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GESTATIONAL DIABETES MELLITUS

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The world is currently facing a global epidemic of Diabetes Mellitus (DM).WHO estimates that presently more than 418 million, about one in ten adults people, are suffering from this metabolic disorder worldwide and the projected figure for 2040 is exceeding 600 million,about 70% in low-& middle income countries. India is the world capital with 50-60 million, followed by China with 45 million with largest age group 40-59 years[1]. Type 2 DM is the most common form with incidence of 85-95%.

Diabetes is hard on women as this is associated with lot of problems in all stages of conception and has got important implications for the newborn. Besides patients with type 1 or type 2 DM becoming pregnant, there is a high prevalence of gestational diabetes mellitus (GDM), as much as 60 percent in somestudies. By definition GDM is the development of glucose intolerance during pregnancy typically happening in the mid trimester. Recent data have shown that the GDM prevalence has increased by 16% to 27% in several race/ethnicity groups particularly Asians during the past 20 years.[2]

GDM accounts for 90% of all cases of diabetes in pregnancy. Unrecognized and untreated GDM leads to serious health problems for mothers and their children. Higher prevalence was observed in the higher age group, higher gravidity, higher BMI, and those with hypertension and family history of diabetes.As with type 1 or 2 DM, GDM is also associated with adverse maternal and fetal outcome. Large number of studies including the landmark HAPO study has confirmed association of GDM with increased incidence of miscarriages, congenital malformations, and intrapartum complications including C-section besides having increased risk of early cardiovascular disease[3].

Pregnancy is diabetogenic; besides altered glucose metabolism and increase in placental counter regulatory hormones during second trimester, increase weight also contributes to altered glucose tolerance. Weight gain and obesity is a regular feature of pregnancy. Obesity is linked to insulin resistance leading to hyperinsulinaemia which can result in hypertension, hyperlipidemias, glucose intolerance, increased Plasminogen Activator Inhibitor 1(PAI-1) and endothelial dysfunction. WHO recommends that all pregnant women should undergo a glucose challenge test (GCT) by 24 weeks of gestation with 50gm glucose. A value greater than 153mg/dl at one hour is an indication for standard glucose tolerance test. The 75-g oral Glucose tolerance test (OGTT) is best performed after an overnight fast; the diagnosis is made if fasting plasma glucose is documented at 92mg/dL or higher, a 1-hr plasma glucose of 180 mg/dL or higher, or a 2-hr plasma glucose of 153 mg/dL or higher. The diagnosis of gestational diabetes is confirmed with a minimum of one abnormal value.[4]In the UK NICE guidelines,GDM is diagnosed if the woman has either fasting plasma glucose level of ≥5.6 mmol/L, ora 2-hour plasma glucose level of ≥7.8 mmol/L. Women at high risk for GDM are screened at the first prenatal visit. A 75-g 2-hour OGTT is the test of choice in both groups.The risk factors for GDM includes increased weight (ie, BMI greater than or equal to 25), decreased physical activity, first degree relative with diabetes, ethnic group with high prevalence of diabetes (African American, Latino, Native American, Asian American, Pacific Islander), past history of GDM or delivery of a baby greater than 9 pounds, and metabolic abnormalities likeHypertension, HDL less than 35 mg/dL, triglyceride level greater than 250 mg/dL,HbA1C 5.7% or higher.

The management of gestational diabetes is undertaken in the same way as any other patient with DM consisting of life style modification,

diet and pharmacotherapy aiming for more strictcontrol. The so called glucose mapping or glucogram which take into account HBA1c, fasting blood sugar, post prandial and random blood sugar at variable periods will guide the treatment choice and selection of proper type and dose of insulin.[5]Diet and life style modifications will help particularly those who are obese and generally speaking, these patients are usually very well motivated and keen to follow all the advices given at this stage.A patient with history of GDM has a 64% higher risk of developing the condition in her next pregnancy. Post-partum screening is recommended in all women with GDM 6 weeks after delivery, using a 75g oral glucose tolerance test (OGTT), as per guidelines of the World Health Organization (WHO).The OGTT should be repeated every 3 years, and annually if the results suggest a prediabetic status. Monitoring for other risk factors, e.g., dyslipidemia should be performed as required. The OGTT should also be performed prior to planning the next pregnancy. Management of metabolic parameters (glucose) and other cardiovascular risk factors (weight, smoking, physical inactivity) must continue in the post-partum period.Lactation is an important aspect of postpartum care as well. Women should be encouraged to breast-feed, as this has undoubted maternal and infant benefits.

Insulin remains the gold standard treatment of diabetes in all form and stages and more so in pregnancy. Those who fail to achieve the desired glycemic controls on diet and life style modifications need to be started on insulin and the glucose mapping will guide the clinician to choose the most suitable form of treatment. It is generally recommended that insulin therapy must be under supervisionof a diabetic clinic orclinician with special interest in the disease. Insulin is currently available in many different forms including the synthetic analogues. There are short and long acting forms including premixed and the clinician should sort out the right form and dose of insulin for each of his patient based upon patient glycemic profile.[6,7]

There is a general perception in medical community at large that there is no role of oral hypoglycemic agents (OADA) in the management of gestational DM and they are absolutely contraindicated. This scenario has changed in the last few years and there are several clinical trials now available in favor of oral OADA. The use of Metformin during pregnancy decreases the rates of early pregnancy loss and preterm labour and prevents foetal growth restriction. With the use of metformin during pregnancy, no teratogenic effects, intrauterine deaths or developmental delays have been reported.[8-11]Despite its crossing the placenta, apparently there are no serious safety concerns with metformin. Women on metformin for PCOS can continue the drug up to end of 1st trimester.

During pregnancy, the use of OADA is not recommended by the American Diabetes Association (ADA) or US Food and Drug administration (FDA). UK National Institute for Health and Care Excellence (NICE) guidelines consider metformin and glibenclamide safe in pregnancy and lactation.[12]The Endocrine Society suggests that glibenclamide may be considered as a suitable alternative to insulin therapy for management of hyperglycaemia in women with GDM who fail to achieve target blood glucose values after a week trial of diet and exercise[13]. The exception is for those women with a diagnosis of GDM before 25 weeks of gestation and for those women with FPG > 110 mg/dl, where insulin therapy is preferred. Recommendation for the use of metformin is in those women with gestational diabetes, who do not have adequate glycaemic control despite step 1, and who refuse or cannot use insulin or Glibenclamide, and are not in the 1st trimester. Even though metformin crosses the placenta freely, follow-up of MiG study (Metformin in Gestational Diabetes) had shown favorable effects on children in metformin group compared to those in the insulin group[14]. Such data for Glibenclamide is not available. International Federation of Gynaecology and Obstetrics (FIGO) 2015 recommendations for

pharmacological therapy of GDM state that insulin, glibenclamide, and metformin are safe and effective therapies for GDM during 2nd and 3rd trimester, and may be initiated as first-line treatment after failing to achieve glucose control with lifestyle modification.[15] Among OADs, metformin may be a better choice than glibenclamide.

Gestational Diabetes Mellitus is quite a common condition and is associated with considerable morbidity which is preventable. Proper comprehensive preconception counseling, screening of all pregnant women in general and those at special risk in particular at 24 weeks gestation, regular monitoring and proper management tailored towards individual patient will definitely achieve this goal. The long term follow up of these patients is also part of proper management of these cases for early diagnosis and management of DM.

REFRENCES:

1. Globel report on Diabetes. World Health Organisation. Geneva 2016.
2. Kim C, Newton KM, Knopp RH. Gestational diabetes and the incidence of type 2 diabetes: a systematic review. Diabetes Care 2002;25:1862-8.
3. HAPO Study Cooperative Research Group. Hyperglycemia and adverse pregnancy outcomes. N Engl J Med. 2008; 2008(358):1991-2002.
4. http://bestpractice.bmj.com/best-practice/monograph/665/diagnosis/criteria.html (retrived 1-2-2017)
5. Egan AM, Murphy HR, Dunne FP. The management of type 1 and type 2 diabetes in pregnancy.QJM. 2015 Dec 1; 108(12):923-7.
6. Kalra S, Gupta Y. Insulin initiation: bringing objectivity to choice. Journal of Diabetes & Metabolic Disorders. 2015 Mar 25; 14(1):
7. Bhutani G, Kalra S. Posology of insulins: A review of standard textbooks and product inserts. Indian J EndocrMetab 2015; 19:625-9
8. Maymone AC, Baillargeon JP, Menard J, Ardilouze JL. Oral hypoglycaemic agents for gestational diabetes mellitus. Expert Opin Drug Saf 2011; 10: 227-38.
9. Dhulkotia JS, Ola B, Fraser R, Farrell T. Oral hypoglycemic agents vs. insulin in management of gestational diabetes: a systematic review and meta-analysis. Am J ObstetGynecol 2010; 203: 457:1-9.
10. Castillo WC, Boggess K, Stürmer T, Brookhart MA, Benjamin DK, Funk MJ. Association of adverse pregnancy outcomes with glyburide vs insulin in women with gestational diabetes.JAMA pediatrics. 2015 May 1; 169(5):452-8.
11. McGrath RT, Glastras SJ, Hocking S, Fulcher GR. Use of metformin earlier in pregnancy predicts supplemental insulin therapy in women with gestational diabetes. Diabetes Research and Clinical Practice.2016 Jun 30; 116:96-9.
12. Mugglestone MA. Management of diabetes from preconception to the postnatal period: summary of NICE guidance. BMJ 2008; 336: 714-7.
13. Blumer I, Hadar E, Hadden DR, Jovanovic L, Mestman JH, Murad MH, et al. Diabetes and pregnancy: An endocrine society clinical practice guideline. J ClinEndocrinolMetab 2013; 98: 4227-49
14. Rowan JA, Rush EC, Obolonkin V, Battin M, WouldesT,Hague WM. Metformin in gestational diabetes: the offspring follow-up (MiG TOFU): body composition at 2 years of age. Diabetes Care 2011; 34: 2279-84.
15. Hod M,Kapur A, Sacks DA, Hadar E, Agarwal M, Di Renzo GC, et al. The international federation of gynecology and obstetrics (FIGO) initiative on gestational diabetes mellitus: A pragmatic guide for diagnosis, management, and care.IntJGynecolObstet 2015; 131(Suppl 3): S173-211.

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