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Safety of Metformin and Insulin in the Management of Gestational Diabetes Mellitus: A Systematic Review and Meta-analysis

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Abstract: Introduction: The prevalence of gestational diabetes mellitus (GDM) is expected to increase especially in the Asia region due to increase in maternal age and obesity. Metformin use in pregnancy has been a concern since it could cross the placenta and accumulate in the foetal tissue, therefore ongoing safety for both mother and neonates and efficacy evaluation need to be carried out. This study aims to identify, evaluate, and summarize the safety and efficacy of the main treatment choices that comprise of metformin and insulin in GDM through maternal and neonatal outcomes. **Methods:** Randomised controlled trials (RCT) comparing insulin and metformin in GDM management were systematically searched in PubMed, Ovid MEDLINE and clinicaltrials.gov from databases inception to February 2021. The relevant data were extracted and reported according to the PRISMA guideline. **Results:** The 27 included RCTs compared the effect of metformin or insulin in 4884 women with GDM. Meta-analysis showed that metformin has lower risk of gestational weight gain (GWG) ($p < 0.0001$), neonatal hypoglycaemia ($p < 0.0001$), NICU admission ($p = 0.008$), macrosomia ($p = 0.03$), large for gestational age ($p = 0.003$), and respiratory distress syndrome ($p = 0.03$). **Conclusion:** Safety profile of metformin when used as first-line treatment for GDM is comparable to insulin.

Keywords: gestational diabetes mellitus; biguanide; antihyperglycemic agent; safety;

1. Introduction

Gestational diabetes mellitus (GDM) has been recognised as one of the most common metabolic disorders in pregnancy in which it carries the potential of imposing adverse outcomes to both maternal and neonatal perspectives. It was reported in 2019 that 84% of the reported 20 million of world population who had hyperglycaemia during their pregnancy comprised of those who had GDM [1]. The prevalence of GDM is expected to increase especially in Asia region due to increase in maternal age and obesity in [2]. In the National Health and Morbidity Survey 2016, it was reported that the prevalence of GDM among pregnant women in Malaysia between the age of 15-49 years old was 13.5% [3]. In a more recent report by International Diabetes Federation (IDF), it was reported that Malaysia was the third country with the highest GDM prevalence (22.5%) among the Southeast