September 2016

Glucose monitoring in pregnancy complicated by diabetes.

Aisha Sheikh
Agha Khan University, aisha.sheikh@aku.edu

Abdul Jabbar
Aga Khan University

Glucose monitoring in pregnancy complicated by diabetes

Aisha Sheikh, Abdul Jabbar

Abstract

Diabetes in pregnancy is associated with adverse maternal and neonatal outcomes. Due to variations in insulin resistance throughout pregnancy there is a continuous need to implement Medical Nutrition Therapy (MNT), exercise and pharmacological treatments which have to be escalated. Self-monitoring of blood glucose (SMBG) is integral to the management of diabetes in pregnancy. Proper implementation of SMBG in pregnant women with diabetes requires patient education and understanding of its applications and limitations. Real-time results enable individuals to make informed daily self-care decisions regarding diet, exercise, and insulin. Retrospective analysis of SMBG data enables clinicians to develop individualized care plans, informing decisions related to insulin initiation and adjustment and the possible needs for interventions or hospitalization to improve inadequate self-monitoring.

Keywords: Pregnancy, Diabetes Mellitus, Self-monitoring of blood glucose, hyperglycaemia.

Introduction

The St. Vincent Declaration in 1989 in a meeting arranged by World Health Organization (WHO) and International Diabetes Federation (IDF) highlighted in one of its clause in the Five-year targets as "……Achieve a pregnancy outcome in the diabetic woman that approximates that of the non-diabetic woman…..".[1] But as yet we are far from achieving such an outcome globally. The troubling aspect is the increasing incidence of Diabetes Mellitus in the young. The IDF Atlas 2015 gave an estimate that 86,000 children under 15 years develop Type 1 diabetes Mellitus (T1DM) annually worldwide.[2] Interestingly the incidence of Type 2 Diabetes Mellitus (T2DM) is increasing in children and adolescents in some countries. Rising incidence/prevalence of Diabetes Mellitus in young means that these individuals will be starting their reproductive lives with Diabetes as a co-morbid and more and more pregnancies will be complicated by diabetes. In the year 2015, 20.9 million (16.2%) live births were affected by hyperglycaemia in pregnancy out of which 85.1% were due to Gestational Diabetes and 7.4% and 7.5% were due to overt diabetes and pre-existing diabetes respectively.[2] The South-East Asian region is facing the major brunt with 24.2% pregnancies complicated by some form of hyperglycaemia.[2] Sadly, the vast majority (87.6%) of hyperglycaemia in pregnancy is from low and middle-income countries where the access to maternal care is already compromised.[2]

Pregnancies complicated by Hyperglycaemia whether it's Gestational, Overt or Pre-existing T1DM or T2DM are associated with significant maternal and foetal/neonatal morbidity and mortality.[3] However, with the discovery of insulin and its safety for use in pregnancy and then in later years the evidence on the safety of some oral anti-hyperglycaemic agents in pregnancy resulted in improved outcomes of such pregnancies. Another major technological advancement, however, is the availability of glucose meters for personal use through which self-monitoring of blood glucose (SMBG) helps the patient and the health care provider in making treatment decisions and modifications.[4]

Need to self-monitor blood glucose during pregnancy

Optimizing glycaemic control improves the maternal and neonatal outcomes but achieving such tight control as recommended for preconception and pregnancy are not easy (Table).[5] Achieving such targets are quite challenging and if the woman is at risk of frequent hypoglycaemic events especially those with T1DM who often get hypoglycaemia unawareness then the targets can be relaxed to a little extent.[4] Since the insulin physiology alters throughout pregnancy there is a great need to modify pharmacological treatments throughout pregnancy which is impossible without dedicated SMBGs. In early pregnancy, there is insulin sensitivity in T1DMs and some variability to this insulin sensitivity which results in frequent modifications of insulin doses.[4] However, for most of Prediabetes, T2DMs and overt DM of pregnancy will notice increasing insulin requirements during pregnancy. The insulin resistance rises exceptionally during the late second and third trimester of pregnancy and

Table: Recommended glycemic targets in pre-conception period and during pregnancy.

	Timing	Goal	
		mg/dl	mmol/l
Fasting	On awakening	60-90	3.3-5.0
Preprandial	Before every meal	60-90	33.5.0
1-hour postprandial	1 hour after every meal	70-140	3.9-7.8
2-hour postprandial	2 hour after every meal	70-120	3.9-6.7

Department of Medicine, The Aga Khan University Hospital, Karachi.
Correspondence: Aisha Sheikh. Email: aisha.sheikh@aku.edu

plateaus towards the end of third trimester necessitating insulin dose adjustments accordingly based upon SMBG.[4]

Timing and frequency of Self-monitoring of blood glucose

There is no "one size fit all" approach and the advice on how and when to test in a particular pregnant woman has to be individualized.[6] To achieve a good metabolic control in a pregnant woman with hyperglycaemia, the timing and frequency of SBMG has to be tailored based upon following factors:

- Diagnosis — whether the woman has Pre-existing T1DM, Pre-existing T2DM, Overt Diabetes of pregnancy or Gestational Diabetes Mellitus

- Stage of pregnancy — whether she is in her first, second or third trimester of pregnancy.

- Hypoglycaemia awareness — whether she is hypoglycaemia aware or unaware. Someone who has unawareness of hypoglycaemia will need more frequent SMBG.

- Evidence of polyhydramnios and foetal macrosomia on foetal growth scan — Postprandial monitoring is associated with better glycaemic control and lower risk of preeclampsia.[7] However, if there is evidence of polyhydramnios and foetal macrosomia on foetal growth scan despite an apparent normal control based upon fasting and post-prandial measurements then there is a need to increase the frequency of SMBG to detect unusual hyperglycaemic peaks that are leading to such problems in growth scan.

SMBGs in women with Pre-existing T2DM or Overt diabetes of pregnancy

In early weeks of pregnancy, the high maternal blood glucose increases the risk of miscarriages and congenital malformations thus frequent SMBGs and insulin dose adjustments are required. Ideally fasting, premeals and 1 or 2-h post meals glucose values should be obtained on daily or alternate days and this data should be utilized to look for adherence to medical nutrition therapy and to make necessary and frequent insulin dose adjustments. The frequency of testing can be reduced in early second trimester but has to be increased again later since the hyperglycemia during the late second trimester and third trimester directly leads to fetal hyperinsulinemia that leads to macrosomia and neonatal hypoglycemia.[8] The increasing insulin resistance of pregnancy at this stage warrants frequent insulin dose adjustments based on SMBGs. Another problem could be severe hypoglycemia that is highlighted in a study on 27 pregnant women with T2DM. In the year before pregnancy only 0.1 event/patient-year were reported but during pregnancy 0.9 events patient-year were reported with frequencies of 0.5, 0.8 and 1.2 events/patient-year in 1st, 2nd and 3rd trimester respectively.[9] Patient education and SMBGs with tailored treatments can lessen the risk of these hypoglycemic episodes.

SMBGs in women with Pre-existing T1DM

Due to the changes in insulin sensitivity in the 1st trimester of pregnancy and since this is the crucial period of organogenesis, the need for frequent SMBGs cannot be over-emphasized. Women with T1DM in their 1st trimester are at risk of frequent hypoglycaemia including severe hypoglycaemia that can lead to hypoglycaemia unawareness. In 108 pregnant T1DM women; severe hypoglycaemia occurred in 45% of women with the frequencies of 5.3, 2.4 and 0.5 events per patient-year in 1st, 2nd and 3rd trimester of pregnancy respectively.[10] In the same cohort of women, mild hypoglycaemia occurred by 5.5 events/patient-week in early pregnancy and decreased throughout pregnancy.[10] Predictors of severe hypoglycaemia were history of severe hypoglycaemia and impaired awareness.[10] Pregnant women with T1DM should thus be testing their blood glucose at least 6-10 times daily including premeals, post prandials, bedtime, early morning i.e. 3-4 am and modify their MNT and insulin doses according to the advice of their physician.[11]

SMBGs in women with Gestational Diabetes Mellitus

Women with GDM can perform their fasting glucose and 1 or 2 hour post prandial glucose. Initially when they are on MNT and exercise alone the frequency of testing can be reduced to alternate days or every 3rd day.[12] Once they are started on pharmacological treatment then they need to test on daily basis especially in the later part of 2nd trimester and 3rd trimester. Insulin treated patients need more frequent SMBGs as compared to oral antihyperglycaemic agent treated women. Patients who are well controlled can reduce their frequency of testing to alternate day.

Translating the SMBG data for treatment decisions and adjustments

It is important to differentiate between checking blood glucose vs. monitoring as SMBG. A pregnant patient cannot monitor their glucose without checking but unfortunately patients often check their glucose without truly monitoring it which implies that they must understand what to do with the glucose reading and what measures to take. The pregnant diabetic woman is very committed, motivated and compliant and the health care professional has to educate her sufficiently to gain the maximum benefit of these positive attributes to achieve better neonatal and maternal outcomes. This data helps them make changes in their MNT and exercise. Pregnant women can be educated to self-adjust their insulin doses according to their SMBG

logs and this self-adjustment of insulin can be checked for their appropriateness on clinical visits. Similarly these logs help the physician in counseling the patient about the effect of MNT, exercise and relationship of her glucose values to her basal or bolus insulin. This data is extremely useful in making dose escalations in pharmacological treatments as the pregnancy progresses.

Dynamics of Glucose meters

There are several kinds of glucose meters available that vary in terms of different characteristics like volume of blood sample, size, speed of testing, memory capacity, type of technology applied, costs, need for a code and type of strips used.[6] Since the introduction of glucose meters in 1970s, the accuracy (how closely the measured value is to the actual value) and precision (the ability to obtain highly reproducible results) have been steadily improving.[8] The hazards of incorrect readings will be suboptimal treatment decisions including improper adjustments in medication dosage potentially increasing the frequency of both hypoglycaemia and hyperglycaemia. All this can result in a huge impact on the pregnant woman and her baby. Thus a pregnant patient requires the highest accuracy in glucose monitoring especially in those who have hypoglycaemia unawareness as well. If the meter result is ±5% compared to laboratory values, is considered the most accurate while ± 10% and ±15% are considered more accurate and accurate respectively.[8] However, even the most accurate meter today has only 63% acceptable values in the 5% accuracy range.[8] Thus, it can be difficult for the physicians and patients to assess the accuracy of blood glucose monitoring systems and SMBG errors are poorly understood by patients and their providers. The physician can help identify the source of errors that can result in inaccurate results and can help prevent and correct such errors.

Overcoming barriers to self-monitoring of blood glucose during pregnancy

Patient education remains the key to the success of SMBG during pregnancy. They need to be educated about the importance of SMBGs which help in making therapeutic decisions and dose adjustments that has a primary role on reducing the complications during and after pregnancy. The patient must be properly educated about all the aspect of meter use i.e. how to code the meter, wash her hands prior to testing and applying correct amount of blood to the test strip.[6] They need to be educated about the proper storage and disposal of test strips, the fact that they should use test strips before expiration. If the strips are subjected to extremes of temperature and humidity then these have to be disposed of.[6] Similarly, the education should address her fears of inconvenience and pain due to lancet prick, social stigmas of testing in public places. They should be educated about keeping their logs of SMBGs, food, and doses of their insulin on specific charts (Figure-1).

Glucose monitoring chart & diet diary

Patient name_____ Medical Record #:_____

Date	Fasting glucose	Drug/ dose	Breakfast	2 h post breakfast glucose	Drug/ dose	Pre-lunch glucose	lunch	2 h post lunch	Drug/ dose	Pre-dinner glucose	dinner	2 h post dinner	Bedtime insulin	Special comments

Targets: Fasting and premeals: 60-95 (90) mg/dl 1-h post meal: 70-140 mg/dl 2-h post meal: 70-120 mg/dl

Figure-1: Glucose monitoring chart & diet diary.

Continuous Glucose Monitoring systems (CGM)

Real-time CGM generates a detailed profile of glucose excursions that can be helpful when making decisions regarding self-care and treatment planning.[8] A secondary analysis of two European randomized controlled trials of continuous glucose monitoring in 89 patients with T1DM and 28 patients with T2DM showed that a higher mean glucose level (126 compared with 120 mg/dL) in the second and third trimesters (117 compared with 115 mg/dL) occurred in pregnancies with Large for gestational age (LGA) neonates compared with those with non-LGA neonates.[13] This analysis was able to pick some specific patterns of hyperglycaemia which could be target to additional insulin coverage and adjustments.

CGM can identify many episodes of hypo- and hyperglycaemia that would go undetected by SMBG. CGM appears superior to SMBG in this regard, but it remains to be seen whether CGM improves pregnancy outcomes and cost is a major concern in middle and low socioeconomic countries.[8]

The expert suggestion about CGM is to use it during pregnancy complicated by either gestational or pre-existing diabetes Mellitus when SMBGs are not sufficient to assess glycaemic control including both hyperglycaemia and hypoglycaemia.[11]

The Future

Different research groups have developed interactive, smartphone- based, remote blood glucose monitoring systems and have demonstrated their convenience and acceptability to women with GDM.[14] Clinical and economic outcomes of such systems are currently under investigation.

Conclusion

Insulin use and SMBGs have revolutionized management of a pregnancy complicated by diabetes. Achieving adequate glycaemic control is the key to improve maternal and neonatal outcomes. The most important step towards a tight glycaemic control in pregnancy is patient adherence to SMBG. A pregnant woman is the most compliant and motivated patient amongst all the patients with diabetes and for a short period of pregnancy a shared care involving physicians, diabetes educators and nutritionists with the patient at the center is paramount to a successful outcome. With proper education of the pregnant woman, SMBG data can be utilized in real-time by the patient herself to make treatment and lifestyle adjustment and in retrospect by her physician to individualize care and make necessary therapeutic decisions.

References

1. Holleman F. The St. Vincent declaration on the treatment of diabetes. Diapedia 2014. Available from: http://dx.doi.org/10.14496/dia.8105473810.9. [Accessed 28. April,2016--]
2. IDF Diabetes. 7 ed. Brussels, Belgium: International Diabetes Federation, 2015. Available from: http://www.diabetesatlas.org [Accessed on 9. December, 2015--]
3. Tennant PW, Glinianaia SV, Bilous RW, Rankin J, Bell R. Pre-existing diabetes, maternal glycated haemoglobin, and the risks of fetal and infant death: a population-based study. Diabetologia 2014; 57: 285-94.
4. American Diabetes Association. Management of diabetes in pregnancy. Sec. 12. In standards of medical care in diabetes - 2016. Diabetes Care 2016; 39 (Suppl. 1): 94-8.
5. Committee on practice bulletins- obstetrics. Practice bulletin no. 137: gestational diabetes mellitus. Obstet Gynecol 2013; 122: 406-16.
6. Negrato CA, Zajdenverg L. Self-monitoring of blood glucose during pregnancy: indications and limitations. Diabetol Metab Syndr 2012; 4: 54. doi: 10.1186/1758-5996-4-54.
7. Manderson JG, Patterson CC, Hadden DR, Traub AI, Ennis C, McCance DR. Preprandial versus postprandial blood glucose monitoring in type 1 diabetic pregnancy: a randomized controlled clinical trial. Am J Obstet Gynecol 2003; 189:507-12.
8. Bailey TS, Grunberger G, Bode BW, Handelsman Y, Hirsch IB, Jovanovi? L, et al. American association of clinical endocrinologists and American college of endocrinology 2016 outpatient glucose monitoring consensus statement. Endocr Pract 2016; 231-61.
9. Secher AL, Mathiesen ER, Andersen HU, Damm P, Ringholm L. Severe hypoglycemia in pregnant women with type 2 diabetes- a relevant clinical problem. Diabetes Res Clin Pract 2013; 102: 17-8.
10. Nielsen LR, Pedersen-Bjergaard U, Thorsteinsson B, Johansen M, Damm P, Methiesen ER. Hypoglycemia in pregnant women with type 1 diabetes. Predictors and role of metabolic control. Diabetes Care 2008; 31: 9-14.
11. Blumer I, Hadar E, Hadden DR, Jovanovi? L, Mestman JH, Murad MH, et al. Diabetes and pregnancy: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2013; 98: 4227-49.
12. Mendez-Figueroa H, Daley J, Lopes VV, Coustan DR. Comparing daily versus less frequent blood glucose monitoring in patients with mild gestational diabetes. J Matern Fetal Neonatal Med 2013; 26: 1268-72.
13. Law GR, Ellison GT, Secher AL, Damm P, Mathiesen RT, Temple R, et al. Analysis of continuous glucose monitoring in pregnant women with diabetes: distinct temporal patterns of glucose associated with large for gestational age infants. Diabetes Care 2015; 38: 1319-25.
14. Hirst JE, Mackillop L, Loerup L, Kevat DA, Bartlett K, Gibson O, et al. Acceptability and user satisfaction of a smartphone-based, interactive blood glucose management system in women with gestational diabetes mellitus. J Diabetes Sci Technol 2015; 9: 111-5. doi: 10.1177/1932296814556506.