

Preconception Care in Pre-gestational Diabetes

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Keywords: Preconception; Prevalence; Diabetes; Pregnancy; Pre-gestational; Hyperglycemia; Congenital heart; Pre-eclampsia; Polyhydramnios

Data from birth certificates in the US indicate that the prevalence of diabetes in pregnancy is about 2-3% and is likely significantly underestimated [1]. The two forms of diabetes during pregnancy are pre-existing or pre-gestational diabetes and gestational diabetes. Some of the cases in the gestational diabetes category represent undiagnosed pre-gestational diabetes first discovered during the pregnancy. Pre-gestational diabetes accounts for approximately 13% of all diabetes in pregnancy [2]. Prevalence of both forms continues to rise and reflects the overall increase in incidence of both type 1 and type 2 diabetes in women of childbearing age, increasing incidence of obesity and undiagnosed type 2 diabetes in women of childbearing age.

Hyperglycemia has been repeatedly shown to interfere with embryonic and fetoplacental development. Women with inadequately treated pre-gestational diabetes put themselves at risk of progressive maternal complications of diabetes, including spontaneous abortions, pre-eclampsia, polyhydramnios, C-section and death. Risks to the fetus are manifold and include congenital malformations (especially anencephaly, microcephaly and congenital heart disease), prematurity, macrosomia, neonatal hypoglycemia/hypocalcemia and stillbirth [3]. A prospective observational cohort study of women with type 1 diabetes by Temple and colleagues [4] showed that prepregnancy care was associated with improved glycemic control and reductions in fetal malformations, very premature delivery, stillbirth and neonatal death.

Given the potential health risks to both mother and child, it is crucial that all risks be discussed with diabetic women of childbearing age. Those not seeking pregnancy should be offered contraception. Pregnancy risk may be stratified by measuring hemoglobin A1c (HbA1c), serum creatinine, blood pressure, urine protein, thyroid function and the degree of diabetic retinopathy. Those with HbA1c >10%, active proliferative retinopathy, severe diabetic nephropathy (GFR \leq 30%), severe neuropathy or CAD are at significantly increased maternal risk and avoiding pregnancy is recommended [5]. Additional risk factors associated with poor pregnancy outcome include maternal social deprivation, smoking, unplanned pregnancy, and lack of folate supplementation and absence of contraceptive use 12 months prior to pregnancy [6].

It is very important not to forget about all the psychological aspects of pregnancy planning in women with diabetes. Transition to motherhood is a major life-changing event and is a common cause of stress and anxiety in all women but more so in women with pre-existing diabetes. Specific stressors include diabetes-related distress such as intensification of glucose control, fear of hypoglycemia, guilt and fear of passing diabetes to the child, and sense of disconnection with health care professionals [7]. It is of paramount importance that health care professionals recognize, acknowledge, and provide continuous support to women during all phases of this transition period.

Preconception visits should include routine rubella, rapid plasma reagin, Pap smear, cervical cultures, blood typing, hepatitis B and HIV testing [8]. Prior to pregnancy patient's medications should be reviewed. Cholesterol-lowering agents should be discontinued before

or at the time pregnancy is confirmed. During the second and third trimester of pregnancy, use of ACE inhibitors and angiotensin receptor blockers has been associated with renal tubule dysplasia, renal agenesis, and other fetal abnormalities including oligohydramnios, hypoplastic lungs, hypocalvaria, and neonatal hypotension, likely stemming from a decrease in fetal angiotensin or an increase in fetal bradykinin. Recently, the risk of first trimester congenital malformations from ACE inhibitors and angiotensin receptor blockers has been challenged. Conception while on an ACE inhibitor should be individualized [9]. These medications can be replaced by antihypertensive agents that are safe in pregnancy (e.g. methyldopa, hydralazine, prazosin, β -blockers like labetalol or calcium channel blockers like nifedipine). Thyroid function should be corrected before pregnancy. Neural tube defects are more common among women with diabetes and it is important to supplement folic acid (at least 400 μ g daily) until at least 12 weeks gestation. The American Diabetes Association (ADA) guidelines recommend low-dose Aspirin in all diabetic patients for pre-eclampsia prevention [8].

The ADA and International Diabetes Federation (IDF), recommend a pre-pregnancy HbA1c <7.0% [8]. The British National Institute for Health and Clinical Excellence (NICE) recommend an even lower HbA1c <6.5%, if this is safely achievable [7]. Women with diabetes who are planning to become pregnant may be offered monthly measurement of their HbA1c level. They should intensify their glucose monitoring to include pre-meal, 1-hr post-meal and bedtime. Insulin remains first line and preferred treatment option. Short term safety and efficacy have been established in studies using glyburide and metformin for the treatment of gestational diabetes however both agents cross placenta and long term data is not available [8]. All other oral blood-glucose lowering agents should be discontinued before pregnancy and replaced with insulin. In large multicenter retrospective study women using insulin pumps in pregnancy had lower HbA1c without increased risk of severe hypoglycemia or DKA but no improvement in other pregnancy outcomes [10]. During pregnancy basal insulin requirements increase approximately 50% while meal and corrective bolus dosing increased 4-fold from before conception to 36 weeks gestation [11].

Retinal assessment can be carried out at the first appointment for preconception care if annual screen has not been performed in the last 6 months. Patient with severe diabetic retinopathy should be advised to postpone conception until treated and stable for at least 6 months [5]. Rapid optimization of glycemic control should be delayed pending retinal evaluation and treatment.

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Received January 19, 2016; **Accepted** January 20, 2016; **Published** January 27, 2016

Citation: Lal R, Basina M (2016) Preconception Care in Pre-gestational Diabetes. J Women's Health Care 5: e118. doi:10.4172/2167-0420.1000e118

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Women with diabetes should be offered an evaluation of kidney function and referred to a nephrologist prior to conception if serum creatinine >1.36 mg/dL (120 µmol/L), urinary albumin:creatinine ratio >30mg/mmol or the eGFR <45 mL/min/1.73 m² [6]. During pregnancy, diabetic women with no albuminuria tend not to become proteinuric, but a third of women with microalbuminuria will develop overt proteinuria due to physiologic hyperfiltration. The increased proteinuria may not signify worsening renal disease, but in diabetic patients with creatinine >1.4mg/dL (124 µmol/L) there was a 40% chance of progressive nephropathy during pregnancy [9].

As a quality improvement project Queen's University in Northern Ireland assembled a website (womenwithdiabetes.net) with videos to encourage women with diabetes to seek preconception care and healthcare professionals to refer these patients [12]. They identify women with type 2 diabetes as a difficult to reach group, who frequently do not receive care with a specialist who can provide preconception counseling. Given the significant risks to both mother and fetus, it is crucial that both healthcare providers and diabetic woman of childbearing age receive counseling prior to pregnancy.

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