Prevention of Gestational Diabetes Mellitus

Subjects: Health Care Sciences & Services
Contributor: Dan Zhang

Gestational diabetes mellitus (GDM) has for many years been defined as glucose intolerance with the onset or first recognition during pregnancy. Such a definition has serious limitations due to many cases of GDM representing preexisting hyperglycemia. As such, the latest definition of GDM excludes women found to have diabetes by diagnostic criteria applied outside of pregnancy. GDM is one of the most common obstetric complications, with the prevalence varying from 7.5% to 27.0% among different areas, principally depending on different races and diagnostic criteria.

Keywords: gestational diabetes mellitus ; gestational weight gain ; overweight ; obesity

1. Introduction

GDM is associated with a wide variety of adverse maternal and offspring outcomes. Women with GDM are at higher risks of pre-eclampsia, dystocia, cesarean section, postpartum hemorrhage, and future development of type 2 diabetes mellitus. GDM also contributes to macrosomia, childhood obesity, metabolic syndrome and cardiovascular diseases in the offspring [1]. Overweight and obesity are leading global health burdens and constitute major risk factors of GDM [2]. The proportion of overweight and obese women of reproductive age has been increasing considerably in the last decades. It is estimated that among overweight and obese pregnant women, the risk of developing GDM is more than twofold higher than for non-obese women [3]. Furthermore, the combination of overweight/obesity and GDM could aggravate these adverse outcomes caused by GDM alone [4].

The Institute of Medicine (IOM) has recommended the ideal gestational weight gain (GWG) for pregnant women. According to the IOM guidelines, total GWG should be within 12.5–18 kg, 11.5–16 kg, 7–11.5 kg and 5–9 kg for underweight, normal weight, overweight and obese women, respectively [5]. Excessive GWG increases the risk of GDM, hypertensive disorders of pregnancy, large for gestational age infants, macrosomia, caesarean delivery, and postpartum weight retention, as well as obesity of offspring [5][6][7]. As reported by a systematic review and meta-analysis of more than 1 million pregnant women, 47% of the population exceeded GWG goals [5], and overweight and obese women have the highest prevalence of excessive GWG [8]. Therefore, effective interventions targeting women who are overweight or obese are urgently needed to decrease the risk of GDM, restrict GWG and promote the future health of two generations.

There are substantial randomized controlled trials (RCTs) attempting to reduce the incidence of GDM, including diet, physical activity (PA), combined interventions or medication. However, the results are controversial [9][10]. The key issue of whether GDM could be prevented by interventions remains unanswered. Furthermore, the effects of interventions on limiting GWG are also inconsistent [11][12][13][14]. In addition, individual RCTs focusing on diverse interventions present inconsistent effectiveness [3][15][16], indicating that the efficacy of various strategies might be different. In this regard, few studies compare the effectiveness of multiple interventions, especially in overweight/obese pregnant women. Consequently, it is necessary to determine the optimal intervention among this population, as well as to update the meta-analysis since certain new trials have been conducted recently.

2. Prevention of Gestational Diabetes Mellitus

The NMA demonstrated that neither diet, PA, combined diet + PA nor medication intervention could effectively protect overweight/obese women from developing GDM. Despite the discrepancy with other literature studying women without special BMI [9][17][18], this conclusion remains convincing due to consistency with studies targeting overweight/obese pregnant women [19][20]. There are some possible explanations for the insignificance. On the one hand, providing intervention only during gestation, which results in a short duration of these interventions, might not be sufficient to produce remarkable metabolic improvements and eventually prevent GDM. During healthy pregnancy, placental hormones and metabolic adaptations promote the state of insulin resistance (IR), which facilitates the adequate transfer of glucose to the fetus [19][21]. By reasons that the excess of adipose tissue affects the production of adipokines, chemokines and cytokines, IR is exaggerated in overweight/obese pregnant women [19], making them enter pregnancy with increased

IR, which further deteriorates as pregnancy progresses [19]. When insulin secretion does not increase adequately to counterbalance the state of IR in the second half of pregnancy, maternal glucose intolerance appears and may contribute to the increased risk of GDM [22]. This emphasizes the significance of reducing BMI before conception. A large study including 226,958 women also indicated that a 10% reduction in pre-pregnant BMI reduced the risk of GDM by up to 25%, depending on the baseline BMI [23]. In this regard, intervention initiated at the onset of pregnancy or even the preconception period should be recommended among overweight/obese women to prevent GDM. On the other hand, the intensity of interventions, for instance, the dose of metformin administrated and the type of PA intervention (PA counselling vs. supervised exercise sessions, or diet counselling sessions vs. diet brochures), is heterogeneous in included trials. Given that overweight/obesity is an established risk factor for GDM [2], and is closely associated with metabolic disorders [24], participants with overweight/obesity may benefit less from modest interventions. Besides, overweight and obesity are intrinsically linked with long-term excessive calorie intake [21], which might be uneasy to change, resulting in a barrier to diet intervention. The fear of harming self and the baby, pregnancy-induced physical discomfort and discouragement by others [25] constitute barriers to PA intervention. Apprehension regarding the use of medications during pregnancy, for example, anxiety related to metformin crossing the placenta and reaching the fetus, also exists [26]. All of these might contribute to the poor compliance of overweight/obese women to the above interventions, which could be another reasonable factor for their failure to prevent GDM. Therefore, a dose-response phenomenon may be present, where more robust interventions, such as supervised exercise sessions, should be principally examined in the future.

More importantly, there was a tendency that PA and diet + PA interventions played protective roles in GDM development. Of the four included interventions, PA intervention ranked as the optimal strategy to prevent GDM, followed by diet + PA intervention and medication, which is partially supported by Davenport et al. [9]. PA has long been prescribed to patients with diabetes due to improvements in glycemia and insulin sensitivity. Studies have proposed that PA achieves these benefits by promoting the glucose uptake of skeletal muscle and increasing mitochondrial density as well as the expression of glucose transporter proteins [27]. Moreover, PA also improves pancreatic islet cell function, increases myonectin levels, and decreases adipokine levels and oxidative stress [28]. These results laid a solid foundation for the possible effectiveness of PA and PA-based lifestyle intervention on the prevention of GDM. Oral antidiabetics, especially metformin, are another empirically therapeutic strategy for women with polycystic ovary syndrome (PCOS) or obesity. Nevertheless, despite the fact that metformin has the ability to inhibit hepatic gluconeogenesis and glucose absorption, stimulate glucose uptake in peripheral tissues, reduce weight gain and improve insulin resistance [26][28], the NMA cannot provide evidence to support metformin as a feasible regime in overweight/obese women during pregnancy to prevent GDM, which is consistent with a previous Cochrane review [29]. Overall, this finding suggested that diet intervention alone was unable to reverse the deteriorating state of IR and prevent GDM in overweight/obese women. However, despite the failure of all evaluated interventions to reach significance, given that the risk of developing GDM in overweight and obese pregnant women is twofold higher than in non-obese women [3], not providing any intervention for them is unreasonable. Consequently, this NMA indicates that although no specific behavioral or medication interventions were effective enough to prevent GDM in overweight/obese women, exercise or exercise combined with diet counseling could be recommended as relatively ideal strategies if necessary, while diet counseling alone should not be currently considered a viable treatment option for overweight/obese pregnant women to prevent GDM.

References

1. Saravanan, P.; Magee, A.L.; Banerjee, A.; Coleman, M.A.; Von Dadelszen, P.; Denison, F.; Farmer, A.; Finer, S.; Fox-R ushby, J.; Holt, R.; et al. Gestational diabetes: Opportunities for improving maternal and child health. Lancet. Diabetes. Endocrinol. 2020, 8, 793–800.
2. McIntyre, H.D.; Catalano, P.; Zhang, C.; Desoye, G.; Mathiesen, E.R.; Damm, P. Gestational diabetes mellitus. Nat. Re v. Dis. Primers. 2019, 5, 47.
3. Wang, C.; Wei, Y.; Zhang, X.; Zhang, Y.; Xu, Q.; Sun, Y.; Su, S.; Zhang, L.; Liu, C.; Feng, Y.; et al. A randomized clinical trial of exercise during pregnancy to prevent gestational diabetes mellitus and improve pregnancy outcome in overweig ht and obese pregnant women. Am. J. Obstet. Gynecol. 2017, 216, 340–351.
4. Catalano, P.M.; McIntyre, H.D.; Cruickshank, J.K.; McCance, D.R.; Dyer, A.R.; Metzger, B.E.; Lowe, L.P.; Trimble, E.R.; Coustan, D.R.; Hadden, D.R.; et al. The hyperglycemia and adverse pregnancy outcome study: Associations of GDM a nd obesity with pregnancy outcomes. Diabetes. Care. 2012, 35, 780–786.
5. Goldstein, R.F.; Abell, S.K.; Ranasinha, S.; Misso, M.; Boyle, J.A.; Black, M.H.; .Li, N.; Hu, G.; Corrado, F.; Rode, L.; et al. Association of Gestational Weight Gain With Maternal and Infant Outcomes: A Systematic Review and Meta-analysi s. JAMA 2017, 317, 2207–2225.

6. Ferrara, A.; Hedderson, M.M.; Brown, S.D.; Ehrlich, S.F.; Tsai, A.-L.; Feng, J.; Galarce, M.; Marcovina, S.; Catalano, P.; Quesenberry, C.P. A telehealth lifestyle intervention to reduce excess gestational weight gain in pregnant women with o verweight or obesity (GLOW): A randomised, parallel-group, controlled trial. Lancet Diabetes Endocrinol. 2020, 8, 490–500.
7. Champion, M.L.; Harper, L.M. Gestational Weight Gain: Update on Outcomes and Interventions. Curr. Diab. Rep. 2020, 20, 11.
8. Kominiarek, M.A.; Peaceman, A.M. Gestational weight gain. Am. J. Obstet. Gynecol. 2017, 217, 642–651.
9. Davenport, M.H.; Ruchat, S.M.; Poitras, V.J.; Jaramillo Garcia, A.; Gray, C.E.; Barrowman, N.; Skow, R.J.; Meah, V.L.; Riske, L.; Sobierajski, F.; et al. Prenatal exercise for the prevention of gestational diabetes mellitus and hypertensive di sorders of pregnancy: A systematic review and meta-analysis. Br. J. Sports. Med. 2018, 52, 1367–1375.
10. Shepherd, E.; Gomersall, J.C.; Tieu, J.; Han, S.; Crowther, C.A.; Middleton, P. Combined diet and exercise intervention s for preventing gestational diabetes mellitus. Cochrane. Database Syst. Rev. 2017, 11, Cd010443.
11. Bruno, R.; Petrella, E.; Bertarini, V.; Pedrielli, G.; Neri, I.; Facchinetti, F. Adherence to a lifestyle programme in overweig ht/obese pregnant women and effect on gestational diabetes mellitus: A randomized controlled trial. Matern. Child. Nutr. 2017, 13, e12333.
12. Dodd, J.M.; Turnbull, D.; McPhee, A.J.; Deussen, A.R.; Grivell, R.; Yelland, L.N.; Crowther, A.C.; Wittert, G.; Owens, J.; Robinson, J.S.; et al. Antenatal lifestyle advice for women who are overweight or obese: LIMIT randomised trial. Bmj 20 14, 348, 1285.
13. Herring, S.J.; Cruice, J.F.; Bennett, G.G.; Rose, M.Z.; Davey, A.; Foster, G.D. Preventing excessive gestational weight gain among African American women: A randomized clinical trial. Obesity (Silver Spring) 2016, 24, 30–36.
14. Wolff, S.; Legarth, J.; Vangsgaard, K.; Toubro, S.; Astrup, A. A randomized trial of the effects of dietary counseling on g estational weight gain and glucose metabolism in obese pregnant women. Int. J. Obes (Lond) 2008, 32, 495–501.
15. Ding, B.; Gou, B.; Guan, H.; Wang, J.; Bi, Y.; Hong, Z. WeChat-assisted dietary and exercise intervention for prevention of gestational diabetes mellitus in overweight/obese pregnant women: A two-arm randomized clinical trial. Arch. Gynec ol. Obstet. 2021, 304, 609–618.
16. Syngelaki, A.; Nicolaides, K.H.; Balani, J.; Hyer, S.; Akolekar, R.; Kotecha, R.; Pastides, A.; Shehata, H. Metformin vers us Placebo in Obese Pregnant Women without Diabetes Mellitus. N. Engl. J. Med. 2016, 374, 434–443.
17. Guo, X.Y.; Shu, J.; Fu, X.H.; Chen, X.P.; Zhang, L.; Ji, M.X.; Liu, X.M.; Yu, T.T.; Sheng, J.Z.; Huang, H.F. Improving the effectiveness of lifestyle interventions for gestational diabetes prevention: A meta-analysis and meta-regression. Bjog 2 019, 126, 311–320.
18. Du, M.C.; Ouyang, Y.-Q.; Nie, X.-F.; Huang, Y.; Redding, S.R. Effects of physical exercise during pregnancy on materna l and infant outcomes in overweight and obese pregnant women: A meta-analysis. Birth 2019, 46, 211–221.
19. Chatzakis, C.; Goulis, D.G.; Mareti, E.; Eleftheriades, M.; Zavlanos, A.; Dinas, K.; Sotiriadis, A. Prevention of gestationa l diabetes mellitus in overweight or obese pregnant women: A network meta-analysis. Diabetes. Res. Clin. Pract. 2019, 158, 107924.
20. Bennett, C.J.; Walker, R.E.; Blumfield, M.L.; Gwini, S.M.; Ma, J.; Wang, F.; Wan, Y.; Dickinsonef, H.; Trubya, H. Interven tions designed to reduce excessive gestational weight gain can reduce the incidence of gestational diabetes mellitus: A systematic review and meta-analysis of randomised controlled trials. Diabetes. Res. Clin. Pract. 2018, 141, 69–79.
21. Plows, J.F.; Stanley, J.L.; Baker, P.N.; Reynolds, C.M.; Vickers, M.H. The Pathophysiology of Gestational Diabetes Melli tus. Int. J. Mol. Sci. 2018, 19, 3342.
22. Chiefari, E.; Arcidiacono, B.; Foti, D.; Brunetti, A. Gestational diabetes mellitus: An updated overview. J. Endocrinol. Inv est. 2017, 40, 899–909.
23. Schummers, L.; Hutcheon, J.A.; Bodnar, L.M.; Lieberman, E.; Himes, K.P. Risk of adverse pregnancy outcomes by pre pregnancy body mass index: A population-based study to inform prepregnancy weight loss counseling. Obstet. Gyneco l. 2015, 125, 133–143.
24. Barazzoni, R.; Cappellari, G.G.; Ragni, M.; Nisoli, E. Insulin resistance in obesity: An overview of fundamental alteratio ns. Eat. Weight. Disord. 2018, 23, 149–157.
25. Shieh, C.; Cullen, D.L.; Pike, C.; Pressler, S.J. Intervention strategies for preventing excessive gestational weight gain: Systematic review and meta-analysis. Obes. Rev. 2018, 19, 1093–1109.
26. Jiang, Y.-F.; Chen, X.-Y.; Ding, T.; Wang, X.-F.; Zhu, Z.-N.; Su, S.-W. Comparative efficacy and safety of OADs in mana gement of GDM: Network meta-analysis of randomized controlled trials. J. Clin. Endocrinol. Metab. 2015, 100, 2071–20 80.

27. Mijatovic-Vukas, J.; Capling, L.; Cheng, S.; Stamatakis, E.; Louie, J.; Cheung, N.W.; Markovic, T.; Ross, G.; Senior, A.; Brand-Miller, J.C.; et al. Associations of Diet and Physical Activity with Risk for Gestational Diabetes Mellitus: A Systematic Review and Meta-Analysis. Nutrients 2018, 10, 698.
28. Pascual-Morena, C.; Cavero-Redondo, I.; Álvarez-Bueno, C.; Lucerón-Lucas-Torres, M.; Sanabria-Martínez, G.; Poyatos-León, R.; Rodríguez-Martín, B.; Martínez-Vizcaíno, V. Exercise versus Metformin to Improve Pregnancy Outcomes among Overweight Pregnant Women: A Systematic Review and Network Meta-Analysis. J. Clin. Med. 2021, 10, 3490.
29. Dodd, J.M.; Grivell, R.M.; Deussen, A.R.; Hague, W.M. Metformin for women who are overweight or obese during pregnancy for improving maternal and infant outcomes. Cochrane Database Syst. Rev. 2018, 7, Cd010564.