

## **Preconception-Care of Women with Type 2 Diabetes, Pregnancy Preparation and Medication Safety**

**Yasir Mohammed Zaroug Elradi\***

*Family Practice Physician at MOH, Dhaman Company, Kuwait*

**\*Corresponding Author:** Yasir Mohammed Zaroug Elradi, Family Practice Physician at MOH, Dhaman Company, Kuwait.

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### **Abstract**

Type 2 diabetes mellitus is growing up dramatically with more than 460 million globally are having it as mentioned clearly by International Diabetes Federation atlas (IDF atlas 9<sup>th</sup> edition) [1], with recognized risk factors which leading to high incidence and prevalence of type 2 diabetes worldwide particularly in young adults and adolescent where obesity and overweight are most obvious causes, so many young adults women in child bearing age get type 2 diabetes early as well as gestational diabetes rate highly increased, hence definitely they need specific care before, during and after pregnancy that include preconception care (PCC) such as screening, counseling and identifying and managing risk factors which recommended by international guidelines like American Diabetes Association (ADA 2020) [2].

**Keywords:** *Type 2 Diabetes Mellitus; International Diabetes Federation (IDF); American Diabetes Association (ADA)*

### **Introduction**

#### **About type 2 diabetes in childbearing age women**

Diabetes mellitus is one of common chronic diseases in children and adolescents with high incidence and prevalence among those who obese or overweight particularly type 2 diabetes, however due to obesity trends in the gulf countries, one local study considered around 30% of Kuwaiti children are obese [3], so in developed countries like United States 10% of pregnancies have had diabetes, also 1% of pregnancies have been complicated by pre-gestational diabetes, also 30% of pre-gestational diabetes had developed diabetes in subsequent pregnancies, moreover many studies have conducted to show up the possible risk factors of diabetes during pregnancy, beside the impacts of hyperglycemia on the mother and her fetus respectively for example: Spontaneous abortion, increasing caesarian section rate, preeclampsia and eclampsia rate, increasing microvascular complication such as retinopathy, neuropathy and nephropathy and in general gestational diabetes may causing obesity, hypertension and type 2 diabetes in children, in the other hand, fetus have risks of congenital anomalies and malformations, macrosomia, neonatal hypoglycemia, fetal demise and neonatal respiratory distress syndrome that confirmed by ADA recommendations.

#### **Evidence of effectivity of preconception care for diabetic women**

Many studies have conducted to emphasize the effectivity of preconception care elements, ways to preform it and discussing barriers that prevent proper outcomes, hence Shaila and her colleagues have performed study on small group of people around 50 diabetic pregnant patients (28 were having type 1 diabetes) and 50 non-diabetic pregnant women with mean age of them about 34 years old, under

close follow up by endocrinologists in hospital till both groups of ladies got deliveries, they found that: 33 diabetic pregnant women who received PCC had low incidence of miscarriage (78% vs 10%) and other maternal complications related to diabetes by (87.5% vs 58.8%) [4]. In 2013 Jill and his team conducted study over six European countries which include: United Kingdom, Belgium, Denmark, Netherlands, Italy and Sweden, in order to discuss recommendations and guidelines about PCC policies, health care providers system and trying to make one protocol in the region providing extra care for chronic diseases such as type 2 diabetes in child bearing age girls, basically the study demonstrated heterogeneous guidelines in each countries but all of them agreed about effectivity of PCC in maintaining health conditions of both mother and fetus, beside reducing possible complications of chronic diseases during pregnancy, also providing strong data for health authorities to establish real and practical health policies, finally the study recommended making united evidence-based guideline about PCC in the region [5]. Also, in 2013 American Family Physician Academy had released strong recommendations about PCC role in reducing risk and complications of type 2 diabetic pregnant ladies, so that emphasizing use of PCC for diabetic women in normal pre-natal and ante-natal care visits [6].

### Components of preconception care based on current guidelines

Fortunately, in 2020 ADA guideline have organized and simplified protocol of PCC in pre-existing type 2 diabetes before and during pregnancy which start at puberty in all women in reproductive age and include the following:

1. Family planning: All diabetic women in reproductive age should receive information and huge discussions about family planning methods, suitability, risk factors of each one and possible complications of contraception such as oral contraceptive pills is recommended in specific situations, moreover family planning benefits is outweigh pregnancy in many conditions like preventing unwanted pregnancy, reducing complications of diabetes particularly in poorly glycemic control state.
2. Preconception counseling: Should establish the importance of normalizing HbA1c to less than 6.5% (48 mmol/mol) if it possible to minimize risk of macrosomia, fetal anomalies and preeclampsia, hence many observational studies illustrated that maintaining A1C as near normal as possible have reducing complications especially during the first 10 weeks of pregnancy, also one study support recommendation of proper counseling prior to organogenesis period in first trimester of diabetic women had strong positive effect in reducing anomalies and other complications. So American College of Obstetrics and Gynecology Committee have made checklist for PCC counseling in pre-existing diabetic ladies that include:
  - a. Preconception education: It's so important to educate diabetic women about comprehensive dietary assessment and nutritional therapy based on nutritionist care and advise about calories intake and nutrients needed before and during pregnancy, also considering life style modifications is integral part of prevention and treatment for both obesity and type 2 diabetes which include adequate exercise at least 150 minutes/week, beside sufficient sleep and avoidance of hyperthermia.
  - b. Diabetes education program for type 2 diabetes is recommended in each visit to discuss some points such as diabetes self-management education which focus on insulin administration, resistance during pregnancy, preconception glycemic target and possible side effects like diabetic ketoacidosis (DKA) and hypoglycemia which is so common during pregnancy.
  - c. Discussing deterioration of diabetic retinopathy and increasing risk of other complications like: polycystic ovary syndrome and infertility risk with hyperglycemia, finally explaining the impact of diabetes on the mother like hypertension and preeclampsia beside risk on fetus as miscarriage, still birth, macrosomia and congenital malformations.
  - d. Supplementations is advised for whole pregnant women but in case of diabetic pregnant ladies, ADA recommend giving 400 mcg of folic acid as part of PCC because many studies confirmed that folic acid intake prevent occurrence of neural tube defects as spina bifida and anencephaly.

### Medical approach of diabetic pregnant women

PCC start at puberty of after diagnosis of girls with diabetes based on standard criteria of diabetes diagnosis, then ADA advised medical approach that intensify the effectivity of care:

1. Firstly make general assessment of overall health and address risk factors for type 2 diabetes as blood pressure state, body mass index (BMI), cardiovascular risks calculation and manage based on atherosclerotic cardiovascular risk score, possible secondary causes or genetic causes as maturity onset of diabetes in the young (MODY).
2. Evaluating diabetes state and associated complications and comorbidities including severe hypoglycemia and DKA attacks, severe hypoglycemia and hypoglycemic unawareness factors, checking factors that prevent patients from getting access to care and trying seriously to solve them as possible, also addressing comorbidities is quite important like hypertension, hyperlipidemia, non-alcoholic fatty liver disease, thyroid dysfunction both hyperthyroidism and hypothyroidism induce diabetes development, also looking for diabetes complications and monitor them especially micro-vascular complications neuropathy, nephropathy and retinopathy, in the other hand macro-vascular complications should be monitored carefully.
3. Reviewing obstetrics and gynecological histories which include past history of deliveries (normal or cesarean section), postpartum hemorrhage, preterm delivery, past history of contraception use, history of thromboembolic phenomenon as PE/DVT and confirming blood grouping and rhesus incompatibility.
4. Checking medications that is used currently and prescribing appropriate treatment during pregnancy.
5. Performing screening for diabetes complications and comorbidities such as: traffic light system for foot examinations in each visit, slit lamp examination or digital retinal camera to monitor retinal abnormality that affected aggressively during pregnancy, urea albumin creatinine ratio and estimated Glomerular Filtration Rate (GFR) to assess kidney function and nephropathy development, cardiovascular risk score is recommended to identify cardiovascular risks and events possibility meanwhile ECG is advised for symptomatic diabetic ladies if her age 35 years or above, lipid profile is commonly elevated and affected due to diabetes and pregnancy with raised blood pressure and obesity which all called metabolic syndrome. As part of general screening checking hemoglobin level and anemia symptoms because iron deficiency anemia is so common during pregnancy, moreover ADA consider screening of some genetic and familial diseases should be screened in specific races where are common like sickle cell anemia and Thalassemia are very common in the Middle East countries, also screening for infectious diseases is mandatory in Kuwait and gulf countries before making engagement and official marriage from both couple to protect offspring from harmful serious infections such as HIV, hepatitis B&C and some sexual transmitted diseases.
6. Immunization against common dangerous infection which include: Rubella, hepatitis B, influenza, varicella and other vaccines if needed.

### Management of type 2 diabetic pregnant ladies during and after pregnancy

ADA and NICE guidelines have demonstrated medical approach and special care for diabetic pregnant women, so is critical to maintain glycemic targets close to normal by either HbA1C less than 6.5% or post prandial and fasting plasma glucose less than 95 mg/dl in fasting blood glucose or 140 mg/dl in one hour after meal or 120 mg/dl in 2 hour after meal because the physiology of pregnancy increase turnover of red blood cells and so reducing concentration of HbA1c, so that the aim of treatment in keeping HbA1c close to 6 - 6.5% as possible unless hypoglycemic symptoms appeared, so that to achieve these glycemic targets, treatment protocol had established by ADA that include:

1. Life style modification like exercise, weight loss, healthy diet with considerable amount of carbohydrate because pregnancy increase demand, stop smoking because it have very dangerous side effects on both mother and fetus like preterm labor and congenital malformations, also alcohol should be reduced or stopped due to teratogenic effects that leading to alcohol fetal syndrome.
2. Insulin use: If blood glucose still high and post prandial, fasting and HbA1c are all above the target then the drug of choice is insulin and should be prescribed to diabetic pregnant ladies as first line because insulin is the safest drug during pregnancy with excellent glycemic target result as studies and guideline confirmed that and approved globally, hence in first trimester the physiological effect of pregnancy reduce requirement for insulin rather than second and third trimester when the requirement for insulin is doubled

and more pre-prandial insulin is needed due to increased insulin resistance, so insulin could be given either multiple daily injections or through continuous infusion pump to provide adequate glycemic target.

3. Metformin: Many studies have performed to metformin safety during pregnancy and now is acceptable to prescribe metformin for pregnant who have no potential to placental insufficiency, hypertension, preeclampsia and intrauterine fetal restriction, however some studies like Auckland and Adelaide cohort discuss the effect of metformin on offspring BMI and waist circumference with controversies between studies and recently meta-analysis was conducted and concluded that metformin leading to small neonate and surprisingly gain weight and obesity.
4. Sulfonylurea: Are confirmed to increase macrosomia and neonatal hypoglycemic events when compared with insulin or metformin which evidenced by meta-analysis in 2015. By the way, ADA 2020 advise using metformin and 2ed class of sulfonylurea like Gliclazide as alternatives to insulin in case if there are barriers to receive insulin such as shortage of insulin supply in the remote areas, no electricity and facilities to keep it or financial cost particularly in poor rural communities.
5. Aspirin: Is recommended recently low dose of Aspirin 60 - 150 mg once/day for women with type 1 and type 2 diabetes at the end of first trimester to reduce the risk of preeclampsia.
6. Reviewing concomitant medications like ACE inhibitors and ARBs antihypertensive drugs, statins should not be taken, with careful caution when prescribing any medication for pregnant ladies.

### Conclusion

Type 2 diabetes among young girls now is rising up because of obesity trend worldwide, so the model of care system must be multidisciplinary team approach based on recent guidelines of PCC that should be initiated early at puberty or time of diagnosis to achieve optimal glycemic control and improving quality of life for both mother and fetus. Research area in this field is still suboptimal in the gulf countries that need more effort and encouragement to enhance making our own consensus.

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