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The Efficacy of mHealth Interventions in Treatment of Gestational Diabetes Mellitus: A Research Protocol

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Abstract
Introduction: Gestational diabetes mellitus (GDM) is a disease characterized by dysfunctional glucose regulation resulting from issues with insulin production and/or regulation. If not controlled, GDM can have significant impacts on fetal development and may lead to complications in pregnant women. GDM is often treated with regular glycemic monitoring, dietary and lifestyle changes, and in most cases insulin injections. As a result of the number of interventions, managing GDM can add further stress to a pregnancy. In this study, we aim to investigate the effects of mobile health (mHealth) solutions on the outcomes of pregnant women experiencing GDM, and their babies.
Methods: The sample population of pregnant women with GDM will be split into two groups: the control group will receive usual care for glycemic control as outlined by their endocrinologists and/or gynecologists, while the experimental group will receive care for glycemic control using mHealth interventions. Patients will be monitored on a bi-weekly basis from the time they were diagnosed with GDM to the time of the delivery of their babies. Compliance, blood glucose levels, pregnancy and neonatal outcomes, and weight gain will be monitored. A two-sample proportion test and 95% confidence interval will be generated to compare the variables between each category.
Results: We anticipate that the experimental group will have higher compliance, with less emergency outpatient visits, reduced weight gain, and higher satisfaction with their intervention method. We also anticipate the same blood glucose measurements in both pre- and post-prandial states. The same maternal and neonatal post-delivery outcomes are also expected.
Discussion: This study evaluates the effectiveness of mHealth interventions on glycemic control. Future research may investigate the maternal effects of stress in conjunction with diabetes, as well as evaluating existing mHealth solutions for factors such as accessibility, and available features.
Conclusion: We anticipate that mHealth interventions, used alongside traditional glycemic monitoring methods, will improve the outcomes of pregnant women with GDM by reducing stress and empowering them to take control of their own treatment.

Keywords: gestational diabetes mellitus; GDM; mobile health; mobile health interventions; mHealth; remote healthcare; remote patient monitoring; telemedicine; user-directed health technology; eHealth

Introduction

Every year, 2%-10% of pregnancies are affected by gestational diabetes mellitus (GDM), and this number is only increasing [1]. In those with GDM, hormones produced because of pregnancy can cause issues with insulin production and/or regulation (e.g., exaggerated insulin resistance). This can lead to a variety of symptoms stemming from high blood sugar (hyperglycemia) and can increase the risk of complications in both pregnant women and their babies [2]. GDM often develops around the 24th week of pregnancy, and if left untreated, can cause major deficits [1]. Hyperglycemia throughout pregnancy has been shown to increase babies' risk of being born too large (macrosomia), which can also lead to many complications during delivery, and as a result, women diagnosed with GDM are far more

likely to deliver via caesarean section [2]. Macrosomia also increases the risk of the child developing obesity or type 2 diabetes in the future [3]. Furthermore, about 50% of women diagnosed with GDM go on to develop Type 2 Diabetes Mellitus (T2D), a condition characterized by long-term insulin resistance, and associated chronic, adverse health events [1].

For these reasons, it is essential to treat and control GDM as quickly and as effectively as is possible. Most GDM treatments involve dietary and lifestyle changes such as increasing physical activity levels, eating healthier, and losing weight (at a healthy rate) [1]. However other medical interventions can include medications and insulin injections [1]. Regular glycemic monitoring throughout the pregnancy is essential in ensuring the short and long-term health of

both the mother and child. Due to the number of interventions, managing GDM can be difficult for pregnant women, especially when already coping with the stresses of pregnancy [4].

Mobile health (mHealth) is a rapidly expanding field referring to the use of mobile and wireless devices to improve health and deliver care. This is made especially relevant due to the CoVID-19 global pandemic, and the resulting decreased access to/increased fear surrounding in-person healthcare [5]. mHealth can be a valuable healthcare resource, given the rapidly increasing prevalence of smartphone ownership, globally. The number of installations of wellness and health applications (apps) has reached an estimated 3.35 billion worldwide, demonstrating the consumer appeal of mHealth solutions [6]. Many apps exist to aid in monitoring and treatments of diabetes, most including features focussing on [7]:

1. Mobile blood glucose self-measurement and logging
2. Improving diet and healthy eating habits
3. Increasing physical exercise levels
4. Increasing adherence to medications/insulin dosage calculations
5. Increasing the level of education and/or awareness about the condition
6. Real-time, remote conferencing between GDM patients and health care professionals.

The effectiveness of mHealth solutions in the treatment of disease is currently unclear, and few past studies on mHealth and its impacts on the treatment of GDM, specifically, have been conducted [6]. As a result, this research protocol aims to answer the question 'What is the effect of mHealth interventions compared to usual care on glycemic control in women with GDM during pregnancy?', and further the current body of research surrounding mHealth usage in the treatment of GDM. We hypothesize that the use of mHealth solutions in treatment and control of GDM will decrease the number of pregnancy/delivery-related complications in mothers and infants, and will increase new mothers' satisfaction with their quality of care, throughout pregnancy, through a combination of several mechanisms, discussed later in this paper.

Methods
Ethics Approval
This is a project conducted by students that will take place at McMaster University, and a General Research Application form will be submitted to the online application system from Hamilton's Integrated Research Ethics Board (HiREB), where all authors will act as co-investigators. We anticipate receiving ethics approval from HiREB via the application submitted.100 20- to 30-year-old, pregnant female patients with GDM will be recruited for this study from Obstetric Medicine at the Boris Clinic from McMaster

University Medical Centre in Hamilton, Ontario. Additionally, participants who are in their second trimester and are pregnant with only one child will be accepted for this study. Finally, participants who were diagnosed with GDM within two weeks prior to the recruitment will be accepted. We anticipate to partner with obstetrician/gynecologist (OB/GYN) from the Obstetric Medicine at the Boris Clinic to recruit participants. This study requires confidential information regarding the patients from, thus, it will be obtained with consent, with the help of the OB/GYN, through the signing of a contract at the beginning of the experimental period. All information provided will be anonymous by assigning each participant a number from 1 to 100. This is a clinical trial involving pregnant individuals as the subjects of this experiment, so no harm will come to the mother and the child; both the control and experimental groups will receive regular treatments from their OB/GYN.

Data Collection
Once the participants' consent has been obtained, the participants' age, their expected date of delivery, the number of children they have had prior to this pregnancy, weight prior to pregnancy, and the type of diabetes (pre-gestational vs gestational) will be collected [8]. Participants will also need to specify whether they have access to a smartphone before random assignment into control and experimental groups in accordance with a randomized control trial (RCT) study design. Having access to a smartphone indicates the socioeconomic status of the women, so it introduces another factor that may contribute to outliers in the data produced, which will be taken into consideration when analyzing the data. Due to the nature of the intervention (mobile app), blinding of the experimental and control groups is not possible in participants for this experiment. The control group (n=50) will follow usual treatments as outlined by their OB/GYN. The participants in this group will visit their OB/GYN every two weeks with their logbook and monitor to report their blood glucose readings. The experimental group (n=50) will have access to a mobile app that can alert them of treatments they must follow and directly connect them to their doctor. The mobile app will be a replacement for a paper logbook, and it will be directly interpreted and sent to their OB/GYN [9]. The mobile app used will be selected after careful evaluation of currently available apps and their features to ensure prevention of a data breach.

The OB/GYN of each participant will report their data on a bi-weekly basis from the time the participants are recruited to one month after they give birth; this study will run for a full year [10]. The OB/GYN will report blood glucose, pre- and post-prandial, and weight, which will be recorded [9, 10]. Any complications during the pregnancy will be reported by the patients' OB/GYN [12]. During the last month of the experiment, the mode of delivery, neonatal outcomes of both the mother and the baby,

compliance with the recommended treatments, and overall satisfaction with the care received will also be reported in a questionnaire filled out by the patients. Finally, the date of the delivery of the baby will be recorded.

Data Analysis

At the beginning of the experiment, the age of the participants, the number of children they have previously had, the type of diabetes, and the expected and actual delivery dates, will be kept in records to explain any outliers in the observed data.

As the data is being collected on a bi-weekly basis, the mean of both the pre- and post-prandial blood glucose readings for women in both categories will be calculated. With that, the rate of change of the blood glucose will be analysed once the experimental period is over. This analysis will be conducted by plotting the means of the blood glucose readings for the women against a linear regression model that will be shared by both categories [10]. Rates of change will then be compared by calculating a 95% confidence interval.

To compare the other variables in each category, the proportion of women will be calculated as the study progresses. With this, a two-sample proportion test will be conducted to see if the differences in each category are significant, where $p<0.05$ is statistically significant.

Results

As this is a research protocol, no real data was generated. However, based on previous studies, we anticipate having no significant difference between the control group and the experimental groups' blood glucose levels [9]. The difference in the rate of change between the two groups is predicted to be -0.01 mmol/L, where the 95% confidence interval will be somewhere between -0.10 to 0.08, so the difference is not statistically significant [10]. We also expect the proportion of women from each category having a similar mode of delivery and similar healthy maternal and neonatal outcome post-delivery [12]. Each variable will have an insignificant difference because the expected p-value will be greater than 0.05 from the two-sample proportion test conducted.

In contrast, there will be a chance of significant difference between the control and experimental groups for the proportion of women who gained weight, followed the recommended treatments, and their overall satisfaction with their mode of intervention. The two-sample proportion test generates an expected result of $p < 0.01$ for compliance and satisfaction of the treatment, which indicates that experimental group were easily able to comply with their OB/GYN's instructions and were satisfied with their treatment [9]. In addition, the two-sample proportion test generates an expected result of $p < 0.0001$ for weight gain, which indicates that the experimental group had reduced gain in weight [11].

Discussion

The effects of mHealth solutions on the treatment of GDM is unclear, due to a large amount of variability, both in mHealth solutions available, as well as individual treatment plans [6]. Through this research protocol, we aim to further knowledge surrounding the relationship between mHealth and GDM outcomes through a more tightly controlled study design. All participants will be drawn from a single healthcare provider (Obstetric Medicine at the Boris Clinic), providing a larger amount of heterogeneity between individual treatment plans, via the reduction of confounding variables. Additionally, after a thorough evaluation of app features, a single mHealth app will be assigned to all members of the experimental group, eliminating any variability in mHealth solutions used between participants.

Although the mHealth interventions received by the experimental group was not significantly different from the regular interventions received by the control group in terms of blood glucose levels, and maternal and neonatal outcomes post-delivery outcomes, other factors could also play a role in data discrepancies. We expect to see the most significant changes in compliance to the treatment plan between groups. This is a useful measure of the effects of mHealth on overall clinical outcomes, as previous research into mHealth and non-gestational diabetes has demonstrated that compliance is closely associated with clinical outcomes [13]. There is an assumption that all participants will be recruited at the onset of the experiment, with few withdrawals from the experiment, or, the sample size will be large enough to account for a small amount of attrition. It is also assumed that all participants will deliver their child on their expected delivery date. Other factors (e.g., age, number of children, type of diabetes, and socioeconomic status) influencing the data will be overlooked unless there is an outlier that can be explained by those factors. Should withdrawals from the experiment occur, the sample size for each group will be imbalanced, and this can be accounted for in the statistical analysis if both the sample sizes are greater than 30 participants.

Overall, mHealth interventions may improve patient treatment by allowing remote, real-time interactions between patients and their OB/GYNs at any time, setting reminders for their treatments, and making logging blood glucose far easier. The results of previous research on mHealth in treatment of diabetes in all forms, with a larger number of women following their treatments and reporting satisfaction with their intervention method early on, makes this evident [14]. Another important clinical outcome that must be considered is weight gain. In previous research, it was found that women treated using mHealth gained less weight over the course of their pregnancy. This implies that the use of mHealth in treating GDM leads to fewer risks, as weight gain post-pregnancy has been highly correlated to higher rates of negative long-term maternal health outcomes such as type 2 diabetes and cardiovascular

disease [15]. In previous studies, it is also shown that fewer emergency outpatient visits were made by the experimental group than the control group [12].

Conclusions

With a tightly controlled study design we expect to determine a more thorough correlation between mHealth and treatment outcome for GDM than has been done previously. We expect that mHealth will improve outcomes through an interplay of several factors:

1. Reducing the stress of monitoring many health outcomes/treatments simultaneously
2. Motivating adherence to the treatment plan, by facilitating easier following of treatment progress
3. Empowering diabetic patients to take control of their own care
4. Making it easier for patients to get medical advice about diabetes management (accessibility)

Through this study, we aim to increase awareness surrounding mHealth, as well as the importance of holistic (non-pharmacological) intervention in treatment of GDM (as well as other conditions) using mHealth. We also hope to further support the implementation of this type of intervention on a more widespread scale. This is made especially relevant given the current CoVID-19 global pandemic, resulting in lower availability and increased patient hesitancy surrounding seeking in-person care [5]. Should we determine mHealth as an effective treatment mediator, widespread implementation will assuage the fears of expectant mothers with GDM, as well as protecting them from infection, without sacrificing the level of care received.

Further research could focus on the long-term health of mothers who suffered from GDM and used mHealth interventions during their pregnancy relative to those who did not. This could also be examined for the children of these mothers. Examining factors such as blood sugar, and diagnosis of T2D in both mothers and children in the long term would provide even further insight into the efficacy of mHealth solutions, potentially strengthening any existing positive correlations surrounding the efficacy of mHealth in these types of treatments.

List of Abbreviations Used
mHealth: mobile health
GDM: gestational diabetes mellitus
T2D: type 2 diabetes
RCT: randomized control trial
OB/GYN: obstetrician/gynecologist

Conflicts of Interest
The authors declare that they have no conflicts of interest.

Ethics Approval and/or Participant Consent
This study did not require ethics approval and participant consent because no experiments were done, and no live participants were recruited for this research protocol.

However, should this investigation ever be conducted beyond this protocol, ethics approval will be obtained through Hamilton's Integrated Research Ethics Board (HiREB). A contract will be signed by the participants at the start of the study to obtain their consent; however, should they choose to terminate their participation in the study, they can contact the primary researcher(s) to withdraw at any time.

Authors' Contributions
All authors contributed to the design of the study, drafted the manuscript, critically appraised and revised, and gave final approval of the version to be published.

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