GUIDELINES FOR THE MANAGEMENT OF GESTATIONAL DIABETES MELLITUS

COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS, SINGAPORE

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INTRODUCTION

Gestational diabetes mellitus, as defined by some as "any degree of glucose intolerance with onset or recognition during pregnancy", is a common condition in obstetrics. The initial criteria for the diagnosis of GDM chosen 40 years ago was to identify the women at risk for becoming diabetic after pregnancy and was derived from non-pregnant individuals. The Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study in 2008 was the first to address risks of adverse outcome associated with degrees of hyperglycaemia.

This study of 23,316 pregnant women showed a correlation between adverse outcomes and increasing glycemia. There was a continuous relationship between each of the glucose values; fasting, 1 hour, and 2 hours on OGTT and primary outcomes such as the frequency of large-for-gestational-age (LGA, >90th centile) babies, primary caesarean section, clinical neonatal hypoglycemia, and neonatal hyperinsulinemia in the HAPO study. A similar relationship exists with secondary outcomes like fetal adiposity, preeclampsia, and birth trauma/shoulder dystocia even after adjustment for potential confounders. (2)

The Growing Up in Singapore Towards healthy Outcomes (GUSTO) birth cohort study recruited 1136 pregnant women from KK Women's & Children's Hospital and National University Hospital (NUH) in 2009-2010. The study found that using risk factors alone did not sufficiently predict GDM risk, and failed to detect half the GDM cases in Asian women. Asian women should be universally screened for GDM to avoid under-diagnosis to ensure optimal maternal and fetal outcomes. (7) Similarly, a KKH study (8) of 2175 women who had routine screening found that targeted screening failed to detect 15.2% to 27.6% of women with GDM depending on the risk model and diagnostic criteria used. Universal screening has a higher detection rate but a commonly raised concern is its cost-effectiveness. Chen et al. (9) found that universal GDM screening is a cost-effective approach to reduce the complications of GDM in Singapore compared to targeted screening or no screening at all.

The Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) and Maternal-Fetal Medicine Units trials have shown that antenatal treatment of a mild degree of maternal hyperglycemia can reduce adverse outcomes. (10-11) The ACHOIS study was further supported by cost-effectiveness analysis. (12)

This guideline was commissioned by College of Obstetricians and Gynaecologists, Singapore (COGS) to specifically address GDM. It was written with reference to recent evidence, reports, WHO as well as NICE guidelines and recommendations from other international bodies. (3-5,13-14). It aims to address specific issues and will be updated with further new evidence.

SCREENING FOR GESTATIONAL DIABETES

COGS recommends the use of the full three-point IADPSG criteria in clinical practice as each of the three glucose values affect pregnancy outcomes and improves the detection of GDM.

The International Association of the Diabetes and Pregnancy Study Groups (IADPSG) Consensus panel defined diagnostic values on the basis of an odds ratio of 1.75 for adverse neonatal outcomes (birth weight > 90th percentile, cord C-peptide > 90th percentile, neonatal percent body fat > 90th percentile) compared

with mean values, for three time points - fasting plasma glucose, 1-hour, and 2-hour OGTT plasma glucose values (2). This diagnostic criteria has been adopted by the American Diabetes Association (3), the Australasian Diabetes in Pregnancy Society (4), the World Health Organization (WHO)(5), and other global official bodies.(6)

A study in NUH (15) showed that the prevalence of gestational diabetes mellitus among Asian females was lower using a modified two-point IADPSG criteria (using 0 hr and 2 hr level). A study by Tan et al. (16) on the first 366 patients who were screened with the full three-point IADPSG criteria in KKH showed that the GDM prevalence based on two-point IADPSG was lower than the previous two-point WHO 1999 criteria. The three-point IADPSG had the highest prevalence. Adding the 1-hour parameter to the two-point test IADPSG criteria, increased the detection of GDM - an absolute increase of 5.7% in the population and a relative increase of 32.8% for the prevalence of GDM overall. It is important to include glucose levels at the 1 h point as it contributes to about one-third of cases of GDM and is clinically relevant.

COGS recommends universal screening with 75 gm OGTT at 24-28 weeks gestation
In addition to local studies (7-9), universal screening was also recommended by WHO (5) and has also been approved by the United States Preventive Services Task Force. (17)

COGS recommends the use of a pre-mix 75g OGTT beverage drink for the OGTT.
This is easier for consumption, has a more palatable taste and convenient to administer. (22)

DIAGNOSTIC CRITERIA AND CLASSIFICATION

Hyperglycemia first detected at any time during pregnancy should be classified as either
- Diabetes Mellitus in pregnancy (DIP) or
- Gestational Diabetes Mellitus (GDM)

Diabetes Mellitus in Pregnancy (DIP) should be diagnosed by the 2006 WHO criteria for diabetes if one or more of the following criteria are met:
- Fasting PG ≥ 7.0 mmol/L
- 2-hour PG ≥ 11.1 mmol/L following a 75 gram oral glucose load
- Random PG ≥ 11.1 mmol/L in the presence of diabetes symptoms

Gestational Diabetes Mellitus (GDM) is diagnosed from 24 weeks pregnancy if one or more of the following criteria are met (IADPSG criteria):
- Fasting PG 5.1 – 6.9 mmol/l
- 1-hour PG ≥ 10.0 mmol/l following a 75 gram oral glucose load
- 2-hour PG 8.5 – 11.0 mmol/l following a 75 gram oral glucose load

SCREENING FOR PRE-EXISTING DIABETES MELLITUS EARLY IN PREGNANCY

This is under review by the Agency for Care Effectiveness, Ministry of Health Gestational Diabetes Mellitus Appropriate Care Guide committee together with members of this guideline committee and will be adopted by COGS when it is completed.

MANAGEMENT OF GDM IN PREGNANCY

Women diagnosed with GDM in pregnancy should be informed about the implications of the diagnosis and offered appropriate interventions. (10) The woman should be cared for by a multidisciplinary team comprising of dietitians, nurses, obstetricians, and where indicated (as for most times, lifestyle and diet suffice) endocrinologists.

COGS recommends the following management for GDM:
- Refer all women to a dietitian or advise them to eat a healthy diet and recommend foods with a low glycemic index.
- Advise regular exercise (such as walking for 30 minutes after a meal) to improve glycemic control.
- Educate on capillary blood glucose monitoring to maintain in general, aiming for glucose levels at the following targets:
  - Fasting: 4.4-5.5 mmol/l and either
  - 1 hour postprandial: < 7.8 mmol/l or
  - 2 hours postprandial: 5.5-6.6 mmol/l

Note the target values may differ slightly at different centres.

- Assess the best treatment option which may include insulin and/or metformin after reviewing the risks and benefits with the patient.
- Consider starting treatment with insulin, with or without metformin for women who have a fasting PG ≥ 7.0 mmol/l at diagnosis or a fasting PG 6.0 - 6.9 mmol/l but with concomitant complications such as macrosomia or polyhydramnios.

Women diagnosed with hyperglycemia in pregnancy should have regular fetal growth surveillance.

Women with GDM should be delivered by 40 weeks +6 days gestation but the mode and timing of delivery should be tailored according to clinical assessment. Other than the usual obstetric indications, other factors to consider include the estimated fetal weight, presence of polyhydramnios, the degree of glucose control and whether lifestyle, metformin or insulin were needed to achieve optimal glucose levels.

POSTNATAL MANAGEMENT

Women should be encouraged and supported to breastfeed as breastfeeding reduces risk of obesity and diabetes in the offspring. (23,24) The dose of metformin, glibenclamide and / or insulin may be reduced or stopped after birth as indicated. Other forms of oral hypoglycemic agents should be avoided whilst breastfeeding.

Women diagnosed with hyperglycemia in pregnancy should be informed about the increased risk of future DM and hyperglycemia in future pregnancies and should be offered lifestyle advice that includes weight control, diet and exercise.

COGS recommends postnatal testing at 6-12 weeks to exclude existing DM.
There is currently no consensus on the best method for postnatal testing. (25,26)

COGS recommends performing the 75 gram OGTT (2-point test) as this will also identify women with impaired glucose tolerance, in whom lifestyle intervention can reduce subsequent progression to Type2 DM by 31-37% over 2-6 years.(27)

Other options may be a HbA1c, fasting glucose or random blood glucose levels. This should not be a one-off testing but should be performed at regular intervals thereafter.

Women with background risk factors (e.g. obesity, strong family history of DM, insulin required during pregnancy, metabolic syndrome etc.) should have more frequent testing (yearly) than those at lower risk (2 to 3-yearly).

REFERENCES

1. HAPO Study Cooperative Research Group, Metzger BE, Lowe LP, et al. Hyperglycemia and adverse pregnancy outcomes. N Engl J Med 2008;358:1991-2002. (One of the 15 HAPO field centres - KK Women's and Children's Hospital, Singapore City, Singapore: Y.H. Cao, J.J. Chee, A. Koh, E. Tan, V.S. Rajadurai, H.Y. Wee, G.S.H. Yeo)
2. Metzger BE, Gabbe SG, Persson B, et al. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. Diabetes Care 2010;33:67682.
3. American Diabetic Association. Standards of medical care in diabetes – 2011. Diabetes Care 2011;34 (suppl.1):S11-S61.
4. ADIPS Consensus Guidelines for the Testing and Diagnosis of Gestational Diabetes Mellitus in Australia. 2014.
5. World Health Organisation. Diagnostic criteria and classification of hyperglycaemia first detected in pregnancy. 2013.
6. Hod M, Kapur A, Sacks DA, et al. The International Federation of Gynecology and Obstetrics (FIGO) Initiative on Gestational Diabetes Mellitus: A Pragmatic Guide for Diagnosis, Management, and Care. Int J Gynecol Obstet 2015;131(Suppl3):S173212.
7. Chong YS, Cai S, Lin H, Soh SE, Lee YS, Leow MK, Chan YH, Chen L, Holbrook JD, Tan KH, Rajadurai VS, Yeo GS, Kramer MS, Saw SM, Gluckman PD, Godfrey KM, Kwek K; GUSTO study group.Ethnic differences translate to inadequacy of high-risk screening for gestational diabetes mellitus in an Asian population: a cohort study. BMC Pregnancy Childbirth. 2014 Oct 2;14:345
8. Koh DSC, Chia ML, Tan WCJ, Ng MJ, Tey WS, Chern B, Yeo GSH, Tan KH. Universal Screening versus Targeted Screening for Gestation Diabetes Mellitus at a Large Tertiary Hospital in Singapore. Singapore Journal of Obstetrics & Gynaecology. 2017;48(1):35-43
9. Chen PY, Finkelstein EA, Ng MJ, Yap F, Yeo GS, Rajadurai VS, Chong YS, Gluckman PD, Saw SM, Kwek KY, Tan KH. Incremental Cost-Effectiveness Analysis of Gestational Diabetes Mellitus Screening Strategies in Singapore. Asia Pac J Public Health. 2016 Jan;28(1):15-25.
10. Crowther CA, Hiller JE, Moss JR, McPhee AJ, Jeffries WS, Robinson JS. Effect of treatment of gestational diabetes mellitus on pregnancy outcomes. N Engl J Med 2005;352:2477-86.

11. Landon MB, Spong CY, Thom E, et al. A multicenter, randomized trial of treatment for mild gestational diabetes. N Engl J Med 2009;361:1339-48.
12. Moss JR, Crowther CA, Hiller JE, Willson KJ, Robinson JS. Costs and consequences of treatment for mild gestational diabetes mellitus - evaluation from the ACHOIS randomised trial. BMC Pregnancy Childbirth 2007;7:27.
13. NICE. Diabetes in pregnancy: management of diabetes and its complications from preconception to the postnatal period. London: National Institute for Health and Clinical Excellence, 2015.
14. Guidelines for the Management of Gestational Diabetes Mellitus. HKCOG Guidelines No.7 Revised Nov 2016. The Hong Kong College of Obstetricians and Gynaecologists. http://www.hkcog.org.hk/hkcog/Download/Guidelines_on_GDM_updated.pdf (assessed on 6 Aug 2017)
15. Yew TW, Khoo CM, Thai AC1, Kale AS, Yong EL, Tai ES. The Prevalence of Gestational Diabetes Mellitus Among Asian Females is Lower Using the New 2013 World Health Organization Diagnostic Criteria. Endocr Pract. 2014 Oct;20 (10) : 1064-9. doi: 10.4158/EP14028.OR.
16. Tan KH, Kwek K, Ng MJ, Yeo SH, Wright A, Tagore S, Chern B. Introduction of the IADPSG Criteria for Screening and Diagnosis of Gestational Diabetes Mellitus. SingHealth Duke-NUS Scientific Congress 2016. 23-24 September 2016
17. Moyer VA. Screening for gestational diabetes mellitus: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med 2014;160:414-20.
18. Hughes RC, Moore MP, Gullam JE, Mohamed K, Rowan J. An early pregnancy HbA1c ≥5.9% (41 mmol / mol) is optimal for detecting diabetes and identifies women at increased risk of adverse pregnancy outcomes. Diabetes care 2014; 37(11): 2953-9.
19. Kwon SS, Kwon JY, Park YW, Kim YH, Lim JB. HbA1c for diagnosis and prognosis of gestational diabetes mellitus. Diabetes Res Clin Pract 2015; 110(1): 38-43.
20. Soumya S, Rohilla M, Chopra S, et al. HbA1c: A Useful Screening Test for Gestational Diabetes Mellitus. Diabetes Technol Ther 2015; 17(12): 899-904.
21. Amylidi S, Mosimann B, Stettler C, Fiedler GM, Surbek D, Raio L. First trimester glycosylated hemoglobin in women at high risk for gestational diabetes. Acta Obstet Gynecol Scand 2016; 95(1): 93-7.
22. Tan KH, Tan LK. Evidence-based Gestational Diabetes Mellitus Screening – The Next Lap for Singapore. Singapore Journal of Obstetrics & Gynaecology. 2016;47(1):41-3
23. Owen CG, Martin RM, Whincup PH, Smith GD, Cook DG. Does breastfeeding influence risk of type 2 diabetes in later life? A quantitative analysis of published evidence. Am J Clin Nutr 2006;84(5):1043–54.
24. Gunderson EP. Breastfeeding after gestational diabetes pregnancy: subsequent obesity and type 2 diabetes in women and their offspring. Diabetes Care 2007;30(Suppl 2):S161–8.
25. Kim C, Chames MC, Johnson TRB. Identifying post-partum diabetes after gestational diabetes mellitus: the right test. Lancet Diabetes Endocrinol. 2013; 1: 84–6.
26. Venkataraman H, Sattar N, and Saravanan P. Postnatal testing following gestational diabetes: time to replace the oral glucose tolerance test? Lancet Diabetes Endocrinol. 2015; 3: 754–6.
27. Appropriate Care Guide. Managing pre-diabetes – a growing health concern. Ministry of Health Singapore. Updated: 3 August 2017 https://www.moh.gov.sg/content/dam/moh_web/ACE-HTA/public-data/our-guidance/Managing%20Pre-diabetes%20(Updated%20on%203%20August%202017).pdf

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This guideline was produced by the College of Obstetricians and Gynaecologists, Singapore as an educational aid and reference for obstetricians and gynaecologists practicing in Singapore. The guideline does not define a standard of care, nor is it intended to dictate an exclusive course of management. It presents recognized clinical methods and techniques for consideration by practitioners for incorporation into their practice. It is acknowledged that clinical management may vary and must always be responsive to the need of individual patients, resources, and limitations unique to the institution or type of practice.

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SUMMARY OF COGS GDM RECOMMENDATIONS

DIAGNOSTIC CRITERIA FOR Diabetes In Pregnancy (DIP) AND Gestational Diabetes (GDM)

- DIP should be diagnosed if one or more of the following criteria are met:
  - Fasting PG ≥ 7.0 mmol/L
  - 2-h PG ≥11.1 mmol/L following a 75 gram oral glucose load
  - Random PG ≥ 11.1 mmol/L in the presence of diabetes symptoms

- GDM should be diagnosed in 2nd and 3rd trimester if one or more of the following criteria are met following a 75 gram OGTT – IADPSG Criteria:
  - Fasting PG 5.1mmol/l - 6.9 mmol/l
  - 1-hour PG ≥ 10.0 mmol/l
  - 2-hour PG 8.5 mmol/l - 11 mmol/L

SCREENING FOR HYPERGLYCEMIA IN PREGNANCY

- Universal screening by 75 gram OGTT at 24 to 28 weeks of gestation is recommended using the full three-point IADPSG criteria (0hr, 1hr and 2hr).

MANAGEMENT OF GDM IN PREGNANCY

- A multidisciplinary team approach (dietician, diabetic nurse, obstetrician and endocrinologist) is recommended.
- Refer all women to a dietician.
  - Advise on eating a healthy diet and recommend foods with a low glycaemic index.
- Advise regular exercise (such as walking for 30 minutes after a meal) to improve glycaemic control.
- Educate on capillary blood glucose monitoring to maintain glucose levels with the following targets:
  - Fasting: 4.4-5.5 mmol/l and either
  - 1 hour postprandial: <7.8 mml/l or
  - 2 hours postprandial: 5.5-6.6 mmol/l
- Consider metformin and/or insulin as indicated
- There should be regular fetal growth surveillance
- Timing and mode of delivery should be based on clinical assessment no later than 40 weeks+6 days gestation

POSTNATAL MANAGEMENT

- Breast-feeding is encouraged and supported.
- Metformin and glibenclamide can be continued whilst breast-feeding (but avoid all other hypoglycemic agents).
- Inform women diagnosed with hyperglycemia in pregnancy of the risk of future DM and hyperglycemia in future pregnancies and offer lifestyle advice that includes weight control, diet and exercise
- Postnatal test at 6-12 weeks should be performed to exclude DM or IGT preferably with the 75 gram 2 point OGTT
- Women diagnosed with hyperglycemia in pregnancy should be screened for DM at regular intervals thereafter. Women at higher risk for progression to DM should be screened yearly, whilst those at lower risk should be screened at least 3 yearly.