

RESEARCH ARTICLE

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Preconception care of women with diabetes: a review of current guideline recommendations

Maimunah Mahmud^{1,2}, Danielle Mazza^{3*}

Abstract

Background: The prevalence of type 2 diabetes mellitus (T2DM) continues to rise worldwide. More women from developing countries who are in the reproductive age group have diabetes resulting in more pregnancies complicated by T2DM, and placing both mother and foetus at higher risk. Management of these risks is best achieved through comprehensive preconception care and glycaemic control, both prior to, and during pregnancy. The aim of this review was to compare the quality and content of current guidelines concerned with the preconception care of women with diabetes and to develop a summary of recommendations to assist in the management of diabetic women contemplating pregnancy.

Methods: Relevant clinical guidelines were identified through a search of several databases (MEDLINE, SCOPUS and The Cochrane Library) and relevant websites. Five guidelines were identified. Each guideline was assessed for quality using the AGREE instrument. Guideline recommendations were extracted, compared and contrasted.

Results: All guidelines were assessed as being of high quality and strongly recommended for use in practice. All were consistent in counselling about the risk of congenital malformation related to uncontrolled blood sugar preconceptionally, ensuring adequate contraception until glycaemic control is achieved, use of HBA1C to monitor metabolic control, when to commence insulin and switching from ACE inhibitors to other antihypertensives. Major differences were in the targets recommended for optimal metabolic control and opinion regarding the usage of metformin as an adjunct or alternative treatment before or during pregnancy.

Conclusions: International guidelines for the care of women with diabetes who are contemplating pregnancy are consistent in their recommendations; however some are more comprehensive than others. Having established current standards for the preconception care of diabetic women, there is now a need to focus on guideline implementation through an examination of the barriers and enablers to successful implementation, and the applicability of the recommendations in the local setting.

Background

The prevalence of type 2 diabetes mellitus (T2DM) continues to rise worldwide [1,2], with population based studies reporting increases in Malaysia [3], the UK [4], the USA [5], Europe [6] and Australia [7]. In developed countries, more than half of all people with diabetes are older than 65 years, and only 8% of adults with diabetes are younger than 44. In contrast, three quarters of people affected by diabetes in developing countries are under 65 years old, and 25% of all adults with diabetes are younger than 44 [8]. Thus more women of reproductive age in developing countries have diabetes,

resulting in an increased number of pregnancies complicated by T2DM [9-11] placing both mother and foetus at higher risk of morbidity and mortality [12].

Diabetes in pregnancy is associated with higher rates of miscarriage, pre-eclampsia, preterm labour and higher rates of fetal malformation [13]; neural tube defect, urinary tract disorder, macrosomia, birth injury, and perinatal mortality [14]. These risks can be minimised by optimal glycaemic control, both prior to and throughout the pregnancy [15,16], and is best achieved through comprehensive preconception care where other issues such as genetic risks, health status, reproductive history, exposure to environment toxins, immunisation and lifestyle risk factors can also be addressed through a

* Correspondence: danielle.mazza@med.monash.edu.au

³Department of General Practice, School of Primary Health Care, Faculty of Medicine, Nursing and Health Sciences, Monash University, Victoria, Australia

multidisciplinary approach in community based management of diabetes before and during pregnancy [17,18].

Two previous guideline comparisons for the care of pregnant women (including preconception care) with diabetes exist [19,20]. The first was a comparison of international and New Zealand guidelines. This study reported a variation in recommendations for folate supplementation with the dose ranging from 0.4 mg to 5 mg and while the authors comment that the other preconceptional recommendations were broadly similar, the guidelines lacked contraceptive advice, specification of HbA1C targets and recommendations regarding medication review. The second review was conducted by the Centers for Disease Control (CDC); however, this review was restricted to guidelines available in the United States. The aim of this current review was to compare the quality and content of current national and international guidelines that are concerned with the preconception care of women with diabetes, and to develop a summary of recommendations to assist in the management of diabetic women contemplating pregnancy.

Methods

A systematic search was conducted of databases (Ovid Medline, the Cochrane Library, SCOPUS), guideline websites (clinical guidelines on Medical Journal of Australia website, Scottish Intercollegiate Guidelines Network, National Institute for Health and Clinical Evidence, New Zealand Guidelines Group, National Guideline Clearinghouse (US)) and other relevant websites (the American Diabetes Association, the Australasian Diabetes in Pregnancy Society, the Royal Australian College of General Practitioners and the Royal Australian and New Zealand College of Obstetricians and Gynaecologists). Search terms included: preconception care, pre conception care, preconception health, pre conception health, preconception, pre conception, pre-pregnancy care, pre pregnancy care, type 2 diabetes, diabetes mellitus and guidelines.

Our inclusion criteria were national and international English language guidelines published from 2001 to May 2009. We excluded those that were local or hospital based. Five guidelines that matched the criteria were identified [21-25]. Each guideline was scored for guideline quality by two independent appraisers using the AGREE instrument [26]. Differences were discussed and resolved. We compared and contrasted the guideline recommendations under the headings of: management approach, evaluation of previous medical and obstetric history, evaluation and treatment of diabetic complications, review of current medication, assessment of metabolic control, blood glucose management, folate supplementation, preconception counselling, contraindications to pregnancy and thyroid screening (Table 1).

From this, we developed a summary of preconception care recommendations for use by practising physicians.

Results

Of the five guidelines identified, two were from the American Diabetes Association (ADA) (ADA 2009 [21] and ADA 2004 [22]). The ADA 2009 is the generic guideline for medical care in diabetes with a specific chapter on pre-conception care, whereas the ADA 2004 guideline is focussed on preconception care of women with diabetes. The remaining guidelines were produced by the National Institute for Health and Clinical Excellence (NICE) (NICE 2008 [23]), the Scottish Intercollegiate Guideline Network (SIGN) (SIGN 2001 [24]), and the Australasian Diabetes in Pregnancy Society (ADIPS) (ADIPS 2005[25]).

Comparison of guideline quality

All guidelines were rated as being of high quality and strongly recommended for use in practice using the AGREE instrument. Scores for individual guidelines using the AGREE instrument are given in Table 2.

Comparison of guideline recommendations

Management approach and evaluation of previous medical and obstetric history

All the practice guidelines agree that diabetic women contemplating pregnancy should be seen by a multidisciplinary team; however this was not specifically mentioned by the NICE guidelines. Both the ADA 2009 and the SIGN guidelines recommend undertaking a complete preconception evaluation of the women's medical and obstetric history.

Evaluation and treatment of diabetic complications

Evaluating and treating diabetic retinopathy is recommended by all the guidelines and nephropathy by all except SIGN. The ADA and ADIPS guidelines also recommend an assessment of neuropathy and undertaking a cardiovascular assessment prior to conception.

Specifically assessing the women for hypertension is only recommended by ADA 2004 and SIGN with the latter nominating a target blood pressure (BP) of < 140/80 for women with diabetic nephropathy.

Review of current medication

Undertaking a medication review before a diabetic woman gets pregnant is recommended by all the guidelines except NICE. While stopping Angiotensin-Converting Enzyme (ACE) inhibitors is mentioned by all, some guidelines also recommend stopping statins [21,23,25] and angiotensin-II receptor antagonists (ARB) [21,23]. The ADA 2004 also recommends stopping diuretics and β -blockers.

Assessment of metabolic control and blood glucose management

Monitoring metabolic control using HbA1C and achieving a target of < 7% is recommended by all guidelines.

Table 1 A comparison of international guidelines recommendation for preconception care among diabetes

	ADA 2009	ADA 2004	NICE 2008	SIGN 2001	ADIPS 2005
Management by multidisciplinary team	✓	✓		✓	✓
Complete preconception evaluation of medical and obstetric history		✓		✓	
Evaluation and treatment of diabetic complications					
retinopathy	✓	✓	✓	✓	✓
nephropathy	✓	✓	✓		✓
neuropathy	✓	✓			✓
cardiovascular disease	✓	✓			✓
hypertension		✓		✓ target BP should be < 140/80	
Medication review					
Review all current medication	✓	✓		✓	✓
Stop Angiotensin-Converting Enzyme (ACE) inhibitors	✓	✓	✓	✓	✓
Stop Angiotensin-II Receptor Blockers (ARB)	✓		✓		✓
Stop statins	✓		✓		✓
Stop diuretics		✓			
Stop β -blockers		✓	✓	✓	
Assessment of metabolic control					
Measure	Use HbA1C	Use HbA1C	Use HbA1C	Use HbA1C	Use HbA1C
Frequency of testing		1-2 monthly			
Target level	< 7%	Up to 1% above normal value, lower if possible	< 6.1%	optimised HbA1C	< 7%
Blood glucose management					
Self monitoring targets		Before meals 4.4-6.1 mmol/l, 2 hours after meal <8.6 mmol/l		Between 4 and 7 mmol/L	
Educate regarding hypoglycaemia awareness and management			✓		✓
Prescribe insulin to achieve target blood glucose levels	✓	✓	✓	✓	✓
Use metformin as an adjunct or alternative	✓		✓		✓
Folate supplementation					
Commencement			preconception	preconception	Preconception
Dose			5 mg/day	5 mg/day	5 mg/day
Duration			until 12 weeks gestation	until 12 weeks gestation	
Preconception Counselling					
		should be routinely incorporated into diabetic care		is essential	
Advise of risk of malformation with poor metabolic control and unplanned pregnancy	✓	✓	✓	✓	✓
Advise use of effective contraception until good glucose control is achieved before conception	✓	✓	✓	✓	✓

Table 1: A comparison of international guidelines recommendation for preconception care among diabetes (Continued)

Inform woman about how DM affects pregnancy and how pregnancy affects DM	✓	✓	
Encourage smoking cessation			✓
Encourage reduction in alcohol intake			✓
Provide dietary advice		✓	✓
Advice about weight reduction		Aim for a BMI < 27	Encourage weight management and exercise
Contraindications to pregnancy		HbA1C > 10%	Creatinine > 0.2 mmol/L
Measure thyroid function in women with Type 1 DM	✓		✓

NICE however, sets a lower target of < 6.1%. Blood glucose self monitoring is another important recommendation by most of the guidelines apart from ADA 2009 or the ADIPS 2005 guidelines. The ADA 2004 defines a target pre-meal blood glucose level of between 4.4-6.1 mmol/L and 2 hours after meals <8.6 mmol/L. All guidelines, except for the ADA 2009, confirm that blood sugar levels should be maintained as normal as possible whilst avoiding hypoglycaemia. Both the NICE and ADIPS guidelines advocate teaching the patient and partner about hypoglycaemia awareness and management [23,25].

All guidelines recommend prescribing insulin preconceptionally to achieve target levels of blood glucose. Use of metformin as an adjunct or alternative for diabetic treatment preconceptionally when insulin treatment is refused or a patient develops resistance, is recommended by the more recent guidelines [21,23,25].

Folate supplementation

Folate supplementation with a daily dose of 5 mg is recommended by three of the guidelines for those planning to become pregnant up until 12 weeks gestation. ADIPS does not mention the duration of treatment. Both ADA 2009 and ADA 2004 fail to mention the importance of folate supplementation.

Preconception counselling

The routine incorporation of preconception counselling into diabetic clinic visits for all women of child-bearing potential is recommended by ADA 2009. All

guidelines recommend that diabetic women should receive counselling about the effective use of contraception in order to plan pregnancies, and the risk of malformation with poor metabolic control and unplanned pregnancy. Informing the patient about how Diabetes Mellitus (DM) affects pregnancy and how pregnancy affects DM is recommended by two guidelines [22,23]. Other important preconception issues like smoking cessation and reducing alcohol intake is only recommended by ADIPS 2005. ADIPS recommends weight management and exercise as general pre-pregnancy advice and NICE recommends weight reduction for women with a BMI >27 kg/m². Provision of dietary advice such as consuming a diet with high levels of complex carbohydrates, soluble fibre and vitamins, and reduced levels of saturated fats is also recommended [23,24].

Contraindications to pregnancy

The NICE guideline states that an HbA1C > 10% is a contraindication to pregnancy. In contrast ADIPS suggests that impaired renal function as measured by a serum creatinine > 0.2 mmol/L should be a contraindication to pregnancy.

Thyroid screening

Thyroid function screening is recommended by ADA 2004 and ADIPS for women with Type 1 diabetes but not T2DM.

A summary of preconception care recommendations for diabetic women is provided in Table 3.

Table 2 AGREE final scores for identified guidelines

	ADA 2009	ADA 2004	NICE 2008	SIGN 2001	ADIPS 2005
Scope and Purpose	94%	100%	100%	100%	94%
Stakeholder involvement	96%	50%	50%	75%	50%
Rigour of development	71%	71%	100%	100%	71%
Clarity and presentation	96%	100%	100%	100%	83%
Applicability	100%	100%	100%	67%	67%
Editorial independence	50%	50%	50%	50%	50%

Table 3 Summary of recommendations for preconception care among diabetic women

Utilise a multidisciplinary team to manage preconception care issues

Members of the team may include an obstetrician, endocrinologist, family physician, diabetic educator and dietician

Complete a full medical and obstetric evaluation in the preconception period to assess risks

Evaluate and treat diabetic complications including:

Retinopathy (pre-existing retinopathy may progress rapidly in pregnancy and should be treated first before pregnancy)

Nephropathy (patients with pre-existing microalbuminuria are more likely to develop pre-eclampsia)

Neuropathy

Cardiovascular disease

Hypertension

Review all current medication use including complementary medication and change the following to a form of therapy which has less risk:

Angiotensin-Converting Enzyme (ACE) inhibitors

Angiotensin-II Receptor Blockers (ARB)

Statins

Diuretics

β -blockers

Assess level of metabolic control

Measure HbA1C monthly until control is achieved

HbA1C should remain below 7% (1% above normal value), lower if possible

Blood glucose management

Undertake blood glucose self monitoring with targets pre-meal of 4.4-6.1 mmol/l and 2 hour after meal of < 8.6 mmol/l

Maintain blood sugar within normal range without hypoglycaemia

Educate on hypoglycaemia awareness and management

Insulin should be prescribed to achieve target blood glucose levels

Use metformin as an adjunct or alternative

Counselling

Commence folate supplementation 5 mg daily pre-conceptually until 12 weeks gestation to prevent neural tube defects

Inform about risk of miscarriage, congenital malformation and perinatal mortality with poor metabolic control and unplanned pregnancy

Inform about how DM affects pregnancy and how pregnancy affects DM

Use effective contraception until target blood glucose control is achieved before conception

Encourage smoking cessation and reduction in alcohol intake

Encourage regular exercise and management of weight to achieve a BMI < 27

Encourage diet with high levels of complex carbohydrates, soluble fibre and vitamins and reduced levels of saturated fats

Contraindications to pregnancy

HbA1C >10%

Impaired renal function, creatinine > 0.2 mmol/L (increased risk of progression to dialysis during pregnancy)

Measure thyroid function in women with Type 1 Diabetes

Discussion

A key finding of this review is that all the guidelines selected for comparison are of high quality and highly recommended for use in practice. Secondly, the guidelines share consistency regarding counselling about the risk of congenital malformation related to uncontrolled blood sugar preconceptionally and the use of effective contraception until good blood sugar control is achieved. Despite general agreement in all categories of recommendations, there is a lack of specific practice based recommendations in certain areas. These include which type of contraception is most suitable and how long before conception folate supplementation should

be started. While medication review and advice to stop ACE inhibitors is consistently given by all the guidelines, alternative antihypertensives that are safe in pregnancy are only suggested by ADIPS, however, there is considerable evidence supporting the use of methyl dopa, oxprenolol, clonidine, labetalol, prazosin and nifedipine in pregnancy [27].

Key differences observed in the recommendations are target levels of HbA1C to be achieved prior to pregnancy. Aiming the HbA1C level at <1% above the upper limit of normal (generally <7%) is recommended [21,22,24,25,28] in preparation for pregnancy. However, there is evidence of better outcomes if the HbA1C is

maintained within the normal range or lower during early pregnancy [29,30]. In view of this, NICE has chosen the lower value at HbA1C as < 6.1% as a target.

Blood glucose self monitoring is recommended by all the guidelines; however the target levels are again different. When considering the two suggested targets, it may be more helpful to women to use the more specific one (pre-meal at between 4.4-6.1 mmol/l and 2 hour after meal < 8.6 mmol/l [22]).

Deterioration of diabetic complications is another concern in pregnancy among diabetic women [31]. As recommended by all guidelines, evaluating and treating diabetic complications are important actions to undertake before conception. However, not all guidelines outline all the possible complications that need to be evaluated. This may lead to inconsistency in practice amongst physicians.

The other obvious differences in the recommendations are in the use of oral hypoglycaemic agents. Though the safety of currently available oral antidiabetic agents (metformin and glyburide) during pregnancy looks promising, the complete safety and efficacy profile during the full term of pregnancy has not yet been established [32-34]. As such it is recommended to be used as an alternative by ADA 2009, ADIPs and NICE in situations such as refusal of the patient to use insulin or insulin resistance, when the likely benefits from improved glycaemic control outweigh the potential for harm [35].

Counselling is a major component of preconception care. The feasibility of routine incorporation into all practice visits need to be considered. Diabetic women are more likely to be engaged with health system and therefore there are more opportunities for delivery of preventive care. On top of specific counselling for diabetic women with pregnancy, general preconception care [36] for women should not be forgotten and should include depression screening, genetic and family history risk assessment, immunisation, smoking cessation advice, advice regarding reducing alcohol intake, weight management and exercise.

A strength of this review is that all guidelines reviewed in this series are of high quality and highly recommended to be used as practice guidelines according to a respected and validated assessment tool- the AGREE instrument [26]. The limitation of this review is the omission of non-English language guidelines.

Conclusions

International guidelines for the care of women with diabetes who are contemplating pregnancy are consistent in their recommendations; however, some are more comprehensive than others. Having established current recommendations for the preconception care of diabetic women, there is now a need to focus on guideline

implementation. More work is needed to look at the applicability of the recommendations in the local setting, and to specifically examine what barriers and enabling factors exist to ensure successful implementation.

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Author details

¹Department of General Practice, School of Primary Health Care, Faculty of Medicine, Nursing and Health Sciences, Monash University, Victoria, Australia.

²Jinjang Health Clinic, Kuala Lumpur Health Department, Kuala Lumpur, Malaysia. ³Department of General Practice, School of Primary Health Care, Faculty of Medicine, Nursing and Health Sciences, Monash University, Victoria, Australia.

Authors' contributions

MM undertook the study and drafted the manuscript. DM conceived the study and reviewed the manuscript. Both authors read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

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