectively.³²

Socio economic factors play a role in the control of diabetes mellitus specially in the adolescent age group. 33 This is important to highlight because the South Asian region has significant variability in glycemic control, hypoglycemia, complication rates, and diabetes care among young people with T1DM. Most individuals do not achieve adequate glycemic control, placing them at high risk of complications such as severe hypoglycemia SH and diabetic ketoacidosis (DKA). Episodes of severe hypoglycaemia can have an impact on HbA1c levels which has an impact on the development of long term diabetes complications associated with diabetes.34 We found that the severe hypoglycaemic and ketoacidotic episodes in 12 months at the end of the study were fewer in the MTG group. Concern was that a lower HbA1c found in MTG would be associated with an increase in such episodes however this was not the case. Studies have shown that apps overall reduce HbA1c levels from baseline without an increased risk of hypoglycaemia, especially auxiliary type apps and longer intervention durations.35

The study by Zhang et al. showed that app self-management alone was difficult to achieve long-term effective glucose control and further interactive management is required but the focus was on adults with poorly controlled diabetes. Our study did not involve telemedicine follow ups with a health care professional since our focus was observing the independent effect that patient app use had on glycemic control. The use of a diabetes-related smartphone application combined with further support from pharmacists represents an opportunity for mobile apps to be part of the diabetes management ecosystem and long term glycemic control (Figure 4). Regional studies have shown that mobile applications within systems supporting its use and connection to healthcare professionals have increased medication adherence and frequency of blood glucose testing compared with usual care participants. The structure of the structure of

The usage of mobile applications presents a unique underutilized opportunity for pharmacists to engage actively with patients through counselling and even through remote monitoring and intervention. The expansion of such applications allowing direct communication features between patients and pharmacists within such applications could further enhance the pharmaceutical care process and contribute to improved diabetes outcomes. Pharmacists can help address patient motivation, goal-setting, and behavior change strategies.³⁸



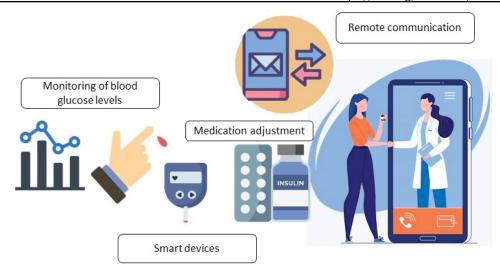


Figure 4. Application of mobile technology for diabetes management

Adolescence is characterized by the need for peer support and this is a vital component of the social experience, leading to improved glycemic control, reduced negative emotions, and enhanced quality of life. Traditionally peer support has been via focus groups and diabetes camps which can be challenging in terms of scheduling and access for many individuals. Mobile applications provide a unique opportunity for peer support and has shown positive outcomes in.^{39,40}

Compared to computer based and web based technologies, the very nature of smartphones makes them much more intuitive to use and convenient. The integration of artificial intelligence will be a valuable asset for diabetes management technologies and can produce patient-specific interventions that more effectively lead to behavior change and glycemic control. Analysis of blood glucose data can identify patterns that can predict hypoglycemic and hyperglycemic events, identify high risk time periods during daily use, provide strategies that can help reduce the risk of such events and even inform the healthcare provider so counselling and treatment can be altered accordingly ⁴¹. The use of artificial intelligence help creates personalized, data-driven predictive models to assist healthcare providers' counselling.⁴²

CONCLUSION

This study revealed that the mobile app-based intervention mode could improve the control rate of HbA1c and the number of acute diabetic related complications in adolescents with T1DM. It showed significant improvement in the patient's glycemic control and acute complication rate when compared to the usual care mode. Further large scale studies are required to support the findings and investigate the benefit of such interventions in the long run for this particularly vulnerable group of individuals.

The use of smartphone apps in patient management is there to complement instead of replacing conventional care models. While smartphone apps can facilitate diabetes self-management, a multidisciplinary healthcare team remains the key to achieving satisfactory patient outcomes. Pharmacists are well positioned to offer patients personalized guidance tailored to each patient's specific needs, considering factors such as their medication regimen, dietary patterns, and lifestyle choices. They can provide valuable insights into the behavioral and psychosocial aspects of diabetes self-management which are vital at the adolescent stage. Ultimately through the appropriate use of counselling with T1DM the aim is to facilitate a holistic and patient-centered care approach for adolescents affected by the condition.

The study has limitations that we recognize. Firstly, during screening the apps to assist participant point, the potential apps were screened for focusing on diabetes self-management but complete or comprehensive usability and content of the apps were not assessed. Secondly the number of apps available in the market increases at a rapid pace and this does not allow an up to date estimation of improved apps or updated apps for the duration of the study. Thirdly apps that had multiple language versions specifically Urdu had to be utilized since this is the national language of Pakistan and the most spoken or understood by the study population involved in our study. Apps with other features but restricted in languages were not selected and this meant that most apps were limited to having been developed within the country. Additionally, relevance to diabetes glucose level self-management is context specific and is dependent on individual requirements however this study covered a wide range of apps to suit the different needs to of the study participants.

DATA AVAILABILITY

Data can be made available upon reasonable request.



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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

FUNDING INFORMATION

The study received the hospital research grant approved by the

AUTHOR CONTRIBUTION

Conceptualization, supervision and data collection were by N.H as well as S.A. N.H, S.A. and A.H.I.A contributed to the methodology and data analysis. N.H, A.H.I.A and S.A. were responsible for the writing – original draft preparation, review and editing.

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